EU project

ROSITA

Roadside Testing Assessment

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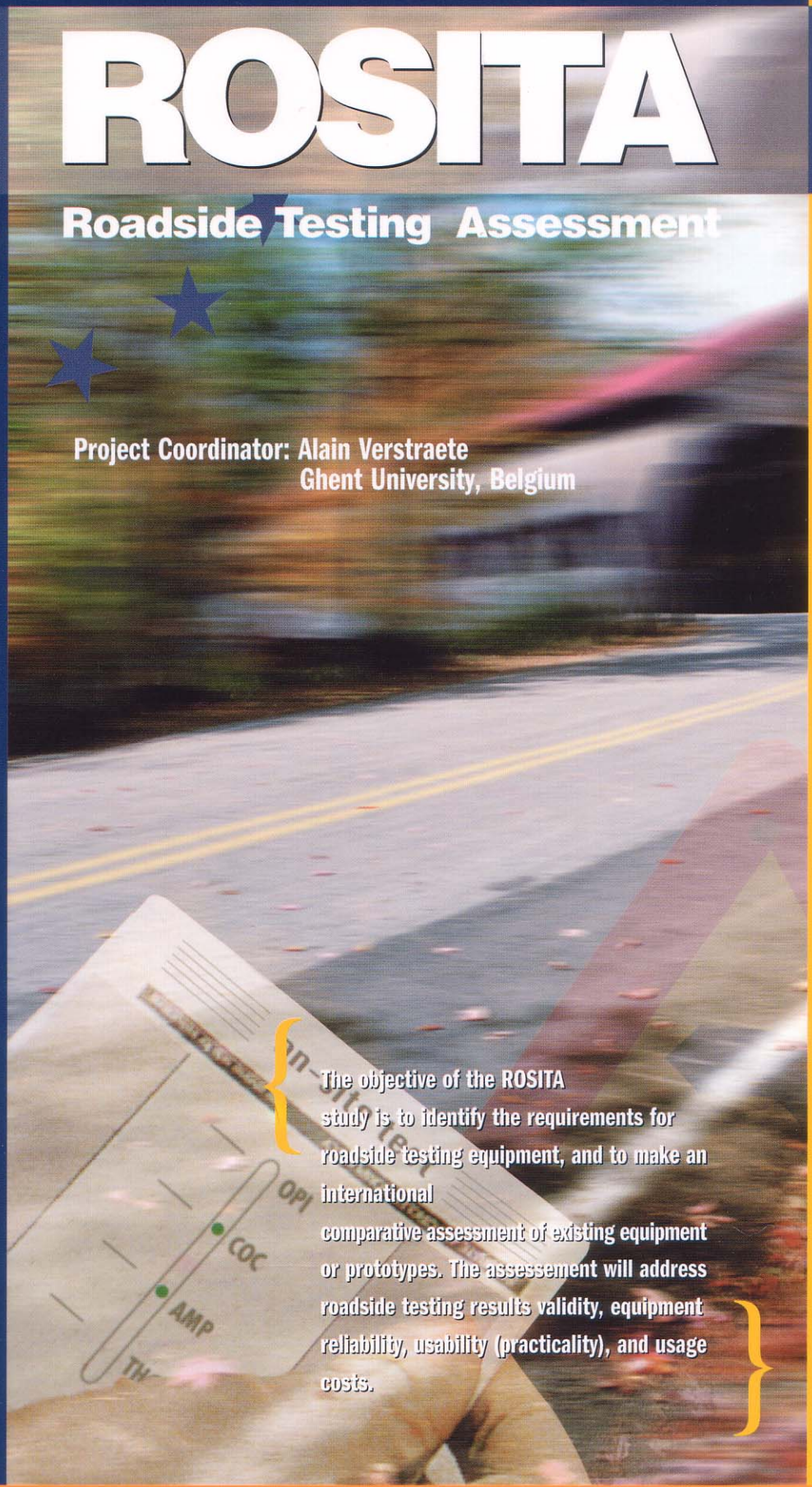

The objective of the ROSITA study is to identify the requirements for roadside testing equipment, and to make an international comparative assessment of existing equipment or prototypes. The assessement will address roadside testing results validity, equipment reliability, usability (practicality), and usage costs.

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ROSITA

Roadside Testing Assessment

Coordinator: Dr. Alain VERSTRAETE

Introduction

This book contains all the reports (deliverables) from the Rosita project. All these reports can be downloaded from our website "www.rosita.org", but we thought that it would also be useful to have them in the form of a printed book.

The Rosita project ran during 1999 and 2000 in 8 European states. A total of 9 European Institutes for Legal Medicine and Toxicology and 3 companies worked together on the 5 different project targets. The following Institutes and Companies were official Rosita Partners:

No.	*Name*	*Country*
1.	University of Gent (Project Management)	Belgium
2.	National Public Health Institute, KTL	Finland
3.	University of Glasgow, Forensic Medicine & Science	UK
4.	Institute of Legal Medicine, Homburg	Germany
5.	National Institute of Forensic Sciences, NICC, Brussels	Belgium
6.	National Institute of Forensic Toxicology, NIFT, Oslo	Norway
7.	University of Santiago de Compostela	Spain
8.	Institute of Legal Medicine, University of Strasbourg	France
9.	Centre of Behavioural and Forensic Toxicology, University of Padova	Italy
10.	Roche Diagnostics	Belgium
11.	Securetec Detektions-Systeme AG	Germany
12.	Dade Behring GmbH	Germany

Official partners of the Rosita project

The Rosita study has been divided into 5 workpackages covering the following five key questions:

1. What are the drugs/medicines that are suspected to have a detrimental impact to road users performance?
2. What is the state-of-the-art roadside testing equipment for urine, sweat and saliva? Are there other tests that can be used to evaluate the impairment of the driver at the roadside?
3. What kind of operational, user and legal requirements exist across Member States of the European Community for roadside testing equipment?
4. How are usability (practicability), sensitivity, specificity and accuracy of available roadside test devices?
5. What can be recommended for the use of roadside testing equipment (in Europe)?

Working for the Rosita project was, for most or all of us, a challenging but rewarding experience. Many people, who were employed by the contractors and police officers worked very long hours for this project, and we are very much indebted to them. Many companies, who were not Rosita contractors, supplied their tests at no or reduced costs. In addition, I would like to thank Dr. Gianpaolo Brusini, who has been our tireless webmaster and who has helped us enormously in the realisation of this book, and our scientific officer René Bastiaans of DG TREN of the European Union, who had the idea of launching the call for this project, who was present at many of our meetings to give us very valuable advice. Our contacts have shown us that the results of Rosita are well known all over the world (more than 400 people downloaded one or more of the deliverables and approximately 100 newspaper articles were devoted to Rosita), and we hope that this book also help in the dissemination of our results.

Dr. Alain Verstraete
Co-ordinator
Gent, August 2001

Deliverable D1

Drugs and medicines that are suspected to have a detrimental impact on road user performance.

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: The Toxicological Society of Belgium and Luxembourg (BLT) as subcontractor of University of Gent (RUG)

Authors: Viviane MAES, Corinne CHARLIER, Olivier GRENEZ and Alain VERSTRAETE

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EXECUTIVE SUMMARY

Driving is a complex task where the driver continuously receives information, analyses it and reacts. Substances that have an influence on brain functions or on mental processes involved in driving will clearly affect the driving performance.

Different studies provide information about the influence of illicit drugs and licit medicines on driving performance: They can be classified into three main types: epidemiological studies, pharmaco-epidemiological studies and experimental studies.

Epidemiological studies are necessary to estimate the importance of the problem. They can be conducted in three different ways:

- *Descriptive epidemiological studies*: the prevalence of psychoactive drugs in the driving population is determined on representative samples selected according to various criteria: the whole driving population, injured or killed drivers, drivers suspected of driving under the influence.
  The most important European studies are summarised in the report.
- *Responsibility analysis studies*: in these studies, the authors try to determine the responsibility of drivers involved in road traffic accidents, to establish if drug use contributes to accidents or not. The responsibility is determined without knowledge of the results of the drug analysis. A study by Drummer (1045 killed drivers) and another one by Terhune (1882 killed drivers) are discussed as examples of responsibility analysis studies.
- *Studies with control groups*: the results of the test group are compared with the same drug analysis performed on a control population consisting of matched drivers or non-responsible subjects. Very few epidemiological studies have included a control population.

Pharmaco-epidemiological studies are very useful as they compare the number of accidents in drivers for whom medicines are prescribed with the number of accidents in a matched control population. The results of the major reports are summarised in the present work. However, this kind of study is difficult to perform with illicit drugs, for easily understandable practical and ethical reasons.

Experimental studies consist in the administration of different doses of medicines or of placebo to selected volunteers. The effects on psychomotor performance and/or on driving skills are measured by laboratory tests, in driving simulators or by real driving experiments. While there is an abundant literature on the subject, methodologies are not well standardised and comparisons of different studies with sometimes conflicting results are difficult to perform.

Illicit drugs possibly influencing driving performances are then presented, with epidemiological and experimental data if available:

- *Cannabis* (used as marihuana, hashish, …) influences perception, psychomotor performance, cognitive and affective functions. This will affect co-ordination, vigilance and alertness, and will impair driving ability. The impairing effects are concentrated in the first 2 hours, but may persist for more than 5 hours. Real driving tests were only performed with low doses and show that a dose of 100–300 µg tetrahydrocannabinol /kg body weight has an effect comparable to blood alcohol concentrations of 0.3-0.7 g/L. Drivers seem to compensate their driving behaviour; however problems may arise in emergency situations. Impairment is more important and persistent for difficult tasks needing continuous attention. One study showed that injured drivers who were positive for cannabis were 2.5 times more likely to be killed. Responsibility analysis showed a trend towards a decrease in relative risk.
- *Opiates* (mostly heroin) induce sedation, indifference to external stimuli, increased reaction time. Miosis has a negative effect on accommodation, mainly in darkness. Impairment of driving performance will be noted, even during the withdrawal syndrome, which is associated with a significant loss of concentration. There are no experimental data on the effect of heroin on driving performance.
- *Cocaine* (free base, crack,…) is also incompatible with safe driving. There are no experimental data on cocaine and driving. The subjectively experienced performance improvement during the phase of euphoria will lead to increased risk-taking in traffic. The objectively observed performance impairment is due to a loss of concentration and attentiveness, and an increased sensitivity for blinding by light (dilated pupils). Moreover the psychological symptoms such as paranoia, delusions, hallucinations will have an influence on driving behaviour.

- There are few studies of the influence of ***amphetamines and designer amphetamines*** (XTC, Eve, ….) on psychomotor function. These stimulating drugs will dangerously increase the self-confidence of the driver with increased risk-taking in traffic. The user becomes aggressive in the beginning and apathetic when the product disappears from the blood. Moreover, the wide pupils can cause blinding. Case reports show that amphetamines have a negative influence on the performance capabilities. However, in many cases of psycho-stimulation, it is not the acute effect of the drug but rather the exhaustion and overexertion resulting from the stimulation as well as other problems arising from misuse that are decisive for driving impairment.
- Finally, ***hallucinogens*** (GHB, LSD, magic mushrooms, mescaline,…) impair psychomotor performance, by producing hallucinations, sleepiness, psychotic reactions,… which are not compatible with safe driving.

Medicinal drugs affecting driving performance are finally presented. Psychoactive medicines can modify behaviour and experience, causing somnolence, loss of psychomotor co-ordination, balance or sensory disturbances,…

- *Benzodiazepines*: with only one exception, all pharmaco-epidemiological studies show an increased accident risk in benzodiazepine-users. The highest risk is observed in the first weeks of treatment, with long-acting benzodiazepines and in young males.
- *Antidepressants*: some, but not all pharmaco-epidemiological studies have shown that there is a dose-dependent increased risk for injurious crash. Newer antidepressants seem to be less impairing.
- *Neuroleptics* are often sedative and induce motor disturbances and a decline of cognitive functions.
- *Narcotics and opioid analgesics* produce sedation, impairment of cognitive functions, mood changes (dysphoria and euphoria), impairment of psychomotor functions and pupil restriction. Absolute driving unfitness exists at onset of the treatment, when important changes in drug dose are introduced and when other CNS depressants or alcohol are co-ingested. In long-term stabilised opioid therapy with unchanged doses no impairment of driving behaviour is observed. Pharmaco-epidemiological studies yield contradictory results.
- *Antihistamines* can impair driving by the sedation they produce. However, newer (second generation) antihistamines cause very little sedation and are likely to have little impairing influence on driving.

Some classifications have been proposed to categorise medicinal drugs according to their influence on driving ability (categories ranging from no impairment to severe impairment): the system proposed by the Dutch study group of Wolschrijn provides a categorisation of about 570 drug doses/formulations and the BLT in Belgium has classified 180 medicines.
The use of categorisation and warning (sticker or label) systems in different European countries (Germany, the Netherlands, the Nordic countries, Italy, France) is discussed and finally, a comparison of the different systems is presented in an overview table.

INTRODUCTION

1) The driving task

Driving is a complex task where the driver continuously receives information, analyses it and reacts. The different steps involved in the driving task are represented in the table below. These functions are closely interconnected. The whole process is also closely related to the knowledge of the driver. Moreover the attitude of the driver will be reflected in his driving behaviour (1).

Table 1: The different steps of the driving task.

Information intake	**Information treatment**		**Action**
PERCEPTION	PREVISION	DECISION	ACTION
Discriminating - to look, to see - to search for information - to identify indices	Anticipating - what one will do - what others will do - what can happen	Deciding as a function of - what one has seen - what one has foreseen - what one knows	- to accelerate - to slow down - to brake - to change lanes etc..

↑ ↓

KNOWLEDGE
- traffic system - driving regulations (law and informal rules) - application of the rules - condition of the vehicle - condition of the driver (illness, medication, alcohol…) - probable risks - situations already encountered or seen (experience)

↑ ↓

ATTITUDES	
- positive towards safety - negative	- wanting to avoid risks - being nervous, aggressive, intolerant, in a hurry

It is clear that substances having an influence on the brain functions and mental processes involved in the driving task will have an influence on driving performance.

2) Methodologies for evaluating the influence of drugs on driving

Information about the influence of drugs (illicit and medicines) on driving performance and accident risks can be derived from different types of studies:

- **Epidemiological studies**
  = surveys in which biological samples (blood, urine, saliva, sweat,…) of drivers are analysed for drugs.

These studies can be categorised into different groups, according to the selection of the subjects:

a. roadside surveys: where a representative sample of the driving population is analysed
b. studies in injured drivers or subjects
c. studies in fatally injured drivers or subjects
d. studies in drivers suspected of driving under the influence of drugs and or alcohol
e. re-analysis studies: analysis of drugs in blood samples taken for the determination of alcohol.

These types of studies are mostly descriptive, i.e. they give information on the percentage of drivers in the studied population that has been exposed to a drug. However, a comparison of the percentages in roadside surveys and injured or killed drivers can show an overrepresentation of drivers who are positive for drugs and thus suggest a causal role.
Further analysis of the data can provide information on the contributory role of drugs in the accidents:

a. comparing the results of the study group (e.g. drivers injured in accident, responsible drivers) with a control group (e.g. matched drivers, non-responsible group); involvement of control groups provides relative risk data
b. responsibility analysis (to determine the responsibility/culpability of drivers involved in accidents for the purpose of establishing if drug use by drivers contributes to accident causation)

- **Pharmaco-epidemiological studies**

  = studies where the incidence of traffic accidents in people who take drugs (mostly medicines) is compared with a control population.

Pharmaco-epidemiological studies are extremely useful, because they provide insight into the relative importance of different types of drugs (which drugs contribute to a significant traffic safety problem). These studies have some limitations such as their lack of assessment of medication compliance and the interval before driving, the medical condition and the concomitant use of alcohol and other medications.
Unfortunately, this type of study is much more difficult to perform for the illicit drugs, and at this time none has been carried out.

- **Experimental studies**

  = the drug (different doses, compared to placebo and positive control) is administered to volunteers and the effects on psychomotor performance and/or driving skills are measured:

  - ***Laboratory tests***

    These tests are dedicated to evaluation of the psychomotor and cognitive performance, vision, body sway, arousal, attention, alertness after taking a drug. Several publications exist, that have reviewed the available tests (2-4). Tests mostly used are:

    Attention tests (simple and divided attention)

    Vigilance tests (ability to sustain attention)

    Auditory and visual tests (visual acuity, accommodation to darkness/light)

    Reaction time (simple and choice reaction time)

    Cognitive tests
    - Digit/symbol substitution test
    - Stroop word/colour test
    - Letter cancellation test
    - Logic test
    - Memory test
    - Mental arithmetic

Flicker fusion test

Visual-motor coordination tests

Body sway

Physiological measurements (EEG, eye movements, pulse, blood pressure, …)

Self-awareness (reported on visual analogue scale)

The laboratory tests, designed to detect a state of hypovigilance, often fail to show significant results even if the tested compound clearly induces somnolence, slower reflexes or impaired driving. This may be explained (5):

- laboratory tests examine a limited number of cognitive functions, contrary to a global driving task
- the test person, submitted to a psychomotor test, can use a certain "capacity reserve" allowing him to perform well over a short period; this reserve can be revealed by prolonging the test time or by submitting the subject to several tests simultaneously
- some side effects of drugs are expressed in a behavioural change of the disinhibition type, with increased risk-taking

Therefore the battery of laboratory tests must be completed with driving tests in conditions as close to reality as possible.

- ***Simulated driving***
  The simulator mimics the actual driving situations in laboratory. However, a lot of variables and stimuli arising in a real situation cannot be reproduced. Another weak point of the test is the low motivation level due to the absence of personal risks.

- ***Real driving***
  Driving experiments are conducted in closed circuit or on the road using a specially instrumented car. Several parameters are recorded:
  - Lane weaving (standard deviation of the lateral position or SDLP: the sideways movement of the vehicle within its traffic lane is measured by using a video camera mounted on the car)
  - Car following
  - Steering manoeuvres
  - Braking
  - Speed…

  Analysis of the multifactorial results is complex.

So far driving tests are mainly focused on sedative effects; there is an important lack of risk evaluation studies. The increase or decrease in risk-taking can be evaluated in tests of inhibition excess (the subjective perception of a sedative effect often leads the subject to increase his inhibition level and decrease his risk-taking) and tests of disinhibition. (5)

Standardisation

While there is an abundant literature in the field, it is sometimes difficult to conclude whether a drug has an influence on driving. Some empirical studies are flawed by methodological deficiencies. Two international Workshops were organised in Padova (1991) and in Cologne (1992) to address this problem and try to standardise the studies. Guidelines have been published and now efforts have to be made to ensure their application (6,7).

- **Evaluation of the effects of drugs, relevant to driving performance**
  = the known effects (psycho-neurological and physiological) of drugs are evaluated in the perspective of their susceptibility to influence driving abilities.

EPIDEMIOLOGICAL DATA

The prevalence of psychoactive substances in the driving population constitutes an important source of information to estimate the importance of the problem. It gives indications about the relative importance of different types of drugs and which drugs might contribute to the traffic safety problem.

1) Descriptive epidemiological studies

Krüger et al. (8) have summarised results from 69 epidemiological studies about alcohol and drugs in traffic. The median percentage of positives for alcohol, illicit drugs and medicines in roadside tests, injured and deceased drivers is represented in the next table.

Table 2: Median exposure rates from 69 epidemiological studies (8).

	Roadside (% positive)	Injured (% positive)	Fatalities (% positive)
Drugs	1	17	19
Medicines	4	13	10
Alcohol	6	35	52

In injured or deceased drivers the mean percentage of positives for alcohol, illicit drugs and medicines is respectively 7, 15 and 2.5 times higher than in a random sampling of drivers.
In his review of investigations of the prevalence of illicit drugs in road traffic in European countries de Gier (9) obtained similar data:

Table 3: Prevalence of drugs in different driver populations (9).

	General driver population	Collision-involved drivers
Illicit drugs	1-5 %	10-25 %
Licit drugs	5-15%	6-21 %

In the general driver population cannabis (majority) and opiates are most frequently observed; the use of amphetamines (younger drivers) increases in some countries (e.g. Norway). Benzodiazepines are the most frequently detected licit drugs.
In the collision-involved drivers (injured or dead) cannabis and opiates are detected in the samples with about equal frequency (2-3 times more than amphetamines). Cocaine is found with low prevalence (exception: Spain 5-7%). Also in these study populations the benzodiazepines prove to have the highest prevalence in the licit drugs (2-14%).
In drivers suspected of driving under the influence an even higher prevalence of licit and illicit drugs is found. The selection of this sample of the driving population is dependent on the perception of the police officers. Once again cannabis and opiates show high prevalence (up to 57 and 42% resp.). For amphetamines up to 21% positives are found. Remarkable differences between countries are observed. The frequency of drugged drivers apprehended in roadside traffic appears to be at least 10-fold higher in Norway than most other countries, probably due to differences between national road traffic acts and the level of attention to the problem (10).

In the following tables details of the most important European epidemiological studies are assembled. Although the absolute prevalence data from the different countries are not comparable due to different study methodologies (e.g. study population, time of sampling,…), the high prevalence of drugs in accident-involved drivers supports the idea that besides alcohol (il)licit drugs are a problem for road safety. Knowledge of the prevalence of drug positive drivers in different populations is not a proof that the use of drugs is a serious safety problem. To determine the accident risks the study needs to match accident-involved drivers with a control group.
There is a serious lack of data on prevalence of drug use in the general driver population: the Dutch study (11) concerns urine and sweat samples collected during weekend nights while in the German survey (8) saliva

samples were collected from drivers. The German results should be considered with reserve as the FPIA method used has a low sensitivity for the detection of cannabinoids in saliva (target molecule is the carboxy-metabolite, scarcely present in saliva) and the saliva-plasma ratio is unfavourable for some important drugs (e.g. morphine 0.2 and benzodiazepines 0.02). On the other hand smoking or snorting drugs will give high concentrations in saliva during the first hours after use due to buccal contamination.

Table 4: Drivers stopped on the road.

	Netherlands (11)	**Germany** (8)
Period	1997-1998 (WE nights)	1992-1993
Number of subjects	293	2234
Biological sample	urine, sweat	saliva
Analytical methods	Drugwipe®,Triage®,Accusign®, HPLC, GC-MS	FPIA, RIA (benzodiaz.)
RESULTS		
Alcohol	12.30%	5.50%
Alcohol only		5.23%
Drugs	8.20%	2.59%
Drugs only		2.32%
Drugs + alcohol		0.27%
Amphetamines	1.37%	0.08%
Barbiturates	0.00%	0.53%
Benzodiazepines	0.34%	2.60%
Cannabinoids	5.12%	0.60%
Cocaine	0.68%	0.01%
Opiates	1.37%	0.70%

Table 5: Drivers injured or killed in an accident.

	Norway (12)	**Spain** (13)	**Belgium** (14)
Period	1993	1992-1995	1995-1996
Number of subjects	394 (injured drivers)	979 (killed drivers)	2053 (injured or killed drivers)
Biological sample	Blood	blood	blood, urine
Analytical methods	GC-MS,HPLC	Immunossay, GC-MS, HPLC	FPIA, HPLC, GC, GC-MS
RESULTS			
Alcohol	62.9%	51.2%	27.0%
Alcohol only	51.8%	44.3%	
Drugs	24.1%	14.3%	19.0%
Drugs only	12.9%	5,9% (2% illicits+ 3,9% medicines)	
Drugs + alcohol	11.2%	6.9%	
Amphetamines	4.1%	0.9%	3.0%
Barbiturates			1.3%
Benzodiazepines	13.7%		8.5%
Cannabinoids	7.6%	1.5%	6.0%
Cocaine		5.0%	0.7%
Methadone			0.4%
Myorelaxants	0.5%		
Opiates	4.3%	3.1%	7.5%
Propoxyphene			0.2%

	Norway (15)	**Switzerland** (16)	**Denmark** (17)	**Finland** (18)	**Italy** (19)	**West-Scotland** (20)		**Germany** (21,22)	
Period	1994	1982-1994	1995	1993	1994-1998	1995-1998		1989-90	1995
Number of subjects	2529 (total of 2819 but 10.3 % BAC>>)	641 (40 % involved In accident)	221 (46 % involved in accident)	332	1123	752		660	632
Biological sample	blood	blood, urine		blood	blood, urine	blood (B), urine (U)		blood	
Analytical methods	immunoassay GC-MS	Emit, RIA, TLC, GC, HPLC		Emit, GC	immunoassay GC-MS	EIA GC, GC-MS, HPLC		RIA, FPIA, GC-ECD, GC-MS	
RESULTS						B (640)	U (112)		
Alcohol	89%	35.9%		95.5%	29.5% >0.8 g/l	25.8%	13.4%	96.2%	
Alcohol only	30%	7.8%		73.2%		16.3%	6.3%	86.4%	
Drugs	59% (in 2529 cases with BAC < 1.5 g/l)	85.0%	86.0% (in 221 cases with BAC < 0.5 g/l)	26.8%	14.0%	68.4%	90.2%	13.1%	30.4%
Drugs only		56.9%				58.9%	83.0%	3.3%	
Drugs + alcohol		28.1%		24.1%	9.4%	9.5%	7.0%	9.8%	
Amphetamines	21.1%	4.2%	10.0%	2.7%	1.3%	2.0%	25.0%	0.45%	6.2%
Antidepressants			< 5.0 %					0.0%	
Benzodiazepines	30.6%	14.8%	53.0%	22.9%		78%	71%	5.45%	12.3%
Barbiturates								1.06%	
Cannabinoids	26.1%	57.3%	17.0%	2.4%	10.0%	26.6%	59.8%	8.2%	22.8%
Cetobemidone			6.0%						
Cocaine	0.04%	10.5%	6.0%	1.2%	4.5%	0.93%	1.8%	0.0%	2.2%
Methadone		10.3%	13.0%			5.5%	11.6%		
Opiates	7.6% M 4.1% C	36.3%	27.0%	0.0%	1.1%	15.2% M 4.1% D	58.0 % M 8.9% D	1.8%	4.3%

M = morphine; **C** = codeine; **D** = dihydrocodeine

Table 6: Drivers suspected of driving under influence.

2) Responsibility analysis studies

1) Study by Drummer on 1045 killed drivers (23). Responsibility was determined after a review of 8 mitigating factors without knowledge of the results of drug analysis. An index of responsibility was calculated using pre-determined scoring guidelines. Drivers were then grouped into one of three categories: culpable, contributory and not culpable. The proportion of culpable drivers (culpability ratio) was then calculated.

Table 7: Responsibility analysis results in fatal accidents (23).

Drug group	Prevalence	Relative risk (all cases)	Relative risk (drug alone)	Relative risk (drug + alcohol)
Drug free	51 %	1.0		
Alcohol	27 %		**6.0**	
Alcohol + drugs	9 %			**9.0**
Drugs	13 %		1.4	
Cannabis	11 %	1.6	0.6	**5.6**
Stimulants	3.7 %	**2.7**	1.6	8.7
Opiates	2.7 %	**5.0**	2.3	2.9
Benzodiazepines	3.1 %	**5.8**	1.9	**9.5**
Misc. Drugs	5.6 %	**4.0**		8.7

Bold = statistically significant

Responsibility analysis: 73 % drivers were considered culpable, 18 % not culpable. Drivers positive for alcohol, stimulants (mostly pseudo/ephedrine and meth/amphetamine), opiates (mostly codeine), benzodiazepines and miscellaneous drugs showed higher culpability ratios. The cannabis-only group had a smaller ratio (0.6, but not significant).

Drivers with drug concentrations higher than what could be considered low therapeutic tended to be culpable. All drivers considered to have drug concentrations much higher than what could be regarded as reflecting therapeutic use were either culpable or contributory to the accident. Drivers in whom more than one drug was detected in blood were invariably found to be responsible for the accident.

2) In the US, Terhune et al. (24) examined 1882 fatally injured drivers (who died within 4 h of the crash) using a method of responsibility analysis to assess the contribution of drugs to accidents (tables 8,9)

This study showed that the responsibility rate increased significantly for drivers with alcohol alone and with all alcohol(≥ 1g/L)-drug combinations The authors also found that the responsibility rate for drivers with THC in their blood decreased compared to the drug-free control group. In contrast, the responsibility rate for amphetamine positive drivers was higher than the drug-free group. Crash responsibility rates increased significantly as the number of non-alcohol drugs in a driver increased. The responsibility analysis suggested little relation between drug use and crash risk, but the sample sizes were small. There appeared to be some potential for increased crash risk when certain drugs were combined with alcohol.

Table 8: Prevalence of drugs in fatally injured drivers (24).

Drug groups	Prevalence
Drug-free	42.1 %
Alcohol-only	40.1 %
Alcohol + drugs	11.4 %
Drugs-only	6.4 %
Cannabis	6.7 %
Cocaine	5.3 %
Benzodiazepines	2.9 %
Amphetamines	1.2 %

Table 9: Responsibility analysis results for fatally injured drivers (24).

Drug groups	% responsible (substance only)	% responsible (drug + alcohol)
Drug-free	*67.7 (= ref. group)*	
Alcohol		
- < 1g/L	**75.8**	
- ≥ 1 g/L	**93.9**	
Cannabis		
- THC + THCCOOH	57.9	**94.6**
- THCCOOH	83.3	**93.1**
Cocaine	57.1	**87.8**
Benzodiazepines	66.7	**100**
Amphetamines	83.3	**91.7**

Bold = statistically significant

3) Studies with control groups

The results of the test group (e.g. injured driver, responsible subject) is compared with a control group (e.g. matched driver, non-responsible subject). Some studies are presented in the next table.

Table 10: Overview of studies with control groups.

Study	Study subject	Drug group	Involved*	Control°
Honkanen et al. (25)	Injured drivers*/ matched controls°	Psychotropics Alcohol	5% pos. 15 % pos.	2.5 % pos. 1 % pos.
Currie et al. (26)	Subjects responsible*(163) / non-responsible° (66) for accident (not limited to traffic accidents)	Benzodiazepines Tricyclic antidepr. BZD + TAD	n = 18 n = 6 n = 4	n = 1 n = 1 n = 0
Marquet et al. (27)	Injured drivers*/ non-trauma patients°	Cannabinoids	NS ↑ Females ↑	

In the BTTS (14) no control group was used but the mortality in the different groups was compared: it was 3.3% in drivers negative for alcohol and drugs, 4.6 % in drivers who were above the legal limit (0.5 g/L) for alcohol, 5.6 % for the drivers who were positive for drugs and 8.6 % in the drivers who were positive for both alcohol and drugs. This relative risk of 2.56 suggests a clear synergistic interaction between alcohol and medication/illicit drugs, because a merely additive effect would have led to a relative risk of 1.60.

PHARMACO-EPIDEMIOLOGICAL DATA: OVERVIEW TABLE

Table 11: Overview of studies with pharmaco-epidemiological data.

STUDY AUTHORS	STUDY POPULATION RISK PARAMETER	DRUG GROUP	OR / RR (confidence interval)	REMARKS
UK 1979 Skegg et al. (28)	Population registered with 16 general practitioners: 57 drivers who were injured in road accidents during a 2-year period (March 1974 – February 1976) (21 car drivers, 22 motor-cyclists, 14 cyclists) 1425 matched controls Risk of accident involvement	Minor tranquillisers Minor analgesics Antiacids Diuretics Cardiovascular med. Asthma med. Antihistamines Any drug	**5.2** (2.2 –12.6) 2.5 (no CI given) 1.7 (") 2.9 (") 4.5 (") 2.9 (") 1.8 (") 2.0 (")	Antihistamines: in motorcycle accidents **5.3**
Tennessee Ray et al.(29)	Elderly (≥ 65 y) 495 injurious crashes/16262 subjects Relative risk of injurious crash	Any kind (psychoactive) BZD CAD 2 BZD or CAD Antihistamines or Opioids	**1.5** (1.2 – 1.9) **1.5** (1.2 – 1.9) **2.2** (1.3 – 3.5) ↑ 4.8 / 9.8 1.1 (0.7 – 1.8)	Risk ↑ with dose ↑ for BZD and CAD No variation with duration use
Quebec 90-93 Hemmelgarn (30)	Elderly (67 – 84 y) 5579 in crash vs 13256 controls Rate ratio of crash involvement	BZD, long half-life - within 1st week - up to 1 year BZD, short half-life	 **1.45** (1.04 – 2.03) **1.26** (1.09 -.1.45) 0.96 (0.88 – 1.05), no↑	No dose effect
Massachusetts Oster et al. (31)	Persons 18 – 64 y 4554 with prescription of BZD 13662 with prescription other drug Probability of accident-related medical encounter	BZD vs control BZD vs self unexposed More than 3 prescriptions over 6 months vs one	**1.15** (1.05 – 1.26) **1.28** (1.04 – 1.56) **1.30** (1.09 – 1.55)	
Washington 87-88 Leveille et al. (32)	Elderly (> 65 y) 234 crashes vs 447 controls Relative risk of crash	CAD Opioid analgesics BZD Antihistamines	**2.3** (1.1 – 4.8) **1.8** (1.0 – 3.4) 0.9 (0.4 – 2.0) 0.7 (0.3 – 1.7)	No dose relationship Risk ↑ with number of drugs
Saskatchewan Neutel (33)	148000 BZD users 98000 controls Odds ratio of hospitalisation	BZD hypnotics - within 4 weeks - within 2 weeks BZD anxiolytics - within 4 weeks - within 2 weeks Anticonvulsants (within 4 w) AD (within 4 w) Antipsychotics (within 4 w)	 **3.9** (1.9 – 8.3) **6.5** (1.9 – 22.4) **2.5** (14.2 – 5.2) **5.6** (1.7 – 18.4) 1.7 (0.6 – 5.7) 1.0 (0.5 – 2.1) 0.6 (0.2 – 1.9)	High risk: young males (20 – 39 y)

STUDY AUTHORSf	STUDY POPULATION RISK PARAMETER	DRUG GROUP	OR / RR (confidence interval)	REMARKS
Saskatchewan Neutel (34)	225796 (> 20 y) with 1st BZD prescr. 97862 controls Risk of injurious accident within 4 weeks use in older vs younger adults	BZD in - all - < 60 y - > 60 y	 **3.1** (1.5 –6.2) **3.2** (1.3 –8.1) **2.8** (1.0 – 8.4)	OR flurazepam 5.1, triazolam 3.2, diazepam 3.1, lorazepam 2.4
Scotland Barbone et al. (35)	Persons > 18 y Within-person case crossover study: 1731 users of psycho-active drugs involved in car crash Odds ratio for accident	BZD - intermediate half-life - long half-life anxiolytics Zopiclone TAD SSRI Other	**1.62** (1.24 – 2.12) 1.59 (0.71 – 3.57) **2.03** (1.41 – 2.93) **4.0** (1.31 – 12.2) 0.93 (0.72 – 1.21) 0.85 (0.55 – 1.33) 0.88 (0.62 – 1.25)	Dose relationship Risk ↓ with age ↑

BZD = benzodiazepines, T/CAD = tricyclic/cyclic antidepressants, SSRI = selective serotonin reuptake inhibitors, OR = odds ratio, RR = relative risk
Bold = significant; NS = non significant

ILLICIT DRUGS WITH AN INFLUENCE ON DRIVING PERFORMANCE

1) CANNABIS

- **Description and use**

  Cannabis is the collective term for the psychoactive substances of the *Cannabis sativa* plant. The cannabis products used are: marihuana (dried parts of the plant), hashish (resin of female flowering tops) and hashish oil (extract from the resin). The main active compound is tetrahydrocannabinol (THC); its content in the cannabis products is variable: hashish contains 2 to 10 % of THC, marijuana is less concentrated (from 0.5 to 7 % of THC, mean = 4 %), the oil contains up to 90% THC.

  Cannabis products are mostly smoked in combination with tobacco ("joint", 5-30 mg THC). They can be ingested in preparations such as tea, cake ("space cake"), sauces… The THC content of actual cannabis products is much higher (up to 40 %!) than twenty or thirty years ago. The effects are not comparable to those described in the sixties or seventies.

- **Pharmacokinetics**

  The bioavailability of THC is higher after smoking than after ingestion. The active compound is rapidly absorbed after smoking (peak 7-8 minutes). The THC plasma concentration rapidly decreases due to distribution in the tissues (THC is very lipophilic) and to metabolism (main metabolite is the inactive THCCOOH, excreted in urine and faeces). The THC in the tissues will be slowly released and metabolised when the intake is stopped, thus responsible for the long detection times of THCCOOH in urine. The presence of THCCOOH in the urine depends on dose and frequency of use and is not correlated with the effect.

- **Effects**

  The cannabis "high" is dependent on the personality of the user, his entourage, his cannabis experience…:
  - euphoria, relaxation, well-being, somnolence
  - increased social interaction, friendliness, laughing
  - changes in visual and auditory perception
  - altered perception of time and space
  - short-term memory loss
  - decreased psychomotor abilities
  - fear and panic
  - dysphoria, hallucinations, flash backs

  Physiological effects: cardiovascular symptoms with tachycardia and blood pressure changes, bloodshot eyes with dilated pupils.

- **Effects on driving performance**

  The influence of cannabis on perception, psychomotor performance, cognitive and affective functions is not compatible with safe driving. Co-ordination, tracking, perception, vigilance, and alertness are impaired.

  - *Experimental data*

    The EMCDDA report (36) mentions several experimental laboratory and simulator tests demonstrating that cannabis impairs tracking ability and attention, affects perception, prolongs response time and affects balance.

    Berghaus et al (37) performed a meta-analysis of the available data on the influence of cannabis (laboratory tests, driving simulator and real driving tests) A total of 324 experiments from 60 experimental studies are discussed. The authors classified the performance areas according to the sensitivity of THC-related impairment, based on the median (the concentration related to 50 % of the cumulated results being significantly negative). These plasma concentrations were not measured, but calculated based on the dose and pharmacokinetic parameters.

Table 12: Order of rank of the performance areas indicating THC-related impairment (37).

Performance area	ng/ml plasma	number of effects
Tracking	6	73
Psychomotor skills	8	29
Attention	9	44
Divided attention	11	59
Visual functions	12	25
Simulator/driving	13	113
En-/decoding	15	63
Reaction time	15	14
All performance areas	11	420

The concentrations are related to the post-smoking interval. The effects reach their maximum after the plasma peak (hysteresis).
Table 13 shows that THC-related impairment is concentrated within the first two hours after the beginning of the smoking procedure. Smoking of marihuana causes impairment of every performance area connected with safe driving. Attention, tracking and psychomotor skills show the highest percentages of deterioration.

Table 13: Percentage of significantly deteriorated parameters in post-smoking intervals (37).

Performance area	Time after the beginning of smoking						
	≤ 20 min	- 1 h	- 2 h	- 3 h	- 4 h	- 5 h	≥ 5 h
Tracking	59	80	67	33	25	0	-
Psychomotor skills	73	69	100	66	0	-	-
Reaction time	75	25	-	-	-	0	0
Visual functions	43	0	20	-	0	0	20
Attention	76	73	50	-	-	-	0
Divided attention	69	71	-	-	-	-	0
En-/ decoding	74	34	30	0	0	-	25
Simulator/driving	46	65	33	33	54	20	42
Number of studies	27	19	9	4	5	5	7

The real driving experiments conducted by Robbe (38) have demonstrated that:
- tracking is impaired (SDLP measurements): a THC dose of 100–300 µg/kg BW has an effect comparable to blood alcohol concentrations of 0.3-0.7 g/L
- in city traffic a dose of 100 µg/kg BW has an effect comparable to a blood alcohol concentration under 0.4 g/L
- drivers tend to overestimate the effect of cannabis and compensate their driving behaviour (speed ↓, following distance ↑, less overtaking)
- reaction time is increased in unexpected stress and emergency situations
- impairment is more important and persistent for difficult tasks needing continuous attention
- the effects are dose-dependent
- there is no correlation between the effect and the plasma concentration of THC or THCCOOH
- the combination of cannabis and alcohol has a major detrimental effect on driving performance

In summary the evidence clearly demonstrates that cannabis causes impairment in several psychomotor abilities. However it should be noted that most studies were conducted with fairly low doses of cannabis which may be different from real cannabis use situations.

- *Epidemiological data*

In most surveys reported in Europe cannabis is the most frequently detected drug (tables 4-6). Important differences in prevalence are observed, partly explained by differences in selecting the examined population and differences in drug use patterns in the European countries.
In Belgium, the BTTS (14) demonstrated that drivers with a positive THCCOOH-urine-test (6%) were 1.9 times more likely to be seriously injured (not significant) and 2.5 times more likely to be killed (significant).

The responsibility analysis of Drummer (23, table7) demonstrates that drivers using cannabis showed a trend to a decrease in relative risk when THC and/or THCCOOH were detected in blood and/or urine. The relative risk compared to drug-free drivers was 0.6 but this was not statistically significant. In his report Drummer mentions other studies suggesting that cannabis users may not have a higher risk of an accident. In combination with alcohol however the higher risk is clearly significant, comparable with the risk of the alcohol-only group. Terhune (24, table 9) also found that the responsibility rate for drivers with THC in their blood decreased compared to the drug-free control group.

2) OPIATES (HEROIN)

- **Description and use**

Opium is the dried milky exudation from the unripe capsules of *Papaver somniferum*-. It contains 4 to 21 % of morphine, 2 to 8 % of noscapine, 0.7 to 3 % of codeine, 0.5 to 1.3 % of papaverine and 0.2 to 1 % of thebaine (=opiates).
Heroin (diacetylmorphine) is synthesised from morphine by a double acetylation. Heroin is more lipophilic and reaches the brain more rapidly than morphine in such a way that euphoric effects are more intense than those of morphine. The purity of street heroin is variable (from < 25 to > 75 %), hence the danger for overdosing.
Heroin can be inhaled (by smoking or inhaling the vapours of heated powder), snorted or injected intravenously (usual dose 10-15 mg).
Morphine is a potent analgesic, therapeutically used for the relief of moderate or severe pain. Abuse is rare in Europe.
Codeine is a licit opiate with antitussive and analgesic properties.

- **Pharmacokinetics**

Heroin is very rapidly metabolised by deacetylation to 6-monoacetylmorphine (6MAM) and morphine (half-life heroin = 3-20 minutes; half-life 6MAM = 9-40 minutes). Morphine is transformed to its glucuronide or to normorphine before excretion in the urine (half-life morphine = 1-7 hours)
Codeine is partly (up to 10%) metabolised to morphine.

- **Effects**

The interaction of opiates with the opiate receptors of the CNS results in sedative, analgesic and antitussive effects. Respiratory depression is the cause of death in case of overdose.
Heroin quickly induces a “high”, a relaxation, a feeling of wellbeing, euphoria and warmth.
After 6-12 hours the very unpleasant sensations of withdrawal appear (cold turkey = sweating, runny nose, yawning, chills, abdominal cramps, muscle pain, nausea, diarrhoea…). The use of opiates leads to development of tolerance with physical and psychological dependence.
Physiological effects of opiates are constricted pupils (miosis), constipation and hypotension.

- **Effects on driving performance**

The sedation induced by opiates induces sleepiness, apathy and indifference to external stimuli, a decrease in concentration, a slowing down and an increase in reaction time. The combination with alcohol enhances the sedation.
The miosis has a negative influence on the accommodation of the eyes to darkness (e.g. when entering a tunnel, driving at night).
Finally the withdrawal symptoms induce loss of concentration and will also impair driving performance.

  - *Experimental data*

    For ethical reasons it is practically impossible to perform controlled experimental research with heroin although some studies with addicts who receive heroin as a substitution therapy are considered in Switzerland.

  - *Epidemiological data*

    In general the use of opiates is less frequently observed in driver populations than the use of cannabis (tables 4-6). Heroin addiction leads to a withdrawal from the social life in such a way that addicted subjects drive more and more rarely.
    In Norway monoacetylmorphine in drivers has increased from ± 10 in 1991 to ± 320 in 1998 (Annual Report 1998, NIFT).
    In the BTTS (14) the drivers who were positive for the illicit opiates (2%) had an increased risk of being seriously injured (x 3.4) and of a fatal outcome (x 2.3). These results were not significant, probably due to the small sample size.

There is a lack of consensus regarding the responsibility of opiates in road accidents. Some studies show a greater incidence of accidents among abusers, while others fail to demonstrate such a link (39).

3) COCAINE

- **Description and use**

  Cocaine is extracted from leaves of the coca plant *Erythroxylon coca*. The coca leaves can be chewed. The cocaine base ("free base" and "crack") is smoked, while the hydrochloride is snorted (25-100 mg) or injected (decomposes on heating).
  In some countries like Belgium, cocaine is still regularly used therapeutically as a local anaesthetic in ear, nose and throat and eye surgery.

- **Pharmacokinetics**

  The plasma peak is reached rapidly after injecting or smoking, later after snorting.
  Cocaine rapidly disappears from the blood (half-life 15-30 minutes), mainly by metabolism to benzoylecgonine and ecgonine methyl ester, inactive metabolites that are excreted in the urine.
  A major danger is associated with crack use, as it penetrates the brain more rapidly than cocaine injected intravenously.
  When cocaine and alcohol are combined, the active compound cocaethylene is formed, which has a longer half-life (produces a longer and more intense “high”) and seriously increases (x 20) the risk of a myocardial infarction.

- **Effects**

  During the cocaine “kick” the user experiences effects of euphoria, of increased alertness, activity, mental energy and self-confidence, sexual excitation, a loss of inhibitions, suppression of hunger and tiredness, sensory hallucinations. The euphoria is followed by a period of anxiety, paranoia and delusions. Finally a depressive phase with exhaustion, aggressiveness and nervousness incites the user to a new consumption.
  Physiological effects: dilated pupils, tachycardia and hypertension.

- **Effects on driving performance**

  All the stages of the cocaine effects are incompatible with safe driving.
  The subjectively experienced performance improvement will lead to increased risk-taking in traffic. The objectively observed performance impairment is due to a loss of concentration and attentiveness, and an increased sensitivity for blinding by light (dilated pupils). Moreover the psychological symptoms such as paranoia, delusions and hallucinations will have an influence on driving behaviour.

  - *Experimental data*

    For ethical reasons it is practically impossible to perform controlled experimental research with cocaine.
    Studies of the effects of cocaine on psychomotor performance are scarce. Cocaine seems to improve performance (attention and reaction time), but probably also risk taking.

  - *Epidemiological data*

    In Europe, but not in the United States, the prevalence of cocaine among drivers is amongst the lowest compared with other illicit substances. (tables 4-6).
    In the BTTS (14) the drivers who were positive for cocaine (0.7 %) had a higher risk of being seriously injured and of a fatal outcome (not statistically significant).

4) AMPHETAMINES / DESIGNER AMPHETAMINES

- **Description and use**

  Amphetamines and designer analogues are synthetic drugs. They are derived from β-phenethylamine.
  These drugs are stimulants and hallucinogens, sold as a powder (amphetamine) or in tablets (designer drugs) with various figure stamps. The composition of the tablets is very variable, the major drug often being mixed with other active compounds such as caffeine, atropine, flunitrazepam, ephedrine, or quinine. The stimulants are mostly used by young persons in raves and megadancings. This drug scene sees a very fast evolution in the choice and offer of stimulants. The drugs are mostly taken orally, although sometimes they are snorted (amphetamine) or injected.

  Amphetamine = speed, pep pills, uppers

Methamphetamine = ice

MDMA = 3,4-methylenedioxymethamphetamine = XTC, ecstasy, love drug, Adam
MDEA = 3,4-methylenedioxyethamphetamine = Eve
MBDB = N-methyl-1-(1,3-benzodioxazol-5-yl)-2-butanamine

- **Pharmacokinetics**

  Amphetamines are excreted unchanged in the urine.
  MDMA and MDEA are partly metabolised to MDA, which is also detected in the urine.

- **Effects**

  Amphetamines are central stimulants. They suppress feelings of tiredness and hunger, and increase mental alertness and physical energy. In addition they stimulate the mood and increase self-confidence.
  The original therapeutic applications of amphetamine were treatment of narcolepsy, of obesity (anorectic effect) and hyperactive behaviour in children. Amphetamines are used by truckers and students to stay awake over long periods. The concomitant effects of euphoria and mood stimulation have lead to drug abuse.
  Because of the tolerance development, some abusers are known to swallow or inject up to 2000 mg daily. High doses lead to hallucinations, psychosis and dysphoria.
  MDMA and analogues have a dual effect: they are stimulants (dance-pills) and entactogens (emotional disinhibition and increased social communication abilities). When these effects decrease negative sensations of fatigue, anxiety, emptiness and depression appear. Later a hangover is experienced with headache, muscle aches, exhaustion, apathy, sweating, nausea, …
  Recent studies (40,41) have revealed the toxic effect of chronic MDMA-use on brain serotonin neurones in humans, associated with mild impairment of memory and serotonergic neuroendocrine function.
  Physiological effects: dilated pupils, tachycardia and dry mouth.

- **Effects on driving performance**

  During the "high", reaction time and vigilance are improved due to the stimulating effect. However increased self-confidence will increase risk-taking in traffic. The user loses his sense of reality. The dilated pupils make the user sensitive to blinding by light.
  After the "high" the feelings of exhaustion and depression of the hangover have a detrimental effect on driving performance.
  The excitation and aggressiveness, induced by these substances, lead to inadequate driving. These stimulants will suppress sleepiness and fatigue, but a rebound effect can occur when the blood concentration becomes low. As a paradigm, either high or low blood concentrations are dangerous for driving.

  - *Experimental data*

    There are few studies of the influence of amphetamines on psychomotor function (36). Sometimes amphetamines are reported to result in psychomotor enhancement (generally at low doses): researchers noted enhanced effects on measures of motor co-ordination and control, monitoring, vigilance and physical endurance. Increased risk-taking appeared at doses of 10-15 mg.
    For MDMA and analogues there is little experimental evidence regarding their effects on psychomotor and driving performance (36). Some studies indicate memory decrements in XTC users. Different test subjects experienced toxic psychosis, dysphoria, anxiety, flashbacks.
    In the Netherlands a study of the influence of MDMA on driving performance is planned to start in October 1999.
    In the conclusions of their literature study, Schulz et al. stated that for amphetamines (as well as for cocaine) "the experimental material analysed is not suitable for indicating the hazard resulting from impairment of the driving ability on the basis of "dimensions and figures". This should not induce the hasty conclusion that the drugs mentioned are of only minor significance for traffic safety. Publications of the non-experimental type and case reports show that amphetamines and cocaine have a negative influence on the performance capabilities in the reality of drug consumption. The fatal effects include euphoria, restlessness, anxiety, agitation and confusion. Moreover, of particular importance are the increase in the willingness to take risks, impairment of the ability to think critically and make judgements, exaggerated sense of self-esteem, misinterpretation of situations and loss of reality.
    However, in many cases, it is not the acute effect of the drug, but rather the exhaustion and overexertion resulting from the stimulation as well as other problems arising from misuse that are decisive for impairment of the driving ability resulting from psycho-stimulation". (42)

- *Epidemiological data*
  The prevalence of amphetamines in different driver populations is, in general, lower compared to opiates (9, tables 4-6). A remarkable exception is the study by Skurtveit (15): in Norway the largest increase in the number of drivers suspected of drugged driving was found for amphetamines (>145% from 1991 to 1994). Recent data show a further increase from 550 cases in 1994 to about 1300 drivers in 1998 (145% again) (Annual Report 1998, NIFT). Norway has the highest prevalence of amphetamines in non-fatal accidents. The detection of methamphetamine in drivers has recently dramatically increased in Finland: a tenfold increase was observed in 1998 compared to the preceding years, the "ice" cases constituting a 20% fraction of the amphetamines-group (unpublished statistics of KTL). The West-Scotland study (20) also revealed a high percentage of amphetamine (amphetamine + MDMA + MDEA) -positive urines (25%) in its tested population of suspected drugged drivers.
  In the BTTS (14) subjects with a positive test for amphetamines (3%) in urine were much more likely to be seriously injured (x 4). In collisions with an obstacle the prevalence of amphetamines was higher than in accidents between road users (5.6 vs. 2.2%, not significant).
  Drivers positive for stimulants (amphetamines and ephedrine) were more often responsible for the accidents than subjects with negative tests (23,24).

5) OTHER SYNTHETIC DRUGS / HALLUCINOGENS

❑ Description, use and effects

- *Gamma hydroxybutyric acid (GHB)*
  Gamma hydroxybutyric acid is a substance that is naturally present in mammal species. It is used as an anaesthetic agent, but other indications have been suggested like the treatment of insomnia, alcohol and opiates withdrawal, and many cerebrovascular disorders.
  After oral absorption, the GHB peak is reached in serum after 20 to 45 minutes, and the half-life is proportional to the amount ingested (more or less 20 minutes). Metabolism occurs in the liver with oxidation in CO_2. Urinary elimination is very limited (1 to 5 % of the absorbed quantity).
  GHB is also abused for non-medical purposes, for its euphoric, sedative and anabolic (bodybuilding) effects. An "amphetamine like" sensation is obtained after 20 to 30 mg/kg, and from 10 mg/kg, amnesia and muscular relaxation can be observed. These properties have led to its use as a rape drug. Physical dependence can be noted; side effects are nausea, vomiting, vertigo, sleepiness, bradycardia and respiratory depression. Coma and seizures have been reported following GHB abuse. Patients regain consciousness spontaneously within a few hours after ingestion. Association with alcohol or other psychoactive drugs is very dangerous (reinforcement of side effects).

- *LSD (lysergide)*
  LSD, familiarly called "acid", is the synthetic version of ergotamine, produced by ergot, a parasite of rice or rye. It is the diethylamide of lysergic acid. Dr Hoffman (Sandoz) studied it in the forties, as a drug for treatment of mental disorders. LSD was misused very quickly after its discovery for its hallucinogenic effects, because the active dose of this hallucinogenic is so small that the drug can be delivered in many forms (microtablets, window pane, stamps).
  The effects appear 15 minutes to 1 hour after ingestion, and can last 6 to 8 hours. Tolerance will develop after only a few days. Cardiac frequency, blood pressure and temperature are increased, spatio-temporal distortion and depersonalisation are frequently reported. Reaction time is significantly increased. Users can be so afraid that they will make suicide attempts. LSD induces a solid psychic dependence.

- *Magic mushrooms*
  Magic mushrooms belong essentially to 3 groups: *psilocybe*, *panaeolus* and *conocybe*. The psychoactive hallucinogenic substances are psilocybin and psilocin, chemically similar to LSD. Effects can be obtained with 10 to 60 mg, and can last 5 to 6 hours. First, the user will be affected by nausea, and then sensations affecting eyes, hearing and consciousness will occur. These products seem to induce less panic than LSD.

- *Mescaline*
  Mescaline is the active compound extracted from the peyote, a cactus from Central America. The chemical structure is 3,4,5-trimethoxy-phenethylamine. After oral ingestion, 66 % can be absorbed. The effects are very similar to LSD, with reinforcement of "colour" visions. Users call mescaline the "mellow LSD", but real hallucinations are more frequent than with LSD. Tachycardia, hypertension,

hyperthermia, hypersalivation and tremor are the most frequent side effects. Mescaline induces tolerance, psychic dependence and sometimes physical dependence.

- **Effects on driving performance**

  The effects of the drugs described in this chapter are not compatible with safe driving. However epidemiological (drugs not systematically screened) and experimental data on these compounds are lacking. Stephens and Baselt (43) report a case of a driver found asleep behind the wheel of his car at rest in a traffic lane with engine running. His symptoms were: nystagmus, muscle flaccidity and severe ataxia. As his urine was highly positive for GHB, the authors conclude that GHB may cause impairment of the psychomotor skills required for safe driving.

MEDICINAL DRUGS WITH AN INFLUENCE ON DRIVING PERFORMANCE

Psychotropic medicines act on psychic function, behaviour and experience; they alter the mental state by affecting the neurophysiological and biochemical activity of the functional units of the CNS (e.g. anxiolytic sedatives, antidepressants, neuroleptics, psychostimulants). The *therapeutic* action of these medicines may have an influence on driving. On the other hand non-psychotropic drugs can impair driving due to certain side effects, often linked to the penetration of the molecules through the blood-brain barrier (e.g. antihistamines, beta-blockers)

Therapeutic or secondary effects of medicines which can have a detrimental effect on driving performance are:
- *somnolence*: induced by many medicines (hypnotics, antidepressants, neuroleptics, antihistamines, narcotic analgesics,..)
- *loss of psychomotor co-ordination*: medical treatment can influence the ability of the patient to integrate data correctly and react adequately (precision and rapidity)
- *behavioural changes*: can lead to risk-taking and altered estimation of speed and distance
- *bilance disturbance*: e.g. vertigo
- *sensory disturbances*: e.g. visual accommodation problems due to ophthalmic medication

Factors that determine the possible influence on driving depend on:
- *the medication*: dose, time after intake, tolerance development,…
- *the patient*: age, individual sensibility, physical and psychological condition (e.g. stress, fatigue, visual acuity), pathologies (e.g. psychotic and neurological disorders, diabetes, epilepsy)

1) HYPNOTICS, SEDATIVES, ANXIOLYTICS

Benzodiazepines were introduced as a safer alternative to barbiturates. Meprobamate has pharmacological properties similar to those of barbiturates. More recently, new compounds such as buspirone, zopiclone or zolpidem have been commercialised.

BENZODIAZEPINES (BZD)

BZD have a widespread use for the short-term treatment of insomnia, the symptomatic relief of anxiety disorders, and as anticonvulsants.

- **Effects**
  BZD produce sedation (low doses) and hypnosis (higher doses). They have a central muscle relaxant activity. They may potentiate other CNS depressants. BZD have a high therapeutic index and the adverse effects are minor. Chronic abuse may induce tolerance; withdrawal symptoms are observed after stopping the BZD use (hypersensitivity to light and sound, tremor, sweating, insomnia, abdominal discomfort, and tachycardia).
  BZD are qualitatively comparable but differ in pharmacokinetic parameters and duration of the effects. Some BZD act quickly and have a short halflife; they are preferably used as hypnotics. Other BZD have an intermediate or long half life and are used as anxiolytics and sedatives. The duration of the effects depends on half life, the formation of active metabolites and the distribution of the drugs.
  BZD abuse, the non-therapeutic use of BZD - often in high doses - as a “drug” to induce euphoria, is extensive.

- **Effects on driving performance**
  The most important (side) effects of benzodiazepines, susceptible of impairing driving performance, are somnolence and sedation, loss of motor co-ordination, memory impairment, behaviour disinhibition and paradoxical agitation.
  BZD are about the most solidly documented drug group with regard to the influence on driving behaviour.

- *Experimental data*
  Numerous studies describing the results of laboratory, simulator and real driving tests after intake of BZD have been published. A common finding is sedation and sleepiness related to impairment in psychomotor tests (36,44). Diazepam is a BZD with a severe influence on driving abilities and is used as a verum in many studies.

- *Epidemiological data*
  BZD are the most frequently detected licit drugs in all driver populations (9, 36, tables 4-6). The prevalence of these drugs in the general driving population is rather low (Germany 3%). BZD are normally used in the older age category (> 40 y). In studies on drivers suspected of driving under the influence. BZD are found with very high prevalence (e.g. Denmark and West-Scotland: 53-78%). In accident-involved drivers the prevalence is lower (up to 13%).

- *Responsibility studies and studies with controls*
  - In his responsibility analysis study Drummer (23) observed higher culpability ratios in drivers, positive for BZD, while Terhune (24) found no difference. However both studies show statistically significant higher culpability when BZD was combined with alcohol.
  - Currie et al. (26) compared blood sample results for BZD from people responsible (n=163) and non-responsible (n=63) for an accident: in the responsible group 18 people were positive for BZD and 4 had combined BZD and tricyclic antidepressants, while in the non-responsible group one person was positive for BZD.

- *Pharmaco-epidemiological studies*
  In most pharmaco-epidemiological studies (table 11) a significantly increased risk for accident involvement was revealed for drivers taking BZD.
  - In a study of elderly drivers (>65 y) Ray et al. (29) found that the relative risk of injurious crash involvement for BZD users was 1.5. The risk increased with dose and was substantial at high doses: 2.4 for ≥ 20 mg diazepam.
  - Hemmelgarn (30) examined records of 5579 elderly people involved in crashes (1990-93) and 13256 controls: there was a significant increase in rate of crash involvement within the first week of long half-life BZD use (1.45); the rate ratio for continuous use up to one year was lower but still significant (1.26). There was no increased risk after initiation or continued use of short half-life BZD.
  - Oster et al. (31) compared 4554 persons who had been prescribed BZD tranquillisers with 13662 controls with prescriptions for other drugs. The probability of an accident-related medical encounter was higher during the months following the prescription of a BZD (1.15. vs control ; 1.28 vs the same person in period when he/she was not exposed to drugs).
  - Leveille et al. (32) performed a matched control study of older drivers involved in injurious crashes (234 cases/447 controls). Current use of BZD had little association with increased risk. This study is an exception to all other observations.
  - A study by Neutel (33) of 148000 people having received a BZD and 98000 controls revealed an odds ratio of hospitalisation of 3.9 within for 4 weeks and 6.5 within 2 weeks after the prescription of a BZD hypnotic, of 2.5 within 4 weeks and 5.6 within 2 weeks of the prescription of a BZD anxiolytic. The highest risk group were the younger males.
  - In another study Neutel (34) compared the risk of injurious traffic accidents in older (>60) and younger adults (225796 persons with a first BZD prescription and 9762 controls). The risk of accidents within the first 4 weeks was increased: 3.1 for all persons, 3.2 for persons under 60, 2.8 for older people. Flurazepam induced the highest risk (5.1), followed by triazolam (3.2), diazepam (3.1) and lorazepam.
  - In the within-person case crossover study of Barbone et al. (35) out of 19386 drivers involved in an accident 1731 used a psychoactive medicine. The odds ratio was increased only for BZD (1.62). Use of an intermediate half-life BZD was not significantly associated with a higher risk. The risk was significantly increased for long half-life anxiolytic BZD. The BZD-associated risk decreased with age. The authors calculated that in the UK 1577 accidents, of which 110 fatal, could be prevented if users of anxiolytic BZD did not drive.

2) ANTIDEPRESSANTS (AD)

This therapeutic class includes
- first generation AD = tricyclic compounds (e.g. amitriptyline, imipramine, clomipramine)
- second generation AD (e.g. maprotiline, trazodone)
- third generation AD = selective serotonin reuptake inhibitors or SSRI (e.g. sertraline, fluoxetine, paroxetine)
- monoamine oxidase (MAO) inhibitors
- lithium salts

Antidepressants are prescribed to treat affective disorders such as different forms of depression, panic disorders, phobias, bulimia nervosa, obsessive-compulsive behaviour,..

- **Effects**

  Among the secondary effects of antidepressant drugs we observe sedation (table 14), tremor, insomnia, blurred vision, mental confusion and dizziness. These effects and their intensity depend on the molecule, on the dose, timing of administration and the individual sensitivity. The side effects of the tricyclic compounds can be quite severe (cardiac arrhythmia). The newer compounds clearly have fewer adverse effects.

  Table 14: Classification of antidepressants according to their sedative properties.

No sedation	***Minor sedation***	***Moderate sedation***	***Severe sedation***
Citalopram	Desipramine	Clomipramine	Amitriptyline
Fluoxetine	Phenelzine	Imipramine	Dosulepine
Fluvoxamine		Maprotiline	Doxepine
Moclobemide		Nortriptyline	Mianserine
Paroxetine			Trazodone
Sertraline			Trimipramine
Viloxazine			

  (Lofepramine: inconclusive data. Opipramol, melitracene, iproclozide, nialamide: absence of data)

- **Effects on driving performance**

  Depressive patients may have an impaired driving behaviour for two reasons:
  - the pathology itself involves cognitive troubles, concentration and attention disturbances, anxiety, irritability, tiredness secondary to insomnia
  - the adverse effects of the antidepressants (sedation) may be detrimental.

  On the other hand adequate treatment may improve the driving performance of depressive patients due to the drug relieving their depressive symptoms.

  The newer compounds with fewer side effects will be a better choice for drivers.

  - *Experimental data*

    In a review of the literature published in 1985 (45) Linnoila and Seppälä have found that studies with healthy volunteers on single doses show that the more sedative drugs induce more impairment. Many studies on psychomotor and driving performance since have analysed antidepressants, the first generation tricyclics (most sedative) often being used as a verum in the studies of the newer drugs (36,44).

  - *Epidemiological data*

    The prevalence of (tricyclic) antidepressants in the general driving population is unknown due to lack of screening data in the reported surveys. Data are scarce in accident-involved or DUI-suspected drivers: prevalences are generally very low (≤ 1.5%) with an astonishing unexplained high prevalence of 21% in fatally injured drivers in a French study (9, tables 4-6).

  - *Responsibility studies and studies with controls*
    - Currie et al. (26), in his study of 229 blood samples, found in the responsible group 6 persons positive for tricyclic antidepressants and 4 persons having combined BZD and tricyclics. In the non-responsible group only one tricyclic positive was detected.

  - *Pharmaco-epidemiological studies*
    - According to the study of Ray et al. (29) patients under cyclic antidepressants have a significantly increased risk for an injurious crash (2.2). The risk is dose-dependent. The intake of amitriptyline at doses ≥ 125 mg daily increases 6 times the risk for road accidents.
    - Neutel (33) and Barbone et al. (35) found no increased risk of accident related to the intake of antidepressants.

3) NEUROLEPTICS

Psychoses are mental disorders characterised by disturbances of the thought process leading to distortions of affective responses and reality. Neuroleptics or antipsychotics are agents used for the treatment of psychosis and include the phenothiazines (e.g. chlorpromazine), the butyrophenones (e.g. haloperidol), the thioxanthenes (e.g. flupenthixol), and the substituted benzamides (e.g. sulpiride).

- **Effects**

  The antipsychotics have variable antagonistic actions on different neurotransmitter systems; the inhibition of the central dopaminergic receptors is a major common characteristic.
  The numerous adverse effects derive from the pharmacological actions. Neuroleptics all are sedative; the degree of sedation depends on the molecule(group). They also cause, with varying degree, the troublesome extrapyramidal effects, such as akathesia (mental and motor restlessness), Parkinsonism-like syndrome, dystonic reactions (e.g. facial grimacing, torticollis) and tardive dyskinesia (e.g. protrusion of tongue and lipsmacking, choreiform movements of trunk and limbs).

- **Effects on driving performance**

  Adverse effects prejudicial for driving are:
  - sedation
  - motor disturbances of the extrapyramidal effects
  - decline of cognitive functions
  - reduction of visuo-motor abilities and vigilance
  - aggressiveness, temporary aggravation of psychotic troubles.

  However, a similar remark as for the antidepressants is in order: without adequate treatment, patients can demonstrate a variety of cognitive problems, attention or motor deficits, that are more detrimental for driving than the adverse effects of the medication. Actually the use of neuroleptics may enable the patient to resume his social activities among which driving his car.

  - *Experimental data*

    A literature search on the effects of neuroleptics reveals an important lack of information in the field of these drugs and their effects on driving behaviour (44). The available data mostly involve observed side effects and results of laboratory tests. Moreover the experimental studies often tested the effects of neuroleptics on healthy volunteers, as it is difficult to maintain sufficient motivation and compliance with psychiatric patients and to compose a homogeneous study population. In healthy subjects neuroleptics induce various effects susceptible of influencing driving ability (somnolence, behavioural changes, decreased vigilance and performances). In studies on patients similar adverse effects were observed, however the results of the research teams are often contradictory or inconclusive. The attenuating effect of the neuroleptics on the psychosis and the heterogeneity of the pathologies may complicate the conclusions.

  - *Epidemiological data.*

    Data on the prevalence of neuroleptics in driving populations are completely lacking.

4) NARCOTIC / OPIOID ANALGESICS

Opioids are all substances with a mechanism of action and side effects comparable to morphine. The opioids include the naturally occurring opium alkaloids (opiates), the semi-synthetic (e.g. dihydrocodeine) and the synthetic (e.g. propoxyphene, methadone) medicines.
The opioid most extensively used in heroin detoxification maintenance programs is methadone, but in some countries (e.g. France) buprenorphine is also used.

- **Effects**

  Narcotic analgesics interact with the opioid receptors in the CNS and produce analgesia, mood changes, mental clouding and narcosis. Their primary use is the treatment of severe pain (burns, trauma, terminal illness).
  They have sedative and respiratory depressant effects, cause miosis and contraction of the smooth muscle, and block peristalsis.

- **Effects on driving performance**

  Effects relevant for driving safety are sedation, impairment of cognitive functions, mood changes (dysphoria and euphoria), impairment of psychomotor functions and pupil restriction. Sedation and cognition impairment are important in the beginning of treatment but seem to wear off in most patients after some days or weeks.

  In a BAST report by M. Lakemeyer (46) about opioid analgesics and driving safety, a survey among pain physicians and their patients led to the following conclusions: absolute driving unfitness exists at onset of the treatment, when important changes in drug dose are introduced and when other CNS depressants or alcohol are co-ingested. In long-term stabilised opioid therapy with unchanged doses no impairment of driving behaviour is observed.

  Experimental studies on cancer patients have demonstrated that long-term treatment with morphine does not increase the risk of road accidents (47,48).

  The review by Friedel and Berghaus (49) and the EMCDDA (36) report mention several experimental studies of the effect of methadone on naï ve subjects, methadone maintenance patients and ex-heroin addicts. Some discrepancies in the study results notwithstanding, the following conclusions can be made: in naï ve subjects acute methadone administration induces a dose-dependent reduction in reaction time, in visual acuity and in information processing, thus when starting up the methadone treatment the subject is unfit to drive. Once stabilised on the program there is little evidence of driving impairment: on different measures of psychomotor performance "optimal" methadone users did not differ from controls. However many methadone users frequently take other psychotropic medication.

  The aim of a methadone programme is the physical and social rehabilitation of heroin addicts, to allow them to lead a normal life (including driving). To evaluate driving abilities a case by case examination is needed that takes into account several circumstances: a substitution period of more than one year, a stable psychosocial integration, a sense of responsibility, therapy compliance, and no intake of other psychotropic substances or alcohol.

  - *Epidemiological data*

    In most epidemiological studies the prevalence of opiates is mentioned but identification of the molecules (illicit = heroin, 6MAM, morphine vs licit = codeine) is seldom described.

    In the BTTS (14): besides a 5.5% positives for licit opiates, very low prevalences for methadone (0.4%) and dextropropoxyphene (0.2%) were observed. Studies in Strathclyde (West of Scotland), Switzerland and Denmark revealed an important prevalence of methadone positives (10-13%) in drivers suspected of driving under the influence. Moreover the Strathclyde survey showed an important use of dihydrocodeine in suspected drugged drivers (table 6).

  - *Pharmaco-epidemiological data*

    The study of Ray et al. (29) showed no increased risk for injurious crash in elderly persons having been prescribed opioids. On the other hand Leveille et al (32) observed a significantly higher risk of crash (1.8) with these analgesics in elderly persons.

5) ANTIHISTAMINES (H1-receptor antagonists)

Antihistamines are used for treating allergies such as hay fever and urticaria, and travel sickness. They act by competitive inhibition and block the effects of histamine.

- **Effects**

  Sedation is observed mostly with the first generation compounds (e. g. diphenhydramine, triprolidine) and is a consequence of their depressive activity on the CNS due to their ability to cross the blood-brain barrier. New agents (e. g. astemizole, terfenadine) do not cause significant sedation because of poor penetration of the CNS.

  Other side-effects include gastro-intestinal disturbances, headache, blurred vision, elation or depression, irritability.

- **Effects on driving performance**

  Adverse effects that can impair driving fitness are mostly sedation-related: drowsiness, dizziness, decreased alertness and concentration, inco-ordination, muscular weakness.

  As the new generation antihistamines cause very little sedation, they are likely to have little impairing influence on driving.

- *Experimental data*
  Many studies comparing the influence of both antihistamine generations on psychomotor skills and driving behaviour have been published. The new drugs both enhance and impair performance depending on the dose; they are free of detrimental effects at low therapeutic doses; sedation may occur at higher doses and in sensitive patients (36,44,50).

- *Epidemiological data*
  Very few epidemiological studies mention this drug category in driving populations. The samples of the BTTS are being analysed for the presence of antihistamines (spin-off study).

- *Pharmaco-epidemiological studies*
  Antihistamines are also seldom mentioned in pharmaco-epidemiological studies. An important reason may be that many antihistamines are over-the-counter products, without the need for a prescription.
  Skegg et al. (28) found a relative risk of accident involvement of 1.8 (not significant) for antihistamine-users. However a significant increase (5.3) was observed in motorcycle accidents.
  Ray et al. (29) and Leveille et al. (32) found no increase in risk of crash involvement associated with the use of antihistamines.

TO THEIR INFLUENCE ON DRIVING PERFORMA WARNING SYSTEMS IN EUROPEAN COUNTRIES (Table 16)

1) CATEGORISATION SYSTEM by Wolschrijn et al.

This categorisation system is based upon expert ratings, assembled by means of a questionnaire with about 30 categorisation of about 570 drug doses/formulations or effects for a -
ratings were summarised and translated into group scores (summing the s
number of ratings => mean). The mean value has been calculated to give an estimation of the impairment

however

research standardised.
It was possible for experts to achieve consensus concerning an important number of drugs in about every macological group. Their rank ordering of drugs/doses is clinically relevant and is important for prescribing

: Description of the categories of the Wolschrijn system.

		iption
I*	1	No impairment presumed
II.2	3	Moderate impairment
III	4	Severe impairment

ABDA (German pharmacist association)
The classification of medicines represented in the German brochure for health
(52) is based on Wolschrijn's categorisation. The mean values of the expert quota represent the relative degree of

Overview table: same mean values as Wolschrijn

2) CATEGORISATION OF MEDICINES IN BELGIUM

About 180 medicinal substances, available in Belgium (1997) and belonging to therapeutic classes susceptible of - -
narcotics, antihistamines, beta blockers, central stimulants and antidiabetics), were classified on the basis of

Wolschrijn et al.: 7 classes ranging from no effect (I) through minor an
(III), completed with the respective * categories (I*, II*, III*) for classes with insufficient scientific data (classes molecules).
The classification of the substances proved to be problematic due to the lack of study data (42% of the -

- he assignment of one category per drug is often inadequate.

The classification was published in a brochure, distributed among the Belgian physicians and pharmacists.

Overview table: mentions the assigned category per molecule

3) ITALY

Ferrara reviewed literature data about laboratory, simulator and real driving tests of the influence of medicines (53). Forty four molecules are listed as provoking driving disability.

Overview table: D = disability for driving

4) NETHERLANDS

The Royal Dutch Society for the Advancement of Pharmacy has composed a list of drugs that can affect driving based on the pharmacodynamic profile or therapeutic class. A yellow warning label with black letters indicates that the drug can affect driving performance (not mandatory).

Overview table: *+ = drug with a yellow warning label*

5) NORDIC COUNTRIES

In 1981 a warning label was introduced in Norway and adopted by Denmark, Finland, Iceland and Sweden. It consists of a red triangle printed by the manufacturer on all packages of drugs considered as "especially dangerous": sedative-hypnotics, opioid analgesics and antitussives, centrally acting muscle relaxants, antihistamines, some antiepileptics and psychostimulants. The red triangle is combined with a warning concerning driving in the specific description in the Norwegian Catalogue for medicinal drugs on the market in Norway.
For other medicines there is only a warning in the Catalogue (no triangle). Physicians and pharmacists should always inform the patients when prescribing/delivering such drugs (instruction not always followed!).
At the request of the prescribing physician, a warning label can also be attached to "potentially dangerous" drugs like non-narcotic analgesics, antidiabetics, anorectics, antiparkinson drugs, hypotensives, neuroleptics, antidepressants, anticholinergics and ophtalmologicals.
Norway has few benzodiazepines compared to other countries (also the Nordic); all benzodiazepines have a red triangle (as in the other Nordic countries).

Overview table: + = drug with a red triangle warning label
w = drug with warning in Norwegian Catalogue

6) FRANCE

As from 3 May 1999 a warning sign (= red triangle with a car in the centre) is legally required on the packages of drugs with possible influence on driving. In a first approach this will be based on the information provided by the drug companies (package insert).

General remark about table 16:
The table does not consider the availability of a product in the concerned countries. When the medicinal substance is available and has a warning label or an assigned impairment category, it is mentioned in the table. A blank case = not available / no label or category.

Table 16: Categorisation and warning systems in European countries

		WOLSCHRIJN							
MOLECULES	**DOSAGE (mg)**	**+ Germany**	**I, II.1, II.2 and III / I*, II* and III***	**Belgium**	**Nether.**	**Italy**	**Norway**	**Finland**	
acarbose				-					ANTIDIABET.
acebutolol				I*					BETA-BLOCK.
acetyldihydrocodeine				II*					NARCOTICS
acrivastine	4	1.6	3/0						ANTI H1
	8	1.6	3/0						
adinazolam	30	3	1/2			D			SED.- ANXIOL.
alfentanil					+	D	w		ANESTHET.
alimemazine					+		+		ANTI H1
allobarbital	30	4	1/1		+				SED.- ANXIOL.
	100	4	1/0						
	200	4	1/0						
alprazolam	0.25	2.5	6/2	II.2	+		+	+	SED.- ANXIOL.
	0.5	2.8	6/2	II.2	+				
	1	3.5	2/4	II.2	+				
alprenolol				I*					BETA-BLOCK.
amfepramone	50	U	0/1	I*					CENT. STIM.
aminogluthetimide							+		ANTINEOPLAS.
amisulpiride	100	1	1/0						NEUROLEPT.
amitriptyline	12.5	3.5	2/0	III	+	D	+		ANTIDEPRESS.
	25	3.9	12/0	III	+	D			
	50	3.9	13/0	III	+	D			
	75	3.9	13/0	III	+	D			
amobarbital	15	4	2/2	III	+				SED.- ANXIOL.
	50	4	3/1						
	100	4	1/1						
	200	4	1/1						
amphetamine	5	3.5	2/1	II.1	+				CENT. STIM.
	10	3	1/1						
antazoine					+				ANTI H1
aprobarbital					+				SED.- ANXIOL.
astemizole	10	1	7/0	I					ANTI H1
	30	1.2	5/0						
atenolol	50-100	1.2	5/0	I					BETA-BLOCK.
atropine	0.4-0.6	3.1	5/1			D			ANTICHOLINERG.
	0.85-1.7	3	2/1						
	2	1	1/0						
azatadine	1	3	3/2	II.1					ANTI H1
	2	3	3/1						
	4	3	1/1						
baclofen	5	1	1/1		+		+	+	MUSCL. RELAX.
	20	2	1/0						
barbital	250-500	U	0/1		+				SED.- ANXIOL.
befunolol				I*					BETA-BLOCK.
benperidol	0.25	1	0/1	II*	+				NEUROLEPT.
benzatropine	0.5	U	0/1						ANTIMUSCARIN.
benzoctamine	10	U	0/1						SED.- ANXIOL.
	20	U	0/1						
betahistine	8-16	1	1/0	I					ANTI H1
betaxolol				I*					BETA-BLOCK.
bezitramide				III*					NARCOTICS
biperiden							w	+	ANTIMUSCARIN.
bisoprolol	5	1	1/0	I*					BETA-BLOCK.
brallobarbital				III*	+				SED.- ANXIOL.
bromazepam	1.5	2.6	7/1	III	+				SED.- ANXIOL.
	3	3.1	6/2						
	6	3.8	6/1						
	12	4	6/1						
bromisoval					+				SED.- ANXIOL.
bromperidol	1	3	0/1	II*	+				NEUROLEPT.
brompheniramine	4	U	0/2	II.2			+	+	ANTI H1
	8	U	0/2						
	12	3	1/2						
brotizolam	0.125	3	0/6	II.2	+				SED.- ANXIOL.
	0.25	3.7	2/3						
	0.5	U	0/1						
buclizine	25	U	0/1						ANTI H1
	50	U	0/1						
bupranolol	50-200	1	1/0						BETA-BLOCK.

MOLECULES	(mg)	WOLSCHRIJN	I, II.1, II.2 II* and III*		Nether.	Italy		Finland	
buprenorphine	0.2-	3.5	2/1		+	D		+	NARCOTICS
	10	2	3/1						ANTIDEPRESS.
buspirone		1.2	13/0		+				SED.-
		1.4	12/0						
	20		9/2						
	30	3							
butalbital	50		1/1		+		+	+	- ANXIOL.
	100	4							
butobarbital	50		1/2		+				SED.-
		4	1/1						
	200		1/1						
butorphanol					+				NARCOTICS
	25	2							ANTIDEPRESS.
	50	1							
camazepam	10		1/1						- ANXIOL.
	20	3							
captopril	1		1/0						
carbamazepine	200		2/1	II.2			+	+	
		3.2	4/0						
							+		ANTIEPILEPT.
carbinoxamine		U	0/1						
		U	0/1						
	12		0/3						
carbromal					+				- ANXIOL.
carisoprodol								+	MUSCL. RELAX.
	10	1		I*					BETA BLOCK.
				II					-BLOCK.
celiprolol									-BLOCK.
cetirizine		1.2	5/0						
		2.3	5/0						
	500 1000		1/1		+				SED. ANXIOL.
							+	+	
chlordiazepoxide		2.9	7/0		+		+	+	- ANXIOL.
	10	3							
	-25	3.5							
chlormezanone	100		2/0		+				SED.-
		2	2/0						
	1	3		II.2		D			
		3.5	4/1						
	12		3/0						
chlorpromazine	-20	3		III	+				NEUROLEPT.
	25-	4	2/2						
				-					ANTIDABET.
chlorprothixene		4	1/0		+				
chlorzoxazone					+				MUSCL. RELAX.
cimetidine		1.4	4/1						
		1.4	4/1						
	800		1/0						
cinnarizine		1	1/1		+	D		+	ANTI H1
	50		1/						
citalopram	40		1/1	II.1					ANTIDEPRESS.
clemastine		3.2	9/1		+		+		ANTI H1
clobazam		1.9	7/0		+		+	+	- ANXIOL.
	20	2.3							
clomethiazol	300				+		+		NEUROLEPT.
	600 1200								
	25	2.7		II.2	+		w		ANTIDEPRESS.
clonazepam		4	1/0				+		SED. ANXIOL.
	0.025	4							CARDIOVASCUL.
	0.075	4							
		4	1/1						
	5	3		II*	+		+		SED. ANXIOL.
	15		1/0						
clotiapine									
clotiaz				III*					SED. ANXIOL.
	75	1							ANTIDEPRESS.
				II.2					SED. ANXIOL.
	100	3							NEUROLEPT.
codeine		2	1/3		+	D		+	NARCOTICS
	100		3/0						

MOLECULES	DOSAGE (mg)	WOLSCHRIJN		Belgium	Nether.	Italy	Norway	Finland	
		+ Germany	I, II.1, II.2 and III / I*, II* and III*						
cyclizine	50	U	0/2		+		+	+	ANTI H1
cyclobarbital	100	4	1/0		+				SED.- ANXIOL.
	400	4	1/0						
cyproheptadine	4	U	0/2	II.2	+				ANTI H1
dantrolene					+				MUSCL. RELAX.
deptropine					+				ANTI H1
desipramine	25	2.5	2/3	II*	+				ANTIDEPRESS.
	50	3	0/2						
	75	4	1/1						
dexchlorpheniramine	2	3	1/1	II.2	+				ANTI H1
dextromethorphan	10-20	1	1/0				+	+	ANTITUSSIVE
dextromoramide				III*	+				NARCOTICS
dextropropoxyphene	65	2.5	2/1	II.2	+	D	+	+	NARCOTICS
	150	3.3	2/1						
diazepam	2	2.8	15/2	III	+	D	+	+	SED.- ANXIOL.
	5	3.2	19/0						
	10	3.9	17/0						
	15	3.9	15/0						
	20	4	14/1						
dibenzepin	80	1	1/0						ANTIDEPRESS.
dihydrocodeine				II*	+				NARCOTICS
diltiazem	90	1	1/0						CARDIOVASCUL.
dimenhydrinate		3	1/1	III	+				ANTI H1
dimethindene	2	2	1/0		+		+		ANTI H1
	4	2	1/0						
diphenhydramine	25	2.8	6/1	III	+	D	+	+	ANTI H1
	50	3.3	8/1						
	100	3.8	6/1						
diphenylpyraline	9	U	0/1						ANTI H1
dixyrazine				II*			w		NEUROLEPT.
domperidone	10-20	U	0/1						ANTIEMETIC
dosulepin	75	2	1/0	II.2	+				ANTIDEPRESS.
doxepin	25	3	7/1	II.2	+	D	w		ANTIDEPRESS.
	50	3.6	5/0						
dronabinol					+				ANTI EMETIC
droperidol	5	U	0/1	II.2	+		w		NEUROLEPT.
ebastine		1	1/0						ANTI H1
enalapril		1	1/0						CARDIOVASCUL.
ephedrine							+	+	SYMPATH. MIM.
ergotamine							+		ANTIMIGRAINE
ethosuximide	250	3	1/0	II*			+	+	ANTIEPILEPT.
ethyl loflazepate				II*					SED.- ANXIOL.
ethylmorphine				II*			+	+	NARCOTICS
etilamfetamine				I*					CENT. STIM.
famotidine	20-40	1	1/0	II.1					ANTI H2
felbamate				II*					ANTIEPILEPT.
femoxetin	200	2	1/0						ANTIDEPRESS.
fenetylline				I*					CENT. STIM.
fenfluramine	20	U	0/1		+		+		CENT. STIM.
	40	2	1/1						
fentanyl				III	+	D	+	+	ANESTHET.
floctafenine					+				ANALG., ANTIINFL.
flunarizine					+				ANTIMIGRAINE
flunitrazepam	0.5	4	3/4	III	+	D	+		SED.- ANXIOL.
	1	4	4/3						
	2	4	4/3						
fluopromazine					+				NEUROLEPT.
fluoxetine	20	1.8	4/1	II.1	+				ANTIDEPRESS.
	40	2	2/2						
	60	2.5	2/1						
flupentixol	1	1	2/0	II.2	+				NEUROLEPT.
	5-15	3	1/1						
fluperlapine	100	4	1/0						NEUROLEPT.
fluphenazine	1	U	0/2	II*	+				NEUROLEPT.
	2	U	0/2						
	5-15	3							
flupirtin	100	3	1/0						ANALG.

MOLECULES	DOSAGE (mg)	+ Germany	I, II.1, II.2 and III / I*, II* and III*	Belgium	Nether.	Italy	Norway	Finland	
									ANTIINFL.
flurazepam	15	4	4/4	III	+		+		SED.- ANXIOL.
	30	4	5/3						
fluspirilene				II*	+				NEUROLEPT.
fluvoxamine	50	2.2	4/2	II.1	+				ANTIDEPRESS.
fosfenytoin								+	ANTIEPILEPT.
gabapentin								+	ANTIEPILEPT.
glafenin	200-400	4	1/0						ANALG., ANTIINFL.
glibenclamide				-					ANTIDABET.
gliclazide				-					ANTIDABET.
glipizide				-					ANTIDABET.
gliquidone				-					ANTIDABET.
glucagon				-					ANTIDABET.
gluthetimide	125	4	1/2						SED.- ANXIOL.
	250	4	1/2						
	500	U	0/2						
granisetron				I					ANTAG 5HT3
guanethidine	10	3	2/1		+				CARDIOVASCUL.
guanfacine					+				CARDIOVASCUL.
halazepam									SED.- ANXIOL.
haloperidol	1	2.3	3/0	II.2	+		w		NEUROLEPT.
	10	3	1/1						
heptabarbital	100	U	0/1						SED.- ANXIOL.
	200	U	0/1						
hexobarbital	250	U	0/2		+				SED.- ANXIOL.
	500	U	0/1						
hydrocodone				II*					NARCOTICS
hydromorphone					+			+	NARCOTICS
hydroxyzine	25	3.5	4/0	III	+		+	+	ANTI H1
	50	4	3/0						
	100	4	3/0						
hyoscine					+	D			ANTIMUSCARIN.
imipramine	25	2.7	3/3	II.2	+	D	w		ANTIDEPRESS.
	50	3.3	3/1						
	75	4	2/1						
indalpine	50	1	1/0						ANTIDEPRESS.
indomethacin	25	2.5	2/1		+				ANALG., ANTIINFL.
		3	1/2						
indoramine	25	3	1/0						CARDIOVASCUL.
insuline				-					ANTIDABET.
iproclozide				II*					ANTIDEPRESS.
isosorbide(dinitrate)	20	1	1/0						CARDIOVASCUL.
kava-kava	100	1.3							ANTIDEPRESS.
ketamine						D			ANESTHET.
ketazolam	30	3	2/1	III	+				SED,ANXIOL.
ketotifen	1	3.5	2/0	II.2	+				ANTI H1
	2	3.3	3/0						
labetalol				I*					BETA-BLOCK.
lamotrigine	120	1	2/0	II*			w	+	ANTIEPILEPT.
	300	1	1/0						
levobunolol				I*					BETA-BLOCK.
levomepromazine	10	4	1/1	III*	+		w		NEUROLEPT.
	25	4	1/0						
lithium	600	2	3/0	II.1	+				ANTIDEPRESS.
lofepramine	70	3	0/1	II*					ANTIDEPRESS.
loprazolam	0.5	U	0/2	II.2	+				SED.- ANXIOL.
	1	3.5	1/2						
	2	4	1/1						
loratadine	10	1	8/0	I					ANTI H1
	20	1.6	5/0						
lorazepam	0.5	3.6	11/3	III	+	D	+	+	SED.- ANXIOL.
	1	3.9	10/1						
	2.5	4	10/0						
	5	4	7/3						
lormetazepam	0.5	3	1/5	II.2	+				SED.- ANXIOL.
	1	3	2/3						
	2	4	2/3						
loxapine				III*	+				NEUROLEPT.

MOLECULES	DOSAGE (mg)	WOLSCHRIJN		Belgium	Nether.	Italy	Norway	Finland	
		+ Germany	I, II.1, II.2 and III / I*, II* and III*						
maprotiline	25	2.2	3/3	II.2	+				ANTIDEPRESS.
	75	3	2/2						
mazindole	1	3	0/1	I	+				CENT. STIM.
mebhydrolin	50	3	3/0		+				ANTI H1
	100	U	0/3						
meclozine	25	4	1/0	II.2	+		+	+	ANTI H1
medazepam	5	2.3	3/3		+				SED.- ANXIOL.
	10	3	2/4						
	15	4	1/4						
melitracen				II*					ANTIDEPRESS.
melperone				II*			w		NEUROLEPT.
mephenoxalone					+				MUSCL. RELAX.
meprobamate	400	3	4/2	III	+		+	+	SED,ANXIOL.
	800	3.5	2/3						
meptazinol	100-200	1.5	4/0						NARCOTICS
	400	1	1/0						
mequitazine	5	1.4	5/0	II.1					ANTI H1
	10	3	3/1						
mesuximide		U	0/1						ANTIEPILEPT.
metaclazepam	7.5	3	0/1						SED.- ANXIOL.
metformine				-					ANTIDABET.
methadone	2.5-10	3	-	II.2	+			+	NARCOTICS
methocarbamol							+	+	MUSCL. RELAX.
methyldopa DL	250	3.5	2/1		+				CARDIOVASCUL.
methyldopa L	250	3	1/0		+				CARDIOVASCUL.
methylphenidate	10	3	0/3	I	+		+		CENT. STIM.
methylphenobarbital	30	U	0/2		+				SED.- ANXIOL.
	100	U	0/2						
	200	4	1/0						
metipranolol				I*					BETA-BLOCK.
metoclopramide	5-10	U	0/1		+				ANTI EMETIC
metoprolol	50-100	1.6	3/0	II*					BETA-BLOCK.
mianserin	10	3	5/2	III	+	D			ANTIDEPRESS.
	20	3.4	7/0						
midazolam	7.5	4	2/2	III	+	D	+	+	SED.- ANXIOL.
	15	4	1/3						
minaprine	50	1	2/0						ANTIDEPRESS.
	100	1	1/0						
moclobemide	100	1		II*					ANTIDEPRESS.
	200	1							
morphine	10	U	0/1	III	+	D	+	+	NARCOTICS
	20	4	1/1						
nadolol	40-80	1	1/1	II*					BETA-BLOCK.
	80-320	1	1/1						
nalbuphine		3	1/0		+	D			NARCOTICS
N-desmethyl-adinazolam						D			SED.- ANXIOL.
nialamide				II*					ANTIDEPRESS.
nicomorphine					+				NARCOTICS
nifedipine		3	1/0						CARDIOVASCUL.
nitrazepam	2.5	3.6	3/4	II.2	+	D	+	+	SED.- ANXIOL.
	5	3.6	5/3						
	10	4	5/2						
nizatidine	150-300	1.6	2/1	II.1					ANTI H2
	600	1	1/0						
nordazepam	5	3	1/2	II*	+				SED.- ANXIOL.
	10	3	1/2						
nortriptyline	10	2.3	4/3	II.2	+		w		ANTIDEPRESS.
	50	2	3/3						
	75	3.5	2/2						
noscapine	15-30	1	1/0						ANTITUSSIVE
ondansetron				I					ANTAG 5HT3
opipramol	50	3	1/0	II*	+				ANTIDEPRESS.
orphenadrine							w	+	ANTIMUSCARIN.
oxaprotilin	25	1.3	3/0						ANTIDEPRESS.
oxatomide	30	U	0/1		+				ANTI H1
oxazepam	10	3	11/1	II.2	+	D	+	+	SED.- ANXIOL.
	20	3	11/1						
	30	4	4/5						
	50	4	6/3						
oxetacaine							+		LOCAL ANESTH.
oxomemazine					+				ANTI H1

MOLECULES	(mg)	WOLSCHRIJN	I, II.1, II.2 II* and III*		Nether.	Italy		Finland	
oxprenolol				II*					BETA-
oxybutine					+				ANTIMUSCARIN.
									ANTIMUSCARIN.
oxycodone					+		+	+	ICS
	20	1		II.1					ANTIDEPRESS.
	30	1.4							
pemoline	37.5		2/1	I*					CENT. STIM.
						D			BETA BLOCK.
	10 20		0/1	II*					NEUROLEPT.
pentazocine	-100	3		III	+		+		NARCOTICS
pentobarbital		4	1/2		+		+		SED.-
		U	0/2						
perazine					+				
perphenazine	4-	U	0/2		+		w		NEUROLEPT.
pethidine	-150	U		III*	+		+		NARCOTICS
phendimetrazine									STIM.
				II*	+				
pheneturid				II*					ANTIEPILEPT.
phenindamine		U	0/1						ANTI H1
	50	U							
pheniramine	40		0/2						
phenobarbital	15		3/0	III				+	SED.-
		3.7	3/1						
	100-	4	3/0						
				I*					CENT. STIM.
phenylbutazon		2.5	2/0						ANALG.,
phenylpropanolamine	25-	U	0/2				+		CENT. STIM.
	200	2		III				+	ANTIEPILEPT.
									ANTITUSSIVE
physostigmine		3							INH. CHOLINESTER.
pimozide	-2	3		II*	+				
pindo				II.2					-BLOCK.
pipamperone					+				NEUROLEPT.
			1/0						- ANXIOL.
pipotiazine					+				NEUROLEPT.
	800	1							NOOTROPIC
				III*					NARCOTICS
pizotifen					+				
prazepam	10		1	II*	+				- ANXIOL.
primidone		U	0/1				+		ANTIEPILEPT.
prochlorperazine		3	2/1		+				
		3.5	2/1						
	2.5	U							ANTICHOLINERG.
				I					CENT. STIM.
promazine	-50	4		III*	+			+	NEUROLEPT.
	25	4		III	+		+		ANTI H1
	50	4							
				III*	+				
propofol									ANESTHET.
	40	1.4		II.2					BETA BLOCK.
	80		3/1						
prothipendyl									
pseudoephedrine	60		1/2						
pyridostigmine	30		1/0						CHOLINESTER.
	15	U				D			SED. ANXIOL.
	150	1.6		I					ANTI H2
	300	1.6							
remoxipride	100		1/0						
reserpine	0.1		3/0		+				CARDIOVASCUL.
	0.25		2/						
risperidone				II*					
ritanserin	5		1/0						- ANXIOL.
scopolamine	-0.8	4				D		+	ANTICHOLINERG.
secobarbital		4	5/1		+				SED.-
		4	2/3						
	200		3/1						
sertraline		2	1/0		+		w		ANTIDEPRESS.

