Driving under the influence of drugs: zero tolerance or impairment limits?

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Results of DRUID project
What is the aim of the DUI laws?

• To deter drugged driving
  – High risk of being detected
  – Certainty of sanctioning
  – Speed of sanctioning
  – Severity of sanctioning

• Can a change in attitude be obtained?
Different legal approaches

**Impairment approach:** driver is prosecuted if he/she shows clear symptoms of impairment (as per his/her personal behaviour or driving style)

**Per se limits:** driver is prosecuted if a drug is found in his/her body fluids (blood, in some countries oral fluid) above a defined cut-off concentration

**Two-tier system:** combining a lighter sanction when drugs are present above the *per se* limit and heavier sanctions when the driver was impaired (e.g. in Germany)
To consider when setting limits (cut-offs)

- The law: ‘under the influence’ or ‘after having used’?
- Time interval between stop and sample collection
- Other parts of the detection procedure:
  - Is suspicion needed?
  - Is screening performed at the roadside?
  - Totally random?
- Performance of the lab(s): LOQs? 1 lab or many?
- Possible drug levels due to “passive” exposure?
- Consequences? Administrative vs penal
What drugs are included?

– Australia: 3: Methamphetamine, MDMA, cannabis
– Belgium, Germany, France: amphetamines, cannabis, cocaine, heroin
– Netherlands: amphetamines, cannabis, cocaine, heroin, GHB
– UK: 16 drugs
– Denmark: 54 drugs
– Sweden: all narcotics
– Italy: all narcotics DPR 309/1990
If fewer drugs

Pros

• Easier to screen for (onsite tests available)
• Less expensive laboratory analysis
• Other drugs are covered by impairment-type law

Cons

• People may shift to use other drugs
• Not all cases will be detected
Including metabolites?

When the parent drug is unstable and is metabolised very rapidly

- Heroin: half-life of 6 minutes => (6-MAM) morphine
- Benzoylecgonine:
  - Cocaine is unstable in blood if not stabilised with fluoride
  - In DRUID: increased risk if only benzoylecgonine is found in blood
  - Some benzodiazepines are really unstable
Biological fluid, screening and confirmation

• Screening
  – Oral fluid in Belgium, France, Spain, Australia, ...

• Confirmation
  – Blood: in most countries
  – Plasma/serum: in some countries: Germany, Belgium
  – Saliva/oral fluid: Australia, Belgium, France
  – Dried blood spots in the future?
  – Exhaled breath in the future?
Types of cut-off

• **Lower limit of quantification (LLOQ) (Sweden)**
  OK If only one central lab

• **Lowest accidental exposure limit (UK):**
  *limit at the lowest level at which a valid and reliable analytical result can be obtained, yet high enough such as passive consumption or inhalation or cross contamination can be ruled out*

• **Lower effect limits:** lowest concentration with effect on driving

• **Risk thresholds:** indicate a certain accident risk or impaired driving
Correlation concentration – fatal crash risk

OR for various alcohol concentrations

OR for various THC concentrations

DRUID deliverable 2.3.2
Risks when not using zero tolerance

• “There cannot be a legal level of an illicit drug”

• Questions will be raised with respect to the dose that can be taken still remaining under the limit $\leftarrow$ deterrent effect use of cut-off $\leftarrow$ communication to the public

• One should realise that establishment of lower effect limits does not mean that one condones drug use
Norwegian approach

• System based on a zero tolerance policy against impaired driving, disregarding individual tolerance and drug-disease interactions

• Legislative concentration limits for impairment of non-alcohol drugs corresponding to a BAC of 0.2 g/L (“impairment limits”) and BACs of 0.5 and 1.2 g/L (“limits for graded sanctions”)

## Cut-offs in Norway

<table>
<thead>
<tr>
<th>DRUGS</th>
<th>Low limits ng/mL</th>
<th>Equiv 0.5 g/L BAC</th>
<th>Equiv 1.2 g/L BAC</th>
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<td>GHB</td>
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<td>Morphine</td>
<td>9</td>
<td>24</td>
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</table>
No graded sanctions for stimulants

• Correlation between drug concentration and risk of traffic accidents/impairment variable or insufficiently documented
  – In experimental studies, at the (rather low) doses that were given, driving performance increases rather than decreases
  – In epidemiological studies the accident risk is increased. Even at low concentrations, substantial impairment can be seen after ingestion of stimulant drugs
• Experimental and epidemiological results should be interpreted together for the determination of cut-offs
Norway: effect of the new legislation

- Number of blood samples taken in suspected DUID cases increased by 20% after introduction of legislative limits (3320 cases in 2010 and 3970 in 2013)
- Number of samples with at least one drug above the per se limit corresponding to BAC of 0.2 g/L increased by 17% (from 2646 to 3090)
- Number of expert witness statements was reduced by the half (from 63.4% to 28.7%)

UK approach

• In addition to 8 illegal drugs, 8 controlled drugs that have recognised and widespread medical uses.

