Expert Panel on Drug Driving – approved minutes of 9th October 2012 meeting, 11:30 – 16:00

Venue: Department for Transport

Attendees:

Dr. Kim Wolff, Chair (King's College London)
Professor Robert Forrest (Sheffield University)
Professor Atholl Johnston (Barts & London School of Medicine, Queen Mary University)
Professor David Osselton (Bournemouth University)
Professor David Taylor (South London and Maudsley NHS Foundation Trust)
Honorary Professor Eilish Gilvarry (Newcastle University)
Dr. Lily Read (Northampton Healthcare NHS Trust)
Dr. Judith Morgan (DVLA)
Dr. Roger Brimblecombe (ACMD representative)

Xxxxxx Xxxxxxx (Centre of Applied Science & Technology)
Xxxxx Xxxxxx (DfT)
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Xxxxxxx Xxxxxxxxx (DfT)

Mark Prunty (DoH) - Observer

Apologies:

Dr. J. Colin Forfar (CHM representative)

1. Minutes from the previous meetings and matters arising

Agreed: The draft minutes of the meeting of 18th September, subject to some factual amendments and inclusion of a reference.

2. Epidemiological Evidence

The panel considered the drug drive screening samples data that Xxxxxx Xxxxxxx presented at the last Panel meeting for evidence of Z drugs, benzodiazepines and morphine concentrations.

Of 1161 blood samples screened positive for at least one substance, only 1 sample contained traces of Z drugs. 597 samples tested positive for benzodiazepines in the screening test, confirmatory analysis for benzodiazepines was carried out for only one of these. (For the other benzodiazepine positive samples the confirmatory analysis would have targeted one of the other drugs found in the screening test.) .

For those samples where confirmatory analysis was carried out for morphine:

- 65 had a concentration of up to 0.1 micrograms per litre,
- 19 had a concentration of between 0.1 and 0.2 micrograms per litre,
- 14 had a concentration of between 0.2 and 0.3 micrograms per litre.

The forensic laboratory confirmed these samples were for free morphine.

Action: Xxxxxx Xxxxxxx agreed to check how many samples contain BZE only, without cocaine.

Action: Seek information from the ACMD about the existence of BZE in the Misuse of Drugs Act

Xxxxxxxx Xxxxx Xxxxxxxx presented some further data from whole blood samples analysed by former Home Office organisation The Forensic Science Service (FSS) over a three year period (from 2004-2007), for drivers suspected of driving whilst impaired following drug use. He had plotted the blood concentrations found for each of the drugs against the percentage of samples found with concentrations below each value. Data for unconjugated morphine was included.

Morphine

The panel returned to the discussion about morphine from the last meeting, when a potential limit of 40 ug/ L for morphine had been considered.

It was noted that the ORs in the literature were lower for opiates when compared to morphine itself

Opiates	OR: 2.35 (95% CI: 0.87-6.32)	4
	OR: 1.41 (95% CI: 0.7-2.9	5
-morphine	OR: 32	6
-morphine □ 20 micrograms/l	OR: 8.2 (95% CI: 2.5-27.3)	7

[4] Movig KL, Mathijssen MP, Nagel PH, van ET, de Gier JJ, Leufkens HG, et at. Psychoactive substance use and the risk of motor vehicle accidents.Accid Anal Prev 2004 Jul;36(4):631-6.
[5] Drummer OH, Gerostamoulos J, Batziris H, Chu M, Caplehorn J, Robertson MD, et at. The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes. Accid Anal Prev 2004 Mar;36(2):239-48.
[6]Assum T, Mathijssen MP, Houwing S, Buttress SC, Sexton RJ, Tunbridge RJ, et al. The prevalence of drug driving and relative risk estimations. A study conducted in The Netherlands, Norway and the United Kingdom. 2005 Jun 22. Report No.: D-R4.2.
[7] Mura P, Kintz P, Ludes B, Gaulier JM, Marquet P, Martin-Dupont S, et al. Comparison of the prevalence of alcohol, cannabis and other drugs between 900 injured rivers and 900 control subjects: results of a French collaborative study. Forensic SciInt 2003 Apr 23;133(1-2):79-85.