MOLECULES	DOSAGE (mg)	WOLSCHRIJN		Belgium	Nether.	Italy	Norway	Finland	
		+ Germany	I, II.1, II.2 and III / I*, II* and III*						
sotalol				I*					BETA-BLOCK.
sufentanil					+		+		ANESTHET.
sulpiride	50	2.5	2/2	II.2	+				NEUROLEPT.
	100	2.3	3/1						
sultopride				II.2					NEUROLEPT.
sumatriptan							+	+	ANTIMIGRAINE
temazepam	5	2.7	6/2	II.1	+	D	+	+	SED.- ANXIOL.
	10	3.4	2/5						
	20	4	2/5						
	30	4	1/6						
temelastine	100	1	1/0						ANTI H1
terfenadine	60	1	11/0	I					ANTI H1
	120	1.7	9/0						
	240	2.2	6/2						
tertatolol				II*					BETA-BLOCK.
tetrazepam				II*					SED.- ANXIOL.
thebacone				II*					NARCOTICS
thiopental						D	+		SED.- ANXIOL.
thioproperazine				II*					NEUROLEPT.
thioridazine	25-100	3.6	3/1	III	+	D	w		NEUROLEPT.
thiothixene					+				NEUROLEPT.
tiagabine								+	ANTIEPILEPT.
tiapride	100	1	1/0	II.1	+				NEUROLEPT.
tiaprophenic acid	400	1	1/0						ANALG., ANTIINFL.
tilidine				III*					NARCOTICS
timolol				II*					BETA-BLOCK.
tizanidine					+		+	+	ANTI SPASTICS
tofisopam	100	1	1/0						SED.- ANXIOL.
tolbutamide				-					ANTIDABET.
topiramate								+	ANTIEPILEPT.
tramadol				II.2	+		+	+	NARCOTICS
tranylcypromine					+				ANTIDEPRESS.
trazodone	50	3.5	2/0	III	+	D			ANTIDEPRESS.
	75	3	8/0						
triazolam	0.125	3	4/3	II.2	+	D	+	+	SED.- ANXIOL.
	0.25	3.7	6/3						
	0.5	4	6/3						
trifluoperazine	5	3	1/1		+				NEUROLEPT.
triflupromazine	5	3							NEUROLEPT.
trimeprazine					+				ANTI H1
trimipramine	12.5	3	1/1	II*	+				ANTIDEPRESS.
	25	3	1/1						
tripelennamine					+				ANTI H1
triprolidine	2.5	3.8	7/0	III		D			ANTI H1
	5	3.8	7/0						
tryptophan	100	1.5	2/2		+				ANTIDEPRESS.
valproate, valproic acid	5mg/kg BW	2	2/0	II.1			+	+	ANTIEPILEPT.
venlafaxine					+		w		ANTIDEPRESS.
veralipride				II*					NEUROLEPT.
vigabatrin		1	1/0	II*			+	+	ANTIEPILEPT.
viloxazine	100	1	2/0	II.1					ANTIDEPRESS.
yohimbine						D			
zolpidem	10	3.5	1/2	II.2	+	D	+	+	SED.- ANXIOL.
	20	3.5	1/2						
zopiclone	7.5	3.8	3/4	II.2	+	D	+	+	SED.- ANXIOL.
zuclopenthixol	10	U	0/1	II.2	+		w		NEUROLEPT.

GLOSSARY

AD	antidepressant
BAST	Bundesanstalt für Strassenwesen
BLT	Toxicological Society of Belgium and Luxembourg
BTTS	Belgian Toxicology and Trauma Study
BZD	benzodiazepine
CAD	cyclic antidepressant
CNS	central nervous system
EIA	enzyme immunoassay
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
FPIA	fluorescence polarisation immunoassay
GC	gas chromatography
GC-ECD	gas chromatography - electron capture detection
GC-MS	gas chromatography - mass spectrometry
GHB	gamma hydroxybutyric acid
HPLC	high performance liquid chromatography
KTL	National Public Health Institute (Finland)
LSD	lysergic acid diethylamide
6MAM	6-monoacetylmorphine
MAO	monoamine oxidase
MDA	3,4-methylenedioxyamphetamine
MDEA	3,4-methylenedioxyethamphetamine
MDMA	3,4-methylenedioxymethamphetamine
NIFT	National Institute for Forensic Toxicology (Norway)
RIA	radio immunoassay
SSRI	selective serotonin reuptake inhibitor
TAD	tricyclic antidepressant
THC	tetrahydrocannabinol
THCCOOH	11-nor-9-carboxy-tetrahydrocannabinol
TLC	thin layer chromatography
XTC	ecstasy, MDMA

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Deliverable D2

Inventory of State-of-the-Art road side drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: Nationaal Instituut voor Criminalistiek en Criminologie (NICC), Universiteit Gent (RUG), Securetec GmbH (SEC), Roche Diagnostics (RDB)

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EXECUTIVE SUMMARY

Market Study

Nineteen original devices have been documented in the market study of this work package. Sixteen are designed for the screening of urine samples; all but one are manufactured in the U.S. They represent a total of approximately 33 brand names on the international market. Of the three devices that were originally developed for saliva, two are manufactured in Europe. One device can also be applied to sweat.

For **urine**, there exist roughly three kinds of test designs to obtain a result with an on-site drugtest: a "dip" test (teststrip or testcard; the device is partially immersed in the urine for a few seconds), a "pipette" test (testcassette; a few drops of urine are brought in the device with a dropper) and a "cup" test (the device is built in the side or top of a cup). Several manufacturers increase the flexibility of their product line by supplying a range of tests: for a single parameter, for multiple parameters, dip and pipette type tests. Most of the tests are available for the detection of amphetamines (AMP), methamphetamine (mAMP), cannabinoids (CAN), cocaine (COC), opiates (OPI) and phencyclidine (PCP). Seventy percent of the devices have a separate AMP and mAMP test. Eighty percent of the urine devices also include benzodiazepines (BZO) and barbiturates (BAR) in their panels, fifty percent include methadone and only thirthy percent offer a test for tricyclic antidepressants.

All devices can be stored at room temperature (15 – 25 °C). The cost of a urine test varies between 2 and 6 Euro for a single parameter, and 10 and 20 Euro for a five panel multitest. The devices for saliva cost between 6 and 18 Euro for one to five parameters. For the Rapiscan, a separate reader has to be purchased, which is expensive.

Since most of the on-site devices were tested in the laboratory, an evaluation of their user friendliness was done by three members of the laboratory personnel. The ease-of-use, the quality of the package insert and the interpretation of the result were taken into account. Approximately sixty percent of the evaluated devices had a users quotation of "good" to "very good", thirty percent was considered "acceptable", only one was "not acceptable".

For the interpretation of the screening result there are different possibilities: for more than ninety percent of the tests, the appearance of a control line and the presence of a second line indicates a negative result. The intensity of the line is not important. A clear distinction between positive and negative results requires some training before routine testing can be carried out. It is very important that the validity of the test is demonstrated by the appearance of a control line. Only Frontline (Roche Diagnostics) and Drugwipe (Securetec GmbH) do not have a built-in control. Ideally, the test data should be read and saved electronically. The Rapiscan saliva tester is the only device with an electronic reader with easy storage of data.

Most of the manufacturers of the on-site urine tests use the SAMHSA cut-offs for drugs of abuse. Some exceptions are observed. If the tests are too sensitive or if the experimental cut-off values are different from the theoretical cut-off values, the number of false positives increases.

In the U.S., the screening cut-offs for the amphetamine class (1000 ng/ml) are only set for amphetamine(s) and methamphetamine(s). In a number of European countries, the increasing abuse of ecstasy requires the use of a screening test sufficiently sensitive for MDMA and its analogues (MDEA, MBDB). Generally, an AMP test also detects MDA (a metabolite of MDMA and MDEA), a mAMP test detects MDMA to a variable extent. Very few data on the other designer amphetamines are available. Moreover, some nasal decongestants and anorectic medication can interfere in an AMP type test. All opiate-type tests cross-react to a high extent with a number of cough suppressants, analgesics and morphine agonists and antagonists. Confirmation by GC/MS is absolutely necessary to establish the cause of the positive screening result.

In conclusion, the main problem issues are the objective interpretation of the result (absence of a reader), the detection of ecstasy and other designer amphetamines, and the specificity of the tests for the illicit amphetamines and morphine.

Experimental Study

Seven non-instrumental urine devices were evaluated in the laboratory for the screening of amphetamines/methamphetamines, cannabinoids, cocaine and opiates: **Testcup**, 4-panel/ AMP-CAN-COC-OPI, **Teststik**, single test, AMP-CAN-COC-OPI, **Frontline**, single test, AMP-CAN-COC-OPI, **Syva Rapidtest**, 4 panel/ mAMP-CAN-COC-OPI + 1 single AMP, **Rapid Drug Screen**, 5 panel/ AMP-mAMP-CAN-COC-OPI, **Rapitest**, 5 panel/ AMP-CAN-COC-OPI-BZO and **Instastrip**, single test, AMP-CAN-COC-OPI. All urines were screened with FPIA with a cut-off of 1000 ng/ml for amphetamines, 50 ng/ml for cannabinoids, 300 ng/ml for cocaine and 300 ng/ml for opiates. All the positive screening results were confirmed with GC/MS using deuterated internal standards of the principal analytes for quantification. The applied cut-off values for confirmation were: 500 ng/ml for amphetamine, methamphetamine, MDA, MDMA, MDEA and MBDB, 15 ng/ml for 11-nor-d9-THC-COOH, 150 ng/ml for benzoylecgonine, 300 ng/ml for morphine, codeine, and 6-acetylmorphine. A large number of the negative screening results were also confirmed with GC/MS, especially if there was a discrepancy between one or more on-site test results and the FPIA result. The performance of the devices was assessed in terms of their "Positive Predictive Values" and "Negative Predictive Values" and percentages of false positive and false negative results.

Syva Rapidtest, **Rapid Drug Screen**, **Rapitest** and **Teststik** showed the best accuracy in the detection of *cannabinoids* in urine. All tests except the Frontline showed sufficient sensitivity and specificity for the detection of the *cocaine* metabolite in urine. All tests showed acceptable results for the detection of *opiates* in urine, the **Rapid Drug Screen** being a very reliable test. **Syva Rapidtest**, **Rapid Drug Screen**, **Rapitest** and **Instatest** all showed good results for the detection of *amphetamine and MDMA* in urine. The Instatest clearly showed very good results. Testcup and Teststik failed to detect MDMA, even in concentrations above 8000 ng/ml.

INTRODUCTION

The aim of this work package was originally defined as an inventarisation of the state-of-the-art devices for roadside testing. The survey was limited to the on-site drug testing devices that are available for the detection of psychotropic substances in urine, saliva and sweat. The so called "impairment testers" are not discussed here as they are not included in the scope of the project.

Since the drug testing business is evolving and new prototypes, new types, even new names are created every day, there was a need to create a simple but clearly structured database. In that way, new devices that appear on the market can be easily added to the inventory, every parameter related to a certain device can be changed without interfering with the other previously determined characteristics e.g. when changing the name of the ABUSIGN device into ACCUSIGN, the correction will automatically be executed on all levels in the database.

Another complicating factor has been the enormous amount of information that has been found on the Internet. Basically identical or very similar test devices were presented with different names by different companies. This problem was thoroughly analyzed by Dr. Crouch in a similar study performed in the United States. We would like to thank Dr. Michael Walsh (The Walsh Group) for providing us with this very interesting study.

The overall characteristics and the information concerning an original device were summarized by means of the following template:

- Name of the original device
- Manufacturer of that device
- Identical devices manufactured by the same company or looking very similar
- Screening matrix: urine, saliva or sweat
- Types available: AMP = amphetamines
  mAMP = methamphetamine
  CAN = cannabinoids
  COC = cocaine
  OPI = opiates
  PCP = phencyclidine
  BZO = benzodiazepines
  BAR = barbiturates
  TCA = tricyclic anti-depressants
  MDN = methadone
- Number of parameters to be tested with one device: single panel or multi-panels
- Price range for a single or multi-test
- Is the device FDA approved, and for which parameters?
- What are the storage conditions mentioned on the package insert ?

- **RESULT**:
  - What is the procedure to obtain the result ?
  - How is the result interpreted ?
  - Is there a possibility to store the result ? Ideally, the test data can be saved electronically. In some cases, the results in the read-out window will not change with time and the test strip can be stored. Simple photocopying of the results is not considered here (not an option for roadside testing).
  - Is there a built-in control to indicate the result is valid ?

- **CUT-OFFs**: the analytical cut-off values for every class of drugs as stated by the manufacturer

- **USER FRIENDLINESS:**
  Since most of the on-site devices were tested in the laboratory, an evaluation of their user friendliness was done by three members of the laboratory personnel. The ease-of-use, the quality of the package insert and the interpretation of the result were taken into account.

- **AVAILABLE INFORMATION:**
  - Inventory of on-site testing devices in the U.S.: evaluation of their user friendliness and accuracy, recent report by Dr. Crouch (Center for Human Toxicology, University of Utah, Salt Lake City)
  - Evaluation studies published in peer reviewed journals (cfr. Annex)
  - Poster presentations at international congresses
  - Internal reports supplied by the manufacturers or distributors
  - The Internet:
    - websites of the different manufacturers/distributors
    - http://www.health.org/workplce/summary.htm
      The division of Workplace Programs (DWP) funded DUO Research: An evaluation of non-instrumented Drug Test Devices (1999).
    - http://www.fda.gov/scripts/cdrh/cfdocs/cfpmn/search.cfm
      The FDA website, where all information about the FDA approval of a device can be obtained.

- **REPORT ON CROSS-REACTIVITIES:**
  For every class of drugs, the cross-reactivity values for the relevant analytes were presented in a separate report. The cross-reactivity of the target analyte was considered as 100 %. This is dependant on the type of device (e.g. cannabis-type) and the matrix the device is designed for e.g. d9-THC-COOH (a metabolite) for urine, d9-THC (the parent drug) for saliva and sweat.
  The distinction between a methamphetamine- and an amphetamine-type device is of major importance in the detection of the different amphetamine analogues (amphetamine, methamphetamine, ecstasy and derivatives, medicines). In most Western European countries, the growing problem of the abuse of ecstasy is an important parameter to consider in the evaluation of the screening tests.

- **COMMENTS AND CONCLUSIONS:**
  Most reported advantages and disadvantages were based on our own evaluation study and on the technical and practical data provided by the manufacturer.
  An analytical quotation was based on conclusions from evaluation studies and cross-reactivity data. The conclusions from the Crouch-study were also taken into account, especially for those devices that were not tested in our laboratory.

To increase the scientific impact of this work, the accuracy of seven on-site urine testing devices for the detection of cocaine, opiates, cannabinoids and amphetamines was evaluated in a laboratory study, using screening with FPIA and quantitative confirmation by GC/MS as the reference method. The results of this study are presented in detail in the last chapter of this work package and are discussed in the conclusions.

LIST OF DEVICES

Accusign
Princeton BioMeditech

identical to:
Syva Rapidtest (Dade Behring)
Status DS (Lifesign L.L.C.)
Mahsan (Mahsan Diagnostika)
Dako (Veda Lab)

Dip Drugscan-one step
Syntron Bioresearch Inc.

identical to:
Quickscan (Syntron) = cassette type paneltest
Quickpack II-one step (Syntron) = cassette type mono test
Quickstrip-One step (Syntron) = dip type mono test

One step Instastrip, Insta test,
multiple drug screen Instastrip, Insta Test
(Cortez Diagnostics, Inc.)

DrugCheck 5
Drug Free Enterprises

identical to:
Drugstop (V-Tech, Inc.)
Teststrips identical to the Dip Drug Scan-one test series (Syntron)

Drugwipe
Securetec GmbH

identical to:

DTx
Forefront Diagnostics

identical to:
Instacheck

First Check
Worldwide Medical Corp.

identical to:

Frontline
Roche Diagnostics Corp.

identical to:

Genie Cup
Point of Care Techn.

identical to:
Syva Rapid Cup d.a.u. 5 (Dade Behring)
Sure Step and PharmScreen teststrips
(American Biomedical Inc)

Oral Screen
Avitar Technologies Inc.

identical to:
Carepoint (Coventry, UK)

Pharmscreen Drug Screen
American Biomedical Inc.

identical to:
Dipro Drugscreen 5 panel (Dipro Diagnostic Products),
Surestep Drug Screen Card II (Biochem Immunosystems)
Clinistrip Drug Check Card (Clinicare Technologies),
Rapitest Multidrug Panel (Morwell Diagnostics),
Ultimed Surestick Drug Screen Card II (The Ultimate Products)
Assurance Drug Screen Card (Applied Biotech)

Quickscreen
PhamaTech

identical to:
Surescreen (Surescreen Diagnostics)

Rapid Drug Screen *AmericanBioMedica Corp.*	identical to:
Rapiscan *Cozart Bioscience Ltd.*	identical to:
Testcup *Roche Diagnostics Corp.*	identical to: **Teststik** (Roche)
Teststik *Roche Diagnostics Corp.*	identical to: **Testcup** (Roche)
Toxiquick *Bionike Laboratories Inc.*	identical to:
Triage *Biosite Diagnostics*	identical to:
Verdict II *Medtox Diagnostics Inc.*	identical to: **Profile II** (Medtox) (only a 5 panel)
Visualine II *Avitar Technologies Inc.*	identical to: **Sunline** (Sun Biomedical Laboratories Inc.)

Accusign

Manufacturer:	***Princeton BioMeditech***
Product identical to	Syva Rapidtest (Dade Behring) - Status DS (Lifesign L.L.C.) Mahsan (Mahsan Diagnostika) - Dako (Veda Lab)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, TCA, MDN
Number of parameters per device:	1 - 10
Cost:	10 - 15 EURO for a five panel, depending on the distributor
FDA:	approved for single and multiple parameter tests
Storage conditions:	2 - 30 °C
Manipulations to obtain a result:	1) Aspirate urine with a plastic pipette (included in the pack) 2) Add 3 drops of sample to the sample well 3) Read the result in 3 - 5 minutes
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
Amphetamine	1000
Barbiturates	300
benzodiazepines	300
Cannabinoids	50
benzoylecgonine	300
Methadone	300
methamphetamine	1000
Morphine	300
PCP	25
Tricyclics	1000

Available information

ACCUSIGN

- Verdonck I and Viaene B, Testing drugs of abuse with non-instrumental immunoassays: a field experience. Poster presented at the TIAFT/SOFT Joint Congress, October-November 1994, Tampa, Florida
- Bogema SC, Performance study of four rapid on-site drug testing devices, presentation at AACC Conference Chicago 1998
- Buchan BJ et al, J Forensic Sci, 43:395 (1998)
- Kintz P and Giroud C, J Anal Toxicol, 21:589 (1997)

ACCUSIGN, SYVA RAPIDTEST

- Hofbauer BM et al., Comparison of immunochromatographic rapid tests for screening of benzodiazepines, amphetamine and its derivatives (ecstasy) in urine. Poster presented at the TIAFT/SOFT Joint Congress, october 1998, Albuquerque, New Mexico

SYVA RAPIDTEST

- Dade Behring: cross-reactivity testing of the Syva Rapidtest AMP and mAMP with MDA, MDMA, MDEA and MBDB
- Mura P et al., Acta Clinica Belgica 1/99:35 (1999)

SYVA RAPIDTEST and STATUS

- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention,
  Division of Workplace Programs. email: wvogl@samsha.gov

STATUS
- Taylor HE et al., J Anal Toxicol 23:119 (1999)

Comments and conclusions

ADVANTAGES
- quick and inexpensive
- easy to use, no messy test after use
- a few drops of urine are sufficient to do the test properly, also when using a multi-panel device
- a large range of single tests and combinations are available
- built-in control line

DISADVANTAGES
- Accusign:
  Sometimes difficult to interpret the result: rather subjective (very faint line = negative?). The study of Verdonck et al. clearly shows that the % of wrong results increases dramatically with non-trained operators.
- PBM also manufacturers Syva Rapidtest and Status DS which are basically identical tests. This leads to confusion and difficulties to evaluate the reliability of the information provided by each distributor. The results of the evaluation-studies of the different tests and the cross-reactivities also show small differences.

ANALYTICAL CONCLUSIONS
- Accusign's positive predictive value and negative predictive value for opiates is excellent.
- Some false positives for cocaine are reported.
- False negatives as well as false positives for the cannabis test.
- Some false positives reported for amphetamine with the AMP test; however, the presence of other amphetamine-like substances was not excluded. LODs of 500 and 10,000 ng/ml reported for MDA and MDMA, respectively, with the AMP test. Some false negatives reported for methamphetamine with the mAMP test. Mean LOD's for MDMA, MDEA and MBDB are 1000, 5000 and 10,000 ng/ml, respectively, with the mAMP test. Kintz et al. found no positive responses for MBDB in concentrations up to 18,577 ng/ml.
  No interference of tyramine, ephedrine, B-phenylethylamine and phenylpropanolamine until 10,000 ng/ml with the Accusign AMP or mAMP tests; influence of B-phenylethylamine reported for Syva Rapidtest AMP. Interference of Phentermine when using the Status AMP test.
- Reasonable LODs for benzodiazepines.

DUE TO THE CONTRADICTORY RESULTS OF THE EVALUATION STUDIES, ONE CAN CONCLUDE THAT THE INTERPRETATION OF THE RESULT IS PERHAPS TOO SUBJECTIVE AND CERTAINLY REQUIRES SOME EXPERIENCE. ACCEPTABLE SENSITIVITY FOR THE DESIGNER AMPHETAMINES WHEN COMBINING BOTH THE AMP and mAMP TEST. MORE STUDY IS NEEDED TO INTERPRET THE "FALSE POSITIVES", POSSIBLY DUE TO THE PRESENCE OF OTHER AMPHETAMINE LIKE COMPOUNDS.

Dip Drugscan-one step

Manufacturer:	***Syntron Bioresearch Inc.***
Product identical to	Quickscan (Syntron) = cassette type paneltest Quickpack II-one step (Syntron) = cassette type mono test Quickstrip-One step (Syntron) = dip type mono test One step Instastrip, Insta test, multiple drug screen Instastrip, Insta Test (Cortez Diagnostics, Inc.)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, MDN
Number of parameters per device:	1 - 6
Cost:	
FDA	approved
Storage conditions:	2 - 28 °C
Manipulations to obtain a result:	Depending on the type of test that you choose, you will either 1) dip the teststrip into the urine 2) pipette 4 drops of urine into the sample well Read the result at 5 min
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	very good

Cut-Off :	ng/ml
amphetamine	500
cannabinoids	50
benzoylecgonine	300
methamphetamine	500
morphine	300

Available information

- Internet: http://www.syntron.net

INSTATEST (Cortez Diagnostics)
- Mura P et al., Acta Clinica Belgica 1/99:35 (1999)
- study performed in the lab of Dr. Verstraete, University of Gent, Belgium

Comments and conclusions

ADVANTAGES
- nice looking test, easy to use and to handle
- built-in control line
- several types of tests are available: single, multi, cassette-type, dip type
- wide range of parameters to test for

DISADVANTAGES
- names of the different types are difficult to distinguish at first
- no published studies on analytical performance

COMMENTS AND CONCLUSION
The Dip Drug Scan One Step test is user friendly and meets the requirements for roadside testing.
One limited evaluation study has found a large number of false positives for opiates.

DrugCheck 5

Manufacturer:	***Drug Free Enterprises***
Product identical to:	Drugstop (V-Tech, Inc.) Teststrips identical to the Dip Drug Scan-one test series (Syntron)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP
Number of parameters per device:	5
Cost:	20 EURO
FDA	approved
Storage conditions:	2 - 28°C
Manipulations to obtain a result:	1) Collect the urine sample directly into the Drugcheck cup 2) Ensure the sample volume is between the lines indicated on the side of the cup 3) The cup contains five detection strips: read the results at 5 min
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	acceptable

Cut-Off :	ng/ml
Amphetamine	1000
Cannabinoids	50
benzoylecgonine	300
Morphine	300
PCP	25

Available information:

- Internet: http://www.drugcheck.com
  comparison chart with other testcups (Testcup and Rapid Drug Screen)
- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov

Comments and conclusions

ADVANTAGES:
- "no" step test; very user friendly, no manipulations other than collecting the sample
- leak-proof cup
- built-in control line

DISADVANTAGES:
- no other format than the five-drug test
- very difficult to read results
- strict time limit: 5 min
- volume of urine important

COMMENTS AND CONCLUSION
Although the test principle seems very practical, there are too many difficulties with the interpretation of the results and the validity of the test.
Evaluation studies with GC/MS data are not available.

Drugwipe

Manufacturer:	***Securetec GmbH***
Matrix:	saliva,sweat
Available for:	AMP, COC, OPI, (CAN)
Number of parameters per device:	1
Cost:	6 -10 EURO per parameter
FDA	not approved
Storage conditions:	15 - 25 °C
Manipulations to obtain a result:	1) disconnect wiping section from the device 2) wipe the surface of the tongue or the body for appr. 10 sec 3) reassemble the device and dip the absorbant pad into water for 10 counts 4) read the result after appr. 2 min
positive/negative control line:	not present
possibility to store result:	Yes
Interpretation of the result:	red/pink color = positive
User friendliness:	good

Cut-Off :	ng/ml
amphetamine	300
MDA	250
MDEA	750
MDMA	250
methamphetamine	300
THC	1000
cocaine	200
morphine	200

Available information:

- Internet: http://www.city-netz.com/securetec/drugwipe 1.html
- Published papers:
  - Kintz P et al., Int J Legal Med 111:82 (1998)
  - Mura P et al., Acta Clinica Belgica 1/99:35 (1999)
  - Samyn N et al., On-site testing of saliva for drugs of abuse in suspected drug users with Drugwipe and determination of drug concentrations in saliva and urine by GC/MS. In: Proceedings of the TIAFT/SOFT Joint Congress, October 1998, Albuquerque, New Mexico
  - Samyn et al. On-site testing of saliva and sweat with Drugwipe and determination of concentrations of drugs of abuse in saliva, plasma and urine of suspected users. Int J Legal Med, 1999, in press
  - Sachs H et al., Sweat testing for drugs using the Drugwipe. In: Proceedings of the 34th TIAFT meeting, august 1996, Interlaken

Comments and conclusions:

ADVANTAGES
- applicable to saliva and sweat (non-invasive, no adulteration, recent abuse)
- not necessary to collect a saliva sample, just wiping of the tongue
- quick result
- appearance of a color = positive result

DISADVANTAGES
- not fully evaluated for saliva and sweat testing
- no drug panel available
- no built in control line

- Interpretation of the result needs training/experience

ANALYTICAL CONCLUSION

- **Saliva**
  Recent abuse of cocaine, amphetamine and designer amphetamines.
  Recent abuse of opiates but with some false negative results if the on-site Drugwipe result was compared to the GC/MS results of saliva and plasma.
  Unreliable results for the cannabis test.

- **Sweat**
  Results for cocaine and amphetamines probably similar to saliva.
  Results for opiates are contradictory: controled study with codeine shows good results - in other studies false positives but comparison with GC/MS on the blood samples, not on sweat samples.

TRIAL ON A LARGE SCALE PROVED IT TO BE RELIABLE TO DETECT DRUGS ON SURFACES. PROMISING FOR SALIVA AND SWEAT. DRUGWIPE IS ALREADY USED FOR SWEAT TESTING ROUTINELY BY THE TRAFFIC POLICE IN CERTAIN PARTS OF GERMANY (trained police forces). RESULT READER IS INTRODUCED BY THE MANUFACTURER. THIS WILL PROBABLY INCREASE THE USER FRIENDLINESS AND DECREASE THE POSSIBILITY OF MISINTERPRETATION OF THE TEST.

DTx

Manufacturer:	***Forefront Diagnostics***
Product identical to:	Instacheck
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, MDN
Number of parameters per device:	1 - 6
Cost:	10 EURO for a four drug panel
FDA	approved
Storage conditions:	2 - 30 °C
Manipulations to obtain a result:	1) Aspirate urine with a plastic pipette (included in the pack) 2) Add 3 drops of sample to the one or the two sample wells 3) Read the result after 3 - 8 minutes, not after 8 min
positive/negative control line:	not present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
amphetamine	1000
barbiturates	300
benzodiazepines	300
cannabinoids	50
benzoylecgonine	300
methadone	300
methamphetamine	1000
morphine	300
PCP	25

Available information

- Internet: http://www.1stepdtx.com
- Bogema SC, Performance study of four rapid on-site drug testing devices, presentation at AACC Conference Chicago 1998
- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov
- Hofbauer BM et al., Comparison of immunochromatographic rapid tests for screening of benzodiazepines, amphetamine and its derivatives (ecstasy) in urine. Poster presented at the TIAFT/SOFT Joint Congress, october 1998, Albuquerque, New Mexico

Comments and conclusions

ADVANTAGES
- quick, easy one step test
- built-in control line
- custom made to test for the required drugs

DISADVANTAGES
- strict time limit (the results cannot be read after 8 min)
- difficult to read

COMMENTS
"The manufacturer claims" that they participated in the study of Bogema SC and that there were no false positives and no false negatives, meaning high accuracy for a low price, the most effective test!

First Check

Manufacturer:	***Worldwide Medical Corp.***
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BARB, MDN
Number of parameters per device:	1 - 5
Cost:	3 EURO for a single test
FDA	approved
Storage conditions:	4 - 30 °C
Manipulations to obtain a result:	1) Aspirate urine with a plastic pipette 2) Add 3 drops of sample to the sample well 3) Read the result after 3 - 5 minutes
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
amphetamines	1000
cannabinoids	50
benzoylecgonine	300
morphine	300

Available information

- Internet: http://www. ibchannel.com/emerging/wmedproducts.htm

- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention,
  Division of Workplace Programs. email: wvogl@samsha.gov

Frontline

Manufacturer:	***Roche Diagnostics Corp.***
Matrix:	urine
Available for:	AMP, CAN, COC, OPI, BZO
Number of parameters per device:	1
Cost:	3 EURO
FDA	approved for CAN, COC and OPI
Storage conditions:	15 - 25 °C
Manipulations to obtain a result:	1) dip test strip in specimen up to the mark for 3-5 sec 2) place strip on a non-absorbant surface 3) wait 2 min before reading the result and match the reaction colour against a colour scale
positive/negative control line:	not present
possibility to store result:	No
Interpretation of the result:	pink color = positive - by comparing to a scale: semi-quantitative result
User friendliness:	acceptable

Cut-Off :	ng/ml
amphetamine	300
MDA	250
MDEA	750
MDMA	250
methamphetamine	300
benzodiazepines	50
cannabinoids	50
benzoylecgonine	300
morphine	200

Available information

- internet: http://www.roche.com
- Workshop report Frontline, Luxembourg, November 1994
- Goerlach-Graw et al., Rapid screening test for the detection of drugs of abuse in urine. Poster presented at the TIAFT/SOFT Joint Congress, October-November 1994, Tampa, Florida
- Beck O et al., Evaluation of three immunochromatographic rapid tests for screening of amphetamines/methamphetamines, benzodiazepines and cocaine in urine. Poster presented at the TIAFT/SOFT Joint Congress, October 1998, Albuquerque, New Mexico
- Hofbauer BM et al., Comparison of immunochromatographic rapid tests for screening of benzodiazepines, amphetamine and its derivatives (ecstasy) in urine. Poster presented at the TIAFT/SOFT Joint Congress, October 1998, Albuquerque, New Mexico
- Wennig R et al., J Anal Toxicol 22:148 (1998)
- Mura P et al., Acta Clinica Belgica 1/99:35 (1999)

Comments and conclusions

ADVANTAGES
- simple cheap "dip and read" test - easy to use and easy to store

- quick result (1 min)

DISADVANTAGES
- wet strip messy after dipping
- no panel available
- no built in control line
- interpretation of the result too subjective: difference between creamcoloured (negative) and a faint pink color not distinct enough, time consuming to compare to a colour scale

ANALYTICAL CONCLUSION
- Excellent results reported for opiates.
- False positives for the cocaine test in subjects involved in a methadone maintenance program (cross-reactivity with a methadone metabolite and with clozapine). However, the new improved cocaine test is claimed to have eliminated this problem.
- High % of false negatives reported for cannabis in one study.
- Low detection limits for designer amphetamines; possibly some false positives (e.g. interference of ephedrine).
- Benzodiazepines test results seem promising: high sensitivity to detect a broad spectrum of substances.

Genie Cup

Manufacturer:	***Point of Care Techn.***
Product identical to:	Syva Rapid Cup d.a.u. 5 (Dade Behring) Sure Step and PharmScreen teststrips (Biomedical Inc)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, TCA, MDN
Number of parameters per device:	6
Cost:	20 EURO
FDA	approved combination AMP, mAMP, CAN, COC, OPI, PCP
Storage conditions:	15 - 30 °C
Manipulations to obtain a result:	1) collect sample, ensuring that the cup is filled above the minimum line 2) replace the lid, turning it until the arrow on the tamper-evident lid is aligned with the STOP on the cup and the upper tab on the cup rests in the notch just below the arrow on the lid 3) turn the lid one revolution to the fully closed position (when the lower tab on the cup rests in the notch of the tamper-evident ring)
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	very good

Cut-Off :	ng/ml
amphetamines	1000
cannabinoids	50
benzoylecgonine	300
methamphetamine	1000
morphine	300
PCP	25

Available information

- Internet: http://www.pointofcare.com

- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention,
  Division of Workplace Programs. email: wvogl@samsha.gov
- Dade Behring: cross-reactivity testing of the Syva Rapid Cup dau 5 mAMP, with MDA, MDMA, MDEA and MBDB

Comments and conclusions

ADVANTAGES
- the tester is not handling urine at any time; collection, testing and storage in the same cup
- easy to use and results easy to read
- built-in control line
- only a small part of the sample is actually used in the test - the remainder of the sample is unalterated for future testing
- temperature check

DISADVANTAGES
- only available test that we know of is the 6 drug test
- Dade Behring distributes the Rapid Test Cup which is a 5 drug test (no amphetamine)
- rather expensive
- volume of urine should be sufficient to match the minimum fill line

COMMENTS
- not fully evaluated in litterature
- data for the Syva Rapid Cup dau 5 indicate lack of cross-reactivity for MDA but acceptable sensitivity for the other designer amphetamines
- teststrips are basically identical to Pharmscreen, Sure Step… (Biomedical Inc.) cfr. evaluation of those tests.

Oral Screen

Manufacturer:	***Avitar Technologies Inc.***
Product identical to:	Carepoint (Coventry, UK)
Matrix:	saliva
Available for:	OPI - OPI/COC/CAN (sept '99)
Number of parameters per device:	1 - 3
Cost:	6 EURO
FDA	not approved
Storage conditions:	2 - 30 °C
Manipulations to obtain a result:	1) collect an "oral fluid" sample (Accusorb foam, FDA approved): slide the plastic hood back and place the foam end in the mouth; move around for 30 to 60 sec to allow the oral fluid to enter the foam 2) remove and slide the hood forward to cover the foam and squeeze the hood between the fingers to expel 4 drops in the sample well 3) read the result after 10 min
positive/negative control line:	present possibility to store result: No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	acceptable

Cut-Off :	ng/ml
morphine	25

Available information

- Internet: http://www.avitarinc.com, manufacturer

Comments and conclusions

ADVANTAGES
- applicable to saliva (non-invasive, no adulteration, recent abuse)
- collection of a saliva sample with a specially designed device based on the Accusorb foam which is FDA approved material
- principle of the test is simple
- three panel test will be available in the near future
- built-in control line

DISADVANTAGES
- full procedure needs training
- few evaluation studies

COMMENTS
Avitar Inc. and Sun Biomedical Labs are working together on the further development of this technique. A complete evaluation might be possible in the ROSITA trials at the roadside.

Pharmscreen Drug Screen Card

Manufacturer:	***American Biomedical Inc.***
Product identical to:	Dipro Drugscreen 5 panel (Dipro Diagnostic Products), Surestep Drug Screen Card II (Biochem Immunosystems) Clinistrip Drug Check Card (Clinicare Technologies), Rapitest Multidrug Panel (Morwell Diagnostics), Ultimed Surestick Drug Screen Card II (The Ultimate Products) Assurance Drug Screen Card (Applied Biotech, Inc.)
Matrix:	urine
Available for:	mAMP, CAN, COC, OPI, PCP
Number of parameters per device:	5
Cost:	17 EURO
FDA:	approved
Storage conditions:	2 - 28 °C
Manipulations to obtain a result:	1) Immerse the test strip into the urine specimen for about 30 s (the plastic of the device should not touch the urine) 2) the strip is removed and the cover is placed over the strips 3) read the results between 3-8 min Also available as a cassette (pipette and read)
positive/negative control line:	present possibility to store result: No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
cannabinoids	50
benzoylecgonine	300
methamphetamine	1000
morphine	300
PCP	25

Available information

Published papers:
- Rapitest: Korte T et al., J Anal Toxicol, 21:49 (1997)
- Pharmscreen: Taylor HE et al., J Anal Toxicol 23:119 (1999)
- Dipro10/Drugscreen 5 panel (Dipro Diagnostic Products) An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of workplace Programs. email: wvogl@samsha.gov
- Ultimed Surestick Drug Screen Card (The Ultimate Products) Bogema SC, Performance study of four rapid on-site drug testing devices, presentation at AACC Conference Chicago 1998

Comments and conclusions

ADVANTAGES
- quick and inexpensive
- no handling of urine
- built-in control line
- the other distributors also provide other combinations of drugs in the multi-tests

DISADVANTAGES
- strict time limit: read after 3 min but before 8 min
- several identical tests distributed by different companies. This leads to confusion and difficulties to evaluate the reliability of the information provided by each distributor. The results of the evaluation-studies of the different tests and the cross-reactivities also show differences.

COMMENTS AND CONCLUSION
- high negative predictive value (no false negatives) for cocaine, cannabinoids and opiates according to litterature
- amphetamine/methamphetamine: same problem as most urine devices manufactured in the U.S., not sufficiently evaluated for the detection of designer amphetamines

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Quickscreen

Manufacturer:	***PhamaTech***
Product identical to:	Surescreen (Surescreen Diagnostics)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BARB, TCA, MDN
Number of parameters per device:	1 - 6
Cost:	14 EURO for a 5 drug panel
FDA	approved for AMP, mAMP, CAN, COC, OPI, PCP, BZO
Storage conditions:	0 - 28°C
Manipulations to obtain a result:	teststrip (dip and read) and cassette (pipette and read) format Drug Multi test: 1) collect urine in a cup but limit the volume to a height of 1.25 cm 2) dip the device in the urine for at least 1 min 3) read result: a negative one after 1 min, positive one after 10 min
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	acceptable

Cut-Off :	ng/ml
Amphetamines	1000
Barbiturates	200
Benzodiazepines	200
cannabinoids	50
benzoylecgonine	300
methadone	300
methamphetamine	500
morphine	300
PCP	25

Available information

- manufacturer: Phamatech, UK and Surescreen Diagn., UK
- Internet: http://www.phamatech.com
- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov

Comments and conclusions

ADVANTAGES
- no specimen handling
- built-in control line
- a large range of single tests and combinations of tests to a multi-test are available
- cheap

DISADVANTAGES
- card gets messy
- strict time limit: read after 3 min but before 10 min

COMMENTS
- excellent assistance by the manufacturer and its distributors, full documentation
- test should be very accurate according to their evaluation study (comparison with EMIT and GC/MS)
- same principle as the ABM test but less user friendly

Rapid Drug Screen

Manufacturer:	***AmericanBioMedica Corp.***
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, TCA
Number of parameters per device:	1 - 9
Cost:	17 EURO for a five drug panel
FDA	approved
Storage conditions:	15-30 °C
Manipulations to obtain a result:	1) collect urine to fill the cup to a certain mark; do not exceed this level 2) insert the blue end of the test card into the slot in the top of the cap by breaking the seal 3) push the card into the cup until it touches the bottom of the cup and wait for about 5 min
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	very good

Cut-Off :	ng/ml
amphetamines	1000
barbiturates	300
benzodiazepines	300
cannabinoids	50
benzoylecgonine	300
methamphetamine	1000
morphine-3-glucuronide	300
PCP	25

Available information

- manufacturer: study carried out by American Medical Laboratories
- Internet: http://www.rapiddrugscreen.com
- Bogema SC, presentation at AACC Conference Chicago 1998
- Taylor HE et al., J Anal Toxicol 23:119 (1999)
  An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov

Comments and conclusions

ADVANTAGES
- cup can be used to collect urine; no handling of the sample at any stage
- panel available with AMP and mAMP test
- built-in control line
- built-in temperature check

DISADVANTAGES
- sufficient volume of sample necessary; at least 25 ml required to do the panel test properly; single tests also available requiring 8-10 ml of sample

ANALYTICAL CONCLUSION
- accuracy of the cut-offs is heavily criticised in the paper of Bogema: too many false positive results at concentrations below (50 %) the proposed cut-off

- positive predictive value poor (false positives) for THC but sensitivity excellent (no false negatives);
- some false negatives for amphetamines with the AMP test

PROBLEM WITH FALSE POSITIVES IF THE ANALYTICAL CUT- OFF VALUES DO NOT MATCH THE REQUIRED SAMHSA and EUROPEAN CUT-OFFs. RELIABILITY OF THE AMPHETAMINE AND METHAMPHETAMINE TESTS NEEDS TO BE EVALUATED PROPERLY.

Rapiscan

Manufacturer:	***Cozart Bioscience Ltd.***
Matrix:	saliva
Available for:	AMP, CAN, COC, OPI, BZO
Number of parameters per device:	5
Cost:	18 EURO
FDA	not approved
Storage conditions:	room temp.
Manipulations to obtain a result:	1) collect a saliva sample with the Cozart Rapiscan Saliva Collection pack - based on the Omni-Sal saliva sampler (dilution with buffer) 2) pipette a required volume of oral fluid into the cartridge (disposable pipettes) 3) the cartridge, which houses the immunoassays, is placed into the instrument and an incubation period of 10 min is activated 4) digital read-out for each drug tested and saving of results
positive/negative control line:	not present
possibility to store result:	Yes
Interpretation of the result:	digital read-out
User friendliness:	acceptable

Cut-Off :	ng/ml
amphetamine	30
MBDB	30,000
MDA	30
MDEA	30,000
MDMA	3,000
methamphetamine	3,000
THC	600
cocaine	150
morphine	30

Available information

- Internet: http://www.cozart.co.uk/drugtest/rapiscan.html
- Malcolm C. et al., Evaluation of an on-site method for the detection of drugs of abuse in saliva. Poster presented at the TIAFT/SOFT Joint Congress, October 1998, Albuquerque, New Mexico
- presentation by Dr. John Oliver (University of Glasgow) for the police forces

Comments and conclusions

ADVANTAGES
- applicable to saliva (non-invasive, no adulteration, recent abuse)
- panel of drugs tested within 10 minutes
- interpretation of result objective and storage of results possible
- quantitative results - distinction positive/negative based on a pre-established cut-off value

DISADVANTAGES
- pricy (+ cost of the instrument: 3000 EURO)
- rather complicated procedure for sampling and application of the sample
- training of the operator absolutely necessary
- no evaluation study available; a large trial of the previous Rapiscan model was carried out in some regions of Scotland in cooperation with the police forces
- cut-offs for cannabinoids are too high

COMMENTS
- the previous model accepted as "user friendly" by police forces
- good results for opiates, benzodiazepines and methadone in the laboratory
- no data for the other drugs

DEFINITE ADVANTAGES ARE: THE USE OF SALIVA, THE POSSIBILITY TO SCREEN FOR A WIDE RANGE OF DRUGS, CLEAR PRESENTATION OF A "QUANTITATIVE" RESULT AND STORAGE OF THE RESULTS FOR ALL DRUGS. ACCURACY, ESPECIALLY FOR CANNABIS, NEEDS TO BE EVALUATED IN THE FIELD TRIALS. DEMONSTRATIONS FAILED TO CONVINCE US.

Testcup

Manufacturer:	***Roche Diagnostics Corp.***
Matrix:	urine
Available for:	AMP, CAN, COC, OPI, PCP, BZO, BAR
Number of parameters per device:	4 or 5
Cost:	17 Euro for the NIDA-5; 15 Euro without PCP
FDA	approved
Storage conditions:	15-30°C
Manipulations to obtain a result:	1) collect urine in cup and close 2) turn the cup in the direction of the test windows so that 1/2 to 1/3 of the lid is covered, for 10 counts 3) control lines show after 2-5 min 4) pull of the plastic label that covers the test windows and read the result for each parameter
positive/negative control line:	present
possibility to store result:	Yes
Interpretation of the result:	white + is positive/ blue - is negative
User friendliness:	good

Cut-Off :	ng/ml
amphetamine	1,000
MDA	2,000
MDMA	ND
methamphetamine	ND
barbiturates	200
benzodiazepines	200
cannabinoids	50
benzoylecgonine	300
morphine	300
PCP	25

Available information

Manufacturer (Internet: http://www.roche.com)
- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov
- reports from the U.S. Court on on-site tests
- Bogema SC, presentation at AACC Conference Chicago 1998
- Tsai J et al., American Academy of Forensic Sciences, February 1997

Published papers
- Crouch DJ et al., J Forensic Sci 43:35 (1998)
- Crouch DJ et al., J Anal Toxicol 22:493 (1998)
- Buchan BJ et al, J Forensic Sci, 43:395 (1998)
- Towt J et al., J Anal Toxicol, 19:504 (1995)
- Taylor HE et al., J Anal Toxicol 23:119 (1999)

Comments and conclusions

ADVANTAGES
- no manipulation of urine; cup = sample container
- clear interpretation of result: + = positive; – = negative
- control line available
- temperature check possible
- panel testing: in the near future, a testcup with benzodiazepines instead of PCP will be available

DISADVANTAGES
- a minimum volume of 15 ml of urine is recommended
- some experience of handling the device is needed
- risk of contamination of the test area if urine is spilled during collection
- detection times can be long depending on the quality of the urine sample

ANALYTICAL CONCLUSION
- High positive predictive value for all drugs. In two studies a definite % of false negatives for cannabis is reported. The corresponding THC-COOH concentrations were in the range 21- 46 ng/ml.
- Low rate of false positives except in the study of Buchan et al.
- Lack of detection of designer amphetamines ! "Conservative test"

THE MANUFACTURER WILL HAVE TO DEAL WITH THE TYPICAL EUROPEAN PROBLEM OF THE DESIGNER AMPHETAMINES.

Teststik

Manufacturer:	***Roche Diagnostics Corp.***
Matrix:	urine
Available for:	AMP, CAN, COC, OPI, PCP, BAR, BZO
Number of parameters per device:	1
Cost:	6 EURO per parameter
FDA	approved
Storage conditions:	15-30 °C
Manipulations to obtain a result:	1) remove the protective sleeve - dip in specimen for 5 -10 sec 2) replace the sleeve - and put down the test horizontally 3) wait 2-5 min until the control line appears 4) remove the lid that covers the test window and read result

positive/negative control line: present
possibility to store result: Yes
Interpretation of the result: white + is positive/ blue - is negative
User friendliness: very good

Available information

- Hofbauer BM et al., Comparison of immunochromatographic rapid tests for screening of benzodiazepines, amphetamine and its derivatives (ecstasy) in urine. Poster presented at the TIAFT/SOFT Joint Congress, October 1998, Albuquerque, New Mexico

- An evaluation of Non-Instrumented Drug Test Devices. Report of the Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Prevention, Division of Workplace Programs. email: wvogl@samsha.gov

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Toxiquick

Manufacturer: ***Bionike Laboratories Inc.***
Matrix: urine, saliva
Available for: AMP, mAMP, CAN, COC, OPI, BZO, BAR, MDN
Number of parameters per device: 1 or 6
Cost: 2 EURO for a single test
FDA approved
Storage conditions: 4 - 30°C
Manipulations to obtain a result: SINGLE TESTS
1) dip test strip in the urine sample up to the mark
2) read the result within 3 to 10 min., do not interprete the result after 10 min

PANEL TEST 5+1 (mAMP, CAN, COC, OPI, BZO, MTD)
1) put 18 drops of urine into the sample window

positive/negative control line: present
possibility to store result: No
Interpretation of the result: 1 line = positive / 2 lines = negative
User friendliness: acceptable

Cut-Off :	ng/ml
amphetamine	500
barbiturates	100
benzodiazepines	100
cannabinoids	20
benzoylecgonine	50
methadone	250
methamphetamine	500
morphine	20

Available information

- Internet site currently under construction: http://www.bionike.com
- more information can be found at Biomar, Germany - several German evaluation studies including one study with saliva
- Hofbauer BM et al., Comparison of immunochromatographic rapid tests for screening of benzodiazepines, amphetamine and its derivatives (ecstasy) in urine. Poster presented at the TIAFT/SOFT joint Congress, october 1998, Albuquerque, New Mexico

Comments and conclusions

ADVANTAGES
- simple, cheap dip test
- small volume of urine acceptable
- tests possibly applicable to saliva samples, because of the high sensitivity
- large range of single tests

DISADVANTAGES
- flimsy dip tests, not really user friendly
- cross-reactivities are not clearly indicated in the information booklet from Biomar
- major drawback: cut-offs are different from the NIDA cut-off values for all drug classes tested
- in the evaluationstudies, no cut-off values for confimation with GC/MS or HPLC are mentioned
- Saliva testing is recommended after freezing and thawing of the collected saliva sample, which is not practical to do at the roadside.

COMMENTS
For urine testing, there will be too many false positives as a result of the discrepancies between Bionike's cut-off values and the SAMSHA cut-offs. On the other hand, such a sensitivity might be advantageous to test with saliva.
In one study, the test has the lowest limit of detection for different benzodiazepines and shows excellent cross-reactivities with designer amphetamines for the AMP and mAMP test. Ephedrine interferes in the mAMP test.

Triage

Manufacturer:	***Biosite Diagnostics***
Matrix:	urine
Available for:	AMP, CAN, COC, OPI, PCP, BZO, BAR, TCA
Number of parameters per device:	5 or 7
Cost:	20 EURO for a five drug panel
FDA	approved
Storage conditions:	15 - 25 °C
Manipulations to obtain a result:	1) urine is incubated for 10 min in the reaction cup 2) transfer to the detection zone using a syringe 3) add 3 drops of wash solution and the results are ready
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	presence of a line = positive result - negative = no line
User friendliness:	not acceptable

Cut-Off :	ng/ml
Amphetamine	1000
methamphetamine	1000
barbiturates	300
benzodiazepines	300
cannabinoids	50
benzoylecgonine	300
methadone	300
morphine	300
tricyclics	1000

Available information

A great number of evaluation studies published at international congresses (SOFT, A.A.C.C.), provided by the manufacturer.
Published articles:
- Fitzgerald R.L. et al., Clin. Chem. 40/3:373 (1994)
- Wu A.H.B. et al., J. Anal. Toxicol. 17:241 (1993)
- Koch T.R. et al., J. Anal. Toxicol. 18:168 (1994)
- Buechler K.F. et al., Clin. Chem. 38:1678 (1992)
- Schwartz J.G. et al., American Journal of Emergency medicine 12:513 (1994)
- Buchan BJ et al, J Forensic Sci, 43:395 (1998)

Comments and conclusions

ADVANTAGES
- easy to read color endpoint results
- Test results are very accurate!! Plenty of evaluation studies!
- Positive and negative built-in controls

DISADVANTAGES
- not user friendly, procedure rather complicated
- handling of urine
- expensive
- strict time limit (10 min)

CONCLUSION
Although very accurate, not recommended for Roadside Testing!

Verdict II

Manufacturer:	***Medtox Diagnostics Inc.***
Product identical to:	Profile II (Medtox) (only a 5 panel)
Matrix:	urine
Available for:	AMP, CAN, COC, OPI, PCP
Number of parameters per device:	1 - 5
Cost:	
FDA	approved
Storage conditions:	2 - 25°C
Manipulations to obtain a result:	1) Aspirate urine with a plastic pipet 2) Add 2 drops of sample to the sample well 3) Read the result after 5 minutes but within 7 minutes
positive/negative control line:	not present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
amphetamine	1000
cannabinoids	50
benzoylecgonine	300
morphine	300
PCP	25

Available information

- Internet: http://www.medtox.com

Comments and conclusions

This product is manufactured by the same company who introduced the EZ Screen urine tests many years ago. The Verdict-II and Profile-II have an improved quality and user friendliness.
A Profile II-A (with an adulteration panel) and Profile-ER (with BZO, BARB, TCA and MDN included in the panel) are currently under development.

Visualine II

Manufacturer:	***Avitar Technologies Inc.***
Product identical to:	Sunline (Sun Biomedical Laboratories Inc.)
Matrix:	urine
Available for:	AMP, mAMP, CAN, COC, OPI, PCP, BZO, BAR, MDN
Number of parameters per device:	1 or 4 - 5
Cost:	15 EURO for a five panel
FDA	approved for CAN, COC, OPI, PCP, BZO
Storage conditions:	2 - 30°C
Manipulations to obtain a result:	1) Aspirate urine with a plastic pipet (included in the pack) 2) Add 3 drops of sample to the sample well 3) Read the result after 5 minutes
positive/negative control line:	present
possibility to store result:	No
Interpretation of the result:	1 line = positive / 2 lines = negative
User friendliness:	good

Cut-Off :	ng/ml
cannabinoids	50
cocaine	300
methamphetamine	500
morphine	100
PCP	25

Available information

- Internet: http://www.avitarinc.com
- Manufacturers: Avitar Techn, Inc. and Sun Biomedical Lab., Inc.

Comments and conclusions

ADVANTAGES
- quick and very inexpensive
- easy to use, no messy test after use
- clear interpretation of the test results in the multipanel (detection window for every parameter)
- a few drops of urine are sufficient to do the test properly
- a large range of single tests and any combinations of 4 or 5 tests to a multi-test can be custom made
- built-in control line

DISADVANTAGES

- multi panel tests are quite large; urine has to be added to every well which is a bit time consuming
- no extensive evaluation
- cross-reactivity values are not reported clearly e.g. for cannabis
- cut-off for opiates different from SAMHSA

COMMENTS AND CONCLUSION

Sun Biomedical Labs are the manufacturers of the Sunline products and formerly also manufactured Visualine II. They offer very competetive prices and absolute guarantee that their tests work! We presume that the Visualine and Sunline tests are basically identical.

Avitar claims 99% accurate test results but an abstract provided by Sun Biomedical Labs shows some false positives compared to FPIA and EMIT because of the higher sensitivity of the device for the drugs or their metabolites.

HIGHER SENSITIVITIES FOR MORPHINE WILL PRODUCE FALSE POSITIVES e.g. with ingestion of food containing poppy seeds. HIGH CROSS-REACTIVITY FOR COCAINE MIGHT BE ADVANTEGEOUS FOR APPLICATION TO SALIVA.

Cross-reactivities of the "AMPHETAMINE" type devices

DEVICE	ANALYTE	%
Accusign		
	MDA	200
	d,l-amphetamine	100
	d-amphetamine	100
	p-hydroxymethamphetamine	33
	phentermine	20
	l-amphetamine	14
	3-OH-tyramine	11
	MDMA	10
	β-phenylethylamine	5
Dip Drugscan-one step		
	d-amphetamine	100
	MDA	83
	d,l-amphetamine	83
	B-phenylethylamine	6
	pseudoephedrine	5
	l-amphetamine	2
	phenylpropanolamine	1
DrugCheck 5		
	MDA	180
	d,l-amphetamine	100
	d-amphetamine	100
	l-amphetamine	4
	phenylpropanolamine	2
	tyramine	1
	B-phenylethylamine	1
	pseudoephedrine	1
	ephedrine	
Drugwipe		
	p-chloramphetamine	300
	p-methoxyamphetamine	150
	MDA	120
	MDMA	120
	d-methamphetamine	100
	d-amphetamine	100
	p-hydroxymethamphetamine	60
	MDEA	40
	l-methamphetamine	12
	ephedrine	12
	N-hydroxy-MDA	12
	tyramine	6
	B-phenylethylamine	6
	l-amphetamine	3
	phentermine	2
DTx		
	d-amphetamine	100
	MDA	20
	l-amphetamine	10

DEVICE	ANALYTE	%
First Check		
	phentermine	500
	MDA	200
	d-amphetamine	100
	d,l-amphetamine	20
	tryptamine	3
	3-OH-tyramine	1
Frontline		
	MDA	120
	MDMA	120
	methamphetamine	100
	d-amphetamine	100
	MBDB	40
	MDEA	40
Genie Cup		
	d-amphetamine	100
	MDA	20
	l-amphetamine	10
	B-phenylethylamine	1
	tyramine	1
Pharmscreen Drug Screen card		
	d-amphetamine	100
	MDA	20
	l-amphetamine	10
Quickscreen		
	d-amphetamine	100
	phentermine	66
	MDA	22
	B-phenylethylamine	10
	d,l-amphetamine	10
	tyramine	8
	l-amphetamine	1
	mephentermine	1
Rapid Drug Screen		
	d-amphetamine	100
	d,l-amphetamine	66
	MDA	33
	l-amphetamine	13
	methamphetamine	11
	MDEA	2
Rapiscan		
	d-amphetamine	100
	MDA	100
	d-methamphetamine	1
	imipramine	1
	MBDB	1
	MDEA	1
	MDMA	1

DEVICE	ANALYTE	%
Testcup		
	d-amphetamine	200
	p-hydroxyamphetamine	100
	d,l-amphetamine	100
	MDA	50
	l-amphetamine	4
	B-phenylethylamine	1
	phenylpropanolamine	1
Teststik		
	d,l-amphetamine	100
	p-hydroxyamphetamine	50
	MDA	25
	l-amphetamine	8
Toxiquick		
	d-amphetamine	100
	MDA	100
Verdict II		
	d-amphetamine	100
	l-amphetamine	13
	phentermine	10
	tyramine	1

Cross-reactivities of the "METHAMPHETAMINE" type devices

DEVICE	ANALYTE	%
Accusign		
	d-methamphetamine	100
	d-amphetamine	33
	MDMA	14
	p-OH-methamphetamine	10
	ephedrine	1
	MDA	1
	d,l-amphetamine	1
Genie Cup		
	d-methamphetamine	100
	MDMA	50
	procaine	10
	l-methamphetamine	4
	d-amphetamine	2
	chloroquine	2
	B-phenylethylamine	2
	ranitidine	2
	ephedrine	2

DEVICE	ANALYTE	%
Pharmscreen Drug Screen Card		
	d-methamphetamine	100
	MDMA	25
	procaine	5
	l-methamphetamine	2
	B-phenylethylamine	1
	d-amphetamine	1
	ranitidine	1
	pseudoephedrine	1
Quickscreen		
	d-methamphetamine	100
	isoproterenol	33
	d,l-amphetamine	25
	MDMA	14
	nylidrin	10
	ephedrine	5
Rapid Drug Screen		
	pseudoephedrine	100
	d-methamphetamine	100
	MDMA	50
	d-amphetamine	5
	ephedrine	4
	l-methamphetamine	4
	MDA	2
Toxiquick		
	d-methamphetamine	100
	MDMA	100
Visualine II		
	d-methamphetamine	100
	MDMA	50
	pseudoephedrine	6
	d,l-amphetamine	5
	d-amphetamine	5
	MDA	5

Cross-reactivities of the "CANNABIS" type devices

DEVICE	ANALYTE	%
Accusign		
	11-nor-Δ9-THC-COOH	100
	cannabinol	33
	Δ9-THC	5
Dip Drugscan-one step		
	11-nor- Δ9-THC-COOH	100
	Δ9-THC	12
	11-OH- Δ9-THC	5
DrugCheck 5		
	11-nor- Δ9-THC-COOH	100
Drugwipe		
	11-nor- Δ9-THC-COOH	100
	11-OH- Δ9-THC	10
	Δ9-THC	5
	cannabinol	5
DTx		
	11-nor- Δ9-THC-COOH	100
	cannabinol	5
	Δ9-THC	5
	11-OH-Δ9-THC	2
First Check		
	11-nor-Δ9-THC-COOH	100
	Δ9-THC	5
	cannabinol	3
Frontline		
	11-nor-Δ9-THC-COOH	100
	11-OH-Δ9-THC	10
	Δ9-THC	5
	cannabinol	5
Genie Cup		
	11-nor-Δ9-THC-COOH	100
	11-OH-Δ9-THC	2
Pharmscreen Drug Screen		
	11-nor-Δ9-THC-COOH	100
	Δ9-THC	5
	11-OH-Δ9-THC	2
Quickscreen		
	11-nor-Δ9-THC-COOH	100
	Δ9-THC	100
	11-OH-Δ9-THC	5

DEVICE	ANALYTE	%
Rapid Drug Screen		
	11-nor-Δ9-THC-COOH	100
	cannabinol	1
	Δ9-THC	1
	11-OH-Δ9-THC	1
Rapiscan		
	11-nor-Δ9-THC-COOH	1000
	11-OH-Δ9-THC	100
	Δ9-THC	100
Testcup		
	11-OH-Δ9-THC	125
	11-nor-Δ9-THC-COOH	100
Teststik		
	11-OH-Δ9-THC	125
	11-nor-Δ9-THC-COOH	100
Toxiquick		
	11-nor-Δ9-THC-COOH	100
Verdict II		
	11-nor-Δ9-THC-COOH	100
	Δ9-THC	2
	11-OH-Δ9-THC	2

Cross-reactivities of the “COCAINE” type devices

DEVICE	ANALYTE	%
Accusign		
	benzoylecgonine	100
	cocaine	60
	ecgonine	30
Dip Drugscan-one step		
	benzoylecgonine	100
	cocaine	100
DrugCheck 5		
	benzoylecgonine	100
	cocaine	100
Drugwipe		
	cocaine	150
	benzoylecgonine	100
DTx		
	benzoylecgonine	100
	cocaine	100

DEVICE	ANALYTE	%
First Check		
	benzoylecgonine	100
	cocaine	60
	ecgonine	30
Frontline		
	cocaine	300
	benzoylecgonine	100
Genie Cup		
	benzoylecgonine	100
	cocaine	100
Pharmscreen Drug Screen Card		
	cocaine	100
	benzoylecgonine	100
Quickscreen		
	benzoylecgonine	100
	cocaine	100
	metoclopramide	12
Rapid Drug Screen		
	cocaine	375
	benzoylecgonine	100
	cocaethylene	100
Rapiscan		
	benzoylecgonine	500
	cocaine	100
Testcup		
	benzoylecgonine	100
	cocaine	4
Teststik		
	benzoylecgonine	100
	cocaine	75
Toxiquick		
	benzoylecgonine	100
	cocaine	100
Verdict II		
	benzoylecgonine	100
	cocaine	30
Visualine II		
	cocaine	100
	benzoylecgonine	100

Cross-reactivities of the “OPIATE” type devices

DEVICE	ANALYTE	%
Accusign		
	morphine	100
	codeine	100
	hydrocodone	60
	morphine-3-glucuronide	60
	hydromorphone	50
	nalorphine	30
	levorphanol	6
	thebaine	6
Dip Drugscan-one step		
	hydromorphone	100
	nalorphine	100
	morphine-3-glucuronide	100
	morphine	100
	heroin	100
	codeine	100
	hydrocodone	60
	levorphanol	50
	naloxone	30
	oxycodone	30
	thebaine	20
	N-norcodeine	15
DrugCheck 5		
	codeine	100
	morphine	100
	nalorphine	100
	morphine-3-glucuronide	100
	hydromorphone	100
	heroin	100
	hydrocodone	60
	levorphanol	50
	naloxone	30
	oxycodone	30
	thebaine	20
	N-norcodeine	15
Drugwipe		
	codeine	100
	morphine	100
	dihydrocodeine	100
	ethyl morphine	100
	heroin	66
	hydrocodone	66
	morphine-3-glucuronide	66
	thebaine	66
	hydromorphone	40
	levorphanol	8
	oxycodone	2
	nalorphine	1
	N-norcodeine	1

DEVICE	ANALYTE	%
DTx		
	codeine	100
	ethyl morphine	100
	morphine	100
	hydromorphone	75
First Check		
	codeine	120
	morphine-3-glucuronide	100
	hydromorphone	42
	hydrocodone	30
Frontline		
	morphine	100
	ethyl morphine	100
	codeine	100
	dihydrocodeine	100
	heroin	66
	hydrocodone	66
	morphine-3-glucuronide	66
	hydromorphone	40
Genie Cup		
	ethyl morphine	100
	morphine	100
	codeine	100
	heroin	100
	hydrocodone	85
	hydromorphone	75
	morphine-3-glucuronide	60
	oxycodone	2
	meperidine	1
	N-norcodeine	1
	thebaine	1
Oral Screen		
	6-acetyl-morphine	100
	morphine-3-glucuronide	100
	morphine	100
	hydromorphone	100
	hydrocodone	100
	codeine	100
	heroin	100
	thebaine	5
Pharmscreen Drug Screen Card		
	ethyl morphine	100
	morphine	100
	codeine	100
	hydrocodone	80
	hydromorphone	75
	morphine-3-glucuronide	60
	oxycodone	2
	meperidine	1
	N-norcodeine	1
	thebaine	1

DEVICE	ANALYTE	%
Quickscreen		
	heroin	100
	codeine	100
	morphine-3-glucuronide	100
	morphine	100
	ethyl morphine	85
	naloxone	75
	hydrocodone	75
	hydromorphine	75
	oxycodone	70
	levorphanol	60
	N-norcodeine	60
	dextromethorphan	60
	thebaine	50
	nalorphine	50
	deoxyephedrine	30
Rapid Drug Screen		
	codeine	100
	morphine	100
	morphine-3-glucuronide	100
	ethyl morphine	56
	heroin	56
	6-acetyl-morphine	56
	hydrocodone	45
	thebaine	35
Rapiscan		
	pholcodine	333
	6-acetyl-morphine	100
	morphine	100
	heroin	100
	codeine	100
	dihydrocodeine	100
	morphine-3-glucuronide	40
	nalorphine	2
Testcup		
	ethyl morphine	100
	morphine	100
	codeine	100
	morphine-3-glucuronide	86
	dihydrocodeine	75
	dihydromorphine	75
	hydrocodone	60
	6-acetyl-morphine	60
	hydromorphone	43
	thebaine	30

DEVICE	ANALYTE	%
Teststik		
	ethyl morphine	100
	codeine	100
	dihydrocodeine	100
	morphine	100
	morphine-3-glucuronide	75
	dihydromorphine	75
	6-acetyl-morphine	75
	hydrocodone	50
	hydromorphone	43
	thebaine	15
Toxiquick		
	dihydromorphine	100
	morphine-3-glucuronide	100
	morphine	100
	hydromorphine	100
	thebaine	100
	dihydrocodeine	100
	codeine	100
	6-acetyl-morphine	100
	hydrocodone	100
	ethyl morphine	100
Verdict II		
	hydrocodone	250
	morphine	100
	hydromorphone	100
	ethyl morphine	100
	codeine	100
	6-acetyl-morphine	100
	heroin	100
	morphine-3-glucuronide	50
	thebaine	25
	dihydrocodeine	1
Visualine II		
	Morphine	100
	Codeine	33
	Hydromorphine	10
	Levorphanol	

Cross-reactivities of the "BENZODIAZEPINE" type devices

DEVICE	ANALYTE	%
Accusign		
	alprazolam	6000
	chlorazepate	2000
	estazolam	600
	bromazepam	300
	diazepam	300
	flunitrazepam	300
	prazepam	100
	oxazepam	100
	flurazepam	66
	triazolam	30
	nitrazepam	30
	lorazepam	6
Frontline		
	triazolam	100
	temazepam	100
	alpha-hydroxy-alprazolam	100
	alprazolam	100
	bromazepam	100
	diazepam	100
	flunitrazepam	100
	flurazepam	100
	nitrazepam	100
	nordazepam	100
	7-amino-flunitrazepam	100
	alpha-hydroxy-triazolam	66
	7-amino-nitrazepam	66
	7-aminoclonazepam	66
	oxazepam	50
	lorazepam	50
Quickscreen		
	nitrazepam	100
	oxazepam	100
	temazepam	80
	chlordiazepoxide	66
	diazepam	50
	flunitrazepam	50
	lormetazepam	50
	triazolam	40
	alprazolam	40
	clonazepam	40
	lorazepam	40
	bromazepam	33
	desmethyldiazepam	27
	flurazepam	20
	prazepam	20
Rapiscan		
	temazepam	100
	oxazepam	5
	diazepam	1

DEVICE	ANALYTE	%
Toxiquick		
	oxazepam	100
	nitrazepam	100
	flurazepam	100
	estazolam	100
	diazepam	100
	desmethyldiazepam	100
	alprazolam	100
	temazepam	100
	chlorazepate	100

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CONCLUSIONS

Of the 19 original devices that have been summarized, 16 were designed for the screening of urine samples, 3 for saliva and 1 for sweat. They represent a total of approximately 37 devices on the international market.

USER FRIENDLINESS

Ease-of-use

For urine, there exist roughly three kinds of test designs to obtain a result with an on-site drugtest:
- "dip" and read, single test strip and multiple test-strip
- "pipette" and read, single testcassette and multiple testcassette
- cup principle

Several manufacturers increase the flexibility of their product line by supplying a range of tests: single, multiple, dip and pipette type tests, whatever the customer wants.

For the cassette type tests, urine needs to be pipetted, either in one well (e.g. Syva Rapidtest, Dade Behring) or in several wells (e.g. Visualine, Avitar techn.). There are single and multiple parameter tests. A few drops of urine are sufficient to do the test. This might not be important during roadside testing since the collected volume of urine is generally higher than 20 ml.
Teststik (Roche Diagnostics) is without any doubt the most practical one of the "dip" tests for a single parameter. The robustness and the housing of the test are perfectly suitable for the roadside. A multi-panel "dip" and read test consists of one large testcard (e.g. Quickscreen) or several teststrips combined in one housing; the latter is preferred because of the special cap used to cover the test strips after they had been dipped into the urine e.g. Dip Drugscan-one step (Syntron Bioresearch), multiple drug screen Instastrip (Cortez Diagnostics), Rapitest (Morwell Diagnostics), Dipro Drugscreen 5 panel (Dipro Diagnostic Products)…
The Rapid Drug Screen (ABM) combines the principle of a testcard with a cup to collect the urine sample. A slot in the cap allows the test card to be inserted in the cup containing the urine. Unlike the other testcups, the ABM test offers a wide range of panels to test for. The principle of a testcup seems the most suitable one for roadside testing but this needs to be confirmed in WP 4. The number of manipulations is restricted and the tester is not handling urine at any time. The cup always includes a temperature check. The Testcup (Roche Diagnostics) is the most evaluated cup test but the DrugCheck 5 (Drug Free Enterprises) seems the easiest to use.

Interpretation of the result

Again different principles to evaluate the screening result of the urine test:
- > 90 % of the tests: always the presence of a control line (test is valid); presence of a second line = negative result, absence of a second line = positive result.
- Roche Testcup and Teststik: the presence of a control line (test is valid);
  blue – = negative; white + = positive
- Frontline and Drugwipe: Appearance of a color = positive
- Triage: positive and negative control line; an additional line = positive result

It is very important that the validity of the test is demonstrated by the appearance of a control line. Only Frontline (Roche Diagnostics) and Drugwipe (Securetec GmbH) do not have a built-in control. The evaluation of the Frontline and the Drugwipe test is also difficult since the appearance of a pink color and the comparison with a colour scale is rather subjective.
A clear interpretation of the result is possible for Testcup, Teststik (Roche Diagnostics) and Triage (Biosite Diagnostics). However, the use of the Triage is not recommended for routine roadside testing. The blue line (negative result) for Testcup and Teststik can be easily distinguished from the white plus (positive result).

Unfortunately, all the other tests show a negative result when a second reddish-pink line appears in addition to the control line. The intensity of the color is not important. A clear distinction between positive and negative results requires some training before routine testing can be carried out.

Saliva and Sweat

- Drugwipe (Securetec GmbH) is the only test not requiring the collection of a saliva sample; the test is also applicable to sweat. Although the absence of a built-in control and of a multi-panel test are definite disadvantages, Drugwipe is very easy to apply.
- The Oral Screen Morphine test (Avitar Techn.) combines an inventive saliva sampling system with a common urine "pipette" and read device. Although a three panel test will be introduced, the lack of an amphetamine test is a disadvantage.
- The Rapiscan system appears to be the most objective system applicable for roadside testing. Extensive training is needed but the screening for several drug classes in one saliva sample is innovative. The accuracy of the test remains to be demonstrated.

Large-scale trials have to be carried out to demonstrate wheather one or several of these saliva tests meet the requirements of a simple road-side screening test. The presence of drugs in saliva points to recent use and demonstrates the impairment at the moment of sampling to a higher extent than the presence of drugs in urine.

CUT-OFF VALUES

The use of analytical cut-off values for the screening and confirmation of a sample enables the analist to distinguish between a positive and a negative result. The screening cut-off values should be based on the sensitivity of the assay, as well as on its pharmacological relevance. Cut-off values that are too low will result in an excessive number of GC/MS negative samples, and cut-off values that are too high will result in too many false negative samples.

Saliva and Sweat

For the screening of drugs in saliva and sweat, no official cut-off values have been recommended. The application of a cut-off value for a certain analyte is determined by the reported concentrations in saliva and sweat and by the analytical sensitivity of the technique.

Urine

The reference guidelines set by SAMHSA (Substance Abuse and Mental Health Services Administration, formerly NIDA) in the U.S. for the screening of drugs of abuse in urine are intended for workplace drug testing.

- Amphetamines 1000 ng/ml
- Cannabinoids 50 ng/ml
- Cocaine metabolite 300 ng/ml
- Opiates (morphine) 2000 ng/ml
- PCP 25 ng/ml

A working group of the European Union has introduced somewhat different cut-off values adapted to the needs of the European countries. PCP is not included, ecstasy and its analogues represent an increasing problem. In the new Belgian law on driving under the influence of illicit drugs, the cut-off values for the on-site screening of a urine sample are:

- Amphetamines (amphetamine, MDA, MDMA, MDEA, MBDB): 1000 ng/ml
- Cannabinoids: 50 ng/ml
- Cocaine Metabolite: 300 ng/ml
- Opiates (Morphine): 300 ng/ml

Most of the manufacturers of the on-site urine tests use similar cut-off values for the illicit drugs. Some exceptions are observed. The screening cut-off for opiates is lower for Visualine (100 ng/ml) (Avitar Techn.), Toxiquick (20 ng/ml) (Bionike Lab.) and Frontline (200 ng/ml) (Roche Diagnostics). Toxiquick also sets

lower screening cut-offs for benzoylecgonine and cannabinoids. If the tests are too sensitive or if the experimental cut-off values are different from the theoretical cut-off values, the number of false positives increases.

Amphetamines

The screening of amphetamine, methamphetamine and ecstasy-like substances is an interesting but complex issue in the drug testing industry.
In the U.S., the screening cut-offs for the amphetamine class (1000 ng/ml) are only set for amphetamine(s) and methamphetamine(s). They are detected with a separate AMP and mAMP test, respectively. Visualine, Toxiquick, the Syntron and Cortez tests (500 ng/ml) and Frontline (300 ng/ml) adopted lower cut-off values for amphetamine and methamphetamine.
In a number of European countries, the increasing abuse of ecstasy requires the use of a screening test sufficiently sensitive for MDMA and its analogues. For the Frontline amphetamine test a table of cut-off values for the designer amphetamines is available. Dade Behring provided us with an evaluation study in which the designer amphetamines were screened with the Syva Rapidtest AMP and mAMP. Generally, an AMP test also detects MDA, a mAMP test detects MDMA and occasionally MDEA and MBDB.

CROSS-REACTIVITY VALUES

Saliva and Sweat

Two major issues are important here: (1) saliva and sweat generally contain the parent drug whereas urine contains metabolites; (2) concentrations in saliva and sweat are much lower than in urine. The former is related to the specificity of the screening test, the latter focuses on sensitivity.
For the three devices applicable to saliva, the cross-reactivity of the test for the parent drug should be sufficiently high. Drugwipe provides acceptable values for amphetamines, cocaine and opiates. The Oral Screen is sufficiently sensitive to detect low morphine concentrations. The Rapiscan cross-reacts to a high extent with amphetamine and morphine, shows acceptable cross-reactivity with cocaine but lacks sensitivity for MDMA (ecstasy) and THC, the active substance in marihuana.

Urine

The cross-reactivity for the AMP test is set at 100 % for d-amphetamine. MDA, also a metabolite of MDMA, cross-reacts in the assay from 20 to 200 %. Few AMP tests show a substantial cross-reactivity for MDMA (Frontline, Accusign). Some nasal decongestants and anorectic medication (β-phenylethylamine, l-amphetamine, phentermine, phenylpropanolamine, pseudoephedrine and ephedrine) can interfere to a variable extent in an AMP type test.
The cross-reactivity of the mAMP test is set at 100 % for d-methamphetamine. MDMA cross-reacts in the assay from 14 to 100 %. Very few data on the other designer amphetamines are available. D-amphetamine, l-methamphetamine and some medication can interfere in the mAMP test.
The cannabis test for urine is very specific for 11-nor-d9-THC-COOH, the principal urinary metabolite of delta-9-tetrahydrocannabinol (d9-THC), the active substance of marihuana. The active metabolite 11-OH-d9-THC and d9-THC itself cross-react in most tests from < 0.5 to approximately 10 %. Teststik and Testcup show high cross-reactivity for the 11-OH-d9-THC, Quickscreen shows a high cross-reactivity for d9-THC.
The cocaine test specifically detects one of the principal urinary metabolites of cocaine, benzoylecgonine. Cocaine itself shows a cross-reactivity from 4 to 375 %. All opiate-type tests cross-react to a high extent with a number of substances: morphine and morphine-3-glucuronide, the metabolites of heroin, but also codeine and other cought supressants, mild analgesics and morphine agonists and antagonists. Confirmation by GC/MS is absolutely necessary to establish the cause of the positive screening result.
The reported cross-reactivity values for the benzodiazepine-class clearly reflect the diversity of these drugs. Most common benzodiazepines cross-react in the assay but the on-site screening assays for benzodiazepines need to be evaluated by comparison with GC/MS and HPLC.

LABORATORY EVALUATION OF THE ACCURACY OF 7 ON-SITE URINE DEVICES FOR THE SCREENING OF DRUGS OF ABUSE

Devices

- TESTCUP (TC), 4-panel/ AMP-CAN-COC-OPI
  Roche Diagnostics
  "cup" test

- TESTSTIK (TST), single test, AMP-CAN-COC-OPI
  Roche Diagnostics
  "single dip" test

- FRONTLINE (FR), single test, AMP-CAN-COC-OPI
  Roche Diagnostics
  "single dip" test

- SYVA RAPIDTEST (RAPI), 4 panel/ mAMP-CAN-COC-OPI + 1 single AMP
  Dade Behring
  "pipette" test

- RAPID DRUG SCREEN (ABM), 5 panel/ AMP-mAMP-CAN-COC-OPI
  AmericanBioMedica Corp.
  "panel testcard and cup" test

- RAPITEST (MW, Morwell), 5 panel/ AMP-CAN-COC-OPI-BZO
  Morwell Diagnostics
  "panel dip test"

- One Step INSTASTRIP (CO, Cortez), single test, AMP-CAN-COC-OPI
  Cortez Diagnostics
  "single dip" test

Study Protocol

- Previously centrifuged urine samples were stored in polypropyleen tubes of 50 ml and brought to room temperature
- The above mentioned devices were used to screen the urine samples for amphetamines/methamphetamines, cannabinoids, cocaine and opiates.
- The tests were applied according to the manufacturers' instructions.
- For TESTCUP, RAPID DRUG SCREEN and RAPITEST, the volume of urine was the predominant factor to do the test. For the INSTASTRIP, we only received 60 tests per parameter.
- All urines were screened with FPIA (Fluorescence polarization immuno assay; ADx, Abott Diagnostics) for amphetamines, cannabinoids, cocaine metabolite and opiates. The sensitivity and specificity of this technique is well-known and evaluated. The screening cut-off values were: 1000 ng/ml for amphetamines, 50 ng/ml for cannabinoids, 300 ng/ml for cocaine and 300 ng/ml for opiates.
- All the positive screening results were unambiguously confirmed with GC/MS using deuterated internal standards of the principal analytes for quantification. The applied cut-off values for confirmation were:
  - 500 ng/ml for amphetamine, methamphetamine, MDA, MDMA, MDEA and/or MBDB; other amphetamine analogues could be detected qualitatively.
  - 15 ng/ml for 11-nor-d9-THC-COOH
  - 150 ng/ml for benzoylecgonine
  - 300 ng/ml for morphine, codeine, 6-acetylmorphine; other opiates could be detected qualitatively.
- A large number of the negative screening results were also confirmed with GC/MS, especially if there was a discrepancy between one or more on-site test results and the FPIA result.

For every test device and for a certain drug class, different types of results are obtained:

- **TP = true positives** = the number of urine samples that provided a positive result with the on-site screening test and that were confirmed positive by GC/MS
- **TN = true negatives** = the number of urine samples that provided a negative result with the on-site screening test and that were confirmed negative by FPIA and/or GC/MS
- **FP = false positives** = the number of urine samples that provided a positive result with the on-site screening test and that were confirmed negative by GC/MS
- **FN = false negatives** = the number of urine samples that provided a negative result with the on-site screening test and that were confirmed positive by GC/MS

Using these results some important parameters can be calculated:

- **SENSITIVITY:** the ability of the assay to identify those urine samples that truly contain a concentration of target analyte above a certain cut-off level
- **SPECIFICITY:** the ability of the assay to identify those urine samples that are truly drug-free or that contain a concentration of target analyte below the cut-off level
- **POSITIVE PREDICTIVE VALUE:** probability that a positive test result is a true positive
- **NEGATIVE PREDICTIVE VALUE:** probability that a negative test result is a true negative

$$\textbf{Sensitivity} = \frac{\textbf{TP} \times 100}{\textbf{TP} + \textbf{FN}}$$

$$\textbf{Specificity} = \frac{\textbf{TN} \times 100}{\textbf{TN} + \textbf{FP}}$$

$$\textbf{PPV} = \frac{\textbf{TP} \times 100}{\textbf{TP} + \textbf{FP}}$$

$$\textbf{NPV} = \frac{\textbf{TN} \times 100}{\textbf{TN} + \textbf{FN}}$$

Where:

TP = True Positives
TN = True Negatives
FP = False Positives
FN = False Negatives
PPV = Positive Predictive Value
NPV = Negative Predictive Value

Results

***** CANNABIS *****

A full report of the results is enclosed. Confirmation values of 11-nor-d9-THC-COOH reported as "High" exceeded 500 ng/ml.

	n results	TP	TN	FP	FN	borderline*
TESTCUP	69	36	24	8	1	2
TESTSTIK	87	48	35	4	0	3
FRONTLINE	87	40	37	2	8	2
RAPIDTEST	87	46	39	0	2	2
ABM	60	31	26	3	0	2
MORWELL	56	30	23	3	0	1
CORTEZ	59	25	24	1	9	2

* Samples with a 11-nor-d9-THC-COOH concentration near the cut-off (15 ng/ml) and reported as a FN or a FP.

	n results	SENS	SPEC	PPV	NPV
TESTCUP	69	97	75	82	96
TESTSTIK	87	100	90	92	100
FRONTLINE	87	83	95	95	82
RAPIDTEST	87	96	100	100	95
ABM	60	100	90	91	100
MORWELL	56	100	88	91	100
CORTEZ	59	74	96	96	73

***** COCAINE *****

A full report of the results is enclosed. Confirmation values of benzoylecgonine reported as "High" exceeded 10,000 ng/ml.

	n results	TP	TN	FP	FN	borderline*
TESTCUP	69	18	49	2	0	1
TESTSTIK	85	17	66	0	2	1
FRONTLINE	86	14	66	1	5	1
RAPIDTEST	86	19	67	0	0	0
ABM	60	15	43	0	2	1
MORWELL	56	15	41	0	0	0
CORTEZ	59	9	49	0	1	1

* Samples with a benzoylecgonine concentration near the cut-off (150 ng/ml) and reported as a FN or FP.

	n results	SENS	SPEC	PPV	NPV
TESTCUP	69	100	96	90	100
TESTSTIK	85	89	100	100	97
FRONTLINE	86	74	99	93	93
RAPIDTEST	86	100	100	100	100
ABM	60	88	100	100	96
MORWELL	56	100	100	100	100
CORTEZ	59	90	100	100	98

***** OPIATES *****

A full report of the results is enclosed. Confirmation values of opiates reported as "High" exceeded 5,000 ng/ml.

	n results	TP	TN	FP	FN	borderline*
TESTCUP	69	15	53	1	0	0
TESTSTIK	82	16	65	0	1	0
FRONTLINE	86	14	68	0	4	0
RAPIDTEST	86	16	65	3	2	0
ABM	60	14	46	0	0	0
MORWELL	56	10	44	1	1	0
CORTEZ	59	17	39	2	1	0

*Samples with an opiate concentration near the cut-off (300 ng/ml) and reported as a FN or FP.

	n results	SENS	SPEC	PPV	NPV
TESTCUP	69	100	98	94	100
TESTSTIK	82	94	100	100	98
FRONTLINE	86	78	100	100	94
RAPIDTEST	86	89	96	84	97
ABM	60	100	100	100	100
MORWELL	56	91	98	91	98
CORTEZ	59	94	95	89	98

***** AMPHETAMINES *****

A full report of the results is enclosed. Confirmation values of amphetamines reported as "High" exceeded 10,000 ng/ml.

	n results	TP	TN	FP	FN	MDMA only	borderline*
TESTCUP	68	12	46	0	10	10	3
TESTSTIK	85	16	56	0	13	11	3
FRONTLINE	85	25	48	8	4	11	1
RAPIDTEST	85	26	50	6	3	11	2
ABM	59	15	38	0	6	9	3
MORWELL	55	16	35	0	4	8	3
CORTEZ	58	28	28	1	1	11	1

* Samples with an amphetamine or MDMA concentration near the cut-off (500 ng/ml) and reported as a FN or FP.

	n results	SENS	SPEC	PPV	NPV
TESTCUP	68	55	100	100	82
TESTSTIK	85	55	100	100	81
FRONTLINE	85	86	86	76	92
RAPIDTEST	85	93	89	81	96
ABM	59	88	100	100	95
MORWELL	55	80	100	100	90
CORTEZ	58	97	97	97	97

Discussion

The performance of the devices was assessed in terms of their "Positive Predictive Values" and "Negative Predictive Values" and percentages of false positive and false negative results. These are standard analytical measures of the certainty of obtaining a correct positive and negative result, respectively. Thus, a high percentage or high PPV indicates that there is a high certainty that a positive result from the device will be confirmed as positive, or as negative for a high NPV. The combination of all correct negative and positive results represents an estimate of the overall accuracy for both positive and negative results for each device. The perfect device has no false positives nor false negatives and an PPV and NPV of 100.
In order to establish an analytical quotation of the devices, the number of borderline samples that were detected as a false negative or a false positive, was also taken into account. These samples have concentrations of the target analyte near the pre-established cut-off level for confirmation; their classification as positive or negative is somewhat theoretical and the result of the on-site test is less important than for clearly positive and negative samples.
Some devices were able to identify a higher percentage of positive results but also revealed a higher number of false positives: they are referred to as an aggressive test. Other devices were giving few false positives but missing many true positives: they are referred to as a conservative test.

Cannabis
The *Syva Rapidtest*, the *Rapid Drug Screen* (ABM) and the *Rapitest* (Morwell) showed the best accuracy in the detection of cannabinoids in urine. Of the 4 FP results with the *Teststik*, 3 were obtained with borderline samples so the Teststik also proves to be a reliable test. However, *Testcup* revealed 8 FP results, two for borderline samples and two for samples with a 11-nor-d9-THC-COOH concentration of 7 and 8 ng/ml, leaving 4 really false positive results. The FN result for Testcup was obtained with a sample with a 11-nor-d9-THC-COOH concentration of 41, but the result was noted down as +/- and the Teststik was positive.
We can not explain the discrepancies between the Testcup and Teststik results. Possibly, the validity of the Testcup can be questionned when the time to obtain the result increases; this occurred with some urine samples and was not registrated.
The Frontline and Instatest (Cortez) showed too many false negatives that were not considered as borderline samples to be reliable in the detection of cannabinoids in urine. In addition, there might have been a problem to interpret the result.

Cocaine
All tests except the *Frontline* showed sufficient sensitivity and specificity for the detection of the cocaine metabolite in urine.
Of the 2 FP results for the *Testcup*, one was obtained with a borderline sample, the other sample showed a benzoylecgonine concentration of 106 ng/ml. The 2 FN results for *Teststik* corresponded to one borderline sample and one sample with a benzoylecgonine concentration of 313 ng/ml for which the result was noted down as +/-.
The Rapid Drug Screen unfortunately showed one negative result for a clearly positive confirmation with GC/MS. Possibly, the result was misinterpreted.

Opiates
All tests showed "acceptable" results for the detection of opiates in urine, the *Rapid Drug Screen* (ABM) being a very reliable test. Of the 3 FP results with *Syva Rapidtest*, 2 showed a morphine concentration of respectively 74 and 120 ng/ml, the latter also being positive with the Cortez test. Although the FPIA and GC/MS result were high for codeine, one urine sample produced a negative result for three tests, a +/- result for two and a positive result for ABM and Testcup, but not for Teststik. The sample was very dark coloured.

Amphetamines
The *Syva Rapidtest (Amp and mAMP panel)*, the *Rapid Drug Screen* (*ABM, AMP and mAMP panel*), the *Rapitest* (*Morwell, AMP*) and the *Instatest* (*Cortez, AMP*) all showed good results in the detection of amphetamine and MDMA in urine. The Instatest clearly shows very good results. Of the 6 FN results for the ABM test, 3 were considered as borderline; of the 4 FN for the Rapitest, 3 corresponded to borderline samples. Also for the Syva Rapidtest, of the 3 FN, 2 were considered as borderline. However, the Rapidtest revealed 6 FP results; neither GC/MS nor FPIA were positive for those samples. The presence of amphetamine-like compounds which do not cross-react in the FPIA assay, cannot be completely excluded.
Very consistent results were obtained for *Testcup and Teststik*. Both assays failed to detect MDMA, even in concentrations above 8000 ng/ml. Amphetamine was detected with good sensitivity.

Analytical quotation

	CANNABIS	COCAINE	OPIATES	AMP/MDMA
TESTCUP	++	+++	+++	–
TESTSTIK	+++	+++	+++	–
FRONTLINE	–	–	+	++
RAPIDTEST	+++	+++	++	++
ABM	+++	++	+++	++
MORWELL	+++	+++	+++	++
CORTEZ	–	+++	+++	+++

– = not acceptable
+ = acceptable
++ = good
+++ = very good

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Deliverable D3

Operational, user and legal requirements across EU member states for roadside drug testing equipment

Status P
Contract DG VII RO 98-SC.3032

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EXECUTIVE SUMMARY

Information Basis

To gain a representative overview of the situation in the area of traffic controls for DUI of drugs, a questionnaire was designed, covering the following topics:

- Legislation: Current situation and expected changes
- Restrictions on the application of roadside alcohol tests and drug tests
- Operational and user requirements
- Introduction of new test devices and training

All questions were intended to be answered with the help of suitable representatives of the police forces in each country, i.e. one selected police expert in the area of roadside drug testing, or several persons with expertise in different areas of road side testing.

Sixty-five questionnaires were distributed in 21 different European countries. In total, 26 completed questionnaires from 19 different countries (13 EU countries and 6 countries not belonging to the EU) were returned. Two countries (Sweden and Portugal) did not send in their questionnaires.

From most countries only one questionnaire was returned. Germany has supplied 5, Spain, the Czech Republic and France have returned 2 questionnaires each.

Applicable Legislation within the European Union

All countries of the European Union (EU) have legal provisions on driving under the influence of drugs (DUID). Generally, participation in street traffic is only allowed if one is capable of driving a motor vehicle in a safe and proper way. If driving ability is impaired by substance abuse, one can be sanctioned, but impairment has to be clearly proven in court. This legislative approach is difficult to enforce, because it is difficult to document the impairment objectively.

Some states try to circumvent the difficulty of proving impairment by using legislation solely based on the analytical detection of drugs in the blood. Germany introduced such a law in August 1998 and in March 1999 Belgium put similar legislation into force. A few other states have comparable law proposals in their parliaments and will implement similar legislation in the near future. However, the biggest part of the European Union is still waiting and carefully following the activities of those states in the forefront. Table 1 summarises the situation on drugs and driving in the countries included in this survey.

The enforcement of legislation of this type depends mainly on the ability of the police forces to obtain the appropriate specimens from the population participating in street traffic. At this point, the authority of the police forces to collect human specimens - either for roadside testing or for confirmatory analysis - is of importance. This authority is regulated by further legislation and differs from country to country.

In some countries the police forces are allowed to control and test the driving population randomly. Suspicion of an offence is not necessary for testing. The majority of countries however treat any roadside testing procedure as an intrusion into personal rights which can only be done if an initial suspicion exists.

Table 1: Overview on the legal situation in the area of DUID and the use of roadside drug tests

Country	Does legislation covering DUID exist?	Impairment or analytical approach?	Roadside testing for DUID allowed at this point of time?	Initial suspicion needed to apply a roadside drug test?	Roadside drug test devices in routine use?
Austria	yes	Impairment	yes	yes	no
Belgium	yes	Analytical/Impairment	yes	yes	yes
Czech Republic	yes	Impairment	yes	yes	no
Denmark	yes	Impairment	no	no	no
Finland	yes	Impairment/Analytical	yes	yes	no
France	yes	Impairment	no	-	no
Germany	yes	Analytical/Impairment	yes	yes	yes
Greece	yes	Analytical/Impairment	yes	no	no
Iceland	yes	Impairment	yes	no	no
Ireland	yes	Impairment	yes	yes	no
Italy	yes	Impairment	yes	yes	no
Luxembourg	yes	Impairment/Analytical	yes	no	no
Netherlands	yes	Impairment/Analytical	no	-	no
Norway	yes	Impairment	yes	yes	no
Poland	yes	Impairment	yes	yes	no
Slovenia	yes	Impairment	yes	yes	no
Spain	yes	Impairment	yes	yes	no
Switzerland	yes	Impairment	yes	yes	no
Unit. Kingdom	yes	Impairment	no	yes	no

To improve the process of gaining an initial suspicion, some states have introduced a training program for their police forces which should enable them to identify intoxicated drivers in street traffic on the basis of physical and psychomotor signs. Roadside testing devices are so far only used in Germany (here sweat or urine are the target specimens) and in Belgium (urine testing) on a routine basis, but some other countries have used urine, saliva or sweat test devices on an experimental basis with voluntary participation of the drivers.