• Proposed limits avoid catching drivers who have taken properly prescribed drugs in accordance with the directions of a healthcare professional, or with any accompanying instructions given by the manufacturer.

• In the majority of cases the limits recommended by the Expert Panel are above normal therapeutic ranges.

## Limits in the UK

<table>
<thead>
<tr>
<th>Drug</th>
<th>Threshold limit in blood (μg/L)</th>
<th>Drug</th>
<th>Threshold limit in blood (μg/L)</th>
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<td>6-acetylmorphine</td>
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Comparison of the cut-offs in blood, serum or plasma

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<th>Sweden</th>
<th>Switzerl</th>
<th>France</th>
<th>UK</th>
<th>NL</th>
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Combinations and sampling interval

How to deal with combined consumption?

- Combination of alcohol and drugs, or the combination of more than one drug, increases the accident-risk exponentially
- In case of combined use the cut-offs could be the limit of detection. Problem: consumption could be too far behind. Better: limit of detection + signs of impairment

How to deal with the interval between the accident and the blood sampling?

- For ethanol, back-calculation is used in many countries, but for drugs, because of the variable pharmacokinetics, back-calculation is very rare.
- One could set the limit lower in order to compensate for the delay, or allow for back calculation (standardised from experts in one jurisdiction).
CASE STUDY

• **Objective.**
  
  – To present the prevalence and concentrations of drugs in blood samples of drivers involved in road traffic accidents
  
  – To discuss the effects of adopting different concentration cut-off values on the number of DUID offences
MATERIALS AND METHODS

Blood Samples

Drivers involved in Road Traffic Accidents
Padova Province 2014-2017
MATERIALS AND METHODS

Alcohol was analysed by HS-GC-FID.

Screening and confirmation for substances were based on immunoassay, liquid chromatography high-resolution mass spectrometry (LC-HRMS) gas chromatography mass spectrometry (GC-MS).

The panel of substances included: opiates, cocaine, cannabinoids, amphetamines and amphetamine-like drugs, methadone, ketamine, benzodiazepines and barbiturates.
MATERIALS AND METHODS

Prevalence of subjects positive to each class and substance was reported adopting either the LOQs of our laboratory or the following concentration values, proposed and/or applied in some European countries.

- **GTFI** - *Minimum performance limits* proposed by the Italian Group of Forensic Toxicologists in 2017, to be adopted by laboratories delivering analysis for forensic purposes to report a positive case
- **DRUID** - *Analytical cut-off values*, adopted in the “European Union’s research project on Driving Under the Influence of Drugs, Alcohol and Medicines” aimed at analysing the prevalence of alcohol and other drug in drivers and in drivers seriously injured or killed in RTA
- **Denmark** - *Danish per se limits* that represent blood concentrations expected a short time after the intake of illicit drugs
- **Germany** - *German per se limits*, established by the ‘Grenzwertkommission’, which is a multi-disciplinary working group that informs Germany’s national government in the determination of limit value
- **England and Wales** - *Per se limits* applied in the “*England and Wales Drug Driving Regulations 2014*”, which came into force in March 2015
- **Wolff** - *Per se limits* proposed by Wolff et al., an expert panel on drug driving asked to make recommendations concerning blood concentration of drugs that should be set in the English regulations to improve road safety
- **Norway** - *Norwegian per se limits* corresponding to a BAC of 0.2, 0.5 and 1.2 g/L
# CUT-OFFS

<table>
<thead>
<tr>
<th></th>
<th>COCAINE</th>
<th>BZE</th>
<th>THC-COOH</th>
<th>THC</th>
<th>-MAM</th>
<th>MORPHINE</th>
<th>CODEINA</th>
<th>METHADONE</th>
<th>MDMA</th>
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RESULTS

4443 blood samples from drivers involved in RTA

- Alcohol: 22%
- Drugs: 18%
- Alcohol-Drugs: 6%
- No: 64%
RESULTS

<table>
<thead>
<tr>
<th>Drug Category</th>
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# CUT-OFFS APPLICATION

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DUI of COCAINE

- Padova LOQs
- GTFI
- DRUID

Cut-off ng/mL

- COCA
  - 1
  - 2
  - 10

-36% 9%
The image contains a bar chart titled "DUI of COCAINE." The chart compares the levels of COCAINE in different regions and countries, with a focus on Padova LOQs, GTFI, DRUID, Denmark, Germany, and England Wales. The y-axis represents the concentration levels of COCAINE, ranging from 0 to 200 ng/mL, and the x-axis lists the regions and countries.

