Drug Driving Advisory Panel

Interim Report 3
Setting Statutory Limits for Blood Drug Concentrations Relating to Impaired Driving

Background

This is the third report from the Independent Expert Panel on Drug Driving (the Panel). It brings together our thinking on cannabis, methamphetamine, and other (including prescription) drugs in an impaired driving context. In this report, we offer advice to ministers on what we consider appropriate blood drug concentrations at both infringement and criminal levels – the latter will be specified in the legislation. Recommended criminal limits in this report supersede the initial advice on criminal limits the Panel provided in its first report. The Panel has used data from the scientific literature, considered statutory limits in overseas jurisdictions, and used New Zealand (NZ) data on drug blood concentrations in road traffic accidents to develop its advice.

Executive summary

The table below summarises the Panel's recommendations for setting blood threshold and criminal (statutory) limits for drugs. The data the Panel used to support these recommendations are presented in this report (page numbers shown in the table).

Drug	Page	Criminal (Statutory) Limit ng/mL	Blood Threshold ng/mL
THC (Cannabis)	8	3	1
Methamphetamine	17	50	10
Amphetamine	19	100	20
MDMA	19	50	10
MDA	21	No limits proposed	
Cocaine	21	20	5
GHB	22	50,000 (50 µg/mL)	10,000 (10 µg/mL)
Ketamine	23	50	10
Alprazolam	26	50	20
Clonazepam	27	50	20
Diazepam	28	200	100
Lorazepam	28	30	10
Midazolam	29	30	10
Nitrazepam	29	50	20
Oxazepam	30	800	200

Temazepam	31	800	200
Triazolam	31	4	4
Zopiclone	32	50	20
Buprenorphine	36	1	1
Codeine	37	200	50
Dihydrocodeine	37	200	50
Fentanyl	38	0.5	0.5
Methadone	39	200	50
Morphine	40	20	10
Oxycodone	41	50	20
Tramadol	41	250	100

Introduction

There are two basic types of law for dealing with impaired drivers. The first is an assessment of impairment by a qualified individual whereby a driver suspected of driving under the influence of drugs undergoes a physical test to determine if that driver is safe to drive a vehicle. Such a regime has been in place for drug impaired drivers since December 2009. The second type of law is known as *per se* law whereby it is an offence to drive a vehicle with a concentration of alcohol or other identified drugs in the blood above a specified threshold. This type of law has been in place for alcohol for decades. *Per se* concentrations for drugs are considered a more effective means of dealing with drug impaired drivers.

There are many drugs that can adversely affect driving ability whether used recreationally or medicinally. The drugs recommended by the Panel for inclusion in *per se* legislation are those widely acknowledged as having significant risk in relation to safe driving as determined by overseas studies and inclusion in *per se* legislation overseas.

The drugs recommended for inclusion in *per se* legislation in NZ include methamphetamine, amphetamine, methylenedioxymethamphetamine (MDMA), cocaine, tetrahydrocannabinol (THC, the main psychoactive constituent of cannabis), gammahydroxybutyrate (GHB) and ketamine. Additionally, some opioid and sedative medicines have been recommended. The opioids are buprenorphine, codeine, dihydrocodeine, fentanyl, methadone, morphine, oxycodone and tramadol. The sedatives are alprazolam, clonazepam, diazepam, lorazepam, midazolam, nitrazepam, oxazepam, temazepam, triazolam and zopiclone.

The Panel has been asked to provide objective advice for the Associate Minister of Transport and the Minister of Police (together Joint Ministers) and make non-binding recommendations on the following topics:

- the 'blood-drug' limits to be specified in legislation (criminal limits)
- the low-level tolerance thresholds to be applied to the detection of drugs in blood (blood thresholds)
- the cut-off thresholds to be included in oral fluid testing devices (oral fluid thresholds).

In preparing advice on criminal limits, the Panel has based its recommendations for criminal limits on:

- limits set in other jurisdictions
- drug concentrations in impaired drivers in NZ
- data from the scientific literature.

The Panel has considered whether its recommendations align with the outcomes sought by Ministers whereby the criminal limits and blood and oral fluid thresholds should align with the Government's policy intent and desired outcomes for the regime:

- Criminal limits should be such that there is a high level of confidence that the individual is impaired.
- Criminal penalties are only applied where the drug is at a concentration likely to impair driving.
- The blood thresholds should be such that there is a high level of confidence that the individual has recently consumed the drug.
- The blood thresholds should not penalise drivers who have been accidentally or passively been exposed to drugs.
- The Ministers expect that drivers taking normal prescription amounts should not be detected.

However, with regard to the drugs selected for inclusion in the *per se* legislation the following should be noted:

- The opioids and sedatives will impair driving skills with normal therapeutic use and patients prescribed these drugs should be warned not to drive.
- Not all of the drugs selected can be detected by the oral fluid testing devices currently available.
- The use of any of these drugs in combination with alcohol, or in combination with each other, will likely result in enhanced impairment.
- While there are reports from overseas jurisdictions that abuse of prescription medicines such as fentanyl and ketamine is common, there is no evidence that these are being abused by NZ drivers.

The Panel has considered blood concentration limits for the drugs in a number of ways, dependent on the drug:

- Where drugs are typically used for recreational purposes, the limits have been based on data from the scientific literature, the concentrations determined in NZ drivers and the limits set in overseas jurisdictions.
- For prescription medicines, the criminal limits have been determined by considering what dose of the drug is known to impair, the maximum dose of the drug that may typically be prescribed, and the blood concentrations expected from such a dose.

Table 1 gives the recommended blood concentrations for criminal limits and blood thresholds. These are compared with the range of values used in other jurisdictions. Many jurisdictions have *per se* limits for a smaller selection of drugs than proposed by the Panel. Some jurisdictions have graduated blood drug limits that are associated with increasing penalties.

Table 1 *Recommended blood concentration criminal limits and thresholds compared with corresponding limits for other jurisdictions.*

Drug Type/Drug	**Recommended Blood Concentration ng/mL**		**Blood Concentrations Set by Overseas Jurisdictions* ng/mL**
	Criminal Limit	**Threshold**	
Recreational			
amphetamine	100	20	20 to 250
cocaine	20	5	20 to 50
GHB	50000	10000	10300 to 123600
ketamine*	50	10	20 to 329
MDMA	50	10	10 to 48
methamphetamine	50	10	10 to 50
THC	3	1	1 to 9
Opioids			
buprenorphine	1	1	0.5 to 0.9
codeine	200	50	10
dihydrocodeine	200	50	x
fentanyl	0.5	0.5	0.3
methadone	200	50	25 to 500
morphine	20	10	10 to 80
oxycodone	50	20	20
tramadol	250	100	50
Sedatives			
alprazolam	50	20	3 to 15
clonazepam	50	20	1 to 50
diazepam	200	100	60 to 550
lorazepam	30	10	15 to 100
midazolam	30	10	30
nitrazepam	50	20	20 to 98
oxazepam	800	200	170 to 860
temazepam	800	200	1000
triazolam	4	4	x
zopiclone	50	20	10 to 58

*ketamine is frequently administered by medical personnel to drivers injured in a crash

x = No concentration set
*Data from Norway, Denmark and the UK [1-3]

Overview of drug use by NZ drivers

ESR is the main provider of forensic services for the NZ Police. This includes all of the toxicological analyses in relation to criminal, coronial and Land Transport Act 1998 (LTA) samples. Through these analyses, data on drug use by NZ drivers has been collated for many years. The data includes the prevalence of alcohol and other drug use from analyses carried out since 2004.

Over this time there have been legislative changes to the LTA, including changes to the blood alcohol limits and the introduction of drugged driving legislation.

In 2009, changes to the LTA enabled Police to stop and test suspected drug-impaired drivers, i.e. those observed to be driving poorly. The drivers are first breath tested for alcohol use. If the breath test result is negative, the drivers are asked to undergo a compulsory impairment test (CIT) conducted by a trained police officer. If the CIT cannot be completed satisfactorily, a blood sample can be taken for analysis.

The ESR Toxicology laboratory carries out analyses for the presence of alcohol and a range of other drugs in samples taken from four subsets of drivers and the results of these analyses can be used to provide evidence of drug use by a portion of the NZ driving population in the following categories:

1. Deceased drivers – drivers who have died as a result of a motor vehicle crash. Blood samples from most drivers are sent to ESR for analysis. It is important to recognise that some drivers may have suffered a medical event that precipitated the crash and thus drugs might not be involved.

2. Drug impaired drivers – drivers stopped by Police due to observed poor driving who have not used alcohol as determined by a breath alcohol test. These drivers have failed to satisfactorily complete a compulsory impairment test and have provided a blood sample for analysis.

3. Hospitalised drivers – drivers in hospital following a motor vehicle crash are obliged to provide a blood sample for analysis. The blood is initially analysed for alcohol. Analysis for evidence of drug use by these drivers is carried out at the specific request of the Police. However, if the concentration of alcohol in the blood is greater than the legal limit, analyses for drugs are not generally carried out. For many reasons blood samples are not always sent for analysis.

4. Drunk drivers – drivers who failed the evidential breath test are not obliged to provide a blood sample for analysis but may accept the evidence of the breath test. Some drivers elect to have a blood sample taken for analysis. Samples taken from these drivers are analysed to determine the concentrations of alcohol but are rarely analysed for evidence of drug use.

Deceased drivers

2004 to 2009
From July 2004 to June 2009, 1177 drivers died on the road in NZ. Blood samples from 1046 (89%) deceased drivers were analysed for the presence of a wide range of drugs.

Analysis of these samples showed:

- 48% had not used alcohol or other drugs (analytical techniques cannot detect all potentially impairing drugs),
- 32% were positive for alcohol
- 30% had used cannabis
- 13% had used both alcohol and cannabis, but no other drugs
- 4% had used methamphetamine,
- 4% had used opioid type drugs and
- 4% had used sedative type drugs.

2013 to 2018
During these five years, there were 1342 identified driver fatalities. Analyses were carried out on blood samples from 1069 (80%) of this group.

Analyses of these samples showed:

- 41% had not used alcohol or other drugs (analytical techniques cannot detect all potentially impairing drugs),
- 27% were positive for alcohol,
- 25% had used cannabis
- 7% had used both alcohol and cannabis, but no other drugs,
- 8% had used methamphetamine,
- 8% had used opioid type drugs and
- 7% had used sedative type drugs.

Drug impaired (failed the CIT) drivers

From 2013 to 2018, 1899 samples from impaired drivers who failed the CIT were submitted for analysis.

- 9% had not used alcohol or other drugs (analytical techniques cannot detect all potentially impairing drugs)
- 59% had used cannabis
- 37% had used methamphetamine,
- 22% had used opioid type drugs and
- 16% had used sedative type drugs.
- Multiple drug use was common with 36% of drivers using more than one drug.