Interestingly, the application of roadside drug test devices is prohibited by regulations in only very few European countries. In most countries drug test devices are not in use because of their low level of validation or their unavailability.

Operational Needs and Requirements of the Police Forces

Based on the national experiences and circumstances, European police forces have a rather clear picture what they need under their specific operational conditions. However, these needs and requirements differ from country to country and sometimes even from state to state within one country. Nevertheless, average tendencies for the requirements on roadside drug test devices have been established from the results of the survey.

Concerning drugs that have to be detected, the following classes of drugs are considered to be very important (in decreasing order of frequency): cannabis, benzodiazepines, amphetamines, cocaine, opiates.

The preferred test configuration is a single use, multi parameter test, which is able to provide a clear, unambiguous test result on the above mentioned groups of drugs within 5 minutes. According to the respondants, saliva is the preferred test specimen for roadside testing due to its easy availability, the low invasiveness of sampling and the good correlation with impairment. Sweat, on average, is the second preference because it allows testing without the collaboration of a driver, in combination with low invasiveness and good availability at the roadside.

The average price which was considered in the context of this survey as reasonable for a single parameter device was 3,9 Euro, for a 4-parameter device 14,0 Euro.

Conclusion and Outlook

For the future it is necessary to further validate existing devices which are applicable to the detection of the abuse of drugs in street traffic. This includes urine tests but also saliva and sweat test devices. For that, we hope that the ROSITA project will be able to provide a significant contribution.

More effort has to be made on the investigation of the correlation between impairment and pharmacokinetics of illegal drugs in easily accessible body fluids (sweat, saliva). This will help to develop more reliable devices for roadside testing.

It is essential for most countries, to train police forces in the detection of drivers under the influence of illegal drugs. In most countries of the European Union further legal measures (e.g. taking a blood or urine sample but also the application of a roadside device) depend on an initial suspicion of DUID.

The development of optimal roadside test devices for the examination of saliva or sweat is a technological challenge. Whereas alcohol is present in the parts per thousand level in the blood as well as in the breath of intoxicated drivers, drugs are usually present in the parts per billion level in body fluids. Most relevant medical and illegal drugs do not appear in detectable concentrations in the breath of drugged drivers.

Industry will be more ready to invest in new products if there are clear regulations, which demand the usage of drug test devices, thus generating a sufficient market size. Therefore developmental activities can either be triggered by new Traffic Safety Regulations or by

harmonisation of the national laws (increasing the market size for a certain kind of test device). Alternatively the provision of public funds can help to support the necessary development efforts.

Due to the fact that road safety is of broad public interest, legal and funding activities should go hand in hand.

INTRODUCTION

Goals of Workpackage 3

To trigger such (further) developmental activities, Workpackage 3 specifically addresses the needs and requirements of the police forces in the different European countries for roadside testing equipment. In addition the legal circumstances and prerequisites in the countries of the EC have been investigated, because legislation is greatly influencing the route and frequency of application of roadside test devices. In this context also the area of alcohol testing has been evaluated as far as it is of importance for drug testing.

Interestingly, the application of roadside drug test devices is prohibited by regulations in only very few European countries. In most countries drug test devices are not in use because of their low level of validation or their unavailability. Based on the national experiences, European police forces are urgently requesting the validation and improvement of the existing drug test devices according to their operational needs and requirements or the development of novel roadside test devices to efficiently combat DUID.

For saliva or sweat test devices, validation is an essential point. Only very few devices exist and the extent of validation is quite different. Urine test devices were broadly validated for laboratory applications, but not for roadside applications, and most police forces do not want or are unable to test urine. Unavailability may be interpreted as a "lack of knowledge", which on site applicable devices are available on the market. The ROSITA project is not only providing an extensive field validation, it also supplies information on a international basis to elimate this "lack of knowledge".

How has the Information been collected?

In the initial months of the project a questionnaire was designed with a set of specific questions on the legal situation in the European Countries and the needs and requirements of their police forces (See Appendix).

Supported by this questionnaire the members of the Consortium, together with selected representatives of countries not directly included in the ROSITA Consortium, conducted detailed interviews with experts on legislation, police and traffic safety to gain the necessary information basis.

Sixty-five questionnaires were distributed in 21 different European countries: **Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Poland, Portugal, Slovenia, Spain, Sweden, Switzerland, United Kingdom**.

In total, 26 completed questionnaires from 19 different countries were returned. At the point of time when this report was finalised the answers of two countries (Portugal and Sweden) had not been received.

From most countries only one questionnaire was sent back. However, Germany has supplied 5, and Spain, the Czech Republic and France returned 2 questionnaires each.

To crosscheck the results of this study, a study initiated by the Pompidou Group has been used as a source of information. This study was performed recently by the Interdisziplinäres Zentrum für Verkehrswissenschaften" (Würzburg, Germany, Prof. Dr. Hans-Peter Krüger, 1998) and was mainly focussed on legislative aspects of "Illicit Drugs in Road Traffic".

LEGAL REQUIREMENTS

Introduction

Basically, legislation sets the regulative environment for the application of roadside testing equipment. Most European countries have a very well established legislative system to cover and deal with the abuse of alcohol in street traffic. To deal with the problem of DUID the countries of the European Union use the 'impairment approach' and they are considering further legal changes to make DUID offences comparable to driving under the influence of alcohol (DUIA), i.e. 'per se' legislation.

Legislative conditions not only empower the police forces of a country to use roadside testing equipment, they also determine the intensity of application and thus the general awareness of drugs and driving in the population. A lack of enforceable legal regulations and the absence of appropriate testing equipment have a detrimental effect on road safety.

Taking these considerations into account, we had a closer look at the individual legislation in the different European countries and analysed the legal prerequisites for applying roadside drug test devices.

Most countries have currently regulated this matter in a very general way. Applicable clauses are included in the penal code or the traffic law, but the traffic police are not empowered to apply roadside testing equipment to enforce these regulations efficiently. Only Belgium, Germany and Switzerland have recently put their police forces in a position to apply test devices.

Austria

General Legislation
Up to now, the government in Austria is very much following an impairment approach in its legislative system. Impaired driving is generally covered by §4 of the national Traffic Law (Straßenverkehrsordnung, StVO). This clause also refers to the Law on Drugs of Abuse (Suchtmittelgesetz) from 1997 and explicitly forbids driving under the influence of those substances mentioned in the Austrian "Suchtmittelgesetz". At present, an amendment of the StVO is under discussion to cover the abuse of medical drugs.

Drug and Alcohol Testing in Austria
Any examination for driving under the influence of drugs is so far a part of the general procedure to test for DUIA. If the police in the context of a suspects DUID, the driver has to be taken to a hospital emergency room or a doctor's office for a medical examination. The doctor´s observations on the state of impairment are part of the evidential chain to prove driving under the influence of drugs. Blood or urine test results are accepted by the court to prove drug consumption, but those specimens can only be taken on a voluntary basis. If the driver is not willing to co-operate, no drug testing is possible.

In contrast to the situation in the area of DUID, Austrian police are authorized by law to submit drivers to a breath test without any initial suspicion for drunkenness. A positive breath test result (=BACs above the legal limit) can be used directly for punishment by the court on the basis of the Austrian Traffic Law. If the breath alcohol test is negative and there are no indications of impairment, the driver is considered innocent. If the breathalyzer test result turns out to be negative (or if the driver is not able to co-operate) and sufficient indications for impairment exist, a medical examination can be performed. A refusal of the breath test is an infringement of a valid regulation (equal to a BAC of more than 1.6 g/L). The driver loses his or her driving licence and regranting depends on attendance at a psychological training course.

The basis for a conviction for DUIA is the police report and the result of the breath test. In the case of a suspicion for DUID the results of the medical examination, the results of a blood and/or urine analysis (if available), and an expert witness on the driving capabilities of the suspect at the time of the traffic control are additionally necessary to prove impairment.

The actual legal situation allows the application of roadside drug test devices, but currently they are not in use in Austria, because tests are missing which fulfil the operational demands of the police at the roadside. Theoretically, any drug testing device can be applied at the roadside or at the nearest police station under the

same circumstances as roadside alcohol tests, however an initial suspicion is needed, or the driver has to be involved in an accident with personal or fatal injury.

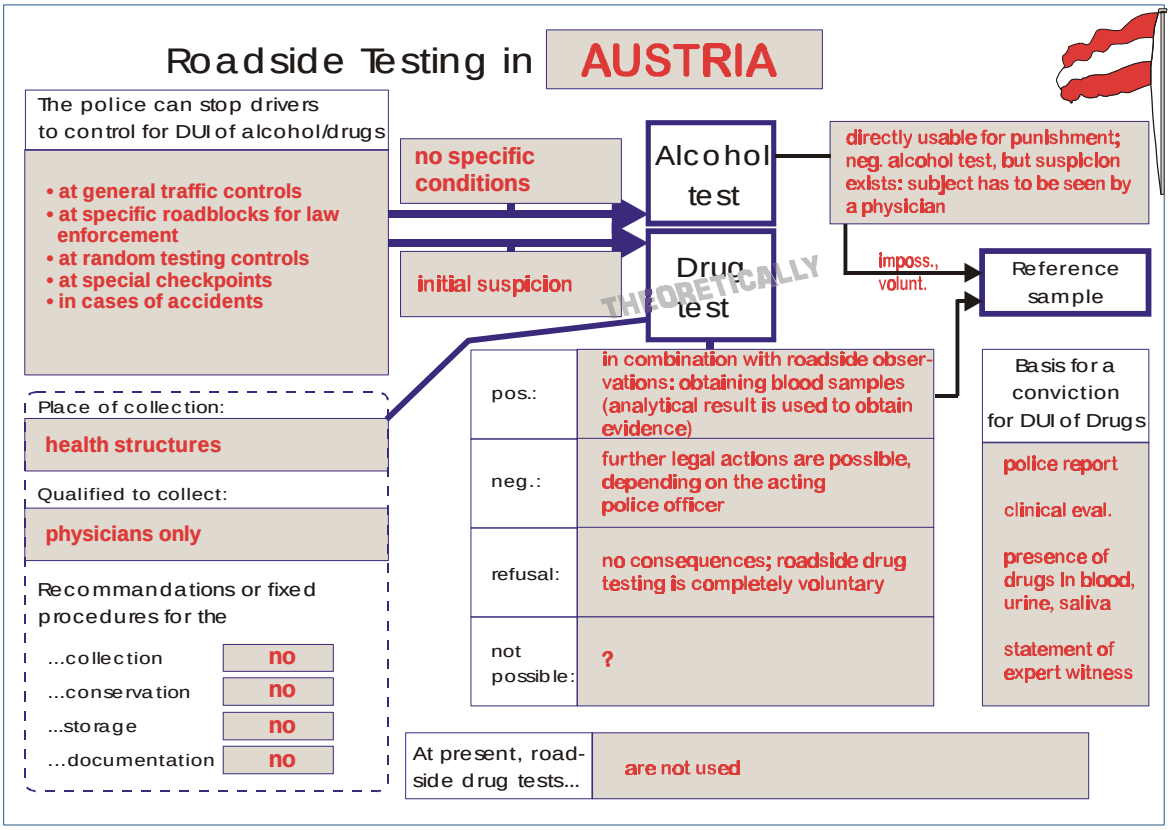


Figure 1: Roadside Testing in Austria

Belgium

General legislation

On March 30th 1999, a new version of the traffic law was adopted by the Belgian parliament. This new law punishes driving under the influence of cannabis, cocaine, opiates and amphetamines and includes not only specific substances, but mentions also - and this is currently unique in Europe – analytical legal limits for these substances in plasma. Drivers identified with a plasma concentration higher than 2 ng/ml THC, 20 ng/ml morphine or 50 ng/ml of amphetamine, MDMA, MDEA, MBDB, cocaine or benzoylecgonine, are infringing the new 'per se' regulation and can be condemned to a fine and/or a prison sentence. In addition, their driving licence can be withdrawn for a limited time (12 hours). Although this new specific regulation is a zero tolerance-type law, blood sampling and analysis is only allowed if signs of impairment are obvious, and if a roadside urine test is positive for amphetamines, cannabis, cocaine or opiates.

Drug and Alcohol Testing in Belgium

The identification of "drugged" drivers at the roadside is currently strictly oriented at the determination of signs of impairment by the police. If signs of impairment are observable during traffic controls, roadside testing for DUID is justified.

Roadside testing consists of a three step procedure. To detect and clarify signs of impairment police forces apply a modified field sobriety test, which was derived from the US drug recognition program. Positive suspects are subjected to an immunological urine screening test. Urine drug tests can be performed by police forces at any place where the privacy of the subject is guaranteed and sampling can be performed under hygienic conditions.

Drug testing (and especially alcohol testing) is done on the occasion of general and random traffic controls (at the roadside or at special checkpoints close to discotheques) and in the context of specific roadblocks for law enforcement reasons. Additionally, the police are allowed to control all persons who are involved in traffic accidents for DUIA or DUID.

If no alcohol consumption is detectable and significant signs of impairment exist, the driver under suspicion is tested for the abuse of illegal drugs. The legislative difference between alcohol and drug testing is that alcohol tests can be done without any initial suspicion, whereas drug testing depends on an initial suspicion. A positive alcohol test can be used as the single reason for an evidential test and its result is already the basis for punishment. Provided that a suspicion for impairment exists, the application of a drug screening device has to be accepted by the suspect.

A positive urine test leads to a blood analysis and the presence of illegal drugs in blood is the basis for the conviction. If the test result is negative, but there are signs of impairment, further legal action can be undertaken under the direction of a prosecutor. If the driver refuses or is unable to give a urine sample, he can be forced to give a blood sample for a laboratory analysis. In this case the driver is infringing a valid regulation and this will be equated to a positive result (prohibition to drive during 12 hours + conviction, similar to alcohol > 0.8 g/L). A negative screening result and the absence of any indication for impairment exonerates the suspect.

For the conviction, the observed signs of impairment are usually not taken into consideration; Article 35 of the Belgian Traffic Law stipulates that driving while being impaired is forbidden, but that statement is very broad, and until now very few subjects have been convicted in Belgium by Article 35.
In the past Dade Behring´s ECOM and Frontline tests from Roche Diagnostics have been evaluated for urine testing. For the examination of saliva or sweat Drugwipe (Securetec GmbH) has been tested in a small study by the National Institute of Forensic Science in Brussels.

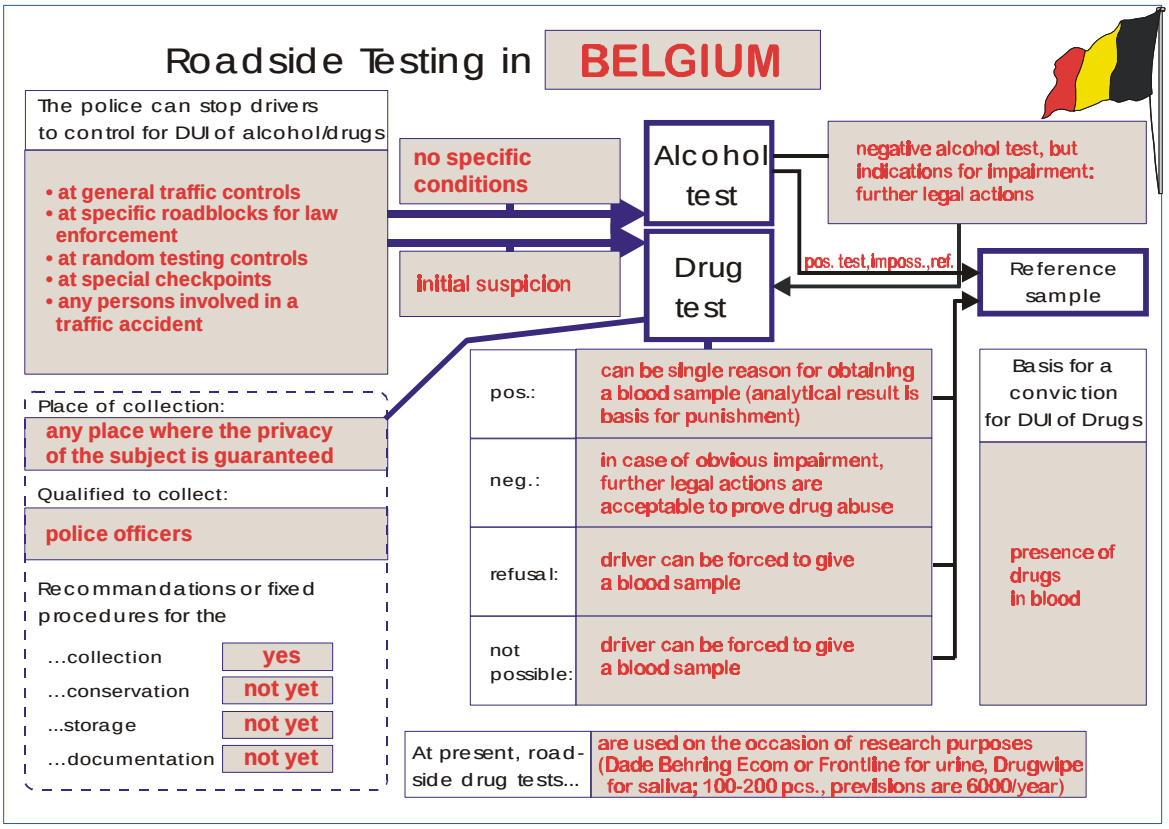


Figure 2: Roadside Testing in Belgium

Czech Republic

General Legislation

Although no specific legislation for DUID exists in the Czech Republic, any offences of impaired driving are generally covered by the Czech Penal Code (Section 13, §89 and §201). Besides alcohol, narcotic and psychoactive substances are mentioned. The applicable clauses of the different laws are cited in table 5.
Generally the Czech Government is following an impairment oriented approach to sanction offences of DUIA and DUID. For alcohol, two different legal blood levels exist: a zero limit during driving is required (this is equal to 0.2 g/L). Impairment is assumed to exist at 1 g/L or higher BACs. However, even at a BAC of 0.3 - 0.4 g/L the driver is considered to be unable to drive in a safe way, and a small fine can be imposed.

Drug and Alcohol Testing in the Czech Republic

If the police suspect the influence of drugs, they are authorized to transfer the suspect directly to a clinical laboratory for a medical examination and the testing of a blood or urine sample. The result of the medical examination together with the analytical result (proving the presence of drugs in blood (urine)) are the basis for a conviction concerning DUI of drugs.

So far drug testing devices are not in use in the Czech Republic. Drug test devices (like immunological urine tests) can be applied at the roadside in cases of general driving faults or accidents by specifically trained officers. The basic prerequisite is, that there is an initial suspicion for DUID and the possibility to take a urine sample at the roadside, which seems to be the main problem. At present suspect drivers are taken to a physician for sampling and the sample is then sent to a toxicology laboratory.

Czech police are allowed to control all persons who show unsafe driving behaviour or seem to be impaired. The police forces perform general traffic controls (e.g. speed controls), as well as specific roadblocks for law enforcement or alcohol test reasons (e.g. near discos) or random traffic controls. Any driver involved in a traffic accident is tested for DUID.

During traffic control actions the police mainly screen for alcohol abuse (based on different types of breath alcohol devices). A positive breath screening test and roadside observations of impairment lead to a medical examination in a hospital or at a physician’s office. In the case of refusal of co-operation the driver has to pay a fine.

During the medical examination the actual physiological status of the patient is checked by means of psychomotor tests and the police officer may ask the physician to take a blood sample. Additionally he can ask the driver to give a urine specimen for toxicological analysis. It is not compulsory for the driver to give a blood or urine specimen, but if the driver refuses to co-operate a fine and/or the suspension of the driving licence are obligatory.

If the breath alcohol test result is negative, and there are signs of impairment, further legal actions like a mandatory medical examination are acceptable to prove alcohol or drug abuse. If this test is negative and there are no indications of impairment, the driver has to be considered innocent.
Refusal to co-operate can result in imposition of penalties or sanctions according to the Misdemeanour Act. If positive screening test results are obtained, they cannot be used for court purposes, but confirmation by substance specific analytical methods is necessary. To prove impairment a medical examination is allowed (according to the Penal Code).

Any result of a screening device applied in this context is not sufficient for prosecution (breath test results are only judged according to the Misdemeanour Act), but requires applicable medical and toxicological findings. Similar to other states only the analytical result of a blood analysis with approved laboratory based methods can be taken as evidence in court. However, tests for drugs are not common, in contrast to alcohol testing. The reasons are financial –the blood analysis for alcohol is much cheaper and more traditional than for a broad variety of drugs.

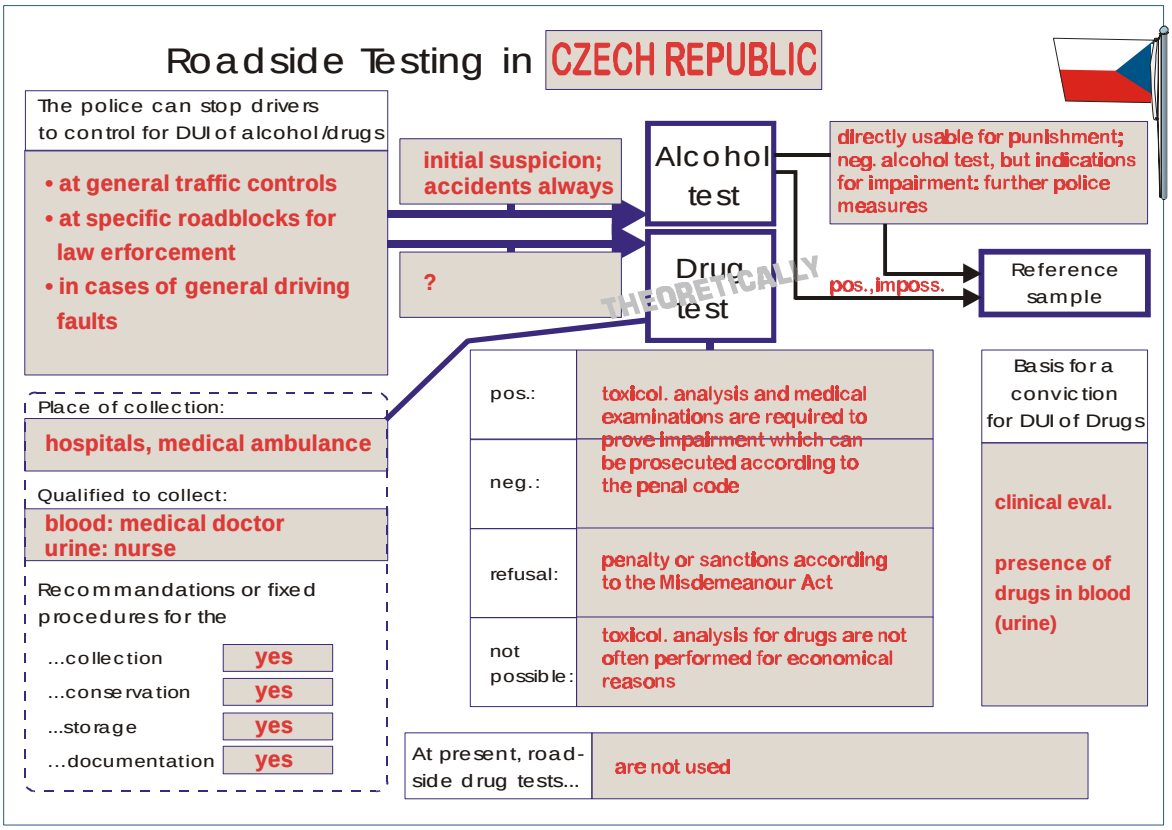


Figure 3: Roadside Testing in the Czech Republic

Denmark

General Legislation

In Denmark, Driving under the Influence of Drugs is covered by the Danish Traffic Act, § 54, 1. This law generally includes all psychoactive substances. Specific substances or legal limits are not explicitly mentioned.

Alcohol and Drug Testing in Denmark

Until today, the Danish police are not allowed to perform roadside drug screening tests, because they are not mentioned in the Danish law. Drivers impaired by illegal drugs are identified on the occasion of controls for alcohol abuse, which can be ordered on the occasion of traffic accidents, general traffic controls, specific roadblocks or random controls. Breath screening tests can be enforced without any suspicion. Specific controls for "drugged" drivers are not conducted.

If the subject seems to be under the influence of alcohol only, no medical examination will be performed. On the other hand, if a breath test is refused or if there is an obvious suspicion for drug consumption (or consumption of both) a medical examination will be carried out at a police station. In this context blood and urine samples will be taken and examined for alcohol and (if required) for drugs. The basis for a conviction for DUI in Denmark is the police report, the clinical evaluation, and the result of the laboratory analysis of the blood/urine specimen.

If the breath test is negative and no other indications for impairment exist, the driver will be released.

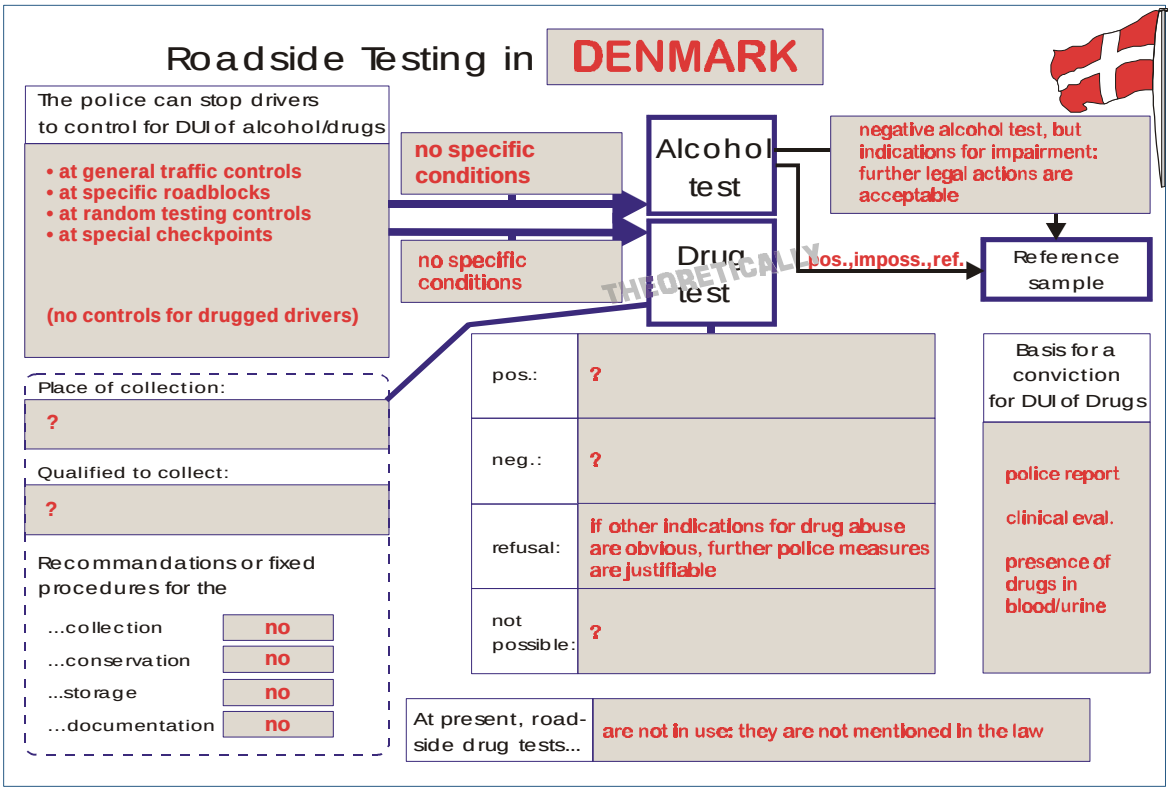


Figure 4: Roadside Testing in Denmark

Finland

General Legislation

To combat driving under the influence of drugs the Finnish government pursues a combination of an analytical and an impairment approach. Since 1977 § 23 of the penal code has regulated DUID. For punishment of a driver it has to be demonstrated that the driving capability is impaired and significant amounts of drugs are present in the bloodstream of the respective driver. Included are all substances that can cause impairment of performance.

Drug and Alcohol Testing in Finland

If signs of impairment or drug utensils indicate the abuse of illegal drugs, the subject is taken to a hospital for obtaining a blood (and on a voluntary basis also urine) sample; usually breath testing for alcohol is the introductory step during a traffic control situation, but this is not obligatory. Under certain circumstances drivers under suspicion can be brought directly for a medical examination and blood sampling.

In contrast to alcohol screening devices drug test devices have not been used in Finland up to now. Breath alcohol tests can be applied without any initial suspicion in order to identify drunken drivers. The main reasons are usually impaired or dangerous driving, road traffic accidents, random or general traffic controls. Due to the broad legal basis, Finland, with its population of approximately 5.1 million inhabitants, is performing approximately 1 million breath alcohol tests for screening purposes per year. When a breath test result comes out positive or breath testing is refused or impossible, the driver can be forced to give a blood specimen at the forensic clinic in Helsinki or at an outpatient clinic and hospital emergency room in Turku and Tampere, respectively, at which time, on request of the police, a clinical examination of the status of drunkenness can be performed. This medical examination is not mandatory, but is recommended in all cases where the abuse of drugs is suspected.

Conviction is based on the demonstration of insufficient driving capability in combination with the analytical detection of alcohol in breath, or in blood. For all cases where the BAC is below the legal limit, but a

suspicion for the influence of drugs exists the police can request a drug analysis to gain the necessary evidence for DUID.

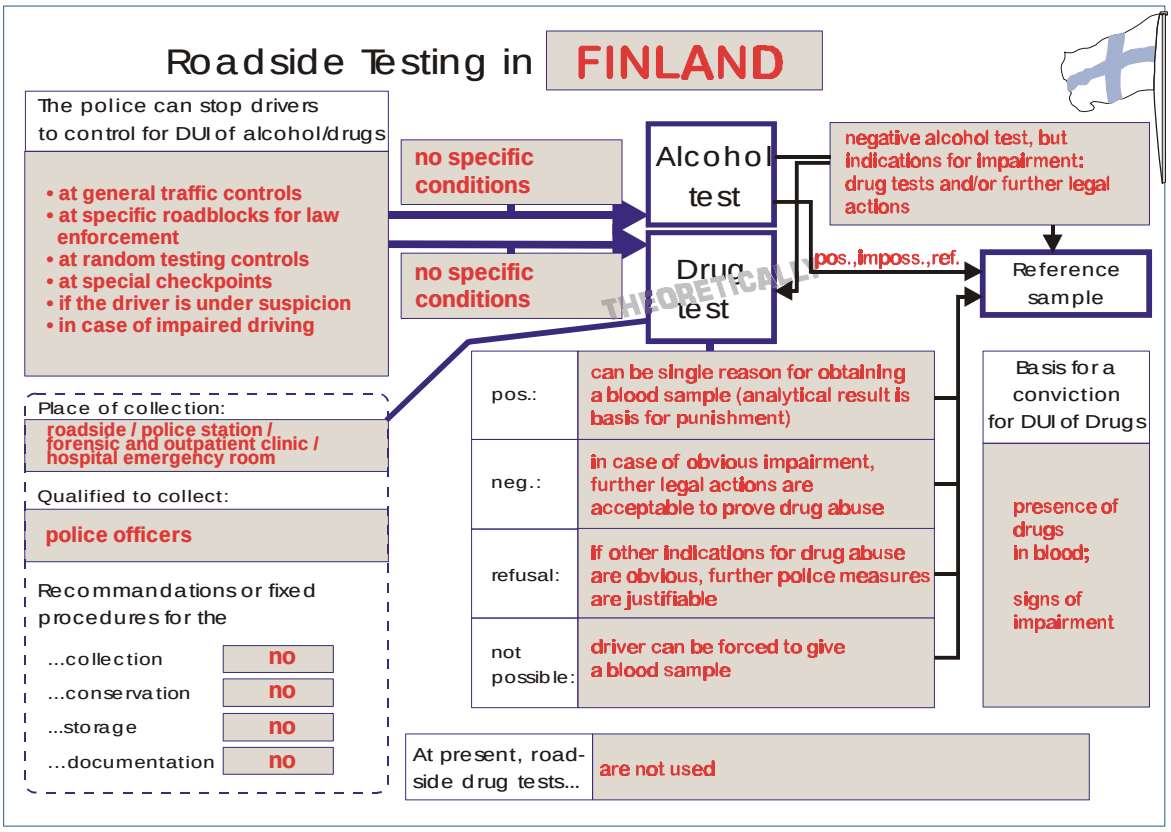


Figure 5: Roadside Testing in Finland

France

General Legislation
A specific regulation covering the offence ”Driving under the Influence of Drugs” has passed the French parliament in March 1999 and should become applicable in January 2000. This new law is part of the penal code and regulates that any driver involved in a fatal accident has to be examined for epidemiological reasons for illegal drugs in blood. Opiates, cocaine, cannabis and amphetamines are explicitly mentioned in the new law whereas benzodiazepines are subject to further discussions and evaluations. Legal limits will not be introduced.

On a more general level the public health codes L 626 and L 630 regulate DUID. To convict someone on the basis of these regulations it is necessary to prove that a traffic offence has happened or that a driver has endangered somebody; relatively few apprehensions are due to driving while impaired. In the annex different drugs of abuse as well as intoxicating plants are explicitly listed, but no exact legal limits are described. Medical drugs are not covered by this law, but the listing can be extended if necessary.

Specific legal restrictions for roadside testing
In France roadside testing for drugs is not allowed by law. Even impairment testing is currently not performed. Exceptionally -in the case of a fatal accident- the police are allowed to ask for a blood specimen to be tested for drugs.

In contrast to this it is estimated that approximately 8.000.000 alcohol tests are performed annually in France to check drivers for alcohol abuse. French police are empowered to test drivers not only under the prerequisite of an initial suspicion, but can apply a roadside alcohol test randomly to the general population.

This may happen on the occasion of general traffic controls or in the case of accidents or infractions. Specific roadblocks for law enforcement or random testing reasons are organized.

Every driver stopped for testing reasons has to undergo a roadside breath alcohol screening test. If indications for alcohol abuse are apparent, the driver is taken to a police station (arrested if necessary) for a confirmatory breath test. If the confirmatory test shows a higher breath alcohol concentration than the legal limit, usually no additional drug testing will be carried out. If the screening test result is negative and there are no indications of impairment, the driver is released. But if a suspect seems to be impaired, although his breath test is negative, the police can force him to provide a blood sample. Any refusal to co-operate in breath testing is treated as the maximum level of alcohol.

The basis for a conviction for DUI is either a BAC of more than 0.5 g/L or a breath alcohol concentration of more than 0.25 mg/L.

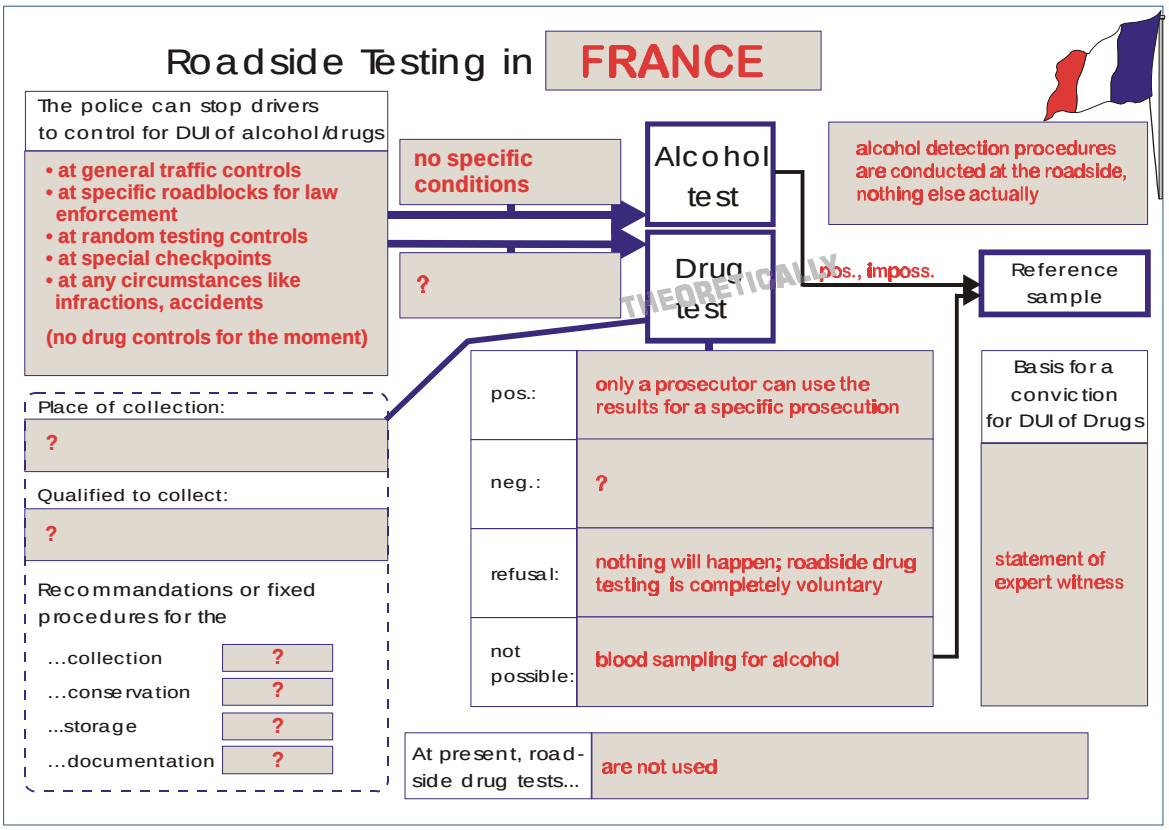


Figure 6: Roadside Testing in France

Germany

General Legislation
Since August 1998 (with the amendment of §24a StVG) Germany pursues an analytical approach with a zero-tolerance limit. The new law prohibits driving under the influence of the drugs cannabis, cocaine, heroin, morphine, amphetamine and the designer drugs ecstasy and MDE, if any of these specially listed drugs is detectable in the blood of a driver. For heroin and cocaine their degradation products morphine and benzoylecgonine have to be measured to provide the necessary evidence. Any infringement of this new law is dealt with an administrative offence and is punished with a fine of up to 1500 Euro. In cases of repetition an additional driving ban of up to three months may be decided.

§24a contains explicit exceptions for substances which are taken due to a prescription for a specific illness. For the moment, this is only the case for morphine.

In addition to the administrative level of offence, there are regulations covering the offence of DUID in the penal code. §§316 and 315c StGB generally sanction the offences of DUIA and DUID where impairment of a driver is proven.

Specific legal restrictions on the application of drug screening devices
In Germany, roadside drug tests have been introduced on a routine basis in Saarland (urine tests), Baden-Württemberg (sweat test), Berlin (sweat test) and Sachsen (sweat test).
Generally, drug test devices help the police officer to decide on the necessity of a blood analysis. Detectable blood concentrations of drugs are the only objective criterion for DUID accepted by court. In addition to the police report, the suspect´s statement, results of a clinical evaluation and a statement of an expert witness are used by the courts to decide on DUID.

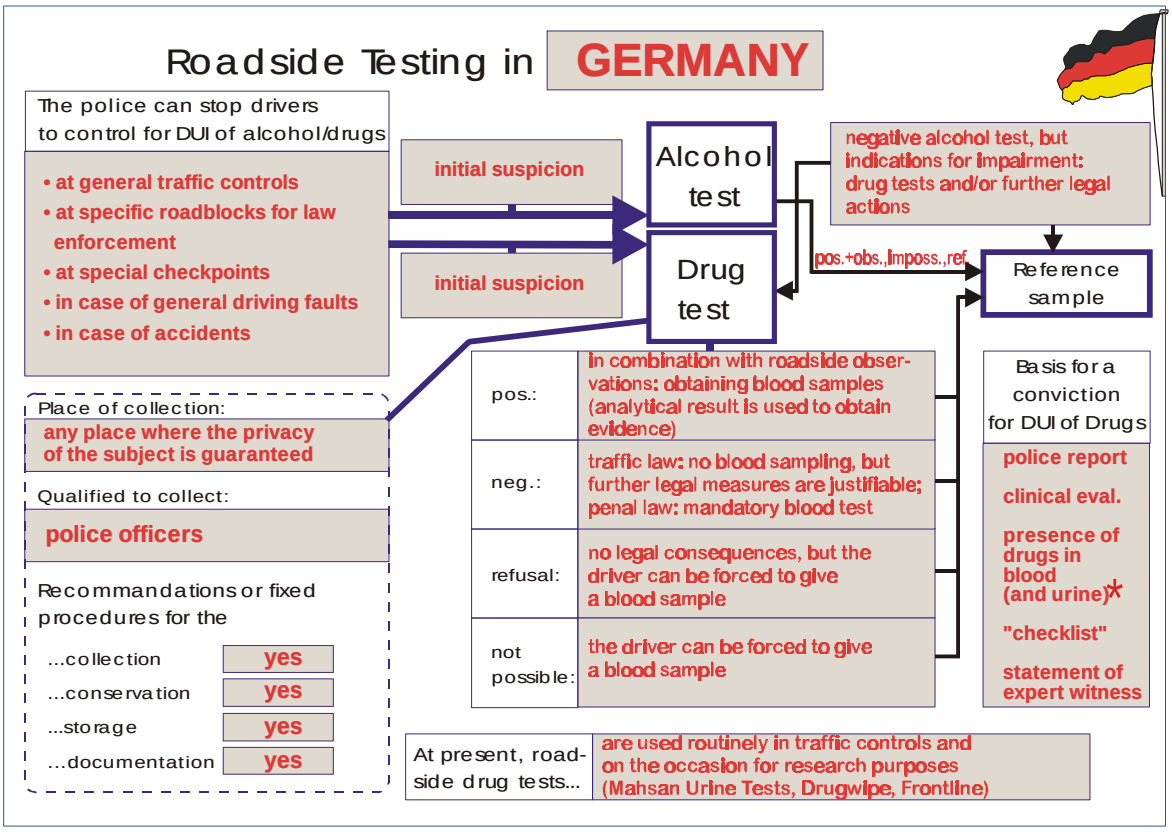
If in a traffic control situation (or in a specific drug control action) indications of the use of drugs are obvious, the police officer interviews the suspect and offers a roadside drug test to confirm or deny his initial suspicion. In the case of refusal the provision of a blood sample can be enforced. In case of a positive test result the officer can order a blood sample to be taken to give evidence to support the statement of the police officers.

If a test was performed because of a suspicion regarding §24a and the result is negative, there is no more basis for further action. If the test result is negative, but indications according to §316 exist for a criminal offence, the blood sample has to be taken to gain the necessary evidence in court (the toxicological analysis is extended to all ”intoxicating” substances).

In cases when a negative roadside test result is obtained or in cases when co-operation is refused and clear signs of impairment are obvious, further legal actions are acceptable to prove alcohol or drug use. If a driver seems to be too influenced so that he is not able to co-operate, he can directly be forced to give a blood specimen. In addition an evaluation by an expert witness can be requested.

The different types of roadside test devices can be applied everywhere where the dignity of man is protected. Saliva and sweat samples can be collected and tested directly at the roadside, whereas urine samples should only be collected and tested at police stations or at public lavatories.

Reasons for testing drivers for the abuse of alcohol or drugs are general traffic controls, specific roadblocks, special checkpoints, accidents and if general driving faults are observed.



* only evidence in the court by offences according to the traffic law; no proof of impairment required

Figure 7: Roadside Testing in Germany

Greece

General Legislation

Until May 1999, impairment whilst driving a motor vehicle in Greece was covered by the Traffic law clauses 614 from 1977, section 42 and by the ministerial decisions 13382 φ. 705.11 / 4 δ / 25-10-77 and 1330 φ 705.11 / 4 ξθ /15-2-85. Toxic substances are mentioned in these regulations only in a very general manner.

Since the 23d of May 1999, a new law (L. 2696 / 99) is valid and regulates the offence DUID in a slightly different way. Section 42 of this new law specifically refers to ”Driving under the influence of alcohol, toxic substances or drugs that according to their instructions for use influence driving ability”. It is requested in the law that the currently applicable ministerial decrees are replaced in the near future by appropriate regulations.

Alcohol and Drug testing

Roadside testing for ”drugged” drivers is currently not performed in Greece, because suitable test devices are missing. The Greek legislation is proposing to control the abuse of narcotics in street traffic, but only laboratory based analytical methods for testing blood or urine are used to prove intoxication.

The Greek police are authorised by law to apply alcohol screening devices to the broad population without an initial suspicion. If the initial breath test turns out to be positive (according to the valid legal limits), the result is the legal basis for punishment by the court. If the breath alcohol test result turns out to be negative and clear signs of impairment are visible (or if the driver is not capable of co-operating), drivers are subject to a more detailed clinical evaluation including blood or urine analysis with laboratory methods. The results of the clinical evaluation together with the alcohol screening test result are then used by the courts to evaluate the state of impairment. In the case of a driver who refuses to co-operate, he (or she) is infringing a valid law and is prosecuted.

Additional reasons for blood or urine sampling are involvement in traffic accidents or a suspicion of the consumption of illegal drugs. Any driver with a negative breath test result and no visible signs of impairment is treated as innocent and is allowed to drive on.

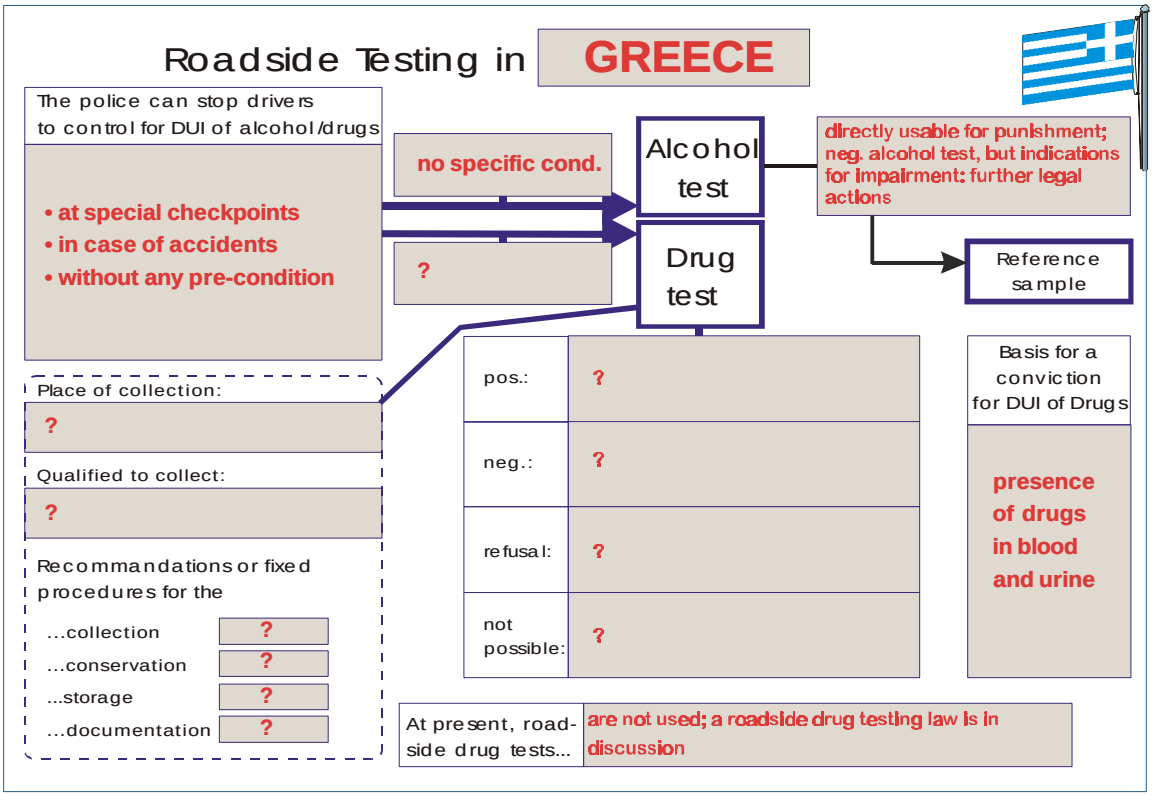


Figure 8: Roadside Testing in Greece

Iceland

General Legislation
Iceland is pursuing an impairment oriented approach in its legislation. Offences of DUID are covered by the Traffic Law No. 50/1987 , Article 44, Paragraph 2.

Drug and Alcohol Testing in Iceland
In most cases testing for DUID is a part of the general control procedure for DUIA. The police in Iceland are authorised by law to submit drivers to a breath test independently of an initial suspicion. Alcohol testing is usually done on the occasion of general or random traffic controls or specific roadblocks for law enforcement reasons at special checkpoints. If a breath test result turns out to be positive, a blood sample is taken in the nearest police station. By law a positive driver has to co-operate.
If breath testing is refused, or a driver is unable to submit a breath sample, or when there is a suspicion of the abuse of other drugs than alcohol, the driver can be forced to provide a blood specimen.

Roadside drug tests are currently not in use in Iceland, because of the lack of appropriate devices. The legislation does not inhibit the application of roadside screening devices for the detection of drug impaired drivers. Therefore, in theory, any drug test device can be used under the same legal circumstances (without an initial suspicion) as roadside alcohol tests.

Drug testing may be done by police officers at the roadside or in the police station. A positive result is then sufficient to obtain a blood sample on a mandatory basis from a suspect. If the test result is negative, police are allowed to perform further measures, like prohibition to continue driving or taking a blood sample. The results of roadside tests alone are not generally usable as evidence.

The result of a roadside test device can not be used as evidence in court. The basis for a conviction for DUIA is the presence of alcohol in breath or blood. In some cases the results of a medical examination to determine the status of impairment of a driver are taken into account by the court.

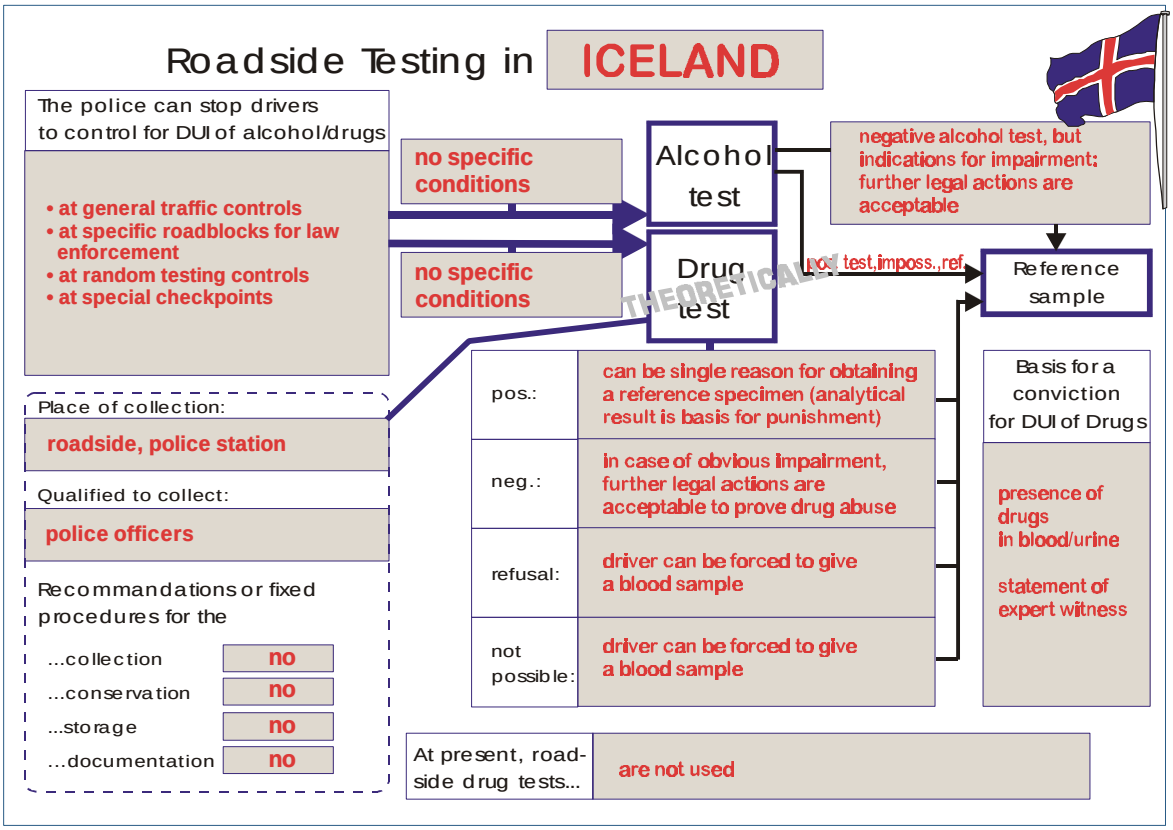


Figure 9: Roadside Testing in Iceland

Ireland

General Legislation
In general, in Ireland offences of DUI of drugs are covered by the Road Traffic Act, Section 49 from 1961. The law belongs to the criminal law and covers all illegal substances, but does not mention specific drugs. Legal limits are not specified.

Drug and Alcohol Testing in Ireland
In Ireland the application of roadside drug test devices is actually not prohibited by any valid regulation, but no devices are routinely used because of the absence of validated test systems. Compared to the alcohol test numbers, the numbers of persons tested for the abuse of drugs is very low. Drug testing is so far solely based on the analysis of a blood or urine specimen in the laboratory, thus requiring the presence of the police, and toxicologist as well as the medical doctor in court.

Blood and urine samples can be gained in cases, when clear indications for alcohol or drug use are obvious and the responsible police officer can request the examination of the obtained specimen for illegal drugs.

During general traffic control actions the behaviour of a driver is evaluated for signs of impairment. In this context the police officer decides on the driving capability of the suspect and may take further legal measures. He may arrest the suspect if she/he has the opinion that a driver is incapable of having proper control over a vehicle due to the consumption of alcohol or drugs. His decision is supported by roadside breathalyser tests, which can be applied without an initial suspicion.

If a driver refuses or is unable to provide a breath sample, he can be found guilty of a drink driving offence. Based on the visible signs of impairment the police officer is authorised to request a urine or blood sample to test for the abuse of alcohol and/or drugs. If the subject is willing to co-operate, a medical doctor will obtain those specimens in the police station or in a hospital. The driver cannot be forced to give any specimens, but can be found guilty of an offence ín the case of refusal. To avoid any blood testing in cases of DUIA the Irish government is currently introducing evidential breath test devices.

Finally, the basis for a conviction for alcohol and driving is the presence of alcohol in breath, the result of the clinical evaluation and the statement of an expert witness. The police officer reports on the observed signs of impairment and the result of the breath screening test, and he presents a Certificate of blood or urine alcohol analysis issued by the Medical Bureau of Road Safety (MBRS) in court; less frequently, a clinical examination of the driver by the doctor at the station can be used in court instead of the Certificate.

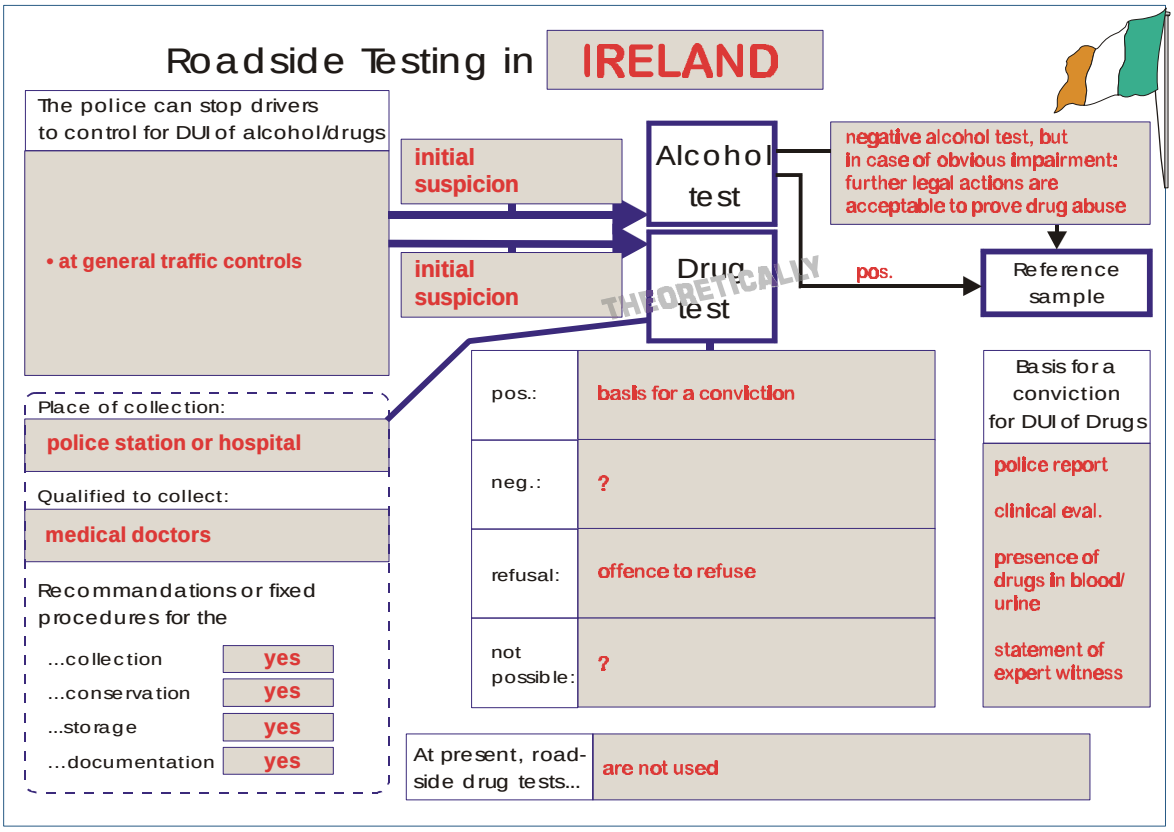


Figure 10: Roadside Testing in Ireland

Italy

General Legislation

Since 1992, a specific legislation on DUI of alcohol and psychoactive substances is valid in Italy (Art. 186 and 187 respectively of Law 285/1992, the New Highway Code). It covers alcohol (BAC limit 80 mg/100 ml) and stupefying and psychotropic substances (without mentioning specific substances or legal limits). In general, the Italian legislation pursues an impairment approach. Sanctions are imposed against drivers who have a documented impaired driving performance or who are involved in traffic accidents and found positive for alcohol and drugs.

Drug and Alcohol Testing in Italy

Since 1994-95, roadside drug tests are in use in Italy for research purposes. Scientific institutions in collaboration with police have tested urine test devices from Syva and Merck and sweat tests from Securetec (Germany). Altogether the annual frequency of use is approximately 1000 - 1500 per year.

The combination of visible signs of impairment and a positive result of a roadside drug test device can be used for gaining a blood and/or urine sample. The analytical results from the analysis of these samples by approved laboratory based methods in addition to the roadside observations are then the basis for punishment.

The application of drug tests as well as breath alcohol tests is mandatory in Italy and cannot be refused by the driver. If the roadside drug test result is positive and the driver refuses to co-operate with the police forces, he will be punished with the same administrative and penal sanctions which are applicable in cases of a positive evaluation.

If the test result is negative, but there are indications for impaired driving (due to various reasons) further legal actions are acceptable (e.g. stopping driving or withdrawing the driving licence).

The basis for a conviction for drugs and driving is the police report which contains a description of the roadside observations as well as the clinical and analytical data.

In the case of road accidents or suspicion of physical and psychic alterations the police may accompany the driver to health care facilities (hospitals or roadside in special equipped ambulances) where samples of biological fluids, usually blood and urine, are taken. Medical examinations have to be carried out under conditions of clinical safety. In this context, coercive blood sampling for judicial reason is considered invasive and thus forbidden. Therefore, the driver has to provide his informed consent for clinical examination and taking a specimen.

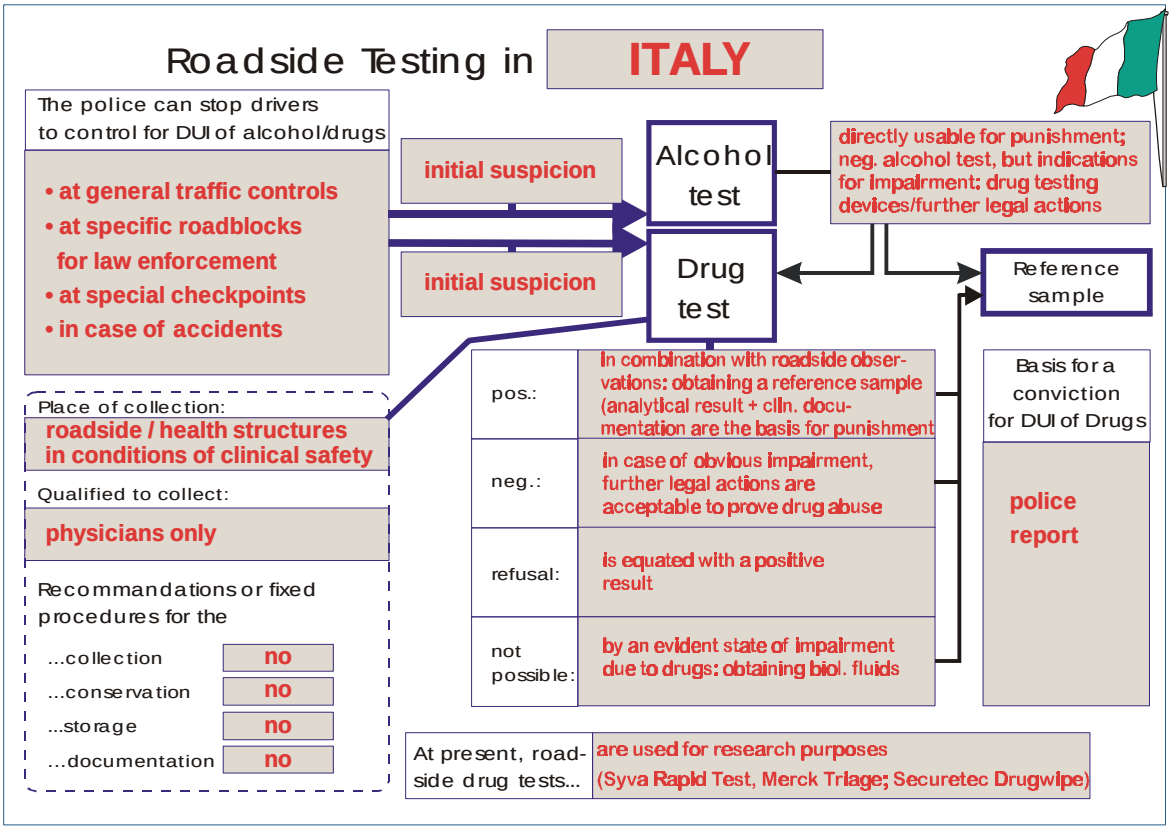


Figure 11: Roadside Testing in Italy

Luxembourg

General Legislation
Luxembourg pursues a combination of an analytical approach and an impairment approach. No specific legislation for DUID exists so far, but these offences are covered by other laws. To infringe these laws the actual status of impairment together with a significant concentration of drugs in blood have to be proven.

Drug and Alcohol Testing in Luxembourg
In general the application of roadside drug test devices is not prohibited by legislation in Luxembourg, but no drug test devices are actually in use. Any validated drug test devices can be applied under the same circumstances as roadside alcohol tests.

In order to identify drunken drivers in Luxembourg, the police have only the possibility of performing roadside alcohol tests in cases of accidents with severely injured participants or general roadblocks ordered by the chief prosecutor.

Based on the extent of impairment (which is evaluated by the police forces) a breath screening test is performed to check the influence of alcohol. The driver is requested to co-operate. Otherwise his refusal is equated with a positive result. If a test result is positive, it can directly be used for punishment provided that the additional roadside observations confirm the abuse of alcohol. In cases when the breath alcohol concentration is below the legal limit, but additional signs of impairment are present, further police actions like stopping the vehicle are justified.

If abuse of illegal drugs is suspected and the driver is willing to co-operate, he will be brought to a hospital to collect a blood or urine sample for laboratory examination. If the driver does not give a blood or urine specimen voluntarily, there is no possibility to test for illegal drugs.

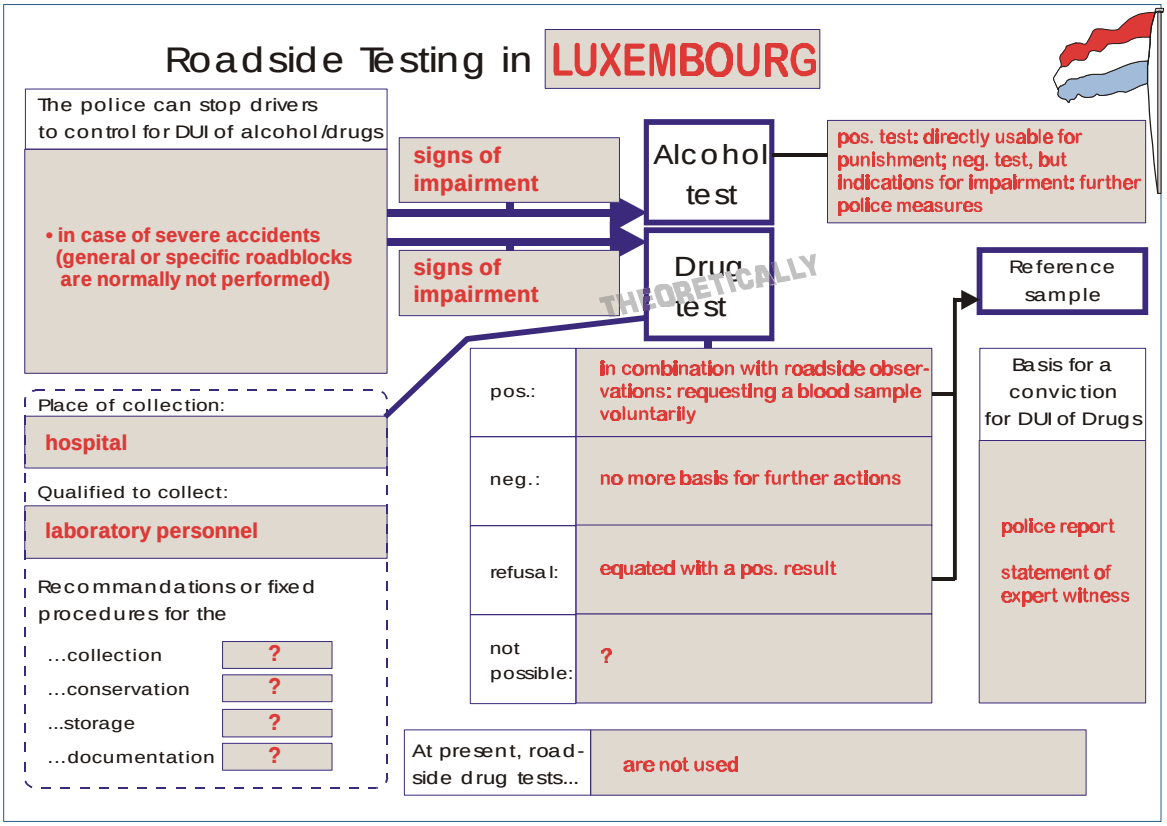


Figure 12: Roadside Testing in Luxembourg

The Netherlands

General Legislation
In The Netherlands both an analytical approach and an impairment oriented approach are pursued. Since 1974 (last change 1987), article 8 of the Traffic Act (section 1) makes driving under the influence of illegal drugs punishable. Impairment of driving performance as well as the presence of significant concentrations of drugs in a driver's blood have to be demonstrated. Included are all substances that might influence driving behaviour. At present, the introduction of specific cut-off values is in preparation as well as specific legislation covering the offence of DUI of prescribed drugs.

Drug and Alcohol Testing in The Netherlands
At present no roadside devices for the detection of the abuse of illegal drugs in street traffic are in use in the Netherlands.

The Dutch Traffic Act does not contain any regulation concerning drug screening devices or their application. Any new roadside test device must be approved by the Minister of Justice. This official approval will authorise the police to use it in the context of traffic control situations. The homologation of screening devices for saliva, urine etc. by the Minister of Justice is prepared by the Dutch Forensic Laboratory at the request of the police forces. The preparatory work is leading to technical specifications for a roadside drug test which has to be fulfilled by any product to be sold in the Netherlands for roadside testing.

Recently the Dutch Institute for Road Traffic Research, SWOV, has performed roadside studies to investigate the drinking and driving habits of motorists during weekend nights. These studies were connected with an on-site evaluation of screening devices (urine tests, sweat test).

From the point of view of the police the collection and analysis of specimens for drug screening can be performed at the roadside under the same conditions as alcohol testing. Any approved roadside screening devices can be used on-site to confirm an initial suspicion of impairment. Evidential testing might be done at the police station or - depending on the kind of evidential test - at any other location.

Today the Dutch police are mainly looking for alcohol abuse. If no alcohol is involved, but there are indications for impairment, the police officer tries to prove the abuse of other substances. Distinct indications of intoxication are required to suspect a driver of DUID and to request blood/urine sampling. To gain suspicion roadside observations provide the necessary indications, but no impairment specific test program is in regular use. Any observation is documented in a protocol. In case when a driver is willing to provide a blood sample, the results of a blood analysis can be used to confirm or contradict the suspicion of the police. In addition the medical doctor performs an examination for the abuse of illicit substances.

In case of alcohol abuse the Dutch police are authorised by law to submit drivers to a breath test without a suspicion of drunkenness; if alcohol influence is suspected, the driver is usually taken to the police station for a second evidential test of the breath alcohol concentration. Its result is used as a guideline for punishment. For traffic safety reasons random controls and general traffic controls are performed as well as specific roadblocks for law enforcement at special checkpoints. Per year, an estimated number of more than 250 000 screening breath tests are done in the whole country.

The evidence of drug-impaired driving must be given by the police report including a description of roadside observations, by the results of the medical examination, the analysis of the driver's sample (if obtained) and by an expert statement of a forensic laboratory.

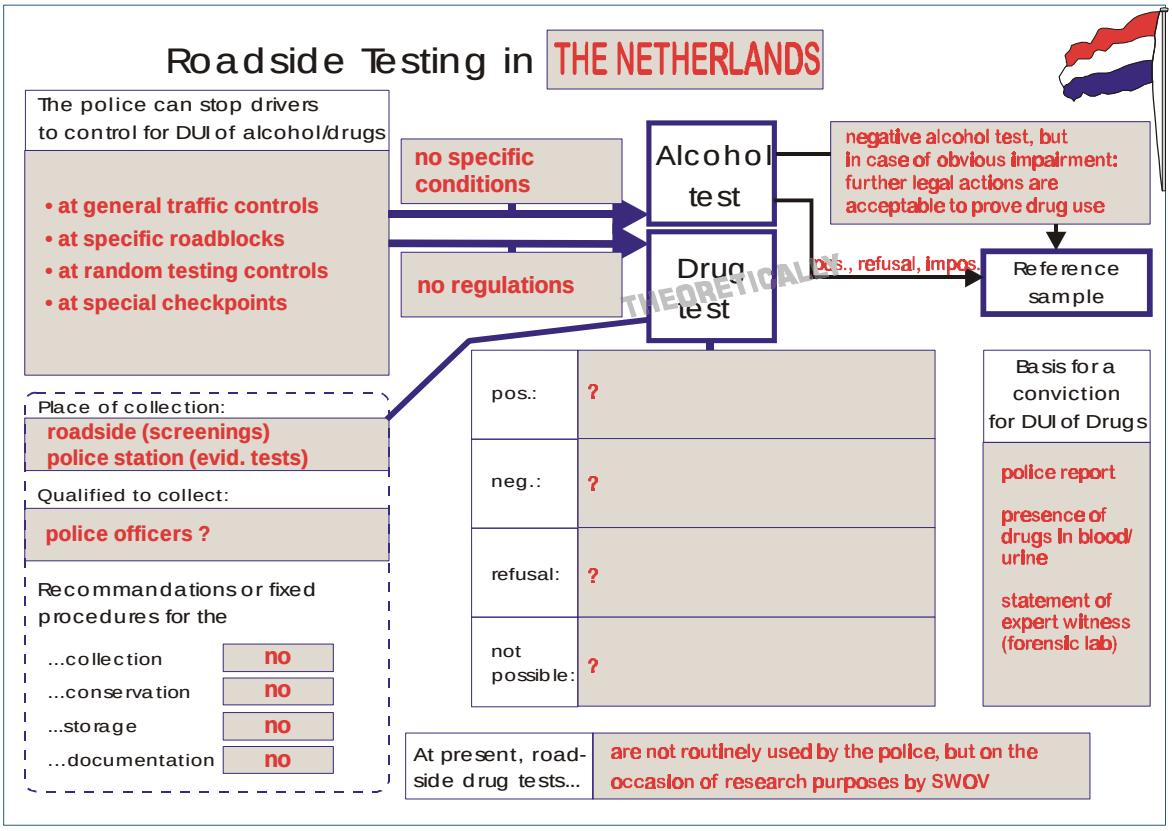


Figure 13: Roadside Testing in The Netherlands

Norway

General Legislation

As early as 1936 the Norwegian Government introduced a fixed legal limit for the concentration of alcohol in blood. In 1959, the Norwegian Road Traffic Act was extended to offences covering drugs others than alcohol. The Road Traffic Act is a part of the penal law and covers generally all psychoactive drugs without mentioning any specific substance or any legal limit in a body fluid. Punishment is based on the proof of impairment which has to be documented by the police forces.

Testing for Drug and Alcohol Abuse in Norway

Annually, Norwegian police forces test approximately 1.000.000 motorists for the abuse of alcohol. For that, general traffic controls or specific roadblocks for law enforcement reasons are performed. Additionally drivers can be tested in cases of accidents, or if the driver is known by the police from earlier offences. Random roadside controls are of minor importance.

At the roadside, the operating police forces have to decide on the type of substance influencing the capability of the driver to drive a motor vehicle. Based on the officer's experience and on his "drugs of abuse-know-how" he may decide on the presence of alcohol or drug abuse or a combination of both. If a reasonable suspicion for the presence is gained, or if e.g. medical or other drugs or consumption utensils are discovered in the car, the driver is usually taken to the police station for a second evaluation with an "Evidential" breath tester. If this test device is not available or the driver is not able to co-operate (because he is injured or severely sick), a blood (and urine) sample is taken.

If the suspicion is maintained for alcohol only, blood samples are collected and sent to the National Institute of Forensic Toxicology (NIFT) in Oslo where all blood samples are analysed (not only for the presence of alcohol, but also for the most common drugs). The result is reported back to the police, which submit a complete protocol to the court for decision. If drug abuse is suspected at the roadside, a clinical examination is performed by a physician at the police station or in a hospital before the respective blood sample is analysed by NIFT for alcohol and drugs. The NIFT prepares and provides an evaluation report on the degree of the driver's impairment based on blood concentrations and medical examination results. If illegal drugs are

detected, but impairment cannot be proven for the court, the driver can be convicted for the use of illegal drugs.

So far roadside drug screening tests are not applied routinely. For the first time this will happen now within the ROSITA project. Roadside screening devices are used by the police to confirm or contradict their initial suspicion. However it is not yet legally allowed to force drivers to provide a saliva sample. This is in contrast to the authority of the police to request and gain a blood or urine sample.

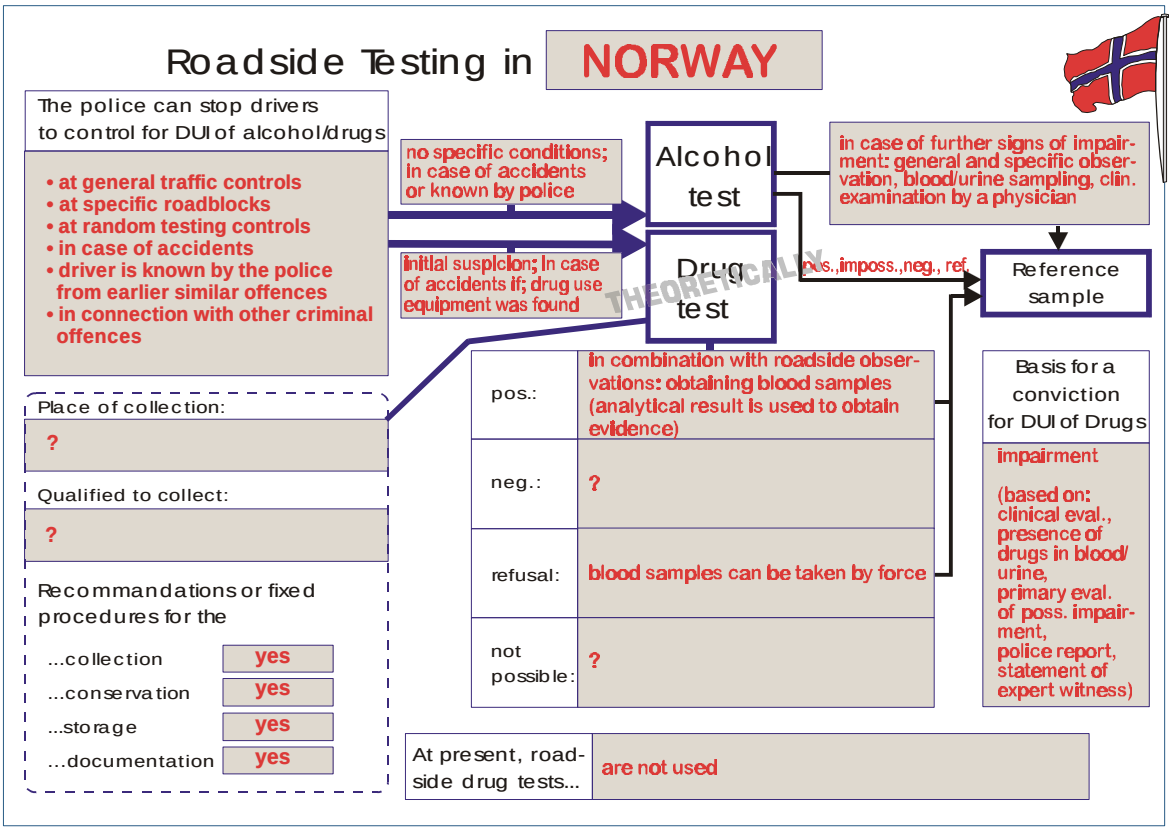


Figure 14: Roadside Testing in Norway

Poland

General Legislation
In Poland, impaired driving falls under a general legislation covering alcohol and driving. All drugs of abuse which are listed in the Drug Addiction Counteraction Act of 24 April 1997 (about 120 substances) as well as all substances with a similar effect on driving capability as alcohol are included in this legislation. "Alcohol similar" substances are officially listed in Poland in a table, which is updated every year (about 230 substances in 1997). Among forensic toxicologists, it is in discussion to explicitly mention drugs like morphine, cocaine and metabolites, THC, amphetamine, MDA, MDE and MDMA. For these drugss a zero limit approach shall be introduced, but up to now no specific limits exist.

Testing for Alcohol and Drugs in Poland
The application of roadside drug test devices is not prevented by any valid regulation in Poland. In theory any reliable drug test devices can be used under the same circumstances as roadside alcohol tests. In the context of general traffic control actions or accidents with personal or fatal injuries an initial suspicion is needed to apply such a device. However due to the absence of validated test devices, only laboratory proven test procedures are currently in use (blood and/or urine tests). Theoretically, a positive screening test result in combination with roadside observations could be an argument to request a mandatory blood sample. If the driver is not willing to co-operate, no negative consequences follow, however he will be brought to a medical clinic in order to give a blood sample for laboratory analysis provided obvious signs of impairment are visible.

Usually police officers become suspicious of drug abuse in the course of a control for alcohol abuse. After confiscation of the driving licence a breathalyser test is performed at the roadside. Furthermore, the police officer has the power to transport the subject directly to the nearestt hospital to take a mandatory blood or urine sample. Prerequisites for a blood or urine sample are a suspicion for drug consumption or a refusal or the inability to co-operate. Alcohol tests and blood and/or urine sampling can be carried out without the driver's agreement.

The basis for a conviction for DUI and driving in Poland is the police report with the observed signs of impairment, the results of the clinical evaluation and the result of the breath screening /or the laboratory's analysis of a blood specimen (if taken). Either misdemeanour board or court decide on the punishment.

Per year, in Poland about half a million drivers are tested at the roadside for possible alcohol abuse mostly on the occasion of routine traffic controls. In all cases of accidents with personal or fatal injuries alcohol testing is obligatory.

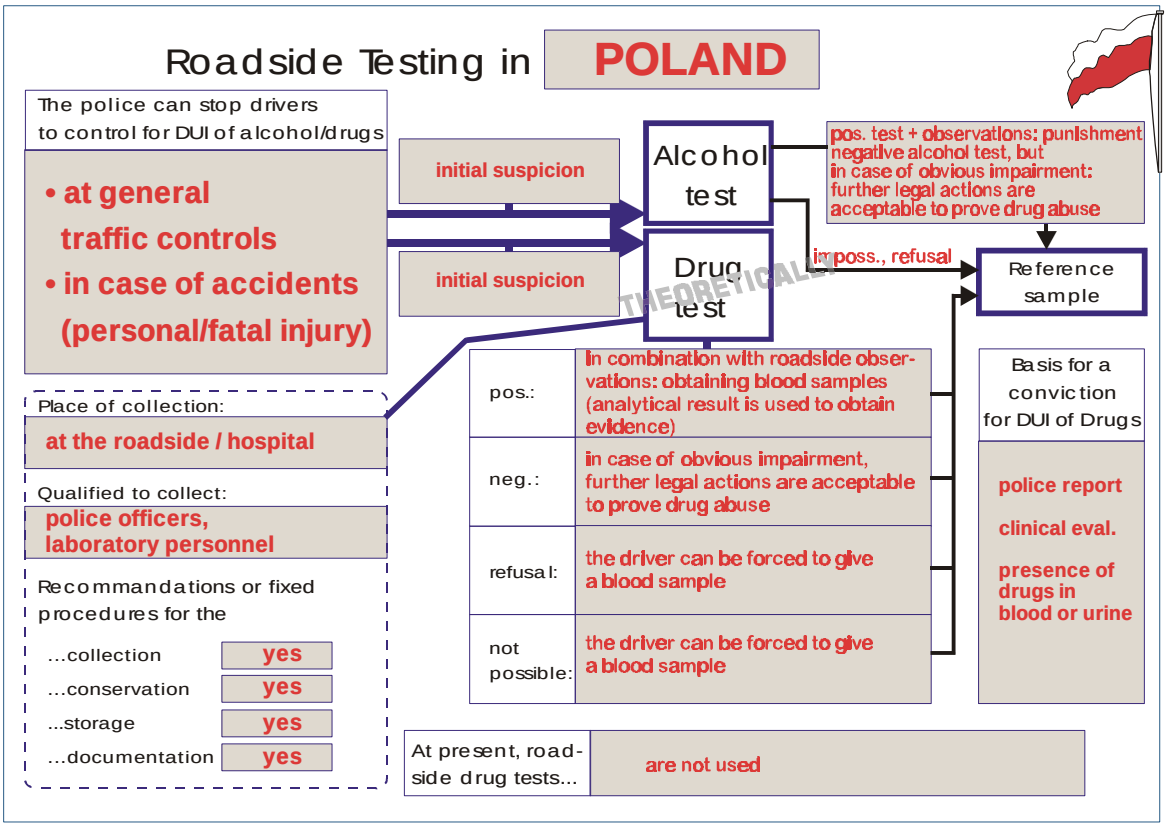


Figure 15: Roadside Testing in Poland

Slovenia

Drug legislation
Since 1998 offences against DUID are covered in Slovenia by § 118 of the Road Traffic Safety Act. This law belongs to the traffic law and includes all hypnotic, psychoactive medicines and other psychoactive substances which negatively influence driving ability. Legal limits are not specified.

Alcohol and Drug Testing in Slovenia
§ 120 of the Road Traffic Safety Act stipulates that, besides alcohol test devices, the police should also apply roadside test devices for illicit drugs, but until today no drug test devices are routinely in use. In all cases in which drug influence is suspected, the driver is usually taken to the nearest hospital for a medical examination. This examination is ordered by the police forces and includes the laboratory analysis of blood and urine specimens to determine the presence of illegal substances. Urine samples are generally not taken at

the police station. Therefore the application of urine-based roadside test devices is useless. Great expectations exist concerning the new saliva test devices. In cases of minor severity the courts decide on the basis of the toxicological findings. In cases where persons or personal items are damaged (traffic accidents), any documented signs of impairment are included in the decision of the courts.
During a traffic control action the investigating police forces decide on the involvement of substance abuse. If alcohol consumption is suspected, the driver is requested to participate in a breathalyser test. If the driver refuses to co-operate, he will be submitted to a medical examination which includes mandatory blood and urine samples. Refusal to co-operate with the police can even be punished more severely than a positive test result. The driver is automatically obliged to pay a fine, he can be arrested or his motor vehicle can be confiscated.
A positive breath test can directly be used for punishment if the driver agrees with the measured result by written consent. If a suspected driver does not agree, punishment is based on the results of a blood (and urine) analysis with laboratory based methods and the police report on the investigated signs of impairment.

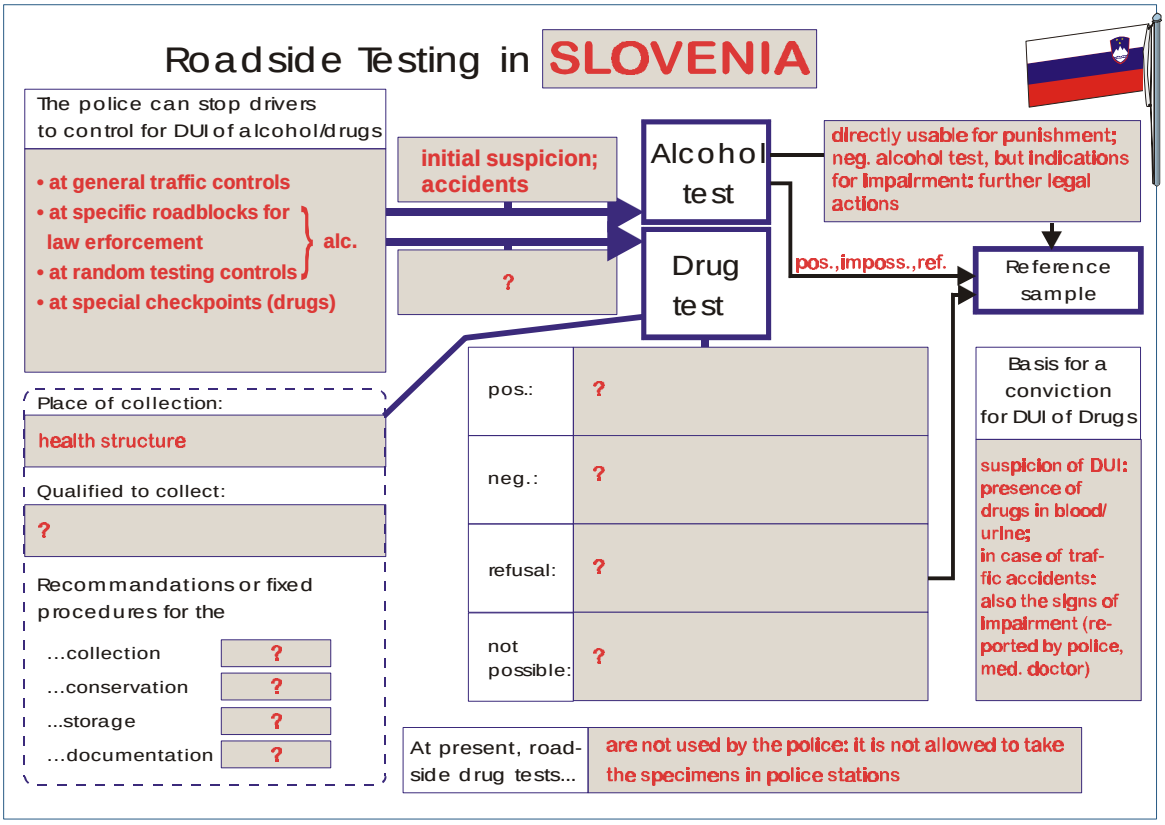


Figure 16: Roadside Testing in Slovenia

Spain

General Legislation
The Spanish Penal Code contains within the Section "Crimes against Public Safety" a subsection related to crimes against road safety. In this subsection driving under the influence of drugs, narcotics, hallucinogenic substances or alcoholic drinks is regulated. The Law on Traffic and Road Safety stipulates in article 12.1: "If the driver of a vehicle exceeds the legal limits pertaining to alcoholic drinks, narcotics, hallucinogenic substances, stimulants or other analogous substances, he may not drive upon any public road". Unfortunately, only alcohol limits are mentioned.

The current Spanish approach to deal with DUID is impairment-oriented. This is in contrast to the alcohol control field, where Spain relies on both: exact analytical limits for the allowed alcohol concentrations in blood as well as examined signs of impairment.

Testing for Drugs and Alcohol in Spain
Under legislative aspects there is no difference between the abuse of alcohol or drugs in street traffic; this is due to the formulation of the Spanish Traffic Act referring to alcohol, toxic drugs, and other substances influencing driving ability. But from the technical point of view, there is no drug test device available which can be used in the same way as a breathalyser.

For testing the influence of intoxicating substances other than alcohol, Spanish regulations stipulate that a procedure should be applied which will consist of:

- a medical examination and
- a clinical analysis which the forensic scientists and medical expert may deem appropriate

Actually, Spanish police forces are only applying breathalyser devices. Current legislation states that police shall use accurate breath test devices for testing drivers for alcohol abuse. Suspected drivers can be punished on the basis of the result of the roadside test device, together with the police report. When the suspect or a judge insists, the analysis of blood, urine or equivalent body fluids is carried out (but due to the occurring time delay the analysis of blood very rarely occurs because of the time that elapses between the incident and the judge's decision).

The following groups of the motorists can be forced to participate in breath testing (without an initial suspicion):

- any participant in street traffic, directly involved in a road accident
- anyone driving a vehicle displaying obvious signs or manifestations which may lead an officer to suspect that the driver is under the influence of alcoholic drinks
- drivers denounced for infractions of current legislation
- participants in alcohol abuse prevention programs.

With regard to the other substances mentioned in the Spanish Traffic Law the possibility is already foreseen, that roadside test devices to detect the presence of other substances than alcohol (Article 12.3) will be developed and introduced; currently, in Spain it is not possible to attempt the detection of any substance other than alcohol, and until now nobody has been arrested for driving under the influence of drugs. There have been no sentences in connection with cases of drugged driving. Any data on the prevalence of drug abuse in street traffic are based on the systematic toxicological studies with victims of traffic accidents.

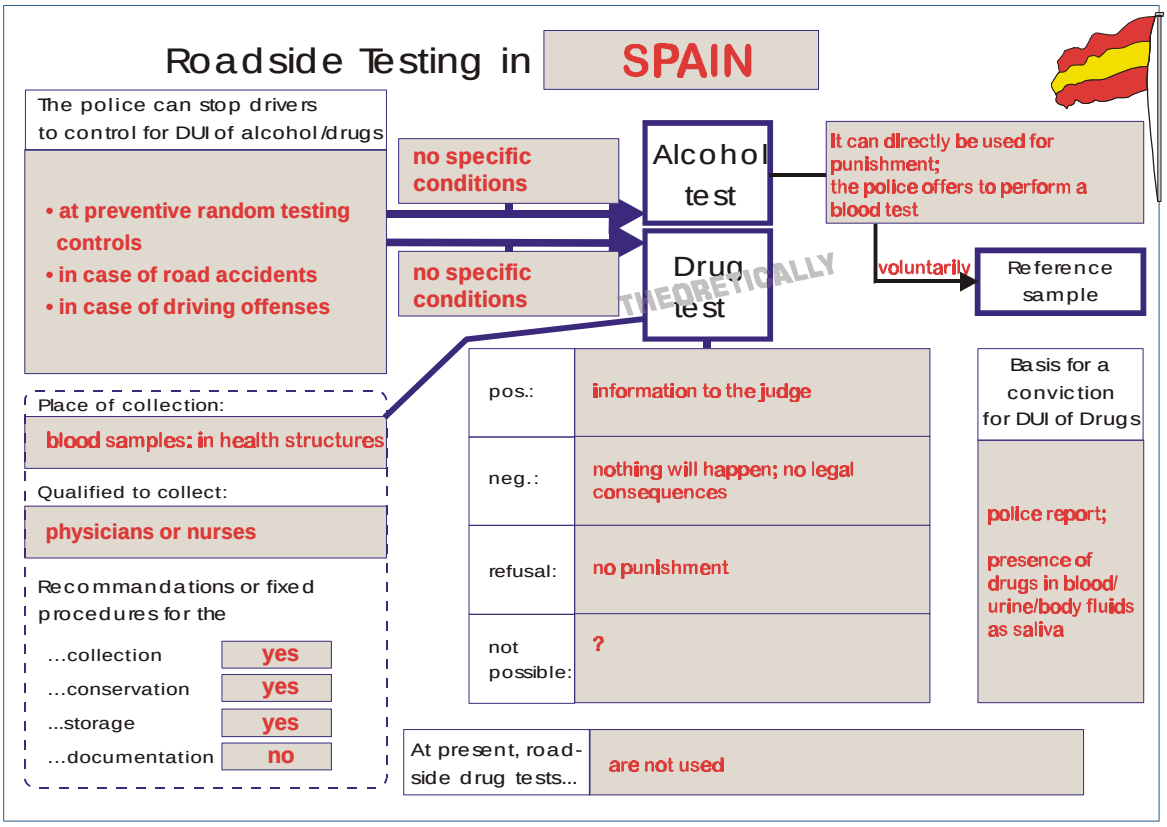


Figure 17: Roadside Testing in Spain

Switzerland

General Legislation
In general, in Switzerland offences of DUI of drugs are covered by two laws: the Road Traffic Act stipulates in section 31, paragraph 2 (SVG; SR 741.01) that a person who is drunk, overtired or otherwise not able to drive, may not drive a vehicle. In Section 2, paragraph 1 of the Traffic Rules Decree (VRV; SR741.11), is more specific regarding the inability to drive due to alcohol/drug/medicine influence. All drugs and medicines are included without explicitly mentioning any substance. There are, except for alcohol (0.8 g/kg whole blood) no legal limits specified.

Approx. in the year 2001, an amendment of the Swiss Road Traffic Act will come into force; apart from some general changes, in the alcohol sector the BAC limit will be reduced to 0.5 g/kg whole blood. DUI of alcohol cases will be punished more severely and the police will get the power to check drivers for drunkenness even without a suspicion in order to intensify the task of general prevention. Regarding drugs, the federal council is going to fix legal limits for psychoactive substances; for illicit drugs like heroin and cocaine, probably a zero-tolerance will be introduced.

Testing for Drugs and Alcohol in Switzerland
Until today, in Switzerland the police officers may perform breath screening tests for drunkenness on each occasion if a driver seems to be under the influence of alcohol. These occasions are general and random traffic controls (bulk controls are performed two times per year, and smaller ones are held around the clock, performed spontaneously or in the case of driving faults) and accidents. A primary decision is made at the roadside, and if the police officer has the opinion that a driver is incapable of having proper control over a vehicle due to the consumption of alcohol, he will request a breath screening test. Information on his rights and duties is given to the subject usually at the beginning of a control, but at the latest by refusal. If the test result is positive (> 0.6 g/kg), or the driver refuses co-operation, a blood sample will be taken and a medical examination will be performed mainly in health structures like hospitals or doctor's offices, sometimes in police stations and very rarely at the roadside. After laboratory analysis, the obtained alcohol content at the

time of taking the blood specimen is calculated back to its level at the time of incident; the results are reported back to the police, the case goes to court and drivers with BACs above the legal limit are convicted according to the Road Traffic Act.
If the breath test turns out to be negative, but signs of impairment are obvious, further investigations are justifiable to prove drug use, including blood and urine sampling, due to the observed signs of impairment.