Key points:
- Padova LOQs: 186 ng/mL
- GTFI: 92 ng/mL
- DRUID: 119 ng/mL
- Denmark: 20 ng/mL
- Germany: 10 ng/mL
- England Wales: 10 ng/mL

Additionally, there is a legend indicating cut-off levels in ng/mL for different regions:
- COCA: 1 ng/mL
- 2 ng/mL
- 10 ng/mL
- 20 ng/mL
- 10 ng/mL

The chart illustrates a significant difference in the levels of COCAINE across these regions, with Padova LOQs showing the highest value, followed by GTFI and DRUID. The percentages at the end of the bar chart indicate a comparison of these levels with a baseline, showing differences of -9%, -36%, -51%, -36%, and -36% respectively.

The chart effectively communicates the disparity in COCAINE levels across different regions, highlighting the need for targeted interventions and policy adjustments.
Increase of the overall number of DUI of cocaine offences in German and English and Wales legislations; when using a *per se limit* for the inactive metabolite benzoylecgonine.
DUI of COCAINE

- Cut-off ng/mL
  - COCA
    - 1
    - 2
    - 10
    - 20
    - 10
    - 80
    - 24

- Countries and Cut-off Levels:
  - Padova LOQs
  - GTFI
  - Denmark
  - Germany
  - England Wales
  - Wolff
  - Norway (0.2)

- Percentage Changes:
  - -9%
  - -36%
  - -51%
  - -36%
  - -36%
  - -81%
  - -53%
DUI of CANNABINOIDS

<table>
<thead>
<tr>
<th>Country</th>
<th>THC Cut-off ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>0.2</td>
</tr>
<tr>
<td>GTFI</td>
<td>1</td>
</tr>
<tr>
<td>DRUID</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>1</td>
</tr>
<tr>
<td>Germany</td>
<td>1</td>
</tr>
<tr>
<td>England Wales</td>
<td>-10%</td>
</tr>
<tr>
<td>Wolff</td>
<td>-10%</td>
</tr>
<tr>
<td>Norway (0.2)</td>
<td>-10%</td>
</tr>
<tr>
<td>Norway (0.5)</td>
<td>-10%</td>
</tr>
<tr>
<td>Norway (1.2)</td>
<td>-10%</td>
</tr>
</tbody>
</table>
DUI of CANNABINOIDS

Cut-off ng/mL

THC
0.2 1
1 1
1 2

-10% -10% -10% -32%

THC
Padova LOQs
GTFI
DRUID
Denmark
Germany
England Wales
Wolff
Norway (0.2)
Norway (0.5)
Norway (1.2)
DUI of CANNABINOIDS

THC levels and cut-off values for different countries:
- Padova LOQs: THC 0.2, 1, 2, 5, 1.3, 3, 9 ng/mL
- GTFI: THC 0.2, 1, 1, 1, 1, 1, 1 ng/mL
- DRUID: THC 0.2, 1, 1, 1, 1, 1, 1 ng/mL
- Denmark: THC 0.2, 1, 1, 1, 1, 1, 1 ng/mL
- Germany: THC 0.2, 1, 1, 1, 1, 1, 1 ng/mL
- England Wales: THC 0.2, 1, 1, 1, 1, 1, 1 ng/mL
- Wolff: THC -32%, -14%, -66%, -92%
- Norway (0.2): THC -10%, -10%, -10%, -10%
- Norway (0.5): THC -10%, -10%, -10%, -10%
- Norway (1.2): THC -10%, -10%, -10%, -10%

The graph shows the comparison of THC levels and cut-off values across different countries and organizations.
DUI of OPIATES

Padova LOQs
GTFI
DRUID
Denmark
Germany
England Wales
Wolff
Norway (0.2)
Norway (0.5)
Norway (1.2)

Cut-off ng/mL
MOR
1
2
10
10
10

-10%
-52%
-52%
-52%
DUI of OPIATES

<table>
<thead>
<tr>
<th>Cut-off ng/mL</th>
<th>MOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-10%</td>
</tr>
<tr>
<td>2</td>
<td>-52%</td>
</tr>
<tr>
<td>10</td>
<td>-52%</td>
</tr>
<tr>
<td>10</td>
<td>-52%</td>
</tr>
<tr>
<td>80</td>
<td>-97%</td>
</tr>
<tr>
<td>80</td>
<td>-97%</td>
</tr>
</tbody>
</table>