Hospitalised drivers

Drivers hospitalised following a crash are unable to undergo an impairment test. Hospitalised drivers may be prosecuted for drug impaired driving, without proof of actual impairment, if a Class A controlled drug is detected in their blood. The Class A drugs most likely to be encountered in NZ are methamphetamine, LSD, cocaine and heroin.

From 2013 to 2018, 1939 blood samples from drivers hospitalised following a crash have been analysed for evidence of drug use.

The number of samples submitted to ESR from hospitalised drivers is considerably more than this. All samples from hospitalised drivers are analysed for alcohol and for many cases alcohol is the only analysis requested. If a drugs analysis is requested and the BAC is above the legal limit, drugs analyses will not be carried out unless further work is requested.

Of the 1939 drivers, no drugs were detected in 33% of the samples;

- 37% had used cannabis
- 28% had used methamphetamine
- 15% had used opioid type drugs
- 14% had used sedative type drugs
- Two drivers had used cocaine
- One driver had used LSD
- No drivers had used heroin

Drunk drivers

Generally, samples from drivers who have blood alcohol concentrations greater than the legal limit are not analysed for evidence of drug use. In 2011 a study was commissioned by the NZ Transport Agency (NZTA) to look at drug use by this portion of the driving population. 3050 samples received by ESR between 2011 and 2015 were analysed for a wide range of drugs. These blood samples were taken from drivers who were not in hospital but had failed a breath alcohol test and elected to have a blood sample taken.

All of these samples had blood alcohol concentrations (BAC) greater than the legal limit - 59% of the drivers had only used alcohol (i.e. no other drugs were detected). Of the remaining 41% of the drivers:

- 27% had used cannabis,
- 3.5% had used sedative type drugs
- 2.3% had used opioid type drugs
- 1.6% had used methamphetamine

Drivers who have breath alcohol concentrations equivalent to BACs between 50 and 80 milligrams per 100 millilitres (mg/100 mL) are not given the option to provide a blood sample. This breath alcohol concentration automatically incurs an infringement charge and consequently possible drug use by these drivers is unknown.

Cannabis

The potential impairing effects of cannabis on driving include disorientation, altered sense of time and distance, lack of concentration, difficulty in thinking, loss of coordination, increased reaction time, lateral travel and impaired sustained vigilance [4]. Cannabis plants produce a large number of compounds unique to the species, called cannabinoids. Tetrahydrocannabinol (THC; Fig. 1), is the primary psychoactive cannabinoid of the cannabis plant itself and any product made from the plant. The other cannabinoids present in the plant are generally at very low concentrations and contribute little or no psychoactive effects.

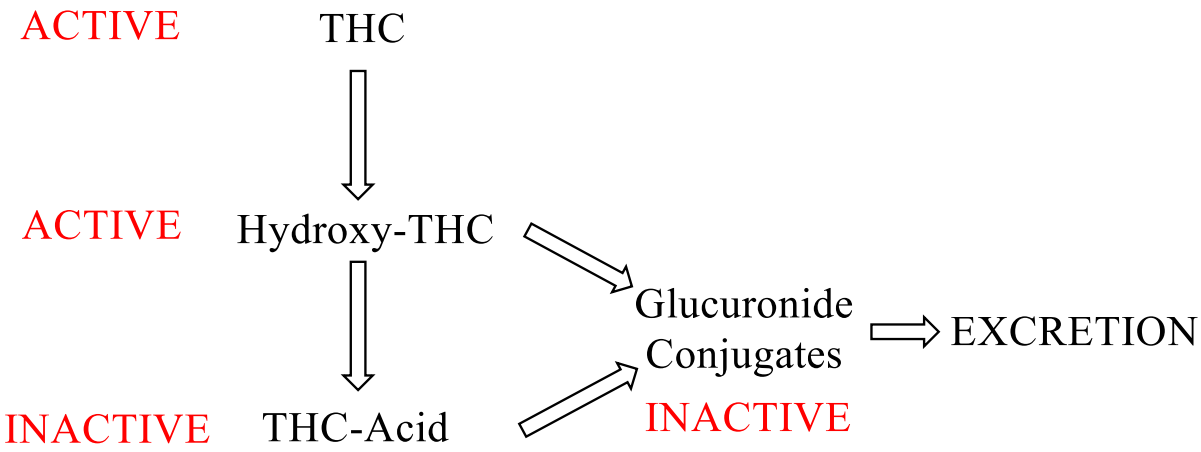

Figure 1 Metabolism and excretion of THC showing pharmacological activity.

The amount of THC in cannabis plants and products may vary greatly. The concentration of THC ('potency') of cannabis plants currently being grown in NZ is largely unknown. Extracts of the cannabis plant can contain a significantly higher proportion of THC, but if plant material or extracts are included in edibles the final concentration of THC may be lower than that in the original plant.

Cannabis material may be taken in a variety of ways and is generally inhaled (smoked or vaped) or ingested for recreational purposes.

There is increased availability of cannabis-based products as foods and medicines. Food products made using hemp seeds do not contain enough THC to give a positive oral fluid screening test or detectable THC in blood samples. Cannabis based medicines may contain THC and/or cannabidiol (CBD). If medicines contain high concentrations of THC, these may cause impairment, positive oral fluid tests and blood THC concentrations. CBD-based medicines have legally restricted, low concentrations of THC that will not result in impairment, positive oral fluid tests or blood THC levels.

Differences between products and routes of administration will affect resulting blood and oral fluid THC concentrations and their pharmacological effects.

Blood THC concentrations following inhalation

Cannabis plant material is generally smoked in the form of cigarettes. Other forms of cannabis, such as cannabis oil and hashish or extracts of the plant, may be heated and inhaled using a variety of techniques including vaping. Although the following information usually refers to 'smoking cannabis', similar findings are expected for all methods of inhalation.

When cannabis is inhaled, maximum blood THC concentrations occur within minutes of dosing, then the blood THC concentrations decrease rapidly at a rate that varies between individuals. Blood THC concentrations reach the maximum while a cannabis cigarette is being smoked. Blood THC concentrations then drop rapidly as the THC is distributed around the body, particularly into fatty tissues. THC principally acts at sites in the brain (where it interacts with receptors), consequently blood concentrations correlate poorly with the effects of the drug (because it is the concentration in the brain that determines effect).

Figure 2 shows an amalgamation of blood THC concentrations from nine smoking studies [5-13] in which experienced smokers smoked cannabis cigarettes containing 15 or 30 mg THC. Approximately 10 minutes was allowed to smoke the cigarette. Blood THC concentrations were measured over an extended time period. Maximum blood THC concentrations of approximately 100 ng/mL occurred during smoking and started declining immediately to below 10 ng/mL within 1 hour. At 3 hours the blood THC concentrations of all smokers had decreased to below 3 ng/mL and at 4 hours the blood THC concentrations were all below 2 ng/mL. These studies did not consider impairment but showed the rapid decrease and wide variability in blood THC concentrations when smoking cannabis in a standardised environment.

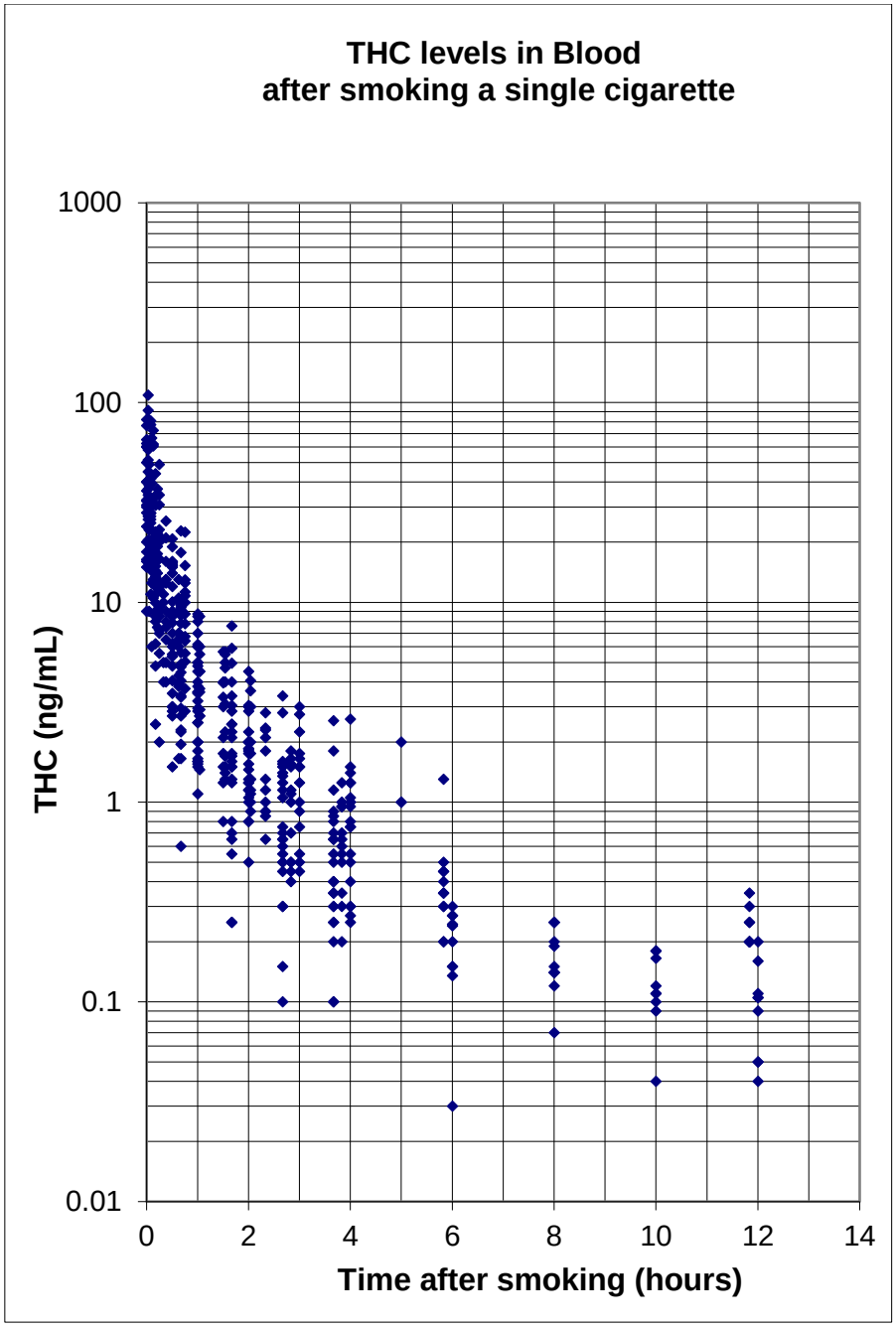

Figure 2 *Concentration of THC in blood of volunteers after inhalation (smoking) of cannabis cigarettes containing 15 or 30 mg THC where the time allowed to smoke the cigarette was 10 minutes (data from references 5-13)*

The rapid decrease in blood THC concentrations, as well as the inconsistency of this decrease between individuals, have led some scientists to state that it is not advisable to set a *per se* blood THC concentration. The delay between the time a driver is stopped at the roadside and the time a blood sample is taken can result in a significant and unpredictable decline in blood THC concentrations [14].