The DRUID report found that opiates and medicinal opioids were mainly detected among drivers of 35 years and older. The logistic regression results indicate a general higher prevalence among female drivers as well*. "Based on case-control studies, the relative risk of serious injury or fatality for ….*

medicinal opioids is estimated to be about 2-10 times (with medicinal opioids in the upper part of the interval)."

The Panel discussed a threshold of 40 ug/L, which would be equivalent to a blood alcohol concentration of 80 mg/ 100 ml. The limit of 40 ug/L was noted to be at the higher end of the therapeutic range for morphine according to the data produced by the Netherlands Forensic Institute[1] below:

Active concentrations of the most common drugs found in plasma (or serum) and blood which are known to be a hazard when driving

Substance	**Expected concentration in plasma after taking an active dose[a] (micrograms/L)**	**Blood/serum ratio [b]**	**Estimated concentration in blood after taking an active dose[c] (micrograms/L)**	**Median in blood NFI 1999-2008 (micrograms/L)**
Morphine	10-120	1.0	10-120	40
Codeine	50-250	0.87	40-250	20

It was noted that OR information regarding Road Traffic Accidents had led some European countries to set a limit of 20 ug/ L. The 20ug/L limit could be justified by using odds ratio information, discussed in previous meetings

The Panel agreed that both health care providers and patients should be properly informed and aware of the potential risks associated with the use of psychoactive medicines.

It was noted that the limit of 40ug/L would be specifically responding to the panel's Terms of Reference of identifying a drug concentration with an impairment effect broadly equivalent to a blood alcohol concentration of 80 mg alcohol per 100 ml blood. The panel discussed the option of including the merits of both a higher and a lower morphine threshold in its recommendations to the Government, as both could be justified from a scientific basis.

It was also agreed that a lower threshold should be recommended for morphine when it was detected in combination with alcohol. It was agreed that in the absence of specific evidence about risk associated with the combination of morphine and alcohol this should be set at half the threshold for morphine on its own. The panel agreed that a threshold for morphine at 20ug/L could be recommended where alcohol was detected in the body above 20mg/100ml blood. (This is the lowest level of alcohol where there is scientific evidence of an effect on driving performance, and it is used in civil aviation as well as work place drug testing. It is also the limit specified for aviation in the Railway and Transport Act 2003.)

[1] [1] Netherlands Advisory Committee, Recommendation with respect to limits for drugs in the context of the proposed amendment to the Road Traffic Act 1994 (March 2010)

The Panel discussed the need for medical information that warned individuals prescribed morphine about the risks of consuming the drug and driving particularly if alcohol had also been consumed concurrently.

Action: Xxxxx Xxxxxx agreed to send the panel a list of what warnings about driving and/ or the use of alcohol were included for the drugs the panel were considering from the British National Formulary.

It was agreed that the panel's methodology needed to be explained fully in the report: There needed to be an explanation of the limitations in data and what this meant for the methodology of recommending thresholds.

It was noted that the panel had adopted a hierarchy of methods based on risk estimates calculated as Odds Ratios to inform the recommended thresholds, where this data was available. In the absence of this evidence of concentrations of drugs in blood in drivers known to be under the influence of psychoactive drugs and involved in serious injury or fatal accidents were investigated.

3. Scientific literature and evidence for specific drugs:

a) Cocaine/ benzoylecgonine

The panel considered additional information from Clockwork Research on the detection windows and road traffic risks associated with cocaine and benzoylecgonine. The panel discussed whether to recommend a threshold for cocaine or whether in addition, there should be a threshold for benzoylecgonine (BZE), as cocaine had a very short half-life.

The Panel noted that BZE was not listed by name in the Misuse of Drugs Act 1971, but a proposed amendment to the Drug Driving provisions in the Crime and Courts Bill is planned to allow for a limit to be set for the metabolite of a controlled drug where it can be uniquely linked back to that drug.

A suggestion was made to table an amendment which would allow the inclusion of a metabolite which can be linked back to a controlled drug *'the presence of which can be proven'* to allow a limit to be set in BZE only when cocaine was also present.