- Padova LOQs
- GTFI
- DRUID
- Denmark
- Germany
- England Wales
- Wolff
- Norway (0.2)
- Norway (0.5)
- Norway (1.2)
DUI of OPIATES

- Padova LOQs
- GTFI
- DRUID
- Denmark
- Germany
- England Wales
- Wolff
- Norway (0.2)
- Norway (0.5)
- Norway (1.2)

Cut-off ng/mL

<table>
<thead>
<tr>
<th>MOR</th>
<th>Cut-off ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-10%</td>
</tr>
<tr>
<td>2</td>
<td>-52%</td>
</tr>
<tr>
<td>80</td>
<td>-97%</td>
</tr>
<tr>
<td>80</td>
<td>-97%</td>
</tr>
<tr>
<td>9</td>
<td>-48%</td>
</tr>
<tr>
<td>24</td>
<td>-88%</td>
</tr>
<tr>
<td>61</td>
<td>-94%</td>
</tr>
</tbody>
</table>
DUI of OPIOIDS

- Padova LOQs
- GTFI
- DRUID
- Denmark
- Germany
- England Wales
- Wolff
- Norway (0.2)

Cut-off ng/mL

<table>
<thead>
<tr>
<th>METHADONE</th>
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</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>10</td>
</tr>
</tbody>
</table>

Bar chart showing methadone levels with cut-off proposed in the range of -3% to -9%.

× = no cut-off proposed
DUI of OPIOIDS

- Padova LOQs: 69, 67, 63, 41
- GTFI: 69, 67, 63, 41
- DRUID: 69, 67, 63, 41
- Denmark: 69, 67, 63, 41
- Germany: 69, 67, 63, 41
- England Wales: 69, 67, 63, 41
- Wolff: 69, 67, 63, 41
- Norway (0.2): 69, 67, 63, 41

Cut-off ng/mL:
- METHAD
  - 1
  - 2
  - 10
  - 50

-3% - 9% - 41%

\[\times\] = no cut-off proposed
DUI of OPIOIDS

- Padova LOQs: -96%
- GTFI: -41%
- DRUID: -9%
- Germany: -3%
- Denmark: -3%
- England Wales: -96%
- Wolff: -96%
- Norway (0.2): -96%

Painted bars indicate no cut-off proposed.
DUI of AMPHETAMINES

- Padova LOQs
- GTFI
- DRUID

Denmark
Germany
England Wales
Wolff
Norway (0.2)

<table>
<thead>
<tr>
<th>Cut-off ng/mL</th>
<th>MDMA</th>
<th>AMPH</th>
<th>METH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

-23%
DUI of AMPHETAMINES

<table>
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<th>Cut-off ng/mL</th>
<th>MDMA</th>
<th>AMPH</th>
<th>METH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>GTFI</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>DRUID</td>
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<tr>
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</tr>
<tr>
<td>Germany</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>England Wales</td>
<td>-23%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolff</td>
<td>-23%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norway (0.2)</td>
<td>-23%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DUI of AMPHETAMINES

<table>
<thead>
<tr>
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<th>AMPH</th>
<th>METHAMPH</th>
<th>DRUID</th>
<th>Germany</th>
<th>Sussex</th>
<th>GTFI</th>
<th>Padova LOQs</th>
<th>Wolff</th>
<th>England Wales</th>
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<th>Denmark</th>
<th>Wolff</th>
<th>England Wales</th>
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</thead>
<tbody>
<tr>
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<td>1</td>
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<td>2</td>
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<td>20</td>
<td>20</td>
<td>20</td>
<td>25</td>
<td>25</td>
<td>10</td>
<td>250</td>
</tr>
</tbody>
</table>

- 0% = no cut-off proposed

-23% = no cut-off proposed
-46% = no cut-off proposed
DUI of AMPHETAMINES

<table>
<thead>
<tr>
<th>Cut-off ng/mL</th>
<th>MDMA</th>
<th>AMPH</th>
<th>METH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>GTFI</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>DRUID</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Denmark</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Germany</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>England Wales</td>
<td>10</td>
<td>250</td>
<td>200</td>
</tr>
<tr>
<td>Wolff</td>
<td>300</td>
<td>600</td>
<td>200</td>
</tr>
</tbody>
</table>

- No cut-off proposed for Norway (0.2)