Finally, the basis for a conviction for alcohol and driving is the police report (including the observations at the roadside), the medical examination (including the observations of the physician), and the presence of alcohol in whole blood.

If indications for drug abuse are obvious, the police officers start to interview the subject regarding consumption of drugs and medicines, and a medical examination including the taking of blood and urine for toxicological analysis is ordered. The procedure of sampling differs generally between the Swiss cantons, because it is not regulated federally. Subsequently, an expert opinion will be stated.

Roadside drug tests are not used routinely for traffic controls, but a small number of devices have been and are used for evaluation purposes at the roadside. As a result one current conclusion is that the test devices can be used as a tool to underline the suspicion. Due to the fact, that for the taking of blood/urine specimen no appropriate federal regulations exist to authorise the police forces in Switzerland to apply a roadside test device, the cantonal rules of procedure are applied.

Generally, the devices can be used by police officers at the roadside and at police stations as well as in all kinds of health structures. Recommendations to collect the specimens, to conserve, to store and to analyse them are given by the Swiss justice and police department.
If a roadside drug test could be carried out and turns out to be positive, the result could be used as a single reason or in combination with observations for gaining reference samples, such as urine to prove the consumption of drugs, and blood for the interpretation of the effects and the degree of impairment.

If in spite of a negative test result or in cases of refusal impairment is obvious, further legal actions are acceptable to prove alcohol or drug use. If the driver seems to be too influenced so that he is not able to co-operate, he can directly be forced to give a blood specimen. Furthermore, inquiries can be conducted to obtain more evidence, like statements made by witnesses.

Generally, the test devices can only be used as a means of assisting the police officer to decide if the driver is unfit to drive due to drugs; in court, objective criteria for DUID are the presence of drugs in blood, the police report, the results of the clinical evaluation and a statement of an expert witness; if available, the confession of an accused person is also taken into consideration.

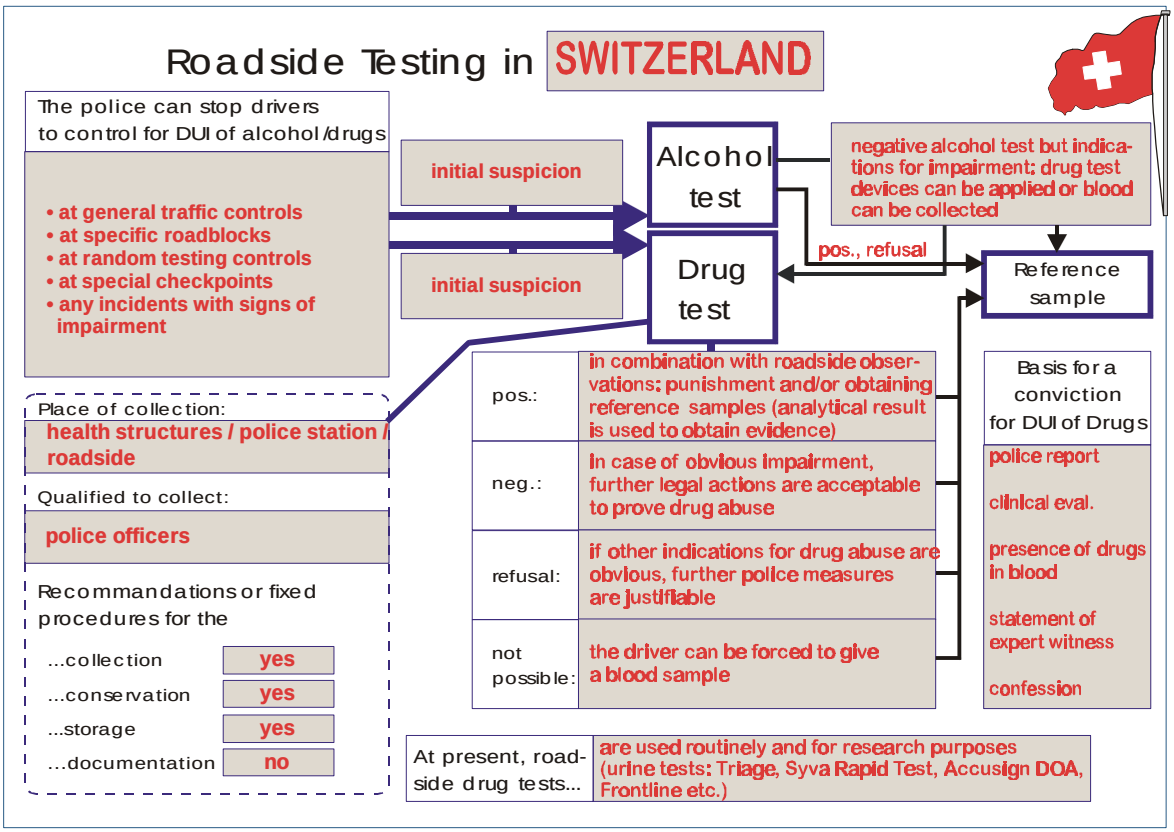


Figure 18: Roadside Testing in Switzerland

United Kingdom

General Legislation
In the United Kingdom, the Road Traffic Act from 1988 (Section 4) covers alcohol and all substances causing impairment.

Testing for Drugs and Alcohol in the UK
UK police forces have the power to stop any motor vehicle on the road for safety reasons and check the driver for his driving capability. Per year, approximately 800.000 roadside alcohol breath tests are performed with breathanalyser tubes and handheld breath test devices. For drugs, no tests are used routinely at the roadside, because the law does not allow specimens to be taken except for alcohol (e.g. breath samples). However, the Cozart saliva test and Drugwipe for sweat testing have been used for evaluation purposes.

Roadside testing depends on an initial suspicion. Such a suspicion can be based on observed signs of impairment, on the information of an informer, a traffic offence whilst a vehicle was in motion or the involvement of a driver in an accident.

In all these cases the suspect driver has to participate in breath testing. If the suspicion for alcohol abuse or the influence of other substances is confirmed, the driver is taken to a police station (arrested if necessary) for a second test with a confirmatory breath analyser. The driver can be prosecuted on the basis of the test result of the evidential breath test system, but has to be handled by regular UK courts according to the Road Traffic Act.

If the breath alcohol test result comes out negative, a medical examination of the suspect is performed by a police surgeon and blood or urine samples are requested for further investigations. If the suspect does not consent to a physical examination, only the behaviour of the suspect can be observed. Drivers can not be

forced to provide a blood sample. Prosecution in such cases is based on the results of the medical examination and further observations of the police surgeon. Refusal of the breath test is equivalent to the infringement of a valid regulation and is punished similarly to a positive result.

Provided that police forces suspect the abuse of other substances than alcohol (e.g. due to signs of impairment), a blood or urine sample can be requested from the suspect driver. Police forces can decide on the type of specimen, the target drugs as well as on the laboratory for analysis. Only laboratories can be selected which have been authorised by the Home Secretary in England or Secretary of State in Scotland.

The basis for a conviction for DUI and driving are the results of the medical examination and of the blood/urine analysis (if obtained), the police report, a statement of an expert witness and, of course, the confession of accused persons.

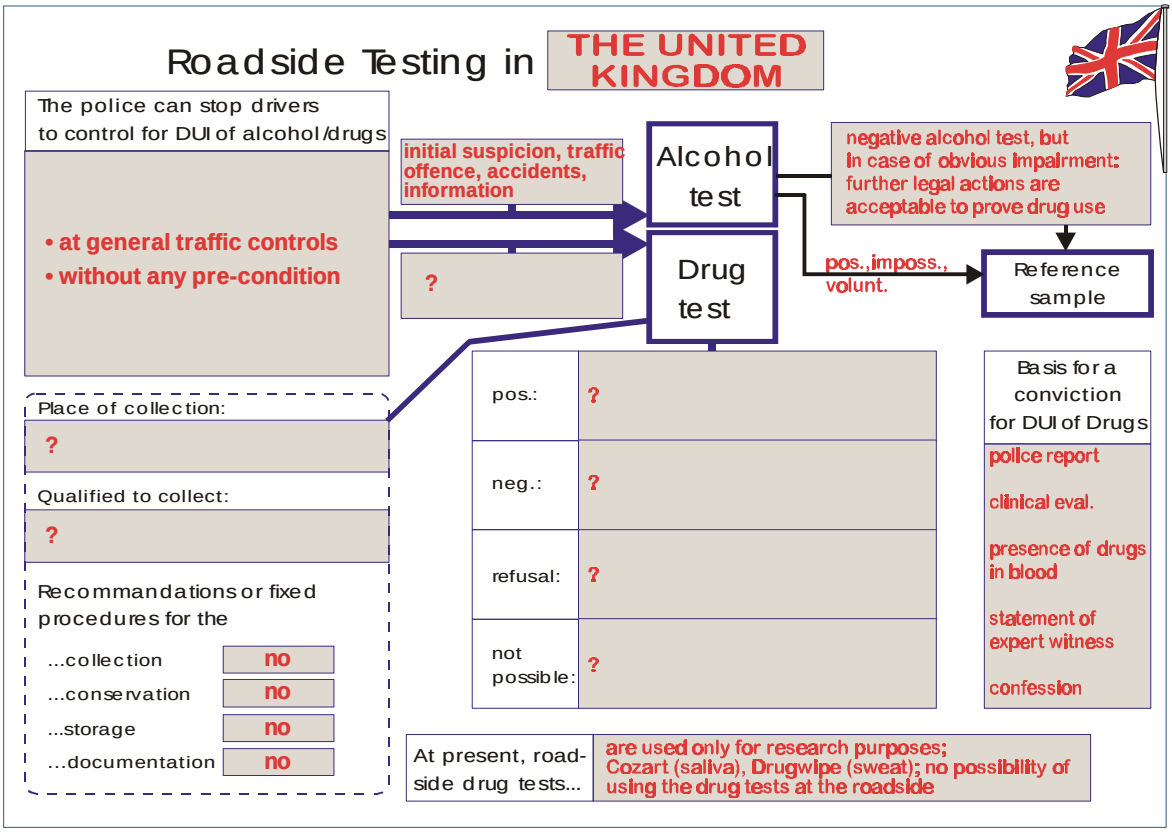


Figure 19: Roadside Testing in the United Kingdom

OPERATIONAL REQUIREMENTS ON ROADSIDE TEST DEVICES FOR DUID

Introduction

The Questionnaire

The individual legal prerequisites in the different European Countries set the frame conditions for the future application of available roadside drug test devices. Within these frame conditions every device has to comply with the operational requirements of the individual police forces.
Police forces all over Europe are very much influenced by the high level of precision and user convenience of the alcohol test devices introduced up to now. These instruments are setting the milestones for drug test devices with respect to handling, logistics, storage and maintenance.
However, alcohol is present in the parts per thousand level in the blood as well as in the breath of intoxicated drivers. Drugs are usually present in the parts per billion level in body fluids and do not appear in detectable concentrations in the breath of drugged drivers. Such prerequisites make the development of suitable test devices technically more complicated and sophisticated and, last but not least, more expensive than alcohol devices.
We collected and summarised the needs and requirements of the police forces in the different European Countries.
The participating countries were asked to provide the following information:

- What are the main target drugs in your county?
- What are the preferred specimens for roadside testing?
- How should a roadside test device be configured (single or multitest, throw-away or reusable device, acceptable test time, provision of the result, reasonable target price, etc.)?
- Are there existing (accreditation/homologation) procedures which have to be followed before the introduction of a new test device.
- Are there any plans to introduce a training program for drug recognition?

With the exception of Portugal and Sweden, police forces of all countries have provided sufficient information and most responders had a rather clear picture of what they need under their operational conditions. On the European level information can therefore be considered as representative.

Warning: Significant National Differences

However, needs and requirements of the individual European states are significantly different. Even in a federal system like Germany the Consortium noted considerable differences in the preferences concerning specimen or test configuration between different states. This observation is not unexpected, but is due to the independent authorities of State or Federal governments to enact and implement traffic laws.

Mathematical treatment

To make tendencies or preferences overall in Europe clearer a European average was calculated from the contributions of the individual countries. If several sets of answers were available from one single country an average national answer was calculated first. This average national answer was then used to calculate an average European answer. Each European Country contributes equally in this evaluation process.
An average quantitative ranking in the importance of the different target drugs was reached by weighting the individual answers according to the total population of this country. More exactly, the given importance for each drug in percentage was multiplied by a factor representing the population of the respective country in relationship to the population of all participating countries.
For the 19 countries which returned their questionnaire a total number of inhabitants of 410 Million was calculated. This number does not only include the countries of the European Union but also countries like Poland, Slovenia or Czech Republic, so far not members of the European Union.

Results

Spectrum of Target Drugs

Which target drugs will be most important for testing at the roadside? Each country was asked to evaluate different drugs concerning their general importance for being included in a test panel at the roadside. In addition a classification of the different types of drugs with percentages due to the experiences of the individual countries was requested.
All the following classes of drugs were classified as very important target analytes for roadside traffic controls:

- cannabis
- opiates
- cocaine
- amphetamines (including designer amphetamines like MDMA)
- benzodiazepines

Further drugs mentioned by selected countries were methadone (most important other drug), antidepressants and ephedrine/pseudoephedrine.

Figure 20 provides an overview of the distribution of the important illicit drugs in Europe on a national level as well as on a European level.

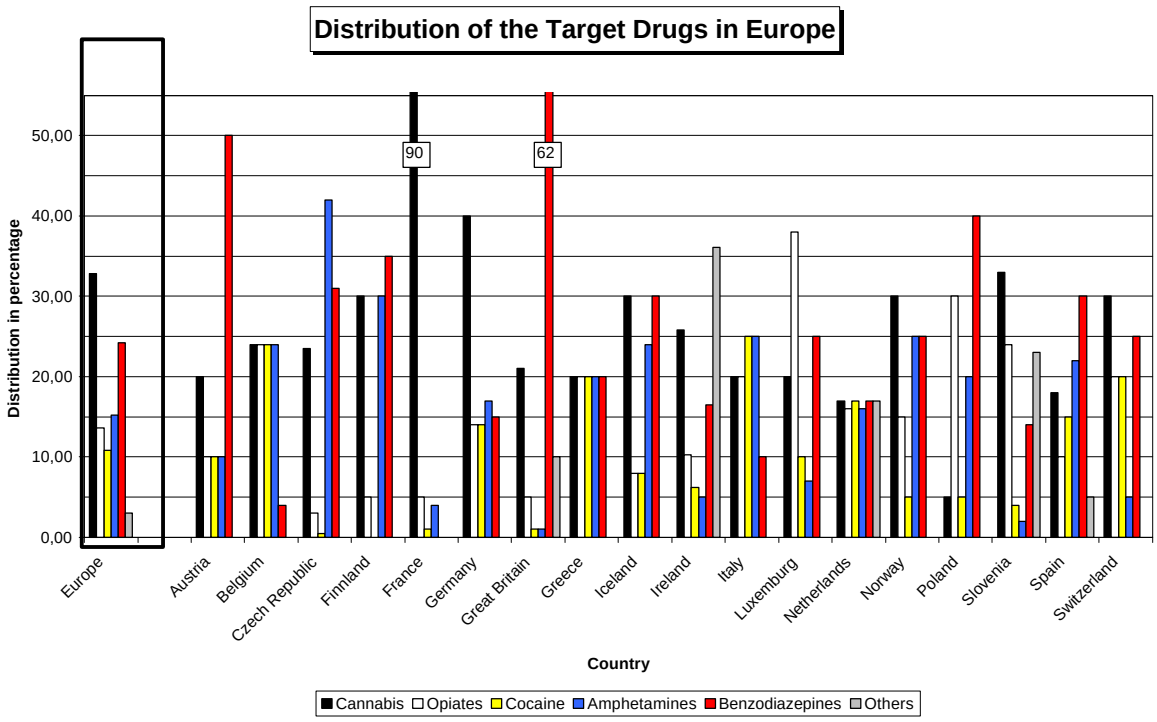


Figure 20: Distribution of the target drugs in Europe

Based on the quantitative information of the responding countries, cannabis is the illegal drug appearing with the highest frequency in street traffic (estimated 33 percent of all cases) followed by benzodiazepines (24 percent). The other groups of illegal narcotics (opiates, cocaine and amphetamines) amounting to values of 10 to 15 percent each. Other illegal drugs play a minor role on the European level, but on a local level they can be very important.
The classification of the different groups of drugs was mainly influenced by regional and national epidemiological studies and the results of the ongoing analytical examinations of blood samples. An additional factor of influence has been the experience of the police officers in the field.

Preferred Test Specimen

Theoretically a policeman at the roadside can ask for a blood, urine, saliva or sweat/skin sample of a suspect driver. Legal, operational and pharmacological conditions finally determine which body fluids are best suited to be used in traffic control situations.

On average the questioning of the representatives of the different European countries brought the result, that most countries prefer to use saliva as an on-site test specimen. This is due to the low invasiveness and the simplicity of obtaining saliva samples. Also the general availability during traffic control situations was considered as good. Further arguments in favour of saliva have been the close correlation of the saliva concentration with the blood concentration (which means a good correlation to impairment) and a low risk of infection.

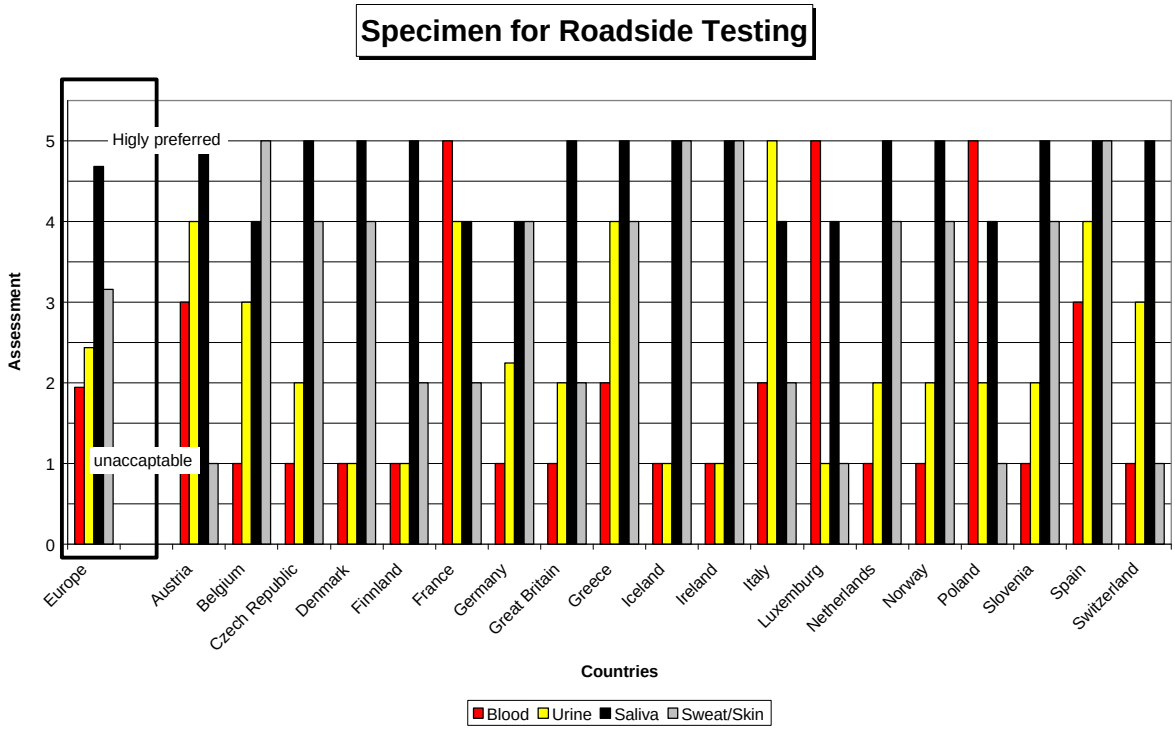


Figure 21: Preferred Specimen for Roadside Testing

Sweat/skin was considered as an acceptable alternative to saliva. The main disadvantage of sweat in relation to saliva, the weak drug correlation of sweat concentrations with impairment, was mentioned . Concerning invasiveness, simplicity and availability sweat seems to be comparable to saliva. The biggest advantages of sweat are, that the intrusion into the personal rights of a driver is lower and that sampling can be performed without any collaboration of the suspect driver.

Sampling and testing of blood at the roadside was considered by most participants as impossible under their legislation. Nevertheless it provides the closest correlation to the state of impairment. The main drawback for urine testing was, that a positive urine test only demonstrates consumption but may not mean impairment. Furthermore, in some states it seems to be legally difficult or impossible to obtain a urine sample.

Device Configuration

Multi- Single or Combination Tests

In general, each test device can be configured as single parameter test or a multi parameter device. Individual tests are cheaper in use than multi test devices. However the officer needs a preselection mechanism (e.g. he must be trained in the detection of other signs of impairment, or the most probable target drug is known because of the control circumstances). A multi test device will have a higher price than individual tests, but will provide more comprehensive information.

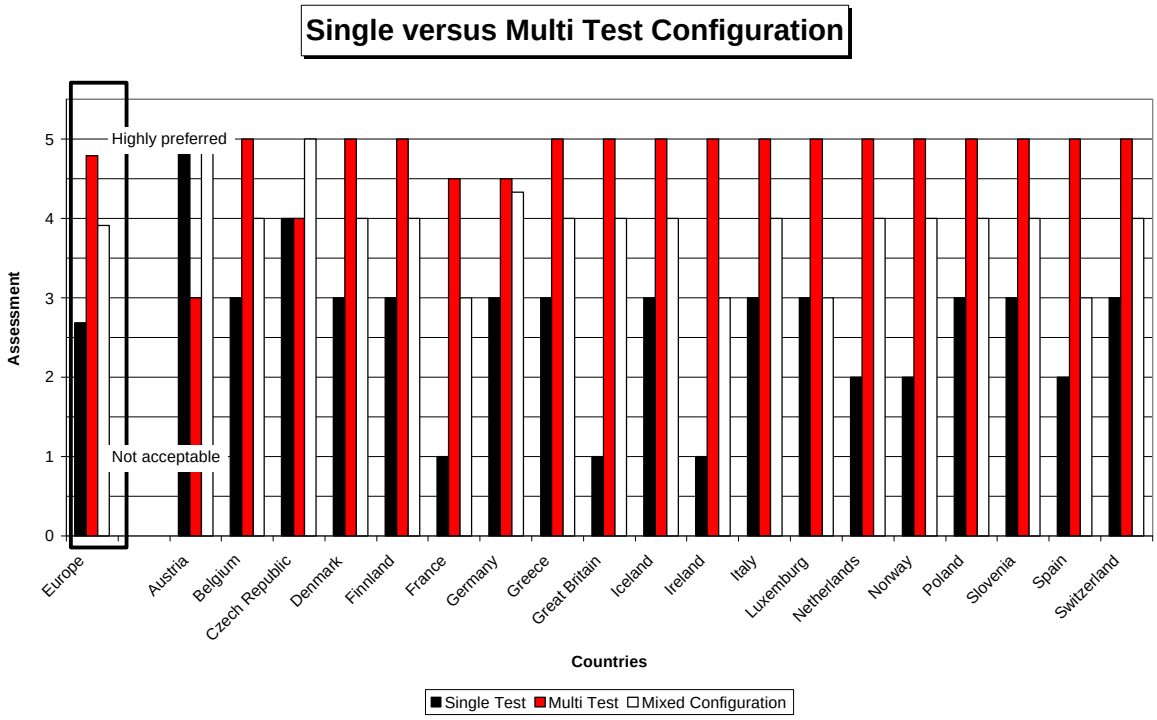


Figure 22: Single versus Multitest configuration

Nearly all countries prefer to use a drug multi test, which supplies a complete "narcotic profile in one shot". A combined solution (with single tests for the low probability drugs and double or triple tests for the high frequency drugs) seems to be acceptable also in most countries, whereas single test systems are considered as difficult to use.
This is due to the above mentioned necessity to have a selection mechanism. Not all police forces will be trained adequately and therefore will need a comprehensive multi drug test for their control activities. In addition a multi test is considered as easier to use and time saving for the police.Well trained policemen are able to preselect suspect drivers and only in a few questionable cases a confirmatory screening test is necessary to secure their initial suspicion. For such "drug recognition experts" a single test would be most cost effective.
The main arguments for a test configuration comprising a double or triple test for the most prevalent narcotics and single tests for the parameters appearing with a lower probability in street traffic have been better price performance ratio, trained police forces will be able to use such a test configuration and the country specific spectrum of drugs makes a 5 or 6 parameter test unnecessarily expensive.

Acceptable duration for a roadside test for DUID
The time demand for testing a single driver at the roadside is a critical parameter. Usually police forces need to test a lot of drivers within one traffic control action. The shorter the time for each test, the more persons can be tested. Furthermore a short examination time means a minimum degree of inconvenience and obstruction for each person, which increases the general acceptance of a control measure.
The general tendency was to prefer very short measurement times (2 to 5 minutes). More than 10 minutes is generally considered as unacceptably long for an on-site examination process.

Throw away concept or reusable instrument
The consortium asked in the questionnaire whether a single use system (= throw away device) or a reusable instrument is preferred. A single use system can only be applied to test one person. Then it will be thrown away or stored for documentation purposes. With a reusable device the police officer is able to test several people. For hygienic reasons one may have to exchange a sampling tool or other consumables, but the basic system is applicable for several measurements. However such a device will need service, maintenance and some sort of calibration.

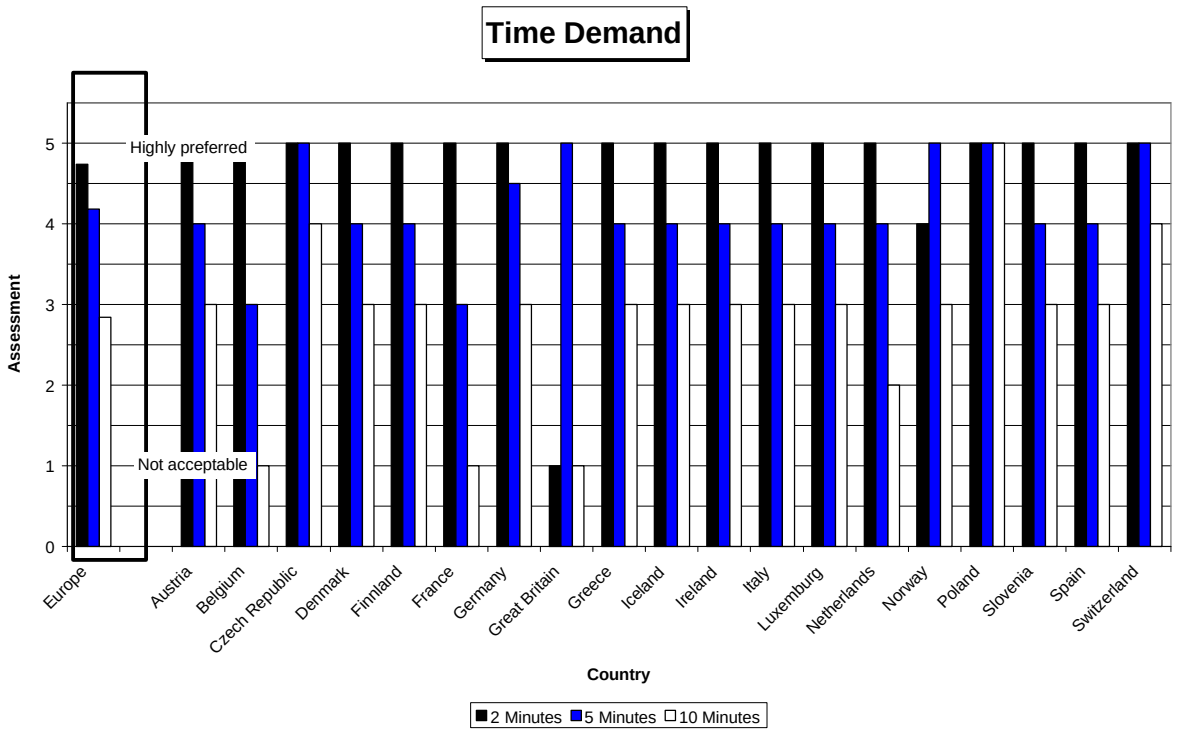


Figure 23: Single versus Multitest configuration

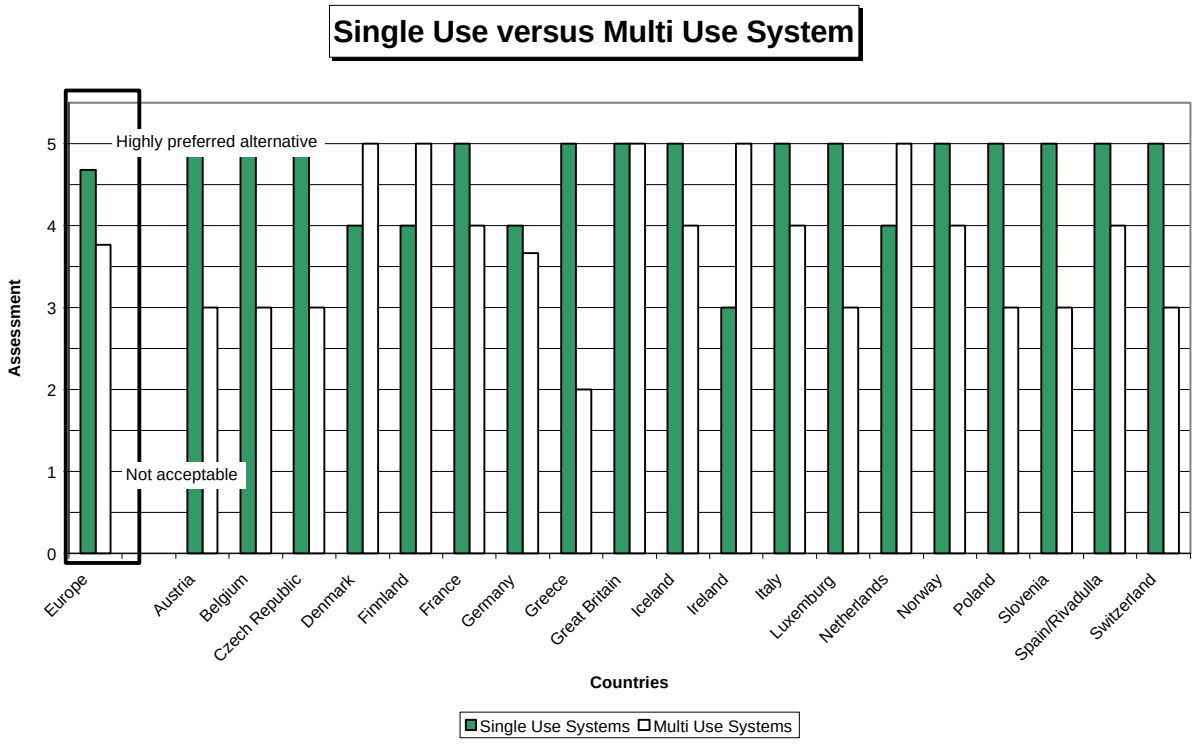


Figure 24: Comparison of single use and reusable drug test systems

In the case of this question most representatives answered they would prefer a single use system, but a clear preference does not exist. Most countries would also introduce a reusable device provided it will have similar technical features and it will be more cost efficient. General arguments for the preference for a single use test

system were avoidance of cross contamination and infections, greater simplicity and therefore ease-of-use and absence of maintenance.

Storage and Place of Application
Only 30 percent of the asked police groups claimed that drug test devices have to withstand extreme temperatures during a long term storage in the police car. The great majority of the participants stated that it is possible to store the test devices in the office and take them out for control actions.
Due to the answers of the respondents more than 86 percent of all drug tests should be performed at the roadside. And about 70 percent of all tests are used during the darkness – a fact which supports the necessity of a signal output mechanism which is independent from the environmental light conditions.

Further Requirements (Reliability, Portability, Readability)
Further important and very important requirements (according to the answers) have been that any device should show the examination result clearly and without any room for interpretation and that only minor training should be necessary before a police officer can use a drug test device.
In some countries it is important to have a measurement result stored or printed for documentation purposes. In other countries this feature is of no interest at all. Of medium importance is, that a drug test device shows the test result optically or acoustically.

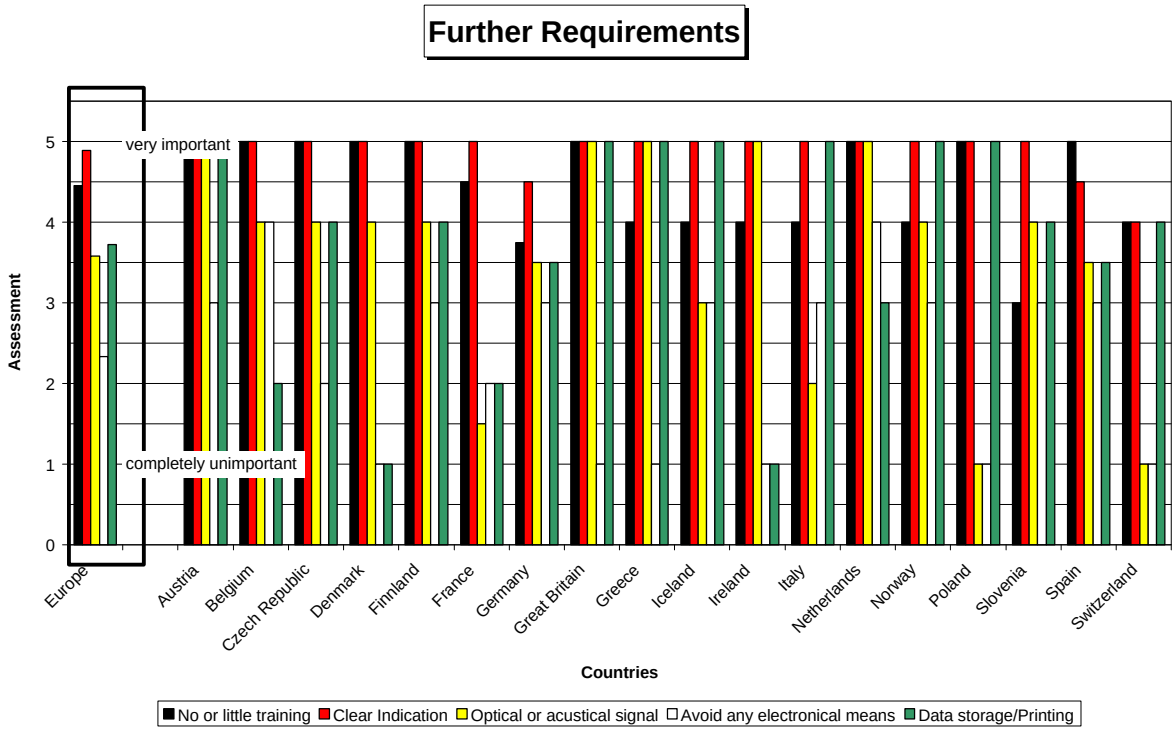


Figure 25: Summary of further requirements on training, portability and readability

Additional features mentioned have been readability under all light conditions, portability and usability for on-site applications.

Cost Considerations

The average price which was considered in the context of this questioning as reasonable for a single parameter device was 3,9 Euro (1,9 Euros and 7,5 Euros are the extreme values), for a 4-parameter device 14,0 Euro (including values between 4,5 and 30 Euros).

Based on the final results of workpackage 2, the devices for saliva and sweat testing cost between 6 and 18 Euro for one to five parameters. The cost of urine test devices varies between 2 and 6 Euro for a single parameter, and 10 and 20 Euro for a five panel multitest.
The price level for urine tests is therefore very closely corresponding with the price level, which is acceptable for potential users. The main question will be how the market sizes for saliva and sweat test devices will develop. In comparison to urine test devices, these devices require additional sampling tools and are currently sold in much smaller quantities. Under these circumstances, the price level is necessarily higher.
Furthermore, price estimates are influenced by the actual prices for alcohol test devices (breathalyser tubes, consumables) and it is questionable whether this price level can be realized in the long term for roadside test devices, because the necessary technology is much more complex.

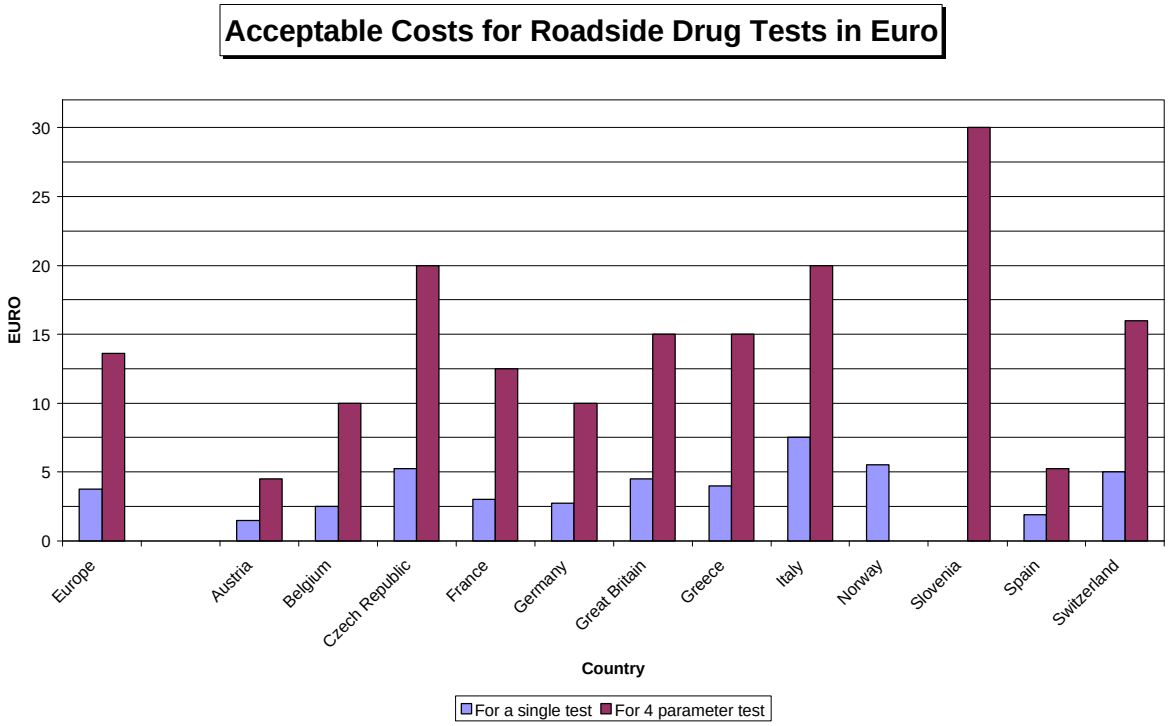


Figure 26: Acceptable Costs for a single and a 4-parameter roadside drug test device

Introduction and Training for New Test Devices

The suggestion to combine the training on a new drug test device with a general drug recognition training is not very practical because only 5 countries so far (Belgium, Germany, Finland, Norway, Switzerland) have introduced such a training program. An additional 5 countries (Greece, Slovenia, Ireland, The Netherlands, United Kingdom) are currently planning the introduction of such a training program, but in the majority of the countries no plans exist to install a drug recognition program.

Accreditation, homologation and approval of roadside test devices

At this time, only 6 of the 19 countries have established specific accreditation or homologation procedures for drug test devices. This is the case in France, Great Britain, the Netherlands, Poland, Slovenia and some states of Germany. In these countries a specific approval procedure has to be passed by new drug test devices before they can be applied to check drivers in street traffic for DUID.

On the European level the European Parliament has adopted a new regulation for in vitro diagnostic medical devices (98/79/EC) in October 1998. According to this regulation, medical devices are defined as instruments

for the examination of human specimens for the purpose of investigating the "physiological or pathological status" of a human being (article 1). Depending on the range of application, manufacturers of such devices have to fulfil more or less strict regulations to be allowed to sell their products within the European Union. Minimum requirements for compliance are a complete technical documentation (including sufficient validation data proving the claimed product features), an established quality control system and a procedure to recall defect products. Compliance is shown by a "CE"-sign on the outside of the packaging.

Every manufacturer printing the CE sign on his products is declaring compliance with the regulation for in vitro diagnostic medical devices. This fact bears the big advantage for the different user groups, that they can be sure, that only products are on the market, which are sufficiently validated and manufactured under good quality conditions.

The main applications covered by the in vitro diagnostic device regulation are laboratory, hospital and home use. But most likely roadside test devices for the examination of urine, sweat or saliva samples will also be covered. Which articles finally have to be applied is a matter of discussion. It is also an open question how the countries, which have actually established procedures for approval of roadside test devices, will deal with this regulation. One future consolidation might therefore be that manufacturers have to fulfil both the EU directive as well as police specific national approval criteria. This makes marketing more difficult, thus lowering the readiness of device manufacturers to invest in a new market. On the other hand a general approval process, which will be accepted by all countries of the European Union will be a positive signal for the manufacturers of in vitro diagnostic devices.

Important for a successful implementation of the new regulation is, that the approval process in total is well structured and can be passed in a short time. This will help to avoid any delay between the development of a new product and the availability in the market, thus giving the police forces access to the newest technologies.

On a national level the countries of the European Union have to adopt the in vitro diagnostic medical device regulation until the 7th of December 1999. From the 7th of June 2000 on, medical devices may comply with this new regulation. For manufacturers as well as users of medical devices it is important to know, that there is a 5-year transitional period for generating compliance with the new regulation for existing products as well as new products coming on the market. After the 7th of December 2003 only products in full compliance with this regulation can be sold within the European Union.

SUMMARY OF THE FINDINGS

Regulations concerning DUI of drugs – Current situation

In the following table (devided in 5 parts) an overview is presented about the valid DUID legislation in the 19 countries; included are the exact laws, named drugs, limits and exemptions, and if amendments of the legislation are planned in the near future

	Austria	**Belgium**	**Czech Republic**	**Denmark**
DUI of Drugs -specific legislation		Art.35,37bis,61bis,61ter,63 3° en 4° (Traffic Law) Law of 16.03.´68; modified on 16.03.´99, in effect since 30.03.´99		Danish Traffic Act §54, 1
- general legislation	§5 StVO (Traffic Law)		-Art. No 89, Sec. 13 (Penal Law) -Law No. 65/1994, §201 (Penal Code) -Law No. 124/1993, §30 (Misdemeanour Act) -Law No. 12/1997, §§6,9 (Traffic Law) -Law No. 40/1995, §6 (Law about protection from alc. and drug abuse) -Law No. 167/1998; (Substances of abuse)	
Substances, Limits	Drugs of abuse as specified by the Law on DOA (´97)	THC (2 ng/ml), MOR (20 ng/ml), AMP, MDMA, MDEA, MBDB, COC, BZE (all 50 ng/ml) Conc. in plasma	No drugs are mentioned	Psychoactive subst.
Exemptions?	No	No	No	No
Future Changes?	Yes	No	No	No

Table 1.

	France	**Finland**	**Germany**	**Greece**
DUI of Drugs -specific legislation			§24a StVG (Traffic Law), changed on August 1st, ´98	L 2696/99, Sect. 42 (Traffic Law), in effect since May 23th, ´99 Minist. decisions -13382 φ. 705.11/4δ/25-10-77 -1330 φ 705.11/4ξΘ/15-2-85
- general legislation	Public Health Code L626, L630 -Driving while impaired -Offence of putting somebody in danger by using drugs on the road	Penal Code 23 (since ´77); impairment has to be demonstrated, although a significant amount of drugs has been measured in blood	§§316, 315c StGB (Penal Law)	
Substances, Limits	Drugs of abuse, and plants listed on an updated list	Subst. which can cause impairment of driving performance	THC, MOR, BZE, AMP, MDE, MDMA; pos detect. in blood -For the penal law: alcohol and/or drugs acting on the CNS	Toxic substances
Exemptions?	No	No	Yes	No
Future Changes?	Yes	No	No, but the list of substances will be updated	No

Table 1. (continued)

	Iceland	**Ireland**	**Italy**	**Luxembourg**
DUI of Drugs -specific legislation		Road Traffic Act, Sect. 49 (criminal law); in effect since ´61	New Highway Code Law 285/1992 Art. 186, 187 (Traffic Law)	
- general legislation	Traffic Law No. 50/1987, Sect. VII, Art. 44, Paragr. 2			Legislation for which an impairment of driving performance has to be demonstrated
Substances, Limits	No substances	All drugs	Stupefying and psychotrop. subst., alcohol	A significant amount of drugs has been measured in drivers blood
Exemptions?	No	No	No	No
Future Changes?	No	No	No	No

Table 1. (continued)

	The Netherlands	Norway	Poland	Slovenia
DUI of Drugs -specific legislation		§ 22.1, Road Traffic Act (Penal Law) in effect since ´59		Road Traffic Safety Act, §118 (Traffic Law); in effect since ´98
- general legislation	Traffic Act, Art. 8, Sect. 1 (Criminal Law); in effect since Nov. ´74, last chance Oct. ´87		Covering DUI of alc. and drugs 1. Penal Code (´98), Chapt. XXI Offences against safety in traffic, Art. 178 2. Traffic Law -On Traffic Law Act (30.06.´97), Art. 45 -Traffic Regulations, Art. 126,127	
Substances, Limits	Any subst. that might influence driving behaviour	All psychoactive drugs	Drugs of abuse, substances similar in action to alcohol	Hypnotics, psychoactive medicines and other psychoact. subst. which diminish drivers ability
Exemptions?	No	No	No	No
Future Changes?	Yes	No, but the government has proposed to lower the BAC limit to 0,02%	No	No

Table 1. (continued)

	Spain	Switzerland	UK
DUI of Drugs -specific legislation	Penal Code: Title XVII: Offences against collective safety Chapter IV: Offences against traffic safety; Art. 379 (Penal Law)		
- general legislation		Art. 31, Sect. 2 StVG Art. 90, Sect. 1,2 StVG Art. 2,1 VRV	Road Traffic Act ´88, Sect. 4 (Traffic Law)
Substances, Limits	Toxic drugs, narcotic and psychotropic substances; No limits	Drugs and drugs of abuse, no list Alcohol 0.80 g/kg in whole blood	All substances causing impairment (only alcohol is specifically mentioned)
Exemptions?	No	No	No
Future Changes?	No	Yes	No

Table 1. (continued)

Regulations concerning DUI of Drugs – Future Changes

Table 2 provides an overview of European countries in which amendments of the legislation are planned in the near future, and which should be amended exactly

	Austria	**France**	**The Netherlands**	**Switzerland**
Regulations which will be chanced	Amendment of StVO (Traffic Law) in discussion Amendment time: not known yet	Penal Law: detection of illicit drugs in drivers involved in a fatal accident in an epidemiological aim (but the results will be sent to the prosecutor) Voted March ´99, will be applied Jan 2000	On a policy level, the introducing of a specific legislation on DUI of (prescribed) drugs is discussed (related to the Traffic Act, Art. 8, Sect. 1)	Revision of Art. 31, Sect. 2 SVG Art. 55, Sect. 1-6 SVG Art. 91, Sect. 1-3 SVG Amendment time: Approx. in 2001
Substances, Limits	The substances are still in discussion, but no limits	OPI, COC, CAN, AMP; BZD are in discussion, but should probably not involved No legal limits (detection)	In discussion: a system of cut-off values	The Federal Council (the Government) will fix which subst. and at which conc. in blood the driving ability definitely has to be denied
Exemptions	Unknown	Actually not	Unknown	Unknown

Table 2.

Needs and Requirements of Future Users of Roadside Drug Test Devices

In the initial 5 months of the ROSITA project the Consortium has collected and evaluated needs and requirements of the traffic police forces of 18 European countries. All responses have been formulated with participation of the respective police forces.

In total, needs and requirements in the European countries are quite different. Nevertheless, average tendencies for the requirements on roadside drug test devices have been determined.

Concerning the detectable drugs the following classes of drugs are considered as very important (in decreasing order): cannabis, benzodiazepines, amphetamines, cocaine, opiates.

The preferred test configuration is a single use, multi parameter test, which is able to provide a clear, unambiguous test result on the above mentioned groups of drugs within 5 minutes. Saliva is the preferred test specimen for roadside testing in Europe due to its good availability, the low invasiveness of sampling and the good correlation to impairment. Sweat, on average, is the second preference because it allows testing without the collaboration of a driver in combination with low invasiveness and good availability at the roadside.

With respect to prices an average amount for a single parameter device of 3,8 Euro and 13,6 Euro for a 4-parameter device was found acceptable.

CONCLUSIONS AND OUTLOOK

Despite the fact that in most countries DUID is forbidden by law and the application of roadside drug test devices is allowed only very few countries so far apply roadside tests for the abuse of illegal drugs. This is mainly due to two reasons:

- Urine tests are validated devices for the examination of drug abuse, but are not applicable under the respective legal systems or the operational conditions of the police forces in most countries.

- Saliva/sweat test devices would fulfil most operational requirements but are still under development or under validation before they will be generally accepted.

However, a few countries or police forces are already using urine or sweat test devices on a routine basis (and saliva test devices will follow soon), but this is not generally the case throughout the European Union.

To date it is necessary to further validate existing devices which are applicable for the detection of the abuse of drugs in street traffic. This includes urine tests but also saliva and sweat test devices. For that, the ROSITA project is providing an essential contribution.

More effort has to be made on the investigation of the correlation between impairment and pharmacokinetics of illegal drugs in easily accessible body fluids (sweat, saliva). This will help to develop more reliable devices for roadside testing.

The development of optimal roadside test devices for the examination of saliva or sweat is a technological challenge. Whereas alcohol is present in the parts per thousand level in the blood as well as in the breath of intoxicated drivers, drugs are usually present in the parts per billion level in body fluids. Most relevant medical and illegal drugs do not appear in detectable concentrations in the breath of drugged drivers.

Industry will be more ready to invest in new products if there are clear regulations, which demand the usage of drug test devices, thus generating a sufficient market. Therefore developmental activities can either be intensified by a harmonisation of the national Traffic Safety Regulations (increasing the market size for certain kinds of test devices) or by the provision of public funds to co-finance the development efforts. Due to the fact, that road safety is of broad public interest, both activities should go hand in hand.

Since the start of the Rosita project, the Consortium has carefully examined the legal and operational situation in a total of 19 European countries. The results clearly demonstrate that optimal test devices will only be available in the future if police forces, national governments, medical and toxicological experts as well as industry co-operate closely to solve legal, operational and technological problems. Only a joint approach will help us to reach our common goal to further increase safety on our roads.

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APPENDIX

"Questionnaire for the identification of operational, user and legal requirements across EU Member states for roadside testing equipment"

Introduction

Background and Goals of this Questionnaire

Several member states of the European Community are implementing or preparing laws on driving under the influence of drugs (DUI). One of the key elements in the enforcement process of a new law is the possibility to perform screening tests rapidly at the roadside.

In January 1999 an international consortium of 12 partners was selected by the European Commission to work on a project for the assessment of roadside test devices (Roadside Testing Assessment, ROSITA). Objectives of this project are to identify the requirements for roadside testing equipment, and to make an international comparative assessment of existing equipment or prototypes. The assessment will address roadside testing result validity, equipment reliability, usability (practicability), and usage costs.

More concretely, the project seeks to answer the five key questions:

1) Which are the drugs/pharmaceuticals that are suspected to have a detrimental impact to road users performance (workpackage 1) ?
2) What is the state-of-the-art roadside testing equipment for urine, sweat and saliva? Are there any other tests which can be used to evaluate the impairment of drivers at the roadside (workpackage 2)?
3) **Which kinds of operational, user and legal requirements exist across EU Member States for roadside testing equipment (workpackage 3)?**
4) Which of the tests meet the criteria set in the methodology and experimental design (testing and evaluation of the instruments, validity, equipment reliability, usability (practicality) and usage costs) (workpackage 4)?
5) What can be recommended for the use of roadside testing equipment in Europe (workpackage 5)?

Workpackage 3 is specifically dedicated to the needs and requirements of the police forces in your country. To gain a complete and representative overview about the situation in the area of traffic controls for DUI of Drugs, we designed the enclosed questionnaire covering the following topics:

- Regulations: Current situation and expected changes
- Restrictions on the application of roadside alcohol tests and drug tests
- Operational and user requirements
- Introduction and Training

Handling Details

Most questions can be answered by simply marking the appropriate box(es) belonging to each question. Using a computer, you must click the left mouse button once; clicking twice, the mark is removed. In some cases we ask you to provide further background information or reasons for your specific choice of an answer. This is to obtain a more detailed insight into the situation in your specific country. If the questionnaire is filled in by means of computers, no room problem should occur; you can write your text into the grey field, which can expand as long as desired. If you prefer to fill in the printed version, and there is not enough room for your comments, please use the back of the page or a separate sheet of paper.

In case of questions not formulated clearly enough we would like to encourage you to contact one of the authors mentioned on the cover page by phone, fax or e-mail.

In generally we tried to design the questionnaire in that way, that it should be filled in by computer (word 6 document), but it can be filled in handwitten also. However, in that case we would like you to take into account, that your handwriting should be readable. After filling in, the questionnaire can be sent back by email (please send your written document back with an unmistakable sign, e.g. your name (moeller.doc), or your name and institute as combination of both (alain_rug.doc) to avoid a data-overlay of identically named questionnaires of various participants) or by mail, if you prefered to fill in the printed version.

Who should answer the questions?

It is extremely important that the questions of this questionnaire will be answered together with the traffic police in your country and that we get a representative overview on the specific conditions under which your traffic police is performing roadside testing today and in the future.

Therefore, all questions should be answered with the help of suitable representatives of the police forces in your country. Who is suitable? This might be one selected police expert in the area of roadside drug testing. In other countries these might be several persons with expertise in different areas of road side testing. In any case we are asking you to note address and telephone/fax-numbers of each of the persons who have dealt with the questionnaire and indicate which section has been filled in by whom. This is important for open queries from our side.

If necessary, copies can be made and forwarded to the different police representatives to save time.

We estimated one month for filling in the questionnaire; this period of time should be sufficient to get in touch with the respective police representatives and to answer the questionnaire in detail.

That means, when dispatching the questionnaire on Tuesday, March 9th 1999, the deadline of returning is at Tuesday, April 6th, 1999.

Participant of the project "Rosita"

Information about the Rosita participant representative(s) who has (have) dealt with this questionnaire or the individual sections:

Title:

First Name:

Family Name:

University/Company:

Department:

Street:

Zip Code and City:

Country:

Telephone Number:

Fax Number:

E-mail:

Contact person(s) of the police

Information about the police representative(s) who has (have) dealt with this questionnaire or the individual sections:

Title:

First Name:

Family Name:

Ranking:

Name of the Police Force:

Department :

Street:

Zip Code and City:

Country:

Telephone Number:

Fax Number:

E-mail:

I agree to be contacted to clarify things that are not clear: ☐ Yes ☐ No

General Regulations - Current Situation

Are there relevant regulations in force in your country, covering offences against driving under the influence (DUI) of drugs?

☐ Yes; a specific legislation for DUI of drugs exists since:
☐ Yes, there are; but although there is no specific legislation for DUI of drugs in force, offences concerning DUI of drugs are covered by another legislation, e.g. by a legislation covering impaired driving or alcohol and driving. Please specify:

Please specify the section(s) and paragraph(s) of the relevant legal code(s) in your country. Please also state to which class of law (penal law, traffic law, others) these regulations are belonging.

Which substances are included in the existing law (drugs of abuse, therapeutic drugs)? Please note the substances explicitly mentioned in your legislation.

Are there any legal limits for drug concentrations specified in the law, which should not be exceeded? In what biological fluid? Please note substances and your legal limits.

Is there any specific/exclusive regulation given (e.g. the exclusion of therapeutic/prescribed drugs, exception for methadone etc.)?

How would you in general (we will ask for detailed information further on) describe your DUI legislation ?

☐ Our country pursue an „impairment approach"; sanctions are imposed against influenced drivers who have an obvious impaired driving performance
☐ Our country pursue an „ analytical approach" ; it focuses on the qualitative presence of drugs in blood

General Regulations – Future Changes

In your country, are there any changes to the legislation concerning DUI of drugs in preparation in the near future?

☐ No, there will be no introduction of a DUI-legislation in the near future
☐ No, there will be no amendment of the valid DUI-legislation in the near future
☐ Yes; A specific legislation for DUI is in preparation and it is expected, that it will come into force from the time:

Please specify the section(s) and paragraph(s) which will be changed in the future. Please state again to which class of law (penal law, traffic law, others) this new regulations will belong.

Which substances will be covered by a future law (drugs of abuse, therapeutic drugs)? Please specify the substances actually in discussion to be included in the future legislation.

Will there be any legal limits for drug concentrations specified in the law, which should not be exceeded? Please provide target substances and foreseen legal limits:

Will there be any specific/exclusive regulations given (e.g. exclusion of therapeutic/prescribed drugs, exception for methadone etc.)?

Legal restrictions for roadside testing

RESTRICTIONS ON THE APPLICATION OF ROADSIDE TESTS FOR ALCOHOL CONSUMPTION

At present, roadside alcohol tests ...

☐ ... are performed routinely on the occasion of general traffic controls
☐ ... are not performed in our country

Which roadside alcohol tests are used? Breathalyser tubes, Handheld breath test devices, others (please name the type, and, if it is known, also the brand name)?

Under which circumstances can the police forces in your country stop drivers at the roadside to control for drunkenness?

☐ General traffic controls, in which the alcohol part constitutes just one item
☐ Specific roadblocks for law enforcement, e.g. speed controls
☐ Random testing controls, in which drivers are stopped on a random basis
☐ Special checkpoints, e.g. in areas around discos etc.
☐ Others:

How frequently are your marked kinds of control conducted:

How many roadside alcohol tests in total are performed per year in your country?

What procedures are conducted at roadside, if a police officer observes a behaviour which is accepted as sign of impairment?

If the police stops someone due to signs of impairment, has the subject to cooperate during the examination?

☐ Yes, otherwise his refusal is treated as an infringement of valid regulations
☐ No, but the driver should cooperate to avoid negative consequences upon refusal
☐ No and there are no negative consequences upon refusal
☐ Others:

Which conditions have to be fulfilled to allow your police forces to check drivers at the roadside with an alcohol test?

☐ No specific conditions have to be fulfilled, roadside alcohol checks are possible without any initial suspicion
☐ An initial suspicion must exist (driving faults, smell of alcohol, etc.)
☐ In the case of an accident
☐ In the case of an accident with personal injury
☐ In the case of an accident with fatal injury
☐ Others:

Please specify the appropriate regulations and quote the essential paragraphs, which authorize the police forces in your country to apply a roadside alcohol test device

Are this legal regulations in practice accepted nation-wide, or does it differ among states, regions, or even among police departments?

The acceptance differ ...
☐ ... among states
☐ ... among regions
☐ ... among police departments
☐ The basis is accepted nation-wide
Notes:

What happens if someone is refusing a roadside alcohol test in your country?

☐ Nothing, because alcohol testing at the roadside is completely voluntary, there are no negative consequences.
☐ If other indications for alcohol abuse are obvious, further police measures are justifiable (e.g. taking directly a blood sample, arresting the person, etc.).
☐ The driver is infringing a valid regulation
  ☐ ... and can be forced to give a blood sample for laboratory analysis
  ☐ ... and has to pay a fine
  ☐ ... and can be arrested
  ☐ ... other consequences: please specify:
☐ The refusal is equated with a positive result
☐ None of the above alternative answers is applicable for our country. The specific consequences of the refusal of a roadside alcohol test are described in the following:

What occurs considering the legal position of your country, if the roadside alcohol measurement ...

... cannot be executed due to too strong influence of alcohol/drugs/medicines?

... for disease reasons cannot be executed (e.g. presence of a pulmonary disease)?

Which legal value has the result indicated by a roadside alcohol test?

☐ It can be directly used for punishment
☐ It can be used for punishment provided that the result is confirmed by other roadside observations e.g. signs of impairment
☐ It can be used as single reason for gaining a reference specimen. The analytical result (with accepted laboratory methods) of the reference specimen is then the basis for punishment.

What is the accepted reference specimen for the determination of alcohol consumption in your country?

☐ The combination of roadside observations and a positive roadside test result can be used for gaining blood samples and the analytical result of the blood sample is used to gain evidence.

Any other possibility:

Which consequences has a negative roadside alcohol test?

☐ There's no more a basis for further actions
☐ Provided that that the alcohol test is negative but there are indications for impairment, drug test devices can be applied to prove the consumption of other "impairing" substances
☐ If there are applicable suspicious criteria (signs of impairment), further legal actions (e.g. taking a blood sample) are acceptable to prove alcohol or drug abuse
☐ It is entirely up to the police what is acted accordingly

More possibilities or notes:

At which point in time during a check does the driver have to be informed of his rights and duties by the police?

To which extent does the driver have to be informed?

☐ An oral information is sufficient
☐ An information pamphlet should be signed
☐ An information pamphlet has to be signed
☐ The subject does not have to be informed upon his rights and duties

What is the basis for a conviction for alcohol and driving?

☐ Police report
☐ Clinical evaluation
☐ Presence of alcohol in blood/urine/other:
☐ Statement of expert witness
☐ Other:

ACTUAL RESTRICTIONS FOR THE APPLICATION OF ROADSIDE DRUG TESTS

At present, roadside drug tests ...

☐ ... are used routinely for traffic controls?
☐ ... are used roadside on the occasion of research purposes
☐ ... are not used in our country

Which roadside drug tests are used? Urine tests, Saliva tests, others? Brand names?

How many roadside drug tests in total are used per year in your country?

Are there any differences between the legal restrictions on the application of drug test devices and those on the usage of alcohol tests?

☐ No, for both types of roadside screening the same legal restrictions (as described in section 6.1) are applicable; nevertheless please go rapidly through the following questions and check your answer
☐ Yes, there are differences in the applicable legal restrictions, the differences are described by answering the following questions

Under which circumstances can the police forces in your country stop drivers at the roadside to detect drugged drivers?

☐ General traffic controls, in which the drug part constitutes just one item
☐ Specific roadblocks for law enforcement, e.g. speed controls
☐ Random testing controls, in which drivers are stopped on a random basis
☐ Special checkpoints, e.g. in areas around discos etc.
☐ Others:

How frequently are your marked kinds of control conducted:

What procedures are conducted at the roadside, if a police officer observes a behaviour which is accepted as sign of impairment?

If the police stops someone due to signs of impairment, has the subject to cooperate during the examination?

☐ Yes, otherwise his refusal is treated as an infringement of valid regulations
☐ No, but the driver should cooperate to avoid negative consequences upon refusal
☐ No and there are no negative consequences upon refusal

Which conditions have to be fulfilled to allow your police forces to check drivers at the roadside with a drug test?

☐ No specific conditions have to be fulfilled, roadside drug checks are possible without any initial suspicion
☐ An initial suspicion must exist (driving faults, physical impairment, unusual pupil size and reaction, etc.)
☐ In the case of an accident
☐ In the case of an accident with personal injury
☐ In the case of an accident with fatal injury
☐ Others:

Please specify the appropriate regulations and quote the essential paragraphs, which authorize the police forces in your country to apply a roadside drug test device

Are this legal regulations in practice accepted nation-wide, or does it differ among states, regions, or even among police departments?

The acceptance differ ...
☐ ... among states
☐ ... among regions
☐ ... among police departments
☐ The basis is accepted nation-wide
Notes:

Where can the specimens for the roadside tests be collected?

☐ At the roadside
☐ At the police station
☐ In clinics
Any other places:

Who is qualified to perform the collection?

☐ Police officers
☐ Only specially trained police officers
☐ Only laboratory personnel
Others:

Are there any recommendations or fixed procedures for the ...

a) ... collection of specimens?
☐ No
☐ Yes;

b) ... conservation of specimens?
☐ No
☐ Yes;

c) ... storage of specimens?

☐ No
☐ Yes;

d) ... documentation of the results (photocopying of the tests etc.)?

☐ No
☐ Yes;

What is happening if someone is refusing a roadside drug test in your country?

☐ Nothing, because drug testing at the roadside is completely voluntary, there are no negative consequences.
☐ If other indications for drug abuse are obvious, further police measures are justifiable (e.g. taking directly a blood sample, arresting the person, etc.).
☐ The driver is infringing a valid regulation
  ☐ ... and can be forced to give a blood sample for laboratory analysis
  ☐ ... and has to pay a fine
  ☐ ... and can be arrested
  ☐ ... other consequences: please specify:

☐ The refusal is equated with a positive result
☐ None of the above alternative answers is applicable for our country. The specific consequences of the refusal of a roadside drug test are described in the following:

What occurs considering the legal position of your country, if the roadside drug measurement ...

... cannot be executed due to too strong influence of alcohol/drugs/medicines?

... for disease reasons cannot be executed (e.g. presence of a pulmonary disease)?

Which legal value has the result indicated by a roadside drug test?

☐ It can be directly used for punishment
☐ It can be used for punishment provided that the result is confirmed by other roadside observations e.g. signs of impairment
☐ It can be used as single reason for gaining a reference specimen. The analytical result (with accepted laboratory methods) of the reference specimen is then the basis for punishment.

What is the accepted reference specimen for the determination of drug consumption in your country?

☐ The combination of roadside observations and a positive roadside test result can be used for obtaining blood samples and the analytical result of the blood sample is used to gain evidence.

Any other possibility:

Which consequences has a negative roadside drug test?

☐ There's no more a basis for further actions
☐ If there are applicable suspicious criteria (signs of impairment), further legal actions (e.g. taking a blood sample) are acceptable to prove alcohol or drug abuse
☐ It is entirely up to the police what is acted accordingly

More possibilities or notes:

At which point in time during a traffic check belonging drugs does the driver have to be informed upon his rights and duties by the police?

To which extent does the driver have to be informed?

☐ An oral information is sufficient
☐ An information pamphlet should be signed
☐ An information pamphlet has to be signed
☐ The subject does not have to be informed upon his rights and duties

What is the basis for a conviction for drugs and driving?

☐ Police report
☐ Clinical evaluation
☐ Presence of drugs in blood/urine/other:
☐ Statement of expert witness
☐ Other:

FUTURE RESTRICTIONS CONSIDERING CHANGES IN LEGISLATION

What will a new legislation for DUI of drugs mean for police control activities for the detection of drugged drivers with regard to ...

... control frequency?

... kind of control?

... drug testing performance?

Do you expect that, together with the modification of the general legislation for DUI of drugs, also your specific laws regulating the application of roadside drug tests will change?

☐ No
☐ Yes; please describe the expected changes

Are there any intentions in your country to enact a specific law allowing the application of roadside drug test devices without any initial/additional suspicion, e.g. to make a broader screening for impaired drivers in the general public feasible?

☐ No, such a law is neither in discussion nor planned

☐ Yes, such a law is in preparation or in discussion; please describe the main content:

For the future, do you expect any differences between the legal restrictions regulating the application of roadside alcohol test devices and those regulating the application of drug test devices?

☐ No, for both types of roadside screening the same legal restrictions during applications (as described in section 6.1) will be valid
☐ Yes, there will be differences in the applicable legal restrictions

In the case of yes, for the description of future differences, please answer the questions 5 to 17 of section 6.2 considering this questions aiming on your specific future situation.

Operational and User Requirements

TARGET DRUGS

Which target drugs will be most important for testing at the roadside? Please consider the expected legal restrictions and your future drug control policy.

The rating scale has to be understood as follows:
1: very important, 2: important, 3: of medium importance, 4: of minor importance,
5: completely unimportant

No	Target drug	Evaluation				
		1	2	3	4	5
1	Cannabis	☐	☐	☐	☐	☐
2	Opiates	☐	☐	☐	☐	☐
3	Cocaine	☐	☐	☐	☐	☐
4	Amphetamines/Methamphetamines	☐	☐	☐	☐	☐
5	Benzodiazepines	☐	☐	☐	☐	☐
6		☐	☐	☐	☐	☐
7		☐	☐	☐	☐	☐
8		☐	☐	☐	☐	☐

Please quantify your above rating with percentages. The total sum is 100.

No	Type of Narcotic	Percentage
1	Cannabis	
2	Opiates	
3	Cocaine	
4	Amphetamines/Methamphetamines	
5	Benzodiazepines	
6		
7		
8		
	Total	100

Can you please explain your ranking? E.g. expected distribution of narcotic consumers in the general population, experiences from the field, ...

PREFERRED SPECIMEN FOR DRUG TESTING

Which specimen would you prefer to use at the roadside for the identification of drivers under the influence of drugs? Please consider your legal restrictions and the environmental conditions during traffic checks.

The rating scale has to be understood as follows:
1: This is the preferred alternative
2: good alternative provided, that the preferred alternative is not feasible
3: acceptable
4: acceptable/feasible with limitations
5: not feasible, unacceptable

No	Specimen	Evaluation				
		1	2	3	4	5
1	Blood	☐	☐	☐	☐	☐
2	Urine	☐	☐	☐	☐	☐
3	Saliva	☐	☐	☐	☐	☐
4	Sweat/Skin	☐	☐	☐	☐	☐
6	Others:	☐	☐	☐	☐	☐

Please explain your ranking (e.g. invasiveness of sampling, infection risk, legal limitations, etc.)

TIME DEMAND

A roadside test device should be able to indicate DUI of drugs within a short time. The total measurement time is defined as sampling time and time of analysis.

Which measurement time is acceptable under your operational conditions:

1: This is the preferred alternative
2: good alternative provided, that the preferred alternative is not feasible
3: acceptable
4: acceptable/feasible with limitations
5: not feasible, unacceptable

No	Measurement Time	Evaluation				
		1	2	3	4	5
1	< 2 Minutes	☐	☐	☐	☐	☐
2	< 5 Minutes	☐	☐	☐	☐	☐
3	< 10 Minutes	☐	☐	☐	☐	☐
4	Other requirements:	☐	☐	☐	☐	☐

Please explain your choice:

SINGLE TESTS OR MULTI TEST DEVICES

In general, individual tests are cheaper in use, than a multi test device. However the officer needs a preselection mechanism (e.g. he must be training in the detection of other signs of impairment, or the most probable target drug is know because of the control circumstances). A multi test device will have a higher price than individual tests, but will provide more comprehensive information. Therefore the question is,

Which test configuration should be available in the future?

1: This is the preferred alternative
2: good alternative provided, that the preferred alternative is not feasible
3: acceptable
4: acceptable/feasible with limitations
5: not feasible, unacceptable

No	Test configuration	Evaluation				
		1	2	3	4	5
1	single test system, you can test for each type of narcotic individually?	☐	☐	☐	☐	☐
2	Multi test system including the most important drugs in one device and providing a complete narcotic “profile” in one shot?	☐	☐	☐	☐	☐
3	a combined system, e.g. a double or triple test for the most important drugs and individual test for the narcotics of minor importance	☐	☐	☐	☐	☐
4	Others:	☐	☐	☐	☐	☐

Please describe your main reasons, which have led to your evaluation result.

SINGLE USE SYSTEM OR REUSABLE DEVICES

A single use system can be applied to test one person. Then it will be thrown away or stored for documentation purposes. A reusable device is able to test several people subsequently. For hygienic reasons you may have to exchange a sampling tool or other consumables, but the basic system is applicable for several measurements. Such a device will need service, maintenance and some sort of calibration

What would you prefer to use in the future?

1: This is the preferred alternative
2: good alternative provided, that the preferred alternative is not feasible
3: acceptable
4: acceptable/feasible with limitations
5: not feasible, unacceptable

No	Test configuration	Evaluation				
		1	2	3	4	5
1	Single use test device	☐	☐	☐	☐	☐
2	Reusable test device	☐	☐	☐	☐	☐
3	Others:	☐	☐	☐	☐	☐

Please provide reasons for your ranking:

Have your police forces internal service departments available for service and maintenance of technical equipment?

In the case of a reusable device: which time intervals (in hours, days, or weeks) are acceptable for ...

... calibration?

... exchange of consumables?

... service and maintenance?

TEMPERATURE, LIGHT AND HUMIDITY CONDITIONS

Environmental conditions during traffic control operations:

Due to your experience with alcohol roadside test devices: which estimated percentage of suspicious drivers is directly tested at the roadside, which percentage is tested later in an office (maybe because of bad weather)?

Percentage of test persons directly tested at the roadside: %

Percentage of test persons tested in an office environment: %

Which percentage of all roadside tests are made directly at the road in the darkness: %

A road side test device must withstand temperatures and humidity in summer as well as in winter. Please describe the typical weather and humidity conditions for traffic control situations in your country?

Temperature range:

In summer: °C

In winter: °C

Relative Humidity Range: %

Environmental conditions during storage:

Any test device can be damaged by extreme temperature or humidity conditions. Is it feasible in your country to store a future drug test device in the office and to take the device out of the office for roadside controls?

☐ Yes, no problem (we have similar procedures for our alcohol devices)
☐ No, we want to store a roadside applicable drug test device in the police car

In the case of no, what would be a minimum acceptable storage time in your police cars?

days

Please provide reasons for your choice:

CHOICE AND COSTS

Who chooses the test devices: the police force, tender on national/regional basis? Are the same devices used in the whole country?

Who pays for the devices: The police force (centrally or locally), or does the driver have to pay if he is positive?

If in your country changes of the valid DUI of drugs regulation are in preparation (chapter 5), do these changes have influence on the answers of the two upper questions?

What do you consider to be an acceptable price for a device (1 test/4 tests)?

FURTHER FEATURES OF IMPORTANCE

Which of the following features are in your opinion most important for a roadside test device?

Please consider additional features (technical, handling, etc.) of importance not yet covered by this questionnaire and note this features in the free space below.

1: very important
2: important
3: of medium importance
4: of minor importance
5: completely unimportant

No	Feature	Evaluation				
1.	A roadside test device	1	2	3	4	5
2.	Should be applicable with no or minor training	☐	☐	☐	☐	☐
3.	Should indicate the result clearly (without any room for interpretation)	☐	☐	☐	☐	☐
4.	Should indicate the result electronically, e.g. with a peep or a red light	☐	☐	☐	☐	☐
5.	Should indicate the result without any electronic means	☐	☐	☐	☐	☐
6.	Should be able to store or print out the result for documentation purposes	☐	☐	☐	☐	☐
7.		☐	☐	☐	☐	☐
8.		☐	☐	☐	☐	☐

Introduction and Training

INTRODUCTION OF NEW EQUIPMENT

Which ministries, police forces, departments, persons are involved in the decision to introduce a new road side testing device for the detection of DUI of drugs?

Which main criteria will be used to decide on the introduction of a new road side drug test device?

Are there any fixed (written) instructions or policies which have to be followed during the introduction of new test equipment?

Please provide editor, title and issue details of these written instructions:

ACCREDITATION SYSTEM

Are there any accreditation or control systems for roadside test devices?

☐ No
☐ Yes; please describe (the responsible institution for the accreditation process, ...)

TRAINING

Does there exist a training system to educate your police officers in the recognition of drug intoxicated drivers in your country?

☐ Yes, we have such a system installed;
what is approximately the percentage of officers who have already received such a training ...
... nation-wide?

... state-wide?

... in special regions?

☐ No, but such a system is under development and will be installed from the date on:

☐ No, but our country is planning to develop such a system
Contact person for the development is:

☐ No, up to now no training program is available

Every future roadside test system will need a certain kind of training to allow the officers to become familiar with handling and evaluation of the new instrument. Are there any applicable instructions or regulations in your country for police training on new equipment?

☐ No written advice exists describing form and extent of training measures for new equipment
☐ Yes, a certain training program by the manufacturer or police experts is claimed.
Please provide editor, title and issue details of these written instructions:

Is it possible to include the training on a new test device into an existing or future drug recognition training program or has training in a test device be seen completely separately?

Further Problems

Which further problems do your police officers report in the detection of DUI of drugs or the respective control measures?

Room for comments

Deliverable D4

Evaluation of different road side drug tests

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: All

Authors: Alain VERSTRAETE and Marina PUDDU

Date: December 19, 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

EXECUTIVE SUMMARY

This part of Rosita consisted of the evaluation of the on-site devices for urine, oral fluid (*in this document, the term 'oral fluid' will be used in preference to 'saliva'. This is based on a recommendation of a working group of the Drug Testing Advisory Board in the USA. The main reason is that saliva is the secretion of the salivary glands, while the fluid we are testing also contains mucosal transudate and crevicular fluid*) and/or sweat in 8 countries. The study was performed on 2968 subjects, 92 % of them male.

- In several countries, the Rosita evaluations were the first experience police officers had with roadside drug tests, and, despite some problems and disappointments, **police officers liked having the tools to detect drugged drivers**. The need is so big that in some countries police officers will settle for imperfect devices, although we strongly advise against using any of the present oral fluid devices for benzodiazepines or cannabis detection.

- **Police did not have major objections to collecting specimens.**
  There was a majority of countries that favoured **oral fluid** as a matrix. In Italy urine was preferred and in Germany, police officers prefer sweat (because it is very easy to obtain a sample).

- **On site testing gives police confidence, saves time, and money.**
  In general, the use of roadside tests offered the following advantages in the enforcement of drug-driving laws, both in countries with an impairment-type law and in countries with 'per se' laws:
  - It gave confidence to the police officer. Without an on-site tool to confirm his impression, a police officer will be more reluctant to press charges. After some time, thanks to the immediate feedback, he rapidly increases his skill at detecting drugged drivers;
  - On-site tests save time, because the subject may not need to be transported to the police station for testing or blood sampling;
  - On-site tests save money, because the more expensive confirmation tests will be limited to cases that are much more likely to be positive;
  - The publicity that accompanied the use of roadside tests (e.g. in Finland) was considered (by the police officers) to have a preventive effect, because people thought they could be controlled everywhere (while in fact the number of actual tests used was limited).

- **Most of the urine devices worked well and generally served as good predictors of blood concentrations.**
  Sampling urine was no problem if appropriate facilities were present. If this was not the case, this was a major problem, and if the subject had to be brought to a health centre of police station, this was seen as a waste of time. In some cases, only a small volume of urine could be obtained. Urine on-site tests are relatively easy to use after some training. There is no clear majority for dip or pipette-type devices, but cup-type devices should require less sample. A preference exists for blue lines and multi-analyte tests. In some countries, 'aggressive' tests (fewer false negatives than false positives) are preferred. For the different drugs (amphetamines, benzodiazepines, cannabinoids, cocaine and opiates), several on-site devices met our analytical criteria for the reliability of analytical results.

- **Oral fluid and sweat are promising specimens and in some cases are better than urine but more research and development will be needed.**
  Sampling of oral fluid and/or sweat are much better accepted by the drivers and the police officers. For some drugs, with reference methods, there was a better agreement between oral fluid and blood than between urine and blood. The oral fluids devices that were tested were not satisfactory for use at the roadside either in terms of ease of use, duration, sample volume needed, sensitivity and reliability (accuracy of 50-81 % for the different drugs in comparison to blood). For sweat, only one device is available and relatively good results were seen for some drugs, but more studies are needed to determine if external contamination and the later appearance of drugs in sweat are an issue.

- **The technology is changing rapidly and more accurate, more sensitive, easier to use devices are expected in the near future.**
  Many development efforts are under way, and new devices and improved versions of the devices that we tested here, are expected soon. Further studies will be needed to evaluate them.

INTRODUCTION

In the last few years, driving under the influence of drugs is recognised more and more as a problem for traffic safety in Europe. There is a universally recognised need for the development of a valid, rapid and affordable roadside test for the major drugs (1). In countries with impairment-type laws, roadside analysis can confirm the suspicion of the police officer and focus the attention on drugs. In countries with 'per se' legislation, screening devices are crucial for the detection of driving under the influence of drugs, before further measures (e.g. blood sampling, temporary driving prohibition, …) can be taken.

During the first phases of the Rosita project, we prepared an inventory of the drugs that cause driver impairment (2) and of the devices that are available to detect drugs in body fluids at the roadside (3), and made a survey of the needs and wishes of the police forces (4). One of the results of this last survey was that oral fluid was the preferred sample to be tested at the roadside.

Work package 4 of Rosita involved the evaluation of the available devices in the field. The reports of each individual country are available separately (5 - 12). The aim of this report is to consolidate all the data and to come to more general conclusions. This analysis of the joint data was not always easy because of the different analytical protocols in the respective countries, which are based on the methods validated in each of the participating laboratories, but also on the different legislation.

Some limitations must be pointed out:

- the analytical methods used in all the countries were not identical;
- the evaluation of the devices was done in different places, at the roadside, in the police station, or in the laboratory
- the devices were evaluated by different persons, which makes the comments on the practical and operational aspects more difficult to compare
- the prevalence of different drug types was different in the different countries, which results in strongly different prevalences in the samples used to test with for different on-site devices, depending on the countries they were tested in.

Before we evaluate the results of the on-site devices, we compare the results of the reference methods in the different biological fluids. This allows us to determine which matrix has the best correspondence with blood, and which is suitable (or not) to be used at the roadside in order to predict that the subject's blood will contain drugs.

This evaluation of the different devices included in the project will consist of two parts:

- A practical evaluation, where all the practical aspects of the use of the devices are considered;
- An analytical evaluation, based on a comparison with a reference method in the same matrix (e.g. comparing on-site urine tests with GCMS in urine), and with the results in blood. Indeed, one of the aims of roadside tests is to select subjects for blood sampling, and an efficient screening method will detect all the subjects who will have a positive result for drugs in blood.

In a final work package, we will make our final recommendations for the future use and development of roadside drug tests.

Only a few similar studies have been published in the literature (13 - 19). Some theoretical aspects have been discussed by Skopp and Pötsch (20).

METHODS

The analytical methods used in the eight collaborating centres are given in Appendix 1.
A comparison of the detection limits in blood or serum for the different drugs or metabolites in the different participating centres is given in Table 1.

Table 1: Detection limits (ng/mL) for selected analytes in the different participating countries

Country	*Belgium*	*Germany*	*Finland*	*France*	*Italy*[1]	*Norway*[2]	*Scotland*
Matrix	Plasma	Serum	Blood	Blood	Blood	Blood	Blood
Amphetamine	5	10	20	5	30	40	50
Methamphetamine	5	5	30	5	30	40	50
MDMA	5	5	40	5	30	40	50
MDEA	5	5	100	5	30	100	50
MDA	5	5	50	5	30	40	50
THC	0.8	0.3	0.25	0.2	2	0.3	1
THCCOOH	1	3.0	5	0.2			1
Cocaine	3	5	10	5	5	60	10
Benzoylecgonine	1	5	2,5	5	5	60	10
Morphine	1	10	50	5	5	10	10
Codeine	1	10	50	5	5	10	10
6-AM	1	5	50	5	5	10	10
Diazepam			30	0.5	50	140	25
Nordiazepam			10	0.5	50	140	25
Flunitrazepam			-	0.5	50	3	

[1]Numbers are cut-offs and not detection limits
[2]Numbers are cut-off limits as reported to the police for evaluation of impairment – and not detection limits.

The data from the evaluations in the eight countries were obtained in Microsoft Excel format. The individual files had to be joined. In order to do that, some transformations of the results were necessary, e.g. to obtain the same units for drug concentrations, or to transform concentrations in serum or plasma into blood concentrations. For this last transformation, the factors in Table 2 were used.

In the end, we obtained a table with 2968 subjects, and 231variables.

The reference method (gold standard) that has been used is gas chromatography-mass spectrometry (GC-MS) or, in some cases, high pressure liquid chromatography with diode array detection (HPLC-DAD) or gas chromatography with electron capture detection (GC-ECD).

In order to simplify the analysis, a manual interpretation of the analytical results (screening and confirmation) was performed, to determine if e.g. cannabis was positive in blood, urine, … The criteria (e.g. cut-offs) used for this interpretation are given under each drug category, under the heading criteria.

Statistical analysis of the data was performed using Microsoft Excel, Medcalc (MedCalc Software, Mariakerke, Belgium), e.g. for calculating ROC-curves, and SPSS (SPSS Inc. Chicago, IL).

Several comparisons were made between the different methods (on-site tests or reference methods) and matrices (blood, urine, oral fluid or sweat).

Table 2: Serum/blood conversion factors for drugs

Drug or metabolite	*Factor serum/blood*
Amphetamine	1
Methamphetamine	1
MDMA, MDEA, MDA, MBDB	1
THC	1.8
Cocaine	1
Benzoylecgonine	1
Ecgonine methylester	1
Morhpine	1
Codeine	1
6-acetyl morphine	1
Diazepam	1.8
Nordiazepam	1.7
Oxazepam	1
Flunitrazepam	1.2
Midazolam	1.9
Triazolam	1.3

In each chapter on a drug class, the following comparisons are made:

1. A comparison between the reference method in blood and the other biological fluids, in order to assess if findings in each matrix correspond well to those in blood. There is a general consensus that blood is the reference sample, as impairment (or recent exposure to drugs) corresponds best to presence of drugs in blood (21);
2. the validity of the roadside test in its own matrix is evaluated by comparison with the reference method for the same matrix;
3. the validity of the roadside test (whichever matrix) for predicting blood positives is by comparison with the blood reference method.

The evaluation of the results was based on classification into the following categories:

- **TN**: True Negatives: numbers of samples in which screening was negative or analyte concentrations are below GC-MS cut-off values and correctly classified by the test;
- **TP**: True Positives: in which analyte concentrations are above GC-MS cut-off and classified correctly by the test.
- **FP**: False Positives: samples misclassified as a positive result with the screening test, that was not confirmed by GC-MS to contain analytes at concentrations above the cut-off values;
- **FN**: False Negatives: samples giving a negative result but in which analytes are present at concentrations above the GC-MS cut-off values and misclassified by the test;

From these 4 categories, the following characteristics were calculated:

- **Sensitivity** = true positives expressed as percent of all positives = TP/(TP+FN)
- **Specificity** = true negatives expressed as percent of all negatives = TN/(TN+FP)
- **Positive Predictive Value** = percent of samples with positive results who are true positives = TP/(TP+FP)
- **Negative Predictive Value** = percent of samples with negative results who are true negatives = TN/(TN+FN)
- **Accuracy** = percent of all samples correctly classified by the tests, percentage of all tests giving correct results = (TP+TN)/(all results)

Our analytical criteria for a good screening test were:

- Accuracy ≥ 95%
- Sensitivity ≥ 90%
- Specificity ≥ 90%

The analytical criteria are somewhat arbitrary, but seem reasonable to the authors. The reader can use other criteria if he wishes, e.g. people who want to detect all positives will use a more sensitive test (even if this sometimes means that there will be more false positives), and people who don't want false positives will choose a very specific test. This evaluates only the analytical performance of the test. The practical and operational aspects are at least as important in the choice of a suitable device.

If possible, we also determined if an on-site test was an 'aggressive' test (more false positives than false negatives), or a 'conservative' test (more false negatives than false positives).

For the determination of the optimal cut-off, we used receiver operating characteristic curves **(ROC curves).** This is a graphic technique for displaying sensitivity and specificity at various decision cut-offs (22). The x-axis plots the fraction of FP for a specific decision threshold and the y-axis plots the TP rate (sensitivity). The curve is drawn through points that represent different decision cut-offs levels. The whole curve is a graphic display of test performance; A curve that is "above" the diagonal line (line extending from the lower left to the upper right represents a test with no discrimination) describes performance that is better than random guessing. The closer the curve comes to the upper left corner, the better the discriminative power of the test. The area under the ROC curve (AUC) describes the overall performance, although usually we are only interested in the performance in a specific region of the curve. Some authors have stated that a good discriminative power corresponds to an AUC > 0.9.

SUBJECTS: DEMOGRAPHIC DATA

Sample Size

The study included **2968** subjects, coming from 8 countries. The percentages are shown in Table 3.

Table 3 : Geographical distribution

	Country		
		Frequency	%
	Belgium	180	6.1
	Finland	751	25.3
	France	206	6.9
	Germany	617	20.8
	Italy	302	10.2
	Norway	314	10.6
	Scotland	214	7.2
	Spain	384	12.9
Total		2968	100.0

Sex distribution

The sex distribution was **92%** male, **8%** female (no data from Belgium). These data correspond well with data from other studies, which show a large majority of male subjects in driving under the influence of drugs (DUID) cases.

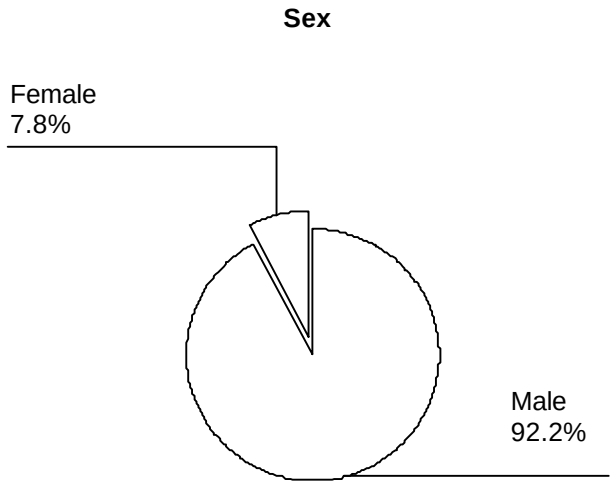

Figure 1: Pie chart of the sex distribution of the subjects

Age

For the whole sample of tested persons, the mean age is *29.6 (SD 10.3) years, median 26, range 66 (min 13; max 79).* Figure 2 and Table 4 give the age distribution.

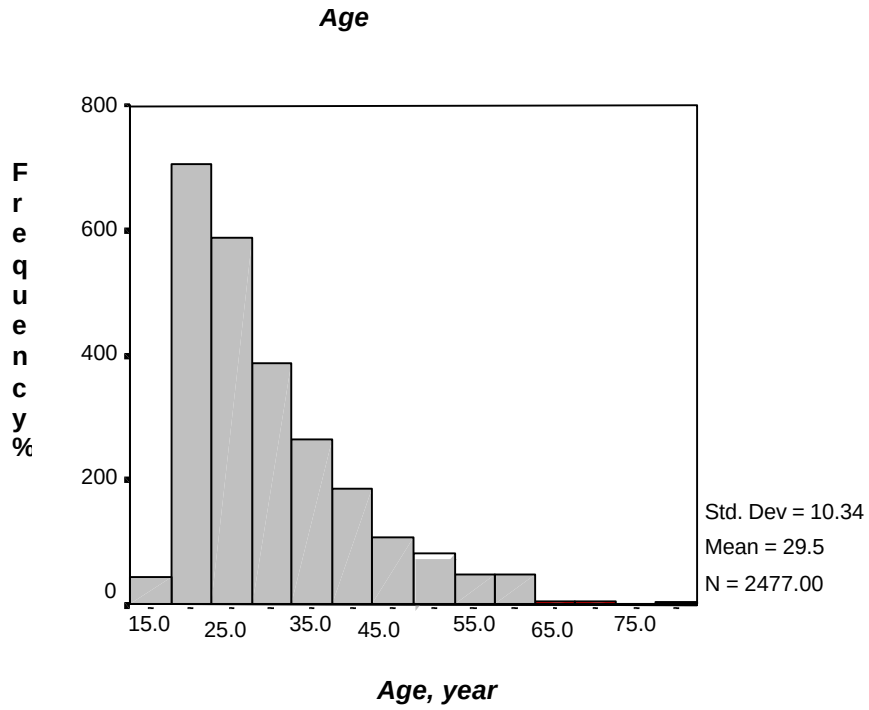

Figure 2: Age distribution of the subjects included in the Rosita study

Table 4: Age distribution of the subjects in the Rosita study

	Age			
	Age class	Frequency	Valid %	Cumulative %
Valid	13-20	414	16.7	16.7
	21-30	1175	47.4	64.2
	31-40	519	21.0	85.1
	41-80	369	14.9	100.0
Total		2477	100.0	
Missing		491*		
Total		2968		

*Belgium and Scotland not recorded

OPERATIONAL ASPECTS

Before describing the different experiences in the countries, we give an overview on the circumstances under which the tests were performed.

- Spain: the on-site tests were performed by the agents of the Traffic Police. Reading and interpretation of the results were done together by the members of the ILM present during the control and by the same traffic agents. The traffic Police was trained in the use of the devices. The tests were performed at the roadside, except for the TesTcup.
- Belgium: the samples collected at the roadside were first screened by the Police with the Dipro Drugscreen 5 and then by lab technicians with the other devices.
- Norway: the on-site urine tests were performed by the police officers in the laboratory at NIFT, in collaboration with representatives from two out of three of the manufacturers as assistants. On the other hand, for oral fluids, the tests (Cozart Rapiscan and Drugwipe) were performed at the police station, because it was impractical to have one test for roadside (Drugwipe could have been performed roadside) and the other not.
- Italy: the on-site tests were performed at the roadside by police personnel or ambulance volunteers. Some of them and RDS tests were performed at CBFT by trained technicians. Roadside collection of blood, urine and oral fluid samples was made by medical personnel.
- Finland: urine was collected under Police supervision in the hospital and not at the roadside. Police and laboratory staff mainly performed the urine tests at the laboratory of drug abuse. The oral fluid tests were performed roadside by trained police officers.
- Germany: the test was performed by police officers during police controls. Oral fluid and sweat samples were collected and tested directly at the roadside, whereas urine samples were normally collected and tested at police stations or at public lavatories. In Germany, the control actions were performed during the night, so the reading of the results occurred in more difficult circumstances than in a police station, hospital or laboratory.
- France: the on-site tests were evaluated in the lab.
- Scotland: the on-site tests were performed by at least two members of the research team, either within the prison or in the laboratory.

Choice of the biological fluids for the On-site tests

Based on the individual country reports, we conclude that urine was preferred in Italy, oral fluid was preferred in Finland, Norway, France, Spain, Scotland and Belgium and sweat was preferred in Germany (followed by oral fluid). The reason for preferring sweat is that it was very easy to obtain a sample.
The choices were not always very clear-cut, because each matrix has its advantages and disadvantages. In the Nordic countries, the use of urine at the roadside was unacceptable, while in Germany, urine was rather well accepted, due to the good experience with the test devices (multi-testing, less problems with urine collection than expected before the ROSITA field study) and due to the practical and analytical inferiority of oral fluid/sweat test devices (collection methods, dependency of consistence of specimen, reading, not all substances covered). There also was better co-operation from the subjects for providing sweat or oral fluid.
There seems to be a majority for oral fluid, but as was remarked in Finland, oral fluid was suitable for roadside testing, but the equipment was not.

Practical aspects

Urine

Sampling
Sampling urine was not a problem if appropriate facilities (like a sanitary van) were available, which was the case in Belgium, Italy, and partly in Germany (parking lot at the Autobahn). In other cases, drivers had to be taken to a

police station or health centre, which took time. In Spain, obtaining urine was a problem, because the lack of suitable facilities; only 58 % of men and 23 % of women gave a urine sample.
Another problem is that drivers and others often refuse to give a urine sample, while the refusal rate is much less for oral fluid. In a study in Canada, only 41 % of drivers who were asked to give a urine sample, complied. Of those that refused to give a urine sample, 70 % accepted to give a saliva sample (23). In a roadside study in the Netherlands people were not particularly enthusiastic when they heard that they had to give a urine sample. The reactions varied from hilarity to peevishness and suspicion. Fifteen % did not succeed in producing a sample. On the other hand people were enthusiastic about sampling sweat with the Drugwipe (24).
Sometimes it was very difficult to obtain urine. The problem was solved by waiting and drinking.
In many countries the volume of urine was not sufficient for the cup-tests (SRC, TesTcup, RDS). This was e.g. a problem in 3 % of the cases in Germany. In that respect, RDS has the advantage that in case of low sample volume, the urine can be pipetted onto the card.