Blood THC concentrations and impairment

An impairing dose of THC is considered to be approximately 5 mg. The bioavailability of THC is variable but generally higher when the drug is smoked rather than ingested. A recent study found that vaping cannabis extracts resulted in greater impairment and higher blood THC concentrations compared with smoking [15].

The greatest impairment to driving occurs 60 to 90 minutes following inhalation, a time range at which blood THC concentrations have already declined significantly [4,16]. The effects of cannabis are reported to last about 3 to 4 hours.

There have been many studies and reports trying to relate blood THC concentrations to impairment, including:

- A study of blood THC concentrations and field sobriety testing found no correlation between blood THC concentrations and the ability to perform sobriety tests [17].
- Drivers assessed as impaired had blood THC concentrations ranging from 0.3 to 45.3 ng/L (median 2.5 ng/mL). Those drivers assessed as not impaired had blood THC concentrations ranging from 0.32 to 24.8 ng/mL (median 1.9 ng/mL) [18].
- A systematic review of the literature relating cannabis effects on driving found that blood THC concentrations of 2 to 5 ng/ml were associated with substantial impairment [19].
- A study found blood THC concentrations in arrested drivers had a mean of 5 ng/mL and a median of 3 ng/mL (half the arrested drivers had blood concentrations less than 3 ng/mL) [20].
- Blood THC concentrations of 3.5 to 5 ng/mL may achieve reasonable separation of impaired from unimpaired drivers [21].

Furthermore, culpability studies are often used to determine crash risk related to a drug. For example:

- A study of Australian fatalities indicated crash risk increased at THC concentrations greater than 5 ng/mL [22].
- A study of NZ driver fatalities found a greater crash risk at blood THC concentrations less than 2 ng/mL compared with concentrations greater than 2 ng/mL [23].

Oral fluid and blood THC concentrations from various means of exposure

Inhalation

Like blood, maximum oral fluid concentrations occur while cannabis plant is being smoked, however the correlation between oral fluid and blood THC concentrations is poor.

Oral fluid concentrations cannot be used to predict a blood THC concentration. After smoking cannabis concentrations of THC are higher in oral fluid than in blood for several hours [24,25].

There are wide variations in oral fluid/blood THC concentration ratios between individuals, but also for an individual, following smoking or vaping cannabis [24]. One study found that, after smoking cannabis, the oral fluid/ blood THC ratio at 1 hour ranged between 0.2 to 350 (median = 6) [26].

Passive exposure

Smoking can expose other people in the vicinity to THC (passive exposure), thus there are concerns that passive exposure to cannabis smoke may result in a positive oral fluid roadside test. Several studies have addressed this issue directly:

In a 2005 study, four passive and four active smokers were placed in an unventilated eight-seater van. Oral fluid was collected inside and outside the van [27]. When the oral fluid was collected in the contaminated environment inside the van, the highest oral fluid THC concentration was 7.5 ng/mL. After the passive smokers left the van for the testing process, oral fluid THC concentrations up to 1.2 ng/mL were detected. The oral fluid concentrations declined sufficiently to give a negative result 30 minutes after leaving the van.

In a 2011 study, participants were exposed to cannabis smoke for 3 hours in a coffee shop in the Netherlands [28]. Oral fluid specimens were collected outside after exposure for 20, 40, 60, 120 and 180 minutes, then 12 hours later. THC was detected in oral fluid but the amount varied, likely depending on the number of cannabis smokers in the coffee shop. Few of the oral fluid samples collected from the passive participants exceeded 5 ng/mL during the three hour exposure period, and all were below 5 ng/mL 1 hour after exposure.

In a 2015 study designed to produce extreme cannabis smoke exposure, six passive and six active smokers were placed in a closed chamber [29]. Two sessions were carried out with no ventilation and one session allowed ventilation of the chamber. Oral fluid concentrations greater than 5 ng/mL were detected for up to 2 hours after exposure in the unventilated environment. When the chamber was ventilated, results were variable, and only some of the passive participants achieving oral fluid concentrations greater than 5 ng/mL. THC was detected in the blood in the passively exposed participants. In the unventilated environment THC blood concentrations generally decreased to below 1 ng/mL with 1 hour. When the chamber was ventilated blood THC concentrations did not reach 1 ng/mL

Taken together, these studies indicate that it is possible for a person to test positive for THC after passive smoking, and also to achieve a concentration associated with impaired driving ability, but only under conditions where the driver was subjected to extreme and prolonged exposure, which they would unlikely do so unwittingly.

The other methods used for inhalation of cannabis products are unlikely to result in similar environmental exposure to THC, but this requires further investigation.

Based on these studies, it is unlikely that passive exposure to cannabis smoke under realistic exposure conditions will result in a positive oral fluid test at the roadside.

Ingestion of cannabis edibles

Both blood and oral fluid THC concentrations are lower when food containing cannabis (cannabis edibles) is ingested, when compared with smoking [30,31].

Maximum blood THC concentrations occur 2 to 4 hours after ingestion. Psychoactive effects are also delayed, although they are reported to be more intense than when the drug is smoked. One study found that the concentrations of THC in oral fluid and blood were similar when the blood THC concentration was at its maximum [32].

Hemp-based food ingestion

Hemp is the common name for low potency cannabis. Hemp has been grown in NZ for over 20 years but it is only since 2018 that food products made from hemp seeds have been allowed to be sold commercially. Hemp seeds can be used to make a variety of food products: hemp seed oil, hemp milk, hulled hemp seeds, hemp protein powders and hemp seed butter (used like peanut butter).

Hemp seed oil (i.e. edible oil made from the kernels of hemp seeds) contains the most THC when compared with other hemp seed food products. As in most countries where hemp food products are sold, regulations require THC concentrations in food products to be less than 10 milligrams of THC per kilogram (mg/kg) of oil. Therefore, ingestion of 15 mL (approx. one tablespoon) of hemp seed oil containing the maximum allowed amount of THC, is equivalent to ingestion of 0.15 mg of THC.

A study carried out by Swinburne University in Melbourne Australia showed that ingestion of 5 mL (approx. one teaspoon) of spiked oil containing 10 or 20 mg/kg THC, did not result in a positive oral fluid test or detectable THC in the blood [33].

Cannabis as a medicine

Currently the only medicinal products containing high levels of THC available in NZ are the imported Sativex and Tilray products, typically administered as an oral spray. These and future medicinal products may deliver impairing doses of THC that will be detected in the oral fluid and blood.

A study compared THC blood concentrations following oromucosal administration and capsulated forms [34] of medicinal Sativex, 5 and 15 mg doses. The higher dose formulations

resulted in maximum blood THC concentrations ranging from 1.6 to 19 ng/mL anywhere from 1.2 to 5.5 hours after administration.

Concern within the medical profession led to a review of the literature that found that most driving experiments are only carried out for 2 to 3 hours after administration, and they recommended that patients should not drive for 8 hours after use [35].

Chronic cannabis use

With chronic use of cannabis, blood THC concentrations can remain elevated. Chronic use may be defined as daily use of the equivalent of several cannabis cigarettes. Chronic use of cannabis will result in elevated blood THC concentrations being detected for a longer time than following a single dose. In addition, a recent study [36] indicates that chronic cannabis users also have an extended duration of impairment.

In one study [37] 30 chronic smokers were held in a secure research unit and abstained from cannabis for one month. Blood THC concentrations on admission ranged from 0.3 to 6.3 ng/mL (median 1.4 ng/mL). The median blood THC concentration on day 1 was less than 2 ng/mL and the median concentration on day 2 was less than 1 ng/mL. However, it was only after day 10 that blood THC concentrations of all 30 participants blood fell below 2 ng/mL.

Oral fluid THC concentrations may also remain elevated following heavy use of cannabis. One study [38] found that oral fluid concentrations took between 2.5 and 30 hours to drop below 5 ng/mL and blood THC concentrations took between 2.5 and 150 hours to drop below 2 ng/mL.

A number of studies have also assessed the driving performance of chronic cannabis users, with mixed results. The findings of these studies vary, from the finding that heavy use had little effect on critical thinking or divided attention tasks [39], to finding persistent cognitive decrements after weeks of abstinence, including deficits in attention, concentration, decision making, concept formation and planning [40]. This conjecture illustrates the significant variability when attempting to link blood THC concentrations to degree of impairment.

Time after administration that THC might be detected in biological samples

There is a common misconception that cannabis use can be detected for weeks after use. The time after administration for the detection of any drug will depend on which biological sample is tested. Drugs are detectable for the shortest time in oral fluid and blood, and are detectable for a longer period in urine, and even longer in hair samples.

After smoking cannabis, blood THC concentrations drop rapidly. After the use of a single cannabis cigarette, assuming the blood was clear of any previous cannabis use, THC may be

detected for up to 12 hours. For some individuals blood THC concentrations may drop to below detection limits within a few hours of smoking.

Like blood, maximum oral fluid concentrations occur while cannabis is being inhaled. However, following smoking cannabis, oral fluid THC concentrations can decline more slowly and may remain higher than blood concentrations for several hours [24].

Chronic use of cannabis will result in higher THC blood concentrations that persist for longer. In line with this, one study [36] has shown that chronic users also have an extended duration of impairment.

The misconception of extended detection times of cannabis use comes from the detection of THC-acid, a metabolite of THC, in urine following use of the drug. For the infrequent cannabis user, THC-acid may be detected in urine for two or three days after the use of the equivalent of a single cannabis cigarette. Chronic use (several cigarettes daily for an extended time) results in an extended detection period of the metabolite in the urine. A study involving 22 chronic drug abusers [41] found that it took between 0 and 19 days to obtain a negative urine result after cessation of cannabis smoking.

Blood THC concentrations in NZ drivers

Deceased drivers

Table 2 shows occurrence of cannabis taking and THC concentrations in the blood of NZ drivers killed in road traffic accidents.

Table 2 Occurrence of cannabis taking and THC concentrations in deceased NZ drivers.

Years	Number of Drivers	Cannabis Positive	THC Concentration Range ng/mL	Mean THC Concentration ng/mL	Median THC Concentration ng/mL
2004 to 2009	1046	314 (30%)	0.2 to 44	5.5	3
2013 to 2018	1069	266 (25%)	0.2 to 100	7.2	4

It is interesting to note that:

- In the 2013 to 2018 period, 72% of deceased drivers had blood THC concentrations greater than 1 ng/mL and that 50% had blood THC concentrations greater than 3 ng/mL.
- In the 2013 to 2018 period, 38% of the drivers using cannabis had also used alcohol.