The Panel agreed that a threshold for BZE would need to be set high so that the concentration in blood was indicative of road safety risk because of the earlier consumption of cocaine. The reasoning and rationale behind such a limit in BZE which is not itself psychoactive would have to be fully explained in the panel's report.

The Panel considered the risk estimate Odds Ratios for cocaine and BZE, which are listed separately in the DRUID report (Main Druid Results, Deliverable 7.3.2), though the panel noted the limitations in data, highlighted in the footnote to the table:

Table 21: Overview of OR (illicit drugs alone)

	BZE*	Cocaine*
crude OR/ serious injury	5.36	3.41**
adjusted OR/ serious injury	3.70	3.30
crude OR / killed	6.87	22.34
adjusted OR / killed	n/a	n/a

* In the case of 0 counts in one of the groups: Positive cases, negative cases, positive controls and negative controls, 0.5 was added to all four cells in the data from each such country when calculating crude OR (Greenland et al., 2000);
** Cocaine or cocaine + benzoylecgonine;

The panel agreed that their original view on a threshold of 80 ug/L cocaine in blood should stand and be recommended for cocaine.

After considering the 2004-2007 DUID data from the FSS on blood drug concentration it was felt that a high threshold of 500 ug/L for BZE in blood would capture recent cocaine use. A threshold of 40 ug/L should be recommended for cocaine when combined with alcohol above a limit of >20mg/100ml. The panel would not recommend a limit for BZE in combination with alcohol.

The panel also agreed that unless scientific evidence was available to the contrary, that the recommended limit for other illicit drugs (including opiates) should be halved to arrive at a limit for the drug where blood alcohol was above 20mg alcohol per 100ml blood.

The panel agreed that its report should emphasise the need to take evidential blood samples ideally within two hours of the screening test and analyse them quickly. This is particularly important with regards to detecting cocaine and other drugs with short half-lives.

b) Methadone and buprenorphine

Xxxx Xxxx presented a paper on methadone and buprenorphine. It was noted that there is some evidence to indicate that those on a stable dose of methadone without any other drug or alcohol use are not likely to pose a significant road safety risk provided dosing has been stable for over 3 months. However, if methadone or buprenorphine are used in combination with alcohol or other drugs there is significant risk.

The panel noted that all methadone and buprenorphine preparations contain a warning not to use alcohol but was unclear whether these were taken on board by those prescribed the drug.

It was noted that drivers on a methadone/buprenorphine programme for the treatment of heroin dependence are required to notify their status to the DVLA and undertake an annual medical review to keep their driving licence. However, of around 160,000 adult methadone and buprenorphine users in treatment contact with substance misuse services in the UK (April 2011 - March 2012, NDTMS statistics, 2012), the DVLA has been notified of only around 3,000.

The Panel considered that if all those prescribed methadone/buprenorphine were properly registered with the DVLA there may be no need to set a threshold for methadone and buprenorphine, as the DVLA has the power to withdraw a licence but were concerned that the number of patients prescribed methadone registered with the DVLA was so low.

The Panel noted that the DRUID report states that even at low dosages methadone and buprenorphine caused impairment when given as a single dose to healthy subjects. No clear evidence exists if patients under maintenance treatment are able to drive safely. DRUID recommended that many maintenance patients use other substances in addition, so it is recommended that a screening for other substances is done if a maintenance patient should be allowed to drive.

The panel agreed that thresholds should be considered for methadone and buprenorphine in combination with alcohol.

The panel looked at the thresholds at which methadone and buprenorphine are considered to impair driving and attract legal sanctions set in legislation in Norway. The Norwegians have set a limit of 25ug/ L which was considered to be very low by the panel and thought to equate to daily doses of 30 mg methadone/day or less.

The panel would consider whether a concentration of 25 ug/L for methadone in blood would be appropriate for the British context and sensible as a threshold in combination with alcohol where blood alcohol above 20mg/ml was present at its next meeting.

Action: Xxxx Xxxxx would provide information about buprenorphine concentrations in Britain, and the same rationale as above would be used to set a limit for buprenorphine in combination with alcohol.