Performing the tests
With training, the tests could be reliably performed by the police officers.
In Germany, there was concern for the officer's safety, which means e.g. the use of plastic gloves to prevent contamination with the specimen.
The preference for a specific test or type of test differed among the countries.
Cup-test were not preferred in any country. The advantage of not coming into contact with urine was balanced by leaking of the container (TesTcup, mainly in Scotland, but also mentioned in Belgium and Germany) or by problems (need for excessive force) in opening and closing them (SRC). Some police officers said that with more experience, the cup test became a good alternative.
Pipette tests had the great advantage of requiring a small volume of urine, and were preferred in Italy and Germany. However, in other countries, police officers did not like pipette-type tests, which they consider more suitable for a laboratory. In Norway, it was considered that SRT was not easy to perform at the roadside.
In Italy, SRT was considered the test that was the most easy to use, followed by RDS and Triage, which was judged difficult to handle. Triage was considered very complicated to use in Finland as well. In Germany the Mahsan DOA4 was the preferred test, followed by SRC.
Dip-tests were preferred in Belgium and Finland. In Finland, they were followed by pipette-tests. The cup tests were not found as easy to use as expected, due to the large sample requirement,
In summary, there is no consensus on the type of test that is preferable.
In Germany, Finland and Norway, **multi-analyte tests** were preferred.
Blue lines were easier to read than red lines.
The duration of a test varied: in Norway, all tests (TesTcup, SRT and OneStep) took 4-5 minutes. In Germany, the time needed to perform a test was mostly 6-10 minutes, with Frontline, Mahsan and SRC being quicker.
In several countries, in case of low temperatures, the execution of the test took more sample and/or more time. Sometimes the device froze in countries with a colder climate.
In Germany, Finland and Norway, police officers prefer false positive results to false negative results (which would allow the driver to continue while under the influence).
One should not forget that even if on-site tests were developed for 10 groups of drugs (amphetamine, methamphetamine, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, opiates, phencyclidine and tricyclic antidepressants), some other drugs (like LSD, gamma-hydroxybutyric acid, ketamine, antihistaminics, psilocybine, …) cannot be detected on-site.
At this time, the devices that have been evaluated here are considered 'borderline products' for the EU in vitro diagnostic (IVD) directive (A. Manns, Dräger, personal communication). Although directive is intended for in vitro diagnostic devices for medical use, and not for medico-legal use, it could be essential as a first harmonising standard.

Reading the results
In Italy, all devices were considered to be easy to read. The presence of control lines was considered important. In Norway, OneStep was considered difficult to read. This was also the case in Finland, where sometimes weak lines were seen for SureScreen and Rapidtest Multidrug.
Triage and Roche TesTcup seemed to score best for the reading of the results.
An electronic reader does not seem to be a necessity for urine tests, but no reader was available for any device. So, it is impossible to know if it would be seen as an advantage or a disadvantage. For the reactions to an electronic reader, we refer to the discussion in the oral fluid section.

Oral fluids

Sampling
Sampling is still a big problem for oral fluid testing. The sampling method for Drugwipe (wiping over the tongue), was appreciated everywhere, because of minimal discomfort and low sample requirement.
Four other sampling methods were used: the devices that came with the Cozart Rapiscan or ORALscreen, spitting into a tube or a Salivette®.

- In Germany and Scotland,, the ORALscreen was considered 'disgusting' because of the many complications that occurred during sampling, and in nearly all cases, the fingers of the officers and researchers came into contact with oral fluid. This was certainly less acceptable to them than working with urine.
- Sampling with Cozart Rapiscan was problematic: it took a long time, was cumbersome, and in Spain, some subjects found it annoying to keep the oral fluid collection pad in their mouth. This was worse if they had little oral fluid (and then it took even longer). Is some cases, not enough oral fluid was obtained, either because the subject did not have enough, or because he refused to co-operate. Also in Finland, the use of the Cozart Rapiscan was problematic in case of dry mouth. In Spain, the average duration for sampling was 4 minutes, with extremes between 1 and 12 minutes. The total sampling + analysis time was 20 minutes (13 to 33 minutes), which was considered too long for roadside use. One advantage of Cozart Rapiscan is the availability of the remainder of the (diluted) sample for confirmation in the lab, although the available volume was considered insufficient for performing all the confirmation analyses needed (this of course only applies if confirmation is performed on oral fluid, not on blood), and due to the high pH, cocaine was hydrolysed to BE. The analysis time is shorter for single tests and double tests.
- In Belgium, oral fluid was sampled by spitting into a tube, but some water was supplied to moisten the mouth of the subject. In Scotland, subjects had to be cautioned against clearing the nasal passages and throat when producing oral fluid by spitting.
- Sampling with a Salivette was sometimes uncomfortable as well. The absorption of THC to the Salivette was noted, as was the variable (50-1000 µL) volume of oral fluid absorbed.

In Norway the test devices were sometimes swallowed by the subjects. In Belgium, complex devices, like the Omni-Sal® were not accepted by the police. In Finland, police officers prefer to handle oral fluid than urine.
In summary, if sampling by wiping the tongue was well accepted (but this requires a very sensitive detection method because of the low volume and it does not provide sample for confirmation analysis), the other methods have some drawbacks, and more research will be needed to find an acceptable and rapid sampling method. Another concern is that different sampling methods result in different concentrations of drugs in oral fluid, as was recently demonstrated for codeine (25).

Performing the tests
None of the devices was fully acceptable to the police officers. In Germany, the general acceptance of the oral fluid test was much less than all the urine tests.

- Drugwipe: Drugwipe was considered simple in terms of training needed. The requirement for a small sample volume and rapid turn around time were appreciated. Less appreciated were the limited test panel, the availability of only single tests, the difficult reading of the results, and the need for water to perform the test. The electronic reader was considered impractical to use in Norway, but was considered essential in all other countries. In Italy, it was considered that oral fluid was quite easy to test at the roadside, at least by using the Drugwipe, although the results of the amphetamine test had to be discarded.
- Avitar ORALscreen: in Germany, problems were encountered in transferring the oral fluid from the sampling device to the test. In Scotland, problems were encountered with the transfer of viscous oral fluid, and some fluid oral fluid failed to migrate to the analytical strip as a result of manufacturing faults.
- Cozart RapiScan: The multiple pieces of equipment and the need to place them on a flat surface made the use of Cozart Rapiscan impractical for a police officer on a motorbike, and restricts its use to police officers driving a van. For the Cozart Rapiscan in Norway, commercial presentations had raised high hopes, for a quick (5 minutes), easy to use device, and expectations were high. However, during the training course, the equipment proved to be rather complicated to use and the total time needed to obtain a result (sample collection, sample preparation, run time) was at least 15 minutes. With real drugged drivers, at least 15 minutes were often needed to collect sufficient oral fluid sample only, as these persons often had very dry

mouth caused by their drug use. In addition, the police had the opinion that the sample preparation procedure was rather complicated (filtration, pipetting, handling of samples tubes), feeling that some laboratory experience was necessary. Soon it was rather clear that the equipment was not suitable for roadside use. Too many items had to be handled and the duration of 15 to 25 minutes was much too long. Moreover, the police discovered that the electronic reader could be disturbed from police-car radio (according to the manufacturer, this is only the case if the reader is placed directly on top of the radio) and that the electronic reader had to be placed horizontally, which was not always easy to arrange in a police car. It was therefore decided that the testing should mainly be performed at the police station. The problems were discussed with the manufacturer, but it took a long time before the improved devices arrived, and the first batch was defective and no results appeared in the display of the electronic reader after waiting for ten minutes. Large efforts were needed to convince representatives for the producers that something was wrong. All these problems resulted in that during 2 –3 months, no working Cozart Rapiscan® equipment was available and valuable time was lost. When the police used the equipment with production defects, they thought that something was wrong with their procedure. Several unsuccessful tests were performed (reference band not detected) which were never reported. After this time, it was more difficult to motivate the police to take more samples, even when new devices without any faults had arrived. Some improvements had been made to the new equipment, however, the collection of oral fluid samples still takes too long time and sample preparation is still complicated. However, some police officers claim that with more experience it is rather easy to perform the tests at a permanent place e.g. police station, but the Cozart Rapiscan is still not useable roadside. Similar problems were encountered in Finland, where the delays were also a big setback, despite the efforts of the retailer Ferle Produkter who were very helpful in trying to get information. In Germany, the duration of the test was 2-5 minutes for Drugwipe and 6-10 minutes for ORALscreen, while in Finland, it was 22 minutes for Cozart Rapiscan and 7 minutes for Drugwipe. However, in some countries like Finland, according to the police, the need for a roadside device is so big that even an imperfect device is better than no device!

Reading the results

Some problems with reading the ORALscreen were reported. Faint lines were produced, especially for cannabinoids resulting in difficulty in distinguishing presence and absence.

In Italy and Spain, Drugwipe was considered difficult to read, and the availability of an electronic reader made reading much more reliable.

An automatic reader also ‘impresses’ the drivers more (i.e. it gives the impression of being more reliable). Tests that are more complicated to perform have the same effect.

Coloured substances in the mouth seemed to give a positive test result. In Finland, it was observed that both Cozart Rapiscan and Drugwipe gave false positive results when cacao or snuff were present. For the Cozart Rapiscan, the manufacturer recommends waiting 10 minutes after food or drink before testing

Conclusion

Despite the many practical problems, police officers still thought that oral fluid tests would be very valuable for evaluation of apprehended drugged drivers. If it is rapid and reliable, such equipment will simplify the police work and save time. The case can be decided immediately, e.g. releasing the drivers or contact a medical doctor for blood sampling and clinical evaluation. They need equipment for the roadside as well as for the police station. But the tests must be easier to use and take less time. There was preference for multi-analyte drug tests, and electronic readers. A reference band is necessary.

The devices available at the moment of the study all had some disadvantages from the practical point of view, and the analytical evaluation was not satisfactory. But the need for such devices is so big that in one country, police officers prefer to use an oral fluid test that is imperfect, than no test at all. In other countries, police will rather use urine tests.

Sweat

Sampling by wiping the skin was very well accepted. The only available on-site device is the Drugwipe, and for the practical aspects we refer to the section on oral fluid.

ANALYTICAL EVALUATION: AMPHETAMINES

Criteria

All subjects were scored as being positive or negative for amphetamines and/or ecstasy, according to the following criteria:

Blood: positive if amphetamine, methamphetamine, MDMA, MDEA, MDA, MBDB or BDB present (at any concentration) by GC-MS, negative if screening was negative or confirmation was negative.

Urine: negative if screening was negative, positive if confirmation demonstrated amphetamine, methamphetamine, MDMA, MDEA, MDA, MBDB or BDB at a concentration higher than 200 ng/ml; if qualitative confirmation was done, positive if one of these substances was detected. Seven urine samples contained ephedrine or pseudoephedrine, and were not considered further.

Oral fluid or sweat: positive if amphetamine, methamphetamine, MDMA, MDEA, MDA, MBDB or BDB were present (at any concentration by GC-MS), negative if screening was negative or confirmation was negative.

Results

The overall results are given in the Table 5

Table 5: Overall results for amphetamines

	Total	*Number positive*			*Number negative*	*Percentage positive*
		AMP	XTC	A+X		
Blood/serum	1496	401	80	107	908	39%
Urine	1973	387	34	80	1471	25%
Oral fluid	271	81	27	45	118	56%
Sweat	43	6	10	57	0	100%

Comparison of blood GC-MS with GC-MS in other biological fluids

In a two-by-two analysis of the results in the different fluids, with blood as the reference, the results shown in Table 6 were found. The performance of the different fluids is evaluated according to three sample series: all the samples, the samples that contained (met)amphetamine (with or without XTC), and the samples that contained XTC (with or without) (met)amphetamine.

For predicting the presence of amphetamines in blood, all three fluids have a good predictive value. Sweat has apparently the highest accuracy, but the number of subjects is low, and no negative samples were included.

On-site Urine tests

On-site (meth)amphetamine urine tests versus urine GC-MS

Evaluation of the on-site devices, compared to the reference method in urine, are shown in Table 7. The performance of the different tests is evaluated according to three sample series:

- All: all the samples
- AMP: the samples that contained (met)amphetamine (with or without XTC)
- XTC: the samples that contained XTC (with or without) (met)amphetamine.

Table 6: Urine, Oral fluid and Sweat GC-MS versus blood GC-MS. The table gives the results of a two by two analysis of the results in the different fluids, with blood as the reference. In this analysis, for example, true positives are those for which positive GC-MS results were obtained with urine or other fluid and were also obtained with blood. False positives, for example, were those cases which were positive by GC-MS in urine etc but were negative in blood.

		Urine	*Oral fluid*	*Sweat*
Analyte	total	(n=992)	(n=231)	(n=70)
A	TP	240	65	11
X	TP	41	34	32
AX	TP	48	28	25
	TN	606	93	0
	FP	50	9	2
A	FN	1	2	0
X	FN	6	0	0
AX	FN	0	0	0
All (A+X+AX)	TP	327	127	68
	TN	606	93	0
	FP	50	9	2
	FN	7	2	0
	Prevalence	34%	56%	97%
	Sensitivity	98%	98%	100%
	Specificity	92%	91%	0%
	PPV	87%	93%	97%
	NPV	99%	98%	NA
	Accuracy	94%	95%	97%
AMP (A+AX)	TP	288	93	36
	TN	606	93	0
	FP	50	9	2
	FN	1	2	0
	Prevalence	31%	48%	95%
	Sensitivity	100%	98%	100%
	Specificity	92%	91%	0%
	PPV	85%	91%	95%
	NPV	100%	98%	NA
	Accuracy	95%	94%	95%
XTC (X+AX)	TP	89	62	57
	TN	606	93	0
	FP	50	9	2
	FN	6	0	0
	Prevalence	13%	38%	97%
	Sensitivity	94%	100%	100%
	Specificity	92%	91%	0%
	PPV	64%	87%	97%
	NPV	99%	100%	NA
	Accuracy	93%	95%	97%

A= samples containing only amphetamine and/or methamphetamine
X= samples containing only MDMA and/or MDEA and/or MDA and/or MBDB
AX= samples containing (met)amphetamine and ecstasy (MDMA and/or MDEA and/or MDA and/or MBDB)
AMP= A+AX, XTC=X+AX

Table 7: On-site tests versus urine GC-MS

	Tests	*Mahs A*	*RDS A*	*RDS MA*	*Dipro A*	*Dipro MA*	*Cort A*	*Cort MA*	*Fron A*	*MD A*	*SDS A*	*SRC A*	*SRC MA*	*SRT A*	*SRT MA*	*SS A*	*SS MA*	*Tcup A*	*Tria A*
	Total	157	578	468	126	122	361	186	68	95	92	52	47	874	561	121	106	527	395
	Prevalence	20%	12%	14%	49%	50%	26%	41%	26%	46%	41%	17%	43%	21%	12%	41%	42%	19%	12%
A	TP	14	9	2	6	1	73	11	8	36	36	6	4	103	2	36	12	42	36
X	TP	0	8	19	10	19	3	0	0	1	1	0	0	16	20	1	1	5	2
AX	TP	14	34	34	27	30	2	1	10	1	1	3	2	40	35	2	2	28	4
	TN	124	510	397	64	61	253	110	28	49	64	43	25	686	492	64	60	425	345
	FP	1	1	5	0	0	15	0	22	2	3	0	2	7	0	3	1	2	3
A	FN	1	1	7	1	6	13	63	0	6	7	0	14	10	6	7	30	10	4
X	FN	1	11	0	10	1	0	1	0	0	0	0	0	8	1	0	0	10	0
AX	FN	2	4	4	8	4	2	0	0	0	0	0	0	4	5	0	0	5	1
All	TP	28	51	55	43	50	78	12	18	38	39	9	6	159	57	39	15	75	42
	TN	124	510	397	64	61	253	110	28	49	64	43	25	686	492	64	60	425	345
	FP	1	1	5	0	0	15	0	22	2	3	0	2	7	0	3	1	2	3
	FN	4	16	11	19	11	15	64	0	6	7	0	14	22	12	7	30	25	5
	Sensitivity	88%	76%	83%	69%	82%	84%	16%	100%	86%	85%	100%	30%	88%	83%	85%	33%	75%	89%
	Specificity	99%	100%	99%	100%	100%	94%	100%	56%	96%	96%	100%	93%	99%	100%	96%	98%	100%	99%
	PPV	97%	98%	92%	100%	100%	84%	100%	45%	95%	93%	100%	75%	96%	100%	93%	94%	97%	93%
	NPV	97%	97%	97%	77%	85%	94%	63%	100%	89%	90%	100%	64%	97%	98%	90%	67%	94%	99%
	Accuracy	**97%**	**97%**	**97%**	**85%**	**91%**	**92%**	**66%**	**68%**	**92%**	**91%**	**100%**	**66%**	**97%**	**98%**	**91%**	**71%**	**95%**	**98%**
AMP	TP	28	43	36	33	31	75	12	18	37	38	9	6	143	37	38	14	70	40
	TN	124	510	397	64	61	253	110	28	49	64	43	25	686	492	64	60	425	345
	FP	1	1	5	0	0	15	0	22	2	3	0	2	7	0	3	1	2	3
	FN	3	5	11	9	10	15	63	0	6	7	0	14	14	11	7	30	15	5
	Prevalence	20%	9%	10%	40%	40%	25%	41%	26%	46%	40%	17%	43%	18%	9%	40%	42%	17%	11%
	Sensitivity	90%	90%	77%	79%	76%	83%	16%	100%	86%	84%	100%	30%	91%	77%	84%	32%	82%	89%
	Spec	99%	100%	99%	100%	100%	94%	100%	56%	96%	96%	100%	93%	99%	100%	96%	98%	100%	99%
	PPV	97%	98%	88%	100%	100%	83%	100%	45%	95%	93%	100%	75%	95%	100%	93%	93%	97%	93%
	NPV	98%	99%	97%	88%	86%	94%	64%	100%	89%	90%	100%	64%	98%	98%	90%	67%	97%	99%
	Accuracy	**97%**	**99%**	**96%**	**92%**	**90%**	**91%**	**67%**	**68%**	**93%**	**89%**	**100%**	**64%**	**98%**	**98%**	**87%**	**70%**	**92%**	**98%**
XTC	TP	14	42	53	37	49	5	1	10	2	3	3	2	56	55	3	3	33	6
	TN	124	510	397	64	61	253	110	28	49	64	43	25	686	492	60	60	425	345
	FP	1	1	5	0	0	15	0	22	2	3	0	2	7	0	1	1	2	3
	FN	3	15	4	18	5	2	1	0	0	0	0	0	12	6	0	0	15	1
	Prevalence	12%	10%	12%	46%	47%	3%	2%	17%	4%	4%	7%	7%	9%	11%	5%	5%	10%	2%
	Sensitivity	82%	74%	93%	67%	91%	71%	50%	100%	100%	100%	100%	100%	82%	90%	100%	100%	69%	86%
	Specificity	99%	100%	99%	100%	100%	94%	100%	56%	96%	96%	100%	93%	99%	100%	98%	98%	100%	99%
	PPV	93%	98%	91%	100%	100%	25%	100%	31%	50%	50%	100%	50%	88%	100%	75%	75%	94%	60%
	NPV	98%	97%	99%	78%	92%	99%	99%	100%	100%	100%	100%	100%	98%	99%	100%	100%	97%	100%
	Accuracy	**97%**	**97%**	**98%**	**85%**	**96%**	**94%**	**99%**	**63%**	**96%**	**96%**	**100%**	**93%**	**98%**	**99%**	**98%**	**98%**	**96%**	**99%**

The TesTstik methamphetamine was tested in Belgium on 14 samples: sensitivity was 67 %, specificity and PPV 100%, NPV was 92 % and accuracy was 93 %.

The SRC amphetamine satisfies our analytical criteria (accuracy ≥ 95 %, sensitivity and specificity ≥ 90 %), but only a few samples were analysed. Mahsan, SYVA Rapid test amphetamine, and Triage come very close to satisfying the analytical criteria. The Cortez methamphetamine test and Syva Rapid Cup methamphetamine have very poor sensitivity. On the basis of our results, RDS (both amphetamine and methamphetamine), Dipro (both), SRC (methamphetamine), SRT (both) and SureScreen (both) are 'conservative' tests, while Frontline is an 'aggressive' test. For the complete sample series, the methamphetamine tests of RDS and Dipro have a better sensitivity than the amphetamine tests, but this is not the case for Cortez, SRC, SRT and SureScreen. If only the samples containing amphetamine are considered, the sensitivity of the methamphetamine test is always less than that of the amphetamine test. For the samples containing MDMA or related substances, all methamphetamine test show increased sensitivity compared to amphetamine test, with the exception of the Cortez test.

Combination of the on-site urine tests for amphetamine and methamphetamine versus urine GC-MS

For the on-site tests where both a test for amphetamine and methamphetamine exists (and for the combination of Mahsan and Frontline that was used in Germany), we considered the combination of both results, i.e. the (combination of) test(s) is negative if both tests are negative and the (combination of) test(s) is positive if either test is positive. The results are shown in Table 8.

Table 8: Evaluation of the results in comparison to urine for the combination of the amphetamine and methamphetamine result.

	Tests	*RDS*	*Dipro*	*Cortez*	*SRT*	*SS*	*Frontline+ Mahsan*
	Total	(n=468)	(n=122)	(n=186)	(n=558)	(n=106)	(n=60)
	Prevalence	14%	50%	41%	12%	42%	28%
A	TP	8	6	65	6	39	8
X	TP	19	20	1	20	1	0
AX	TP	38	33	0	38	2	9
TN		397	61	102	492	58	25
FP		5	0	8	0	3	18
A	FN	1	1	9	0	3	0
X	FN	0	0	0	0	0	0
AX	FN	0	1	1	2	0	0
All	TP	65	59	66	64	42	17
	TN	397	61	102	492	58	25
	FP	5	0	8	0	3	18
	FN	1	2	10	2	3	0
	Sensitivity	98%	97%	87%	97%	93%	100%
	Specificity	99%	100%	93%	100%	95%	58%
	PPV	93%	100%	89%	100%	93%	49%
	NPV	100%	97%	91%	100%	95%	100%
	Accuracy	99%	98%	90%	100%	94%	70%

For SRC, the sample size was too small

If the results of amphetamines and methamphetamine are considered jointly (i.e. if one considers the test to be positive if either the amphetamine **or** the methamphetamine test is positive) **RDS, Dipro and Syva RapidTest** satisfy our analytical criteria.

On-site urine tests versus blood GC-MS

The comparison with blood is given in the Table 9.
The performance of all on-site tests is (expectedly) a little worse in comparison to blood than to urine, except for Frontline, that is an 'aggressive' test. For the whole sample population, and for the samples that contained amphetamine, SRT amphetamine and Triage meet the analytical criteria, with results comparable to those in the urine comparison. For XTC, in comparison to blood, the best results are obtained by RDS methamphetamine and SRT methamphetamine.

Table 9: On-site tests versus blood GC-MS

	Tests	*Mahs A*	*RDS A*	*RDS MA*	*Dipro A*	*Dipro MA*	*Cort A*	*Cort MA*	*Front A*	*MD A*	*SDS A*	*SRC A*	*SRC MA*	*SRT A*	*SRT MA*	*SS A*	*SS MA*	*Tcup A*	*Tria A*
	total	165	393	288	66	63	123	80	103	47	46	72	35	490	373	50	48	297	353
A	TP	52	19	3	8	1	68	10	27	31	30	23	4	87	4	32	11	40	34
X	TP	13	21	34	19	33	4	0	15	1	0	10	4	29	33	1	1	10	3
AX	TP	47	32	33	16	16	5	1	35	1	1	22	7	23	19	1	1	24	1
	TN	34	296	192	5	2	22	17	4	7	6	12	7	329	306	7	10	190	306
	FP	11	3	5	0	1	18	1	21	5	5	5	1	12	1	5	2	10	6
A	FN	2	1	13	1	8	5	50	0	2	4	0	12	2	7	2	23	3	2
X	FN	3	18	6	15	1	0	1	0	0	0	0	0	7	1	0	0	18	1
AX	FN	3	3	2	2	1	1	0	1	0	0	0	0	1	2	0	0	2	0
All	TP	112	72	70	43	50	77	11	77	33	31	55	15	139	56	34	13	74	38
	TN	34	296	192	5	2	22	17	4	7	6	12	7	329	306	7	10	190	306
	FP	11	3	5	0	1	18	1	21	5	5	5	1	12	1	5	2	10	6
	FN	8	22	21	18	10	6	51	1	2	4	0	12	10	10	2	23	23	3
	Prevalence	73%	24%	32%	92%	95%	67%	78%	76%	74%	76%	76%	77%	30%	18%	75%	75%	33%	12%
	Sensitivity	93%	77%	77%	70%	83%	93%	18%	99%	94%	89%	100%	56%	93%	85%	94%	36%	76%	93%
	Specificity	76%	99%	97%	100%	67%	55%	94%	16%	58%	55%	71%	88%	96%	100%	58%	83%	95%	98%
	PPV	91%	96%	93%	100%	98%	81%	92%	79%	87%	86%	92%	94%	92%	98%	87%	87%	88%	86%
	NPV	81%	93%	90%	22%	17%	79%	25%	80%	78%	60%	100%	37%	97%	97%	78%	30%	89%	99%
	Accuracy	**88%**	**94%**	**91%**	**73%**	**83%**	**80%**	**35%**	**79%**	**85%**	**80%**	**93%**	**63%**	**96%**	**97%**	**85%**	**48%**	**89%**	**97%**
AMP	TP	99	51	36	24	17	73	11	62	32	31	45	11	110	23	33	12	64	35
	TN	34	296	192	5	2	22	17	4	7	6	12	7	329	306	7	10	190	306
	FP	11	3	5	0	1	18	1	21	5	5	5	1	12	1	5	2	10	6
	FN	5	4	15	3	9	6	50	1	2	4	0	12	3	9	2	23	5	2
	Prevalence	70%	16%	21%	84%	90%	66%	77%	72%	74%	76%	73%	74%	25%	9%	74%	74%	26%	11%
	Sensitivity	95%	93%	71%	89%	65%	92%	18%	98%	94%	89%	100%	48%	97%	72%	94%	34%	93%	95%
	Specificity	76%	99%	97%	100%	67%	55%	94%	16%	58%	55%	71%	88%	96%	100%	58%	83%	95%	98%
	PPV	90%	94%	88%	100%	94%	80%	92%	75%	86%	86%	90%	92%	90%	96%	87%	86%	86%	85%
	NPV	87%	99%	93%	63%	18%	79%	25%	80%	78%	60%	100%	37%	99%	97%	78%	30%	95%	99%
	Accuracy	**89%**	**98%**	**92%**	**91%**	**66%**	**80%**	**35%**	**75%**	**85%**	**80%**	**92%**	**58%**	**97%**	**97%**	**85%**	**47%**	**94%**	**98%**
XTC	TP	60	53	67	35	49	9	1	50	2	1	32	11	52	52	2	2	34	4
	TN	34	296	192	5	2	22	17	4	7	6	12	7	329	306	7	10	190	306
	FP	11	3	5	0	1	18	1	21	5	5	5	1	12	1	5	2	10	6
	FN	6	21	8	17	2	1	1	1	0	0	0	0	8	3	0	0	20	1
	Prevalence	59%	20%	28%	91%	94%	20%	10%	67%	14%	8%	65%	58%	15%	15%	14%	14%	21%	2%
	Sensitivity	91%	72%	89%	67%	96%	90%	50%	98%	100%	100%	100%	100%	87%	95%	100%	100%	63%	80%
	Specificity	76%	99%	97%	100%	67%	55%	94%	16%	58%	55%	71%	88%	96%	100%	58%	83%	95%	98%
	PPV	85%	95%	93%	100%	98%	33%	50%	70%	29%	17%	86%	92%	81%	98%	29%	50%	77%	40%
	NPV	85%	93%	96%	23%	50%	96%	94%	80%	100%	100%	100%	100%	98%	99%	100%	100%	90%	100%
	Accuracy	**85%**	**94%**	**95%**	**70%**	**94%**	**62%**	**90%**	**71%**	**64%**	**58%**	**90%**	**95%**	**95%**	**99%**	**64%**	**86%**	**88%**	**98%**

Combination of the urine tests for amphetamine and methamphetamine versus blood GC-MS

For the on-site tests where both a test for amphetamine and methamphetamine exists (and for the combination of Mahsan and Frontline that was used in Germany), we considered the combination of both results, i.e. the (combination of) test(s) is negative if both tests are negative and the (combination of) test(s) is positive if either test is positive. The results are shown in Table 10.

If the results of amphetamines and methamphetamine are considered jointly (i.e. if one considers the test to be positive if either the amphetamine or the methamphetamine test is positive), **RDS and Syva RapidTest** satisfy the analytical criteria.

Table 10: Evaluation of the results in comparison to blood for the combination of the amphetamine and methamphetamine result.

	tests	*RDS*	*Dipro*	*Cortez*	*SRT*	*SS*	*Frontline + Mahsan*
	total	(n=287)	(n=63)	(n=80)	(n=371)	(n=48)	(n=84)
	Prevalence	31%	95%	78%	17%	75%	80%
A	TP	15	8	57	33	33	25
X	TP	33	34	1	9	1	11
AX	TP	35	17	1	20	1	31
TN		191	2	8	306	5	2
FP		6	1	10	1	7	15
A	FN	1	1	3	0	1	0
X	FN	6	0	0	1	0	0
AX	FN	0	0	0	1	0	0
All	TP	83	59	59	62	35	67
	TN	191	2	8	306	5	2
	FP	6	1	10	1	7	15
	FN	7	1	3	2	1	0
	Sensitivity	92%	98%	95%	97%	97%	100%
	Specificity	97%	66.7%	44%	100%	42%	12%
	PPV	93%	98%	86%	98%	83%	82%
	NPV	96%	67%	73%	99%	83%	100%
	Accuracy	95%	97%	84%	99%	83%	82%

For SRC, the sample size was too small.

On-site (meth)amphetamine Oral fluids tests

The comparison of the on-site amphetamine tests with the reference method in blood and oral fluid are given in Table 11.

The accuracy of the on-site tests is not satisfactory, when one compares them with the reference method. Sensitivity is between 80 and 90 %, but specificity is much lower. There is no big difference between the two devices. Compared to blood, on-site tests for urine give much better results.

The Cozart Rapiscan has a single test specifically for detecting ecstasy. It is not included in a panel test, so two cartridges must be used.

Several countries (Belgium, Norway, Finland) reported that amphetamine concentrations were higher in oral fluid than in blood, which was also reported by other authors (14).

On-site (meth)amphetamine Sweat tests

The results of the Drugwipe on sweat are given in the Table 12

The performance of the Drugwipe for amphetamines in sweat seems good, but very few negative samples were analysed, so we don't have a very good idea of the specificity (1 false positive/3 samples), and more studies will be needed to confirm these findings.

Table 11: On-site tests versus oral fluids and blood GC-MS

		Oral fluid		*Blood*	
	tests	RapiScan	Drugwipe	RapiScan	Drugwipe
	Total	(n=80)	(n=120)	(n=113)	(n=172)
A	TP	47	25	45	37
X	TP	1	17	1	26
AX	TP	0	35	1	29
	TN	15	17	43	38
	FP	7	14	15	31
A	FN	9	5	7	5
X	FN	0	4	1	4
AX	FN	1	3	0	2
All	TP	48	77	47	92
	TN	15	17	43	38
	FP	7	14	15	31
	FN	10	12	8	11
	Prevalence	73%	74%	49%	60%
	Sensitivity	83%	87%	85%	89%
	Specificity	68%	55%	74%	55%
	PPV	87%	85%	76%	75%
	NPV	60%	59%	84%	78%
	Accuracy	79%	78%	80%	76%
AMP	TP	47	60	46	66
	TN	15	17	43	38
	FP	7	14	15	31
	FN	10	8	7	7
	Prevalence	72%	69%	48%	51%
	Sensitivity	82%	88%	87%	90%
	Specificity	68%	55%	74%	55%
	PPV	87%	81%	75%	68%
	NPV	60%	68%	86%	84%
	Accuracy	78%	78%	80%	73%
XTC	TP	1	52	2	55
	TN	15	17	43	38
	FP	7	14	15	31
	FN	1	7	1	6
	Prevalence	8%	66%	5%	47%
	Sensitivity	50%	88%	67%	90%
	Specificity	68%	55%	74%	55%
	PPV	13%	79%	12%	64%
	NPV	94%	71%	98%	86%
	Accuracy	67%	77%	74%	72%

Table 12: On-site test versus sweat and blood GC-MS

	Tests	*Drugwipe*			*Drugwipe*		
		Sweat			Blood		
	total	(n=63)			(n=63)		
A	TP	8			11		
X	TP	26			32		
AX	TP	24			25		
	TN	2			0		
	FP	1			2		
A	FN	1			0		
X	FN	0			0		
AX	FN	1			0		
		All	AMP	XTC	All	AMP	XTC
	TP	58	32	50	68	36	57
	TN	2	2	2	0	0	0
	FP	1	1	1	2	2	2
	FN	2	2	1	0	0	0
	Prevalence	95%	92%	94%	97%	95%	97%
	Sensitivity	97%	94%	98%	100%	100%	100%
	Specificity	67%	67%	67%	0.0%	0%	0%
	PPV	98%	97%	98%	97%	95%	97%
	NPV	50%	50%	67%			
	Accuracy	95%	92%	96%	97%	95%	97%

Determination of the optimal cut-off for (meth)amphetamine and ecstasy

Oral fluids

In this evaluation, we determined what would be the optimal cut-off for the analytes (measured by GC-MS) in oral fluid, in order to 'predict' that the bloodanalysis would be positive for amphetamines (or ecstasy).

Our reference method is thus the analysis of amphetamines in blood with GC-MS. Analysis of a ROC curve for the sum of MDMA, MDEA and MDA showed an optimal cut-off of 72 ng/mL, with a sensitivity of 100 % and a specificity of 98.6 % (n = 130, AUC 0.999). Samples that contained amphetamine or methamphet-amine were not included in this comparison.

Analysis of a ROC curve for the sum of amphetamine and methamphetamine showed an optimal cut-off of 74 ng/mL, with a sensitivity of 96.8 % and a specificity of 95.5 % (n = 205, AUC 0.976). Samples that contained XTC were not included in this comparison (Figure 4).

Analysis of a ROC curve for the sum of all amphetamines showed an optimal cut-off of 90 ng/mL, with a sensitivity of 98.6 % and a specificity of 100 % (n = 130, AUC 0.993).

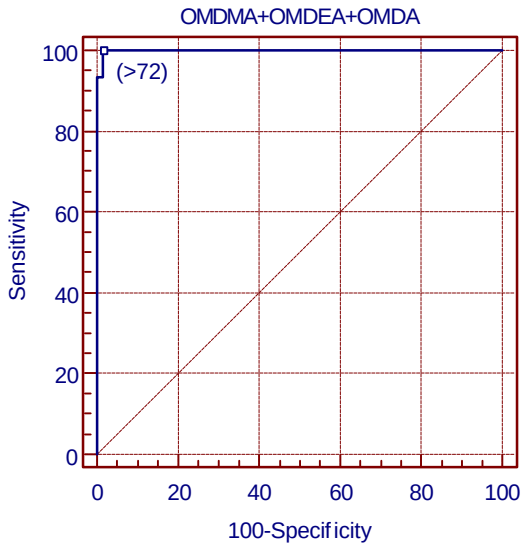

Figure 3: ROC curve for the sum of MDMA, MDEA and MDA in oral fluid, compared to analysis in blood

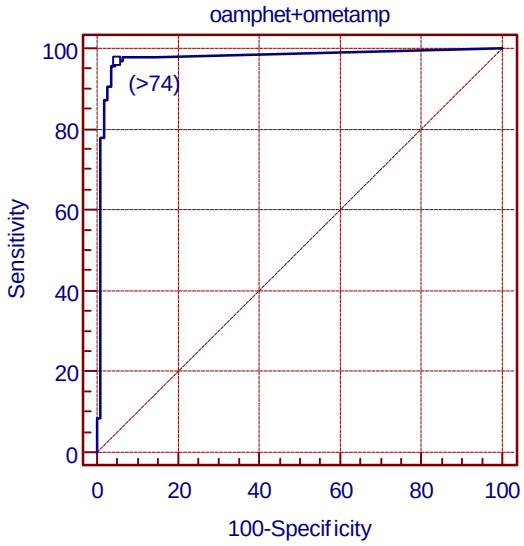

Figure 4: ROC curve for the sum of amphetamine and metham-phetamine in oral fluid, compared to the analysis in blood.

Discussion and conclusion

Our results for amphetamines show that with the reference methods, all fluids could be used to predict the presence of amphetamines in blood. Both urine and oral fluid have good accuracy and predictive values. Eighteen different on-site tests for amphetamine or methamphetamine were evaluated. Only one test (Syva Rapid Cup) satisfied the analytical criteria, but it was tested only on a low number of samples. Three other tests came close to satisfying the analytical criteria (Mahsan, SYVA rapid test amphetamine, and Triage). Most methamphetamine tests succeed better in detecting samples that contain MDMA or related compounds.

If the results of amphetamines and methamphetamine are considered jointly (i.e. if one considers the test to be positive if either the amphetamine or the methamphetamine test is positive), RDS, Dipro and Syva RapidTest satisfy the analytical criteria. This strategy seems to be an good way of obtaining excellent sensitivity and specificity.
In comparison to on-site urine tests (7/18 have accuracy > 95 %), tests for oral fluid have much lower accuracy (80 % or less in all cases). For sweat, the low number of samples (nearly all positive) does not permit definite conclusions, but use of sweat seems promising. The optimal cut-off for amphetamines in oral fluid would be in the range of 70-90 ng/mL. Using the proposed SAMHSA cut-off of 160 ng/mL yields a sensitivity of 87 % and a specificity of 97 %.

ANALYTICAL EVALUATION: BENZODIAZEPINES

Criteria

Each sample was scored as negative or positive according to the following criteria:
Blood: positive if a benzodiazepine was identified or quantified by a confirmation method;
Urine: positive if a benzodiazepine was identified or quantified by a confirmation method. If screening was positive and no confirmation was done in urine, the urine was scored as positive if benzodiazepines were identified in blood. If however, screening in urine was positive, but no benzodiazepines could be found in the confirmation analysis, the sample was considered negative in urine.
Oral fluid: positive if a benzodiazepine was identified or quantified by a confirmation method;

Results

The overall results are given in the Table 13.

Table 13: Overall results for benzodiazepines

	Total	*Number positive*	*Number negative*	*Percentage positive*
Blood/serum	1270	508	762	40%
Urine	1762	535	1227	30%
Oral fluid	71	33	38	46%

Comparison of blood GC-MS versus GC-MS in other biological fluids

In a two-by-two analysis of the results in the different fluids, with blood as the reference, the results shown in Table 14 were found.

Table 14: Comparison of reference methods (screening + GCMS) in urine and oral fluid versus reference method in blood. The table gives the results of a two by two analysis of the results in the different fluids, with blood as the reference. In this analysis, for example, true positives are those for which positive GC-MS results were obtained with urine or other fluid and were also obtained with blood. False positives, for example, were those cases which were positive by GC-MS in urine etc but were negative in blood.

	Oral fluids	*Urine*
Total	(n=35)	(n=1100)
Prevalence	83%	42%
TP	6	415
TN	4	567
FP	2	66
FN	23	52
Sensitivity	21%	89%
Specificity	67%	90%
PPV	75%	86%
NPV	15%	92%
Accuracy	29%	89%

The sensitivity and specificity of a urine (reference) test for the detection of benzodiazepines in blood, is relatively good. For oral fluid, a limited number of samples were analysed, and very low sensitivity and low specificity were

observed. A possible explanation could be that the methods used for oral fluid did not have the necessary sensitivity in some centres.

On-site Urine tests for benzodiazepines

The performance of the on-site tests (versus urine and blood) are given in Table 15 and Table 16.
Seven different tests were used. The number of used tests, and the prevalence of positives in the population varies significantly, which makes the comparisons rather difficult.

On-site tests versus urine

Table 15: On-site tests versus Urine GC-MS

Tests	*RDS*	*Cortez*	*Multidrug*	*SyvaRapidtest*	*SureScreen*	*TestStik*	*Triage*
Country	F I Scot	FIN	FIN	F N Scot	FIN	FIN	FIN I
Total	(n=219)	(n=189)	(n=92)	(n=354)	(n=102)	(n=15)	(n=394)
TP	10	108	61	53	62	10	61
TN	203	47	23	253	28	4	325
FP	5	9	5	47	4	1	4
FN	1	25	3	1	8	0	4
Prevalence	5%	70%	70%	15%	69%	67%	16%
Sensitivity	91%	81%	95%	98%	89%	100%	94%
Specificity	98%	84%	82%	84%	88%	80%	99%
PPV	67%	92%	92%	53%	94%	91%	94%
NPV	100%	65%	88%	100%	78%	100%	99%
Accuracy	**97%**	**82%**	**91%**	**86%**	**88%**	**93%**	**98%**

On the basis of our results, **RDS, Cortez and SureScreen** are 'conservative' tests, while **Syva Rapidtest** is an 'aggressive' test.
RDS and Triage meet our analytical criteria for a good test. Teststik seems promising as well, but these findings should be confirmed in a larger study.

On-site tests versus blood

Table 16: On-site tests versus Blood GC-MS

Tests	*RDS*	*Cortez*	*Multidrug*	*Syva Rapidtest*	*SureScreen*	*TestStik*	*Triage*
Total	(n=124)	(n=138)	(n=67)	(n=214)	(n=69)	(n=5)	(n=370)
TP	7	97	55	55	54	5	51
TN	105	7	3	142	5	0	296
FP	7	13	7	4	4	0	13
FN	5	21	2	13	6	0	10
Prevalence	10%	86%	85%	32%	87%	100%	16%
Sensitivity	58%	82%	96%	81%	90%	100%	84%
Specificity	94%	35%	30%	97%	56%	NA	96%
PPV	50%	88%	89%	93%	93%	100%	80%
NPV	95%	25%	60%	92%	45%	NA	97%
Accuracy	90%	75%	87%	92%	86%	100%	94%

When compared to blood, the results are somewhat worse (accuracy between 75 and 94 %) with Cortez being a 'conservative' test, and SRT (also a 'conservative' test) being better compared to blood than urine.

On-site Oral fluids tests for benzodiazepines

The only on-site device that was tested was the Cozart RapiScan. One problem was the high number of failures (14 %). More details can be found in a following chapter.

Table 17: On-site tests versus oral fluids and blood GC-MS

Tests	*RapiScan*	
	Oral fluid	Blood
Total	(n=60)	(n=133)
TP	10	11
TN	16	63
FP	17	7
FN	17	52
Prevalence	45%	47%
Sensitivity	37%	17%
Specificity	48%	90%
PPV	37%	61%
NPV	48%	55%
Accuracy	43%	56%

The Cozart RapiScan is not sufficiently reliable (accuracy of 56 % versus blood and 43 % versus oral fluid). This seems to be due to insufficient sensitivity (17 % versus blood). Cozart Bioscience has informed us that a new benzodiazepine assay is available (sensitivity of 60 ng/mL temazepam), but it was not evaluated by us. The low specificity observed in oral fluid could possibly be explained by the fact that the detection limit of the confirmation methods used in oral fluid was not low enough, as the specificity is much better in comparison to blood (this was also the case for the comparison of the reference methods, see Table 14). Probably the detection limit should be around 1 ng/mL.

Determination of the optimal cut-off for benzodiazepines

No reliable cut-off could be determined. In a comparison of the sum of the benzodiazepine concentrations in oral fluid versus the results in blood, the AUC was 0.589.

Discussion and conclusion

In summary, with the methods that were used in our study, urine seems to be a better fluid to detect benzodiazepines at the roadside. Out of the tested on-site urine tests, **Triage and RDS** were the only one that met our analytical criteria for a good test. This is probably explained by the extremely low concentrations of benzodiazepines in oral fluid, that have been described by other authors as well. In the review by Kidwell, the detection limits of the methods used to detect benzodiazepines in oral fluid range from 0.05 to 5 ng/mL, with the majority being less than 0.3 ng/mL (26). The sensitivity of the on-site test and of some confirmation methods seems insufficient at present. This is even more so for the low dose benzodiazepines like flunitrazepam that are very commonly misused.

ANALYTICAL EVALUATION: CANNABINOIDS

Criteria

Each sample was scored as negative or positive according to the following criteria:

Blood: positive if THC was above the detection limit by a confirmation method. If a screening method was negative, the blood was considered negative;

Urine: positive if THCCOOH was > 15 ng/mL by GCMS. If screening was negative (< 50 ng/mL), the sample was considered negative. If confirmation was qualitative, the urine was considered positive if THCCOOH was found. If screening was positive and no confirmation was done in urine, the urine was scored as positive if THC was identified in blood.

Oral fluid and sweat: positive if THC was identified or quantified by a confirmation method.

Results

Comparison of blood GC-MS versus GC-MS in other biological fluids

Urine versus blood for all countries

Table 18: Urine GC-MS versus Blood GC-MS per country

Country	*All countries**	*Belgium*	*Finland*	*France*	*Germany*	*Italy*	*Norway*	*Scotland*
Total	(n=990)	(n=129)	(n=62)	(n=21)	(n=111)	(n=302)	(n=167)	(n=198)
TP	298	95	19	16	92	5	69	2
TN	557	14	5	4	17	262	94	161
FP	127	19	38	1	0	35	0	34
FN	8	1	0	0	2	0	4	1
Prevalence	31%	74%	31%	76%	85%	2%	44%	2%
Sensitivity	97%	99%	100%	100%	98%	100%	95%	67%
Specificity	81%	42%	12%	80%	100%	88%	100%	83%
PPV	70%	83%	33%	94%	100%	13%	100%	6%
NPV	99%	93%	100%	100%	89%	100%	96%	99%
Accuracy	**86%**	**84%**	**39%***	**95%**	**98%**	**88%**	**98%**	**82%**

* in Finland, confirmation of THCCOOH in urine is always performed but analysis for THC in blood is only performed when other drugs are negative.

As can be expected, many samples were positive in urine, but not in blood ('false positives' in the table). A better correlation would probably have been obtained if THCCOOH was considered in blood as well, but as there is a general consensus to use THC in blood as a marker of recent use, this analysis was not performed. However, large differences were observed between countries, with a good positive predictive value (for urine; > 80 %) in Belgium, France, Germany and Norway, while the PPV was low in Finland (39%), Italy (13%) and Scotland (6%). Two explanations are possible:

- The selection of subjects. If no selection of subjects (based on impairment or signs of recent use) is performed, one can expect many positive urine samples, while the blood is negative (due to the longer detection time of THCCOOH in urine compared to THC in blood). In subjects that have been selected on the basis of signs of recent drug (cannabis) use, a better agreement between urine and blood can be expected.
- The different analytical strategy in some countries, with the possibility that the screening or confirmation are less sensitive than in others. E.g. in Finland, analysis for THC is only performed when other drugs are negative.

Urine, Oral fluids and Sweat versus blood
Table 19 compares the sensitivity, specificity and predictive values for the reference methods in urine, oral fluids and sweat.

Table 19: Urine, Oral fluids and Sweat GC-MS versus Blood GC-MS

	Urine	***Oral fluids***	***Sweat***
Total	(n=1100)	(n=335)	(n=98)
TP	292	101	73
TN	616	205	3
FP	184	14	15
FN	8	15	7
Prevalence	27%	35%	18%
Sensitivity	97%	87%	91%
Specificity	77%	94%	17%
PPV	61%	88%	83%
NPV	99%	93%	30%
Accuracy	**83%**	**91%**	**78%**

With the reference techniques, there is quite a good agreement between oral fluid and blood, with a sensitivity of 86 % and a specificity of 90%.
The correspondence between blood and sweat is not as good as for oral fluid. There are many positives in sweat that were not confirmed in blood (but in many cases the corresponding urine sample was positive).

On-site Urine tests for cannabinoids

On-site tests versus urine

Table 20: On-site test Urine versus Urine GC-MS

Tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*Sure-screen*	*Multi-drug*	*StatusDS*	*Triage*
Total	(n=148)	(n=123)	(n=571)	(n=542)	(n=369)	(n=88)	(n=880)	(n=114)	(n=95)	(n=92)	(n=396)
TP	66	85	152	203	120	38	280	31	30	33	66
TN	73	34	372	300	232	45	576	72	51	51	315
FP	7	3	42	22	11	4	2	1	1	0	2
FN	2	1	5	17	6	1	22	10	13	8	13
Prevalence	46%	70%	27%	41%	34%	44%	34%	36%	45%	45%	20%
Sensitivity	97%	99%	97%	92%	95%	97%	93%	76%	70%	80%	84%
Specificity	91%	92%	90%	93%	95%	92%	100%	99%	98%	100%	99%
PPV	90%	97%	78%	90%	92%	90%	99%	97%	97%	100%	97%
NPV	97%	97%	99%	95%	97%	98%	96%	88%	80%	86%	96%
Accuracy	**94%**	**97%**	**92%**	**93%**	**95%**	**94%**	**97%**	**90%**	**85%**	**91%**	**96%**

The following tests met our analytical criteria for cannabis: **Dipro, Cortez and SRT,** with Mahsan, RDS, SRC, TesTcup and Triage coming close.
RDS is an ‘aggressive’ test (20 out of the 42 false positives contained THCCOOH in urine, but less than 15 ng/mL), while **SRT, SureScreen, MD, StatusDS and Triage** are ‘conservative’ tests.

On-site tests versus blood

Table 21: On-site test Urine versus Blood GC-MS

tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*SureScreen*	*Multidrug*	*StatusDS*	*Triage*
total	(n=338)	(n=98)	(n=479)	(n=435)	(n=144)	(n=106)	(n=558)	(n=5)	(n=6)	(n=6)	(n=308)
TP	282	70	140	165	72	94	142	3	2	2	6
TN	12	8	238	188	36	1	327	0	1	0	268
FP	41	19	101	75	35	11	80	2	3	4	33
FN	3	1	0	7	1	0	9	0	0	0	0
Prevalence	84%	72%	29%	40%	51%	89%	27%	60%	33%	33%	2%
Sensitivity	99%	99%	100%	96%	99%	100%	94%	100%	100%	100%	100%
Specificity	23%	30%	70%	71%	51%	8%	80%	0%	25%	0%	89%
PPV	87%	79%	58%	69%	67%	90%	64%	60%	40%	33%	15%
NPV	80%	89%	100%	96%	97%	100%	97%	N/A	100%	N/A	100%
Accuracy	**87%**	**80%**	**79%**	**81%**	**75%**	**90%**	**84%**	**60%**	**50%**	**33%**	**89%**

The number of comparisons is very low **for SureScreen, Multidrug and StatusDS**.
In comparison with blood, all on-site tests are 'aggressive' tests, and very few false negatives will be observed.

On-site Oral fluids tests for cannabinoids

Table 22: On-site test versus oral fluids and blood GC-MS

	Oral fluid		*Blood*	
Tests Total	ORALscreen (n=190)	RapiScan (n=9)	ORALscreen (n=179)	RapiScan (n=98)
Countries			D Scot	E FIN N
TP	1	1	1	3
TN	157	0	149	74
FP	29	1	28	5
FN	3	7	1	16
Prevalence	2%	(89%)*	1%	19%
Sensitivity	25%	(13%)	50%	16%
Specificity	84%	(0%)	84%	94%
PPV	3%	(50%)	3%	38%
NPV	98%	(0%)	99%	82%
Accuracy	**83%**	**(11%)**	**84%**	**79%**

* very small sample size

The evaluation of the results (Table 22) is difficult, because of the low prevalence of positives and the small number of Cozart Rapiscan results that could be compared to GCMS in oral fluid. However, for nearly 100 results, corresponding blood results are available.
The ORALscreen test for cannabis has a lot of false positives, and a PPV of only 3 %. Many of these false positives were caused by difficulties in distinguishing the presence of a very faint line and the absence of any line. From the information provided by the manufacturer, we know that the Cozart Rapiscan is not able to detect low concentrations of THC. This is confirmed in these results, because, compared to blood, only 2 out of 11 positive samples were detected (sensitivity 18 %), and compared to oral fluid, the sensitivity was 13 % (1 out of 8).
In conclusion, the versions of ORALscreen and Cozart Rapiscan that were tested are not reliable for the detection of THC in oral fluid. Since that time, improvements have been made to the Cozart Rapiscan. The test has been further improved and can detect 25ng/ml Δ9-THC (information provided by the manufacturer), and further tests will be needed to evaluate this new version.

Dot plot for ORALscreen results versus THC in oral fluids and blood

Figures 5-6 provide a dot plot of the blood THC concentrations on the Y-axis, for the subjects whose oral fluid was positive (left of the figure) or negative (right of the figure) by the ORALscreen test. The lack of reliability of the ORALscreen is further illustrated by the dot plot, where negative results were found for many samples that contained THC and vice-versa.

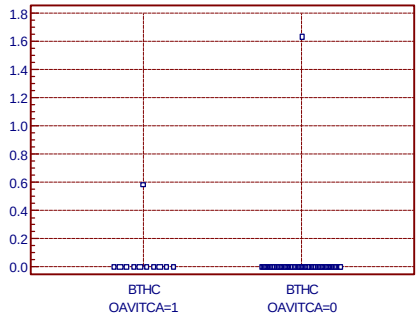

Figure 5: Dot plot of the THC concentrations in blood, according to the result of the Avitar Oralscreen

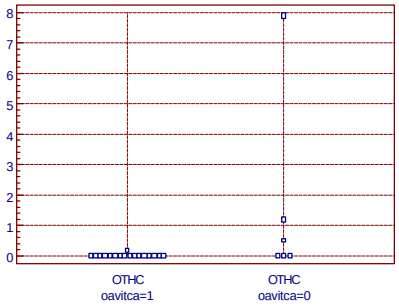

Figure 6: Dot plot of the THC concentrations oral fluid, according to the result of the Avitar Oralscreen

Dot plot for COZART RAPISCAN results versus THC in oral fluids and blood

The following figures provide a dot plot of the blood THC concentrations on the Y-axis, for the subjects whose oral fluid was positive (left of the figure) or negative (right of the figure) by Cozart Rapiscan

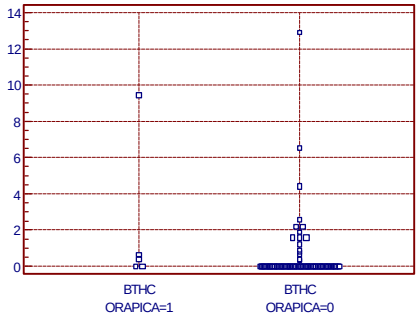

Figure 7: Dot plot of the THC concentrations in blood, according to the result of the Cozart Rapiscan

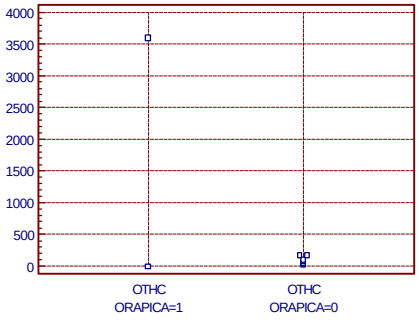

Figure 8: Dot plot of the THC concentrations in oral fluid, according to the result of the Cozart Rapiscan

Determination of the optimal cut-off for cannabinoids

ROC curve: urine versus blood

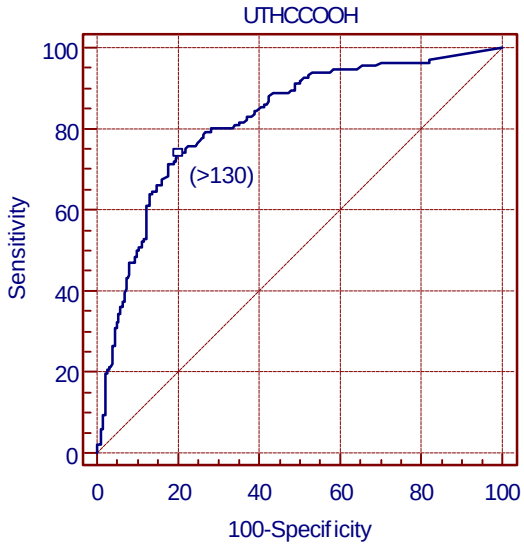

Figure 9: ROC curve of urinary THCCOOH with THC in blood as reference.

We determined the 'optimal' cut-off for THCCOOH in urine, in order to detect subjects in which THC is found in blood. The results are shown in the figure (N= 398, 136 pos, 262 neg). The optimal cut-off is 130 ng/ml (sensitivity 74.3 %, specificity 80.2%), with an AUC = 0.822. At the 15 ng/ml cut-off, the sensitivity is 95.6% and the specificity is 31.3 %.

ROC curves: oral fluid versus blood

We determined the 'optimal' cut-off for THC in oral fluid, in order to detect subjects in which THC is found in blood. The results are shown in the figure (N= 123: 83 pos, 40 neg). The optimal cut-off is 1.9 ng/ml (Sensitivity 86 %, specificity 90%, AUC = 0.888)

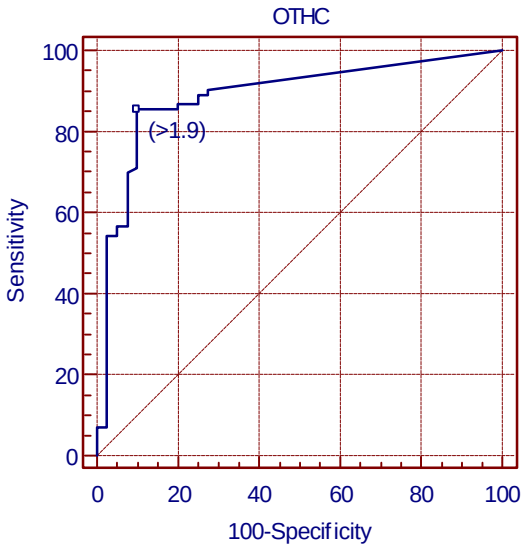

Figure 10: ROC curve of THC in oral fluid by GCMS with THC in blood as reference.

In France and Belgium, THC was measured in the Salivette. In the comparison that was done in Belgium, concentrations in the Salivette were much higher than concentrations in liquid oral fluid. The comparison involved 51 samples, 42 positive and 9 negative. The optimal cut-off was calculated to be 61 ng/ml (Sensitivity 100 % Specificity 52%; AUC = 0.730). In the discussion a possible explanation is given.

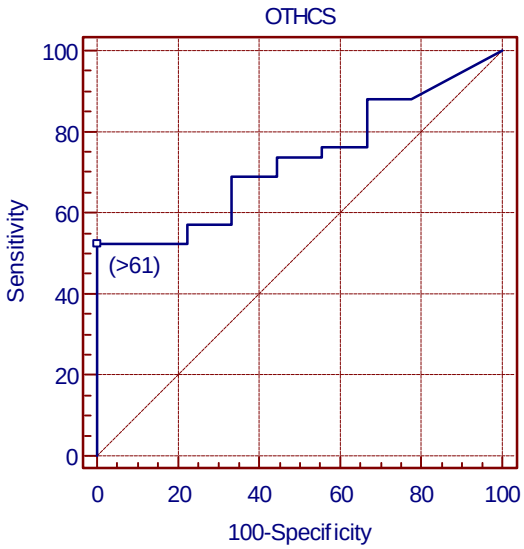

Figure 11: ROC curve of THC on a Salivette® with THC in blood as reference

ROC curves: sweat versus blood

We determined the 'optimal' cut-off for THC in sweat, in order to detect subjects in which THC is found in blood. The results are shown in figure 12. The number of subjects was 116, (98 pos., 18 neg.). The optimal cut-off is 32.1 ng/ml (sensitivity 67.5 %, specificity 66.7%), with an AUC = 0.698).

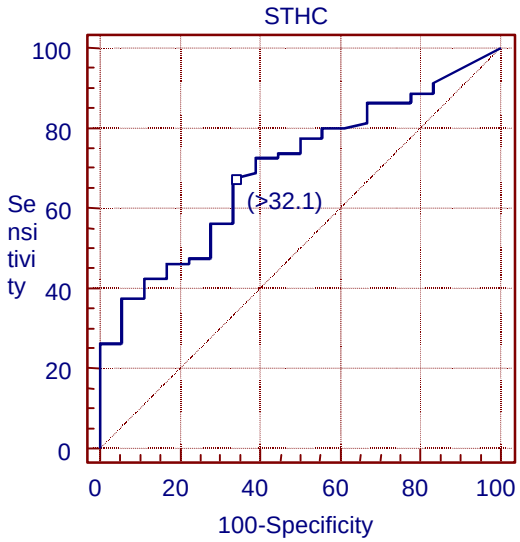

Figure 12: ROC curve of salivary THC with THC in blood as reference

Comparison of ROC curves: oral fluid and sweat versus blood

When ROC curves were determined for the subjects for whom we had values in oral fluid and in sweat, no significant difference could be demonstrated (N=61; Oral fluid AUC 0.884, sweat AUC 0.809, p=0.273).

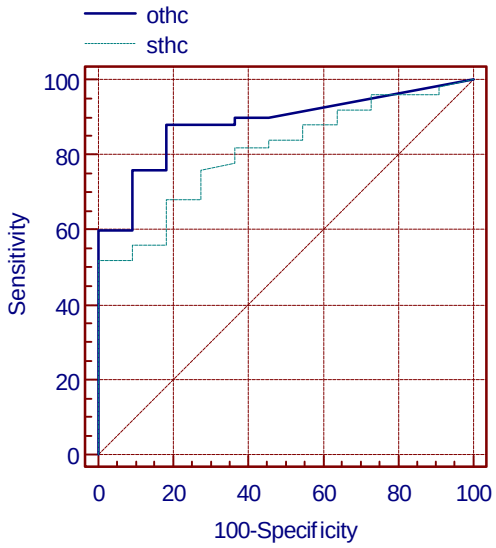

Figure 13: Comparison of ROC curves for THC in oral fluid and sweat

In a comparisons of oral fluid and sweat, oral fluid has a better AUC, but the difference with sweat is not statistically significant.

Discussion and conclusion

For cannabinoids, the comparison of the performance of the different matrices shows a small advantage for oral fluids, which is not unexpected considering the much longer window of detection of cannabis metabolites in urine compared to the presence of THC in blood. Three out of 11 on-site tests for urine showed results that met the analytical criteria: **Dipro, Cortez** and **Syva Rapidtest.** In comparison to blood, the accuracy of the best on-site tests was close to 90 %. For the on-site oral fluid tests, the sensitivity was too low (18 to 25 % compared to blood), so at present they cannot be recommended. The required sensitivity of on-site tests is 2 ng/mL of THC. No on-site tests were available for sweat.

The much higher concentrations of THC that can be extracted from the cotton of the Salivette, in comparison to the THC-concentrations in oral fluid, are difficult to explain. A possible explanation could be that the cotton of the Salivette absorbs the THC which has been sequestered on to teeth and gum, but this hypothesis needs further confirmation. Kauert (14) has shown that 90 % of the THC sampled with a Salivette could be retrieved by extracting the cotton of the Salivette, and only 10 % remained in the liquid phase. This phenomenon could be useful in order to increase the sensitivity of oral fluid analysis for THC, if a suitable extraction method can be found to release the THC trapped on the fibres of the sampling device. However, on-site tests that use liquid oral fluid should be sensitive to the very low THC concentrations found in liquid oral fluid.

ANALYTICAL EVALUATION: COCAINE

Criteria

All subjects were scored as being positive or negative for :

Blood: positive if cocaine and/or benzoylecgonine and/or ecgonine methyl ester were present (at any concentration) by GC-MS, negative if screening was negative or confirmation was negative.

Urine: negative if screening was negative or when only EME was present, positive if confirmation demonstrated BE at a concentration higher than 150 ng/ml if qualitative confirmation was done, positive if one of these substances was detected.

Oral fluid or sweat: positive if cocaine and/or benzoylecgonine and/or ecgonine methyl ester were present (at any concentration by GC-MS), negative if screening was negative or confirmation was negative.

Results

Comparison Blood GC-MS with other biological fluids GC-MS

Table 23: Urine, oral fluids and sweat versus blood GC-MS

	Urine	*Oral fluids*	*Sweat*
total	(n=773)	(n=282)	(n=27)
TP	55	26	24
TN	698	253	0
FP	17	2	3
FN	3	1	0
Prevalence	8%	10%	89%
Sensitivity	95%	96%	100%
Specificity	98%	99%	0%
PPV	76%	93%	89%
NPV	100%	100%	N/A
Accuracy	**97%**	**99%**	**89%**

In our study population, analysis of cocaine in urine and oral fluid GC-MS has a good correlation with blood. The positive predictive value of urine is only 76 %, while it is 93 % in oral fluid. The number of subjects tested for sweat is low, so no valid conclusions can be made.

On-site Urine tests for cocaine metabolites

On-site tests versus Urine GC-MS

The following tests meet the analytical criteria: **Dipro, RDS, TesTcup, Syva Rapid Cup, Syva Rapid Test, SureScreen, Status DS and Triage.**
Mahsan and RDS are 'aggressive' tests.

Table 1: On-site Urine tests versus Urine GC-MS

Tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*SureScreen*	*Multidrug*	*StatusDS*	*Triage*
Total	(n=156)	(n=128)	(n=580)	(n=570)	(n=393)	(n=90)	(n=904)	(n=116)	(n=96)	(n=92)	(n=396)
Countries	D	B	B D F I Scot	B D FIN E N Scot	D E F FIN N	D FIN	B F FIN I N	FIN	FIN	FIN	FIN I
TP	12	20	32	35	11	6	50	4	3	3	20
TN	134	107	539	529	372	82	847	112	92	88	375
FP	10	1	9	4	8	2	5	0	0	1	0
FN	0	0	0	2	2	0	2	0	1	0	1
Prevalence	8%	16%	6%	6%	3%	7%	6%	3%	4%	3%	5%
Sensitivity	100%	100%	100%	95%	85%	100%	96%	100%	75%	100%	95%
Specificity	93%	99%	98%	99%	98%	98%	99%	100%	100%	99%	100%
PPV	55%	95%	78%	90%	58%	75%	91%	100%	100%	75%	100%
NPV	100%	100%	100%	100%	99%	100%	100%	100%	99%	100%	100%
Accuracy	**94%**	**99%**	**98%**	**99%**	**97%**	**98%**	**99%**	**100%**	**99%**	**99%**	**100%**

Frontline: sample size too small

On-site tests versus Blood GC-MS

Table 24: On-site Urine tests versus Blood GC-MS

tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*Triage*
total	(n=63)	(n=25)	(n=331)	(n=306)	(n=99)	(n=25)	(n=426)	(n=298)
Countries								
TP	23	19	36	24	5	8	39	15
TN	19	3	281	270	83	12	374	279
FP	21	2	14	11	11	5	12	3
FN	0	1	0	1	0	0	1	1
Prevalence	37%	80%	11%	8%	5%	32%	9%	5%
Sensitivity	100%	95%	100%	96%	100%	100%	98%	94%
Specificity	48%	60%	95%	97%	88%	71%	97%	99%
PPV	52%	90%	72%	69%	31%	62%	76%	83%
NPV	100%	75%	100%	100%	100%	100%	100%	100%
Accuracy	**67%**	**88%**	**96%**	**96%**	**89%**	**80%**	**97%**	**99%**

Frontline, Multidrug, Status DS, SureScreen: sample size too small

Compared to blood**, RDS, Roche TesTcup, Syva Rapidtest and Triage** fulfil the analytical criteria for a good test. All tests are 'aggressive' tests, and the most 'aggressive' ones are Mahsan, Cortez and RDS.

On-site Oral fluids tests for cocaine and metabolites

Table 25: On-site Oral fluids tests versus Oral fluids and Blood GC-MS

	Oral fluid			*Blood*		
Tests	ORALscreen	Drugwipe	RapiScan	ORALscreen	Drugwipe	RapiScan
Total	(n=180)	(n=118)	(n=33)	(n=200)	(n=34)	(n=4)
Countries				D Scot	B D E I	E FIN
TP	0	17	0	0	15	1
TN	178	82	33	188	3	1
FP	2	7	0	2	1	1
FN	0	12	0	0	5	1
Prevalence	0%	25%	NA	0	59%	50%
Sensitivity	NA	59%	NA		75%	50%
Specificity	99%	92%	100%	99%	93%	50%
PPV	0%	71%	NA	0%	94%	50%
NPV	100%	87%	100%	100%	72%	50%
Accuracy	**99%**	**84%**	**100%**	**99%**	**82%**	**50%**

A problem for the interpretation is the small number of positive subjects included in the study. Interpretable results are only seen for Drugwipe, and show rather low sensitivity.

On-site Sweat tests for cocaine and metabolites

Table 26: On-site sweat tests versus sweat and blood GC-MS

	Sweat	***blood***
tests	Drugwipe	Drugwipe
total	(n=22)	(n=22)
TP	17	15
TN	0	0
FP	0	2
FN	5	5
Prevalence	100%	91%
Sensitivity	77%	75%
Specificity		0%
PPV	100%	88%
NPV	0%	0%
Accuracy	**77%**	**68%**

The results are difficult to interpret because of the very limited number of negative samples, so nothing can be said about the specificity. There is a considerable number of false negatives, in comparison to blood as well as sweat.

Determination of the optimal cut-off for cocaine and metabolites

ROC curves: urine, oral fluids and sweat versus blood

ROC curves were calculated for cocaine, benzoylecgonine and ecgonine methyl ester and for the sum (in ng/ml) of all three analytes. The number of positive and negative samples, the area under the ROC curve and the cut-off are given in Table 27. The AUC's for cocaine and BE in urine and oral fluid are equivalent. For sweat the AUC's are much lower. In oral fluid, the optimal cut-off is the detection limit for all individual analytes. The optimal cut-off for BE in urine is 1030 ng/ml.

Table 27: AUC and cut-offs determined by analysis of the ROC curves for cocaine and metabolites.

	Urine				*Oral fluid*				*Sweat*			
Analytes	Pos	Neg	Area	Cut-off	Pos	Neg	Area	Cut-off	Pos	Neg	Area	Cut-off
Cocaine+ EME+ BE	21	31	0.974	1589	17	55	0.965	19	21	3	0.698	98
Cocaine	22	39	0.977	29	27	58	0.955	0	24	3	0.722	86
EME	22	31	0.949	161	17	56	0.875	0	21	3	0.619	17
BE	37	35	0.973	1030	27	57	0.974	0	24	3	0.674	13

The correlation between the concentration of BE in oral fluid and serum is BE (ng/ml) in oral fluid = 4.6 + 0.65 * serum (R^2= 0.798)

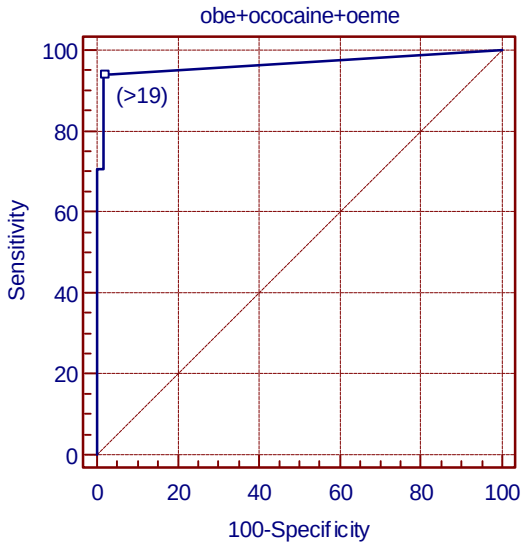

Figure 14: ROC curve for the sum of cocaine, BE and EME in oral fluid (presence of cocaine in blood as the gold standard).

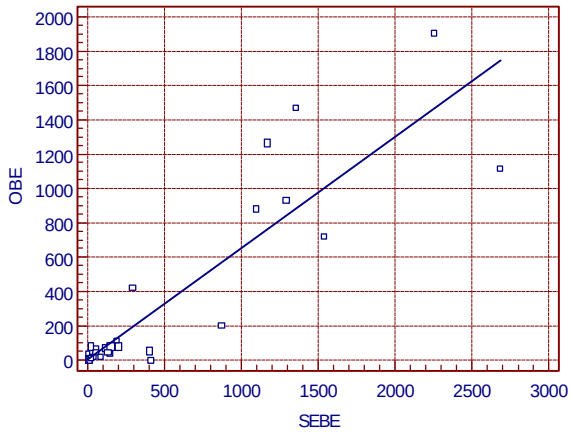

Figure 15: Linear regression and correlation of benzoylecgonine in oral fluid and in blood

Discussion and conclusion

For the prediction of positivity in blood with the reference methods, both oral fluid and urine gave good results. Eight of the 11 on-site tests met the analytical criteria: **Dipro, RDS, TesTcup, Syva Rapid cup, Syva Rapid Test, SureScreen, Status DS** and **Triage.** Even compared to blood, 4 tests have an accuracy > 95 % and sensitivity and specificity > 90 %: **RDS, Roche TesTcup, Syva Rapidtest and Triage.** In oral fluid, the evaluation of the result was hampered by the low number of positive samples in the evaluation. Some comparisons that show good accuracy include a very small number of positive samples. For Drugwipe, an evaluation seems possible, and the sensitivity is too low. For sweat, the number of samples that could be evaluated was rather small as well, and the evaluation was done with positive samples only, the accuracy of Drugwipe was 77 %. The optimal cut-off for oral fluid is the detection limit of the assay.

ANALYTICAL EVALUATION: OPIATES

Criteria

All subjects were scored as being positive or negative for:

Blood: positive if 6-AM and/or morphine were present (at any concentration) by GC-MS, negative if screening was negative or confirmation was negative.

Urine: negative if screening was negative, positive if confirmation demonstrated 6-AM a concentration higher than 10 ng/ml, or morphine > 200 ng/mL or codeine > 200 ng/mL. If qualitative confirmation was done, positive if one of these substances was detected.

Oral fluid or sweat: positive if 6-AM or morphine or codeine were present (at any concentration by GC-MS), negative if screening was negative or confirmation was negative.

Results

Comparison of blood GC-MS versus GC-MS in other biological fluids

The interpretation of the data was such that all opiates (codeine, morphine, …) were considered true positives.

Table 28: Urine Oral fluids and sweat versus Blood GC-MS

	Urine	*Oral fluid*	*Sweat*
Total	(n=841)	(n=321)	(n=25)
TP	69	34	15
TN	655	257	5
FP	115	26	3
FN	2	4	2
Prevalence	8%	12%	68%
Sensitivity	97%	89%	88%
Specificity	85%	91%	63%
PPV	38%	57%	83%
NPV	100%	98%	71%
Accuracy	86%	91%	80%

The predictive value of urine, oral fluid and sweat for a positive result in blood were compared (table 28). The best agreement was observed for oral fluid, with relatively less false positives than urine. The numbers for sweat are too low to draw meaningful conclusions.

Norway, Belgium and Finland reported that opiate concentrations were higher in oral fluid than in blood. It was also pointed out that 6-AM was found in several samples, while it was not detected in blood, which indicates that oral fluid could be a better matrix than blood to confirm heroin use.

On-site Urine tests for opiates

On-site tests versus urine GC-MS

Table 29: On-site test versus Urine GC-MS

Tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*SureScreen*	*Multidrug*	*Status DS*	*Triage*
Total	(n=137)	(n=34)	(n=472)	(n=474)	(n=387)	(n=85)	(n=782)	(n=118)	(n=97)	(n=94)	(n=396)
TP	0	7	42	58	57	1	78	9	7	6	10
TN	133	23	406	387	311	81	671	104	87	85	382
FP	4	4	23	27	18	3	29	3	1	3	4
FN	0	0	1	2	1	0	4	4	2	0	0
Prevalence	0%	21%	9%	13%	15%	1%	10%	9%	9%	6%	3%
Sensitivity		100%	98%	97%	98%	100%	95%	82%	78%	100%	100%
Specificity	97%	85%	95%	93%	95%	96%	96%	97%	99%	97%	99%
PPV	0%	64%	65%	68%	76%	25%	73%	75%	88%	67%	71%
NPV	100%	100%	100%	99%	100%	100%	99%	98%	98%	100%	100%
Accuracy	**97%**	**88%**	**95%**	**94%**	**95%**	**96%**	**96%**	**96%**	**97%**	**97%**	**99%**

Frontline: sample size too small

The following tests meet our analytical criteria: **RDS, Cortez, SRC, SRT, Status DS and Triage**. Mahsan has good results, but only negative samples were included, so the sensitivity cannot be determined. ‘aggressive’ tests are: Dipro (low number of evaluated samples), RDS, TesTcup, Cortez and SRT. No ‘conservative’ tests were observed.

On-site tests versus blood

Table 30: On-site tests versus blood GC-MS

Tests	*Mahsan*	*Dipro*	*RDS*	*Roche TesTcup*	*Cortez*	*Syva Rapidcup*	*Syva Rapidtest*	*SureScreen*	*Multidrug*	*Status DS*	*Triage*
Total	(n=60)	(n=11)	(n=331)	(n=295)	(n=132)	(n=28)	(n=463)	(n=11)	(n=10)	(n=7)	(n=309)
TP	20	6	26	27	27	8	42	2	0	0	2
TN	27	1	260	209	59	13	362	1	4	2	299
FP	13	4	44	57	46	7	58	8	6	5	8
FN	0	0	1	2	0	0	1	0	0	0	0
Prevalence	33%	55%	8%	10%	20%	29%	9%	18%	0%	0%	1%
Sensitivity	100%	100%	96%	93%	100%	100%	98%	100%	NA	NA	100%
Specificity	68%	20%	86%	79%	56%	65%	86%	11%	40%	29%	97%
PPV	61%	60%	37%	32%	37%	53%	42%	20%	0%	0%	20%
NPV	100%	100%	100%	99%	100%	100%	100%	100%	100%	100%	100%
Accuracy	**78%**	**64%**	**86%**	**80%**	**65%**	**75%**	**87%**	**27%**	**40%**	**29%**	**97%**

Frontline: sample size too small

Compared to blood, it appears that Triage meets the analytical criteria, but the number of positives is very low, so it is not possible to estimate the sensitivity. All tests have a high sensitivity.

On-site Oral fluids tests for opiates

Table 31: On-site versus Oral fluids and Blood GC-MS

	Oral fluid			*Blood*		
tests	ORALscreen	Drugwipe	RapiScan	ORALscreen	Drugwipe	RapiScan
total	(n=183)	(n=46)	(n=37)	(n=180)	(n=214)	(n=109)
TP	4	9	11	1	17	10
TN	163	19	5	154	156	78
FP	13	5	14	24	31	16
FN	3	13	7	1	10	5
Prevalence	4%	48%	49%	1%	13%	14%
Sensitivity	57%	41%	61%	50%	63%	67%
Specificity	93%	79%	26%	87%	83%	83%
PPV	24%	64%	44%	4%	35%	38%
NPV	98%	59%	42%	99%	94%	94%
Accuracy	**91%**	**61%**	**43%**	**86%**	**81%**	**81%**

For opiates, the sensitivity of on-site tests in oral fluid is rather low. Compared to blood, the sensitivity is 50 – 67 %, and the specificity is 83 – 87 %. ORALscreen appears to have the best results, but the prevalence in the study population is much lower than with the other tests.

On-site Sweat tests for opiates

Table 32: On-site tests versus sweat and blood GC-MS

	Sweat	*Blood*
Tests	Drugwipe	Drugwipe
Total	(n=9)	(n=12)
TP	8	8
TN	0	2
FP	0	2
FN	1	0
Prevalence	100%	67%
Sensitivity	89%	100%
Specificity	NA	50%
PPV	100%	80%
NPV	0%	100%
Accuracy	**89%**	**83%**

Because of the very low numbers, interpretation is impossible.

Determination of the optimal cut-off for opiates

We determined the 'optimal' cut-off for codeine, morphine and 6-AM in oral fluid, in order to detect subjects in whom these substances were positive in blood. The results are shown in figure 16. The number of samples was 142 (37 pos, 115 neg.)

The optimal cut-off is the detection limit (Sensitivity 91.9 % Specificity 77.4%, AUC = 0.869).

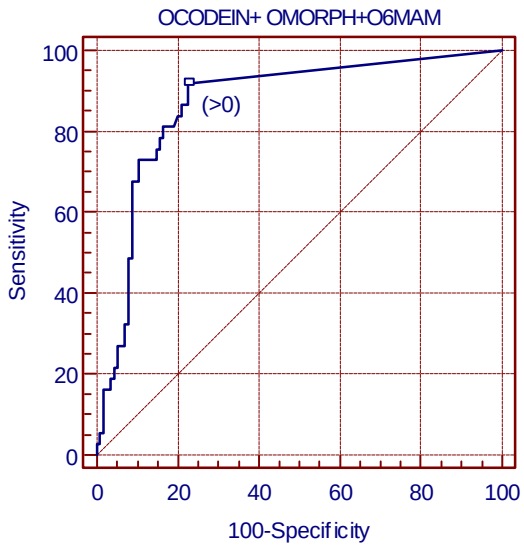

Figure 16: ROC curve for the sum of morphine, codeine and 6-AM in oral fluid (presence of opiates in blood as the gold standard)

Discussion and conclusion

In the comparison of the different fluids with reference methods, oral fluid has slightly better results than urine.
Six of the eleven on-site tests met the analytical criteria: **RDS, Cortez, SRC, SRT, Status DS and Triage**.
In oral fluid, the on-site tests showed less accuracy than urine tests. The sensitivity in particular, was too low. An ideal oral fluids test should have a low detection limit (2 - 5 ng/mL) for opiates.
For the purposes of WP4, we have considered positive specimens only those which contained morphine, 6-AM, or codeine. It should be noted that other substances may give positive results with on-site tests, for example dihydrocodeine or pholcodine.

PROBLEMS IN THE EXECUTION OF THE TESTS AND READING OF THE RESULTS

The number of tests that yielded doubtful results or that failed to give results are given in the following tables. These numbers are underestimated, because not all participating countries reported on the failed results. The following criteria were used:

Doubtful = a test result that it could not be correctly interpreted (e.g. too faint line)
Failed = when the test failed because of malfunction of the device

Urine

Table 33. Number of doubtful tests in urine

Tests	*(Met)amphet.*	*tot*	*Benzodiaz.*	*tot*	*Cannabin.*	*tot*	*Cocaine*	*tot*	*Opiates*	*tot*	*%*
Mahsan	24	442			9	468	8	443	7	441	2.68
Dipro	4	260			3	130	3	134	5	131	2.29
RDS	11	1187	0	386	4	652	3	656	3	651	0.59
RocheTesTcup	4	640			8	655	3	659	3	656	0.69
Frontline	16	185									8.65
Cortez	2	628	0	196	3	434	8	434	6	433	0.89
Syva Rapidcup	4	226			2	203	5	202	3	201	1.68
Syva Rapidtest	3	1474	0	363	2	908	3	913	0	909	0.18
SureScreen	0	237	0	128	0	127	0	126	0	127	0
Multidrug	0	99	0	99	0	99	0	99	0	99	0
Status DS	0	95			0	95	0	95	0	95	0
Teststik			0	27							0
Triage	0	400	0	399	0	400	0	400	0	400	0

The very high percentage of doubtful results for Frontline is obvious. Only the amphetamine test was evaluated, and it is known that it gives many difficulties to interpret the results.

Table 34. Number of failed tests in urine. Failures could be that the lines did not appear, that the control line did not appear, also included failures due to handling problems due to insufficient training.

Tests	*(Met)amphet.*	*tot*	*Benzodiaz.*	*tot*	*Cannabin.*	*tot*	*Cocaine*	*tot*	*Opiates*	*tot*	*%*
Mahsan	1	442			1	468	1	443	1	441	0.22
Dipro	0	260			0	130	0	134	0	131	0
RDS	2	1187	0	219	5	652	5	656	5	651	0.51
RocheTesTcup	32	640			32	655	32	659	32	656	4.9
Frontline	0	185									0
Cortez	2	628	0	196	1	434	1	434	0	433	0.19
Syva Rapidcup	12	226			12	203	12	202	12	201	5.8
Syva Rapidtest	0	1474	0	363	0	908	0	913	0	909	0
SureScreen	0	237	0	128	0	127	0	126	0	127	0
Multidrug	0	99	0	99	0	99	0	99	0	99	0
Status DS	0	95			0	95	0	95	0	95	0
Teststik			0	27							0
Triage	0	400	0	399	0	400	0	400	0	400	0

The number of 'failures' also includes failures due to handling problems due to insufficient training.

Many failed tests were reported from Scotland for the Roche TesTcup. This was much less the case for the other countries. It is possible that insufficient training in the use of the TesTcup was the cause for this, but other countries (e.g. Germany, 5/84 or 6 % failures) also reported problems, e.g. in the closing of the cup, so we think that training could be more critical for this device. The Scottish report reads: "*There were, however a significant number of failures with this device in our hands (tests were carried out by several different laboratory staff) in which the urine failed to enter the analysis chamber. We understand that some contractors had later batch numbers that had been modified. In a few cases, the lid seal failed, leading to a leakage of urine. If particular care is needed in carrying out routine procedures such as replacing the lid, requiring pressing of the top etc., then these manipulations should be described and emphasised in the instructions accompanying the test kit" (6).*

Oral fluids and Sweat

Table 35: Number of doubtful tests in oral fluid and sweat

	Tests	*(Met)amph.*	*tot*	*Benzod.*	*tot*	*Cann.*	*tot*	*Cocaine*	*tot*	*Opiates*	*tot*	*%*
oral fluids	ORALscreen					0	161	0	201	6	201	**1.07**
	Drugwipe	22	425					6	281	0	402	**2.53**
	RapiScan	0	488	0	414	0	489	0	391	0	486	**0**
Sweat	Drugwipe	6	73					7	33	6	22	**14.8**

For oral fluid and sweat, many doubtful results were reported with Drugwipe, especially for amphetamines, but interpretation was much easier with the experimental electronic reader.

Table 36: number of failed tests in oral fluid and sweat

	Tests	*(Met)amph.*	*tot*	*Benzod.*	*tot*	*Cann.*	*tot*	*Cocaine*	*tot*	*Opiates*	*tot*	*%*
oral fluids	ORALscreen					0	161	6	201	0	201	**1.1**
	Drugwipe	103	699					0	358	6	476	**7.0#**
	RapiScan	70	488	85	499	72	489	63	391	72	486	**15.4s***
sweat	Drugwipe	0	73					0	33	0	22	**0**

*the number is probably underestimated, as not all cases of failed tests were reported in Norway.
percentage probably too high, because 2500 Drugwipes were provided for the study.

Many failed tests were reported with the Cozart Rapiscan, in all countries that used them. The reason was a bad lot of test strips. This caused a lot of problems, and also decreased the motivation of the police officers, who initially thought that the problems were due to a mistake they made. This caused a significant waste of efforts for the project. The number of failed tests included all the Drugwipe amphetamine tests that were used in Italy.

SUMMARY OF THE COMPARISON OF THE ANALYTICAL FLUIDS

The accuracy, sensitivity and specificity of GC-MS in urine, oral fluid and sweat, in comparison to the reference methods in blood, are summarised in the Table 3.

Ability to predict the presence of drugs in blood from analysis of other body fluids

Table 37: GC-MS versus GC-MS in blood

	Accuracy			***Sensitivity***			***Specificity***		
Analyte	Urine	Oral fluids	Sweat	Urine	Oral fluids	Sweat	Urine	Oral fluids	Sweat
Amphetamine	94%	95%	97%	97%	98%	100%	92%	91%	0%
Benzodiazepines	89%	29%	NA	89%	21%	NA	90%	67%	NA
Cannabinoids	86%	89%	78%	97%	86%	91%	81%	90%	17%
Cocaine	97%	99%	89%	95%	96%	100%	98%	99%	0%
Opiates	86%	91%	80%	97%	89%	88%	85%	91%	63%

The results are of course also dependent on the timing of sampling relative to the last intake. If a drug was taken very recently, it is possible that it can only be found in blood (and oral fluid), but not yet in urine. If a drug was taken a longer time ago, it is possible that it is not detectable anymore in blood, but only in urine (and possibly in sweat).

Optimal cut-offs

The optimal cut-offs, calculated with ROC-curve analysis, in the different fluids are summarised in Table 38. The cut-offs are based on **confirmation** (GC-MS) analysis. It was not possible to do the analysis with screening results, because they were not quantitative.

Table 38: Calculated optimal cut-offs (ng/ml) in the Rosita study (with number of samples, area under the ROC curve and the sensitivity and specificity at that cut-off). As a comparison, the SAMHSA proposed confirmation cut-offs in oral fluids are given with the calculated sensitivity and specificity in our series at the SAHMSA cut-offs. Finally, the sweat cut-offs that we calculated are also mentioned.

	Oral fluid								*Sweat*
	Rosita					SAMHSA			
Analyte	Cut-off (ng/ml)	N	AUC	Sens.	Spec.	Proposed confirmation cut-off*	Sens.	Spec.	Cut-off (ng/ml)
A+MA	74	205	0.976	97%	96%	160*	87%	97%	226
MDMA+MDEA+MDA	72	130	0.999	100%	99%	160*	100%	99%	721
A+MA+MDMA+MDEA+MDA	90	130	0.993	99%	100%	160*	99%	100%	NA
THC	1.9	123	0.888	86%	90%	2	85%	90%	32
BE	0	84	0.973	96%	96%	8	93%	96%	13
COC + BE	0	84	0.975	96%	96%	8*	85%	98%	
COC+BE+EME	19	72	0.965	94%	98%	8*	94%	98%	98
COD+MORPH+6-AM	0	142	0.869	92%	77%	40(6-AM: 4)*	78%	84%	NA

* The SAMHSA cut-offs are for one molecule, while we added the concentrations of the molecules.

With the exception of cannabis, the cut-offs obtained in the ROSITA study are lower than the SAMHSA (confirmation) cut-offs. Use of the SAMHSA cut-offs would somewhat reduce the sensitivity of the oral fluid assays, but increase the specificity. Although the number of subjects is not low, further confirmation of these cut-offs would be welcome, because in this multi-centre study, we are not sure of the uniformity of the analytical methods. Moreover, the methods for analysis of oral fluid are still evolving, and efforts at organising quality controls are only starting. With the data we had, it was not possible to determine screening cut-offs. The screening cut-offs will depend on the specificity of the antibodies, and the presence of other cross-reacting metabolites in oral fluid or sweat.

SUMMARY OF THE PERFORMANCE OF ON-SITE TESTS

In this part, we give an overview of the analytical and operational characteristics of the devices that were evaluated. For the user friendliness, we rely on the evaluation that was performed in Finland, the country that tested the majority of the tests.

Urine tests

Mahsan

Country
The test was evaluated in GERMANY only.

Analytical results and comments

Table 39: Analytical results for Mahsan

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	157	88%	99%	97%	97%	97%
Cannabinoids	148	97%	91%	90%	97%	94%
Cocaine	156	100%	93%	55%	100%	94%
Opiates	137	n/a	97%	0%	100%	97%

Mahsan comes close to meet our analytical criteria for amphetamines, cannabinoids and cocaine.
For opiates the results are good, but as only negative samples were present the sensitivity can not to be calculated.
Mahsan is an 'aggressive' test for cannabinoids and cocaine.

Advantages

- Easy handling
- Few failures (0.2%)
- Low volume needed
- Suitable card size

Disadvantages

- Metamphetamine not included
- Risk of contamination with urine during the test procedure
- Long time of reaction when used at low temperatures
- 2.7% of results are doubtful

Dipro Drugscreen 5 panel test

Country
It was evaluated in BELGIUM only.

Analytical results and comments

Table 40: Analytical result for Dipro Drugscreen 5 panel test

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	126	69%	100%	100%	77%	85%
Metamphetamine	122	82%	100%	100%	85%	91%
Combined Amp + Metamph.	122	97%	100%	100%	97%	98%
Cannabinoids	123	99%	92%	97%	97%	97%
Cocaine	128	100%	99%	95%	100%	99%
Opiates	34	100%	85%	64%	100%	88%

Dipro meets our analytical criteria for the combined use of amphetamine and methamphetamine, cannabinoids and cocaine.
It could be considered ‘aggressive’ for opiates while it is ‘conservative’ for amphetamine and metamphetamine

Advantages
- Very well accepted by Police for its design (diptest)
- Low volume needed
- No failures

Disadvantages
- High number of doubtful results (2.3%)

Triage

Country
It was evaluated in FINLAND and ITALY.

Analytical results and comments

Table 41: Analytical results for Triage

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	395	89%	99%	93%	99%	98%
Benzodiazepines	394	94%	99%	94%	99%	98%
Cannabinoids	396	84%	99%	97%	96%	96%
Cocaine	396	95%	100%	100%	100%	100%
Opiates	396	100%	99%	71%	100%	99%

The test met the analytical criteria for benzodiazepines, cocaine and opiates.
It comes very close to satisfying the analytical criteria for amphetamines and cannabinoids.
Triage is 'conservative' for cannabinoids.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (good): ease of performance 1.7, ease of interpretation 2.8, reliability 2.6, appearance (look and size) 2.0.

Advantages

- Only few drops required (I)*
- Easy to read because of good result lines (I, FIN)
- No doubtful or failed results reported

Disadvantages

- Long measurement time, approximately 15 minutes, which is much longer than the other tests (I)
- It has been considered too difficult in respect of training requirements.(I)
- Very complicated to use (I, FIN). Two pipetting steps are needed, which is very difficult to perform at the roadside.
- Static electricity (FIN)

*In parenthesis the countries that mention the advantage or disadvantage.

Cortez

Country
It was evaluated in FINLAND, FRANCE, GERMANY, NORWAY and SPAIN.

Analytical results and comments

Table 42: Analytical results for Cortez

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	361	84%	94%	84%	94%	92%
Metamphetamine	186	16%	100%	100%	63%	66%
Combined amphet. + methamphet.	186	87%	93%	89%	91%	90%
Benzodiazepines	189	81%	84%	92%	65%	82%
Cannabinoids	369	95%	95%	92%	97%	95%
Cocaine	393	85%	98%	58%	99%	97%
Opiates	387	98%	95%	76%	100%	95%

Meets the analytical criteria for cannabinoids and opiates.
The test for metamphetamine has very poor sensitivity.
It is an 'aggressive' test for cocaine and opiates and 'conservative' for benzodiazepines.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.9, ease of interpretation 1.3, reliability 1.7, appearance (look and size) 2.5.

Advantages

- Few failed results (<1%)
- Suitable card size (D)
- Easy handling (FIN, D, N)
- Little sample was needed (N)
- Short time of reaction (N)

Disadvantages

- Risk of contamination with urine (D)
- Long time of reaction when employed at low temperatures (D)
- Reading was difficult in some cases (N)
- Very weak result lines (FIN, N)

Rapid Drug Screen

Country
It was evaluated in BELGIUM, FRANCE, GERMANY, ITALY and SCOTLAND.

Analytical results and comments

Table 43: Analytical results for Rapid Drug Screen

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	578	76%	100%	98%	97%	97%
Metamphetamine	468	83%	99%	92%	97%	97%
Combined amphet. + methamphet.	468	98%	99%	93%	100%	99%
Benzodiazepines	219	91%	98%	67%	100%	97%
Cannabinoids	571	97%	90%	78%	99%	92%
Cocaine	580	100%	98%	78%	100%	98%
Opiates	472	98%	95%	65%	100%	95%

The test met the analytical criteria for amphetamine and methamphetamine (if both tests are combined), benzodiazepines, cocaine and opiates.
It is an 'aggressive' test for cannabinoids, cocaine and opiates; it is 'conservative' for amphetamine, metamphetamine and benzodiazepines.