Impaired drivers

For the period 2017 to mid 2020, blood samples from 1679 impaired drivers were analysed. Of these drivers:

- 1023 (61%) had used cannabis.
- 523 (31%) had used cannabis and no other drugs. Blood THC concentrations ranged from 0.2 to 40 ng/mL (mean 9.8 ng/mL, median 7 ng/mL).
- 52 (10%) had blood THC concentration less than 1 ng/mL.
- 96 (18%) had blood THC concentration less than 2 ng/mL.
- 132 (25%) had blood THC concentration less than 3 ng/mL.

Hospitalised drivers

For the period 2017 to mid-2020, blood samples from 2796 hospitalised drivers were analysed. Of these drivers:

- 1036 (37%) had used cannabis.
- 426 (15%) had used cannabis and no other drugs. Blood THC concentrations ranged from 0.2 to 40 ng/mL (mean 4.4 ng/mL, median 2.7 ng/mL).
- 110 (26%) had blood THC concentrations less than 1 ng/mL.
- 173 (41%) had blood THC concentrations less than 2 ng/mL.
- 227 (54%) had blood THC concentration less than 3 ng/mL.

Use of blood THC concentrations in evidence

The following points taken from scientific literature and analysis of blood THC levels in NZ drivers killed in road traffic accidents are important when considering the use of blood THC concentrations as evidence:

- Blood THC concentrations will likely drop below 3 ng/mL within 3 hours of smoking an impairing dose.
- Impairment following the use of cannabis would be expected to last for 3 to 4 hours.
- There will inevitably be a delay between stopping a driver and obtaining a blood sample.
- Of 523 drivers found to be impaired by a police CIT test, 25% had THC blood concentrations less than 3 ng/mL, 10% had blood concentrations less than 1 ng/mL.
- Overseas jurisdictions have set *per se* limits for THC ranging from 1 to 9 ng/mL.

Proposed statutory limit

Based on the findings discussed in this section, the blood drug concentrations detected in NZ drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood THC limit of 3 ng/mL and a blood threshold limit of 1 ng/mL**.

Stimulants

Stimulants (psychostimulants) are a class of drugs that increase activity of the central nervous system (CNS) via interactions with specific receptors in the brain; as a result of this they can increase nervous stimulation of other parts of the body resulting increased activity and performance. They are prescribed (e.g. methylphenidate for treatment of Attention Deficit Hyperactivity Disorder (ADHD)) and used illicitly (e.g. methamphetamine) as performance enhancing or recreational drugs.

It may be dangerous to drive after using psychostimulants due to:

- overconfidence in driving skill that is not supported by actual improvement in driving ability,
- propensity to take unnecessary risks,
- aggressive and dangerous driving,
- impaired ability to react appropriately,
- drivers suddenly falling asleep as the stimulant effects wear off [4].

A case controlled study [42] estimated accident risk for alcohol, medicines and illegal drugs (using data from the Driving Under the Influence of Drugs (DRUID) project) and, for single drug use, the study attempted to determine the threshold at which a significant increase in risk was observed. For amphetamine type drugs, no clear threshold could be determined; indeed, there was a similar high risk at all drug blood concentrations.

Methamphetamine

Methamphetamine is a central nervous system stimulant: low dose administration increases alertness, but with increased dosing and duration of use there are disorienting effects on cognition, reasoning and psychomotor ability. After high-dose or chronic use, delusions and psychotic episodes may also occur [43].

Blood methamphetamine concentrations depend on the route of administration, the dose and the frequency that the drug is taken. Methamphetamine may be smoked, snorted, injected or ingested. The onset of effects is significantly faster for the first three routes of administration compared to the oral route.

Peak blood methamphetamine concentrations occur shortly after injection, a few minutes after smoking, and around 3 hours after oral dosing [4].

Methamphetamine blood concentrations do not decline quickly. The half-life of the drug ranges from 6 to 15 hours [44]. As a consequence, the drug can be readily detected for 24 hours or longer after use.

Onset of effects is rapid following intravenous use and smoking, while the effects are felt more slowly following oral use. Overall, the stimulatory effects typically last 4 to 8 hours but

residual effects can persist for up to 12 hours. Methamphetamine is known to affect the ability to drive safely. It has been suggested that low dose stimulants may improve performance. Indeed, driving simulation studies have shown increased alertness following low dose administration of methamphetamine [45]; however, such doses are not typical of recreational methamphetamine use and do not apply to drug abuse situations.

Studies have found no correlation between methamphetamine blood concentrations and increased risk of crashing because the use of methamphetamine increases crash risk at all blood concentrations determined [42].

Oral fluid devices cannot distinguish between methamphetamine and MDMA. A positive oral fluid result could be due to use of either drug [46]. The oral fluid devices can generally detect methamphetamine at concentrations from 35 to 50 mg/L.

Methamphetamine is generally detected in oral fluid at higher concentrations than is present in blood. Although there have been no controlled methamphetamine smoking studies, long-term users are likely to have detectable methamphetamine in oral fluid for several days after dosing [47].

In the years from 2017 to mid-2020, blood taken from 1679 NZ impaired drivers was analysed for evidence of drug use. Of these, 823 (49%) had used methamphetamine. Of these 823 drivers, methamphetamine was the only drug detected in 326 drivers (19% of the total impaired drivers tested). Of the 326 methamphetamine positive drivers who had used methamphetamine alone, 305 (94%) had blood methamphetamine concentrations greater than 50 ng/mL.

In the years from 2017 to mid 2020, blood taken from 2796 hospitalised drivers has been analysed for evidence of drug use. Of these 771 (28%) had used methamphetamine. The blood methamphetamine concentrations in these 771 drivers ranged from 10 to 2000 ng/mL (average 240 ng/mL, median 170 ng/mL) and 645 (84%) of the drivers had blood methamphetamine concentrations greater than 50 ng/mL.

The UK, Norway and Denmark governments have set *per se* limits for methamphetamine at 10, 48 and 32 ng/mL respectively [1-3].

Proposed statutory limit

Based on the blood drug concentrations detected in NZ drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood methamphetamine limit of 50 ng/mL and a blood threshold limit of 10 ng/mL.**

Amphetamine

Amphetamine is a central nervous system stimulant with effects similar to methamphetamine albeit with lower potency [48]. Amphetamine is more commonly used than methamphetamine in many European countries but to date, amphetamine itself is not commonly used in NZ.

Amphetamine is also a metabolite of methamphetamine and is usually detected when methamphetamine is present in blood. However, blood concentrations of amphetamine from metabolism of methamphetamine are rarely greater than 10% of the blood concentration of methamphetamine itself [4], thus it is possible to distinguish the use of amphetamine itself from its presence due to methamphetamine use and its consequent metabolism.

Like other stimulants, oral fluid amphetamine concentrations are greater than blood concentrations [47]. That said, amphetamine is not detected by the same immunoassay screen as methamphetamine, so will not be detected by the methamphetamine channel on an oral fluid screening device. A separate channel is used for amphetamine. Oral fluid devices claim to detect amphetamine in oral fluid at 50 to 60 ng/mL.

From 2017 to mid 2020 amphetamine use has been detected in three impaired drivers in NZ. Blood amphetamine concentrations were 40, 70 and 170 ng/mL in these three drivers.

The UK, Norway and Denmark have set *per se* limits for amphetamine of 250, 41 and 32 ng/mL respectively [1-3].

Proposed statutory limit

Based on the blood drug concentrations detected in NZ drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood amphetamine limit of 100 ng/mL and a blood threshold limit of 20 ng/mL.**

Methylenedioxymethamphetamine (MDMA)

MDMA is a mild to moderate central nervous system stimulant with hallucinogenic properties. MDMA toxicity may include symptoms of hyperthermia, seizure, tachycardia and hypertension [49].

No clear correlation exists between MDMA blood concentrations and effects [4]. Toxicity due to MDMA is variable among individuals and there is a significant overlap between concentrations associated with minimal toxicity, impairment and concentrations associated with fatal overdose.

An intoxicating dose of MDMA is considered to be approximately 100 mg. Such doses can cause acute changes in cognitive performance and impair information processing, which in turn impair driving ability [4]. A simulator study was carried out to determine the effect of methamphetamine and MDMA on driving [50]. Volunteers were dosed with either 100 mg MDMA or 0.42 mg/kg body weight methamphetamine. The mean peak MDMA blood concentration at 3 h was 200 ng/mL, and the mean peak methamphetamine blood concentration was 90 ng/mL. In this study MDMA drivers performed less well than methamphetamine drivers.

MDMA tablets are not commercially prepared; therefore, users/buyers do not know the MDMA content per tablet (i.e. strength of the tablet) or purchased batch. The UK expert panel [51] reported that MDMA tablets contained 40 to 75 mg. In a recent ESR study of 37 tablets seized at the border in 2019, the MDMA content ranged from 44 to 290 mg per tablet (mean 176 mg, median 168 mg).

In general, the oral fluid concentrations of stimulant type drugs are higher than blood concentrations but this depends on the route of administration. MDMA is commonly found in tablet form and may be swallowed resulting in low oral fluid concentrations.

As discussed previously, oral fluid devices cannot distinguish between methamphetamine and MDMA: a positive result could be due to use of either drug, although the sensitivity of devices is greater for methamphetamine than MDMA [46]. Information provided in relation to the Dräger device specifies this difference with detection of methamphetamine at 35 ng/mL and MDMA at 75 ng/mL.

The use of MDMA is often combined with alcohol and other drugs. Of the 44 NZ impaired drivers found with MDMA in their blood from 2017 to mid-2020, only two had not used other drugs. Similarly, of the 73 hospitalised drivers over the same time period, only nine were found with only MDMA in their blood.

Blood MDMA concentrations for the 44 impaired NZ drivers ranged from 10 to 1700 ng/mL (mean 250 ng/mL, median 80 ng/mL). Blood MDMA concentrations from the 73 hospitalised drivers ranged from 10 to 7300 ng/mL (mean 260 ng/mL, median 70 ng/mL).

The UK, Norway and Denmark governments have set *per se* limits for MDMA of 10, 48 and 21 ng/mL respectively [1-3].

Proposed statutory limit

Based on the blood drug concentrations detected in NZ drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood MDMA limit of 50 ng/mL and a blood threshold limit of 10 ng/mL.**

Methylenedioxyamphetamine (MDA)

MDA is a drug in its own right and a metabolite of MDMA. It is a CNS stimulant with considerably greater potency [4] than MDMA. When MDMA is detected in blood, MDA is also usually detected. The finding of a metabolite in blood is not generally reported in LTA certificates, so when MDA is detected in the blood with MDMA, only MDMA is reported (this is to avoid 'double counting' of drug use). Use of the drug MDA itself can be distinguished readily from its presence due to MDMA use because the blood concentration of MDA when present as the metabolite is rarely greater than 10% of the concentration of MDMA.