Xxxxxx Xxxxxxx would report back from the DVLA panel on whether it needed to strengthen its guidelines in relation to methadone/ buprenorphine prescribing.

c) Z Drugs

Xxxxxxx Xxxxxx Xxxxxxxx presented a paper on Z drugs to supplement the previous papers tabled about this group of drugs.

The panel noted that Zolpidem is the only Z drug listed in the Misuse of Drugs Act 1971, and therefore the only one within the scope of the terms of reference.

There is some evidence of an increased risk of an RTA through the use of Z drugs. Barbone (1998) reported on a case-crossover study conducted in the United Kingdom in 1992–1995, which reported an OR (95% CI) of 1.62 (1.24–2.12) for all benzodiazepines.

This same study found a strong association between the use of Zopiclone and the risk of traffic accidents (OR = 4.00, 95% confidence interval (CI) (1.31–12.2). Two reviews that addressed the residual effects of hypnotics recommended that users of Zopiclone should be advised not to drive, whereas the use of Zolpidem was considered safer (Vermeeren 2004, Verster 2004). Elvik (2012) noted an odds ratio (OR) for injury for Zopiclone of 1.42, but a French study (Orriols 2011) showed no link between Zopiclone and accident risk. Zaleplon, the least prescribed of the Z drugs, also appears to have few residual risks (though there are few studies).

Although these drugs are beginning to be more prevalent in the context of abuse there is insufficient evidence to recommend limits for them.

Action: Seek information from the ACMD about the presence of Zolpidem and not Zopiclone on the Misuse of Drugs Act

d) Amphetamines

Xxxxxxxx Xxxxxx Xxxxxxxx discussed the literature available on amphetamines. It was noted that only 44 articles were available following a search of pub med, and they pointed to an increased risk of a road traffic accidents (RTA) when on the drug and coming off it.

The odds ratios (summarised by Clockwork research from available literature and discussed at the last panel meeting) relating to an RTA when driving and ORs for amphetamines were considered from the DRUID main results report (Deliverable 7.3.2, 2011), and also from 2 papers by Alan Wayne Jones[2] and are as follows:

Substance	*OR*	*95% CIs*	*Basis of the OR*	*Refs*
Amphetamine	4.46 (p<0.05)	2.21 - 9.00	Meta analysis of 8 studies analysing presence of amphetamines in drivers fatally injured in road crashes	9
Amphetamine	8.88 (p<0.001)	4.54 - 17.39	Case control study (Thailand) comparing urine samples from 200 cases after road accidents with 849 controls.	16
Amphetamine	8.35	3.91 - 17.83	Analysis of blood samples collected from individuals seriously injured in road accidents in 6 European countries between 2007-2009.	4
Amphetamine	24.09	9.72 - 59.71	Analysis of blood samples collected from individuals killed in RTAs in 4	4

[2] JONES, A. W. 2007. Age- and gender-related differences in blood amphetamine concentrations in apprehended drivers: lack of association with clinical evidence of impairment. Addiction, 102, 1085-1091.
JONES, A. W., HOLMGREN, A. & KUGELBERG, F. C. 2008. Driving under the influence of central stimulant amines: age and gender differences in concentrations of amphetamine, methamphetamine, and ecstasy in blood. J Stud Alcohol Drugs, 69, 202-8.

			European countries between 2007-2009.	
Amphetamine	2.1	0.66 - 6.73	Case-control study Netherlands comparing 110 drivers hospitalised after a road accident with 816 drivers randomly selected from moving traffic.	13
All stimulants including cocaine	2.27	0.9 - 5.6	Case-control study of 3398 fatally-injured drivers in Australia to assess the effect of alcohol and drug use on the likelihood of them being culpable.	8

It was noted that the ORs for risk of a RTA were higher following amphetamine than for cannabis or cocaine.