Advantages

- Few doubtful and failed results (<1%)
- Metamphetamine included (D, B)
- Suitable cup size (D)
- Easy handling (D, B, Scot)
- Good interpretation of results (B, Scot)
- If not too much urine available, possibility to pipette (D)
- Fast test (I)
- The bag supplied could be used to storage the card after use (Scot)

Disadvantages

- Risk of contamination with urine after removing the test card (D)
- Long time of reaction when employed at low temperatures (D)
- Test card still wet after use (D)
- A large volume of urine needed (I), but in that case, the possibility to pipette the urine onto the card exists (D).

Syva â RapidCup d.a.u.

Country
It was evaluated in FINLAND and GERMANY.

Analytical results and comments

Table 44: Analytical results for Syva RapidCup

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	52	100%	100%	100%	100%	100%
Metamphetamine	47	30%	93%	75%	64%	66%
Cannabinoids	88	97%	92%	90%	98%	94%
Cocaine	90	100%	98%	75%	100%	98%
Opiates	85	100%	96%	25%	100%	96%

Only few samples were analysed for amphetamines, but the results seem promising.
Meets our analytical criteria for cocaine and opiates. It comes close to be a good test for cannabinoids.
It is a very 'conservative' test for metamphetamine, with low sensitivity

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 1.8, ease of interpretation 2.3, reliability 2.3, appearance (look and size) 1.3.

Advantages

- Metamphetamine included (D)
- Operating instructions very clear (D)
- Easy handling (D)
- Low risk of contamination of urine (D)
- Collection cup and test in one (FIN)

Disadvantages

- Cup too big, transport and storage problem (D, FIN)
- Difficult to open and close (D, FIN)
- Many failures (5.8%)
- 1.7 % of results doubtful
- Large sample volume needed (D, FIN)
- Long reaction time when employed at low temperatures (D)

Syva â RapidTest d.a.u.

Country
It was evaluated in BELGIUM, FINLAND, FRANCE, NORWAY and SCOTLAND.

Analytical results and comments

Table 45: Analytical results for Syva RapidTest

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	874	88%	99%	96%	97%	97%
Metamphetamine	561	83%	100%	100%	98%	98%
Combined amphet. + methamphet.	558	97%	100%	100%	100%	100%
Benzodiazepines	354	98%	84%	53%	100%	86%
Cannabinoids	880	93%	100%	99%	96%	97%
Cocaine	904	96%	99%	91%	100%	99%
Opiates	782	95%	96%	73%	99%	96%

Meets our analytical criteria for the combined use of amphetamine and methamphetamine, cannabinoids, cocaine and opiates.
It is a 'conservative' test for amphetamine, metamphetamine and for cannabinoids.
It is 'aggressive' for benzodiazepines and opiates.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.5, ease of interpretation 1.8, reliability 2.0, appearance (look and size) 2.5.

Advantages

- Good pipette (FIN, Scot)
- Easy to perform (FIN, N, Scot)
- No failures (FIN)
- Low percentage of doubtful results (<1%)
- Easy to read (N, Scot)

Disadvantages

- Sometimes more than 3 drops of urine are needed (FIN)
- Not easy to perform roadside (N)

OnTrak TesTcup5

Country
It was evaluated in BELGIUM, FINLAND, GERMANY, NORWAY, SCOTLAND and SPAIN.

Analytical results and comments

Table 46: Analytical results for OnTrak TesTcup

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	527	75%	100%	97%	94%	95%
Cannabinoids	542	92%	93%	90%	95%	93%
Cocaine	570	95%	99%	90%	100%	99%
Opiates	474	97%	93%	68%	99%	94%

The methamphetamine test was evaluated on a small number of samples in Belgium, and the results are not included here.
The OnTrak TesTcup meets our analytical criteria for cocaine.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.0, ease of interpretation 2.8, reliability 2.5, appearance (look and size) 2.3.

Advantages

- Low percentage of doubtful results (<1%)
- Easy to perform, also roadside (N, E, Scot)
- Collection cup and test in one (FIN, N, D, Scot)
- Easy to read results (N, E, B, Scot), the psychological aid given by the cross pattern on the results' plate was an advantage (Scot)
- Operating instruction clear and informative (D)
- Low risk of contamination of urine (D)

Disadvantages

- High level of failed results (5%), which could be explained by lack of familiarisation.
- Large amount of urine needed (N, D, S)
- Needs careful closing
- Long reaction time when employed at low temperatures (D)
- Adequate training is necessary (B)

SureScreen 6 Drug MultiTest

Country
It was evaluated in FINLAND

Analytical results and comments

Table 47: Analytical results for SureScreen6DrugMultiTest

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	121	85%	96%	93%	90%	91%
Metamphetamine	106	33%	98%	94%	67%	71%
Combineds amphet + metamph.	106	93%	95%	93%	95%	94%
Benzodiazepines	102	89%	88%	94%	78%	88%
Cannabinoids	114	76%	99%	97%	88%	90%
Cocaine	116	100%	100%	100%	100%	100%
Opiates	118	82%	97%	75%	98%	96%

It meets the analytical criteria for on-site tests for cocaine.
It is a 'conservative' test for both amphetamine and metamphetamine

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.8, ease of interpretation 2.4, reliability 2.2, appearance (look and size) 2.0.

Advantages

- Easy to use and economical
- No failures and doubtful results

Disadvantages

- Messy
- Sometimes weak lines

Rapitest Multidrug panel

Country
It was evaluated in FINLAND.

Analytical results and comments

Table 48: Analytical results for Rapitest Multidrug panel

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	95	86%	96%	95%	89%	92%
Benzodiazepines	92	95%	82%	92%	88%	91%
Cannabinoids	95	70%	98%	97%	80%	85%
Cocaine	96	75%	100%	100%	99%	99%
Opiates	97	78%	99%	88%	98%	97%

It is a ‘conservative’ tests for cannabinoids and ‘aggressive’ for cocaine

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.9, ease of interpretation 2.2, reliability 2.3, appearance (look and size) 2.5.

Advantages

- No failures and doubtful results
- Easy to use
- The part that had been dipped in urine can be protected by a cover

Disadvantages

- Sometimes weak lines

Status DS

Country
It was evaluated in FINLAND

Analytical results and comments

Table 49: Analytical results for Status DS

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	92	85%	96%	93%	90%	91%
Cannabinoids	92	80%	100%	100%	86%	91%
Cocaine	92	100%	99%	75%	100%	99%
Opiates	94	100%	97%	67%	100%	97%

Status DS meets our analytical criteria for cocaine and opiates. Status DS is a 'conservative' test for cannabinoids while it is 'aggressive' for opiates.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.5, ease of interpretation 2.2, reliability 2.1, appearance (look and size) 2.3.

Advantages

- No failures and doubtful results

Disadvantages

- Stiff pipette

Frontline

Country
It was evaluated in GERMANY

Analytical results and comments

Table 50: Analytical results for Frontline

	n	***Sensitivity***	***Specificity***	***PPV***	***NPV***	***Accuracy***
Analyte						
Amphetamines	68	100%	56%	45%	100%	68%

The sample size was small for amphetamines and for the other drugs too small for any evaluation.
Frontline is an 'aggressive' test for amphetamine.

Advantages

- Very simple design
- Short, clear and informative operating instructions
- Easy handling
- No prolongation of reaction time in case of low temperature
- Usable even in case of small volume of urine
- No failures

Disadvantages

- No cup provided
- High risk of contamination with urine
- No control line
- Too many doubtful results (9%)

Oral fluid and sweat tests

Drugwipe

Country
It was evaluated in BELGIUM, FINLAND, GERMANY, ITALY, NORWAY and SPAIN.

Analytical results and comments

Table 51: Analytical results for Drugwipe

Oral fluid	*n*	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy*
Analyte						
Amphetamines	120	87%	55%	85%	59%	78%
Cocaine	118	59%	92%	71%	87%	84%
Opiates	46	41%	79%	64%	59%	61%
Sweat						
Amphetamines	63	97%	67%	98%	50%	95%
Cocaine	22	77%		100%		77%
Opiates	9	89%		100%		89%

The accuracy of this device is not satisfactory when one compares it with the reference method.
In oral fluid, the sensitivity is quite close to 90% for amphetamines but the specificity is much lower.

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): ease of performance 2.7, ease of interpretation 1.8, reliability 1.9, appearance (look and size) 2.6.

Advantages

- Very simple for training purposes (I)
- Easy to use (I, N, B, E, FIN, D)
- Only few drops of oral fluid needed (I, N, D)
- Less time-consuming (I, N, B, E)
- Easy to use for Police officers on motorbike (E)
- It can be used for both oral fluid and sweat (D)
- Very clear and informative operating instructions (D)
- Very low risk of contamination with oral fluid (D)

Disadvantages

- Many doubtful results (2,5 %) because reading was difficult (I, N, B, Fin), the problem was solved after introduction of an electronic reader into the trial
- Cannabinoids and benzodiazepines lacking (N, D)
- Single test (N, D)
- No reference line included (D)
- Electronic reader unpractical to use (N)
- Water needed to perform the test (N, D)
- One specific production batch has failed (= 4% of all tests supplied, 7% of the tests recorded in the data-base)

Cozart Rapiscan

Country
It was evaluated in FINLAND, NORWAY and SPAIN.

Analytical results and comments

Table 52: Analytical results for Cozart Rapiscan (in comparison to oral fluid)

	n	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy*
Analyte						
Amphetamines	80	83%	68%	87%	60%	79%
Benzodiazepines	60	37%	48%	37%	48%	43%
Cannabinoids	9	13%	0%	50%	0%	11%
Cocaine	33		100%		100%	100%
Opiates	37	61%	26%	44%	42%	43%

User friendliness (evaluation in Finland, 5)

The test scored as follows on a scale from 1 (bad) to 3 (excellent): by health professionals in a clinic: ease of performance 2, ease of interpretation 2.8, reliability 1, appearance (look and size) 2.3. By police officers: ease of performance 1.8, ease of interpretation 2.9, reliability 2.3, appearance (look and size) 2.5.

Advantages

- Possibility of testing several drugs simultaneously (FIN, E)
- Availability of an electronic reader (FIN)
- Reference line (E)
- Very good reading (E)
- No doubtful results at all (electronic reader)

Disadvantages

- Difficult to use (FIN, N, E)
- Sample handling complicated (Fin, N, E)
- Too many menu options on the reader (FIN)
- Time consuming (N, E)
- No printed report (E). However, a printer was presented during the June 2000 Rosita meeting
- Extra time needed to train police (N)
- Electronic reader can be disturbed by police-car radio (N)
- Too many failed tests (15%). One batch was found to be defective.

Avitar ORALscreen

Country
It was evaluated in GERMANY and SCOTLAND.

Analytical results and comments

Table 53: Analytical results for ORALscreen

	n	*Sensitivity*	*Specificity*	*PPV*	*NPV*	*Accuracy*
Analyte						
Cannabinoids	190	25%	84%	3%	98%	83%
Cocaine	180		99%	0%	100%	99%
Opiates	183	57%	93%	24%	98%	91%

The Oralscreen for cannabis has a lot of false positives, and a PPV of only 3%.
In its present form is not reliable for the detection of THC in oral fluid. For cocaine and opiates, the evaluation was performed in a sample series with a very low prevalence.

Advantages

- Operating instruction acceptable (D)

Disadvantages

- Difficult collection of the sample (Scot, D)
- Risk of contamination of the personnel with oral fluid (Scot)
- Not good performance with viscous oral fluid (Scot)
- Difficult to read (very faint lines) (Scot)
- Many oral fluid specimens of positive donors in blood failed to migrate in the on-site device (Scot)
- No amphetamine included
- Large sample volume of oral fluid needed
- Approximately 1 % failed and doubtful tests
- Not accepted by the police

Conclusions

In several countries, the Rosita evaluations were the first experience police officers had with roadside drug tests.

In general, the use of roadside tests offered the following advantages in the enforcement of drug-driving laws, both in countries with an impairment-type law and in countries with 'per se' laws:

- It gives confidence to the police officer. Without an on-site tool to confirm his impression, a police officer will be more reluctant to press charges;
- On-site tests save time, because the subject does not need to be transported to the police station for testing or blood sampling (although in some settings this would only apply to the subjects who test negative, as all who test positive are brought to the police station for evaluation by a medical doctor and/or blood sampling);
- Subjects are impressed by the result (even more so if the procedure was complex or if the result is read electronically) and confesses when confronted with the positive result, sometimes after a long and vehement denial.
- On-site tests save money, because the more expensive confirmation tests will be limited to cases that are much more likely to be positive.
- The publicity that accompanied the use of roadside tests (e.g. in Finland) was considered (by the police officers) have a preventive effect, because people thought they could be controlled everywhere (while in fact the number of actual tests used was limited).

In the German Federal State Saarland, the tests were so successful that purchasing roadside tests was budgeted for 2001 by the minister of the Interior. This is also a consequence of the professional and effective test procedure, done by the three traffic police departments in the state, which also tripled the number of positive cases during the ROSITA project. In Norway, NIFT frequently receives requests for further test devices.

There was a majority of countries that favoured oral fluid as a matrix, but the present devices are not satisfactory in terms of ease and duration of use, sensitivity and reliability. However, many development efforts are under way (27, 28, and communications by Securetec, Avitar and Cozart Bioscience during Rosita meetings), and new devices or prototypes are expected soon (e.g. by Orasure Inc./Dräger Sicherheitstechnik GmbH and Lifepoint Inc.).

Before oral fluid can be used for roadside testing, the following criteria should be met:

- a simple and validated sampling procedure, that takes little time;
- a test that needs a small sample volume (100 µL) and that can also analyse viscous samples;
- development of devices targeted to the parent molecules, with suitable detection limits, e.g. 2 ng/mL of THC.
- an electronic reader.

For sweat, only one device, the Drugwipe, is available. Relatively good results were seen for some drugs with Drugwipe.

In the meantime, police officers in some countries will settle for imperfect devices, although we strongly advise against using any of the present devices for benzodiazepines or cannabis detection (the newer improved devices presented by the manufacturers still have to be evaluated). In other countries, urine will be used. The experience with Rosita has shown that some urine on-site devices have good to very good performance.

Finally, one should not forget that on-site test are only preliminary tests, and that a sanction can only be based on a positive analysis in a laboratory, with or without the documentation of driving impairment (depending on the type of legislation).

ABBREVIATIONS

On-site tests

Table 54: Abbreviations of the On-site test

Abbreviations	*Name of the test*	*Manufacturer*
AVIT	ORALscreen™	Avitar Technologies, Inc.
CORT	5 Drug Screen InstaStrip In Finland: OneStep DipDrugscan	Cortez Diagnostics
DIP	Dipro Drugscreen 5 panel test	Dipro Diagnostic Products
DW	Drugwipe®	Securetec GmbH
FRON	Frontline®	Roche Diagnostics Corp.
MD	Rapitest Multidrug panel	Morwell Diagnostics GmbH
MAHS	Mahsan	Mahsan Diagnostika
RAPI	Cozart Rapiscan	Cozart bioscience Ltd.
RDS	Rapid Drug Screen™	American Bio Medica Corp.
SRC	Syva® RapidCup d.a.u™.	Dade Behring
SRT	Syva® RapidTest d.a.u.™	Dade Behring
SDS	Status DS™	Lifesign LLC.
SS	SureScreen 6Drug Multi Test	SureScreen diagnostics Ltd.
TCUP	OnTrackTesTcup®5	Roche Diagnostics Corp.
TRIA	Triage®8	Biosite Diagnostics
TST	OnTrack TesTstik®	Roche Diagnostics Corp.

* In Finland (Syntron Bioresearch Inc; USA) was used

Analytes

11OHTHC=11-hydroxyTHC
6-AM=6-acetyl morphine
A= amphetamine
AX= amphetamine and/or ecstasy
BDB= benzodioxazolylbutanamine
BE= Benzoylecgonine
BENZODIAZ= Benzodiazepines
EME= Ecgonine methyl ester
MA= Metamphetamine
MBDB= Methylbenzodioxazolylbutanamine
MDA= Methylenedioxyamphetamine
MDEA= Methylenedioxyethylamphetamine
MDMA= ecstasy, Methylenedioxymethylamphetamine
MET(AMPHET)= amphetamine and/or Metamphetamine
THC= δ-9-tetrahydrocannabinol
THCCOOH= 11-nor-δ-9-tetrahydrocannabinol carboxylic acid
X= ecstasy

Participating countries

B	Belgium
D	Germany
E	Spain
F	France
FIN	Finland
I	Italy
N	Norway
Scot	Scotland

Miscellaneous

AUC	=	area under curve
CBFT	=	Centre for Behavioural and Forensic Toxicology, Padova, Italy
FN	=	false negative
FP	=	false positive
GC-MS	=	gas chromatography-mass spectrometry
ILM	=	Institute of Legal Medicine
NA	=	not applicable or not available
ND	=	not done
NIFT	=	National Institue of forensic Toxicology, Oslo, Norway
NPV	=	predictive value of negative test
P	=	p value (probability in the sense of statistical significance)
PPV	=	predictive value of positive test
R	=	coefficient of correlation
ROC	=	receiver operating characteristic curves or relative operating characteristic curves
SD	=	Standard deviation
TN	=	true negative
TP	=	true positive

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Deliverable D4a - Finland

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: KTL, Finland

Authors: Marielle GRÖNHOLM and Pirjo LILLSUNDE

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INTRODUCTION

In the Finnish part of the ROSITA evaluation both urine and saliva devices were included. The saliva tests were performed roadside and urine test in a laboratory. All samples were obtained from drivers suspected to be driving under the influence of drugs. Police started to perform an impairment evaluation (1.11.1999) (appendix 1). The law on coercive means allows the police to do tests, for example behavioural and on-site tests. The physicians evaluation was reformed in order to recognise the symptoms of other drugs as well as the symptoms of alcohol (1.2.2000) (appendix 2). The law (penal code 23) was slightly modified 1.11.1999 so that the driving under influence of drugs and driving under the influence of alcohol were combined into the same paragraph. At the same time, driving under the influence of drugs was divided into two crime categorises. The material for police training was produced (a book, transparencies and a CD-ROM). Police officers in six towns were trained (total of 400) to recognise the symptoms of drug use of drivers under the influence of drugs and to perform behavioural tests. Simultaneously they were trained to do the on-site tests. The collaborators of the National Public Health Institute (KTL) in Finland were; the Ministry of Interior/Police Department (Mr. Pertti Luntiala, General Inspector), Ministry of Transportation and the Forensic Institute/Helsinki University (Prof. Antti Penttilä).

METHODS

The testing was performed during September 1999 until May 2000 on drivers suspected to be under the influence of drugs. The Rapiscan and/or Drugwipe tests were performed roadside or at police stations when the police suspected drug use. The urine tests were not suitable to be tested roadside according to the police. Therefore police and laboratory staff mainly performed the urine tests at the Laboratory of Drug abuse. If driving under the influence of drugs was suspected, the police performed an impairment evaluation (from 1.11.1999). A physician made the clinical performance test and took the blood and urine samples. The handling of drunken and drugged driving cases in Finland is illustrated in figure 1.

The samples were sent to the Laboratory of Substance Abuse where they were stored at 5 °C before analyses. Oral fluid samples were collected with the Rapiscan and diluted with the elution buffer. The sample was separated from the cotton and stored in a glass test tube at –20 °C. The delay between oral fluid sampling and analyses varied from a couple of days to several months. The on-site urine tests were performed normally a few weeks after the sampling. The urine samples were tested for amphetamines (AMP), cannabinoids (THC), opiates (OPI), benzodiazepines (BZO), cocaine (COC), barbiturates, methadone and PCP with the Dade Behring VIVA analyser (EMIT). Additionally a TLC-system (including benzodiazepines) combined with GC/MS screening (including amphetamines) was performed (1) on the urine. This comprehensive screening system detects approximately 200 drugs. Positive illicit drug findings were confirmed separately (except amphetamines) in urine. Quantitation analyses on blood was performed as two parallel analyses.

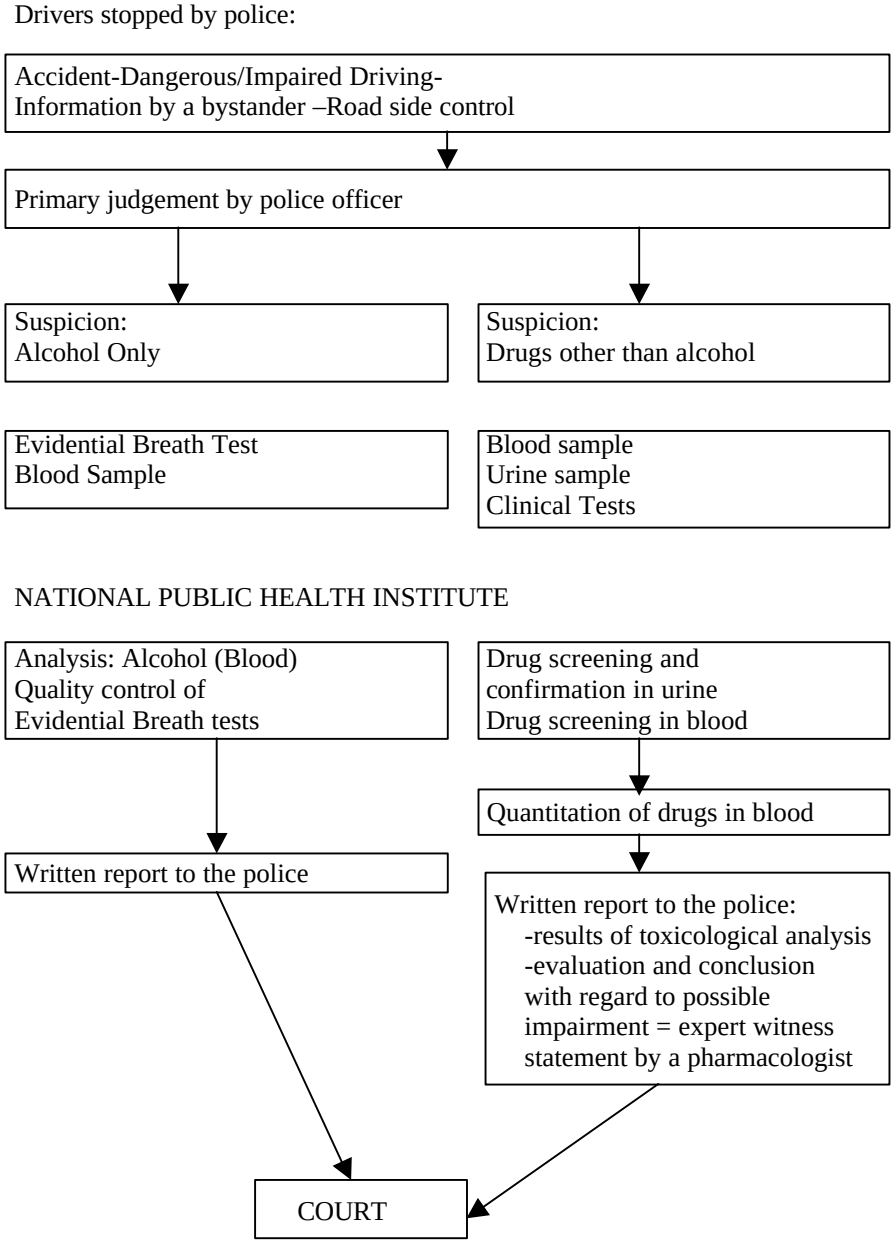

Figure 1: Handling of drunken and drugged driving cases in Finland

The urine on-site tests included were; Syva Rapid Cup d.a.u. 4 (SRC) (Dade Behring Inc., USA/ THC, OPI, BZO, MET), Syva Rapid test d.a.u. 4 (SRT) (Dade Behring Inc., USA/ AMP, THC, COC, OPI), Surescreen (SS) (Surescreen Diagnostics Ltd., UK/ AMP, THC, COC, OPI, BZO, MET), Triage 8 (TRI) (Biosite Diagnostics, USA/ AMP, THC, COC, OPI, BZO, MET), OneStep DipDrugscan 6 (DD) (Syntron Bioresearch Inc., USA/ AMP, THC, COC, OPI, BZO, MET), Rapitest Multidrug (MD) (Morwell Diagnostics GmbH, Switzerland/ AMP, THC, COC, OPI, BZO), Status DS (SDS) (LifeSign, LLC, USA /AMP, THC, COC, OPI), Ontrak TesTcup (RTC) (Roche Diagnostics Systems Inc., USA/ AMP, THC, COC, OPI) and Ontrak TesTstik (RTS) (Roche Diagnostics Systems Inc., USA/BZO). The two tests for oral fluid testing were Rapiscan (COZ) (Cozart Biosciences Ltd., UK/ AMP, THC, COC, OPI, BZO) and Drugwipe (DW) (Securetec GmbH, Germany/ AMP, OPI).

Cut-off concentration's of 20 ng/ml for cannabinoids, 200 ng/ml for benzodiazepines, 300 ng/ml for amphetamines (class specific), benzoylecgonine and opiates and additionally 1000 ng/ml for amphetamines (monoclonal) were applied for the EMIT screening.

The cut-offs for the confirmation methods for blood is listed in table 1, urine in table 2 and oral fluid in table 3. The criteria for accepting a GC/MS results were:

- the peak (MS) heights of the ions correspond well to each other in standards and samples
- the ion peaks in the selected ion chromatogram (GC) are on top of each other
- the retention times can vary ± 5% between standards and samples
- if the cut-off standard is not detected, all samples below the lowest detectable standard are reanalyzed
- control samples are between acceptable limits
- zero sample is negative considering the drugs analyzed

Table 1: Analytes, standard concentrations, control concentrations, limit of detection (LOD) and limit of quantitation (LOQ=used cut-off) for blood.

BLOOD	**standards (mg/l)**	**control (mg/l)**	**LOD**	**LOQ**
amphetamines				
amphetamine	1000, 500, 100, 0, 4000	500	20	100
metamphetamine	1000, 500, 100, 0, 4000	500	30	100
MDA	1000, 500, 100, 0, 4000	500	50	100
MDMA	1000, 500, 100, 0, 4000	500	40	100
MDEA	1000, 500, 100, 0, 4000	500	100	100
MBDB	1000, 500, 100, 0, 4000	500	-	100
BDB	1000, 500, 100, 0, 4000	500	-	100
pseudoephedrine	1000, 500, 100, 0, 4000	500	100	100
opiates				
morphine	500, 250, 50, 0	200	-	50
ethylmorphine	500, 250, 50, 0	200	-	50
Codein	500, 250, 50, 0	200	-	50
MAM	500, 250, 50, 0	200	-	50
THC				
Δ9THC	10, 5, 2,5, 1, 0,5, 0	2,5	0.25	0.5
Benzodiazepines				
diazepam	1000, 500, 100, 50, 0	700	30	50
desmethyldiazepam	1000, 500, 100, 50, 0	700	10	50
oxazepam	1000, 500, 100, 50, 0	700	10	50
temazepam	1000, 500, 100, 50, 0	700	10	50
chlordiazepoxide	2000, 1000, 200, 0	1400	200	200
midazolam	300, 150, 30, 15, 0	210	3	15
alprazolam	100, 50, 10, 0	70	5	10
lorazepam	100, 50, 10, 0	70	5	10
clonazepam	100, 50, 10, 0	70	5	10
nitrazepam	100, 50, 10, 0	70	5	10
triazolam	100, 50, 10, 0	70	10	10
zopiclone	500, 250, 50, 0	350	25	50
zolpideme	100, 50, 10, 0	70	1	10

Table 2: Analytes, standard concentrations, control concentrations, limit of detection (LOD) and limit of quantitation (LOQ=used cut-off) for urine.

URINE	**standards (mg/l)**	**control (mg/l)**	**LOD**	**LOQ**
amphetamines				
amphetamine	2000, 1000, 200, 0	500	50	200
metamphetamine	2000, 1000, 200, 0	500	50	200
MDA	2000, 1000, 200, 0	500	50	200
MDMA	2000, 1000, 200, 0	500	50	200
MDEA	2000, 1000, 200, 0	500	50	200
MBDB	2000, 1000, 200, 0	-	50	200
BDB	2000, 1000, 200, 0	-	50	200
pseudoephedrine	2000, 1000, 200, 0	500	50	200
ephedrine	2000, 1000, 200, 0	500	50	200
opiates				
morphine	2000, 1000, 200, 0	500	50	200
ethylmorphine	2000, 1000, 200, 0	500	50	200
codein	2000, 1000, 200, 0	500	50	200
6-MAM	500, 250, 50, 0	100	20	50
dihydrocodein	2000, 1000, 200, 0	500	50	200
pholcodine	2000, 1000, 200, 0	-	-	-
THCC				
THCC	200, 100, 15, 7, 0	40-50	5	7
Benzodiazepines (GC/MS)				
diazepam	1000, 500, 100, 50, 0	700	30	50
desmethyldiazepam	1000, 500, 100, 50, 0	700	10	50
oxazepam	1000, 500, 100, 50, 0	700	10	50
temazepam	1000, 500, 100, 50, 0	700	10	50
chlordiazepoxide	2000, 1000, 200, 0	1400	200	200
midazolam	300, 150, 30, 15, 0	210	3	15
alprazolam	100, 50, 10, 0	70	5	10
Benzodiazepines (TLC)				
Hydrolysis products				
MACB	5000, 500	500	<500	-
ACB	5000, 500	500	<500	-
ANB	5000, 500	500	<500	-
ACCB	5000, 500	2000	<500	-
ANCB	5000, 500	-	<500	-

Table 3: Analytes, standard concentrations, control concentrations, limit of detection (LOD) and limit of quantitation (LOQ=used cut-off) for oral fluid.

ORAL FLUID	standards (ng/ml)*	control (ng/ml)	LOD	LOQ
amphetamines				
amphetamine	1000, 500, 100, 50, 25	500	-	50 (16,7)
metamphetamine	1000, 500, 100, 50, 25	500	-	50 (16,7)
MDA	1000, 500, 100, 50, 25	500	-	50 (16,7)
MDMA	1000, 500, 100, 50, 25	500	-	50 (16,7)
opiates				
morphine	500, 250, 50, 25	200	-	50 (16,7)
ethylmorphine	500, 250, 50, 25	200	-	50 (16,7)
codein	500, 250, 50, 25	200	-	50 (16,7)
6-MAM	500, 250, 50, 25	200	-	50 (16,7)
dihydrocodein	-	-	-	-
pholcodine	-	-	-	-
THC				
Δ9THC	200, 100, 15, 7, 3.5, 0	2,5	-	1.5 (0,5)
Benzodiazepines				
diazepam	1000, 500, 100, 50, 0	700	30	50 (16,7)
desmethyldiazepam	1000, 500, 100, 50, 0	700	10	50 (16,7)
oxazepam	1000, 500, 100, 50, 0	700	10	50 (16,7)
temazepam	1000, 500, 100, 50, 0	700	10	50 (16,7)
chlordiazepoxide	2000, 1000, 200, 0	1400	200	200 (66,6)
midazolam	300, 150, 30, 15, 0	210	3	15 (5,0)
alprazolam	100, 50, 10, 0	70	5	10 (3,3)

* the actual concentrations in the standards were one third of the concentrations mentioned above (Buffer solution:oral fluid 3:1)

Questionnaire

The urine on-site tests were performed at the Laboratory of substance Abuse by 2 non professionals (police) and 4 laboratory staff. The oral fluid tests were performed by trained police officers in the different towns on-site.
The persons performing the urine on-site tests evaluated some user friendliness characteristics of the devices on a scale of 1 (bad) to 3 (good).
A questionnaire (appendix 3) was answered by the police (non professionals) on the characteristics of the Rapiscan, Drugwipe and roadside testing. An a-clinic (health care professionals, not laboratory staff) using the Cozart Rapiscan also evaluated the user friendliness of the device.

GC/MS was used as the confirmation method (reference method). For the benzodiazepines in urine also TLC was accepted as reference method. In discrepancy cases an GC/MS quantitation analysis on benzodiazepines was performed additionally to the TLC.
Negatives below the on-site tests cut-of values were concluded as true negatives (TN). Positives with substances other than listed in the manufacturers cross reactivity lists very concluded as false positives (FP). Sensitivities, selectivities, accuracies, positive predictive values (PPV) (the probability that a positive on-site result is a true positive) and negative predictive values (NPV) (the probability that the on-site test result is a true negative) were calculated (10).

RESULTS

URINE

Analytical results

A total 545 urine samples were tested with on-site devices. The number of positives for each analyte by reference method is TP+FN and for the onsite methods TP+FP. Calculation of accuracy, sensitivity, specificity for the on-site assays, using the reference method as the gold standard are listed for the amphetamines in table 4, cannabinoids in table 6, opiates in table 8 and benzodiazepines in table 10. Sometimes the Syva Rapid test needed more than 3 drops of urine (as stated by the manufacturer), but with an addition it was possible to perform the test successfully. Because of lack of sample (less than 40 ml) 11 Syva Rapid Cup's failed.

Amphetamines

Table 4: Amphetamine results

	Syva Rapid Test	*Surescreen*	*Triage*	*Dip Drugscan*	*Multidrug*	*Status DS*	*Roche TesTstik*
Total	248	116	98	196	99	94	113
TP	100	45	45	76	41	40	35
FP	3	0	1	7	0	0	0
FN	1	3	4	6	2	4	1
TN	144	68	48	107	56	50	77
Sensitivity	99.0 %	93.8 %	91.8 %	92.7 %	95.3 %	90.9 %	97.2 %
Specificity	98.0 %	100.0 %	98.0 %	93.9 %	100.0 %	100.0 %	100.0 %
PPV	99.0 %	93.8 %	91.8 %	92.7 %	95.3 %	90.9 %	97.2 %
NPV	99.3 %	95.8 %	92.3 %	94.7 %	96.6 %	92.6 %	98.7 %
Accuracy	98.4 %	97.4 %	94.9 %	93.4 %	98.0 %	95.7 %	99.1 %

Table 5: False Negative Amphetamine results, concentrations in ng/ml

Sample no	*Amphetamine*	*Metamphetamine*	*MDA*	*Ephedrine*	*Negative on*
00-36	153 120	16 900	0	15 270	All urine devices
00-40	1900	0	0	0	SS, DD, MD
00-47	3130	30	0	0	SS, TRI
00-76	1210	960	1210	0	TRI
00-96	3640	960	0	0	SS, DD, SDS
00-180	2060	0	0	0	TRI
00-104	84 540	0	0	0	DD
00-112	73 770	0	0	0	DD
00-169	>> 5000	0	0	0	DD
00-42	5 000	0	0	0	SDS
00-58	>> 5000	0	0	0	SDS

The results for amphetamines using different on-site test are presented in table 4. In two of the false positive Syva Rapid tests, the Triage false positive and six of the Dip Drugscan false positive results no amphetamines were detected. Metamphetamine gave a positive result though not listed in the amphetamine crossreactivity list in one of the Syva Rapid test results and one Dip Drugscan result. The large amount of false positive Dip Drugscan results might be explained with the difficulty of interpreting the test result (table12). The false negatives are listed in table 5, some of them at rather high concentrations.

Cannabinoids

Table 6: Cannabinoid results

	SRC	*SRT*	*SS*	*TRI*	*DD*	*MD*	*SDS*	*RTC*
Total	48	248	116	98	205	99	94	113
TP	18	90	33	34	80	31	33	37
FP	0	0	1	1	3	0	0	0
FN	1	2	1	1	1	3	1	1
TN	29	156	81	62	121	65	60	75
Sensitivity	94.7 %	97.8 %	97.1 %	97.1 %	98.8 %	91.2 %	97.1 %	97.4 %
Specificity	100.0 %	100.0 %	98.8 %	98.4 %	97.6 %	100.0 %	100.0 %	100.0 %
PPV	94.7 %	97.8 %	97.1 %	97.1 %	98.8 %	91.2 %	97.1 %	97.4 %
NPV	96.7 %	98.7 %	98.8 %	98.4 %	99.2 %	95.6 %	98.4 %	98.7 %
Accuracy	97.9 %	99.2 %	98.3 %	98.0 %	98.0 %	97.0 %	98.9 %	99.1 %

Table 7: False Negative Cannabinoid (THCCOOH) results, concentrations in ng/ml

Sample no	*THCCOOH*	*Negative on*
00-36	352	All urine devices
99-1163	73	SRT
00-27	123	MD
99-1992	68	MD

All urine devices had a cut off at 50 ng/ml. Both positives below 50 ng/ml and negatives above 50 ng/ml were observed, when confirmed with GC/MS. An explanation for the positives (nineteen cases) could be that only the major metabolite (tetrahydrocannabinolic acid) was analysed in the urine samples. In all false positives (Surescreen 1, Triage 1, Dip Drugscan 3 and Rapiscan 1) no THCCOOH or THC (Rapiscan) could be identified by GC/MS (table 6).
The concentrations of false negatives are given in table 7.

Opiates

Table 8: Opiate results

	SRC	*SRT*	*SS*	*TRI*	*DD*	*MD*	*SDS*	*RTC*
total	48	248	116	98	195	99	94	113
TP	1	42	9	8	21	7	5	8
FP	3	7	3	4	4	1	4	6
FN	0	0	1	0	0	1	0	0
TN	44	199	103	86	170	90	85	99
Sensitivity	100.0 %	100.0 %	90.0 %	100.0 %	100.0 %	87.5 %	100.0 %	100.0 %
Specificity	93.6 %	96.6 %	97.2 %	95.6 %	97.7 %	98.9 %	95.5 %	94.3 %
PPV	100.0 %	100.0 %	90.0 %	100.0 %	100.0 %	87.5 %	100.0 %	100.0 %
NPV	100.0 %	100.0 %	99.0 %	100.0 %	100.0 %	98.9 %	100.0 %	100.0 %
Accuracy	93.8 %	97.2 %	96.6 %	95.9 %	97.9 %	98.0 %	95.7 %	94.7 %

The opiate results are listed in table 8. All tested urine devices showed a response for pholcodine, although it was not listed in any of the crossreactivity tables. All pholcodine positives were concluded as false positives. The sensitivity for pholcodine varied between the devices. Syva Rapid Cup and Dip Drugscan tested positive for pholcodine three of three times, Syva Rapid Cup, Triage 8 and Roche TesTcup tested positive for pholcodine four of four times. Surescreen tested positive for pholcodine two of three times and Multidrug only one of three cases.
Other false opiate positives were obtained with Syva Rapid test (three cases) and Dip Drugscan (one case), without any opiate findings with GC/MS.

The false negatives and the opiate concentrations are shown in table 9.

Table 9: False Negative opiate concentrations in ng/ml

Sample no	*6-MAM*	*Morphine*	*Codeine*	*Device*
00-170	0	671	349	SS
99-1971	0	470	0	MD

Benzodiazepines

Table 10: Benzodiazepine results

	SS	*TRI*	*DD*	*RTS*
Total	104	97	196	89
TP	64	64	113	30
FP	1	0	1	2
FN	4	3	19	0
TN	35	30	63	57
Sensitivity	94.1 %	95.5 %	85.6 %	100.0 %
Specificity	97.2 %	100.0 %	98.4 %	96.6 %
PPV	94.1 %	95.5 %	85.6 %	100.0 %
NPV	89.7 %	90.9 %	76.8 %	100.0 %
Accuracy	95.2 %	96.9 %	89.8 %	97.8 %

Benzodiazepines are the most complicated group in on-site testing. The results are shown in table 10. Benzodiazepines on the market vary in different countries, and the tests are not be sensitive for all of them. Additionally sometimes crossreactivity for other medical drugs like mirtazapine and citalopram was seen.
The false negative benzodiazepine results for urine devices are presented in table 11.

Table 11 False Negative benzodiazepine concentrations in ng/ml

Sample no	*Temazepam*	*Nordiazepam*	*Oxazepam*	*Other benzodiazepines*	*Device*
99-1175	970	0	0	0	DD
99-1185	420	0	6550	midazolam 220	DD
99-1186	300	0	440	0	DD
99-1189	8590	0	440	0	DD
99-1201	0	920	2640	0	DD
99-1215	650	210	130	0	DD
99-1239	5390	0	0	0	DD
99-1242	490	0	0	0	DD
99-1252	8600	0	0	0	DD
99-1348	150	4700	400	Chlordiazepoxid 710	DD
99-1357	0	0	26230	0	DD
99-1395	0	0	4210	0	DD
99-1436	220	160	610	0	DD
99-1970	0	0	0	0	DD
99-1992	0	0	0	0	DD
00-110	0	0	0	0	DD
00-183	580	1140	110	0	TRI
00-2	0	0	0	Clonazepam	SS, DD
00-36	17 000	42	2370	Clonazepam 33, Alprazolam 180	SS, TRI, DD
00-50	0	0	0	Clonazepam	SS, TRI
00-96	270	58	350	0	DD

Practical results

Obtaining urine
The urine samples were obtained under supervision of police at health centres (in connection to blood sampling and physician's evaluation). The urine sampling was not obligatory. Sometimes it was not possible to get the urine sample immediately, so the driver got some water to drink or the urine was collected at a later time by the police and sent to KTL. Because the samples were tested in the laboratory it was possible to select samples with sufficient urine for the on-site testing. All urine samples have been tested for pH, creatinine, glutaraldehyde and nitrite (Adulta check).
Urine on-site testing is not suitable for road site testing in Finland. The public opinion in Finland is opposed to sampling at road side because of privacy reasons. Additionally it is not always possible to get a sample immediately and cold or rainy weather is also a problem. In addition the longer detection window might be problematic; although urine test positive, driver may not be under the influence. Police prefers handling saliva to urine.

Performing the test on-site
The persons performing the urine on-site tests evaluated some user friendliness characteristics of the devices on a scale of 1 (bad) to 3 (good), the results are presented in table 12.

Table 12: User friendliness characteristics of the urine devices

	Syva Rapid Cup	*Syva Rapid Test*	*Surescreen*	*Triage*	*Dip Drugscan*	*Multidrug*	*Status DS*	*Roche TesTcup*
Ease of performance	1,8	2,5	2,8	1,7	2,9	2,9	2,5	2,0
Interpretation	2,3	1,8	2,4	2,8	1,3	2,2	2,2	2,8
Reliability	2,3	2,0	2,2	2,6	1,7	2,3	2,1	2,5
Appearance	1,3	2,5	2,0	2,0	2,5	2,5	2,3	2,3

It was seen that the "dip" test were the easiest to use, followed by the traditional "pipetting" tests. The "cup" test were not found easy to use as expected, but with growing experience it seemed easier. The cups needed a large amount of urine (30-40 ml minimum) which is not always possible to obtain. The interpretation of the test result varied, but the Dip Drugscan results were not acceptable, it was very difficult to interpret. In the test situation each result was considered either positive or negative, in borderline cases a second or third opinion was asked. When comparing the sense of reliability of the tests it seems that the more complicated the test, the higher the sense of reliability. The sense of reliability is not in correspondance with the accuracies. The users felt that the size of the test (Syva Rapid Cup) was a bigger inconvenience than extra equipment needed to perform the testing, as shown by the appearance numbers (table 12). The advantages and disadvantages of the urine testing devices are described in table 13.

SALIVA

Analytical results

A total of 206 persons were tested with on-site devices. The number of positives for each analyte by reference method is TP+FN and for the onsite methods TP+FP. Calculation of accuracy, sensitivity, specificity for the on-site assays, using the reference method (GC/MS) as the gold standard are listed for the amphetamines in table 14, cannabinoids in table 16, opiates in table 18 and benzodiazepines in table 19. These calculations includes true positive and true negative cases when compared to blood also, due to insufficient saliva sample. False positive or false negative cases where saliva was not available is not included in the tables.

Table 13: Advantages and disadvantages of the urine devices

	Advantages	*Disadvantages*
Syva Rapid Cup	Collection cup and test in one	Needs a large amount of urine, difficult to close, very bulky
Syva Rapid Test	Good pipette	Sometimes needs more than 3 drops
Surescreen	Easy to use, economical	Messy, sometimes weak lines
Triage	Good result lines	Very complicated to use, reagents get electrostatic and do not stay in the reaction cup (contamination risk), slow
Dip Drugscan	Easy to use, a cover for the part dipped in urine	Very weak result lines
Rapidtest Multidrug	Easy to use, cover for the part dipped in urine	Sometimes weak result lines
Status DS		Pipette is stiff
Roche TesTcup	Collection cup and test in one	A bit difficult to use, need careful closing
Roche TesTstik	Good result line, easy to use	Only one substance

Amphetamines

Table 14: Amphetamine results

	Rapiscan	*Drugwipe*
Total	104	50
TP	53	25
FP	5	11
FN	6	0
TN	40	14
Sensitivity	89.8 %	100.0 %
Specificity	88.9 %	56.0 %
PPV	89.8 %	100.0 %
NPV	87.0 %	100.0 %
Accuracy	89.4 %	78.0 %

Table 15 False Negative Amphetamine results, concentrations in ng/ml

Sample no	*Amphetamine*	*Metamphetamine*	*MDA*	*Ephedrine*	*Negative on*
99-1443	290	550	0	0	Rapiscan
99-1887	1930	0	0	0	Rapiscan
00-483	34	0	0	0	Rapiscan
00-546	78	0	0	0	Rapiscan
00-549	663	0	0	0	Rapiscan
00-S421	250	0	0	0	Rapiscan

The results for amphetamines using different on-site test are presented in table 14. The difficulty of reading the Drugwipe (AMP) test is probably the biggest reason for the false positive results. In both Drugwipe and Rapiscan false positive cases no amphetamine or amphetamine related substances were identified with GC/MS.
The false negatives are listed in table 15, some of them at rather high concentrations. With Drugwipe no false negatives were reported, but for Rapiscan false negatives were obtained at 34, 78, 250, 290 663 and 1930 ng/ml.
A linear relationship (Saliva-Plasma ratio) between oral fluid and blood concentration was observed. S/P ratio of 2.9 was received, and it is about the same magnitude (2.8) as reported earlier (2).

Cannabinoids

Table 16: Cannabinoid results

	Rapiscan
Total	97
TP	1
FP	1
FN	0
TN	95
Sensitivity	100.0 %
Specificity	99.0 %
PPV	100.0 %
NPV	100.0 %
Accuracy	99.0 %

In the false positive Rapiscan result no THC could be identified by GC/MS (table 16).
THC has been the target molecule for oral fluid assays. The theoretical calculated S/P-ratio's of THC and it's metabolites are approximately 0.1 as reported earlier (3). However the actual measured concentrations in oral fluid are likely to be equal to or greater than concentrations in serum (13). Because the cut-off of the Rapiscan is 200 ng/ml, oral fluid concentrations of 10-180 ng/ml THC measured by GC/MS were not considered as false negatives (this means no false cannabinoid results were obtained). That is the reason of the misleading "good" results for THC Rapiscan. This means that Rapiscan is not able to detect cannabinoid use in reality. The used cut-off is absolutely too high.

Opiates

Table 17: Opiate results

	Rapiscan	*Drugwipe*
total	102	17
TP	8	0
FP	12	4
FN	5	0
TN	77	13
Sensitivity	61.5 %	-
Specificity	86.5 %	76.5 %
PPV	61.5 %	-
NPV	93.9 %	100.0 %
Accuracy	83.3 %	76.5 %

Table 18: False Negative opiate concentrations in ng/ml

Sample no	*6-MAM*	*Morphine*	*Codeine*	*Device*
99-1632	334	645	161	Rapiscan
00-90	0	81	0	Rapiscan
00-S369	0	940	0	Rapiscan
00-S370	3470	6130	44000	Rapiscan
00-716	0	129	0	Rapiscan

The opiate results are listed in table 17. Also the Rapiscan tested positive for pholcodine (see urine devices).
Other false opiate positives were obtained with Drugwipe (four cases) and Rapiscan (twelve cases) without any opiate findings with GC/MS. In eight of the twelve false positives with Rapiscan no opiates were detected in oral fluid or blood, but opiates were present in urine (in two cases no urine was available). Another interesting finding was that 6-MAM was detected in oral fluid three times when

also seen in urine but not in blood and three times detected in oral fluid but not in blood when urine was not available. This might be explained by the short half life of opiates and the favourable S/P-ratio (6-MAM S/P=6 (4)). Since saliva reflects the free unbound blood concentration (2-9), it can still be found at measurable concentrations in saliva although not detectable in blood.
The false negatives and the opiate concentrations are shown in table 18. The false negative results with Rapiscan varied between 81 and 5300 ng/ml total opiate concentration.

Benzodiazepines

Table 19: Benzodiazepine results

	Rapiscan
total	75
TP	3
FP	9
FN	0
TN	63
Sensitivity	100.0 %
Specificity	87.5 %
PPV	100.0 %
NPV	100.0 %
Accuracy	88.0 %

Benzodiazepines are the most complicated group in on-site testing. The results are shown in table 19.
With Rapiscan we got twelve positive results which were quantitated. In ten of these cases no benzodiazepines were detected, in one case diazepam at 20 000 ng/ml and the other true positive diazepam at 14 300 ng/ml. These positives are clearly not at concentrations that reflect the free unbound blood concentration, rather contamination after oral administration. Our experience is that the use of benzodiazepines was not detectable with Rapiscan. There were no false negative benzodiazepine results. In cases where blood quantitation was positive there where no benzodiazepines in saliva (n>20).
Suggestions for cut-offs for oral fluid testing, see SAMSHA recommendations.

Practical aspects

A questionnaire (appendix 3) was answered by the police (non professionals) on the characteristics of the Rapiscan, Drugwipe and roadside testing. A total of 33 policemen answered the questionnaire. The characteristics of the devices are described in table 20. An a-clinic (health care professionals) using the Cozart Rapiscan also evaluated the user friendliness of the device.

Table 20: User friendliness characteristics of the oral fluid devices

	Rapiscan A-clinic	*Rapiscan Police*	*Drugwipe Police*
Ease of performance	2	1,8	2,7
Interpretation	2,8	2,9	1,8
Reliability	1	2,3	1,9
Appearance	2,3	2,5	2,6

When the user friendliness of the devices were evaluated the police compared Rapiscan and Drugwipe, but the clinic personel had earlier used an automated imunnological urine screening device and they seemed to compare the Rapiscan testing with the immunological urine testing. The police complained a lot that the Rapiscan was difficult to use. The sample handling was too complicated. It was pointed out that the police is not a physician nor chemist. Additionally there are too many “menu” options on the reader. The Drugwipe was found to be very easy to use, but the interpretation was very difficult. The

electronic reader for the Drugwipe was not available for most of the policemen during the study, and the colour change interpretation was found too confusing. A majority (Rapiscan users 75 % (n=24) and Drugwipe users 65 % (n=17)) found an automatic reader necessary to help interpret the result, but also to impress the suspected drivers. Reliable impression was given when an electronic reader was available or when the use of both saliva and urine on-site devices was complicated, and looked professional. The automatic reader and complicated use was also found to give a reliable impression, not correlating with the actual accuracies of the devices.

The low reliability of Rapiscan given by the clinic personal reflects the intention of testing; the clinic was screening for drug abusers, not impaired persons. The oral fluid was often negative when the drugs where still detectable in urine (longer detection window). It was expected that the Drugwipe appearance would have been better accepted than Rapiscan. The Rapiscan needed a lot of additional equipment for the testing, but it seemed that it was inconvenient for the police to always have the water bottle for Drugwipe ready to use. The device should take little space in the police cars, because the police are getting more and more new equipment.

Other problems that came up in the questionnaire were the rate of refusal, which was very low. Only 13 % 0f the answering police had met an uncooperative driver. Talking, instructing and persuading were the solutions. The big problem when testing with Rapiscan was the dry mouth of the drivers. In 92 % of the answers this was the main (only) problem. Solutions like waiting, giving something to drink, telling the driver to collect saliva in the mouth before starting collecting or placing the cotton some other place than under the tongue was tried. The Drugwipe is clearly preferable in situations with dry mouth, because it needs very little oral fluid. The police felt that saliva was suitable for road side testing, but the equipment was not. Additionally the cold winter is a problem; either the test freezes when it is below zero, or if the weather is cold, it takes a longer time for the tests to run. No known adulteration problems were documented. However (coloured) substances in the mouth seemed to give a positive test result (snuff and cacao).

Overall it was an interesting study for the police, they learned a lot and felt that trying out new equipment is good. All police that had used the test wanted to continue use some kind of drug testing device. A majority the police wanted to continue use Drugwipe (64 %) rather than the Rapiscan (45 %), but most of all a more developed than the used tests were wanted. In the future a possibility of having the Rapiscan at the police station and Drugwipe in the patrol car was suggested. The police have also noted the preventive effect of having a drug testing device.

The advantages of the Rapiscan is the possibility of testing several drugs simultaneously and the electronic reader. The disadvantages are the complicated handling procedure and slow (police estimate of needed time 22 minutes). Drugwipe advantages are the easy and rapid (police estimate 7 minutes) use. The Drugwipe disadvantages were the difficulty of interpreting the result without an electronic reader. It only tests for one drug at a time and has no test for the benzodiazepines or cannabinoids.

BLOOD

The physician who performs the behavioural evaluation collects the blood sample. Sometimes the blood vessels are so small that a minimal volume is obtained, or the driver himself has taken the blood sample. If necessary the blood sample can be taken by force. The samples where collected in test tubes containing NaF and K_2Ox as preservation agents. The analyses are performed on whole blood.
Since blood is the matrix to be used for juridical purpose and saliva tests seemed to be the most appropriate for road side testing, an evaluation between saliva on-site tests and blood findings was also performed. The results for amphetamines are presented in table 21 and opiates in table 22. The variation between confirmation results in saliva (table 14 and 17) and blood (table 21 and 22) are mostly due to statistical variation. These results confirm that cannabis (table 23) and benzodiazepine (table 24) use (or even influence) was not detectable with the saliva on-site tests. The cut-offs used for the blood analyses are listed in table1.

Table 21: Amphetamine results

	Rapiscan	*Drugwipe*
Total	94	42
TP	47	22
FP	8	5
FN	5	0
TN	34	15
Sensitivity*	90.4 %	100.0 %
Specificity*	81.0 %	75.0 %
PPV*	85.5 %	81.5 %
NPV*	87.2 %	100.0 %
Accuracy*	86.2 %	88.1 %

* Calculated by comparing different matrices (saliva on-site test and blood confirmation)

Table 22: Opiate results

	Rapiscan	*Drugwipe*
Total	96	20
TP	6	0
FP	11	7
FN	1	0
TN	78	13
Sensitivity*	85.7 %	- %
Specificity*	87.6 %	65.0 %
PPV*	35.3 %	0 %
NPV*	98.7 %	100.0 %
Accuracy*	87.5 %	65.0 %

* Calculated by comparing different matrices (saliva on-site test and blood confirmation)

Table 23: Cannabis results

	Rapiscan
Total	72
TP	0
FP	4
FN	5
TN	63
Sensitivity*	0 %
Specificity*	94.0 %
PPV*	0 %
NPV*	92.6 %
Accuracy*	87.5 %

* Calculated by comparing different matrices (saliva on-site test and blood confirmation)

Table 24: Benzodiazepine results

	Rapiscan
Total	98
TP	7
FP	4
FN	35
TN	52
Sensitivity	16.7 %
Specificity	92.9 %
PPV	63.6 %
NPV	59.8 %
Accuracy	60.2 %

DISCUSSION

In general it seems that urine on-site tests correlate well with confirmation done by GC/MS. But since the overall specificity of any devices were not 100 %, proper confirmation is extremely important. The crossreactivity lists given by most manufacturers are far from complete. For instance in this study a lot of false positives were obtained with pholcodine, but also other medical substances like ephedrine, codeine, mirtazapine and citalopram gave a positive on-site test result. On the other hand we got a false negative on a sample containing a large amount of amphetamine (153 120 ng/ml), metamphetamine (16 900 ng/ml), ephedrine (15 270 ng/ml) and THCCOOH (352 ng/ml), it gave a negative result on all urine devices. The pH of the sample was 5 and nitrate, glucose and creatinine concentrations were normal. The EMIT analyser (VIVA) gave correctly positive results for both amphetamines and cannabinoids.

Clinical impairment evaluation has been performed, but the results have not yet been compered with laboratory findings.

CONCLUSION

The concentrations in oral fluid reflect the free unbound drug concentration in serum (2-9). The saliva-plasma ratio of benzodiazepines in not as favourable (S/P=0.3 (6)) as that of basic drugs like opiates (6-MAM S/P=6 (4), codeine S/P=1-3 (6)) and amphetamines (S/P=2.8 (2)), therefore the cut-offs for benzodiazepines should be very low in oral fluid devices. It seems that cannabis use could be detected with oral fluid testing because of the residues after smoking (4, 6), still it would be preferable to have a lower cut-off than 200 ng/ml for THC. In practice our experience is that oral testing can be performed on amphetamines and opiates but not yet for benzodiazepines and cannabinoids (cocaine is not found in Finland).

Saliva is better accepted as a screening matrix than urine. The police prefers to have a device at the road side that would be comperable to the breath alcometer test. The device should be very easy to use and simple to interpret (electronic reader preferable). The device should be fast and screen for most commonly detected drug (amphetamines, cannabinoids, opiates and benzodiazepines) in a singel test. An alternative is to have a device at the police stations which could be used if necessary (immediate confirmation of suspicion or to avoid urine and blood sampling and further investigations). But the police would at the moment rather have a device that needs development than be without a device.

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APPENDIX 1

OBSERVATIONS DRUGS/TRAFFIC **Draft translation of empairment evaluation (police)**

Crime/violation number	Date	Laboratory sample-number (filled by KTL)
Last name	First name	Social security number

OBSERVATIONS OF THE WAY OF DRIVING, WEATHER AND ROADWAY

Way of driving
- ☐ No own observations
- ☐ Steady
- ☐ Unsteady
- ☐ Winding, deviation from straight line up to _____ meters. The number of deviations _____ on a _____ meter observation section.
- ☐ Improper speed
- ☐ Violation of priority
- ☐ Other remarks

Control of the device of the vehicle
- ☐ Drive at low revolutions, jerking
- ☐ Unsecure use of gears
- ☐ Roaring of the motor
- ☐ Othe

Weather and lighting
- ☐ Rain
- ☐ Hard wind/storm
- ☐ Snow/sleet
- ☐ Fog
- ☐ Daylight
- ☐ Dusk
- ☐ Dark

Defects and faults of
- ☐ no
- ☐ yes, what

Roadway
- ☐ Good
- ☐ Bad
- ☐ Roadwork
- ☐ Good lighting
- ☐ Bad lighting
- ☐ Dry
- ☐ Wet
- ☐ Icy/snowy

OBSERVATIONS DURING STOPPING AND CONFRONTING

Reactions
- ☐ Normal
- ☐ Slow
- ☐ Very slow

Fysical abnormalities
- ☐ None
- ☐ Sweting
- ☐ Shuddering
- ☐ Vomiting
- ☐ Restlessness

Appearance
- ☐ Neat
- ☐ Unkempt
- ☐ Dirty/messy

Can speak Finnish or Swedish
- ☐ Yes
- ☐ No
- ☐ Defectively/passable

Speech
- ☐ Clear
- ☐ Mumbling/slurred
- ☐ Thick
- ☐ Faltering

Communication, sense of time and
- ☐ Sense of time and place clear
- ☐ Sleepy
- ☐ Wakes up easily
- ☐ In deep sleep/unconscious
- ☐ Confused

Mood, behaviour
- ☐ Peaceful, Controlled
- ☐ Agitated
- ☐ Aggressive
- ☐ Familiar
- ☐ Overly cheerful
- ☐ Bored
- ☐ Defiant
- ☐ Weepy

Getting out of the vehicle
- ☐ Normal
- ☐ Loss of balance
- ☐ Has to lean on the vehicle

Walking
- ☐ Steady
- ☐ Dragging
- ☐ Tottering
- ☐ Loss of balance

Smell of alcohol
- ☐ Yes
- ☐ No

Alcohol breath test
- ☐ Yes, at _____ 0/00
- ☐ No
- ☐ Cannot be done
- ☐ Refused

Positive on-site tests

Cozart
- ☐ Amphetamine
- ☐ Opiates
- ☐ Benzodiazepines
- ☐ THC
- ☐ Cocaine

Drugwipe
- ☐ Amphetamine
- ☐ Opiates
- ☐ Cocaine

Other, specify _____
- ☐ Amphetamine
- ☐ Opiates
- ☐ Benzodiazepines
- ☐ THC
- ☐ Cocaine

Eyes	**Pupils**	**Lighting during**
☐ No abnormalities	Right ab. _____ mm	☐ Daylight
☐ Red	Left ab. _____ mm	☐ Dusk
☐ Watery, glowing	☐ React quickly to light	☐ Night, street lights
☐ Restless	☐ React slowly to light	☐ Night, room lights
	Nystagmus	☐ Other
	☐ Jerky movement	_____
	☐ No jerking observed	

Conspicuous behaviour

☐ did not change during examination ☐ increased during examination ☐ decreased during examination

The test began at

The test ended at

The ability of the driver to carry out the tests demanded

☐ has not been impaired ☐ has been impaired ☐ has been considerably impaired

Other information, like other observations, confiscated drugs, tablets, equipment etc. can be written overleaf

Place and time _____ Signature of the observer _____

Sisäasianministeriö/Poliisi Editahu 2.2000

APPENDIX 2

Draft translation of physician's empairment evaluation

Orderer of the examination……

Examination place ……

Name of the subject …… Social security number ……

Proving of identity ☐ proved by the police ☐ other ……

The reason for examination ☐ drunken driving ☐ other crime ☐ other

Wanted examination ☐ blood sample ☐ urine sample ☐ clinical examination

---

Deceases
According to the subject ☐ no ☐ yes What? ☐ no answer Blood pressure ……../…..… mmHg Pulse ……/min
Observed symptoms ☐ no ☐ yes What?

Observed injuries ☐ no ☐ yes What? Liquid treatment of the injured ☐ no ☐ yes What, how much?

Drugs and medication. Has the subject used these before or after the happening? What, when, how much?
Injection marks ☐ no ☐ yes
According to The subject ☐ no ☐ yes regularly ☐ yes occasionally ☐ no answer

On-site test ☐ saliva ☐ urine ☐ neg. ☐ pos. What? Alcohol breath test …….o/oo

---

Clinical examination
Weight ..…… kg ☐ weighed ☐ given Height …….…… cm ☐ measured ☐ given
Body structure ☐ normal ☐ slim ☐ fat

Examinations, observations	normal	slightly deviating	clearly deviating (underline the observations)
Consciousness	☐		☐ numb, sleepy, almost unconscious
Fixing of the date and time, memory	☐	☐	☐
Walking straight forward	☐	☐	☐
Full turn while walking	☐	☐	☐
Romberg's test with eyes closed	☐	☐	☐
Finger to finger test	☐	☐	☐
Pulling oneself together			☐ observed
Behaviour	☐		☐ uninhibited, aggressive, angry, talkative, arrogant, unresponsive, limp, absentminded
Speech	☐		☐ inarticulate, stumbling, thick, faltering
Train of thought	☐		☐ illogical, jumpy, muddled
Mood	☐		☐ euphoric, irritated, distressed, varying, restless, upset, bored
Size of the pupils	☐		☐ strongly dilated, pointed
Pupils' reaction to light	☐		☐ slowed down, non-reacting
Nystagmus			☐ strong ☐ after following the object ☐ spinning induced
Other unusual findings		☐	☐ sweating, spasms, chills, dry mouth, running nose, trembling, watering or bloodshot eyes

Other observation:

Samples* The skin was cleaned with ☐ water ☐ other. What? ……

Blood sample ……/…… at …….. ☐ 2 tubes according to the instructions ☐ other ……
Urine sample ……/…… at …….. under supervision ☐ yes ☐ no
quality of urine ☐ normal ☐ unusual How?
Urine test slip glucose ☐ no ☐ yes keto compounds ☐ no ☐ yes

Signature** …… Clarification of name and job position ……

Evaluation of the degree of the functional disorder (the total degree of errors)

1. Functional disorders ☐ were not observed ☐ were observed ☐ examinations were not carried out, because……

2. The degree of the functional disorder ☐ is in the limits of normal variation
☐ deviates from the normal state and is at least ☐ mild ☐ of medium strength

3. To my knowledge these functional disorders/errors have been caused by
☐ drugs and/or ☐ medication and/or ☐ alcohol ☐ decease ☐ injury ☐ I can't evaluate

This I swear by my honour and conscience

Date …… Signature ……

Clarification of name and job position ……

*Personal data and sampling time must be written on the sample tubes.
**The signature of the person who took the samples, if not the same as the signature in the end.

APPENDIX 3

A QUESTIONNAIRE FOR ALL USERS OF THE SALIVA TESTS

Return to (latest return date 29.05.2000): Marielle Grönholm,
KTL/Laboratory of substance abuse, Mannerheimintie 166, 00300 Helsinki
Fax: 09-4744 8553 or e-mail: marielle.gronholm@ktl.fi
Comments by phone: 09-4744 8294

INFORMATION ON THE USER OF THE TEST

Sex: Male Female Year of birth: 19_____

Used tests:
- ❑ Cozart Rapidscan (cotton swab)
- ❑ Drugwipe (wiper)
- ❑ Other:_____

Area:
- ❑ Helsinki
- ❑ Turku
- ❑ Tampere
- ❑ Vaasa-Oulu

Occupation:
- ❑ Police
- ❑ Laboratory/Hospital staff
- ❑ Other: _____

THE COLLECTION OF SALIVA

1. Which problems did you encounter in the field?
   - ❑ Insufficient volume of saliva
   - ❑ Refusal of the subject
   - ❑ Aggressive behaviour while testing
   - ❑ Intention of manipulation
   - ❑ Other:
     _____
     _____

2. How did you solve the problems?
   _____
   _____
   _____
   _____

3. Do you think saliva is a suitable sample for roadside use? (Police)
   - ❑ Yes
   - ❑ No
     Why?_____

THE TEST PROPERTIES

1 – bad/weak 2 – good 3 – very good/excellent (circle the most suitable choice)

4. Cozart Rapiscan:

Ease of use:	1	2	3
Ease of reading the results:	1	2	3
Credibility of the test:	1	2	3
User instructions/Training:	1	2	3
Look and size of the test:	1	2	3

Other:
_____
_____
_____

5. Estimate the time required to carry out the test: _____ minutes.

6. Other comments:
_____
_____
_____

7. Would you prefer an automatic reader? (the other choice is manual reading)
- ❑ Yes
- ❑ No
- ❑ Depends on the situation:_____

8. If the automatic reader has been available, report your experiences and comments.
_____
_____
_____

9. Drugwipe

Ease of use:	1	2	3
Ease of reading the results:	1	2	3
Credibility of the test:	1	2	3
User instructions/Training:	1	2	3
Look and size of the test:	1	2	3

Advantages and disadvantages:
_____
_____
_____

10. Estimate the time required to carry out the test: _____ minutes.

11. Other comments:
_____
_____
_____

12. Would you prefer an automatic reader? (the other choice is manual reading)
- ❑ Yes
- ❑ No
- ❑ Depends on the situation:_____

13. In the future I would like to use

a) Cozart Rapidscan b) Drugwipe

c) Some other/better on-site test d) no on-site test at all

Comments:

_____

_____

_____

THANK YOU FOR ANSWERING!!!

Deliverable D4b - Scotland

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: FMS, SCOTLAND

Authors: Robert A. ANDERSON, John S. OLIVER and Calum M. MORRISON

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

This report contains the results from the Scottish part of the ROSITA evaluation of urine and saliva test devices. The approach adopted in this study involved two principal aims: (a) to test the reliability of the test devices, (b) to test their roadside practicality. Since UK law does not permit roadside testing for drugs, an approach was made to the Scottish Prison Service to obtain volunteers from within the prison inmate population as donors of matched saliva, urine and blood samples. The prisoner population is known to exhibit a significant incidence of drug use, as indicated by the results of the UK Mandatory Drug Testing scheme, and satisfies the requirements of sub-project (a). Once ethical approval for the project protocol had been obtained, consent for the project was given. Access to the prison was however significantly delayed as a result of industrial action. Access was gained late November 1999, enabling matched samples to be obtained from then until February 2000. A limited panel of tests was performed on site by the research team to allay the anxiety of the volunteers lest the prison staff have access to their results. Project collaborators within the Scottish Prison Service were Mr N. Royle, Mr E. Murch, Mr S. McFarlane and Dr M. McQueen. Acknowledgement is also given to the Healthcare staff and prison officers who assisted in the project.

For sub-project (b), training in the use of saliva and urine test devices was given to Police Officers for their evaluation at the roadside. The final protocol for the project stipulated that a series of tests would be carried out with motorist volunteers, based on informed consent. A fully equipped caravan belonging to the Occupational Health Department was obtained for the purpose. Also, support was obtained from the Royal Automobile Club and the Automobile Association. Although enthusiastic, for unforeseen operational reasons, Police Co-operation was withdrawn less than 24 hours prior to the start. Consequently, roadside evaluation by the Police Officers was not undertaken. Collaborators in the project within Strathclyde Police were Chief Superintendent J. Gilmore and Inspector P. Fleming.

Within the Forensic Medicine Department, a GC-MS instrument scheduled to be delivered in January 2000 was not delivered and installed until late May 2000. This caused further delays for the research team.

METHODS

Protocol

Two hundred and fourteen prisoner volunteers from admission groups between November 1999 and February 2000 provided matched blood, urine and saliva samples. Each prisoner was addressed by a member of the research team and informed both verbally and in writing of the purpose of the exercise. It was stressed that participation was entirely voluntary. Once a consent form had been signed, venous blood samples (10ml) were obtained and immediately transferred into lithium heparin containers. In some cases provision of blood was refused or was not possible to collect because of prior damage to the veins caused by drug abuse. Saliva (5ml) was obtained by expectoration directly into a universal container. For volunteer Nos. 115-214, an additional saliva sample was collected using the sponge device supplied by Avitar Technologies Inc. This was used for immediate testing on-site with the Avitar OralScreen device. Urine samples (target volume 100 - 200 millilitres) were collected under supervision in supplied containers. Aliquots were used for initial on-site testing. The specimens of blood, saliva and urine were frozen and stored in dry ice for transport to the Forensic Medicine Department for analysis. Specimens were stored in the freezer at -20°C until analysed. All initial and repeat analyses were completed within a 6-month period following collection. Any repeated analyses were completed within a further 2-month period.

All specimens were analysed in the laboratory using on-site test kits supplied by ROSITA Partners and by routine laboratory methods based on instrumental enzyme immunoassay (EIA) and gas

chromatography- mass spectrometry (GCMS) for the presence of drugs of abuse. Saliva samples, following the late withdrawal of the Cozart Rapiscan Device for this project, were analysed using the Avitar OralScreen device only and by instrumental methods for the presence of opiates, cocaine and cannabinoids. In addition, the laboratory analysis of urine specimens was carried out by the Laboratory of the Government Chemist, Teddington, UK and instrumental immunoassay of the saliva specimens was carried out by Altrix Healthcare, Birkenhead, UK.

The following table summarises the sample processing carried out.

SAMPLE PROCESSING

Specimen: Blood

200 specimens

Onsite Tests: *Not applicable*

Laboratory Analyses
all carried out at Department of Forensic medicine and Science, University of Glasgow

Instrumental Immunoassay
ELISA, using test kits from STC Technologies and Cozart Bioscience. No cut-off was applied. Analytes and lowest calibrator concentration: amphetamine (25 ng/ml), methamphetamine (25 ng/ml), benzodiazepines (10 ng/ml), cannabinoids (2 ng/ml), cocaine metabolite (10 ng/ml), methadone (5 ng/ml), opiates (10 ng/ml).

GC-MS Confirmatory Analyses:
All samples analysed (ELISA positives and negatives) using Thermoquest Model MD 800, for the following analytes in three separate groups:
amphetamine, methamphetamine, MDA, MDMA, MDEA, chlordiazepoxide, diazepam, nordiazepam, oxazepam, temazepam, THC, 11-hydroxy-THC, THCCOOH, cocaine, benzoylecgonine, ecgonine methyl ester, methadone, EDDP, morphine, 6-acetylmorphine, codeine, dihydrocodeine.
Blood standard concentrations were 0, 25, 50, 75 and 100 ng/ml except for amphetamines, which were 0, 100, 250, 500 and 1000 ng/ml and THC, which were 0, 10, 20 and 50 ng/ml.
The criteria for accepting a GC/MS results were: (a) qualifier ion ratios agreed between standards and samples within 20%, (b) retention times agreed between standards and samples (usual within-batch variation was less than 1%), (c) quantification ions and qualifier ions for each substance show same retention time and deuterated internal standards show marginally earlier retention times than the non-deuterated compounds.

Specimen: Urine

209 specimens: Nos 1-114 tested only in the laboratory, Nos 115-214 tested on-site. Each on-site test was read by two people minimum.

Onsite Tests:

American Biomedica Rapid Drug Screen:

Analyte	Cut-Off (ng/ml
d-Amphetamine	1000
Benzodiazepines	300
Benzoylecgonine	300
Cannabinoids (11-nor-9-carboxy-delta-9-THC)	50
Methamphetamine	1000
Opiates (morphine-3-glucuronide)	300

Roche TestCup:

Analyte	Cut-Off (ng/ml
Amphetamines	1000
Cocaine metabolites	300
Marijuana metabolites	50
Opiate metabolites	300
Phencyclidine	25

Syva Rapid Test:

Analyte	Cut-Off (ng/ml
d-Amphetamine	1000
Barbiturates (secobarbital)	300
Benzodiazepines (oxazepam)	300
Benzoylecgonine	300
Cannabinoids (11-nor-9-carboxy-delta-9-THC)	50
d-Methamphetamine	1000
Opiates (morphine)	300
Phencyclidine	25
Tricyclic antidepressants (nortriptyline)	1000

Laboratory Analyses
all carried out at the Laboratory of the Government Chemist using validated and UKAS accredited methods

Instrumental Immunoassay
All specimens analysed using Roche EIA: analytes: cannabinoids, cocaine, amphetamine, opiates, methadone.

GC-MS Confirmatory Analyses:
Confirmation of EIA-positive samples only. Blood standard concentrations were in the following ranges: THC (10-100 ng/ml), morphine, codeine, dihydrocodeine (133-1000 ng/ml), 6-acetylmorphine (6.5-50 ng/ml), methadone (200-1500 ng/ml), benzoylecgonine (100-1500 ng/ml), amphetamines (300-4000 ng/ml), nordiazepam, temazepam, oxazepam and lorazepam (150-1500 ng/ml).

Specimen: Saliva

214 Specimens. Nos 1-114 tested only in the laboratory, Nos 115-214 tested on-site. Each on-site test was read by two people minimum.

Onsite Tests:

Avitar OralScreen:

Analyte	Cut-Off (ng/ml
Cocaine	15
Cannabinoids (THC)	Several*100
Morphine	10

Laboratory Analyses

Instrumental Immunoassay
all specimens tested by Altrix Healthcare by ELISA for cannabinoids (cut-off 1.4 ng/ml), cocaine (cut-off 5 ng/ml) and opiates (cut-off 10 ng/ml). All specimens also tested at the Department of Forensic

Medicine and Science, University of Glasgow by ELISA for cannabinoids, cocaine and opiates, no cut-off applied.
GC-MS Confirmatory Analyses
all positives and those showing indeterminate results with the OralScreen were analysed by GC-MS for cannabinoids (THC and THCCOOH), cocaine alkaloids (COC, BZE and EME) and opiates (morphine, 6-acetylmorphine, codeine and dihydrocodeine). Saliva standard concentrations were 0, 25, 50, 75 and 100 ng/ml except for THC, which were 0, 10, 20 and 50 ng/ml.

User questionnaire

As noted above, on-site tests were performed both at the Department of Forensic Medicine and Science and in the Prison environment by two or three ROSITA project personnel. As the roadside sub-project was unable to proceed, the planned questionnaire concerning user opinion of the devices was not used. Comments on the usability of the devices were therefore restricted to laboratory personnel.

Analysis of Results

As agreed at ROSITA participants' meetings in Oslo and Santiago de Compostella, GC/MS was used as the confirmation method following the results of immunoassay screening. All blood specimens were confirmed, whether positive or negative in the screening test. For urine specimens, analysed at the Laboratory of the Government Chemist, only those samples showing positive results in the screening test were confirmed. Saliva samples showing positive in the immunoassay screen carried out by Altrix Healthcare, plus those showing indeterminate results in the on-site test with Avitar OralScreen (or where there was a difference in opinion between two personnel on the result of the test) were confirmed by GC-MS.

Evaluation of results

Standard criteria were used in the evaluation of results:

- *True Negatives (TN)*: negatives in which analyte concentrations are below GC-MS cut-off values (SAMSHA cut-off values used);
- *False Negatives (FN)*: samples giving a negative result but in which analytes are present at concentrations above the GC-MS cut-off values;
- *False Positives (FP)*: positives which are not confirmed by GC-MS to contain analytes at concentrations above the cut-off values or which are due to substances other than those listed in the manufacturer's cross reactivity list;
- *True Positives (TP)*: positives which are confirmed by GC-MS to contain analytes at concentrations above the cut-off values or which are due to substances listed in the manufacturer's cross reactivity list.

Sensitivities, selectivities, positive predictive values (PPV) (the probability that a positive on-site result is a true positive), negative predictive values (NPV) (the probability that the on-site test result is a true negative) and accuracies were calculated (1) as follows:

- Sensitivity = percent of true positives which are detected = TP/(TP+FN)
- Specificity = percent of true negatives which are detected = TN/(TN+FP)
- Positive Predictive Value = probability (%) that a positive test result is a true positive = TP/(TP+FP)
- Negative Predictive Value = probability (%) that a negative result is a true negative = TN/(TN+FN)
- Accuracy = percentage of all tests giving correct results = (TP+TN)/(Total no of results)

RESULTS

In this project, carried out in an environment similar to a room in a police station, no problems were experienced in obtaining adequate urine specimens within a 15-20 minute period. Similarly, for the purposes of the project, time was available to collect saliva for confirmatory analysis by expectoration into a tube.
On-site tests were carried out by ROSITA personnel. Each test was read by a minimum of two people, independently. In a significant number of cases, especially for cannabinoids, the lines on the results' panel were faint and considerable difficulty was experienced in these circumstances whether a line was present or not. The decision was made to simulate what a police officer is likely to have done in these circumstances and fall on the side of caution. These samples would have been considered to be probably positive and would have been sent for confirmation.

URINE

Analytical results

209 urine samples were tested with 3 on-site devices. The results are summarised in Tables 1-5.

Table 1: Summary of urine test results for **Amphetamine and Methamphetamine** groups

	American Biomedica Rapid Drug Screen	Roche TestCup	Syva Rapid Test
Total attempted	201	209	209
No. of failed tests	0	27	0
Net no. of results	201	182	209
TP	0	0	0
FP	1	1	2
FN	0	0	0
TN	200	181	207
Sensitivity	Not applicable	Not applicable	Not applicable
Specificity	99.5%	99.5%	99.0%
PPV	0	0	0
NPV	1	1	1
Accuracy	99.5%	99.5%	99.0%

Table 2: Summary of urine test results for **Cannabinoids**

	American Biomedica Rapid Drug Screen	Roche TestCup	Syva Rapid Test
Total attempted	201	209	209
No. of failed tests	0	27	0
Net no. of results	201	182	209
TP	33	26	35
FP	24	8	12
FN	4	8	3
TN	140	140	159
Sensitivity	89.2%	76.5%	92.1%
Specificity	85.4%	94.6%	93.0%
PPV	57.9%	76.5%	74.5%
NPV	97.2%	94.6%	98.1%
Accuracy	86.1%	91.2%	92.8%

Table 3: Summary of urine test results for **Opiates**

	American Biomedica Rapid Drug Screen	Roche TestCup	Syva Rapid Test
Total attempted	201	209	209
No. of failed tests	0	27	0
Net no. of results	201	182	209
TP	24	18	24
FP	14	11	21
FN	1	0	1
TN	162	153	163
Sensitivity	96.0%	100.0%	96.0%
Specificity	92.0%	93.3%	88.6%
PPV	63.2%	62.1%	53.3%
NPV	99.4%	100.0%	99.4%
Accuracy	92.5%	94.0%	89.5%

Table 4: Summary of urine test results for **Cocaine**

	American Biomedica Rapid Drug Screen	Roche TestCup	Syva Rapid Test
Total attempted	201	209	209
No. of failed tests	0	27	0
Net no. of results	201	182	209
TP	1	1	1
FP	1	0	1
FN	0	0	0
TN	199	181	207
Sensitivity	100.0%	100.0%	100.0%
Specificity	99.5%	100.0%	99.5%
PPV	50.0%	100.0%	50.0%
NPV	100.0%	100.0%	100.0%
Accuracy	99.5%	100.0%	99.5%

Table 5: Summary of urine test results for **Benzodiazepines**

	American Biomedica Rapid Drug Screen	Roche TestCup	Syva Rapid Test
Total attempted	201	209	209
No. of failed tests	0	27	0
Net no. of results	201	182	209
TP	6		32
FP	3		37
FN	18		0
TN	158		140
Sensitivity	25.0%		100.0%
Specificity	98.1%		79.1%
PPV	66.7%		46.4%
NPV	89.8%		100.0%
Accuracy	88.6%		82.3%

Comments on Devices

American Biomedica Rapid Drug Screen

This device was easy to use and the results' panel was clear and easy to read. Also, compared to problems with other devices used in the project, there were no failed tests. The bag in which the test card is supplied could be conveniently used to store the card after use. The screw cap was easy to put on and no leaks were found. This device gave a significant number of positive results for cannabinoids at concentrations below the manufacturer's stated cut-offs, as indicated by GC-MS analysis. In some instances these were below the GC-MS cut-off of 15 ng/ml.

Syva Rapid Test

The plate device was easy to use and convenient because all drugs were on a single test. The lines on the test result panel were usually clear and easy to read. The use of the micropipette presented no problems in either the prison environment or the laboratory and would have been advantageous if only small volumes of urine were obtained. Overall, the device was popular with the members of the team and the observing prison medical practitioner.

Roche TestCup

This device was in principle easy to use and read. The bands formed were clear and the psychological aid given by the cross pattern on the results' plate was an advantage. The incorporation of the test plate in the cup was very convenient. There were, however a significant number of failures with this device in our hands (tests were carried out by several different laboratory staff) in which the urine failed to enter the analysis chamber. We understand that some contractors had later batch numbers that had been modified. In a few cases, the lid seal failed, leading to a leakage of urine. If particular care is needed in carrying out routine procedures such as replacing the lid, requiring pressing of the top etc., then these manipulations should be described and emphasised in the instructions accompanying the test kit.

SALIVA

Analytical results

214 Saliva samples were tested with the single on-site device that was made available for this study. The results are summarised in Table 6.

Table 6: Results obtained with the Avitar OralScreen device

Total attempted	214
No. of failed tests	23
Net no. of results	191

	Cannabinoids	Cocaine	Opiates
TP	2	Not applicable – no positives	4
FP	30		21
FN	0		2
TN	159		164
Sensitivity	100.0%		66.7%
Specificity	84.1%		88.6%
PPV	6.3%		16.0%
NPV	100.0%		98.8%
Accuracy	84.3%		88.0%

Comments on the Avitar OralScreen Device

The collection device was problematical in our experience and did not protect the operator from contamination with oral fluid. Gloves would be essential when manipulating the collector. The device itself often gave very faint lines and was therefore difficult to read, particularly the test for cannabis, and subjective judgements had to be made as to presence or absence of a line. There were a significant number of devices in which apparently normal, fluid saliva failed to migrate to the analysis strip. Also, the device did not perform well with viscous saliva. An interesting observation made during the analysis of results was that many of the donors giving positive results in blood gave saliva specimens that failed to run in the on-site device.

BLOOD

Blood specimens were collected from 200 volunteer participants in the project, to serve as the reference specimen for other tests, particularly saliva. Blood is also considered to be the best reference specimen when the question of impairment is important and is used in the UK under the Road Traffic Act for this purpose, as indicated in Work Package 3. A comparison is given in Table 7of results for cannabinoids and opiates in blood, saliva and urine. Cocaine was the other analyte measured with the Avitar device but there were no confired positives.

Table 7: Summary of Cases giving positive analytical results for blood and comparison with saliva and urine results.

Cannabinoids		
Case No.	Saliva Results (Avitar OralScreen)	Urine Results by GC-MS [THCCOOH] (ng/ml)
172	Failed to run	5
173	positive	420
178	negative	34
187	Failed to run	216
190	negative	56
192	negative	204
195	negative	99
202	negative	14
210	negative	176
Opiates		
Blood Positives	Saliva Results (Avitar OralScreen)	Urine Results by GC-MS [Morphine] (ng/ml)
59	negative	negative
61	Failed to run	2285
89	Failed to run	3348
101	positive	1957
141	positive	14535
177	negative	521

DISCUSSIONS AND CONCLUSIONS

The study protocol adopted in this project, involving the prison population, was determined by the UK traffic law, which does not currently permit roadside testing other than for alcohol. The volunteers who participated provided a significant number of drug-positive biological specimens, reflecting the drug use patterns currently seen in forensic practice in our area. The percentage of positives was, however, lower than seen in other ROSITA projects in which subjects were selected on a for cause basis by traffic police, often involving roadside impairment assessment procedures. This underlines the consensus opinion that roadside drug tests would be an adjunct, and not necessarily a replacement for, roadside impairment assessment carried out by a police officer. In addition, the project in Scotland was carried out within a background which included previous roadside studies, for example involving saliva collection (2). The latter found a high public acceptance of this type of procedure. No similar study has been carried out for urine collection with suitable roadside facilities. It should therefore be recalled and emphasised that the UK legislation currently permits urine collection at the police station. Amendment of the law would be required, however, to permit on-site testing and for subsequent collection of blood if a positive urine test was obtained. Under these circumstances, the current project exactly simulated the most likely scenario if the law was in fact amended in this way.

The devices used in this study were inevitably from one generation of development amongst a continuing line of similar innovations. Already the manufacturers have improved on the devices used in ROSITA and newer technology stands waiting to be released. The ROSITA project has indicated that on-site/roadside testing is possible but that the generation of devices used is probably insufficiently sensitive, accurate or practicable for routine use. It seems that electronic reading devices are essential, from the viewpoints of both the tester and the suspect. Neither has been comfortable with the subjective nature of many on-site tests. These then are definable targets which undoubtedly will be achieved now that ROSITA has given support to the case that such devices are needed and will be used.

It is also worth noting an important ancillary conclusion, within the wider context of drug testing. There is a general tendency in many parts of the world to move away from laboratory testing and analysis, usually to save money but also to save time. The results of this study indicate the importance of reference methods such as GC-MS for laboratry confirmation of on-site tests in maintaining the general forensic science approach of using at least two different methods of analysis .

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Deliverable D4c - Germany

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: University Homburg/Saar, Institute for Legal Medicine, Germany

Authors: Manfred MÖLLER, Stefan STEINMEYER, Hartwig OHR

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

In the development of drug test devices, a major contention continues to be the accuracy, specifity, sensitivity, and the evaluation of individual results, mostly under laboratory conditions [1, 2, 3]. In the Workpackage 4 of the ROSITA project [4] it has to be found out which of the tests meet the criteria set in the methodology and experimental design (testing and evaluation of the instruments, validity, equipment reliability, usability, and usage costs) especially for the purposes of the police for the use of test devices at the roadside.
In order to realize this intend, the Saarland police could be enlisted to perform and assess the roadside drug tests. To establish general conditions to the cooperation between the Institute of Legal Medicine Homburg (ILMH) and the police within ROSITA, the Ministry of Interior of Saarland was asked for official support.
On 25 June 1999, an official decree – based on the experiences of the police and on arrangements with the ILMH – was issued by the Ministry of Interior of Saarland addressing the three state traffic police departments (TPD, centre, east, west), in which the organisational and practical use of roadside devices within the ROSITA project was regulated. With this decree, it became possible to perform and evaluate the on-site tests directly at the roadside to prove the DUID within police traffic controls, analogue to the testing for alcohol. For that, the performance of ROSITA was not depending on voluntary help of the police, it was supported by an official order on an administrative basis.
The role of the police as a partner of ILMH is defined by their competence for the evaluation of the handling and of the practicability of the test devices at the roadside; starting from the date mentioned above, the police officers were authorized to use drug test devices at the roadside on the occasion of traffic controls, for research purposes. In order take advantage of this, as much tests as possible were distributed to the police. The analytical evaluation of the roadside tests was done on basis of the obtained results of serum and/or urine analysis according to the legal requirements. Planning, organization and termination of traffic controls was incumbent on the TPD's within own responsibility.
The field study of ROSITA lasted 14 months from June 1999 to August 2000. The project started to develop a self-dynamics, and instead of the intended (and budgetted) 200 samples, 604 samples were included into the ROSITA evaluation. The evaluation of the on-site tests has been finished now and the results considering the handling of the tests and their acceptance by the police officers are available.

METHODS

Existing DUID Legislation in Germany

In addition to Driving under the Influence of Drugs (DUID) as a criminal offence (§316 of the penal code), a new law came into action in Germany in August 1998, creating sanctions for driving under the influence of certain illicit drugs. It is now an administrative offence (§ 24a of the Road Traffic Regulations) to drive under the influence of Amphetamine, MDMA, MDE, Cannabis, Cocaine, Heroin, and Morphine. The law is applicable if one of these drugs (the target analytes for Heroin and Cocaine are Morphine and Benzoylecgonine, respectively) is detected in blood.
The main criteria to constitute a criminal offense (§ 316 StGB) is the observation of signs of impairment within the area of vegetative symptoms (pupil width, pupil reaction), co-ordination disturbances (walking, physical tests) or psychic disturbances (thinking flow, mood) must usually accumulate, in order to proof driving inability. Also the observation of one symptom of impairment (e.g. unbalanced walk), if it is clearly enough pronounced, is sufficient.
For § 24a StVG, only the evidence of recent consumption is necessary, fulfilled by the positive detection of drugs (listed in in the law's appendix) in the blood.

Target Population / Selection of subjects

Regarding the statistical evaluation 1999 of the frequency of accidents and age, the risk of being involved in an accident is in the group of 18 to 24 years old drivers approximately 3 times higher in comparison to the other age groups of (all registered) drivers in Germany. This special age group has – due to a mostly critical situation connected to problems in the development of self-confidence and of identity, and to dynamics in the change of life-style – higher drug consumption tendencies than other, older age groups. Therefore, in order to find drugged drivers, the policy of the police is to perform target group oriented actions and controls. Drug testing (and certainly alcohol testing) is done – beside general and random traffic controls – mostly on the occasion of special checkpoints close to discotheques, especially on weekends, concerning the starting and ending times of the appropriate events.
The subjects were selected among drivers suspected by the police to be influenced by drugs.
To examine drug influence in traffic, a first suspicion was required: if indications of the use of drugs seemed to be obvious, the police officer interviewed the suspect and offered a roadside drug test to confirm or extenuate his initial suspicion.

On-site Tests

In order to obtain a valid evaluation at the end of the ROSITA study, a sufficient number of examinations had to be achieved with as much different test devices as possible. After an inventory of existing drug test devices by Samyn et al. as workpacke 2 of ROSITA [5], seven urine test devices (one also usable for saliva) and two saliva/sweat test devices were distributed to the traffic police departments.

Used Devices

Used by the police traffic units were:
the urine test devices **DOA 4**, 4-panel/ CAN-COC-OPI-AMP from Mahsan Diagnostics (Reinbek, Germany), **Frontline,** single test AMP, and **Testcup**, 4-panel/ CAN-COC-OPI-AMP from Roche Diagnostics (Indianapolis, USA), **Rapid Drug Screen (RDS)**, 5-panel/ CAN-COC-OPI-AMP-mAMP from American BioMedica Corp. (Hudson, USA), **Syva Rapid Cup**, 5-panel/ CAN-COC-OPI-AMP-mAMP from Dade Behring Diagnostics Inc. (Cupertino, USA), **Toxiquick**, 5-panel/ CAN-COC-OPI-mAMP-BZO-MTD + single test AMP from Biomar (Marburg, Germany), **One-Step-Drug-Scan**, 4-panel/ CAN-COC-OPI-AMP-from Cortez Diagnostics (Calabasas, USA) and for the testing of saliva and/or sweat **Drugwipe**, single tests COC, OPI, AMP from Securetec GmbH (Ottobrunn, Germany), **Oral Screen**, 3-panel test CAN-COC-OPI from Avitar Inc. (Canton, USA), and **Toxiquick** (as for urine) from Biomar (Marburg, Germany).

Each of the TPD's has started with testing a urine test-version and a saliva/sweat test-version; thus, it was ensured that an according test device was available for each body fluid which could be obtained. Per subject, in addition to the roadside test(s) to be assessed, the police officers were required to use a reliable reference system (which would be decisive for further legal measures, e.g. blood sampling), in order to confirm the on-site detection of positive samples. Recommended for reference purposes was the combination of **Mahsan DOA 4** and **Roche Frontline AMP** due to practical experience previously obtained by ILMH [6]. Nevertheless, both tests are also subject to investigation within ROSITA.

Testing Process

If in a traffic control situation indications of the use of drugs are obvious, the police officer interviewed the suspect and offered – on a voluntary basis - a roadside drug test to confirm or attenuate his initial suspicion. In more than 98%, the suspects aggreed with collaborating.
All tests were performed and read by about 100 different officers from the three TPD´s of the Saarland after being instructed into the handling of the test systems (via representatives of the appropriate manufacturers and/or via co-workers of the ILMH). They were responsible for the choice and the

numbers of devices to be tested at the roadside. For better comprehensibility of the testing process, a written overview about the handling in which situations was worked out by the ILMH which could be used on-site as assistance (Figure 1). The different types of test devices could be applied everywhere where the privacy of the subject was protected. Saliva and sweat samples could be collected and tested directly at the roadside, whereas urine samples should only be collected and tested at police stations or at public lavatories.

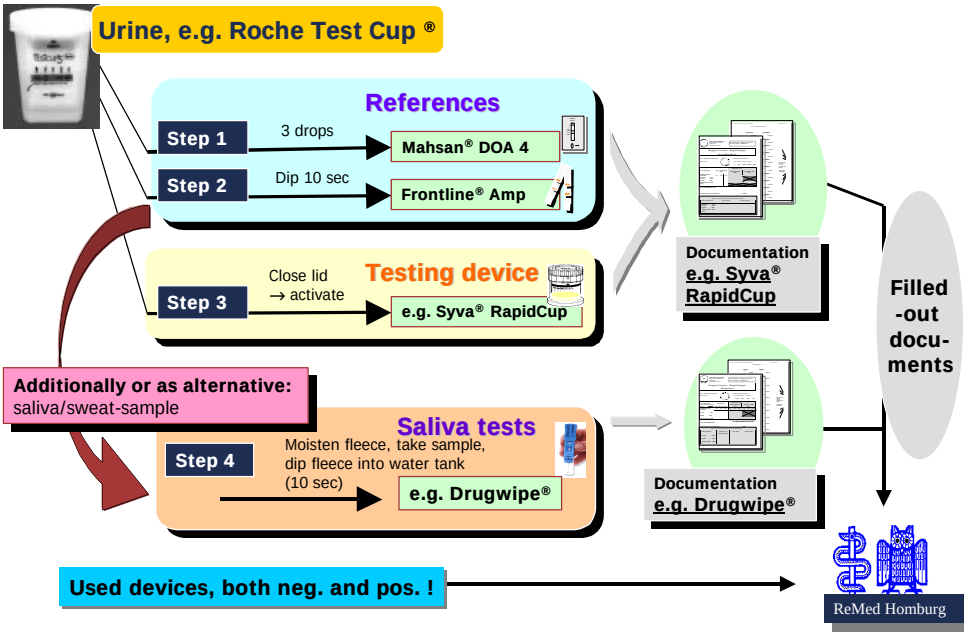


Figure 1: Testing Process

If a test was performed because of a suspicion regarding §24a and the result is negative, there is no more basis for further action. If the test result is negative, but indications according to §316 exist for a criminal offence, the blood sample has to be taken to gain the necessary evidence in court (the toxicological analysis is extended to all ”intoxicating” substances).
If the police officers decided to order a blood sample, they performed an orientating examination by means of a “check-list” in which they noted all traffic-relevant and weather conditions, special observations, and, in regard to the subject, symptoms of drug use and/or signs of impairment. A detailed clinical-physiological examination was done by the physician who took the blood sample. The results of these examinations were documented for legal purposes but they are not a subject of the evaluation for ROSITA.