In NZ, MDA itself is not a commonly used drug. It has been detected in a driver only once in the years from 2017 to mid-2020, at a concentration of 410 ng/mL.

Overseas jurisdictions have not set *per se* limits for MDA.

The Panel does not propose a *per se* limit for MDA.

Cocaine

Cocaine is a potent CNS stimulant. The routes of administration for cocaine are dependent on its form and include snorting, smoking and injection. The onset of effects is rapid, from seconds to minutes irrespective of the route of administration [4].

Cocaine is rapidly metabolized and has a short duration in the body. Any time delay between a driver being stopped and a blood sample being taken will result in a significant reduction in the concentration of cocaine in the blood. Benzoylecgonine is an inactive metabolite and breakdown product of cocaine and its presence in blood is indicative of cocaine use.

Cocaine generally has a higher concentration in oral fluid than blood and may be detected up to 6 hours after smoking and up to 12 hours after snorting [47]. Oral fluid detection devices report detection of cocaine in oral fluid at concentrations between 10 and 30 ng/mL with one device also reported as detecting benzoylecgonine at 70 ng/mL.

Cocaine is rarely detected in NZ drivers. During the period 2017 to 2019 only one cocaine-impaired driver was detected – the person had a blood cocaine concentration of 30 ng/mL. Benzoylecgonine has been detected in the blood of some drivers but this is not generally reported as it is a metabolite, not a drug listed in the Misuse of Drugs Act 1975.

Some countries have set a *per se* limit for cocaine and benzoylecgonine. *Per se* limits for cocaine of 10, 24 and 21 ng/mL have been implemented in the United Kingdom [1], Norway

[2] and Denmark [3] respectively. The UK also set a *per se* limit for benzoylecgonine of 50 ng/mL.

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood cocaine limit of 20 ng/mL and a blood threshold limit of 5 ng/mL.**

Gamma-hydroxybutyrate (GHB)

GHB is a powerful CNS depressant. At low doses, its effects are similar to alcohol's [4]. Signs of behavioural effects and impaired performance when under the influence of GHB include erratic driving, ignoring road signs, and near-collisions [4]. The onset of effects occurs within 10 to 20 minutes of dosing and they generally last for 2 to 5 hours.

Following oral administration, peak plasma concentrations are achieved within 20 to 45 minutes and the half-life of GHB in blood is in the region 20 to 40 minutes [52]. Even after high doses, GHB is swiftly eliminated, meaning that it is undetectable in the blood within 4 to 6 hours. An hour delay between the time of an infringement to the time the blood sample is taken, would mean a blood GHB concentration of 100,000 ng/mL could drop to about 10,000 ng/mL.

A Swedish study of GHB concentrations in blood taken from 473 impaired drivers over a 10-year period reported an average blood concentration of 90,000 ng/mL (maximum 340,000 ng/mL) [53].

GHB is not detected by oral fluid screening tests. Use of the drug is generally determined by observed poor driving and a failed CIT test.

It is not possible for laboratory analytical techniques to detect all drugs at once. GHB is not detected by the analytical methods usually applied to LTA samples. GHB analysis would need to be requested specifically by the police.

The blood GHB concentrations found in samples from three NZ impaired drivers since 2017 were 45,000, 70,000 and 90,000 ng/mL. In each case, use of the drug was suspected and the analysis was specifically requested by the Officer in Charge.

Anecdotal information from Australia indicating that GHB was commonly used with methamphetamine led to an ESR study of 290 drivers who had used methamphetamine. This study found 42 drivers (14%) had also used GHB. Blood GHB concentrations in these

drivers ranged from 15,000 to 200,000 ng/mL (mean 80,000 ng/mL). It is clear from this study that GHB use by drivers is more prevalent than previously thought.

Norway has specified a graduated *per se* limit for GHB of 10,300 to 123,600 ng/mL [2]. A *per se* limit for GHB has not been specified in the UK or Denmark.

Proposed statutory limit

Based on the blood drug concentrations detected in NZ drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood GHB limit of 50,000 ng/mL and a blood threshold limit of 10,000 ng/mL.**

Ketamine

Ketamine is classified as a dissociative anaesthetic (i.e. involves catalepsy, catatonia, analgesia and amnesia, but not necessarily loss of consciousness). It is used in veterinary medicine and in human surgery to induce anaesthesia. Ketamine is also abused recreationally, when it may be administered by injection, smoking, snorting or orally [4].

There is no direct correlation between ketamine concentrations and behaviour. Drowsiness, perceptual distortions and intoxication may be dose related in a concentration range of 50 to 200 ng/mL, and analgesia begins at plasma concentrations of about 100 ng/mL [4]. The half-life of ketamine is 2 to 3 hours. This means the drug is eliminated from the body rapidly.

At this time there is no evidence that ketamine is commonly used recreationally in NZ. While it is frequently detected in blood taken under the LTA, these samples have all come from drivers who have been hospitalised following a crash and it is most likely that the drug has been administered by medical personnel.

Ketamine is not detected by oral fluid screening tests. Use of the drug will generally be determined by observed poor driving and a CIT test.

Some countries have *per se* limits for ketamine - the UK has set a limit of 20 ng/mL [1]. Norway introduced a graduated system with concentrations ranging from 55 to 300 ng/mL [2].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood ketamine limit of 50 ng/mL and a blood threshold limit of 10 ng/mL.**

Sedatives

The drugs under consideration in this section are prescribed medicines used as relaxants, sleep aids, anti-anxiety and anti-spasmodic drugs. These include benzodiazepine-type drugs and zopiclone. Benzodiazepines are also frequently used recreationally particularly in combination with illicit stimulants and opioids.

Reviews of pharmacodynamic studies with healthy volunteers have generally shown that sedatives can cause severe impairment in tests designed to measure psychomotor and driving performance. Sedatives cause impairment following administration of normal therapeutic doses. In addition, performance may be adversely affected the morning after drug ingestion: this is known as the 'hangover' or 'residual' effects of benzodiazepines [49].

The magnitude of impairment is dependent on various factors, including dose, pattern of use and time of administration/intake. However, overall, the significant issues for drivers relate to the sedative effects of these drugs.

The drugs under consideration are those commonly prescribed in NZ and/or those detected in the NZ driving population: alprazolam, clonazepam, diazepam, lorazepam, midazolam, nitrazepam, oxazepam, temazepam, triazolam and zopiclone.

A combination of analytical results of blood samples taken from deceased, impaired and hospitalised drivers gives an indication of the prevalence of use of these drugs by NZ drivers (Table 3). It should be noted that when sedatives are detected in drivers' blood, they are rarely the only drug detected.

Table 3 *Sedative drugs detected in blood of deceased NZ drivers (n = 966) in descending order of occurrence.*

Drug	Number of Detections in NZ Drivers
Diazepam	298
Zopiclone	210
Clonazepam	198
Lorazepam	102
Midazolam	62
Triazolam	49
Temazepam	24
Alprazolam	13
Nitrazepam	8
Oxazepam	2

The intended use (indication) of a particular sedative determines when, why and how often it is dosed. Those (nitrazepam, temazepam, triazolam and zopiclone) used to induce sleep (hypnotics) are generally only prescribed to be taken at night before sleep, which likely means that drivers' blood levels would be lower than for other sedatives because clearance from the circulatory system would occur overnight. Those generally prescribed (daytime dosing) to reduce anxiety (anxiolytics) are alprazolam, clonazepam, diazepam, lorazepam and oxazepam. Clonazepam is also prescribed to treat epilepsy. Midazolam is most commonly administered prior to surgery as a sedative.

These drugs all have different dosage strengths and will therefore be present at different concentrations in blood after use. Individual sedatives are eliminated from the body at different rates and the frequency of their administration varies.

Oral fluid concentrations of benzodiazepines are generally lower than the blood concentrations at the same time. There is not a great deal of detailed information about the oral fluid:blood ratios for these drugs other than the ratio is variable and can range from about 1:2 to over 1:10 [54].

It is important to note that a positive response to the oral fluid screen benzodiazepine channel does not determine which specific benzodiazepine(s) is(are) present.

Dräger lists benzodiazepine oral fluid screen cut-off concentrations as follows: alprazolam (10 ng/mL), clonazepam (15 ng/mL), diazepam (15 ng/mL), midazolam (40 ng/mL), nitrazepam (30 ng/mL), oxazepam (40 ng/mL), temazepam (20 ng/mL) and triazolam (40 ng/mL). This means that based on an oral fluid:blood ratio of 1:10, the oral fluid device will detect recent use of diazepam, oxazepam and temazepam, but not the other benzodiazepines. Even with a lower fluid:blood ratio the device is unlikely to detect triazolam. Furthermore, the screening panel does not detect lorazepam or zopiclone. The latter is not a benzodiazepine, but is used for similar indications and so is included in this section.

All of these drugs when taken at normal therapeutic doses have the potential to significantly impair the ability to drive safely. Patients should be advised not to drive after taking these drugs and not to combine their use with alcohol, but we have no data to indicate whether doctors and/or pharmacists routinely give such advice.

The recommended criminal limit and threshold limit for each of these drugs is based on consideration of the blood concentrations expected following recommended doses, knowledge of the pharmacodynamic properties of the drug, doses that have been shown to cause impairment, the concentrations detected in NZ impaired drivers, and limits set by overseas jurisdictions.

In addition, it is advised that a criminal penalty should be considered for these drugs when detected at the blood threshold concentration in the presence of alcohol or in combination with other sedative/impairing drugs.

Norway, Denmark and the UK have set *per se* limits for a number of sedative drugs [1-3] (Table 4). The difference in *per se* limits for these drugs across these three jurisdictions is significant. Norway has a three-tier system with increasing blood concentrations resulting in increased penalty. The concentrations given in Table 4 are those for the maximum penalty, with the exception of midazolam, which has a single statutory concentration.

Table 4 *Statutory limits for sedatives in the UK, Norway and Denmark compared with limits proposed in this report.*

Drug	**Blood Limits Proposed in this Report ng/L**		**Limits in Other Jurisdictions ng/mL**		
	Criminal	**Threshold**	**UK**	**Norway**	**Denmark**
Alprazolam	50	20	x	15	5.3
Clonazepam	50	20	50	8	5.3
Diazepam	200	100	550	342	110
Lorazepam	30	10	100	x	21
Midazolam	30	10	x	33*	x
Nitrazepam	50	20	x	98	21
Oxazepam	800	200	300	860	110
Temazepam	800	200	1	x	x
Triazolam	4	4	x	x	3
Zopiclone	50	20	x	58	11

x No limit
*Single statutory concentration

Alprazolam

Alprazolam is prescribed for the treatment of anxiety; it is approximately 10 times more potent than diazepam [55]. Alprazolam is available in doses of 0.25 to 0.5 mg dosed 3 times daily with a maximum daily dose of 4.5 mg per day [55,56].