The panel also considered the limits for amphetamine-type drugs in the new law in Norway:

Drugs	**Impairment limits (ng/ml in whole blood)**	**Limits for graded sanctions comparable to blood alcohol 0.05 % (ng/ml in whole blood)**	**Limits for graded sanctions comparable to blood alcohol 0.12 % (ng/ml in whole blood)**
Amphetamine	41	*	*
MDMA	48	*	*
Methamphetamine	45	*	*

** Legal limits cannot be defined because the relationships between blood concentration and accident / driving skills are highly variable, or little documented. For example, pronounced effects may be seen at low concentrations sometime after a large intake of amphetamine / methamphetamine.*

It was noted that in 2010 the Norwegians did not set limits equivalent to blood alcohol levels because of a lack of consistent data. However, the Panel considered UK data.

The panel considered the blood concentration data from the FSS provided by Xxxxxxxx Xxxxxxxx and concluded from this data that a suitable threshold for amphetamine where an increased risk of a RTA was established was 600 ug/L.

Using the previously agreed criteria, the recommended threshold for amphetamine in blood when in combination with above 20mg alcohol per 100ml blood would be 300 ug/L.

The 2004-2007 FSS DUID data was scrutinised and it was found that the levels in blood were as follows:

The mean concentration observed in the 312 cases where amphetamine or amphetamine with MDMA were detected the mean concentration was 0.596 ug/mL (596 ug/L), with a range of 0.022 – 4.84 ug/mL (22 – 4840 ug/L).

For the 101 case were MDMA alone was detected, the mean concentration was 0.38 ug/mL [equivalent to 380 ug/L], with a range of 0.098 - 2.688 ug/mL [equivalent to 98 - 2,688 g/L].

The panel also considered the data from two reports by A.W. Jones.[3]

Based on the these sources the panel proposed a threshold for MDMA of 450ug/L in blood and when MDMA was consumed and detected in the presence of blood alcohol above 20mg per 100ml of blood a threshold for MDMA was agreed at 225ug/L.

4. Policy update

The panel was advised that Xxxx Xxxxx would be briefing Peers on what was likely to be in the Panel's interim report on 24th October at the Home Office and also attending a conference on Impaired Driving held by the Parliamentary Advisory Council for Transport Safety on 16th October.

Action: Xxxxxxx would provide a summary of the panel's progress for the next meeting.

5. AOB

The panel also took note of the points raised by Xxxxx Xxxxxx with regard to licensed medicines.

The panel discussed the issues regarding people driving while on medication which was specified in regulations, and the statutory defence. It was discussed that police will not be able to test drivers for drugs at random. The police will only be able to do so where a driver has committed a moving traffic offence, has been involved in a road traffic accident, or there is reason for a police officer to suspect that a person has been driving under the influence of drink or drugs.

The legislation will provide for a defence if a specified controlled drug is properly prescribed or supplied and taken in accordance with medical advice. This defence is not available if advice about not driving after taking the drug has not been followed.

[3] JONES, A. W. 2007. Age- and gender-related differences in blood amphetamine concentrations in apprehended drivers: lack of association with clinical evidence of impairment. Addiction, 102, 1085-1091.
JONES, A. W., HOLMGREN, A. & KUGELBERG, F. C. 2008. Driving under the influence of central stimulant amines: age and gender differences in concentrations of amphetamine, methamphetamine, and ecstasy in blood. J Stud Alcohol Drugs, 69, 202-8.

The prosecution for a case where the medical defence has been raised must prove beyond reasonable doubt that the defence is not valid. Both the police and Crown Prosecution Service will be aware of the defence in deciding how to deal with any cases before they reach the court.

The specificity and sensitivity of the assay equipment is not the responsibility of the Panel.

The advice given by a pharmacist and a GP is important in terms of medicines which impair driving and the Panel will make note of the importance of accurate communication from healthcare professional in its report.

The Panel acknowledges the significant risk associated with the use of prescribed medications and alcohol and is pleased that Xxx Xxxxxx concurs.

Most of the points raised had already been discussed or fell outside the panel's remit.

Action: Xxxx Xxxxx would draft a response.

Action: Xxxxxxx would provide a summary of the panel's progress for the next meeting.

It was agreed that codeine and ketamine would be discussed at the next panel meeting.