× = no cut-off proposed
DUI of KETAMINE

<table>
<thead>
<tr>
<th>Country</th>
<th>Cut-off ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>0.5</td>
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<tr>
<td>GTFI</td>
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<td>Germany</td>
<td>×</td>
</tr>
<tr>
<td>England Wales</td>
<td>×</td>
</tr>
<tr>
<td>Wolff</td>
<td>×</td>
</tr>
<tr>
<td>Norway (0.2)</td>
<td>×</td>
</tr>
<tr>
<td>Norway (0.5)</td>
<td>×</td>
</tr>
<tr>
<td>Norway (1.2)</td>
<td>×</td>
</tr>
</tbody>
</table>

× = no cut-off proposed
DUI of KETAMINE

- Cut-off ng/mL
   - METHAD
     - Padova LOQs: 0.5
     - GTFI: (X)
     - DRUID: (X)
     - Denmark: (X)
     - Germany: (X)
     - England Wales: 20
     - Wolff:
       - Norway (0.2): (X)
       - Norway (0.5): (X)
       - Norway (1.2): (X)

- (X) = no cut-off proposed
DUI of KETAMINE

- Padova LOQs (0.5)
- GTFI (X)
- DRUID (X)
- Denmark (X)
- Germany (X)
- England Wales (20)
- Wolff (200)
- Norway (0.2) (X)
- Norway (0.5) (X)
- Norway (1.2) (X)

-50% = no cut-off proposed

X = no cut-off proposed
DUI of KETAMINE

- Cut-off ng/mL
- METHAD
  - Padova LOQs: 0.5
  - GTFI: 0.5
  - DRUID: 0.5
  - Denmark: 0.5
  - Germany: 0.5
  - England Wales: 0.5
  - Wolff: 0.5
  - Norway (0.2): -50%
  - Norway (0.5): -60%
  - Norway (1.2): -100%

- x = no cut-off proposed

KETAMINE
DUI of KETAMINE

Cut-off ng/mL
METHAD
0.5

METHAD

Padova LOQs
GTFI
DRUID
Denmark
Germany
England Wales
Wolff
Norway (0.2)
Norway (0.5)
Norway (1.2)

-50%
-100%
-60%
-100%

= no cut-off proposed
DUI of KETAMINE

- Padova LOQs: 0.5
- GTI: X
- DRUID: X
- Denmark: X
- Germany: X
- England Wales: X
- Wolff: X
- Norway (0.2): X
- Norway (0.5): X
- Norway (1.2): X

- Cut-off ng/mL:
  - METHAD: 0.5

- Proposed cut-off: -50% to -100%

- X = no cut-off proposed
OVERALL REDUCTION OF DUI*

*with respect to cases positive for substances for which a cut-off is present
Analytical Threshold

<table>
<thead>
<tr>
<th></th>
<th>COCAINE</th>
<th>THC</th>
<th>MORPH</th>
<th>METHAD</th>
<th>AMPH</th>
<th>KETAMINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>186</td>
<td>145</td>
<td>63</td>
<td>69</td>
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<td>10</td>
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<tr>
<td>GTFI</td>
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<td>57</td>
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<td>13</td>
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<tr>
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<td>119</td>
<td>131</td>
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<td>63</td>
<td>10</td>
<td>❌</td>
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</tbody>
</table>

❌ = no cut-off proposed
"Low" Per Se Limits

<table>
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<tr>
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<th>MORPH</th>
<th>METHAD</th>
<th>AMPH</th>
<th>KETAMINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Padova LOQs</td>
<td>186</td>
<td>145</td>
<td>63</td>
<td>69</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
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<td>10</td>
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<tr>
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<td>99</td>
<td>2</td>
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<td>7</td>
<td>5</td>
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</table>

*= no cut-off proposed*
“Impairment” Per Se Limits

<table>
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<tr>
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<th>MORPH</th>
<th>METHAD</th>
<th>AMPH</th>
<th>KETAMINE</th>
</tr>
</thead>
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<tr>
<td>Padova LOQs</td>
<td>186</td>
<td>145</td>
<td>63</td>
<td>69</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Wolff</td>
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<td>31</td>
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<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
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<td>33</td>
<td>52</td>
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<td>4</td>
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<tr>
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<td>12</td>
<td>4</td>
<td>×</td>
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</tbody>
</table>

× = no cut-off proposed
Conclusions

• The implementation of high analytical limits or impairment-based cut-offs could result in the persecution of a much lower number of “drugged drivers” involved in road traffic accidents, with a decrease of DUID from 8% to more than 90% depending on the limits adopted.

• Cut-offs? at the lowest level at which a robust analytical result can be obtained, high enough such as passive consumption or inhalation or traces can be ruled out - a 'lowest accidental exposure limit’
Ευχαριστώ για την προσοχή σας