Studies have shown that a single 0.5 mg dose of alprazolam is sufficient to cause impairment [45].

Following a single 1 mg oral dose to six male patients, peak plasma concentrations averaged 19 ng/mL at 1.3 hours after dosing [44]. Steady state (blood drug concentration that does not change with time - achieved after repeat dosing) serum (blood minus blood cells) concentrations of 25 to 55 ng/mL have been reported in six patients taking daily oral doses of 1.5 to 6 mg [44].

Alprazolam is not commonly found in NZ driver samples. The blood concentrations found in four impaired drivers were 70, 100, 200 and 200 ng/mL.

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations - 3, 6 and 15 ng/mL [2]. Denmark has a *per se* limit of 5.3 ng/mL [3].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood alprazolam limit of 50 ng/mL and a blood threshold limit of 20 ng/mL.**

Clonazepam

Clonazepam may be prescribed as an anti-anxiety or anticonvulsant drug. It is approximately 20 times more potent than diazepam [55]. In NZ, clonazepam is available as tablets containing 0.5 or 2 mg, oral liquid at 2.5 mg/mL and an injectable formulation at 1 mg/mL. The standard dose is generally 0.5 to 2 mg as a single dose up to a maximum of 8 mg per day depending on the indication (Clonazepam has multiple uses from epilepsy treatment to anxiety, panic and combination with opiate substitution treatments). Doses above 2 mg require split dosing with dose intervals of at least 4 hours [55,56].

Studies have determined that a single dose of 1 to 2 mg clonazepam is sufficient to cause impairment [45].

Therapeutic plasma concentrations of clonazepam, observed in 25 patients undergoing continuous treatment with 6 mg of clonazepam daily for 15 to 26 days were found to range between 29 and 75 ng/mL [57]. An average 55 ng/mL is considered necessary to achieve an optimum therapeutic effect [56].

Clonazepam is one of the more common sedatives found in NZ driver samples. The blood concentrations found in 47 impaired drivers ranged from 10 to 140 ng/mL (mean 30 ng/mL, median 20 ng/mL).

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations of 1.3, 3 and 8 ng/mL [2]. Denmark has a *per se* limit of 5.3 ng/mL [3].

Proposed statutory limit

Based on the concentrations detected in NZ impaired drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood clonazepam limit of 50 ng/mL and a blood threshold limit of 20 ng/mL.**

Diazepam

Diazepam is prescribed for the short-term relief of anxiety, acute alcohol withdrawal, epilepsy, convulsions and for the control of muscle spasms. In NZ, diazepam is available in tablets containing 2 or 5 mg, an oral liquid at 10 mg/mL an injection at 10 mg/2 mL and an enema containing 5 or 10 mg. The standard dose is 2 to 10 mg three times daily, with a maximum recommended dose of 30 mg daily (although some severe conditions require 60 mg) [55,56].

Studies have determined that doses greater than 5 mg diazepam are sufficient to cause impairment [45].

For healthy male volunteers receiving a single 10 mg diazepam dose, the peak plasma concentrations ranged from 250 to 590 ng/mL (mean 400 ng/mL) [58].

Diazepam is the most common sedative found in NZ driver samples. The blood concentrations found in 93 impaired drivers ranged from 10 to 1430 ng/mL (mean 140 ng/mL, median 60 ng/mL).

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations of 57, 143 and 342 ng/mL [2]. Denmark has a *per se* limit of 110 ng/mL [3]. The UK *per se* limit is 550 ng/mL [1].

Proposed statutory limit

Based on the concentrations detected in NZ impaired drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood diazepam limit of 200 ng/mL and a blood threshold limit of 100 ng/mL.**

Lorazepam

Lorazepam is prescribed for the treatment of moderate-to-severe anxiety, insomnia and perioperative use. It is approximately five times more potent than diazepam [55]. In NZ, lorazepam is available in tablets containing 1 or 2.5 mg, and an injection of 2 or 4 mg. The standard dose is 0.5 to 2.5 mg as a single dose, with a maximum dose of 4 mg daily, although in some cases a daily dose up to 8 mg (as divided doses for perioperative use) is prescribed [55,56].

Studies have determined that doses of 1 to 2 mg lorazepam are sufficient to cause impairment [45].

The peak plasma concentration of lorazepam was in the range 22 to 36 ng/mL (mean 28 ng/mL) for six healthy male volunteers given a single oral 2 mg dose [59].

Lorazepam is one of the more common sedatives found in NZ driver samples. The blood concentrations found in 34 impaired drivers ranged from 10 to 230 ng/mL (mean 50 ng/mL, median 30 ng/mL).

Denmark has a *per se* limit of 21 ng/mL [3]. The UK *per se* limit is 100 ng/mL [1].

Proposed statutory limit

Based on the concentrations detected in NZ impaired drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions**, the Panel recommends a statutory blood lorazepam limit of 30 ng/mL and a blood threshold limit of 10 ng/mL.**

Midazolam

Midazolam is a sedative often used as preoperative medication for anaesthetic induction. In NZ, midazolam is available as tablets containing 7.5 mg, an injection containing 5, 15 or 50 mg, and a nasal spray containing 5 mg/mL [55]. The standard dose is 7.5 mg (oral) 1 hour prior to a procedure, with a maximum daily oral dose of 15 mg [55].

Following an oral dose of 10 mg in healthy young adults, peak plasma concentrations averaged 69 ng/mL for males and 53 ng/mL for females [44].

Patients should not drive for at least 12 hours following a 7.5 mg dose [60].

Midazolam is commonly detected in NZ driver samples when the driver has received emergency treatment following a car crash.

Blood concentrations of midazolam found in two impaired drivers were 30 and 150 ng/mL.

Norway has a *per se* limit for midazolam of 33 ng/mL [2].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood midazolam limit of 30 ng/mL and a blood threshold limit of 10 ng/mL.**

Nitrazepam

Nitrazepam is usually prescribed as a hypnotic for the treatment of insomnia. It is approximately two times more potent than diazepam and, in NZ, nitrazepam is available in tablets containing 5 mg. The standard dose is 2.5 to 10 mg, with a maximum daily dose of 10 mg [55].

Studies have determined that doses of 5 mg nitrazepam are sufficient to cause impairment [45].

Following administration of a single 5 mg dose to healthy adults, peak serum concentrations ranged from 25 to 50 ng/mL (mean 35 ng/mL) [44].

Nitrazepam is not often found in NZ driver samples. The blood concentration found in one impaired driver was 40 ng/mL.

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations of 17, 42 and 98 ng/mL [2]. Denmark has a *per se* limit of 21 ng/mL [3].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood nitrazepam limit of 50 ng/mL and a blood threshold limit of 20 ng/mL.**

Oxazepam

Oxazepam is prescribed for the treatment of anxiety, especially anxiety associated with mental depression and for the relief of acute alcohol withdrawal symptoms [55,56]. It is approximately 3 times less potent than diazepam. In NZ, oxazepam is available in tablets containing 10 or 15 mg. The standard dose is 10 to 30 mg three or four times daily, with no maximum specified [53].

Studies have determined that a dose of 15 mg oxazepam is sufficient to cause impairment [45].

The peak serum concentration found in eight volunteers given a single 45 mg oral dose ranged from 880 to 1440 ng/mL (mean 1,090 ng/mL) [61].

Oxazepam is frequently detected in NZ drivers but this is because it is a metabolite of diazepam. The presence of oxazepam due to use of diazepam itself can easily be determined by the presence of diazepam and its metabolites. The concentration of oxazepam in the blood following the use of diazepam is always much lower than diazepam. Oxazepam itself is not commonly found in NZ drivers' blood.

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations of 172, 430, 860 ng/mL [2]. Denmark has a *per se* limit of 110 ng/mL [3] and in the UK it is 300 ng/mL [1].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood oxazepam limit of 800 ng/mL and a blood threshold limit of 200 ng/mL.**

Temazepam

Temazepam is prescribed for the short-term management of insomnia and as a preoperative medication. It is approximately half the potency of diazepam. In NZ, temazepam is available in tablets containing 10 mg. The standard dose is 10 to 20 mg daily, with a maximum dose of 30 mg (as either a single or daily dose) [55].

Studies have shown that doses of 10 to 20 mg temazepam are sufficient to cause impairment [45].

A single 30 mg oral dose of temazepam given to 24 subjects produced a mean peak plasma concentration of 870 ng/mL [62].

Temazepam is frequently detected in NZ drivers but this is because it is a metabolite of diazepam. The presence of temazepam due to the use of diazepam can easily be determined by the presence of diazepam and its metabolites. The concentration of temazepam in blood following administration of diazepam is always much lower than diazepam.

The use of temazepam itself is not common in NZ; therefore, its detection is not common in the blood of NZ drivers (see Table 3).

The blood concentrations found in three impaired drivers were 80, 90 and 350 ng/mL.

The UK has a *per se* limit of 1,000 ng/mL [1].

Proposed statutory limit

Based on our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood temazepam limit of 800 ng/mL and a blood threshold limit of 200 ng/mL**.

Triazolam

Triazolam is used for the treatment of severe or disabling insomnia. It is approximately 20 times more potent than diazepam. In NZ, triazolam is available in tablets containing 0.125 or 0.25 mg. The standard dose is 0.125 or 0.25 mg at bedtime, with a maximum of 0.25 mg as a single or daily dose [55,56].

Studies have determined that doses less than 0.5 mg triazolam are sufficient to cause impairment [45].

Oral administration of a single 0.25 mg dose of triazolam to 6 healthy adults resulted in peak plasma concentrations ranging from 2.3 to 3.7 ng/mL (mean 3.0 ng/mL) [63].

The blood concentrations found in nine impaired drivers ranged from 4 to 14 ng/mL (mean 7 ng/mL, median 4 ng/mL).

Other countries have not set *per se* limits for triazolam.

Proposed statutory limit

Based on the concentrations detected in NZ impaired drivers and our interpretation of the scientific literature, **the Panel recommends a statutory blood triazolam limit and a blood threshold limit of 4 ng/mL.**

Zopiclone

Zopiclone is a hypnotic and sedative used to treat transient, short-term and chronic insomnia. In NZ, zopiclone is available in tablets containing 3.75 or 7.5 mg. The standard dose is 7.5 mg at bedtime [55]. Although this is not recommended for long-term use, this is NZ's most continuously prescribed sleeping tablet. While the recommended maximum dose is 7.5 mg [55,56], anecdotally some patients are prescribed 15 mg per night long-term.

Studies have shown that a dose of 7.5 mg zopiclone is sufficient to cause impairment [45].