Documentation

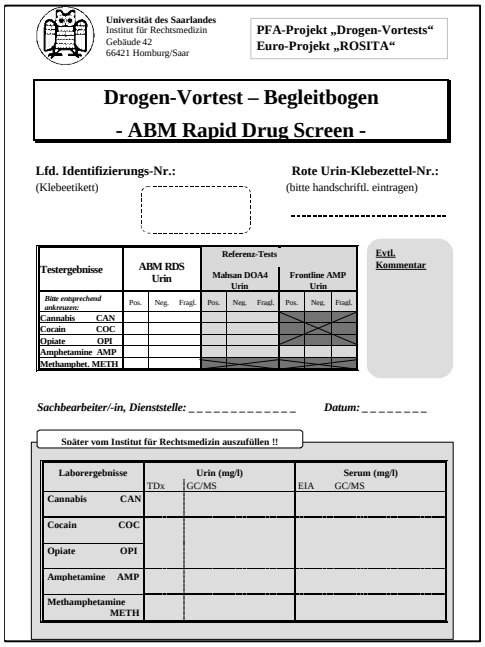
The documentation of the results was also carried out by the police officers on a developed form (Figure 2), which additionally enabled an allocation to the subsequent chemical-toxicological analysis and to the final findings. The documentation system was based on marking in columns for a positive or a negative test result of the appropriate device, or – if the result could not clearly be interpretated – for a doubtful result. In order to ensure maximal data protection, two systems of numbering were in function instead of personal data collection: by these two systems, a perfect allocation of the test results to the analytical results was given.

After Testing

The delay between on-site testing and blood sampling could be within some minutes to one hour. After a control or a testing situation, the collected tests and specimens (positive and negative) as well as the blood samples were stored at the police station at 4°C (fridge) until they were sent on the following working day to ILMH.

Final Police Assessment

To predicate the suitability of the roadside tests, a confidential report for each test system was drawn up (figure 3) which has been filled out by the police officers in charge. The report contains assessments in terms of operating instruction, handling, reaction time, readability etc. of the respective test version. From each TPD one report per test version was delivered; thus, three confidential reports per test version are present which were combined into a total result.



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66421 Homburg/Saar

PFA-Projekt „Drogen-Vortests“
Euro-Projekt „ROSITA“

Drogen-Vortest – Begleitbogen
- ABM Rapid Drug Screen -

Lfd. Identifizierungs-Nr.: (Klebeetikett)

Rote Urin-Klebezettel-Nr.: (bitte handschriftl. eintragen)

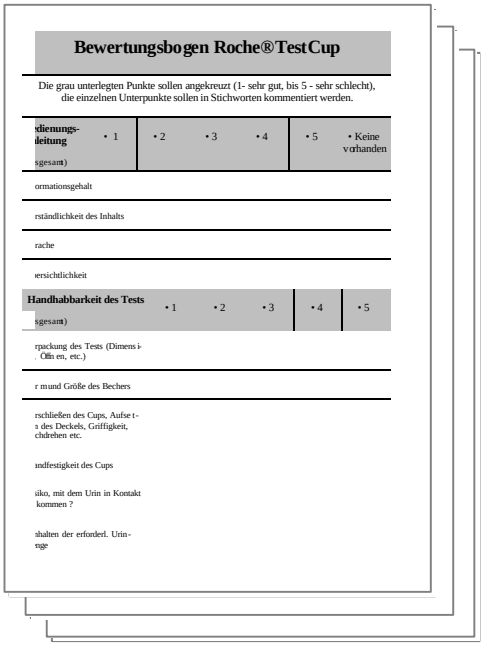
Testergebnisse	ABM RDS Urin			Referenz-Tests: Mahsan DOA4 Urin			Frontline AMP Urin			Evtl. Kommentar
Bitte entsprechend ankreuzen:	Pos.	Neg.	Fragl.	Pos.	Neg.	Fragl.	Pos.	Neg.	Fragl.	
Cannabis CAN										
Cocain COC										
Opiate OPI										
Amphetamine AMP										
Methamphet. METH										

Sachbearbeiter/-in, Dienststelle: _____ *Datum: _____*

Snäter vom Institut für Rechtsmedizin auszufüllen !!

Laborergebnisse	Urin (mg/l) TDx	Urin (mg/l) GC/MS	Serum (mg/l) EIA	Serum (mg/l) GC/MS
Cannabis CAN				
Cocain COC				
Opiate OPI				
Amphetamine AMP				
Methamphetamine METH				

Figure 2: Example Documentation Form



Bewertungsbogen Roche®TestCup

Die grau unterlegten Punkte sollen angekreuzt (1- sehr gut, bis 5 - sehr schlecht), die einzelnen Unterpunkte sollen in Stichworten kommentiert werden.

dienungs-leitung	• 1	• 2	• 3	• 4	• 5 • Keine vorhanden
sgesamt)					
ormationsgehalt					
rständlichkeit des Inhalts					
rache					
ersichtlichkeit					
Handhabbarkeit des Tests	• 1	• 2	• 3	• 4	• 5
sgesamt)					
rpackung des Tests (Dimens i- . Öffn en, etc.)					
r mund Größe des Bechers					
rschließen des Cups, Aufse t- s des Deckels, Griffigkeit, chdrehen etc.					
ndfestigkeit des Cups					
üiko, mit dem Urin in Kontakt kommen ?					
shalten der erforderl. Urin- nge					

Figure 3: Example Final Questionnaire

Role of the ILMH

The ILMH – beside the analytical evaluation of the test devices – is responsible for the organisation of the field study; it is incumbent on the procurement, distribution and eventually on the introduction of the drug versions which can be tested (e.g. *Roche TestCup*, *Cortez One Step Drug Scan*, etc.), of the reference tests (*Mahsan DOA 4*, *Frontline AMP*), of the documentation forms and of further consumables such as gloves, urine cups etc., as well as for the final questionnaires and their evaluation.

Laboratory Analysis and Classification of Roadside tests

By the decree of the Ministry of Interior, the Police of Saarland was placed in an excellent position to utilise the roadside tests directly in traffic controls to put one of the principal objects of ROSITA into practice, namely the assessment of the tests by police officers regarding their functionality at the roadside. In order to hear the opinion of a high number of police officers, as much tests as possible were distributed to the police, whereby due to the high amount of positive samples, as expected, quantitative urine analyses via GC-MS were too expendable. Therefore, the examinations of the cases were based on the routine analyses according to the order of the police, and the classification of the roadside tests was done on the basis of the obtained analytical results.
In order to coordinate the legal requirements concerning blood and urine analysis with ROSITA research and minimisation of analytical expences, the following procedure was used:
After registration via EDP, the blood samples recieved in the ILMH were centrifuged immediately, and the serum was isolated. The serum samples were examined according to the order of the police (administrative or penal offence) via immunoassay for the listed drugs of abuse (§24a admin. offence) or, in a broader screening, additionally for other psycoactive drugs (§§ 316, 315c penal code). A GC-MS confirmation followed in positive cases.
For administrative cases, the procedure used has been applied since the amendment of §24a Road Traffic Law in August 1998. It is the optimisation of administrative, analytical and cost-cutting

measurements. The procedure for penal code cases comprises a wide analytical examination program, including a great number of licit and illicit drugs and pharmaceuticals. Because the actual evaluation was limited to the substances detectable by the roadside tests, the procedure relevant for the evaluation within ROSITA is a part of the analytical procedure practically used in penal cases. Other substances detected by additional analyses were not included into the ROSITA evaluation.
In cases in which a result of a roadside test could not be correlated to serum analysis, urine was analysed to confirm the positive urine test(s). If urine was not available for analysis the serum result was taken for evaluation; however, in less than 1% this way of assessment was needed. Of course saliva/sweat tests were confirmed by serum not by urine results due to the better correlation of the concentrations. In penal code cases, generally the urine – if obtained – was examined and the analytical result could be taken for the evaluation of the roadside tests.

Generally, the assessment of the roadside tests was done having regard to the following aspects:

- The police officer's documentation of the results must be seen as correct. Random mistakes cannot be excluded, but if a result of a roadside test was documented wrongly, the police officer himself unwittingly counted the wrong documentation for right, including the taking of any further actions.
- The analytical procedure was performed according to the order of the police and to the appropriate legal requirements; if no discrepancies appeared, the classification of the roadside test into false positive, correct positive etc., was done according to the obtained analytical results.
- In case of discrepancies, these were clarified by appropiate analytical crosschecks.
- At the tests' evaluation, the appropiate cut-offs of the different devices and given cross-reactivities were taken into account. However, overlaping ranges around the test cut-off were used in favour of the test results.

The specimens were screened by instrumental enzyme immunoassay on the SLT Spectra EIA analyser (Mahsan MTP Microplates), according to the manufacturers' instructions. Urine samples were stored at 4°C until preparation for FPIA screening analysis on the Abbott TDxFLx analyser. The sensitivity and specificity of this techniques are well-known and evaluated. Generally, the delay between sampling and analysis could be within some hours to one week.

GC-MS serum analysis was performed on a 5890/5973 system from Hewlett Packard, and analysis was done by Hewlett-Packard Standard Software (G1701BA, Version 1.0).

Table 1: Laboratory cut-offs and LODs, respectively

	FPIA (ng/ml)	**EIA (ng/ml)**	**GC/MS (ng/ml Serum)**
CAN	20	2	0,3 (THC) 3,0 (THC-COOH)
COC	100	10	5,0 (COC) 5,0 (BZE) 5,0 (ME)
OPI	100	10	10,0 (MOR) 10,0 (COD) 5,0 (MAM)
AMP, Designer Drugs	200	20	10,0 (AMP) 5,0 (MAMP) 5,0 (MDA) 5,0 (MDMA) 5,0 (MDE)

Different types of results are obtained for every drug test device and for a certain drug class:

true negatives / positives: the number of samples that provided a negative / positive result with the on-site screening test and that were confirmed positive by laboratory analysis

false negatives / positives: the number of urine samples that provided a negative / positive result with the on-site screening test and not confirmed by laboratory analysis.

With these results, the following parameters can be determined:

sensitivity: the ability of the test device to identify those urine samples that truly contain a concentration of target analyte above a certain cut-off level

specificity: the ability of the test device to identify those urine samples that are truly drug-free or that contain a concentration of target analyte below the cut-off level

accuracy: probability that the test device gives a correct result in order to qualify systematic and random deviations

positive predictive value, PPV: probability that a positive test result is a true positive

negative predictive value, NPV: probability that a negative test result is a true negative

The calculations are as followed:

Sensitivity	:	true positive / [true positive + false negative]
Specificity	:	true negative / [true negative + false positive]
Accuracy	:	[true pos. + true neg.] / [true pos. + false pos. + true neg. + false neg.]
PPV	:	true positive / [true positive + false positive]
NPV	:	true negative / [true negative + false negative]

RESULTS

In General

Within the period from June 1999 to August 2000, altogether 1315 roadside test devices (1061 urine devices, 254 saliva/sweat devices) were used by about 100 different police officers to test 604 subjects in traffic offences.
In 58 cases no blood sample was taken, due to a total negative test result; however, the urine was sent to the ILMH for investigation. From these drivers, no specification of age and sex is present due to the anonymization. With the remaining 546 cases the balance is clearly on the side of the male drivers. Only approx. 5% of the examined drivers are women (figure 4).

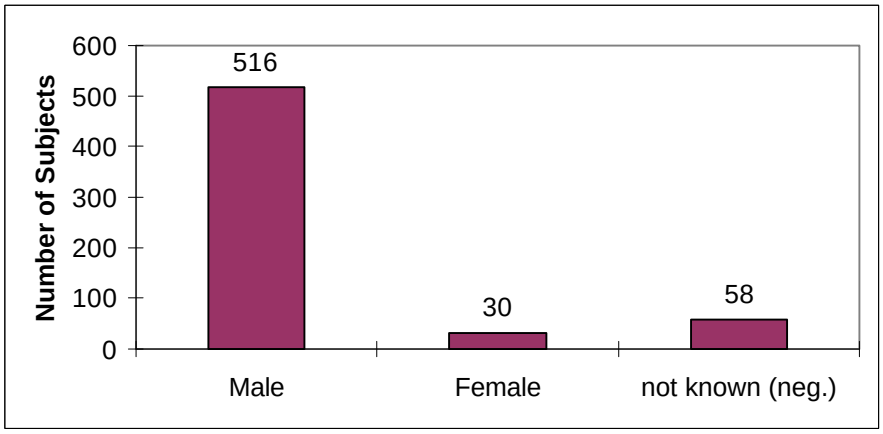


Figure 4: Sex of the positive tested drivers

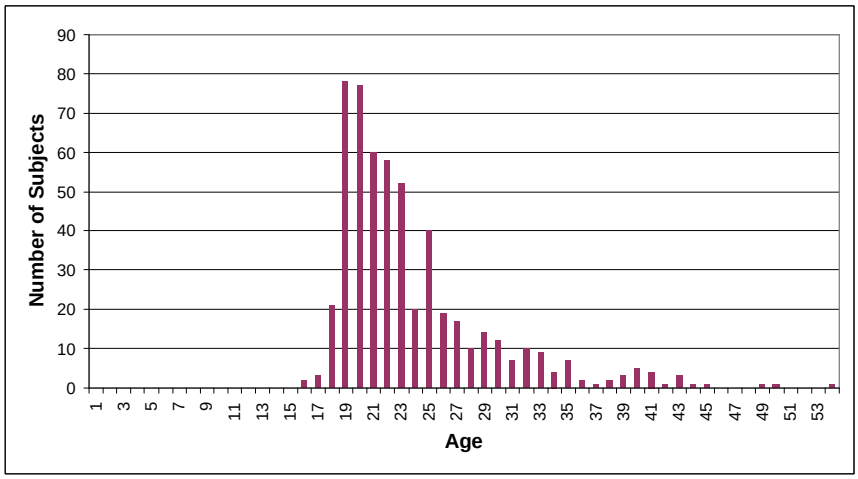


Figure 5: Age Pattern of the positive tested drivers

The majority of the drivers aged between 17 and 30 years (18-24: 366 (67%), 25-30: 112 (20%); 10% were between 30 and 40 years old, and only 2% were older than 40 years (figure 5). This age distribution is not really remarkable: the police has chosen particularly the young drivers as the target group checked for DUI at traffic controls, and those controls are performed in areas around events and places which where tailored to young people (discotheques, concerts etc.)

In Fig. 6 it is shown in how much cases also alcohol could be determined in addition to drugs.

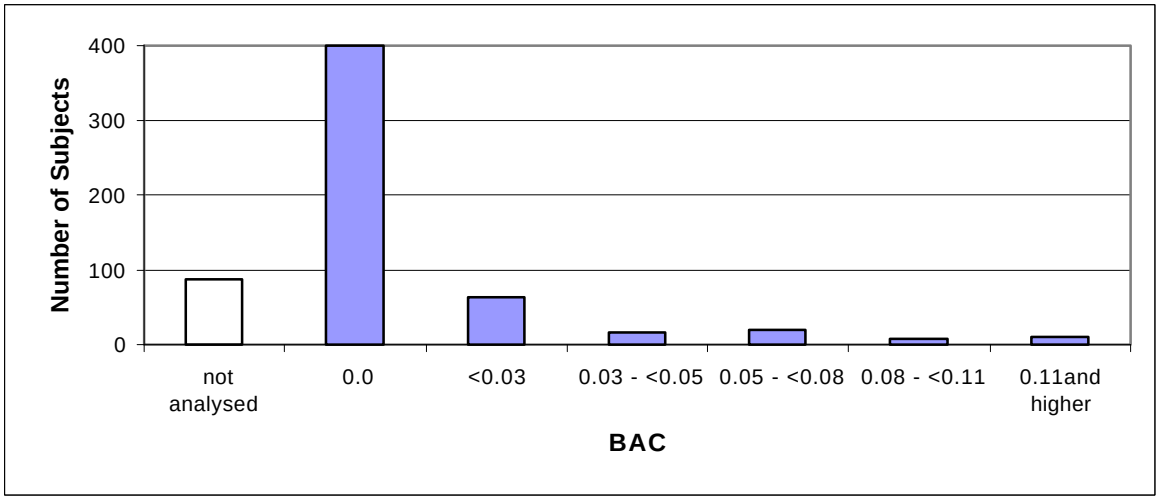


Figure 6: BAC pattern of the positive tested drivers

In 87 of the 604 cases, the BAC was not measured; the remaining cases, in approx. 80 % a BAC of zero was measured; on these drivers, the observations assessed by the police police could be referred completely to the influence of drugs. At BAC higher than 0.05%, it is difficult to differentiate between the influence of drugs and of alcohol, and at BAC's higher than 0.1%, the symptoms observed by the police generally can be referred predominatly to alcohol; the influence of drugs is overlaid.

Practical Aspects of Roadside Testing

In the following, the individual points are listed which have been worked out as important for the police officers:

General

Preferred Specimen

- The Saarland police officers are in complete agreement that the favourite specimen for testing is sweat, followed by saliva. These specimen allow testing with good co-operation of a driver, in combination with good availability at the roadside without beeing invasive. But for the moment, tests with urine as specimen are more accepted mainly due to good experiences with the test devices (multi-testing, less problems with urine collection than expected before the ROSITA field study) and due to the manual and analytical inferiority of saliva/sweat test devices (collection methods, dependency of consistence of specimen, reading, not all substances covered). But there is no doubt that after introduction of an improved saliva or sweat test system which enables the safe detection of all important substances in a clean way, the police officers will be more interested to use on these specimens.

Substances to be detected

- Especially in order to fulfil the requirements of the German legislation regarding §24a Road Traffic Law, a test system should detect all substances listed in the law's annex, namely Amphetamine, MDMA, MDE, Cannabis, Cocaine, Heroin, and Morphine (the target analytes for Heroin and Cocaine are Morphine and Benzoylecgonine, respectively). The more substances are in one shot, the better, but Cannabis and Amphetamine/Designer Drugs should be absolutely included, due to their enormous prevalence in road traffic in Saarland. Tests for only one, two or three substances are also accepted, but under the line an appropiate test must be available for each of the listed drugs. If not, they can be used only in addition to other test systems. Anyway, in order to save time and money, their use requires an experienced police officer who is able to connect observed symptoms to the consumption of the appropiate drug(s).

Urine tests
It is not a problem to detect the substances Morphine and Benzoylecgonine. However, it is more difficult to detect a) THC and b) amphetamine and the designer drugs.

- All roadside test systems for Cannabis are suited to detect THC-COOH, the main urinary metabolite of Cannabis. Independent of the tests‘ analytical ability to detect THC-COOH, there is the question up to what extend this could be assigned to the requirements of the law. In the urine of a chronic Cannabis user who didn't consume cannabis for a week, by sure THC-COOH can be found, but no THC; therefore, a performed urine test with a positive result for CAN of course is correct, but the subject can't be sanctioned regarding §24a StVG. However, it has to be recollected that the police officer needs an initial suspicion before performing drug tests at the roadside. There must be signs of recent drug consumption, delayed pupil reaction, etc. A driver not having smoked for one week does't have these signs, and therefore normally he will not be checked in a roadside test. To draw destinctions of cases, of course it is a precondition that the police officer is experienced and – as far as possible - trained to recognise drug influence.

- Most Amphetamine tests do not crossreact with Methamphetamine, MDMA and analogues (with the exception of Roche Frontline Amphetamine test). They usually have a 40 to 50% cross-reactivity for MDA. The Methamphetamine tests usually have a high cross-reactivity for Methamphetamine and MDMA but NOT for Amphetamine and MDA. As a result, a panel test with Amphetamine and Methamphetamine in the same panel would be ideal for German circumstances to be sure to detect all substances listed in the annex of §24a Road Traffic Law. Regrettably, only two tests used in the field study met this claim with a panel of five drugs (Syva Rapid Test, American Bio Medica Rapid Drug Screen); in the other cases, (next to Cannabis, Cocaine, Opiates) there was only an Amphetamine test provided. As a consequence, the Frontline for Amphetamines was used as a reference test in addition to Mahsan DOA 4. There is a very good sensitivity and specificity, and an easy detection of d-Amphetamine, d-Methamphetamine, MDMA, MDEA and MBDB, so that in combination with Mahsan DOA 4, the police officer has the potentiality to cover the §24a StVG-spectrum.

Additional
In order to understand the difficulties of roadside testing, a special focus must be made to the substancial (structural) problems of the police officers. Absolutely new problems occured with performing roadside testing, especially in drug control actions. The officers have to deal with an age group which is not the same as theirs; people going to discotheques are mostly youngsters, and the peak times of the travelling to and from discotheques are after midnight. For officers who are older than 50 years, the age difference and the time of controls are a problem not to be neglected due to the physical conditions as well as to generation problems. Additionally the dangerousness of the situation must be taken into consideration; of course the party time of discotheques and events is also the high time for dealers which are also "on the road". The officers have to have in mind that the self-protection is of great importance. On one hand against "dealers" possibly carrying weapons, and on the other hand against contamination with body fluids at the testing procedure. Thereby, an wide range of equipment must be used from apparently banal things like latex gloves to bulletproof vests. Beside a high level of motivation, this conditions require flexibility and alertness from the officers.

Testing-related aspects

Collection of specimen
The police officers generally were not acustomed to work with body fluids. Especially in the beginning of the field study, there was only a very small tolerance range to work with them. Therefore, at the conditions at the roadside, for the police officers not only the analytical part of a test system is important, but also the reasonability of the collection method. Even a perfect test from the analytical point of view is not practicable for the police work and will not be accepted when the collection method exceeds a "limit of disgusting". As actual example, the Avitar Oral Screen was rejected very soon by the officers due to the appropiate handling with specimen: saliva has to be collected by a foam in the subject's mouth, and the officer has to squeeze the foam between his fingers until the saliva drops out on a test card into a reaction field. Unfortunately, in no case the testing procedure could be performed without complications: this time, the saliva was very frothy and air bubbles were formed, or it was very viscous and the officers had to press hard the collector. Some other time, not enough saliva could be obtained (Amphetamine consumption? Cannabis consumption?) and finally the subject had to

spit directly on the reaction field of the test card. In one case, the subject bit off the foam of the collector, and in other cases, leftovers of food sticked on the foam after removing the collector of the mouth of the subject. In nearly all cases, the officers' fingers were wetted with saliva. Astonishingly, only the Avitar Oral Screen as system for testing the specimen saliva exceeded the „limit of disgusting", and not, as maybe expected, a testing system for urine or even all urine tests on the basis of handling with urine alone.
Additionally, along with the tests the police officers had to become familiar with other utensils such as plastic gloves, pipettes etc., and the handling of urine-contaminated waste. After a period of habituation, the officers were able to handle the tests even in a "chemistlike" manner. However, this incident should not mislead to the assumption that the kind of handling is not important. On the contrary, the tests must be very easy and secure to handle for the officers in order to minimise those mistakes appearing conditional on the combination of roadside "reallife" conditions and of a tricky drug test system.

- **Urine**
  Normally the collection of urine took place where the privacy of the subject is protected, namely at police stations or at public lavatories. In special cases, the alternative was offered to perform a test directly at the roadside. In most cases the suspected driver cooperated with the police and a urine sample could be obtained. In about 3% of the documented cases the driver was not able to give a urine sample or the given amount was not enough to perform the test. In order to deal with this problem, the police officers tried to achieve a sufficient amount of urine by collecting in several steps, or, due to the availability of different test devices, they could use another test device requiring less urine. As an addition or as alternative, and also in case of refusal, the use of a saliva test or sweat test could be offered to the suspect. The storage and transportation of the collected specimens was sometimes problematic mainly due to the occurrence of leaking cups (especially Roche Test Cup, Syva Rapid Cup). This seems to be a construction problem, but may also have its reason in the special circumstances at the roadside (low temperature, transport, etc.). Doubtful results appeared relatively seldom (in about 2-5%, varying widely between the different test devices). Difficulties with the reading can be mentioned as reason, due to the circumstances (light conditions – blue lines better to read than red lines, temperature, stress, etc.) or test specific (thin or weak lines, etc.), as well as test failures (no valid lines, broken lines, etc.). Urine seems to be an acceptable but not the optimal sample for the roadside use. The performing of the urine-tests requires a higher expenditure of time and personal as a test that can be done directly at the roadside, due to the need of usable places to collect the samples. But nevertheless, the police officers actually ranked the urine tests higher than saliva/sweat tests because of the better reliability and the broader spectrum of drugs which can be tested with one device. Problems of refusal and the disability to give a sample occurred relatively more often than in case of saliva/sweat tests, while the problem of the collection of the necessary amount depended more on the type of the test as on the type of the sample. In this regard, an absolute advantage of pipet tests can be pointed out especially in contrast to cup tests, namely the power to start the reaction with only drops of urine. This aspect was mentioned by the police officers as very important and necessary for the testing at the roadside. On the other hand, by using cup tests, generally the problem of contamination with urine was mastered better than by using pipet tests or dip tests. However, the police officers could not really take this advantage due to the leaking of the used cup tests conditional on complexity of the system (Roche Test Cup; lid position for chromatography is not the final position on which the cup is closed, sealing of vent necessary), on material (Syva Rapid Test; "muscular effort" required to close and to re-open the cup), or conditional on a remaining risk of contamination (American Bio Medica Rapid Drug Screen; urine-wet test card).

- **Saliva**
  The problems in collection of saliva/sweat were minor compared to the collection of urine; the collection of specimens is not invasive and the tests could be performed directly at the roadside without requireing special facilities, maintaining the protection of privacy, so that the expenditure of time and personal remains remarkably lower than in case of the urine tests. The subjects were more willing to co-operate (there were no documented refusals) and the risk of adulteration seems to be low. But depending on the test devices there is a clear difference between the methods of collecting saliva and the necessary volume. In case of the Drugwipe the way to collect the specimen by wiping the tongue or the forehead (sweat) is accepted by the police officers, the necessary amount is very low and does not depend on the consistence of the specimen. In one case, the test was performed successfully even in a subject's nose. Therefore the acceptance of the Drugwipe test by the police officers is good. Unfortunately in very few cases the officers documented the specimen they used, so an evaluation according to this point of view is not possible. The amount and consistence of saliva needed to perform an Oral Screen test or a Toxi Quick test is from much

more importance than in case of the Drugwipe so that problems with viscous saliva and insufficient specimen occured, especially by users of Amphetamine and Cannabis. Furthermore the way of collecting the specimen seems to be disgusting for the police officers so they rejected the Oral Screen and the Toxi Quick very soon. Regarding the reading of the results, the absence of a control line and the irregularity of the color field of the Drugwipe led in borderline cases to a lot of "doubtful" results and, for sure, sometimes to a false result. Therefore, from the practical point of view it is a big advantage that the Dugwipe could be read out by an electronic reader. The appearance of a number higher or lower than 800 degrees instead of a color field facilitates the decision between positive and negative and thereby seem to reduce the doubtful cases dramatically. Unfortunately the reader had been involved very late into the German ROSITA field study. So there are only a few results read out electronically, and of course in terms of sensitivity, specifity etc., the appropriate data do not allow to make final statements. In principle, saliva and sweat are more practicable samples than urine and they are requested by the police officers. They are easy to collect without excessive inconvenience and the specimen can be handled without endangering the officers. However, the short time of experience within the testing with saliva and sweat and the generally low amount of the sample for laboratory confirmation remain reservations. So at this point of time of the police officers saliva and sweat tests ranked behind the urine tests, although they would prefer saliva and sweat as specimen to work with. But it is very important to know that especially regarding the collecting of the saliva samples, a "limit of disgusting" may not be exceeded; the police officer generally is not used to work with body fluids, and there is only a very small acceptance range to work with them. Therefore, for the police officers, at roadside conditions not only the analytical part of a test system is from importance, but also the reasonability of the collection method.

- **Amount**
  The necessary amount of specimen to start the test systems was emphazised as sometimes big problem at the roadside. In this regard, an absolute advantage of pipet tests can be pointed out, especially in contrast to cup tests, namely the power to start the reaction with only drops of urine. On the other hand, by using cup tests, generally the problem of contamination with urine was mastered better than by using pipet tests or dip tests. However, the police officers could not really take this advantage due to the leaking of the used cup tests conditional on complexity of the system (Roche Test Cup; lid position for chromatography is not the final position on which the cup is closed, sealing of vent necessary), on material (Syva Rapid Test; "muscular effort" required to close and to re-open the cup), or conditional on a remaining risk of contamination (American Bio Medica Rapid Drug Screen; urine-wet test card). The same is valid for saliva test systems; the Securetec Drugwipe was more accepted than Avitar Oral Screen and Biomar Toxiquick, among other things, due to the lower amount of necessary sample needed and thereby to minimise the full use of working with this specimen.

Reading

As limitation of roadside tests, in general, it is often mentioned that they only give a result as positive or negative, that nothing can be concluded about the amount of drug present in the specimen. But regarding the German DUI legislation, the police officer doesn't need a quantification of drugs necessarily, he needs a qualification in terms of a clear and unambiguous result in order to confirm or to extenuate his suspicion regarding recent drug consumption. This clearness of the test result was considered as most important for the officers; a safe result plays a prominent role at the roadside to provide security on an handling level (possibility to demonstrate the "corpus delicti" immediately to the suspect) as well as on a psychological level (conviction of doing the right). The analytical correctness of a test becomes important later on. Therefore, all features are from importance which ensure reaching this aim:

- a control instance should exist as working control and as comparison wether a drug line appeared or not or, in case of a field test, if there is a change of colour or not. Due to the absence of such a control at the Roche Frontline and of the Securetec Drugwipe, their amount of false positive and doubtful results is not conclusively due to analytical failures, but likewise they might have occured because of unsureness in reading the results. Unfortunately, this can only be assumed, an examination at a later date is not possible. Anyway, for the police officers the result below the line is the same: these test systems seem not to be done without problems at the roadside.
- At line tests, in positive cases not even the touch of a line should appear in order to avoid interpreting the result as (false) negative. In negative cases, the lines must appear clear, plain, complete and thick – the more intensive, the better. At field tests, a discolouration from white to colour on the indicator field should be also clear and complete. Due to the fact that on large-scaled crossings the German street lighting effuses bright orange light, an orange- or red-line/field and

possibly weak coloured test result is very difficult to read, the contrast is very low. Therefore, also from this reason in the case of the Roche Frontline and the Securetec Drugwipe maybe false or doubtful results were documented. The ABM Rapid Drug Screen has got a red line system as well, but due to the existing of a control line, the problem of color seems – in view of the lower amount of false and doubtful results – not to be that big. However, the blue line system was valued to be more suitable for testing on German streets. In this context, an electronical reading or generally an electronic system with a clear differentiation between positive and negative (by flashing of lamps or, as in case of the electronic reader of Securetec, by appearance of a number higher or lower than 800 units) seems to be the optimal solution. However, it has to be considered that such a system must simplify the testing and not to make it more complicated due to too many working steps.

Analytical results

Urine Tests

Table 2: Roche Frontline AMP

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
AMP Positive		86	25	111
AMP Negative		2	56	58
AMP Total		88	81	169
Doubtful	16			185
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
97,73%	**69,14%**	**84,02%**	**77,48%**	**96,55%**

Table 3: Mahsan DOA4

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
CAN Positive		346	3	349
CAN Negative		1	120	121
CAN Total		347	123	470
Doubtful	9			479
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
99,71%	**97,56%**	**99,15%**	**99,14%**	**99,17%**
COC Positive		46	10	56
COC Negative		0	416	416
COC Total		46	426	472
Doubtful	8			480
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**97,65%**	**97,88%**	**82,14%**	**100,00%**
OPI Positive		38	5	43
OPI Negative		0	428	428
OPI Total		38	433	471
Doubtful	7			478
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**98,85%**	**98,93%**	**88,37%**	**100,00%**
AMP Positive		123	0	123
AMP Negative		7	322	329
AMP Total		130	322	452
Doubtful	25			477
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
94,62%	**100,00%**	**98,45%**	**100,00%**	**97,87%**

Table 4: Roche Test Cup

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
CAN Positive		55	1	56
CAN Negative		1	17	18
CAN Total		56	18	74
Doubtful	2			76
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
98,21%	**94,44%**	**97,30%**	**98,21%**	**94,44%**
COC Positive		5	0	5
COC Negative		0	72	72
COC Total		5	72	77
Doubtful	2			79
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**100,00%**	**100,00%**	**100,00%**	**100,00%**
OPI Positive		3	1	4
OPI Negative		0	74	74
OPI Total		3	75	78
Doubtful	1			79
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**98,67%**	**98,72%**	**75,00%**	**100,00%**
AMP Positive		21	0	21
AMP Negative		0	56	56
AMP Total		21	56	77
Doubtful	1			78
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**100,00%**	**100,00%**	**100,00%**	**100,00%**

Table 5: Cortez One-Step Drug Scan

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
CAN Positive		36	1	37
CAN Negative		0	12	12
CAN Total		36	13	49
Doubtful	3			52
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**92,31%**	**97,96%**	**97,30%**	**100,00%**
COC Positive		5	7	12
COC Negative		0	32	32
COC Total		5	39	44
Doubtful	8			52
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**82,05%**	**84,09%**	**41,67%**	**100,00%**

Table 5 (continued): Cortez One-Step Drug Scan

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
OPI Positive		3	2	5
OPI Negative		0	41	41
OPI Total		3	43	46
Doubtful	6			52
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**95,35%**	**95,65%**	**60,00%**	**100,00%**
AMP Positive		20	5	25
AMP Negative		1	24	25
AMP Total		21	29	50
Doubtful	2			52
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
95,24%	**82,76%**	**88,00%**	**80,00%**	**84,00%**

Table 6: Dade Behring Syva Rapid Cup

Test Results		*Confirmed*		
		Positive	**Negative**	**Total**
CAN Positive		115	0	115
CAN Negative		0	35	35
CAN Total		115	35	150
Doubtful	2			152
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00 %	**100,00 %**	**100,00 %**	**100,00 %**	**100,00 %**
COC Positive		18	0	18
COC Negative		0	129	129
COC Total		19	129	147
Doubtful	5			152
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**100,00 %**	**100,00%**	**100,00 %**	**100,00%**
OPI Positive		17	0	17
OPI Negative		0	132	132
OPI Total		17	132	149
Doubtful	2			151
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**100,00 %**	**100,00%**	**100,00 %**	**100,00%**
AMP Positive		56	1	57
AMP Negative		0	91	91
AMP Total		56	92	148
Doubtful	3			151
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**98,91%**	**99,32%**	**98,25%**	**100,00%**

Table 6 (continued): Dade Behring Syva Rapid Cup

MAMP Positive		10	3	13
MAMP Negative		0	8	8
MAMP Total		10	11	21
Doubtful	1			22
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**72,73%**	**85,71%**	**76,92%**	**100,00%**

Table 7: American Bio Medica Rapid Drug Screen

Test Results		*Confirmed*		
		Positive	**Negative**	**Total**
CAN Positive		74	4	78
CAN Negative		0	27	27
CAN Total		74	31	105
Doubtful	4			109
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**87,10%**	**96,19%**	**94,87%**	**100,00%**
COC Positive		16	6	22
COC Negative		0	85	85
COC Total		16	91	107
Doubtful	2			109
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**83,47%**	**94,39%**	**72,73%**	**100,00%**
OPI Positive		11	3	14
OPI Negative		0	94	94
OPI Total		11	97	108
Doubtful	1			109
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**96,91%**	**97,22%**	**78,57%**	**100,00%**
AMP Positive		30	1	31
AMP Negative		1	74	75
AMP Total		31	75	106
Doubtful	3			109
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
96,77%	**98,67%**	**98,11%**	**96,77%**	**98,67%**
MAMP Positive		20	4	24
MAMP Negative		2	58	60
MAMP Total		22	62	84
Doubtful	8			92
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
90,91%	**93,55%**	**92,86%**	**83,33%**	**96,67%**

Not enough data were available for statistical analysis of **Biomar Toxi Quick** (only 4 tests performed, 3 of them “all doubtful”)

Failures

The failures have been valued by the definition of most manufacturers: if at least one reaction field showed no valid line, the complete test was countered as a failure. But it is worth to mention that in case of those test devices with separate reaction fields (American Bio Medica Rapid Drug Screen, Roche Test Cup, Syva Rapid Cup) the other fields beside the invalid field showed - if they were documented - correct results (exception: Syva Rapid Cup Opiates 1x doubtful).
In the following tables only the cases documented by the police officers are included. The numbers of undocumented cases are probably higher. The number of tests in brackets consists of the documented performed tests (including the doubtful tests) plus the number of documented failures.

Table 8: Failures (documented)

	Total failures (Tests)	***Percentage (referring to total test number)***	***Reasons***
Mahsan DOA4	1 (481)	0,21%	no valid line
Roche Frontline AMP	0 (185)	0,00%	
Roche Test Cup	5 (84)	5,95%	no lines, no test reaction
Syva Rapid Cup	12 (164)	7,32%	no test lines, no valid lines, chamber not filled with urine after closing
ABM Rapid Drug Screen	2 (111)	1,80%	no valid lines
Cortez One Step Drug Scan	0 (52)	0,00%	
Biomar ToxiQuick	2 (6)	33,33%	no test reaction, no valid lines

Table 9: Amount of urine to low for testing (documented)

	Total
Mahsan DOA4	0
Roche Frontline AMP	0
Roche Test Cup	2
Syva Rapid Cup	10
ABM Rapid Drug Screen	2
Cortez One Step Drug Scan	0
Biomar ToxiQuick	0

Table 10: No urine sample given (documented) / only blood available

Total of all cases a urine test was offered	
20	(16 not possible, 4 refusal)

Advantages / Disadvantages

After the testing phase the police officers in charge of all the three TPD´s have been assessed all the used test devices via questionnaires (figure 2), wich in total give a clear overview about advantages and disadvantages of the tests.

Table 11: Advantages/disadvantages

Test	*Advantages*	*Disadvantages*
Mahsan DOA4	• suitable card size • short, clear and informative • operating instruction provided in German • easy handling, very few failures • minimum 3 drops of urine • very positive and reasonable as help for the police at the roadside / station	• no MAMP included • no cup, no package for asservation provided • pipette provided, but separate • risk of contamination with urine • prolongation of reaction time by use at low temperatures
Frontline AMP	• simple design • Operating instruction short, clear and informative • operating instruction provided in German language • easy handling • if not much urine available: bending of test strip possible • no prolongation by low temperature • 2 TPD´s: positive and reasonable as help for the police at the roadside / station	• no cup provided, no package for asservation • high risk of contamination with urine (unprotected fleece) • no control line • 1 TPD : "not optimal"
Roche Test Cup	• suitable size and material • re-closable plastic bag provided • operating instruction clear and informative • low risk of contamination of urine • positive and reasonable as help for the police at the roadside / station	• no MAMP included • operating instruction should be provided in German language • "complicated", but easy after habituation • few failures (1 TPD: 5-10%) • minimum 30 ml (trick: tilting) • prolongation of reaction time by use at low temperatures
Syva Rapid Cup	• MAMP included • operating instruction very clear and informative • operating instruction provided in German language • easy handling • low risk of contamination of urine • positive and reasonable as help for the police at the roadside / station	• cup too big (transport and storage problem) • "strenuous effort" to close (licking in 5-10%) • difficult to open (collecting urine, additional tests, failures) • few failures (1 TPD: 4%); often partial • minimum 40-50 ml • prolongation by use at low temperatures
ABM Rapid Drug Screen	• MAMP included, suitable cup size • operating instruction clear, good illustrations • easy handling, • if not much urine available: possibility to pipette	• operating instruction should be provided in German language • risk of contamination with urine after removing the test cards • test card urine-wet • few failures • prolongation by use at low temperatures
Cortez One Step Drug Scan	• suitable card size • operating instruction acceptable • easy handling • if not much urine available bending of strips • 2 TPD´s : positive and reasonable as help for the police at the roadside / station	• no MAMP included • no cup, no package for asservation provided • operating instruction should be provided in German language • risk of contamination with urine • few failures • prolongation by use at low temperatures (single cases more than 15 minutes) • 1 TPD: "not optimal"
Biomar Toxi Quick		• not accepted by the police officers, only 4 tests performed

Necessary Reaction Time

Reaction time means the interval from the moment of the contact between the specimen and the test (by pipetting, closing of the cup, etc.) until the appearance of the valid line. The additional time to prepare the test device was about 1-2 minutes for each device as well as the time needed for documentation.

Table 12: Necessary Reaction Time

Test	*Necessary Reaction Time*
Mahsan DOA4	approximately 2 minutes
Frontline AMP	approximately 1-5 minutes
Roche Test Cup	approximately 6-10 minutes
Syva Rapid Cup	approximately 2-5 minutes
ABM Rapid Drug Screen	approximately 6-10 minutes
Cortez One Step Drug Scan	approximately 6-10 minutes
Biomar Toxi Quick	not enough tests performed

Reading of the Results

Table 13: reading of the results

Test	*Reading of the Results*
Mahsan DOA4	no problems to interpretate, clear results
Frontline AMP	problems to interpretate (especially in borderline areas and at bad light conditions)
Roche Test Cup	no problems to interpretate, clear results
Syva Rapid Cup	2 TPD´s: no problems to interpretate 1 TPD: sometimes problems to interpretate
ABM Rapid Drug Screen	2 TPD´s: no problems with reading and interpretation 1 TPD: often weak lines (even control line), leads to uncertainty
Cortez One Step Drug Scan	1 TPD: no problems with reading 1 TPD: often unclear or no results (even control), leads to uncertainty 1 TPD: only problems in few cases
Biomar Toxi Quick	not enough tests performed

Ranking

To find out the most suitable urine test for the German police within ROSITA, a ranking list was filled out by the police officers in charge. By each TPD, each test could be rated with a number from 1 to 10, from “completely unacceptable” to “very suitable”; the higher the number, the better. From each TPD one report per test version was delivered; thus, three confidential reports per test version are present which were combined into a total result with a minimum of 3 points and a maximum of 30 points per test.

For the police officers, each urine test is seen as an advantage and needful help in detecting drug influenced drivers with a clear preference to the Mahsan DOA4 and the Syva Rapid Cup. All tests give the possibility to gain an immediate feedback to the initial suspicion of the police officer and give a support to decide about further legal actions. This is especially helpfull in the field of illegal drugs because the detection of drug consumption is not as easy as with alcohol.

From the analytical point of view, as very important can be considered the minimisation of false negative results due to the fact that a negative tested driver who was allowed to drive on remains being a potential risk in traffic. In case of a false positive test outcome legal steps are taken after blood

sampling and withdrawal of the drivers licence, but of course after the laboratory analysis of the serum the legal measures are resolved. Therefore, considering the possible consequences for traffic safety a false negative test result has a higher value than a false positive one.

Table 14: ranking

Test	***Police Ranking***	
	Score (min. 3 max. 30)	⇒ Acceptance
Mahsan DOA4	27/30	90,0 %
Syva Rapid Cup	24/30	80,0 %
Roche Test Cup	20/30	66,6 %
ABM Rapid Drug Screen	19/30	63,3 %
Frontline AMP	16/30	53,3 %
Cortez One Step Drug Scan	15/30	50,0 %
Biomar Toxi Quick	12/20 (two TPD's)	60,0 %

The accuracy as parameter for the reliability of the test can be used to rank the different test devices by comparing the means of the single drug accuracies of each device.

Table 15: accuracy as parameter for the reliability of the test

Accuracy Ranking	***CAN***	***COC***	***OPI***	***AMP***	***MAMP***	***MEAN***
Roche Test Cup	97,30	100,00	98,72	100,00	-	**99,00**
Mahsan DOA4	99,15	97,88	98,93	98,45	-	**98,60**
Syva Rapid Cup	100,00	100,00	100,00	99,32	85,71	**97,00**
ABM Rapid Drug Screen	96,19	94,39	97,22	98,11	92,86	**95,75**
Cortez One Step Drug Scan	97,96	84,09	95,65	88,00	-	**91,42**
Roche Frontline AMP	-	-	-	84,02	-	**84,02**
Biomar ToxiQuick	-	-	-	-	-	**-**

100% as ideal outcome couldn't be reached, but with the **Roche Test Cup**, the **Mahsan DOA4**, the **Syva Rapid Cup** and the **American Bio Medica Rapid Drug Screen**, four tests performed over 95% which can be seen as absolutely acceptable.

Regarding both the police and the analytical results, the **Roche Test Cup**, the **Mahsan DOA4**, the **Syva Rapid Cup** showed themselves as the most practicable and reliable ones. The **American Bio Medica Rapid Drug Screen,** the **Cortez One Step Drug Scan** and the **Roche Frontline** are at a middle region.

These rankings are based on practical experiences and therefore they are not absolute, of course. However, to make use of them, it should be considered that the special conditions of night shifts, bad weather conditions, partly hectic etc. don't show the usefulness of the test systems under reproducible laboratory conditions (daylight, trained technicians, room temperature etc.).

Saliva/Sweat Tests

It is of note that saliva/sweat was not asservated as appropiate reference sample for further analysis after testing. According to the actual legal situation, the confirmation of the saliva/sweat tests was done by blood analysis; in both specimens, the actual circulating concentration of drugs and their metabolites at the time of collection can be estimated. Positive test results were confirmed by serum analysis via EIA and GC/MS. The negative cases were confirmed the same way if a blood sample was taken. If there were no legal actions because of a negative test (urine and/or saliva test), this result was seen as correct negative.

Table 16: Securetec Drugwipe visual read-out

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
COC Positive		5	9	14
COC Negative		3	26	29
COC Total		8	35	43
Doubtful	11			54
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
62,50%	**74,29%**	**72,09%**	**35,71%**	**89,66%**
OPI Positive		16	6	22
OPI Negative		2	31	33
OPI Total		18	37	55
Doubtful	6			61
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
88,89%	**83,78%**	**85,54%**	**72,73%**	**93,94%**
AMP Positive		72	24	96
AMP Negative		0	24	24
AMP Total		72	47	120
Doubtful	17			137
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
100,00%	**51,06%**	**80,00%**	**75,00%**	**100,00%**

Plus 6 tests which were not included into the evaluation, because only urine was collected and therefore no suitable matrix was available for assessment.

Table 17: documented specimen (visual reading)

	Saliva	*Sweat*	*No Comment*	*Others*
Drugwipe Cocain	6	7	41	0
Drugwipe Opiates	8	8	44	1 (within nose)
Drugwipe Amphetamines	41	9	93	0

Table 18: Avitar Oral Screen

Test Results		***Confirmed***		
		Positive	**Negative**	**Total**
CAN Positive		0	0	0
CAN Negative		4	0	4
CAN Total		4	0	4
Doubtful	0			4
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
0,00%	**not applicable**	**0,00%**	**not applicable**	**0,00%**
COC Positive		0	0	0
COC Negative		0	4	4
COC Total		0	4	4
Doubtful	0			4
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
not applicable	**100,00%**	**100,00%**	**not applicable**	**100,00%**
OPI Positive		0	0	0
OPI Negative		1	3	4
OPI Total		1	3	4
Doubtful	0			4
Sensitivity	**Specificity**	**Accuracy**	**PPV**	**NPV**
0,00%	**100,00%**	**75,00%**	**not applicable**	**75,00%**

Not enough data were available for statistical analysis of **Biomar Toxi Quick** (only 1 test performed)

Failures

In the following tables, only the cases documented by the police officers are included. The numbers of undocumented cases are probably higher. The number of tests in brackets consists of the number of documented performed tests (including the doubtful tests) plus the number of documented failures.

Table 19: Failures

Failures	***Total***	***Percent***	***Reasons***
Drugwipe Cocain	0	0,00%	
Drugwipe Opiates	0	0,00%	
Drugwipe Amphetamines	0	0,00%	
Avitar Oral Screen	6	60,00%	test did not flow to valid line, viscous saliva, low volume
Biomar Toxi Quick	1	100%	test did gave no result

Advantages / Disadvantages

After the testing phase the police officers in charge of all the three TPD´s have been assessed all the used test devices via questionnaires (figure 3), wich in total give a clear overview about advantages and disadvantages of the tests.

Table 20: Advantages/disadvantages

Test	*Advantages*	*Disadvantages*
Securetec Drugwipe	• suitable size • usable for saliva and sweat • operating instruction very clear and informative • operating instruction provided in German language • easy handling • low amount of saliva/sweat • very low risk of contamination with specimen • positive and reasonable as help at the roadside / station in addition to urine tests, • electronic reader as an addition seems to be necessary	• single tests • no CAN included • no control line (without electronic reader) • carrying of water "troublesome" • prolongation by use at low temperatures
Avitar Oral Screen	• operating instruction acceptable	• no AMP included • operating instruction provided only in English language • not acceptable system of collection • big amount of saliva necessary • reaction time depends enormously on type of saliva • only very few tests have been working • not accepted as help for the police at the roadside / station
Biomar Toxi Quick		• not accepted by the police officers, only one test with saliva performed

Necessary Reaction Time

Reaction time means the interval from the moment of the contact between the specimen and the test (by pipetting, closing of the cup, etc.) until the appearance of the valid line. The additional time to prepare the test device was about 1-2 minutes for each device as well as the time needed for documentation.

Table 21: Reaction Times

Test	*Necessary Reaction Time*
Securetec Drugwipe	approximately 2-5 minutes
Avitar Oral Screen	approximately 6-10 minutes
Biomar Toxi Quick	not enough tests performed

Reading of the Results

Table 22: Reading of the Results

Test	*Reading of the Results*
Securetec Drugwipe	without electronic reader: often unclear results with electronic reader: optimal reading
Avitar Oral Screen	if the test works: no problems
Biomar Toxi Quick	not enough tests performed

Ranking

To find out the most suitable urine test for the German police within ROSITA, a ranking list was filled out by the police officers in charge. By each TPD, each test could be rated with a number from 1 to 10, from „completely unacceptable“ to „very suitable“; the higher the number, the better. From each TPD one report per test version was delivered; thus, three confidential reports per test version are present which were combined into a total result with a minimum of 3 points and a maximum of 30 points per test.

Table 23: Ranking

Test	*Police Ranking*	
	Score (min.3 max. 30)	Acceptance
Securetec Drugwipe	14/30	46,6 %
Avitar Oral Screen	5/30	16,6 %
Biomar Toxi Quick	4/20 (only two PD´s)	20 %

Blood (Serum)

In Germany to prove DUID in court the illicit drug(s) must be detected in serum. Whenever legal steps because of DUID are initiated by police officers, a blood sample must be taken. In case of refusal this can be enforced be police officers. The blood samples are taken at the police station by a physician who attends the traffic control. Procedures of blood sampling, storage and transport are the same as for alcohol offences.

Table 24

Drug	***Results***		
	Positive*	**Negative***	**not analysed***
THC+TOOH	376	28	146
TOOH	54		
BE/ME	43	71	490
MOR+COD	29		
MOR	9	72	491
other Opiates	3		
AMP/MAMP	84		
Designer Drugs	31	123	296
AMP/MAMP +Designer Drugs	70		

* total number: 604 cases

Having a look at the cases with mono consumption, it can clearly be seen that the most frequent consumed drug is Cannabis (78%), followed by the Amphetamines (17%). This is also confirmed by those cases with two substances identified. Cannabis and Amphetamines are the most frequent combination. In cases with triple consumption, Cannabis was included in all 16 cases. Amphetamines were consumed in 9 cases.

Table 25

Drugs	***Results***
Mono Consumption	
CAN	281
COC	4
OPI	13
AMP/DD	63
Double Consumption	
CAN + COC	14
CAN + OPI	11
CAN + AMP/DD	108
COC + OPI	7
COC + AMP/DD	5
OPI + AMP/DD	0
Triple Consumption	
CAN + COC + AMP/DD	6
CAN + OPI + AMP/DD	3
CAN + COC + OPI	7
all negative (incl. not analysed)	82

DISCUSSION

The German objective of workpackage 4 of ROSITA was to examine the performance of different drug test systems directly at the roadside, as equipment of the Saarland traffic police and done by the police officers. Additionally, an analytic evaluation of the ILMH was done. Due to the successfullness of the program, instead of the intended (and budgetted) 200 samples, 604 samples were included into the ROSITA evaluation. For this reason, not all positive and/or negative roadside tests could be confirmed with GC-MS as gold-standard method in the same specimen. In cases of positive roadside tests, the specimens were included in our laboratory test procedure which consists in confirmation of a positive urine test (in cases of 24a Road Traffic Law) directly in serum by GC-MS. Only if the serum test was negative, further analytical tests were done in urine.
Generally, from both the analytical and the police point of view, roadside drug test devices were assessed as helpful and necessary in detection of drug impaired drivers, and in order to remain and to improve the achievements of ROSITA, it is considered as very important to make the drug tests available to the police officers as soon as possible. Furthermore, it seems that there is a need of action in the general investigation of accidents, due to the high number of positive cases and the low number of known drug-related accidents. As a first consequence of ROSITA, the Ministry of Saarland has budgetted the purchasing of roadside tests for the Saarland police for the year 2001.
The best ranked tests within our field study are the Mashan DOA4, the Syva Rapid Cup and the Roche Test Cup.
The only saliva/sweat test that is accepted by the police officers is the Securetec Drugwipe especially in combination with the electronic reader. Only two test systems were not accepted, in the first place due to a non-perfected method of sample collection.
Generally, all tested versions have their advantages and disadvantages, but after a period of habituation, the officers had no problems to work with nearly all test systems individually and even in combinations in spite of different handling and reading (pipeting, diping, presence of lines, discolouration of indicator fields etc.). It could be shown in daily practice at police work, predominantly other problems occured in comparison with the “clean” and userfriendly laboratory conditions.

CONCLUSION

The detection of DUID has been pushed a big step forward by the roadside tests. There is no doubt that the signs of impairment by drug abuse and/or pharmaceuticals are, in most cases, less visible than those by alcohol, although the effects on driving fitness are comparable or can even be much stronger. At the beginning, the police officers were, in most cases, not much experiences in detecting the signs of impairment caused by drugs of abuse, at least compared with their experience in the field of alcohol. So they hesitated to take legal steps against a driver who showed possibla signs of impairment due to the consumption of drugs. The roadside tests have quickly become a well accepted help in the decision of the police officers to take action, This was both from an „officer-related“ point of view (immediate feedback of an initial suspicion, providing security in acting) and from a „suspect-related“ point of view: in many cases, the subject confessed the consumption of drugs as conclusion of a (sometimes long) period of vehement disputing after seeing the positive test result. The high percentage of positive test results shows that the police officers did not use this tests for random and that their initial suspicions were mostly justified. On the other side the negative test results helped to minimize the consequences for the drivers and reduced costs and work for the police officers. The test results could be validated by the laboratory analyses of the ILMH in a high fraction of correct tests, positive as well as negative.
Up to now, the roadside test results as part of the police observation weren’t objected by the judges in court; the judges had (and used) the possibility to familiarise with the police control work at night shifts.
ROSITA showed us the possibilities of roadside drug testing. The advantages and disadvantages of different test devices were pointed out. It is encouraging to see that the producers of the test devices already reacted on the first results of ROSITA and started to develop a new or revised generation of drug test devices, which of course will need also an evaluation; but with Rosita, the first move was made, a big step forward, and due to its results “Drugs in Traffic” became a topic in the public attention and in the media in Germany.

ACKNOWLEDGEMENTS

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APPENDIX 1

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PFA-Projekt "Drogen-Vortests"
Euro-Projekt "ROSITA"

- MUSTER -

Beginn und Ende der Testphase des ... MUSTER:

_____

Dienststelle :

ZVD Ost **ZVD Mitte** **ZVD West**

Bewertungsbogen ausgefüllt am: _____

von: _____

_____

- Die grau unterlegten, anzukreuzenden Fragen gelten einer allgemeinen Bewertung der Hauptaspekte des Tests; die 1 steht als beste, die 5 als schlechteste Bewertungsmöglichkeit.
- Die Textfragen sollen die Einzelaspekte des Testes wiedergeben; die Kommentare sollten in Stichworten aufgeschrieben werden. Natürlich kann bei Bedarf auf den Rückseiten weitergeschrieben werden.

1. Bedienungsanleitung	**Allgemeine Beurteilung:** (1- sehr gut, 5 - sehr schlecht) 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑
1.1. Informationsgehalt?	
1.2. Verständlichkeit des Inhalts?	
1.3. Übersichtlichkeit?	
1.4. Sprache (deutsche Anleitung vorhanden bzw. überhaupt notwendig?)	

2. Allgemeines	
2.1. Ist dieVerpackung des Testbestecks angemessen?	
2.2. Wieviel Müll entsteht, ergeben sich Probleme bei dessen Entsorgung im Laufe eines Einsatzes?	
2.3. Wie beurteilen Sie Form und Größe bzw. Material des Test-Sets bzw. seiner Bestandteile?	
2.4. Wie beurteilen Sie die Zusammenstellung des Test-Sets (halten Sie Bestandteile für überflüssig, bzw. vermissen Sie noch etwas)?	
2.5. Wie beurteilen Sie die Zusammenstellung der zu erfassenden Substanzen auf dem Test? *Zur Info: die meisten Hersteller bieten sowohl Einzel- als auch Mehrfachtests an, in verschieden kombinierbarer Substanzkonstellation!*	

3. Handhabbarkeit des Tests		**Allgemeine Beurteilung:** (1- sehr gut, 5 - sehr schlecht) 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑
3.1.	Wie beurteilen sie die nötige Testvorbereitung (Öffnen der Verpackung, zwangsläufige Benötigung von Papierunterlagen (wegen kontaminierter Testkarte,-streifen etc.)?	
3.2.	Wie beurteilen Sie die für diesen Test benötigte Mindestmenge Untersuchungsmaterial?	
3.3.	Kann der Test trotz Unterschreiten der Mindestmenge durch bestimmte Maßnahmen dennoch durchgeführt werden (Kippen des Bechers, Pipettieren o.ä.)?	
3.4.	Besteht - bei nur geringer Materialabgabe durch den Probanden - die Möglichkeit, den Urin/Speichel/Schweiß „etappenweise“ zu sammeln?	
3.5.	Wie bewerten Sie das System des Herstellers, das zu untersuchende Material mit dem Test in Kontakt zu bringen (Eintauchen einer Testkarte vs. Pipettieren, Verschließen bzw. Kippen des Bechers, etc.)?	
3.6.	Wie beurteilen Sie generell die Testdurchführung; ist er umständlich bzw. kompliziert, ist ein mehrfaches Studieren der Bedienungsanleitung erforderlich etc.?	
3.7.	Wie hoch ist für Sie das Risiko, bei der Testdurchführung mit dem zu untersuchenden Material in Kontakt zu kommen; bei welchem Schritt sehen Sie die größte Gefahr?	
3.8.	Lassen sich weitere Tests mit dem gesammelten Material durchführen (z.B. Testwiederholung bei Nichtfunktionieren eines Tests, oder zur Durchführung eines weiteren Testsystems)?	
3.9.	Wie beurteilen Sie die Möglichkeiten zur Asser Materials im Anschluß an den Test? Gibt es sp Hersteller gelieferte Einpackmöglichkeiten für Halten Sie diese für erforderlich?	
3.10.	Wie beurteilen Sie den Test unter hygienischen Gesichtspunkten (Dichtigkeit, Kontakt von Uri Speichel zur Unterlage, Kontaminierter Abfall	

4. Zeitaufwand	**Reaktionszeit (in min):** 1 ❑ 2-5 ❑ 6-10 ❑ 11-15 ❑ >15 ❑
4.1. Wieviel Zeit nimmt die Vorbereitung in Anspruch (Auspacken etc.)?	
4.2. Wie beurteilen Sie die Zeitdauer vom Starten des Tests bis zum Vorliegen des Ergebnisses (Reaktionszeit)? Gab es oft (unerklärliche) zeitl. Schwankungen?	
4.3. Konnten Sie konkret beobachten, dass die Reaktionszeit von äußeren Einflüssen abhängig ist (Wetter, Temperatur, etc.)? Falls ja, inwiefern?	
4.4. Stimmt die durchschnittliche Reaktionszeit eines Tests mit den Herstellerangaben überein oder gibt es Diskrepanzen?	
4.5. Wieviel Zeit benötigen Sie für die Nachbereitung (Asservieren, Dokumentation etc. - ohne Ausfüllen der Rosita-Bögen!)?	
4.6. Ist der Gesamt-Zeitaufwand (Vorbereitung + Reaktionszeit + Nachbereiten) für einen Schnelltest angemessen?	

5. Auswertbarkeit	**Allgemeine Beurteilung:** (1- sehr gut, 5 - sehr schlecht) 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑
5.1. Konnten Sie eindeutig zwischen negativen und positiven Testergebnissen unterscheiden? Worin lagen Ursachen für Probleme (Farbintensität, Gleichmäßigkeit der Linien bzw. des Farbfeldes; Sind die Probleme spezifisch für den gesamten Test oder gibt es Unterscheidungen bei den einzelnen Substanzen)?	
5.2. Kam es vor, dass Tests nicht funktionierten? Falls ja, wie oft? Können Sie die Ausfälle beschreiben? wenn möglich, bitte eine Prozentangabe ! Zum Beispiel: - Ausfall des gesamten Systems oder bloß einer Substanz (welche am häufigsten?), - Nichterreichen der Mindestmenge - Zwar Starten, aber kein vollständiges Durchlaufen des Tests	
5.3. Ist eine Kontrollinie vorhanden? Wenn ja, ist sie eindeutig (Farbintensität, Gleichmäßigkeit, evtl. Differenzen bei den einzelnen Drogen)?	
5.4. Wie beurteilen Sie die Art der Ergebnis-Darstellung, würden Sie eine andere Art bevorzugen („Linientest“ vs. „Farbfeldtest“ bzw. elektronische Auswertung)?; bitte Ihre „Rangliste“ angeben)	
5.5. Bestehen Dokumentationsmöglichkeiten für die Ergebnisse (die Rosita-Begleitbögen sind nicht gemeint!!)? Sind in der Routine (nach dem Rosita-Projekt) zusätzliche Dokumentationsvorlagen der Herstellerfirma überhaupt notwendig oder reicht das offizielle Formular „Protokoll und Antrag“?	
<u>Generell zur Auswertbarkeit:</u> 5.6. Erschweren die verschiedenen Ergebnisdarstellungen (Linien auf der einen, Farbfeld auf der anderen Seite) unterschiedlicher Testsysteme das gleichzeitige Arbeiten mit mehreren Testvarianten?	
5.7. Macht das Prinzip „Erscheinen einer Linie bei negativem, Nichterscheinen bei positivem Ergebnis“ Schwierigkeiten?	
5.8. Wie bewerten Sie die der Farbe der Linien bzw. des Farbfeldes (blau, rot); bietet evtl. eine bestimmte Farbe Vor- bzw. Nachteile bei schlechtem Lichtverhältnissen?	
5.9. Finden Sie eine Kontrollinie zur Sicherheit notwendig?	

6. Abschließende Fragen

6.1. Wie sehen Sie die Zumutbarkeit für den Polizeibeamten, diesen Test durchzuführen („Ekelfaktor“)?	
6.2. Wie beurteilen Sie diesen Schnelltest als Hilfe bei Ihrer Verdachtserhärtung? (positiv/negativ; sicher/zu unsicher; akzeptabel; umständlich; unzumutbar für Polizei und/oder Proband; etc.)	
6.3. Haben Sie konkrete Wünsche und Verbesserungsvorschläge für diesen Schnelltest (Einfach-/Mehrfachtest, Temperaturanzeige, Bechergestaltung, etc.)?	
6.4. Wie äußern sich die Probanden zu diesem Schnelltest?	

Eventuell weiterer Kommentar

Deliverable D4d - Belgium

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: Contribution of Belgium, N.I.C.C.

Authors: Nele SAMYN, Bart VIAENE, Bart LAEREMANS and Gert DE BOECK

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

Several EU member states have recently introduced or are preparing 'per se' laws on driving under the influence of drugs [1-3]. In most of these countries, driving under the influence of a drug will be proven by the presence of certain analytes in the blood of the driver. One of the key elements in the enforcement process is the possibility to take immediate administrative measures (short-term driving ban) and the selection of the drivers that will have to undergo venipuncture. An important step to improve the detection of "impaired drivers" has been the extensive training programme for police officers in some countries. A second complementary approach is the use of an acceptable screening device at the roadside to provide the police officer with additional evidence of recent drug use [4].

In march 1999, the Belgian parliament adopted a new law on driving under the influence of illicit drugs. A driver is sanctioned if THC, cocaine, benzoylecgonine, morphine, amphetamine, MDMA, MDEA or MBDB are detected in blood in concentrations exceeding the cut-off values mentioned in the law. Similar « per se » laws were introduced in Germany and Sweden. An initial suspicion of impairment is established using a limited drug recognition test battery, partially based on the German and the American DRE programmes. If there is a suspicion of impairment, a urine test (cannabis, cocaine, opiates, amphetamines, metamphetamines) is performed on-site. A positive test result for at least one parameter leads to immediate withdrawal of the driving licence (usually for 12 hours) and blood sampling by an independent physician.

An inventory of state-of-the-art drug testing screening devices and an extensive laboratory evaluation of seven on-site urine devices has been published earlier this year [4,5]. The presence of certain drugs of abuse or their metabolites in urine can be interpreted as evidence of relatively recent exposure, except for cannabis. However, this does not necessarily mean that the subject was under the influence at the time of sampling. When the drug is detected in blood, there is a higher probability that the subject is experiencing pharmacological effects. Saliva is probably the only body fluid that might parallel blood in some regards and that may be related to behavioral performance [6]. Kidwell et al. [7] also consider sweat testing as a possible part of a roadside sobriety program to reduce driving under the influence of drugs (DUID). Although it has long been known that drugs are excreted in sweat, this has not been extensively used as a drug detection medium. Recently, due to the development of the sweat patch technology, sweat analysis has been proposed as a means for evaluating drug exposure e.g. in detoxification centers, rather than for roadside testing purposes.

When testing for drugs in subjects suspected of impaired driving, some practical aspects should be considered. As for alcohol, police officers with a minimum scientific background must regularly carry out roadside tests that require immediate results. Saliva and sweat sampling is easy, non-invasive, without the intrusion of privacy and with very little chance of adulteration. Securetec (Ottobrunn, Germany) introduced Drugwipe, a non-instrumental immunodiagnostic assay for the detection of drugs on surfaces. The use of Drugwipe for saliva and sweat is currently being investigated in several countries.

During the course of this study, newly trained police officers tested over two hundred drivers. The results of the evaluation by the police and the clinical data will be related to the results of the blood and urine analysis. The features of the different on-site tests will be discussed. For over hundred subjects, saliva and sweat samples were quantitatively analysed and compared to the corresponding blood and urine results. The reliability of Drugwipe is assessed by means of the blood, saliva and sweat confirmatory results.

METHODS

Sample selection

From august 1999 until september 2000, subjects were selected at police controls all over the country to give urine, blood, saliva and sweat. A limited drug recognition test battery followed by a positive urine test supported the suspicion of DUID. We also obtained samples from volunteers, mostly passengers in the car, admitting recent drug use. They agreed to participate through informed consent. The central bureau of investigations of the State Police trained several police officers to obtain sufficient experience in the interpretation of the results of the drug recognition test battery. A number of diverse general observations (e.g. get out of the car and walk, smell, speech, bloodshot eyes, strabisme…) were indicating the unfitness to drive, in addition to four psychomotoric performance tests: walk-and-turn, stand-on-one-leg, finger-to-nose and the Romberg test.

Clinical evaluation

A medical staff from the State Police performed a limited examination of vital functions and physiological signs of drug use. A questionnaire was filled in, including questions about the kind of drugs that had been consumed, the amount, the administration route, and the intake of medication. Blood pressure, heart rate, and temperature were measured. Eye tests were performed: horizontal and vertical gaze nystagmus, strabisme, dilated/constricted pupils, and reaction to light.

On-site screening

Several on-site urine tests were compared during the police controls. Each device was tested on a fresh urine sample, already screened by the police with the Dipro Drugscreen 5 panel test (VDP, Belgium) for amphetamines, methamphetamines, cannabinoids, cocaine metabolite and opiates. Different test principles were compared: a “pipette-type” test (Syva Rapidtest, Dade Behring), a “cup” test (Testcup, Roche Diagnostics) and a “dip” test (Rapid Drug Screen, AmericanBioMedica). Other tests that have been evaluated on their user friendliness at the roadside are: Surescreen test card (Eurodb, Belgium), Toxiquick pipette test (Laméris, Belgium), Ultimed Surestick Drug Screen card (Forlab, Belgium) and Quickscan pipette test (Syntron, USA).
The Drugwipe is wiped on the tongue to test saliva, and on the forehead for the sweat test. Separate strips are available for opiates, cocaine and the amphetamine group. The coloration of the detection field will change from light pink to red depending on the amount of drugs collected. If no drugs are present, the read-out window remains cream coloured. The manufacturer provides a prototype of an electronic reader. The read-out cut-off values for amphetamines and opiates are 800, for cocaine 700.

Sampling

1-2 ml of saliva was collected by spitting in a dry polypropylene tube, supplying some water to moisten the mouth. Occasionally, a salivette was used to obtain a saliva sample; the subject was asked to put the cotton role between cheeck and gum for two minutes without touching it with the bare hands. Sweat was collected by wiping the forehead with a cotton fleece moistened with 70 % of isopropanol. Urine, saliva and sweat samples collected at the roadside were frozen in plastic tubes until analysis in the laboratory. Blood samples were collected with glass venoject tubes (2 x 7 ml) using NaF and KOx as anticoagulant. The tubes were either cooled to –4°C and centrifuged the next day or centrifugation was performed on-site and the corresponding plasma was frozen until analysis.

Analytical procedures and cut-off values

Urine and blood

On-site data for urine were confirmed using screening with FPIA (ADX, Abott Diagnostics) and quantitative confirmation (using the appropriate deuterated standards) by GC/MS as the reference method. The parameters that tested positive in urine during the roadside screening, were confirmed in plasma. The applied solid phase extraction (SPE) procedures for opiates and for cocaine and its metabolites were based on the previously published methods of Wang et al. [8] and of Cone et al. [9]. Benzoylecgonine was derivatized with pentafluoropropionic anhydride and pentafluoropropanol (Sigma). Amphetamine and its derivatives were extracted using Bond Elut Certify columns (Varian Belgium) according to the manufacturers instructions. They were derivatized with heptafluorobutyric anhydride (HFBA). Cannabinoids were extracted from urine and plasma using 5 ml of hexane/ethyl acetate (9/1) (v/v) after acidification of the sample. Derivatization was performed with BSTFA + 1% TMCS or by methylation with iodomethane. Quantitative analyses were performed on a Hewlett-Packard 6890 gas chromatograph equiped with an autosampler (HP7673A) and interfaced with a Hewlett-Packard 5973 mass selective detector. Analytical conditions were optimized for the detection of (1) cocaine, benzoylecgonine (BE), anhydroecgonine methylester (AEME), ecgonine methyl ester (EME), morphine (MORP), 6-acetylmorphine (MAM) and codeine; (2) amphetamine (AMP), 3,4-methylenedioxy-*N*-amphetamine (MDA), 3,4-methylenedioxy-*N*-methylamphetame (MDMA), 3,4-methylenedioxy-*N*-ethylamphetamine (MDEA), *N*-methyl-1-(3,4-methylenedioxy-phenyl)-2-butanamine (MBDB) and ephedrine; (3) Δ-9-tetrahydrocannabinol (THC), 11-hydroxy-Δ-9-tetrahydrocannabinol (OH-THC) and 11-*nor*-Δ-9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH). The MS was operated in SIM mode. At least three ions were monitored for the analytes and two ions for the internal standards. The cut-off values mentioned in the law for the urine screening test and for the confirmation in plasma, are presented in Table 1. The laboratory confirmation cut-off values for urine are also included.

Table 1: cut-off values in urine and plasma for DUID cases

	Legal screening cut-off for urine (ng/ml)	*Laboratory confirmation cut-off for urine (ng/ml)*	*Legal confirmation cut-off for plasma (ng/ml)*
Amphetamines	1000	500	
Metamphetamines	1000	500	
Amphetamine			50
MDMA			50
MDEA			50
MBDB			50
Cannabinoids	50		
THC-COOH		15	
THC			2
Cocaine	300		
Benzoylecgonine		150	50
Cocaine			50
Opiates	300	300	
morphine			20

All available urine samples were also screened with FPIA for benzodiazepines and the corresponding blood samples were analysed with HPLC-DAD. The negative blood samples from subjects that scored "impaired" by the police investigation, were screened for a broad range of medicinal drugs by the same technique. After a liquid extraction of 1 ml of plasma at pH 9.2 with 1-chlorobutane, the organic phase was evaporated and redissolved in 150 µL of mobile phase (phosphate buffer pH 3.8- acetonitrile 67/33(v/v)). An aliquot of 50 µl was injected on a Waters Symmetry C18 (3.9 x 150 mm, 5µm) column at 33°C.

Saliva

Saliva samples were thawed and centrifuged thoroughly. The supernatant was analysed using similar methods as for plasma.
The salivettes were centrifuged and the dried cotton role was extracted with a mixture of hexane and ethylacetate to detect cannabinoids. Internal standard was added directly to the salivette. Confirmation of other drugs was obtained by direct extraction of the wet salivette with methanol, evaporation of the organic phase and further clean up by SPE.

Sweat

Sweat wipes were extracted with acetatebuffer 0.1 M pH 4.0 for cocaine, opiates and amphetamines. Internal standards were added to the wipe. For cannabinoids, direct extraction of the wipe with hexane/ethylacetate was performed. For multiple drug extraction, the wipe was dried, extracted with buffer, centrifuged and extracted with the non-polar phase for cannabis analysis. The aqueous extracts were further analysed with similar SPE and derivatisation procedures as for plasma samples.

Table 2: represents the limits of detection (LOD) and limits of quantification (LOQ) for each analyte and each matrix.

	LOD (ng/ml or ng/wipe)	*LOQ (ng/ml or ng/wipe)*
CANNABINOIDS		
Urine		
THC-COOH	3.0	10.0
Plasma		
THC	0.8	1.0
OH-THC	0.8	1.0
THC-COOH	1.0	4.0
Saliva		
THC	0.8	1.0
Sweat (Salivette)		
THC	3.0	5.0
AMPHETAMINES		
Urine	5.0	25.0
Plasma, Saliva, Sweat	5.0	10.0
COCAINE		
Urine		
Benzoylecgonine	10.0	20.0
EME/Cocaine	20.0	-
Plasma, saliva, sweat		
Cocaine	3.0	5.0
Benzoylecgonine	1.0	3.0
OPIATES		
Urine	10.0	20.0
Plasma, Saliva, Sweat	1.0	2.0

RESULTS AND DISCUSSION

Case selection

Of the subjects that were stopped during the police controls, 137 drivers were selected for immediate administrative measures and blood sampling. They scored positive for at least two signs of impairment, one of them being a psychomotoric performance test. The Romberg test often scored positive after recent smoking of marijuana. Recent use of a stimulant was easily observed by the dilatation of the pupils and a slow reaction to light. In only a few cases, the results of the test battery indicated impairment but the urine test was negative. Of the 175 subjects involved in this study, 38 agreed participation on a voluntary basis.
The results of the on-site screening of urine are shown in Figure 1. In 44 % of the cases cannabis was the only positive parameter, in 23 % combined with a positive amphetamine and/or methamphetamine test. Somewhat unexpected was the prevalence of a significant amount of cocaine positives in the surroundings of "after-clubs", dancings only opening on early sunday morning. Combinations of cocaine and opiates were only observed at the border with France, a high prevalence of marihuana positives was established at the border with the Netherlands. The concentrations of THC in plasma were frequently higher than 5 ng/ml.
Screening of benzodiazepines in urine revealed only 6 positive cases (cut-off 100). However, the low cross-reactivity of certain benzodiazepines in the FPIA assay is well known. The positive screening results were all confirmed in blood. The drugs that were detected in blood were nordiazepam, diazepam, bromazepam, flunitrazepam, clonazepam and temazepam. One blood sample contained a high flunitrazepam concentration (92 µg/ml) and its metabolites, another one revealed a nordiazepam concentration of 2,900 µg/ml.

Clinical data

Of the subjects that were considered "impaired", only 57% showed one or more physiological signs of recent drug use. Mydriasis and horizontal or vertical gaze nystagmus were the most frequently seen in users of stimulants, often in combination with a significantly increased heart rate. The questionnaire revealed that cannabis was the most stated drug, followed by "ecstasy", speed and cocaine (by sniffing). A cause for concern is the reported use of "liquid XTC" (GHB) and even "special K" (ketamine) in the dance scene. Since these analytes are not mentioned in the law on DUID, they are not detected in routine analysis. They are frequently combined with high doses of MDMA and even alcohol.

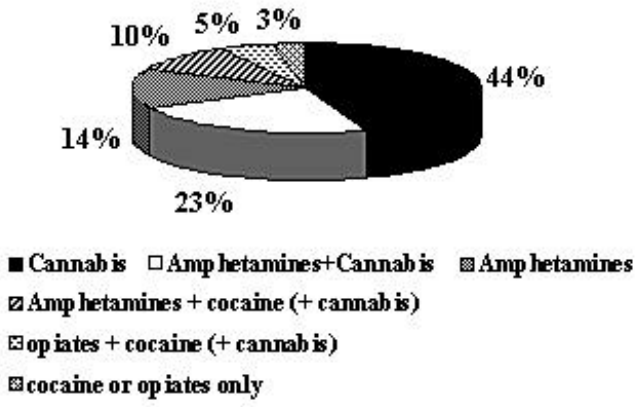

Figure 1: on-site screening results of urine during specific police controls for DUID

Urine on-site screening devices

User friendliness

In 10 % of the legal cases, no urine sample could be provided. Urine sampling showed to be acceptable at the roadside provided that suitable facilities were present (sanitary van) and that police officers were used to the procedure. However, providing a sample is time-consuming and difficult to control. Some attempts to adulterate have already been observed.
Table 3 shows different aspects related to the user friendliness of the four most frequently tested devices in this study. The principle of a **testcup** appears interesting for the police forces because the number of manipulations is restricted and urine is not handled at any time. However, the cup design requires large volumes of urine which is a problem at the roadside, especially for the dancing public. The **pipette-type test** completely rules out this problem but does not seem to be accepted by the police officers. The "laboratory-design" of such a test disturbs them. They will settle for a **dip test** so the DIPRO panel test had been chosen partly to suit the needs of the traffic police.

Table 3: Overview of the user friendliness of the evaluated urine devices

	DIPRO	*SYVA RAPIDTEST*	*RDS*	*TESTCUP*
Ease-of-use at the roadside	very good	less accepted by the police	very good	adequate training is necessary
Volume of urine needed	5 ml	3 drops	25 ml	15 ml
Interpretation of the result	acceptable	very good	good	very good
Number of parameters detected	5 drug classes	4 drug classes + metamphetamine single test	5 drug classes	4 drug classes
Single tests	pipette type different from panel	identical principle to panel	identical principle to panel	very robust "dip" test (Teststik)

Surescreen has the disadvantage of providing a "messy" card after use; the time to interpret a positive result should be 10 min, which is too long. Moreover, the lines are rather diffuse and the interpretation is not clear. **Quickscan** and **Toxiquick** both offer a panel pipette-type test, which is undoubtedly less userfriendly than the Syva Rapidtest. It is important to stress that every test, however userfriendly, requires a minimum training by the manufacturer or distributor to provide accurate results.

Accuracy

For every test device and for a certain class of drugs, different types of results are obtained: *true positives* (TP), the number of urine samples that provided a positive result with the screening test and that were confirmed positive by GC-MS; *true negatives* (TN), the number of urine samples that provided a negative result with the on-site screening test and that were confirmed negative by FPIA and/or GC-MS; *false positives* (FP), the number of urine samples that provided a positive result with the on-site screening test and not confirmed by GC-MS; *false negatives* (FN), the number of urine samples that provided a negative result with the on-site screening test and that were positive with GC-MS. Using these parameters the sensitivity, the specificity, the positive predictive value and the negative predicitve value can be calculated. Some of the results are presented in Figures 2A to 2D.

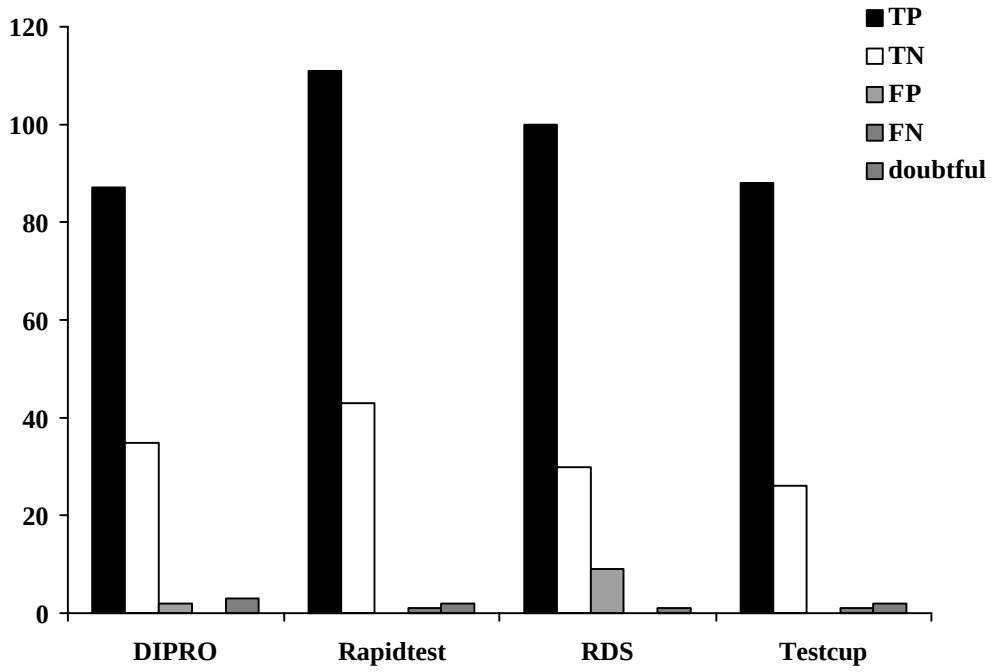

Figure 2A: Performance of on-site tests to detect cannabis in urine at a cut-off level of 50 ng/ml cannabinoids.

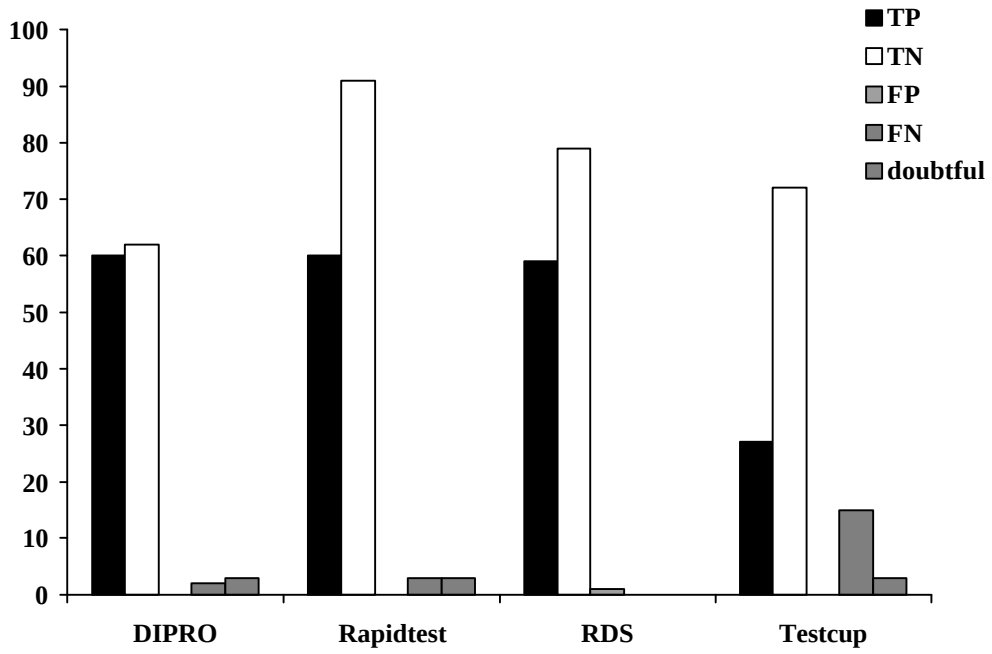

Figure 2B: Performance of on-site tests to detect amphetamine and MDMA in urine at a cut-off level of 1000 ng/ml for amphetamines and methamphetamines

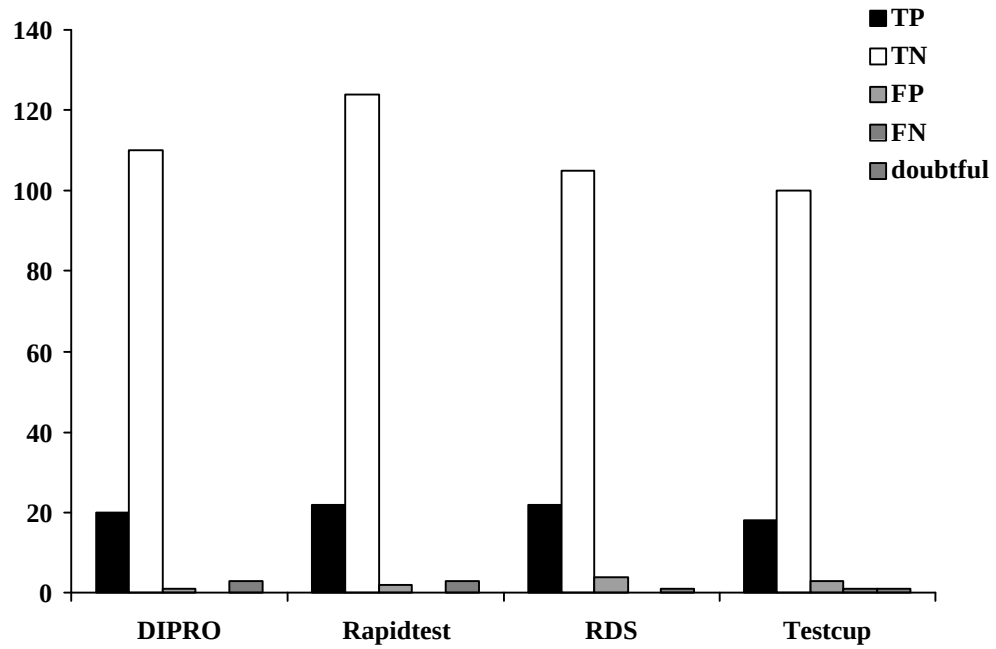

Figure 2C: Performance of on-site tests to detect benzoylecgonine in urine at a cut-off level of 300 ng/ml for the cocaine metabolite

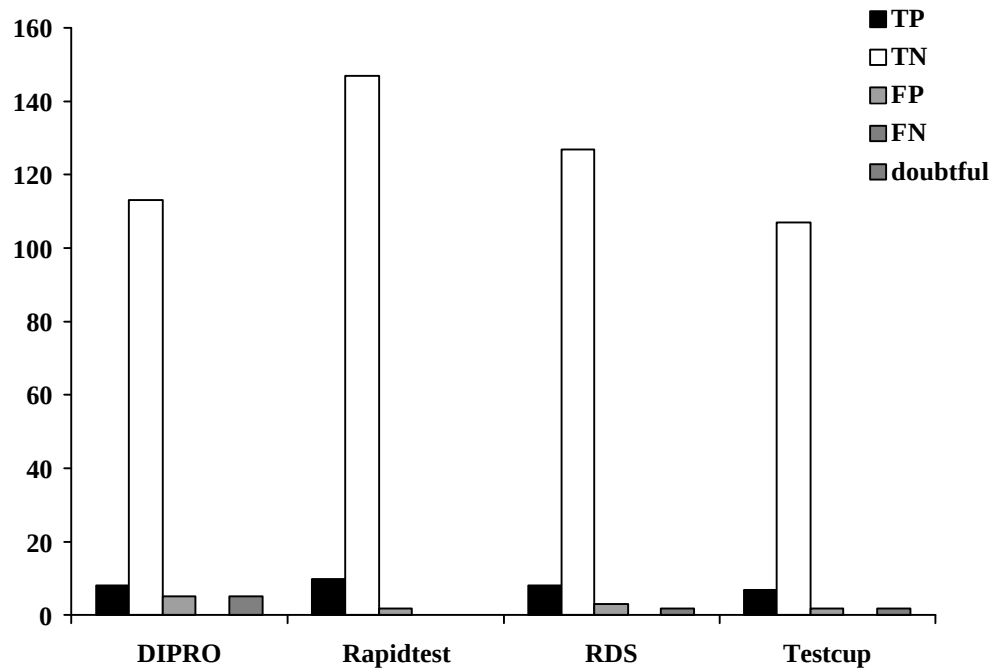

Figure 2D: Performance of on-site tests to detect opiates in urine at a cut-off level of 300 ng/ml

Figure 2A shows nine FP for the RDS in the detection of cannabis in urine. Five samples had a concentration of THC-COOH below 10 ng/ml (= LOQ) but higher than the LOD.
For amphetamines, the on-site result is considered positive if either the amphetamine parameter or the metamphetamine parameter or both show a positive result. **Figure 2B** reflects the lack of MDMA detection with the Testcup in MDMA-only samples. The cross-reactivity values of the amphetamine parameter of the Testcup are negligible for MDMA and about 14% for MDA. A new Testcup is being

marketed with a methamphetamine parameter but this causes problems in the detection of urine samples that only contain amphetamine.
In **Figure 2C** the RDS shows four FP results, coming from urine samples in which benzoylecgonine was detected in a concentration below 150 ng/ml or with an FPIA result lower than 300 but higher than 100.
For opiates, two samples containing respectively 75 ng/ml of total morphine and 105 ng/ml of total codeine produced a positive test result for all four tests. **Figure 2D** shows an elevated number of doubtful and FP results with the Dipro panel test. In a few cases, the paneltest displayed a very weak negative result for opiates (interpreted as positive in conditions of faint luminosity) whereas the single test for morphine was clearly negative. The single tests have a pipette-type design.

Analysis of the plasma samples

Only 5 subjects that participated in the study (drivers and volunteers) did not want to give a blood sample. In 12 of the 137 legal cases, the plasma result was negative for the analytes mentioned in the law. These plasma samples were screened with HPLC-DAD for a broad range of therapeutic drugs. All except one were negative.
In one of the 12 cases, no urine was provided. In two cases, the urine test on-site showed a false positive result; confirmation of the urine sample revealed low concentrations of THC-COOH and morphine. In three cases, the urine result was positive but the plasma concentrations were below the legal limits. One subject had a concentration of 48 ng/ml of MDMA in plasma and was found positive for paroxetine, clonazepam and temazepam in subtherapeutic concentrations. Although the drug recognition test battery indicated “impairment” and the following urine test was clearly positive for cannabis, in six subjects the corresponding plasma samples did not contain THC or medicinal drugs.

Drugwipe

The Drugwipe (DW) had already been introduced in Belgium in the context of a previous roadside study [10]. Difficulties in the interpretation of the result have been overcome by introducing a prototype of an electronic reader. A digital read-out was obtained and preliminary cut-off values were applied to distinguish between a positive and a negative test result. In future, it should be possible to store the read-out result electronically. The Drugwipe is easy-to-use, also for police officers, and provides a result within two minutes.

Drugwipe results versus blood results

Table 4 shows the number of positive samples for urine and plasma using the legal cut-off values. Obviously, for cannabis, cocaine and opiates, the number of positive results in urine is higher than the number of positive results in plasma. This clearly reflects the longer detection window of urine and stresses the fact that a positive urine test is merely an indication of potential drug use.

Table 4: the number of urine and blood positives (using the legal cut-off values) in this study, and the percentage of Drugwipe results that were in agreement with the corresponding blood results, using the cut-off values proposed by the manufacturer

	URINE +	***BLOOD +***		***DRUGWIPE***	
				saliva	**sweat**
CANNABIS	114	85	6*	-	-
COCAINE	23	18	3*	64%	64%
OPIATES	9	5		77%	50%
AMP/MDMA	64	61	13*	74%	92%

* no urine sample available

The agreement between Drugwipe results and blood analysis is acceptable for amphetamine and/or MDMA, especially when using sweat as the screening matrix. However, the reliability of the test to detect cocaine use needs to be improved. For both saliva and sweat, some read-out results near the cut-

off of the reader and not corresponding to a borderline result in plasma were obtained. Some of the positive screening results for opiates in sweat, reflect the longer detection window of sweat in comparison to blood. Table 5 shows the results of the saliva testing in more detail.

Table 5: Comparison between the plasma results (using the legal limits) and the results of the on-site screening test for saliva, taking the manufacturers cut-off values into account

	Plasma + ***DW +***	***Plasma -*** ***DW -***	***Plasma +*** ***DW -***	***Plasma -*** ***DW +***
AMPHETAMINES	51	2	**15**	**4**
COCAINE	13	3	**6**	**3**
OPIATES	4	6	**1**	**2**

Accuracy of the Drugwipe applied to saliva

To determine the accuracy of the saliva test, a saliva sample was taken by spitting and the laboratory analysis by GC-MS was compared to the on-site test result on the tongue. In Table 6 the LOQ is applied as a cut-off level to evaluate the number of TP, TN, FP and FN. The sensitivity of the test is depending upon the TP and FN results; it varies between 45 % for opiates and 77 % for amphetamines. Read-out results near the cut-off of the reader were considered as negative results. Since the number of saliva samples that were confirmed as negative is too low, no conclusion can be drawn about the specificity of the test.

Table 6: Accuracy of the Drugwipe (DW) test on saliva based on confirmation of saliva samples with GC-MS using the LOQ as the cut-off value.

	Saliva + ***DW +***	***Saliva -*** ***DW -***	***Saliva +*** ***DW -***	***Saliva -*** ***DW +***
AMPHETAMINES	51	1	**15**	**0**
COCAINE	15	0	**9**	**0**
OPIATES	5	2	**6**	**0**

There is only a weak indication that the FN results for the amphetamines and cocaine correspond to the saliva samples with the lowest concentrations. The application of confirmation cut-off values for saliva will therefore not alter the results significantly. However, for opiates, the saliva samples with the lowest concentrations (< 200 ng/ml) (e.g. after IV injection of heroin) corresponded to the negative Drugwipe results on the tongue. Establishing a cut-off of 100 ng/ml of morphine in saliva resulted in only one FN result. One subject diluted his saliva sample extensively with water thus producing low concentrations but a positive on-site test.