In a study of 12 subjects who received 15 mg of zopiclone (i.e. twice the recommended therapeutic dose), a mean peak plasma concentration of 130 ng/mL was found [64].

A study investigating concentrations of zopiclone detected in impaired drivers reported a mean blood concentration of 100 ng/mL (maximum 410 ng/mL) [65].

Zopiclone is one of the more common sedatives found in NZ driver samples (see Table 3). The blood concentrations found in 52 impaired drivers ranged from 10 to 600 ng/mL (mean 100 ng/mL, median 54 ng/mL).

The use of zopiclone is not detected by current roadside oral fluid tests.

Norway has three *per se* limits representing increasing penalties with increasing blood concentrations of 12, 23 and 58 ng/mL [2]. Denmark has a *per se* limit of 11 ng/mL [3].

Proposed statutory limit

Based on the concentrations detected in NZ impaired drivers, our interpretation of the scientific literature and consideration of statutory limits in overseas jurisdictions, **the Panel recommends a statutory blood zopiclone limit of 50 ng/mL and a blood threshold limit of 20 ng/mL.**

Opioids

Opioid drugs can be broadly classified as natural opiates (morphine and codeine), semi-synthetic opioids (heroin, oxycodone and dihydrocodeine) or as synthetic opioids (methadone, buprenorphine, tramadol and fentanyl). Although opioid drugs are used globally for analgesia, many have a significant potential for misuse. Methadone is commonly used to treat opioid addiction.

All medicinal and illicit opioids are CNS depressants and universally cause drowsiness and lethargy.

All medicinal and illicit opioids are characterised by the onset of tolerance with regular dosing and a well-defined withdrawal syndrome upon cessation of dosing. The development of tolerance results in the need for administration of larger doses to achieve the required result. The degree of tolerance that an individual achieves following daily dosing with opioid drugs is quickly lost if dosing is interrupted.

There is mounting epidemiological evidence linking the therapeutic use of opioids to increased crash risk, but there is inconsistency in the literature [51, 66-70].

Most available oral fluid testing devices have an opiate channel. This channel detects 6-monoacetylmorphine (6MAM; Fig. 3) a major metabolite of heroin, it also detects codeine, morphine and dihydrocodeine, but cannot distinguish between these drugs. None of the other opioids (buprenorphine, fentanyl, oxycodone or tramadol) are detected by current oral fluid testing devices. Some oral fluid testing device manufacturers include a separate methadone testing channel.

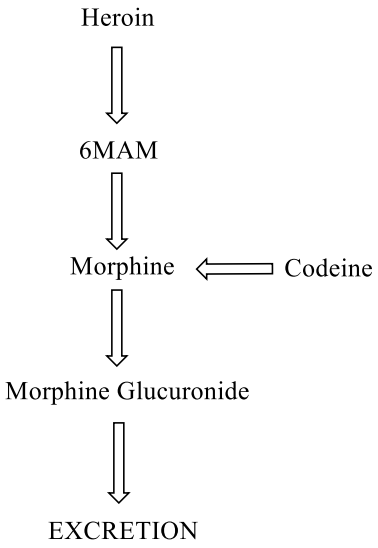

Figure 3 *Simplified metabolic pathways of some of the opiates showing their interrelationships and major route to excretion.*

Opioid use by NZ drivers

Detection of opioids in the blood of deceased drivers has increased in NZ. For the period 2004 to 2009 opioids were detected in 4% of deceased drivers, this increased to 9% for 2013 to 2018.

Opioid use in impaired and hospitalised drivers for the years 2017 to mid-2020 is shown in Table 5. The prevalence of morphine and fentanyl in hospitalised drivers is not given because these drugs are frequently administered for pain relief by medical personnel either *en route* to the hospital or at some stage during admission.

Table 5 *Detected opioids in impaired and hospitalised drivers in NZ.*

Drug	Number of impaired drivers	Number of hospitalised drivers
Buprenorphine	1	0
Codeine	19	66
Dihydrocodeine	7	13
Fentanyl	2	x
Methadone	69	50
Morphine	23	x
Oxycodone	7	6
Tramadol	40	164

x Data not included because these drugs are used for pain relief following traffic crash injury.

It should be noted that when opioids were detected in impaired drivers, it was common to find evidence of other drug use as well. Combinations including cannabis, methamphetamine and/or sedatives were detected in the blood of most of these drivers.

The recommended criminal limit and blood threshold limit for each of these drugs is based on the consideration of concentrations expected in the blood following ingestion of the recommended doses, knowledge of the pharmacodynamic properties of the drug, doses that are known to cause driving impairment, the concentrations detected in NZ impaired drivers and limits set in overseas jurisdictions. Recommending limits for these drugs is complex due to the wide range of doses that may be prescribed and the variety of methods of administration.

In addition, it is advised that a criminal penalty should be considered for these drugs when detected at the blood threshold concentration in the presence of alcohol or in combination with other impairing drugs.

Norway, Denmark and the UK have specified *per se* limits for some of the opioid drugs [1-3]. The difference in *per se* limits for these drugs across these three countries is significant. Norway has a three tier system with increasing blood concentrations resulting in increased penalty, but this has only been applied to morphine.

The criminal and blood threshold limits proposed in this report together with the *per se* limits used by Norway, Denmark and the UK are shown in Table 6.

Table 6 Statutory limits for opioids in the UK, Norway and Denmark compared with limits proposed in this report.

Drug	Limits Proposed in This Report ng/mL		Limits in Other Jurisdictions ng/mL		
	Criminal limit	Blood Threshold limit	UK	Norway	Denmark
Buprenorphine	1	1	x	0.9	0.53
Codeine	200	50	x	9	x
Dihydrocodeine	200	50	x	x	x
Fentanyl	0.5	0.5	x	0.34	x
Methadone	200	50	500	25	53
Morphine	20	10	80	61	10
Oxycodone	50	20	x	16	x
Tramadol	250	100	x	53	x

x No limit set

Heroin

Heroin is a powerful euphoriant and regardless of the route of administration (intravenous or intranasal (snorting)) - it decreases alertness and motor activity [51]. It is approximately five times more potent than morphine. Heroin itself is not detected in blood samples due to its extremely rapid metabolism to 6MAM, which is then further metabolised to morphine. 6MAM can be used to provide evidence that heroin has been used but due to its short half-life (6 to 25 minutes), it may not be detected in blood even as little as 2 hours after heroin use.

In NZ, 6MAM has been detected in one impaired and one hospitalised driver since 2017.

The Panel does not recommend a *per se* limit for 6MAM as the use of heroin will be covered by the *per se* limit for morphine.

Buprenorphine

In recent years, buprenorphine has become an increasingly popular choice in clinical practice as an alternative to methadone for the treatment of opioid dependence. It is less commonly used in the treatment of moderate to severe pain. In NZ, it is dispensed in combination with naloxone as sublingual tablets that contain 2 mg buprenorphine and 0.5 mg naloxone, or 8 mg buprenorphine and 2 mg naloxone for opioid dependence. For the treatment of pain, it is used as transdermal patches, delivering 5, 10, or 20 micrograms (µg)/hour, or as a 300 µg/mL injection [55,56].

The standard opioid substitution maintenance dose is 4 to 24 mg buprenorphine daily as a single sublingual dose, with a maximum dose of 32 mg daily. For treatment in moderate to severe pain doses of 300 to 600 µg may be administered by intramuscular injection or slow intravenous injection every 6 to 8 hours. Alternatively transdermal patches delivering 5 µg/hour increasing up to a maximum of 40 µg/hour may be used [55,56].

A single 4 mg sublingual dose of buprenorphine resulted in a mean peak plasma concentration of 3.3 ng/mL [44].

Sublingual or intravenous administration of 0.4 mg or less of buprenorphine has been found to impair driving skills [45].

Buprenorphine is not detected by currently available roadside oral fluid testing devices.

Buprenorphine is not often found in NZ driver samples possibly due to the low concentrations of the drug in blood and its rapid elimination half-life. The blood concentration found in one impaired driver was 3 ng/mL.

Norway has a *per se* limit of 0.9 ng/mL [2] and Denmark has a *per se* limit of 0.53 ng/mL [3]. These concentrations are below the detection limit of the current ESR technology.

Proposed statutory limit

Based on our interpretation of the scientific literature, with consideration of statutory limits in overseas jurisdictions, and acknowledging the current technological limitations, **the Panel recommends a statutory blood buprenorphine limit and a blood threshold limit of 1 ng/mL.**

Codeine

Codeine is indicated for treatment of mild to moderate pain (and occasionally for diarrhoea or suppression of non-productive cough). It can cause sedation, drowsiness and depress breathing. It has approximately one-tenth the potency of morphine. In NZ codeine is available in tablets containing 15, 30 or 60 mg (it is also available as paracetamol 500 mg + codeine 8 mg combination). The standard dose is 15 to 60 mg up to four times a day, with a maximum daily dose of 240 mg [55].

Oral administration of 60 mg of codeine per 70 kg body weight resulted in peak plasma concentrations ranging from 66 to 413 ng/mL (mean 214 ng/mL) [71]. Similarly, administration of a 120 mg dose resulted in blood concentrations ranging from 184 to 1,158 ng/mL (mean 474 ng/mL) [71].

Since 2017, codeine has been detected in the blood of 19 impaired drivers at concentrations ranging from 10 to 330 ng/mL (mean 98 ng/mL, median 80 ng/mL). Very few of these drivers had used codeine alone. Sedatives, cannabis and/or methamphetamine were commonly detected in the blood of drivers using codeine. The blood codeine concentrations found in 66 hospitalised drivers ranged from 10 to 1,200 ng/mL (mean 100 ng/mL, median 50 ng/mL).

Norway has a *per se* limit of 9 ng/mL [2]. Denmark and the UK have not set *per se* limits for codeine.

Proposed statutory limit

Based on our interpretation of the scientific literature and the concentrations found in NZ impaired drivers, **the Panel recommends a statutory blood codeine limit of 200 ng/mL and a blood threshold limit of 50 ng/mL.**

Dihydrocodeine

Dihydrocodeine is chemically similar to codeine and has approximately one-tenth the potency of morphine. In NZ, dihydrocodeine is prescribed for the treatment of mild-moderate pain. It is available as modified release tablets containing 60 mg dihydrocodeine. The standard dose is 60 to 120 mg every 12 hours, with a maximum daily dose of 240 mg [53].

Following a single oral dose of 60 mg in 12 adult volunteers, peak plasma dihydrocodeine concentrations ranged from 90 to 110 ng/mL (mean 100 ng/mL). Twice daily oral doses of 60, 90 and 120 mg given to the same volunteers resulted in mean peak plasma concentrations of 150, 220 and 280 ng/mL respectively [72].

Since 2017, dihydrocodeine has been detected in the blood of 7 impaired drivers at concentrations ranging from 10 to 420 mg/mL (mean 160 ng/mL, median 130 ng/mL). Very few of these drivers had used dihydrocodeine alone. Sedatives, cannabis and/or methamphetamine were commonly detected in the blood of drivers using dihydrocodeine. The blood dihydrocodeine concentrations found in 13 hospitalised drivers ranged from 10 to 2000 ng/mL (mean 330 ng/mL, median 120 ng/mL).

Other countries have not set *per se* limits for dihydrocodeine. This could relate to low prescribing frequency for the drug in those countries.

Proposed statutory limit

Based on our interpretation of the scientific literature and the concentrations found in NZ impaired drivers, **the Panel recommends a statutory blood dihydrocodeine limit of 200 ng/mL and a blood threshold limit of 50 ng/mL**.

Fentanyl

Fentanyl is a powerful opioid estimated to be 80 times more potent than morphine. Fentanyl is generally used in medical settings as an anaesthetic agent or for postoperative pain [55,56]. In NZ, fentanyl is available as transdermal patches containing 0.0125, 0.025, 0.05 or 0.1 mg fentanyl and as injections containing 0.01, 0.020, 0.1, 0.5 or 1 mg. The standard dose range is 0.0125 to 0.025 mg per hour released transdermally or by injection, with a maximum dose of 0.3 mg per hour. Fentanyl is also used off-label as a nasal spray for palliative care [55].

Studies have determined that intravenous doses of 0.1 mg fentanyl are sufficient to cause impairment [45].

For a fentanyl transdermal patch (delivery 0.025 mg per hour), serum concentrations ranged from 0.3 to 1.2 ng/mL within 24 hours of patch application [44]. Buccal fentanyl tablets containing 0.4 mg fentanyl taken by healthy volunteers for six days produced a mean serum concentration of 1.8 ng/mL following the final dose [44].

Fentanyl is not be detected by current roadside oral fluid testing devices.

Fentanyl is not often found in NZ impaired driver samples. The blood concentrations found in two impaired drivers were 3 and 8 ng/mL. Fentanyl is frequently detected in hospitalised drivers, likely due to its administration by medical personnel.

Norway has a *per se* limit of 0.34 ng/mL [2], which is below the detection limit of the current ESR technology.

Proposed statutory limit

Based on our interpretation of the scientific literature, with consideration of statutory limits in overseas jurisdictions, and acknowledging the current technological limitations, **the Panel recommends a statutory blood fentanyl limit and a blood threshold limit of 0.5 ng/mL.**

Methadone

Methadone is a synthetic opioid used in the treatment of opioid dependence, but also as an analgesic and antitussive. Adverse effects include sedation, cognitive impairment and respiratory depression. Some tolerance to sedation and respiratory depression develops in chronic use [44]. In NZ, methadone is available as tablets containing 5 mg, injection solutions of 10 mg/mL and oral liquids at 2, 5 or 10 mg/mL. The normal oral dose is up to 20 mg daily for naïve patients, with a maintenance dose of 60 to 120 mg daily [55]. Higher doses are used in methadone tolerant patients.

Studies have determined that 10 mg doses of methadone are sufficient to cause impairment in naïve users of the drug, but tolerance (and thus reduced impairment at a particular dose) develops with long-term use [45].

A single 10 mg dose to healthy adults resulted in a mean peak blood concentration of 33 ng/mL [44]. Daily administration of 100 to 120 mg of methadone to tolerant subjects resulted in peak blood concentrations ranging from 440 to 820 ng/mL [73].

Since 2017, methadone has been detected in the blood of 69 impaired drivers at concentrations ranging from 10 to 1200 mg/mL (mean 260 ng/mL, median 200 ng/mL). Very few of these drivers had used methadone alone. Sedatives, cannabis and/or methamphetamine were commonly detected in the blood of drivers using methadone. The blood methadone concentrations found in 50 hospitalised drivers ranged from 10 to 800 ng/mL (mean 280 ng/mL, median 280 ng/mL).

Norway has a *per se* limit of 25 ng/mL [2] and Denmark has a *per se* limit of 53 ng/mL [3]. The UK's *per se* limit for methadone is 500 ng/mL [1].

Proposed statutory limit

Based on our interpretation of the scientific literature, with consideration of statutory limits in overseas jurisdictions, and the concentrations found in NZ impaired drivers, **the Panel recommends a statutory blood methadone limit of 200 ng/mL and a blood threshold limit of 50 ng/mL.**

Morphine

Morphine is used for the relief of severe and chronic pain. Chronic intake of morphine may lead to physical and psychological dependence.

In NZ, morphine is available as immediate release tablets containing 10 or 20 mg, as modified release tablets and capsules containing 10, 30, 60 or 100 mg, as oral liquid at 1, 2, 5 or 10 mg/mL and as injections at 1, 2, 5, 10, 15, 20, 30, 50, 60 or 100 mg. The standard doses are: 5 to 20 mg every 4 to 6 hours (immediate release); 10 to 20 mg twice daily (modified release); 1 to 5 mg every 4 hours (oral liquid); 5 to 10 mg injected at 1 to 2 mg/minute (intravenous) [55]. Maximum doses are difficult to define due to the development of tolerance and extenuating circumstances [55].

Studies have determined that 10 mg doses of morphine are sufficient to cause impairment in naïve users of the drug but tolerance develops with long-term use [45].

Morphine blood concentrations are difficult to interpret because concentrations achieved after morphine administration depend on the route of administration (i.e. intravenous or oral) and the formulation of the medication (i.e. immediate or controlled release) [44].

A single oral dose of 30 mg of morphine in an immediate release tablet gave rise to a mean peak plasma concentration of 24 ng/mL after 0.8 hours [74]. A single oral dose of 60 mg morphine in a controlled release capsule gave a mean peak plasma concentration of approximately 10 ng/mL at 7.9 hours [74].

Since 2017, morphine has been detected in the blood of 23 impaired drivers at concentrations ranging from 10 to 110 ng/mL (mean 40 ng/mL, median 30 ng/mL). Very few of these drivers had used morphine alone. Sedatives, cannabis and/or methamphetamine were commonly detected in the blood of drivers using morphine. Morphine is frequently detected in hospitalised drivers, likely due to administration by medical personnel, before or during the drivers' hospital admission.

Norway has a three tiered *per se* limit range for morphine of 9, 24 and 61 ng/mL [2]. Denmark has a *per se* limit of 10 ng/mL [3], and the UK's *per se* limit for morphine is 80 ng/mL [1].

Proposed statutory limit

Based on our interpretation of the scientific literature, consideration of statutory limits in overseas jurisdictions, and the concentrations found in NZ impaired drivers, **the Panel recommends a statutory blood morphine limit of 20 ng/mL and a blood threshold limit of 10 ng/mL.**

Oxycodone

Oxycodone is a narcotic analgesic approximately equipotent to morphine [44]. In NZ, oxycodone is available as immediate release capsules containing 5, 10 or 20 mg, as modified release tablets 5, 10, 15, 20, 30, 40, 60, or 80 mg, as oral liquid at 5 mg/5 mL and as an injection at 10, 20, 50 or 200 mg. The standard dose is 5 to 20 mg every 4 to 6 hours (immediate release); 10 to 40 mg every 12 hours with a maximum of 200 mg every 12 hours (modified release); 2.5 to 20 mg every 4 to 6 hours (oral liquid) and initially 5 mg every 4 hours (injection). The maximum daily dose is 400 mg. A 2 mg oral oxycodone dose is approximately equivalent to 1 mg parenteral oxycodone [55].

Studies have determined that a 20 mg dose of oxycodone is sufficient to cause impairment [45].

Peak plasma concentrations in 12 adult surgery patients receiving 10 mg immediate release oral dose ranged from 13 to 46 ng/mL (mean 30 ng/mL), whereas subjects receiving 40 or 80 mg modified release tablets attained mean peak plasma concentrations of 30 and 99 ng/mL respectively [44].

Oxycodone is not detected by current roadside oral fluid testing devices.

Oxycodone is not often found in NZ driver samples. The blood concentrations found in seven impaired drivers ranged from 10 to 140 ng/mL (mean 80 ng/mL, median 50 ng/mL). Blood oxycodone concentrations detected in six hospitalised drivers ranged from 10 to 300 ng/mL (mean 90 ng/mL, median 50 ng/mL).

Norway has a *per se* limit of 16 ng/mL [2]. Neither Denmark nor the UK have *per se* limits for oxycodone.

Proposed statutory limit

Based on our interpretation of the scientific literature, consideration of statutory limits in overseas jurisdictions, and concentrations detected in NZ impaired drivers, **the Panel recommends a statutory blood oxycodone limit of 50 ng/mL and a blood threshold limit of 20 ng/mL.**

Tramadol

Tramadol is a narcotic analgesic that is approximately one-tenth the potency of morphine. In NZ, tramadol is available as immediate release capsules containing 50 mg, as modified release tablets containing 50, 100, 150 or 200 mg, as oral liquid containing 10 or 100 mg and as an injection of 50 or 100 mg. The standard doses are:

- 50 to 100 mg every 4 to 6 hours (immediate release capsules),
- 50 to 200 mg every 12 hours (modified release),
- 12.5 mg equivalent to 5 drops or 1 press of a delivery pump up to 100 mg every 4 to 6 hours (oral drops or pump spray),

with a maximum daily dose of 400 mg (reduced to 300 mg in patients 75 years of age and over) [55].

A single 50 mg normal release oral dose given to 24 healthy adults resulted in a mean peak plasma concentration of 107 ng/mL [44], and a single 100 mg normal release oral dose given to 10 healthy adults resulted in a mean peak plasma concentration of 280 ng/mL [44].

Tramadol is not detected by currently available roadside oral fluid testing devices.

Since 2017, tramadol has been detected in the blood of 40 impaired drivers at concentrations ranging from 10 to 1000 ng/mL (mean 280 ng/mL, median 220 ng/ml). Very few of these drivers had used tramadol alone - sedatives, cannabis and/or methamphetamine were commonly detected in the blood of drivers using tramadol. The blood tramadol concentrations found in 164 hospitalised drivers ranged from 10 to 3,000 ng/mL (mean 210 ng/mL, median 130 ng/mL).

Norway has a *per se* limit of 53 ng/mL for tramadol [2]. Neither Denmark nor the UK has *per se* limits for tramadol.

Proposed statutory limit

Based on our interpretation of the scientific literature, consideration of statutory limits in overseas jurisdictions, and the concentrations found in NZ impaired drivers, **the Panel recommends a statutory blood tramadol limit of 250 ng/mL and a blood threshold limit of 100 ng/mL.**

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Expert Panel on Drug Driving

Dr Helen Poulsen (Chair)
Dr Sharon Kletchko
Andrew McGlashen
Professor Ian Shaw
Associate Professor Malcolm Tingle

26th November 2020