Accuracy of the Drugwipe applied to sweat

To determine the accuracy of the sweat test, a sweat wipe was analysed by GC-MS and the results were compared to the on-site test result on the forehead. In Table 7 again the LOQ of the analytes of interest is applied as a cut-off level to evaluate the number of TP, TN, FP and FN. The sensitivity of the test in the detection of opiates, cocaine and amphetamines is respectively 62 %, 67 % and 92 %. Read-out results near the cut-off were considered as negative results. Since the number of saliva samples that were confirmed as negative is too low, no conclusion can be drawn about the specificity of the test.
As for saliva, there is only a vage indication of a correlation between the test results and the concentration of analytes in the screening matrix. Application of confirmation cut-off values will not change the conclusions significantly.

Table 7: Accuracy of the Drugwipe (DW) test on sweat based on confirmation of sweat wipes with GC-MS using the LOQ as the cut-off value.

	Sweat + ***DW +***	***Sweat -*** ***DW -***	***Sweat +*** ***DW -***	***Sweat -*** ***DW +***
AMPHETAMINES	51	3	**4**	**0**
COCAINE	17	0	**8**	**0**
OPIATES	8	0	**4**	**0**

Features of saliva and sweat as a screening matrix

Undoubtedly, saliva and sweat offer a non-invasive way of screening at the roadside with the possibility of direct supervision. This is a major advantage in comparison to urine testing. Police officers recognise these benefits and are very willing to participate in the development of a suitable on-site test.

Sweat testing is very easy but external contamination of the skin needs to be taken into consideration. As for urine, because of the long detection window, any correlation with the presence of a pharmacological effect at the time of sampling is ruled out. However, as an indication of potential drug abuse and in addition to the drug recognition test battery, sweat testing might be preferable to urine testing.

Saliva analysis is considered as the only alternative to blood sampling to obtain some information about impairment due to recent use of medicines or drugs of abuse. Sampling is time consuming because of the high viscosity of the sample and the decrease of the salivary flow after amphetamine use or cannabis smoking. The collection protocol and the route of administration of the drug significantly influence the concentrations in the sample. For roadside testing purposes, the screening test should only require a small amount of sample (e.g. 100 µl) to facilitate the collection. The principle of the Drugwipe (wiping the tongue) is highly recommended. The use of a suitable collection device e.g. a cotton swab is also acceptable for the police. However, complex sampling devices like the Omni-Sal® are not accepted.

Analysis of oral fluid samples

Figure 3 shows a significant number of matching plasma and saliva samples for all four drug classes. Application of the legal cut-off values for amphetamines in plasma and of the proposed cut-off values for amphetamines in oral fluid (160 ng/ml; SAMHSA - mandatory guidelines) results in complete agreement between the two matrices. The saliva/plasma ratio for amphetamine and MDMA is always significantly higher than one.

Detection of morphine, codeine and 6-MAM in saliva is depending upon the route of administration. After intravenous injection, the saliva/plasma ratio can be lower than one. After smoking or sniffing of heroin, the concentrations of the analytes in saliva remain higher than in plasma for 2-3 hours due to a contamination of the buccal cavity. Similar observations have been made in cocaine users. In this study, cocaine is predominantly abused intranasally or by smoking, resulting in high concentrations of the parent drug in saliva. AEME is typically present in saliva after smoking “crack”. The SAMHSA guidelines for oral fluid only mention a cut-off value for benzoylecgonine (8 ng/ml). A slightly higher cut-off value (10-20 ng/ml BE) results in exellent agreement between saliva and plasma results, when also considering the legal limit for the cocaine metabolite in plasma. When a cut-off value of 50-100 ng/ml of morphine in saliva is applied, the positive scores for saliva and plasma matched rather well, again when the legal limit for plasma was taken into consideration. The presence of substantial concentrations of 6-MAM in saliva is shown in table 8.

Application of the SAMHSA cut-off value for THC in oral fluid (2 ng/ml) did not improve the correlation between plasma and saliva samples significantly, when the legal cut-off for THC in plasma was taken into account. One important drawback of using « oral fluid » samples obtained by spitting, is the instability of THC in such specimen. Concentrations detected in the aqueous samples were generally in the low ng range. Due to the adsorption of THC to the cotton role in the salivette®, extraction with a hydrofobic solvent mixture revealed THC concentrations higher than 100 ng/salivette. A major disadvantage of the salivette® was the variability in the volume of saliva absorbed in the cotton role (50-1000 µl). The probablity to obtain a positive saliva sample for cannabis seems higher

but the corresponding blood sample might be negative. Some examples of data obtained with the salivette® in comparison to collection by spitting, are presented in table 9.

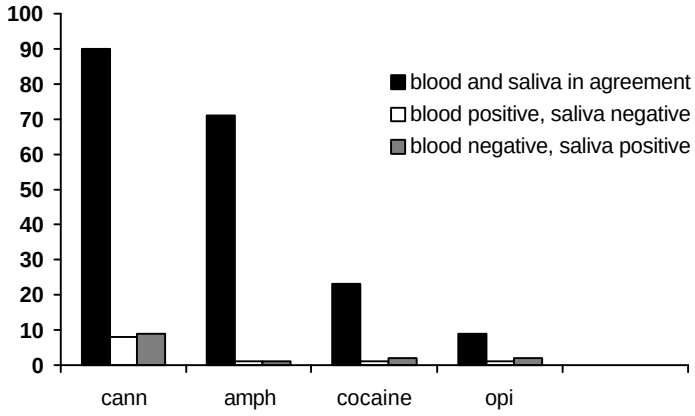

Figure 3: Comparison of plasma and saliva analysis by GC-MS, using the analytical limits as cut-off values

Table 8 : Comparison of some relevant opiate positive samples after different suspected administration routes: intravenous injection (IV), inhalation (SM) or sniffing (SN) of heroin.

Subject ID	***Route?***	***MAM***		***Morphine***		***Codeine***	
		plasma	**saliva**	**plasma**	**saliva**	**plasma**	**saliva**
B4	**SM**	< LOD	6,600	30	6421	9	434
E1	**?**	< LOD	300	158	5000	23	460
E2	**SN, SM**	< LOD	20	15	95	3	91
E6	**IV**	< LOD	19	17	25	2	7
I1	**SN**	< LOD	572	32	323	6	50
I5	**?**	< LOD	56	< LOD	15	< LOD	< LOD
J2	**IV?**	< LOD	61	34	163	10	98
J6	**?**	< LOD	594	36	332	7	43
L7	**SN**	< LOD	5	< LOD	19	< LOD	3

Table 9: Concentration of THC in saliva samples collected by spitting and using a salivette®

ID	***Plasma (ng/ml)***			***THC in saliva (ng/ml)***	***THC in salivette (ng/salivette)***
	THC	**OH-THC**	**THC-COOH**		
F5	17.8	8.8	90	2.7	
H2	11.7	4.8	218	2.2	
H3	4.4	1.8	37	11.0	
H4	5.2	3.7	81	83.0	
I2	13.1	4.2	88	24.2	
O1	6.4	3.6	38	9.4	> 100
O2	12.4	3.7	32	3.5	
O3	7.9	2.6	23	21.3	>100
O5	8.0	3.0	11	15.5	>100
T4	2.4	1.0	15	4.6	71
U6	3.1	1.2	40	5.4	72
X1	20.6	3.3	65		>100
X3	1.2	< LOD	7		>100
X4	< LOD	< LOD	< LOQ		45
X5	< LOD	< LOD	9		61
Z1	12.4	6.0	60		>100
Z3	14.2	3.2	51		> 100
Z9	3.9	< LOD	9		>100

Analysis of sweat wipes

Figure 4 illustrates the correlation between sweat and plasma confirmatory results. In all cases, the parent drug was the predominant analyte in sweat, and concentrations were generally higher than in blood. As for saliva, the results for amphetamines correlate very well, even when the LOQ was taken as a cut-off level. For cocaine and opiates there was a small percentage of positive sweat samples not matching a positive blood sample. Suitable cut-off levels for both plasma and sweat confirmation will certainly decrease this percentage; the sweat samples with the lowest concentrations of the parent drug corresponded to a negative blood sample or blood samples with a low concentration of analytes. For cannabis, the number of positive sweat results not corresponding to a positive plasma result is more significant. The application of a suitable cut-off level for THC in sweat will be more difficult because of the longer detection window and the ”depot” effect of sweat.

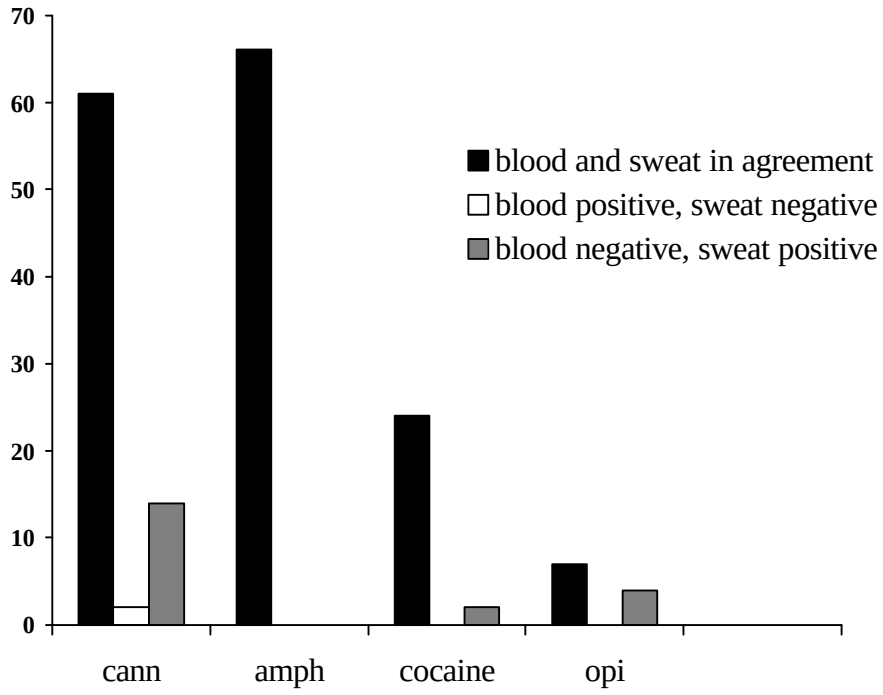

Figure 4: Comparison of plasma and sweat analysis by GC-MS, using the analytical limits as cut-off values

CONCLUSIONS

During the course of the Rosita project, there has been an enormous interaction between certain departments of the State Police and the Section Toxicology from the N.I.C.C. “Rosita” experienced all the benefits but also the drawbacks of the application of a new law. In Belgium, roadside blocks for alcohol controls were already widespread and in certain areas, driving under the influence of drugs (e.g. control on the possession of drugs) was already reported before the introduction of the law. The idea of roadside testing and even urine sampling on-site was not new, but restricted to certain regions of the country. Police officers with experience in the field of drug abuse obviously showed the highest motivation to participate in specific roadside controls for driving under the influence of drugs. The first newly trained police officers gained experience rather fast but had to suffer the consequences of a time consuming procedure. This decreased the number of subjects that could participate in the project enormously. On the other hand, because of the fact that the legal consequences of a conviction were not well known, most positive drivers provided us with saliva and sweat samples and participated in the project on a voluntary basis.

It is very important to point out the importance of the drug recognition test battery. Although it is a first indication of impairment, the urine test result does not provide the police officer with information about recent use especially when cannabis is detected. Most negative blood results corresponded to subjects that were only positive for cannabis in urine. However, during this first year, the number of negative blood results remained below 10 % of the total amount of samples. Caution has to be taken in those areas were the prevalence of roadside controls was low before the application of the law.

The use of saliva, and even sweat, as alternatives for urine testing would facilitate the procedure enormously. Urine sampling is difficult for the subject and for the police officer: too time consuming and the risk of adulteration will be a considerable disadvantage. One important issue is the accuracy of the on-site tests to detect drugs of abuse in fresh urine samples. In our opinion, a pipette-type test avoids problems with low volumes of urine, frequently observed with amphetamine users. The police are more in favour of a dip-test or a testcup. All evaluated tests were sufficiently reliable, with the exception of the Testcup in the detection of MDMA. Unfortunately, this is not the current situation for saliva testing. Although very userfriendly, the application of the Drugwipe to saliva did not produce satisfactory results for amphetamines, cocaine and opiates. For sweat, the only acceptable results were obtained for amphetamine and MDMA by wiping the test on the forehead.

A positive saliva test will be closely related to the presence of a pharmacological effect, a positive sweat test only gives an indication of potential drug use. Sampling should be quick and easy and the development of a reliable screening test will be the biggest challenge in the forthcoming years. Since blood analysis will remain the most reliable confirmation method, cut-off levels of the screening test should correlate well with the plasma results, applying legal limits. Nevertheless, the proposed guidelines for oral fluid by SAMHSA seem to be an important step forward in the analysis of alternative matrices.

ACKNOWLEDGEMENTS

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Deliverable D4e - Norway

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: National Institute of Forensic Toxicology, Oslo, Norway

Authors: Asbjørg S. CHRISTOPHERSEN, Merete GRUNG, and Svetlana SKURTVEIT

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

Drugs and driving in Norway, status per 2000

An increasing number of apprehensions due to driving under the influence of drugs other than alcohol have been recorded in Norway during the last years (1, 2). During the 1990ies, the number of cases increased more than 100% (1990: n=2050; 1999: n=4800), while apprehensions due to alcohol only decreased more than 40%, to a level close to drugged driving cases (1999: n= 4960). The population in Norway is approximately 4,3 million. Compared to other countries, the number of drugged driving cases is probably higher in Norway compared to other countries (2, 3,4).

The Norwegian Road Traffic Acts prohibits driving under the **influence** of alcohol (limit 0,05%) or other intoxicating or narcotic drugs. However, the Norwegian Road Traffic Acts set no limits for drugs other than alcohol, similar to what have been introduced in some other countries. Thus, each case of suspected drugged driving in Norway has to be evaluated for the court with regard to possible **impairment**. This evaluation is based on results from a clinical examination of the suspect performed by a physician at the time of blood sampling, interview and other relevant information from the police, in addition to results from blood sample analyses performed at NIFT. In most cases an expert witness statement is prepared for the court (3).

NIFT receives blood samples from all apprehended drugged drivers from the whole country. A drugged driving case in Norway starts when a driver is stopped by the police due to suspicion of influence by alcohol or drugs, most often because of an accident, reckless or dangerous driving, discovery of a former well-known drugged driver, or reports from the public to the police. Relatively few drivers are arrested due to systematic roadside or roadblock control, as organised in several other countries. According to the instruction for control of driving under the influence, a Norwegian police officer can stop a driver for alcohol screening using a breathalyzer, without any suspicion of driving under the influence. Screening for alcohol is also performed in connection with other type of traffic control (e.g. speed, technical and driving licence control etc), also giving the police the opportunity to evaluate possible drug influence, based on possible detection of syringes, pills or equipment connected to drug use, or specific physical signs. If drugs are suspected on the background of this primary investigation, the driver is taken to the police station where the responsible police officer on duty makes the final decision whether the suspicion of drugged driving is maintained or not. In cases of suspicion, a medical doctor is called for blood (and urine) sampling combined with a clinical examination. If the driver does not accept blood sampling voluntarily, the samples can be taken by force.

The Norwegian police have no equipment or routine for drug testing roadside. However, since many years, the Norwegian police have more frequently increased their focus towards drugs, when driving under the influence is suspected and therefore gained valuable experience in the selection of suspected drugged drivers. Most Norwegian police officers have no special education to detect drugged drivers based on DRE (Drug Recognition Expert) programs, similar to what is practised in USA and at several districts in Germany. However, during the last few years, some special courses have been organised for representatives from the Traffic Police. A training program has recently also been included in the education program at the Police Academy.

In spite of rather good experience to apprehend suspected drugged drivers, the Norwegian police officers have for a long time expressed a need for equipment to use roadside or at the police station to evaluate possible drug intake, before the decision of blood sampling and clinical examination is taken.

During several years, one or more drugs have been detected in close to 70% of the blood samples from suspected drugged drivers in Norway. In some cases, blood samples are collected as a routine because the driver has been involved in an accident. In such cases, and also in addition to other situations, on-site devices for drug testing roadside or at the police station would be valuable. In addition, it is also well known that some suspected drugged drivers (who probably have taken drugs) are released before blood sampling, due to missing signs of impairment or other events to support the suspicion of influence. For these cases, on-site equipment would be useful to discover recent drug use important for traffic safety.

The most frequently detected drugs among Norwegian drivers are amphetamine, tetrahydrocannabinol (THC), benzodiazepines (BZD) (mainly diazepam and flunitrazepam), morphine and 6-monoacetylmorphine (6-MAM). For most cases, two or more drugs are detected. This pattern of drug detection has existed for several years (1,2,3). However, the frequencies of amphetamine and 6-MAM have increased several times during the 90ies. The drug use pattern discovered among Norwegian

drivers, is probably not very different in other countries. Thus, on-site equipment must cover the most frequently detected drugs important for traffic safety.

The aim of the WP4 ROSITA project

The aim of WP4 ROSITA project was to evaluate different equipment to be used by the police for preliminary screening of possible impairment among suspected drugged drivers. Two different criteria had to be evaluated: i) whether the available equipment could reveal recent drug use important for impairment, by comparing results from on-site drug testing with results from blood analyses collected simultaneously, ii) if the equipment was appropriate for use by the police, easy to handle and to interpret positive or negative results.

When Norway (i.e. NIFT) was asked to participate in the ROSITA-project, mainly WP4, it was decided that collaboration with possible users of such equipment in the future, e.g. police officers. Thus, it was important to test the equipment under similar conditions as the "goal" for the future. If testing of on-site devices could be performed on real suspected drugged drivers in Norway, preferentially roadside or at the police station, blood samples would always be collected and analytical results available for comparison. Application to ethical committee would be unnecessary, if the police already suspected the selected test persons.

Formal approval from the authorities

Before the project started, NIFT applied to the Ministry of Justice, organising all Norwegian police districts, for permission to collaborate with some police districts in order to accomplish the ROSITA-project. The following criteria were pointed out: i) the devices should only be used for drivers already suspected for drugged driving; e.g. blood samples were collected anyway, ii) participation from suspected drugged drivers should be voluntary, iii) the drivers were informed that results from on-site testing had no legal purpose and no sanctions could be taken based on these results, iv) extra costs (training, information meetings, travel expenses etc for the police) should be covered by the project, v) extra time for the police officers involved in the project had to be covered by the police districts. NIFT also advised which police districts should preferentially be asked for participation (those sending many samples, geographically not too far from Oslo). From the beginning, 4 different district were selected, later one more district and a division from the Central Mobile Force were selected. All police districts accepted to participate when asked by the Ministry of Justice. From each district a contact person was appointed. All later contacts connected to the project were organised between the contact police officers and a person from the project group at NIFT.

Information meetings

The first part of the project included information meetings with representatives from the different participating police districts. The next step was to train the police officers to use the different equipment, which was organised mainly in collaboration with representatives from the producers. Based on the situation in Norway, it was most interesting and appropriate to test equipment suitable for saliva, being more convenient for use at roadside or at the police station. It was more difficult to organise urine sample testing as explained earlier in this report.

Training of police officers

Training programs for police officers were organised at NIFT, in collaboration with representatives from the producers. The first training course were focused on devices designed for saliva. From each police districts, 2 – 4 police officers participated, together with members from the project group at NIFT. In addition, representatives from each district received extra equipment for exercise and for training of colleagues, in collaboration with members from the project group at NIFT, if necessary. Instructions how to use the equipment was available from the producers and further modified in collaboration with the project group at NIFT. In addition, NIFT designed a protocol to be used for each case, to record person identification, age, date for sampling, results from the testing of saliva (see annex 1). The opposite side of the protocol included additional instructions necessary for the testing process. The police officers were asked to send the protocol to NIFT together with blood and urine

samples and the standard protocol containing results from the clinical examination, drug use and other information connected to the case (person identification, type of case, time for driving, blood sampling, etc) (see annex 2). Members from the project groups later visited all police districts (except one) several times, for information and training of other police officers. On-site saliva tests should be performed roadside or at the police station, shortly before blood (and urine) sampling and clinical examination.

Collection of saliva samples for chromatographic analyses at NIFT.

NIFT also organised training for police doctors working at the main police district in Oslo, who were asked to collect saliva samples for drug analyses at NIFT. In addition, they were also asked to test saliva using on-site saliva devices, when the police officers bringing the suspected drivers to the medical doctor had no experience in using the devices. Written instructions were prepared for the participating doctors.

Urine samples - on-site testing

Urine testing on-site was unpractical and not easy to organise roadside or at the police station. The testing was then performed by the police in the laboratory at NIFT, in collaboration with representatives from two out of three of the producers as instructors. The devices were tested on urine samples from suspected drugged drivers, sent to NIFT together with blood samples and protocols from clinical examinations. A protocol for the recording of urine on-site test results was also designed by NIFT (Annex 3).

METHODS

Target population - selection of subjects

Five different police districts in addition to one division from the Central Mobile Force participated in testing the different devices, mainly police officers frequently involved in traffic control.

Selection of drivers to be tested - on-site testing of saliva

Based on the Norwegian protocol, the police officers were asked to test saliva only and not sweat, using devices designed for saliva. Only suspected drugged drivers should be asked for participating. They should also be informed of the aim of the project and that they could refuse to participate. Shortly after saliva on-site testing, the driver should be brought to a medical doctor for blood (and urine) sampling and clinical examination. The police officer should fill in the ROSITA-protocol (see annex 1) with name, age and sex of the suspect, name of the responsible police officers, special sign of the suspected recorded by the police, in addition to the on-site testing results. The information from the ROSITA-protocol could then be connected to the data file at NIFT, containing analytical results, conclusion from clinical examination and the final interpretation. Protocols should also be filled out if the suspects refused, if the test failed or occurrence of other problems. In any cases, blood samples would always be collected as the drivers were suspected for driving under the influence of drugs.
The ROSITA-protocol should be sent to NIFT (normally by car or mail), together with the standard protocol from clinical examination and other information from the case (annex 2), in addition to blood and urine samples. If saliva samples were collected for chromatographic analyses, they should also be sent to NIFT in the same container especially designed for blood and urine samples and the standard protocols.

Testing period

The testing period started late in September 1999 and lasted to July 2000. However, the frequency of the testing was mainly dependent on whether the police officers on duty were trained to use the devices and that they had unoccupied time to perform testing. In many cases, other work had to be prioritised, resulting in irregularity of the testing. The police had to add all the extra work connected to the project during their daily routine work. Three of the police districts organised roadside control or special patrols out on the road, in order to control drugged driving and to test the devices. At all occasions, members from the project groups at NIFT participated. These three special controls resulted in few extra samples.

Type of on-site saliva devices tested

Two type of devices designed for saliva were tested:
RapiScan^{R} (Cozart) and Drugwipe^{R} (Securetec).

RapiScan^{R} is a 5 drug panel test with an electronic reader. The following drugs were included: Amphetamines, opiates, cannabinoids, benzodiazepines and cocaine. Cocaine is rarely detected in Norway and the cocaine results (mostly negative) are not included in this report. It was discussed with the producer that this drug should be excluded, in order to save time. However, this was difficult to organise and cocaine was included in all tests, though not included in the final result table.

Drugwipe^{R} is a single drug test, covering only amphetamines and opiates. The results are recorded by colour changes, from white to pink. An electronic reader was tested for a short period of time.
Drugwipe^{R} and RapiScan^{R} should be selected randomly. Because the RapiScan^{R} test device was very complicated to use (time consuming to collect sufficient saliva volume, several steps of sample preparation before introducing sample in the electronic reader, long time to wait, approximately 10 minutes before the results were recorded at the reader), it was not convenient to perform the tests roadside. Therefore most of the tests were performed at the police station, mainly by police officers, or sometimes by medical doctors. Totally, approximately 15-20 police officers performed tests, in

addition to 4 – 5 different police doctors (from one police district). Table 1 shows cut-off limits for the saliva on-site tests.

Table 1: Cut-off limits for on-site saliva devices (RapiScan^R and Drugwipe^R)

Drug	*Rapiscan (ng/ml)*	*Drugwipe*
Amphetamine	10	10 ng
Methampehtamine	**1000**	
MDA	10	
MDMA	1000	
MDEA	10 000	
Efedrin	10 000	
Oxazepam	1000	
Diazepam	30	
N-desmethyldiazepam	2000	
Nitrazepam	10 000	
THC	200	
Morphine	10	10 ng
6-MAM	10	
Codeine	10	
Pholcodeine	30	

Collection of saliva samples - handling and chromatographic saliva analyses

Salivette^R (Sarstedt) was used for the collection of saliva samples. The Salivette^R tube contains a cotton roll, which the sample donor chewed for approximately one minute before the cotton roll was transferred back to the tube. The Salivette^R tube was sent to NIFT for analyses together with blood/urine samples and the protocols and stored deep-frozen (-20^o C) before analyses. Storage time: 1- 2 months.

Chromatographic analyses of saliva

At the day of analyses, the saliva samples were thawed, centrifuged (10 min, 3000 rpm) and analysed using standard methods for blood analyses (see later references). Calibrators were made in saliva, by adding known amount of drugs to native saliva obtained from a drug free person, followed by transferring of the calibrators to the Salivette^R cotton rolls, and further handled similarly as real samples. Amphetamines were analysed in all saliva samples collected from suspected drugged drivers. Due to insufficient saliva volume, opiates were analysed only in samples positive for opiates in the corresponding blood samples based on positive results from EMIT and GC/MS. Only one sample was analysed for THC. The cut-off limits for saliva samples are given in table 2. (Cut-off limits are given in both µM (standard denomination used at NIFT) and mg/l as comparison). The results from chromatographic saliva analyses, were compared with blood analyses and on-site saliva tests (when available).

Immunological screening was not performed in saliva, due to insufficient sample volume. In some cases, water (500 µl) had to be added to the Salivette^R cotton roll, due to dry cotton roll which resulted in no saliva available after centrifugation. The Salivette^R tube was then re-centrifuged and analyses were performed using the diluted sample.

The rest of the saliva samples collected in combination with RapiScan^R on-site tests (diluted with buffer, unknown volume), were not sent to NIFT for further analyses. The main reason was that the standard container used for sending of blood and urine samples to NIFT has no sufficient space for the RapiScan^R tubes. A separate sending including correct information of the sample donor was inconvenient to organise for the police.

Table 2. Cut-off limits used at NIFT for whole blood, urine and saliva analyses.

		Urine confirmation		*Blood confirmation*		*Saliva confirmation*	
	Mw	**µM**	**mg/l**	**µM**	**mg/l**	**µM**	**mg/l**
6-monoacetylmorphine base	327,4	0,2	0,07	0,025	0,01	0,025	0,008
Morphine base	285,3	0,2	0,06	0,03	0,01	0,025	0,007
Codeine base	299,4	0,2	0,06	0,03	0,01	0,025	0,007
Ethylmorphine base	313,4	0,2	0,06	0,2	0,06		
Amphetamine base	135,2	1	0,14	0,30	0,04	0,3	0,04
Metamphetamine base	149,2	1	0,15	0,30	0,04	0,3	0,04
Benzoylecgonine base	289,3	0,2	0,06	0,2	0,06		
Cocaine base	303,4	0,2	0,06	0,2	0,06		
Diazepam	284,7			0,5	0,14	0,06	0,017
N-desmethyldiazepam	270,7	0,5	0,14	0,5	0,14	0,1	0,027
3-OH-diazepam (temazepam)	300,7	0,50	0,15				
Oxazepam	286,7	0,50	0,14	2,00	0,57		
Flunitrazepam	313,3			0,01	0,003		
Nitrazepam	281,3			0,2	0,06		
Clonazepam	315,7			0,03	0,009		
MDA	179,2	0,4	0,07	0,2	0,04	0,2	0,04
MDMA	193,2	0,4	0,08	0,2	0,04	0,2	0,04
MDEA	207,2	1	0,20	0,5	0,10		
THC	314,5			0,001	0,0003	0,001	0,0003
THC-acid	344,5	0,03	0,01				
		Urine screening		***Blood screening***			
		µM	**mg/l**	**µM**	**mg/l**		
Amphetamines	135,2	2,2	0,30	0,4	0,05		
Cannabinoides	314,5	0,1	0,02	0,05	0,02		
Benzodiazepines (diazepam)	284,7	0,7	0,20	0,4	0,11		
Opiates	285,3	1,1	0,30	0,3	0,09		
Cocaine	303,4	1,0	0,30	0,3	0,09		

Saliva on-site testing - saliva sample collection performed at NIFT

In order to obtain more saliva samples for chromatographic analyses, which could be compared with on-site saliva tests, a number of on-site tests combined with saliva and blood sample collection, were performed at NIFT and handled by members of the ROSITA project group. These tests were performed in combination with voluntary drug intake (diazepam, codeine) due to other on-going projects at the Institute (method evaluation, psychometric tests). All saliva and blood samples were treated as samples collected at police station from suspected drugged drivers. In some cases clinical examinations were performed.

Urine - on-site testing

As on-site urine testing was difficult to organise at the different police districts or roadside (nor special cars with toilets etc available), all tests were performed at NIFT by police officers from the participating police districts. All police officers performing on-site urine tests had experience using saliva on-site tests. The urine samples used for on-site test were collected from suspected drugged drivers and sent to NIFT together with blood samples. The urine samples were stored deep frozen (-20^{o} C) at NIFT for 1 – 3 months and thawed the day before testing, e.g. the urine samples had room temperature. As corresponding blood samples already were available, all results from on-site urine test were compared with both blood and urine sample results and discussed with the participating police officers after the tests were finished. Special protocols designed for urine on-site tests were used to record results and other information connected to the tests (annex 3).

The following on-site urine tests were included:

Syva^{R} RapidTest (Dade Behring), multitest covering amphetamines, cannabinoids, cocaine and opiates. Syva^{R} RapidTest (Dade Behring), single test, covering BZDs.
Testcup^{R} (Roche), covering amphetamines, cannabinoids, cocaine and opiates.
OneStep^{R} Drug Scan (Cortez), covering amphetamines, cannabinoids, cocaine and opiates.
The cut-off limits for urine on-site tests are not included in the Norwegian report, but can be give from other parts of the ROSITA project.

Evaluation of the devices used for on-site screening of saliva and urine.

An evaluation form was sent to representatives from the participating police districts – asking for evaluation of the devices, usefulness, problems, time used, easiness to evaluate the results, type of equipment would be useful in the future and preferentially biological matrix for on-site screening. The evaluation form is included in annex 4. Representatives from all districts received the form and most of them returned an evaluation.

Blood sample collection and analyses

As explained earlier, blood samples have been collected in all cases where saliva and urine on-site tests have been performed in the corresponding saliva or urine samples. Thus, results from blood sample analyses are available for all on-site tests (except three cases– see later) for comparison with the on-site tests. All blood samples have been collected and handled according to the standard procedure at NIFT e.g. storage, analytical program with screening and confirmation analyses. Immunological screening analyses are performed at the day of registration, while samples for chromatographic analyses are stored at – 20 ^{o}C until analyses.
Standard analytical program for whole blood used at NIFT includes:
Immunological screening using EMIT, covering amphetamines, high-dose BZDs, opiates, cannabinoids, cocaine (5). In addition, chromatographic screening analyses including alcohol (head-space GC), low-dose BZDs and zopiclone (GC with EC-detection) (6) are performed.
Positive samples after screening, are confirmed and the compounds quantified using GC/MS (opiates, amphetamines including MDMA and related compounds, THC, cocaine/benzoylecgonine), an alternative GC-column combined with EC-detector (BZDs) and an enzymatic method (ADH) for alcohol. (7, 8, 9, 3). The cut-off limits used for screening and quantification/confirmation analyses are summarised table 2. (The limits are given in both μM and mg/ml). All results are calculated according to calibrators made in whole blood, except for alcohol. Program for independent control samples are included in all analyses. The results of the unknown samples are accepted according to the results from control samples and deviation from theoretical mean values.
When no drugs are detected after the standard screening program, but impairment has been concluded from the clinical evaluation performed at the time of blood sample collection, other drugs important for driving impairment are looked for. The analytical programs then included are muscle relaxants, dextropropoxyphene, methadone and some antidepressive drugs.
When all analyses are finished, an evaluation is given with regard to possible impairment by a medical officer at NIFT, based on the analytical results and the clinical examination.

External quality control

NIFT regularly participates in several external quality control programs covering both whole blood and urine samples.
During the ROSITA project period, three plasma quality control samples sent to all ROSITA – partner laboratories, have been analysed. The plasma QC samples have been analysed together with whole blood samples and calculated from whole blood reference standards.

Analyses of urine samples

All urine samples received from suspected drugged drivers and included in this study, were handled according the standard procedure at NIFT, e.g. storage and analytical program. The standard analytical

program for urine samples from apprehended drivers, includes immunological screening using EMIT, covering amphetamines, high-dose BZD, cannabinoids, opiates and cocaine. Positive screening results are not always confirmed or reported when the main question is impairment, when blood sample results only are evaluated and reported back to the police. Exceptions are confirmation of samples positive for opiates (GC/MS), looking for 6-MAM and heroin use. In addition, cases where the police suspect illegal drugs use (according to the Narcotic Law). Positive urine samples are then confirmed if no drugs have been detected in blood samples and a Narcotic Law offence is also suspected.
However, some additional confirmation analyses were performed for urine samples included in the ROSITA project, for the comparison of results from on-site urine tests. The confirmation analyses included amphetamines (including MDMA and related compounds), opiates, high-dose BZD, cocaine and THC-acid. For all urine analyses, GC/MS were used for confirmation (7, 10). All calibrators were made from urine and urine control samples were always included. The results were accepted according to the same procedure as described for blood samples. Cut-off limits for screening and confirmation of urine samples are included in table 2 (both μM and mg/L).

Blood as reference biological material

All results from on-site saliva tests, on-site urine tests and saliva analyses, have been compared with results from blood drug analyses, which is considered to be the "gold" reference material at NIFT. Only the blood drug concentrations can be used for evaluation of recent drug intake and possible impairment, which is the standard procedure in Norway. Countries with zero-drug limits introduced also use the results from blood drug analyses for the evaluation of above/below analytical cut-off limits. In some cases, positive urine samples may result from former drug use (e.g. THC-acid etc), but with no drug detected in blood samples means that impairment can not be proven.
The main reason for testing on-site devices (for urine or saliva), was to uncover or reinforce suspicion of recent drug use and possible impairment. Such equipment will support and give valuable information to the police to take the decision of blood sample collection, or that the suspicion is unfounded so that the drivers can be released.

Comparison of results from on-site tests with conclusions from the evaluttion of impairment

The results from on-site tests (both urine and saliva) were compared with the conclution from the evaluation of impairment performed at NIFT when available. This evaluation was based on the information from the clinical examination performed at the time of blood sampling and the results from blood and urine drug analyses. The impairment evaluation is routinely reported back to the police in the responding letter together with the results from blood (and urine) analyses. An on-site test positive for one or more drugs was considered to be in accordance with the impairment conclusions i) "likely impaired" or ii) "possibly impaired". If no drugs was detected by the on-side test, the result was in accordance with the conclusion "not impaired". For some cases, no conclusion of impairment have been given, e.g. cases were alcohol only was detected in the blood samples, or cases with no clinical examination or other important information lacking.

RESULTS

URINE

Age and sex distribution for urine sample donors.

The majority of the urine samples were collected from male (87%) with a mean age of 32 years , range: 19 – 73 years, which is in accordance with the total number sample donors of suspected drugged drivers in Norway (1,3).

Analytical results

The numbers of urine tests performed are given in table 3.

Table 3: performed tests

Test	*Number of tests performed*	*Failures*
RapidTest (4 drug panel)	100	1
RapidTest (benzodiazepines)	50	-
Testcup (4 drug panel)	100	1
Onestep (4 drug panel)	92	1
TOTAL	342	

All results from the urine on-site tests were compared to both blood sample analysis (EMIT and GC/MS) as well as urine sample analysis (EMIT and GC/MS). Some results are summarised in tables 4 - 6. The tables present urine on-site tests compared to results from analyses of the corresponding blood and urine samples. TN denotes negative urine on-site test and corresponding negative blood/ urine sample analysis, TP positive for both on-site tests and blood/saliva, while FN denotes negative urine on-site test and positive by the corresponding blood /urine analysis and FP positive for on-site test while negative for blood/urine analyses. Cannabionoid on-site test results are compared to THC detection in blood or THC-acid detection in urine samples. On-site amphetamine tests are compared to amphetamine, metamphetamine and/or MDMA/ MDA detected in blood or urine, and opiates compared to morphine, 6-MAM, codeine and/or ethylmorphine detected in blood or urine. The same principle has been used for comparison of BZDs.

Table 4: Comparison of results from blood and urine analyses with on-site urine tests.

RapidTest										
	Cannabis		**Amphetamine**		**Cocaine**		**Opiates**		**Benzodiazepines**	
	Blood	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*
TN	39	35	59	55	93	90	60	56	20	20
TP	43	51	29	34	2	4	23	35	22	26
FN	7	11	3	7	0	2	1	4	1	1
FP	10	1	8	2	4	2	15	3	7	3
Failure	1	1	1	1	1	1	1	1	0	0
SUM	100	99	100	99	100	99	100	99	50	50

Table 5: Comparison of results from blood and urine analyses with on-site urine tests.

Testcup								
	Cannabis		**Amphetamine**		**Cocaine**		**Opiates**	
	Blood	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*
TN	38	35	59	56	90	90	59	57
TP	46	55	31	37	7	5	22	37
FN	4	7	2	5	0	1	1	2
FP	11	1	7	0	2	2	17	2
Failure	1	1	1	1	1	1	1	1
SUM	100	99	100	99	100	99	100	

Table 6: Comparison of results from blood and urine analyses with on-site urine tests.

Onestep								
	Cannabis		**Amphetamine**		**Cocaine**		**Opiates**	
	Blood	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*	*Blood*	*Urine*
TN	32	32	52	48	82	82	52	51
TP	41	54	26	31	2	6	22	36
FN	1	1	3	7	0	0	0	1
FP	17	4	9	4	7	3	18	4
Failure	1	1	1	2	1	1	0	0
SUM	92	92	91	92	92	92	92	

Negative blood or urine tests are related to screening analyses. The results from comparing the individual on-site urine tests and blood samples analyses are also illustrated in the figures 1, 2 and 3, respectively.

For more than 85% of the cases, results from on-site tests were in accordance with the confirmation analyses in the corresponding **urine** samples. Testcup^{R} device showed accordance with confirmation analyses in more than 90% for all drugs tested. The largest deviance between urine on-site tests and confirmation analysis was found for RapidTest^{R}, as 11% of positive THC-acid samples were not detected by the device.

For more than 79% of the cases, results from on-site urine tests were in accordance with the confirmation analyses in the corresponding **blood** samples. The largest deviation between urine on-site tests and confirmation analyses in blood was found for opiates and cannabinoids. For opiates, the urine on-site tests showed that 15-20% of the cases could not be confirmed by GC/MS blood analyses. Lower correlation between on-site urine tests and blood drug confirmations compared to urine sample confirmations, can be explained from the detection of drugs for a longer time period in urine samples compared to blood.

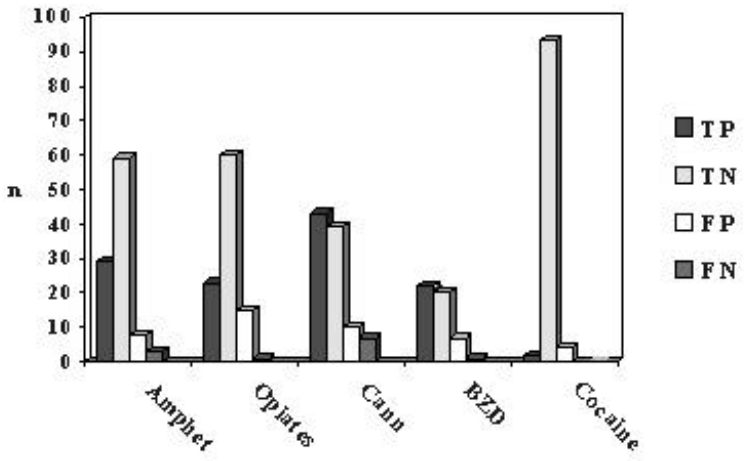

Figure 1: Results from RapidTest urine on-site tests (n) compared with corresponding blood samples for amphetamines - opiates - THC - BZD and cocaine.

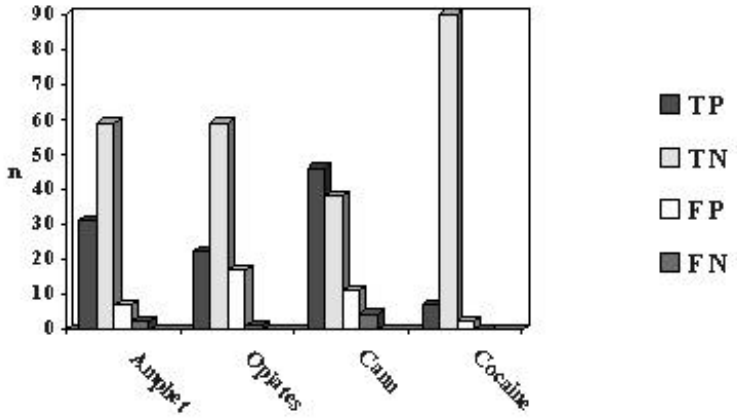

Figure 2: Results from Testcup urine on-site tests (n) compared with corresponding blood samples for amphetamines - opiates - cannabinoids and cocaine.

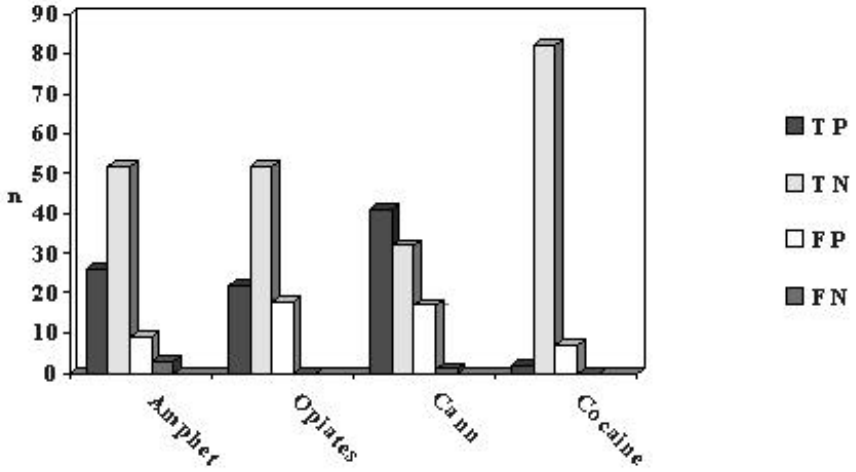

Figure 3: Results from Onestep urine on-site tests (n) compared with corresponding blood samples for amphetamines - opiates - cannabinoids and cocaine.

Evaluation of the on-site testing procedure.

Since the urine samples were not collected road side, it is difficult to answer the question if urine sampling and testing constituted a problem in the field. However, some problems may be encountered during sampling at the police stations, e.g. insufficient volume of urine (rare) or that sample donor argues that urine cannot be delivered. Thus, in a number of cases, urine samples are lacking (but blood samples are taken by force if necessary).
Urine sampling and testing roadside would probably be very complicated to organise for the police in Norway. The equipment needed for roadside sampling of urine, such as cars with toilets etc, is not available for the Norwegian police. In addition, the public opinion would probably not favour a roadside test of urine for privacy reasons.
Testing of the urine samples for this project was performed by 5 policemen in the laboratory of NIFT and with support from the project group. All police officers had experience from using saliva tests. The advantages and disadvantages of the devices are summarised in table 7.

Table 7: Evaluation on urine on-site test equipment

Test	*Advantages*	*Disadvantages*	*Time used*	*Reading of results*
Testcup	a cup allowing both sampling and analysis easy to perform (also roadside)	large amount of urine needed spilling of urine	4-5 min.	easy to read results manual reading was OK
RapidTest	few drops of urine needed easy to perform	extra equipment necessary not easy to perform roadside	4-5 min.	easy to read results manual reading was OK
OneStep	no need for extra transferring equipment little sample was needed easy to perform	colour change was weak	4-5 min.	reading was difficult in some cases

Comparison of results from urine on-site tests with results from evaluation of impairment

The results from comparison of on-site urine tests and the evaluation of impairment based on blood drugs analyses and clinical examination, are illustrated in the figures 4 (RapidTest), 5 (Testcup^{R}) and 6 (OneStep^{R}), respectively. As seen from the figures, one or more drugs were detected by the on-site urine tests in about 80% of the cases with a positive conclusion with regard to impairment. Impairment was also concluded in 5 – 13 % of the cases where no drug was detected by the on-site test. For 4 – 5% of the cases, both impairment conclusions and on-site tests were negative.

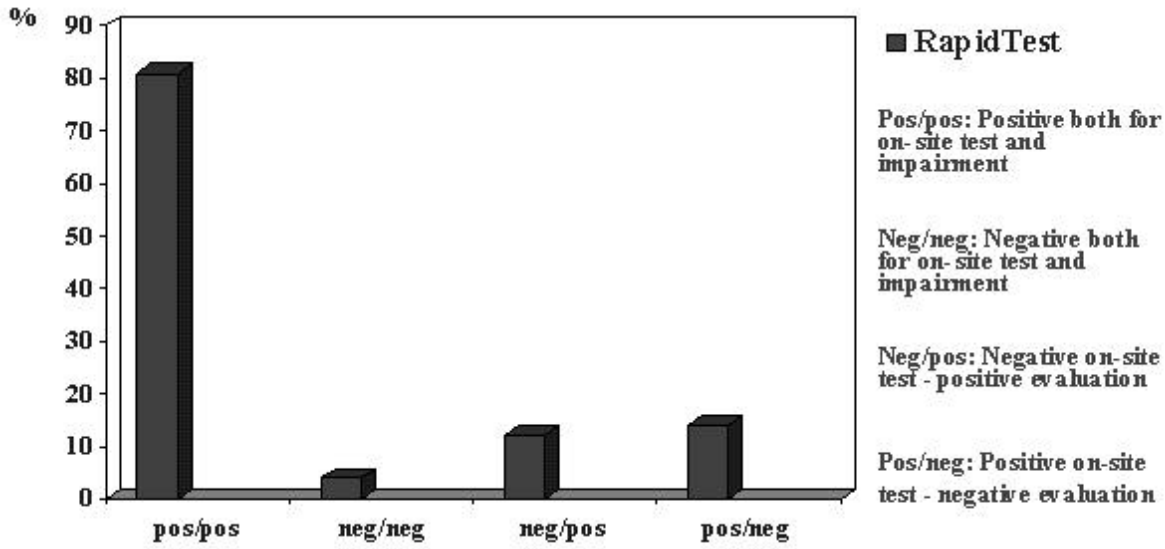

Figure 4: Results from evaluation of impairment based on clinical examination and blood drug analyses – compared with urine on-site tests. Each bar represents the frequency of total number of cases (n=92) evaluated.

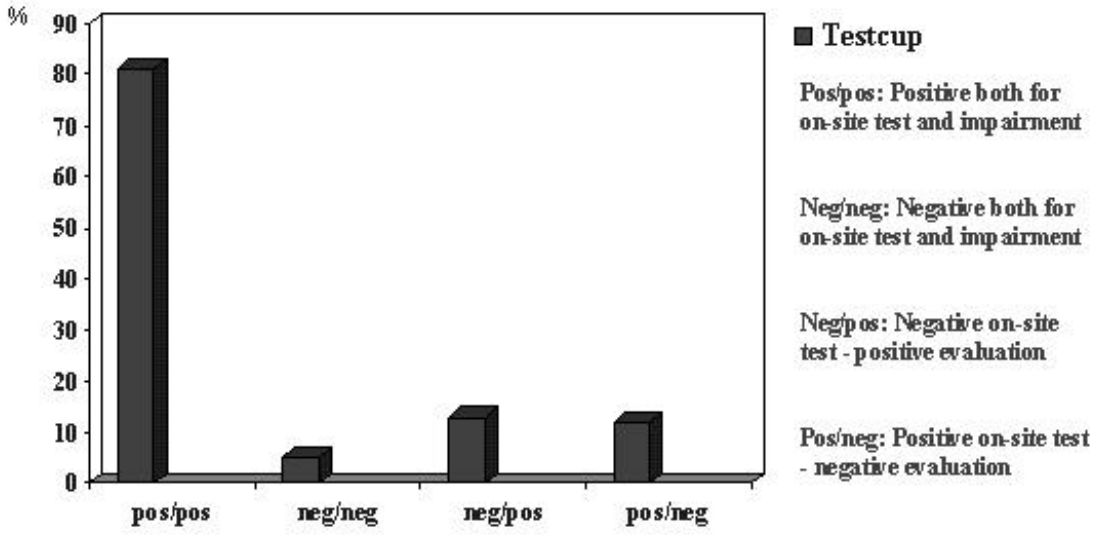

Figure 5: Results from evaluation of impairment based on clinical examination and blood drug analyses – compared with urine on-site tests. Each bar represents the frequency of total number of cases (n=92) evaluated.

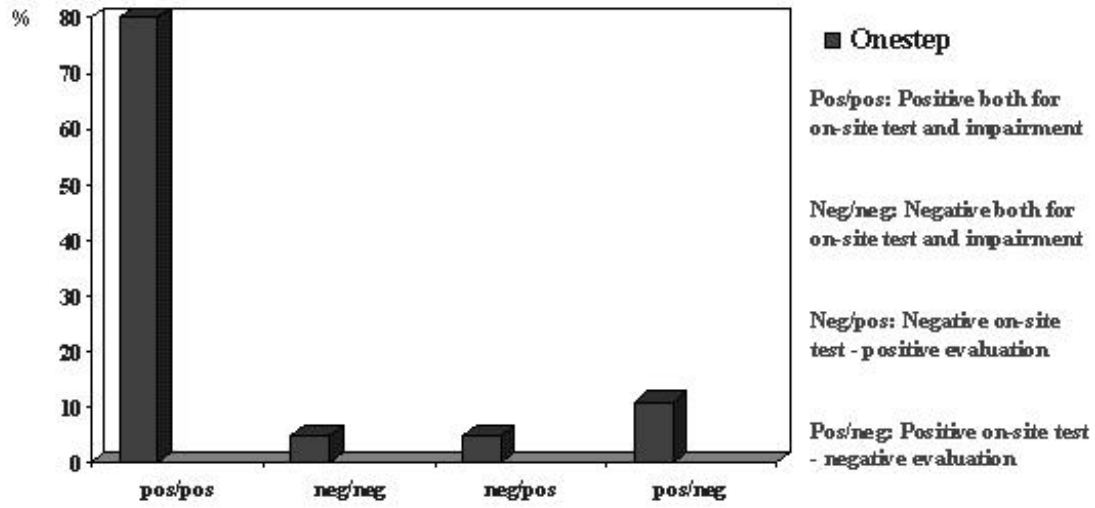

Figure 6: Results from evaluation of impairment based on clinical examination and blood drug analyses – compared with urine on-site tests. Each bar represents the frequency of total number of cases (n=83) evaluated.

SALIVA

On-site saliva tests – collection of saliva samples

The number of saliva samples collected, on-site tests performed, failures and individuals that refused to participate are summarised in table 8.

Table 8: samples collected, on-site tests performed, failures and individuals that refused to participate

Test	*No. of tests performed*	*Failures*	*No. of samples collected*
RapiScan	101	9*	
Drugwipe	142		
Refused to participate both RapiScan and Drugwipe	15		
Salivette^{R} sample collections			85
TOTAL	243 (249-15)		

* The number of failures given in the table is too low, as several unsuccessful tests were performed where the police did not reported the failures. On main reason was that defects were connected to the available RapiScan^{R} tests (see later part, evaluation of on-site tests).

For all saliva tests except three, blood samples were collected and the corresponding analytical results are available. In two of the three cases of missing blood samples, urine samples were collected and the analytical results are available. In one of these cases, results from on-site saliva test (Drugwipe^{R}) was in accordance with urine samples results. In the other cases, the urine sample was positive for amphetamine and opiates, but not detected by on-site saliva test (Drugwipe^{R}). For the third case, neither blood nor urine was collected. The reason was that the suspected drugged drivers swallowed the test device and the police forgot to order blood samples. In some cases, the individuals accepted to be tested by both RapiScan^{R} and Drugwipe^{R}. The results from both devices are presented in Annex 5 (Excel workbook).
Unfortunately, for 23 cases, where on-site tests and saliva collections were performed at the police station, the protocol with the on-site tests results were not sent to NIFT and they could not be traced later. The results from these on-site tests are therefore missing and comparison to blood and saliva analyses not possible. Later, it was not possible for the sample collector to remember test results for each individual.

Age and sex distribution for individuals participating in saliva on-site tests.

The majority of the samples were collected from male (90 %) with a mean age of 32 years, range: 17 – 61 years. The frequency of female (10%) was lower among this group of drivers than the whole group of samples donors of suspected drugged drivers in Norway (1,3).

Comparison of results from saliva and blood analyses

All results from chromatographic analyses of saliva collected by Salivette^{R} and blood samples are summarised in table 9, page 36 (amphetamines), table 10, page 37 (opiates) and table 11, page 38 (BZD) (in addition to Annex 5 – Excel workbook). When available, results from the corresponding on-site saliva tests are also given in the tables.

Amphetamines including MDMA and related compounds:

56 saliva samples were analysed for amphetamines, methamphetamines, MDMA and MDA. In all saliva samples with drug detection, the concentrations were higher compared to blood, even when the saliva samples had to be diluted with water (table 9, p. 36). In some cases, amphetamines was positive in saliva, but not in blood samples (n=3). For two of these cases, the corresponding urine samples were positive for one or more amphetamines. No urine sample was available in the third case. Based on our results, it seems that amphetamines and related compounds can be detected in saliva for a longer time after drug intake compared to blood. High amphetamine concentrations in saliva are thus favourable for on-site test devices.

Corresponding results from on-site devices are missing in 23 cases. For 6 cases when on-site results were available (Drugwipe^{R}), the test results are either false positive or false negative compared to saliva.

Opiates

For all cases, the saliva concentrations for the individual drugs were higher compared to blood samples (table 10, p. 37). In some cases, one or more opiates were detected in saliva but not in blood. However, in most cases the compounds were detected in urine (when available). Special attention must be paid to 6-MAM, which was detected in 10 saliva samples, but in none of the blood samples. When urine samples were available, 6-MAM was not detected in all urine samples with corresponding detection in saliva. Our results thus indicate that saliva may be a better matrix to confirm recent heroin use compared to blood, where the compound is rapidly metabolised to morphine. Table 10 also shows comparison of on-site saliva tests (when available) with saliva analyses. Some false negative or false positive results compared to saliva confirmation analyses were obtained (table 10).

Benzodiazepines (BZD)

In most cases the concentrations of BZD were lower compared to blood (table 11, p. 38). However, diazepam and N-desmethyldiazepam were the only drugs tested. None of the BZD-corresponding on-site tests (RapiScan^{R}) were positive for BZD when detected in the collected saliva samples analysed at NIFT. When comparing blood samples positive for BZDs, few positive results were detected using BZD-on-site tests (RapiScan^{R}) (figure 8 and table 11). The situation is probably more critical for flunitrazepam (low dose BZD), which is the most frequently detected BZD-drug after diazepam among suspected drugged drivers in Norway. It is expected that the concentration for this low-dose BZD is even lower in saliva. This situation complicates the detection of flunitrazepam by on-site tests. The cut-off limits for on-site BZD-tests (RapiScan^{R}) are high for most the BZD-compounds tested (table 1) and flunitrazepam is not mentioned in the table from the producer.

THC

Only one saliva sample was analysed due to insufficient sample volume. This is too insufficient material to evaluate the concentration of THC in saliva compared to blood.

On-site saliva tests compared with blood analyses

Some results from on-site saliva tests are summarised in table 12 (Drugwipe^{R}) and 13 (RapiScan^{R}), respectively. TN denotes negative saliva on-site test and the corresponding negative blood sample analysis, TP positive for both on-site test and blood analyses, FN denotes negative on-site saliva test and corresponding positive blood analysis, while FP denotes positive saliva tests and negative blood results. The positive blood results are related to positive THC for cannabinoids, one or more amphetamines or related drugs detected for amphetamines, morphine, 6-MAM, codeine or ethylmorphine detected for opiates and one or more BZDs detected. Negative blood results are related to screening analyses.

75% of all Drugwipe^{R} tests were in accordance with blood sample results (opiates: 80 % and amphetamines 70 %). Some results from on-site saliva tests compared with blood sample results are also illustrates in figures 7 and 8, respectively.

Table 12: Comparison of results from blood analyses with saliva on-site tests.

Drugwipe		
	Amphetamines	**Opiates**
TN	42	64
TP	34	20
FN	7	10
FP	25	11
Failure	0	0
Total	108	105

Table 13: Comparison of results from blood analyses with saliva on-site tests.

RapiScan				
	Amphetamines	**Opiates**	**Cannabinoids**	**BZD**
TN	58	69	66	49
TP	22	12	4	7
FN	2	4	10	28
FP	11	5	9	6
Failure	9	9	9	9
SUM	102	99	98	99

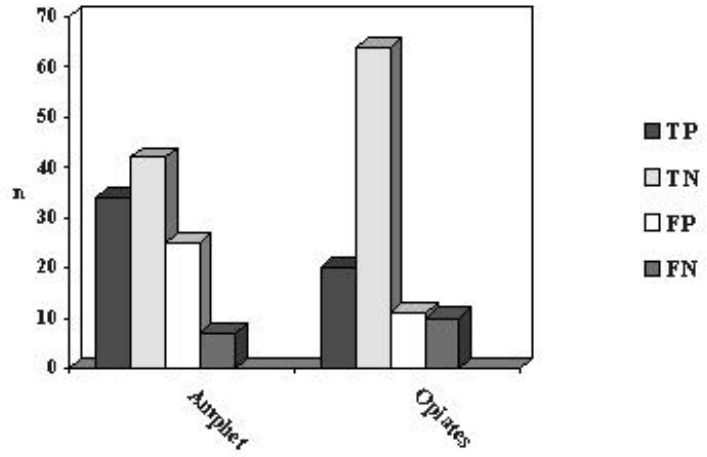

Figure 7: Drugwipe saliva tests compared with results from corresponding samples for amphetamines and opiates.

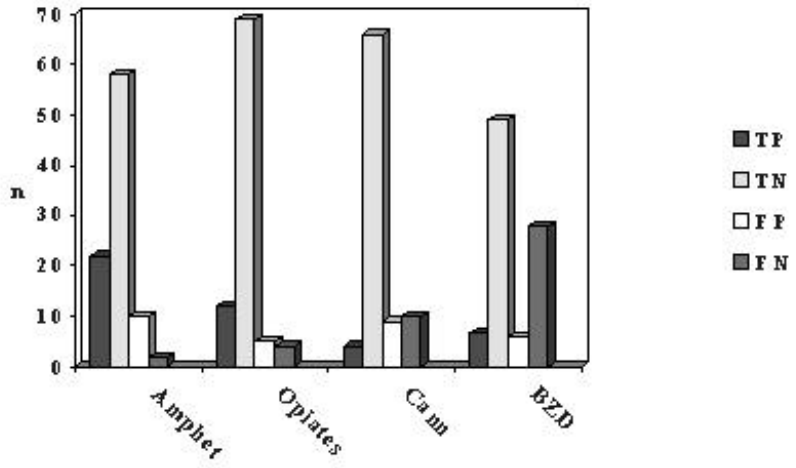

Figure 8: RapiScan saliva tests compared with results from corresponding samples for amphetamines, opiates, THC and BZD.

The reason for different number of individual drug tests as given in table 12, was that both opiates and amphetamines were not always performed on the same person. In some cases, either opiate or amphetamine tests were performed, depending on which drug was suspected. The reason for different values for the individual drug tests when RapiScan^{R} was used, is that all on-site results were not recorded for all drugs on the protocol (forgot to write the results – should be available for multi-drug tests in all cases). When evaluating all RapiScan^{R} results, 80 % were in accordance with blood samples

results, varying from 90% for opiates and 62 % for BZDs. For cannabinoids, few positive cases could be detected using on-site test for saliva, event with high concentrations in blood. The cut-off limit for cannabinoid saliva test as in-dicated by the producer (table 1), is very high and therefore it is not surprisingly that few positive cannabinoid cases were detected. In some few cases with low blood concentrations of flunitrazepam, surprisingly the on-site BZD tests were positive. However, some metabolite(s) of high-dose BZD could have been present which were not covered by the GC-method. Cases where only urine was available are not included.

Comparison of results from saliva on-site tests with results from evaluation of impairment

The results from comparison of on-site saliva tests and the evaluation of impairment based on blood drugs analyses and clinical examination, are illustrated in the figures 9 (RapiScan^{R}) and 10 (Drugwipe^{R}), respectively.

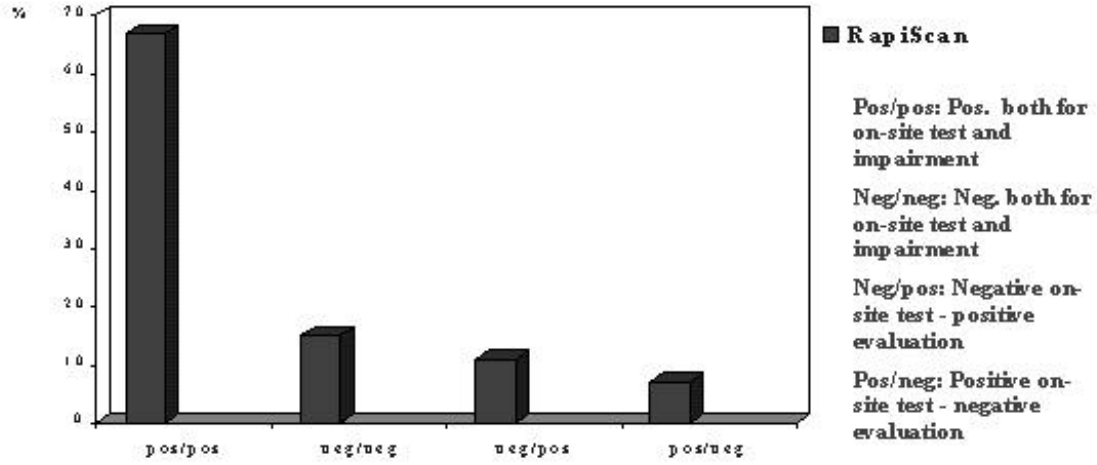

Figure 9: Results from evaluation of impairment based on clinical examination and blood drug analyses – compared with saliva on-site tests. Each bar represents the frequency of total number of cases (n=45) evaluated.

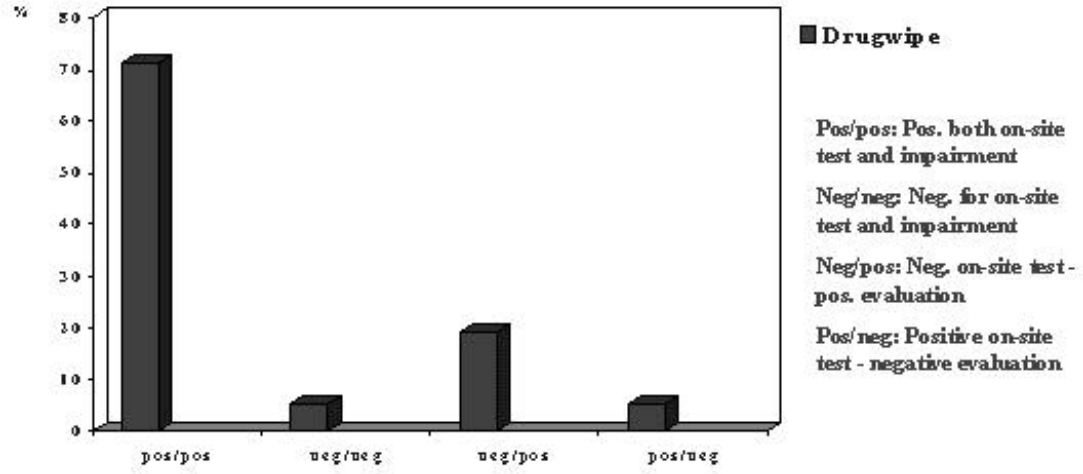

Figure 10: Results from evaluation of impairment based on clinical examination and blood drug analyses – compared with saliva on-site tests. Each bar represents the frequency of total number of cases (n=84) evaluated.

As seen from the figures, one or more drugs were detected by the on-site saliva tests in 67 – 71 % of the cases with a positive conclusion with regard to impairment. Impairment was also concluded in 11

– 19 % of the cases where no drug was detected by the on-site test. These values were at the same level /higher compared to corresponding evaluation of impairment and results from on-site tests. One important reason for positive results from evaluation of impairment and no drug detected by the on-site tests, was that one of the tests (Drugwipe^{R}) could not detect BZDs and cannabinoids, while the sensitivity for the other saliva test (RapiScan^{R}) was too low for detection of these drugs in most of the cases. In some cases where a positive conclusion of impairment was given, however the corresponding negative saliva test was negative, other drugs not covered by any of the on-site tests were detected in the blood samples (e.g. zopiclone, carisprodole, meprobamate). For 5 – 15 % of the cases, both impairment conclusion and on-site saliva tests were negative.

Evaluation of the individual on-site tests

RapiScan^{R}

Based on several presentations from the producer before the ROSITA-project started, RapiScan^{R} devices were expected to be easy to use and the results would be available within approximately 5 minutes. Some police officers also participated at such information meetings, resulting in high motivation and interest for testing of such devices.

The project group had no opportunity to test the devices before the training of police officers started. During the training course, we discovered that the equipment was rather complicated to use. The total time needed for sample collection, sample preparation, running time needed for the electronic reader, was at least 15 minutes. When the equipment was used to test real drugged drivers, at least 15 minutes were often needed to collect sufficient saliva sample only, as these persons often had very dry mouth caused by their drug use. In addition, the police had the opinion that the sample preparation procedure was rather complicated (filtration, pipetting, handling of samples tubes), feeling that some laboratory experience was necessary.

Due to complicated procedures, the police needed extra time for training and instruction of other colleagues not participating in the training course, though extra support from members of the project group for additional training was given. Soon after the testing period started, it was rather clear that the equipment was not suitable for roadside use. Too many items had to be handled. In addition, it was not adequate to use at least 15 minutes roadside, sometimes more than 25 minutes before the test results were available. During some roadside tests, the police discovered that the electronic reader could be disturbed from police-car radio and that the electronic reader had to be placed horizontally, which was not always easy to arrange in a police car. It was therefore decided that the testing should mainly be performed at the police station. Due to these problems, very few samples were collected during the first weeks after the training course. In addition, the police lost their motivation for using complicated and time consuming devices. It was difficult to find extra time for testing, within their daily routine work. Many police officers very early concluded that the device was not what they expected and not very helpful for their evaluation of drugged drivers.

The problems were discussed in November 1999 with representatives from Cozart, a representative from the police officers also participated. The producer then informed that a new type of device that should be more easy and faster to use would be introduced within a very short time period. The old equipment could be discarded. This information was given to all participating police districts.

However, several weeks passed before new equipment arrived, in addition all the electronic readers had to be replaced.

Unfortunately, the first batches of new devices sent to the different police districts had production defects (no reference band was detected) and no results appeared in the display of the electronic reader after waiting for ten minutes. Large efforts were used to convince representatives for the producers that something was wrong. All these problems resulted in that during 2 –3 months, no working RapiScan^{R} equipment was available. During this time period, the participating police districts had planned roadside controls and valuable time was lost. When the police used the equipment with production defects, they thought that something was wrong with their procedure. Several unsuccessful tests were performed (reference band not detected) which were never reported. After this time, it was more difficult to motivate the police to take more samples, even when new devices without any faults had arrived.

Some improvements had been done with the new equipment, however, the collection of saliva samples still takes too long time and sample preparation is still complicated. However, some police officers claim that with more experience it is rather easy to perform the tests at a permanent place e.g. police station (still not useable roadside).

Drugwipe^{R}

This equipment was more easy to use and less time-consuming. One test could be finished within two-three minutes for each individual drug, which could be satisfactory for roadside use. As very small volume of saliva is needed, problems with dry month appeared in few cases. Due to more easy testing procedure than RapiScan^{R}, more samples could have been collected. However, as Drugwipe^{R} and RapiScan^{R} should be selected randomly, problems connected to RapiScan^{R} also influenced the numbers of Drugwipe^{R} tests.

The main drawback with this type of test was that only two drug groups were covered (amphetamines and opiates), while important drugs as cannabinoids and BZD were lacking. Another negative point is that the device is a single test, meaning that the police will evaluate which tests should be selected primary to detect the drug that they suspected had been taken. The evaluation of positive or negative results was often difficult, due to the colour change from white to pink and no reference line included. This may result in extra problems when using the equipment roadside in the dark. An electronic reader was offered during the testing period, but according to the opinion from the police, it was somewhat unpractical to use. Another criticism was that water was needed, both when using visual reading and the electronic reader. This is not very practical roadside at wintertime in Norway. Some police officers became very sceptical to the equipment from the beginning, due to that they used themselves for training and positive results were obtained in several cases. The main reason was probably that the evaluation of colour change was difficult and not very easy to conclude positive or negative reaction, when no reference band was included for comparison.

A multi-test covering several frequently used drugs, easy interpretation of positive/negative results including reference line is therefore necessary.

General use of saliva on-site tests for other occasions

During the investigation period, several other institutions, contacted NIFT for information using saliva devices as an alternative to urine testing, e.g. drug treatment clinics, custom services, those discussing testing of employees and also a companies with an work-place testing agreement. For these institutions, the time aspect of testing was less critical. However, the sensitivity and type of drugs covered by the equipment were also important for these institutions.

Evaluation of on-site tests based on the reports from participating police districts.

In spite of many practical problem connected to on-site saliva testing, the general feedback given by the police in the evaluation (Annex 4) was that saliva tests and suitable equipment would be very valuable for evaluation of apprehended drugged drivers. Such equipment will simplify the police work and save time. The case can be decided immediately, e.g. releasing the drivers or contact a medical doctor for blood sampling and clinical evaluation. This conclusion was more clearly given from police working outside large cities, which have no permanent doctor connected to the police station, resulting in more time spent before the doctor arrives. Equipment available for both roadside testing and at the police station are desirable. All police officers answering the question form clearly pointed out that the equipment had to be easier to use (no laboratory experience necessary) and far less time consuming, especially for roadside use. The Drugwipe^{R} sample collection process was suitable and easy to handle. The police officers want equipment that is comparable to the easiness and time use for breathalyzer. Most police officers expressed that multi-drug tests are preferable, using electronic readers showing positive or negative result, as several police officers pointed out that it was difficult to evaluate positive or negative result using Drugwipe^{R}. However, it is not necessary to know the type of drugs that have been taken, only that one or more drugs had been taken. Reference band is necessary as a control if the on-site test works.

Summary of the main conclusions from the Norwegian police were:

- Saliva tests: Yes – preferable for use both roadside and at the police station
- Multi-drug test preferable.
- Fast and easy to use – less then five minutes.
- Few items to handle
- Electronic reader
- Reference line necessary in cases of colour change recording.
- Comparable with on-site breathalyzer for time needed and easiness to use.

- None of the equipment available was satisfactory for police work
- None of the police officers asked wanted to use urine samples for on-site testing – in spite of available equipment tested during the ROSITA-project were rather easy to use - (but laboratory personnel were available for help all the time)

SWEAT

Sweat samples were not included in the Norwegian part of the project.

BLOOD

Analytical results

All analytical results are included in different tables as earlier described. The collection and storage of blood samples have been explained elsewhere, and they were performed according to standard routine in Norway (3). The evaluation of possible impairment based on blood drugs concentrations and clinical examination are presented in Annex 5 (Excel book).
The Excel book also contains blood alcohol concentrations for all cases and also other drugs detected, not covered by the on-site tests.
The cut-off limits for blood analyses are given in table 2 showing both mg/l and µM, which is the standard denomination, used at NIFT. All cut-off limits are referred to whole blood. For some BZD compounds, the results have to be recalculated if compared to plasma, due to that plasma/blood ratio > than 1.

DISCUSSION

Is saliva usable for on-site testing - what is needed in the future

Saliva should be suitable in the future for on-site drugs testing both roadside or at the police station. However, several improvements have to be done, both with the possibility to detect important drugs at sufficient sensitivity (cannabinoids, BZD) and procedures for handling of the devices.

The criteria for such equipment are given in the evaluation from the participating police districts. Urine testing roadside is not possible to organise for the Norwegian police and will probable give general protests. It is also worth noting that urine samples are not available in many cases when the investigation have been performed at the police station or at doctors office. None of the police officers recommended using on-site urine devices.

Based on results from the Norwegian project, on-site testing using saliva would be very useful for the police, as valuable time can be saved. In spite of rather good experience to evaluate drugged drivers by the Norwegian police (see introduction), the police officers want equipment to simplify their work. As long as the drivers are suspected for drunken or drugged driving in Norway, the police can suspend their driving licence up to 3 weeks if the cases have not been finished for the court. (When sentenced according to the Road Traffic Act, the driving licence is suspended for 2 years).

With on-site tests were available, some negative cases can be concluded immediately. Innocent drivers (e.g. in accident cases) may keep their licence and avoid more suspicion from the police. In addition, such devices would be helpful in cases where the police probably release impaired drivers, due to uncertainty about their possible impairment. Some impaired drivers are clever to hide their drug use and behave rather properly during police investigation. Equipment would also be very useful for untrained police officers with little or no experience to evaluate impaired drivers.

The comparison of evaluation of impairment and on-site saliva tests, showed correlating results for about 76 – 82% of the cases (either positive/positive or negative/negative). For urine on-site-tests, the corresponding values were approximately 85%. The drivers evaluated as impaired, when no drugs was detected by on-site tests could be lost if the on-site test only was used for the decision of blood sampling/clinical examination or not (11- 19 % of the cases compared to saliva tests).

One important moment if on-site devices should be introduced as a routine, is that the police still have to evaluate the drivers for possible impairment and not trust the devices too much. Such problems will mainly be connected to "new" drugs important for traffic safety or other drugs not covered by the device. Devices not covering important drugs or having too low sensitivity, may then contribute to release of too many impaired drivers. Some false positive result from on-site testing can be accepted, as these results can be "deconfirmed" by blood samples and specific analytical methods. It is therefore important that the police maintain their experience and knowledge to evaluation possible impairment of drugs not covered by the on-site tests. The suspicion of impaired driving is also an important reason for apprehension by the police and requisition of clinical examination blood/urine sample fpr drug analyses.

Comments to selection of police districts

During the selection of police districts, it was decided that large police district sending many samples should be included in the project. However, due to many police officers on duty at different time, it was more difficult to obtain experience and more difficult to reach the individual police officers for help and advice if necessary. The project was therefore easier to organise in collaboration with smaller police districts with rather few police officers involved. During the project period, other police districts not involved in the project asked to participate, mainly for testing of saliva samples and more samples could have been collected. However, on the background on the resources from the project group (mainly occupied with daily routine work) at NIFT and long distances to the different police districts, requiring more travel expenses, it was not possible to train and support more districts. A possible new

testing period with new and better equipment would open the possibility to collaborate with other police districts, because of large interest in the project.
During autumn 2000, meeting with the participating police districts will be organised to give a summary of the results obtained from the Norwegian part of the project.

Interest from media

Newspapers, television and broadcasting have shown much interest for the project during the testing period. The ROSITA project has been referred in far more than 50 articles in newspapers from the whole country mainly based on interviews with the leader of the project. In addition, interviews have been given on television (first news at main Norwegian television station) and several broadcasting stations several times. Members from the project group have also been invited to seminars outside NIFT to present the project. Articles describing the project have been published in Journal of the Norwegian Medical Association, Journal of the Norwegian Pharmaceutical Association and Journal for Norwegian Toxicologists. The Ministries of Transport, Justice and Social Affairs, in addition to the Public Main Prosecutor have asked to been informed about the evaluation and conclusions from the projects.

CONCLUSION

In spite of several practical problems connected to the testing of on-site devices, the Norwegian police welcome equipment to be used for primary testing of apprehended drugged drivers, meaning that such equipment will save valuable time. Some police districts have contacted NIFT after finishing the project, asking for devices and when it will be available. However, several improvements connected to the testing procedure are necessary in addition to increased sensitivity for some drugs. Multi-drug panel devices urine electronic readers are preferentially. The Norwegian police welcome saliva as the preferable matrix to use both for road-side testing and at the police station. New drugs and low dose drugs important for traffic safety may arise as a problem if such devices would be routinely used. In spite of satisfactory equipment for on-site testing, it is important that the police are trained to select the suspected drugged drivers from the traffic and to evaluate if the results from on-site testing are in accordance with their impression of the behaviour of the suspects or other equipment in the car connected to drugs use. One main reason for apprehension is that the police suspect drug impairment which means further actions.

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3. A. S. Christophersen and J. Mørland. Drugged driving, a review based on the experience in Norway. Drug and Alcohol Dep. 27, 125-135, 1997.

4. A. S. Christophersen, G. Ceder, J. Kristinsson, P. Lillsunde and A. Steentoft Drugged driving in the Nordic countries- a comparative study between five countries. Forensic Sci. Int. 106, 173-190, 1999.

5. H. Gjerde, A. S. Christophersen, B. Skuterud, K. Klemetsen and J. Mørland.Screening for drugs in forensic samples using EMIT urine assay. Forensic Sci. Int. 44: 179-185, 1990.

6. H. Gjerde, E. Dahlin and A. S. Christophersen. Simultaneous determination of common benzodiazepines in blood using capillary column gas chromatography. J. Pharm.Biomed. Anal. 10, 317-322, 1992.

7. H. Gjerde, I. Hasvold, G. Pettersen, A. S. Christophersen. Determination of amphetamine and methamphetamine in blood using derivatization with perfluoro-octanylchloride and gas-chromatography mass spectrometry. J. Anal. Toxicol. 17, 65.68, 1993.

8. A. S. Christophersen. Tetrahydrocannabinol stability in whole blood: plastic versus glass containers. J. Anal. Toxicol. 10, 129-131, 1986.

9. H. Gjerde, U. Fongen, H. Gundersen and A. S. Christophersen. Evaluation of a method for simultaneously quantification of codeine, ethylmorphine and morphine in blood. Forensic Sci. Int. 51, 105-110, 1991.

10. R.E. West, D.P. Ritz. GC/MS analysis of five common benzodiazepine metabolites in urine as tert-butyl-dimethylsilyl derivatives. J. Anal. Toxicol. 17, 114-117, 1993.

APPENDIX 1

Statens rettstoksikologiske institutt (SRI)
Postboks 495 Sentrum
0105 Oslo
Besøk og prøvelevering: Lovisenberggt. 6
Sentralbord 22 04 27 00
Telefaks 22 38 32 33

ROSITA- PROSJEKT

Testresultater spyttprøver

OPPLYSNINGER OM PRØVEGIVER

Navn _____ _____
(etternavn) (fornavn)

Fødselsnr. ☐☐☐☐☐☐ ☐☐☐☐☐

Kjønn: M ☐ K ☐

REKVIRENT

_____

Adresse: _____

Postnr.: _____ Poststed: _____

Kontaktperson: _____

Tlf.:_____

ROSITA-prosjektet (ROad SIde Testing Assessment) er et felles europeisk prosjekt som skal undersøke testsystemer for andre rusmidler enn alkohol, med henblikk på testing før eventuell blodprøvetaking. I Norge skjer dette i form av et samarbeid mellom enkelte politidistrikter og Statens rettstoksikologiske institutt (SRI). Testing foretas på spyttprøver, ved bruk av testsystemene Rapiscan eller Drugwipe.
Testresultatet i spyttprøven er en screening-analyse, og resultatet er ikke et juridisk bevis.

TESTSYSTEM	STOFFGRUPPE	TESTRESULTAT		
		Pos	Neg	Ikke egnet
RAPISCAN (COZART)	AMFETAMIN	☐	☐	☐
	BENZODIAZEPINER	☐	☐	☐
	CANNABIS	☐	☐	☐
	OPIATER	☐	☐	☐
DRUGWIPE (SECURETEC)	AMFETAMIN	☐	☐	☐
	OPIATER	☐	☐	☐
☐ ØNSKET IKKE Å AVGI SPYTTPRØVE				

PRØVE TATT:
ð UTE
ð INNE

Eventuelle tegn og symptomer på rusmiddelinntak/påvirkning:
Pupiller? Puls?
Nystagmus?
Gange/balanse/koordinasjon?
Annet?

Skjemaet sendes til SRI sammen med undersøkelsesprotokoll og blod/urinprøve. Rekvirenten tar kopi.
Kontaktperson ved SRI: Asbjørg S Chistophersen tlf 22042724.

_____ _____
Sted og dato Underskrift prøvetaker

APPENDIX 2

Statens rettstoksikologiske institutt
Postboks 495 Sentrum
0105 OSLO
Besøk og prøvelevering: Lovisenberggt. 6
Sentralbord: 22 04 27 00 Telefaks: 22 38 32 33

Rekvisisjonsskjema
Analyser av rusmidler og medikamenter
fra politi og påtalemyndighet

Rekvisisjonsskjemaet skal leses maskinelt
Skriv tydelig
Bruk helst svart penn
Sett kryss slik: X
Tallene skal se slik ut: 1 2 3 4 5 6 7 8 9 0

Versjon 202
Sak nr:
Rekvirentens saksnr.
BAV 828

Prøvegivers etternavn
Prøvegivers for- og mellomnavn
Fødselsnummer
Mann / Kvinne
Levende / Død
Høyde: cm
Vekt: kg

Rekvirent
Kontaktperson
Telefon
Postadresse
Postnr.
Poststed

Påvirkning, saken gjelder 1-6 — Analyser i blod
Mistanke om påvirkning av
Alkohol
Alkohol og/eller andre rusmidler: amfetamin, cannabis, kokain, opiater og benzodiazepiner (utvidet prøve) — *Klinisk undersøkelse skal utføres!*
Flyktige stoffer (sniffing)
Andre stoffer/legemidler
Spesifiser

Rusmiddelbruk, saken gjelder 7-8 — Analyser primært i urin
Standard program: amfetamin (unntatt ecstasy), cannabis (hasjis, marihuana o.l.), opiater (heroin, morfin o.l.), kokain, diazepam/oxazepam
Andre analyser
Spesifiser

Tidspunkt for hendelsen:
dato
kl.

Saken gjelder (Kryss av for én eller flere kategorier)
Påvirkning i forbindelse med: (forutsetter blodprøve)
1 Føring av motorvogn
2 Føring av annet
3 Trafikkulykke
4 Annen ulykke
5 Voldsbruk
6 Annet

Rusmiddelbruk (urinprøve anbefales)
7 Brudd på narkotikaloven/legemiddeloven
8 Rusmiddelkontroll ifølge dom

Må kun brettes her

Fylles ut under prøvetakingen

Urin
Temperatur °C
pH
Spesifikk vekt
Utseende

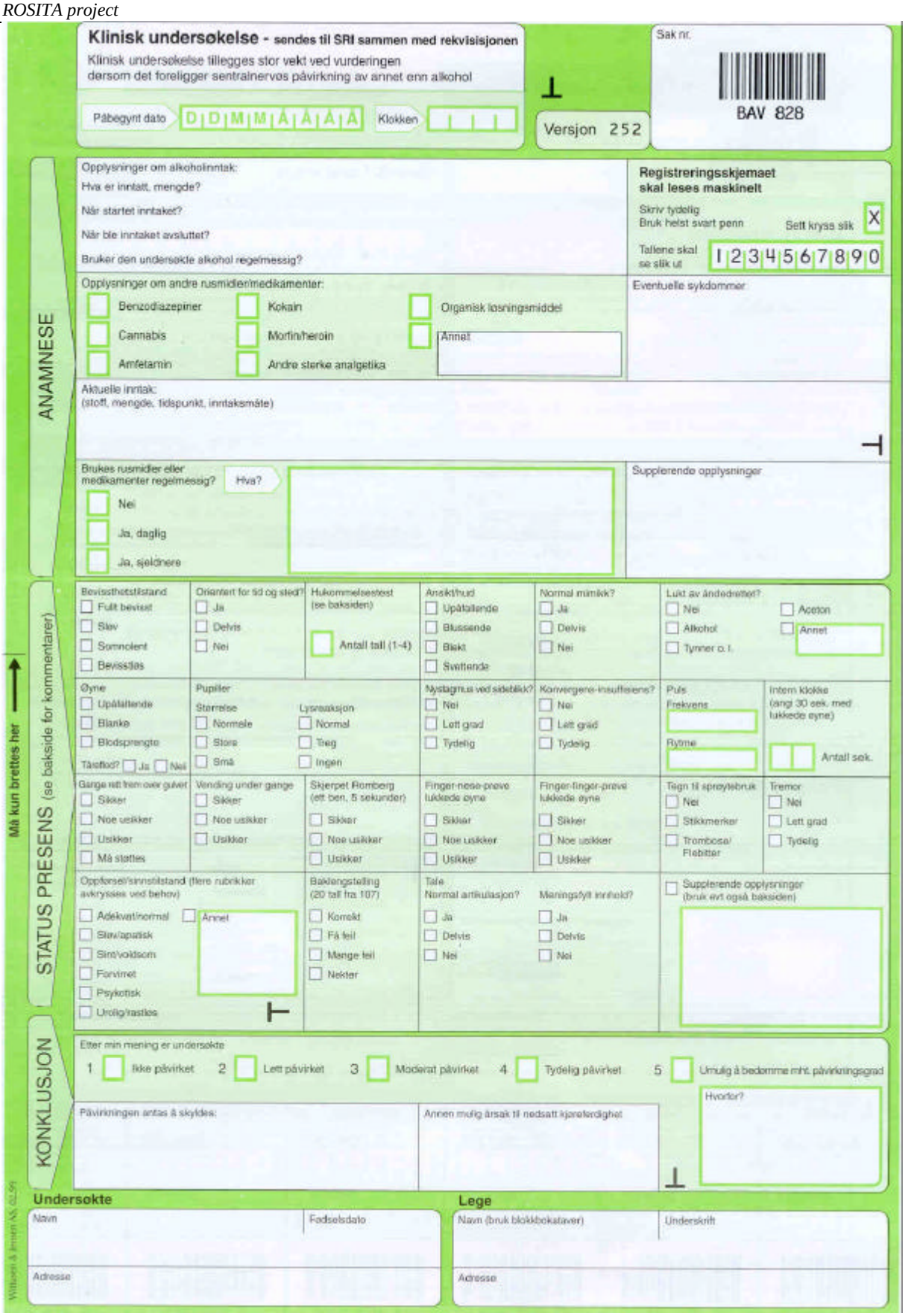
Er klinisk undersøkelse utført?
Ja / Nei

Huden er renset med:
Kompress i prøvetakingssettet
Annet

Prøvetakingssted
Tilstedeværende polititjenestemann
Underskrift prøvetaker

Jeg bekrefter at jeg har avgitt denne prøven.
Underskrift prøvegiver

Prøve A tatt	Prøve B tatt	Prøve C tatt	Prøve D tatt	Prøve E tatt	Prøve F tatt
Dag Mnd År	Dag Mnd År	Dag Mnd År	Dag Mnd År	Dag Mnd År	Dag Mnd År
Klokkeslett	Klokkeslett	Klokkeslett	Klokkeslett	Klokkeslett	Klokkeslett
BAV 828 A	BAV 828 B	BAV 828 C	BAV 828 D	BAV 828 E	



Klinisk undersøkelse - sendes til SRI sammen med rekvisisjonen

Klinisk undersøkelse tillegges stor vekt ved vurderingen dersom det foreligger sentralnervøs påvirkning av annet enn alkohol

Påbegynt dato D D M M Å Å Å Å Klokken

Versjon 252

Sak nr. BAV 828

ANAMNESE

Opplysninger om alkoholinntak:
Hva er inntatt, mengde?
Når startet inntaket?
Når ble inntaket avsluttet?
Bruker den undersøkte alkohol regelmessig?

Registreringsskjemaet skal leses maskinelt
Skriv tydelig
Bruk helst svart penn
Sett kryss slik X
Tallene skal se slik ut 1 2 3 4 5 6 7 8 9 0

Opplysninger om andre rusmidler/medikamenter:
Benzodiazepiner; Kokain; Organisk løsningsmiddel
Cannabis; Morfin/heroin; Annet
Amfetamin; Andre sterke analgetika

Eventuelle sykdommer

Aktuelle inntak:
(stoff, mengde, tidspunkt, inntaksmåte)

Brukes rusmidler eller medikamenter regelmessig? Hva?
Nei
Ja, daglig
Ja, sjeldnere

Supplerende opplysninger

Må kun brettes her

STATUS PRESENS (se bakside for kommentarer)

Bevissthetstilstand: Fullt bevisst; Sløv; Somnolent; Bevisstløs
Orientert for tid og sted?: Ja; Delvis; Nei
Hukommelsestest (se baksiden): Antall tall (1-4)
Ansikt/hud: Upåfallende; Blussende; Blekt; Svettende
Normal mimikk?: Ja; Delvis; Nei
Lukt av åndedrettet?: Nei; Alkohol; Tynner o. l.; Aceton; Annet

Øyne: Upåfallende; Blanke; Blodsprengte; Tåsefall? Ja Nei
Pupiller: Størrelse: Normale; Store; Små; Lysreaksjon: Normal; Treg; Ingen
Nystagmus ved sideblikk?: Nei; Lett grad; Tydelig
Konvergens-insuffisiens?: Nei; Lett grad; Tydelig
Puls: Frekvens; Rytme
Intern klokke (angi 30 sek. med lukkede øyne): Antall sek.

Gange rett frem over gulvet: Sikker; Noe usikker; Usikker; Må støttes
Vending under gange: Sikker; Noe usikker; Usikker
Skjerpet Romberg (ett ben, 5 sekunder): Sikker; Noe usikker; Usikker
Finger-nese-prøve lukkede øyne: Sikker; Noe usikker; Usikker
Finger-finger-prøve lukkede øyne: Sikker; Noe usikker; Usikker
Tegn til sprøytebruk: Nei; Stikkmerker; Trombose/ Flebitter
Tremor: Nei; Lett grad; Tydelig

Oppførsel/sinnstilstand (flere rubrikker avkryssbar ved behov): Adekvat/normal; Sløv/apatisk; Sint/voldsom; Forvirret; Psykotisk; Urolig/rastløs; Annet
Baklengstelling (20 tall fra 107): Korrekt; Få feil; Mange feil; Nekter
Tale: Normal artikulasjon?: Ja; Delvis; Nei — Meningsfylt innhold?: Ja; Delvis; Nei
Supplerende opplysninger (bruk evt også bakside)

KONKLUSJON

Etter min mening er undersøkte
1 Ikke påvirket; 2 Lett påvirket; 3 Moderat påvirket; 4 Tydelig påvirket; 5 Umulig å bedømme mht. påvirkningsgrad

Påvirkningen antas å skyldes:
Annen mulig årsak til nedsatt kjøreferdighet
Hvorfor?

Undersøkte
Navn; Fødselsdato
Adresse

Lege
Navn (bruk blokkbokstaver); Underskrift
Adresse

Wilhelm & Jensen AS 01.99

APPENDIX 3

Statens rettstoksikologiske institutt (SRI) Postboks 495 Sentrum 0105 Oslo Besøk og prøvelevering: Lovisenberggt. 6 Sentralbord 22 04 27 00 Telefaks 22 38 32 33	ROSITA- PROSJEKT **Testresultater urinprøver**
OPPLYSNINGER OM URINPRØVEN Prøvenr: _____	HVEM ANALYSERTE PRØVEN _____ POLITIKAMMER _____

ROSITA-prosjektet (ROad SIde Testing Assessment) er et felles europeisk prosjekt som skal undersøke testsystemer for andre rusmidler enn alkohol, med henblikk på testing før eventuell blodprøvetaking. I Norge skjer dette i form av et samarbeid mellom enkelte politidistrikter og Statens rettstoksikologiske institutt (SRI). Testing foretas på urinprøver, ved bruk av testsystemene Rapiscan eller Drugwipe.

Testresultatet i urinprøven er en screening-analyse, og resultatet er ikke et juridisk bevis.

TESTSYSTEM	STOFFGRUPPE	TESTRESULTAT		
		Pos	Neg	Ikke egnet
TESTCUP (ROCHE)	AMFETAMIN	☐	☐	☐
	KOKAIN	☐	☐	☐
	CANNABIS	☐	☐	☐
	OPIATER	☐	☐	☐
RAPID TEST (SYVA)	AMFETAMIN	☐	☐	☐
	KOKAIN	☐	☐	☐
	CANNABIS	☐	☐	☐
	OPIATER	☐	☐	☐
RAPID TEST (SYVA)	BENZODIAZEPINER	☐	☐	☐
Kommentar				

SRI 10/02-2000 _____

Underskrift

APPENDIX 4

EVALUERING AV TESTUTSTYR TIL SPYTT I ROSITA-ROSJEKTET

Vennligst returner skjemaet til Asbjørg Christophersen, pb. 495 Sentrum, 0105 Oslo.
Fax: 22 38 32 33 e-mail: a.s.christophersen@labmed.uio.no - Telefon: 22 04 27 00

INFORMASJON OM DEG SOM BESVARER SPØRRESKJEMAET

Kjønn: ☐ Mann ☐ Kvinne Fødselsår: 19_____

Tester som har blitt benyttet:
☐ Cozart Rapidscan
☐ Drugwipe
☐ Andre:_____

Distrikt:
☐ Nord-Jarlsberg
☐ UP
☐ Kristiansand
☐ Asker/Bærum
☐ Oslo

Yrke:
☐ Politi
☐ Laboratorie/Helsepersonell
☐ Annet:_____

SAMLING AV SPYTTPRØVER:

1. Hvilke problemer møtte du?
☐ Utilstrekkelig mengde spytt
☐ Prøvegiver nektet å avgi spyttprøve
☐ Agressiv oppførsel under prøvetakning
☐ Forsøk på å manipulere prøven
☐ Annet:

_____
_____

2. Hvordan løste du problemene?

_____
_____

3. Tror du spyttprøver egner seg for bruk i (forutsatt hensiktsmessig utstyr):

Vegkanten?
☐ Ja
☐ Nei
Hvorfor? _____

Politistasjon?
☐ Ja
☐ Nei
Hvorfor? _____

SPYTT-TESTENE

1 – svært dårlig; 2– dårlig; 3– OK; 4 – bra; 5 – svært bra (sett en ring rundt det som passer best)

4. Cozart Rapiscan:

Hvordan var utstyret å bruke:	1	2	3	4	5
Avlesning av resultater:	1	2	3	4	5
Pålitelighet av testen:	1	2	3	4	5
Bruksanvisning/opplæring:	1	2	3	4	5
Utseende/størrelse:	1	2	3	4	5
Generell vurdering	1	2	3	4	5

Fordeler og ulemper:

_____

_____

5. Estimater hvor lang tid en typisk test varte: _____ minutter.

6. Andre kommentarer:

_____

_____

_____

7. Vil du foretrekke en automatisk avleser? (I motsetning til manuell avlesning)

☐ Ja
☐ Nei
☐ Avhengig av situasjonen: _____

8. Har du noen kommentarer til den automatiske avleseren?

_____

_____

_____

9. Drugwipe:

Hvordan var utstyret å bruke:	1	2	3	4	5
Avlesning av resultater:	1	2	3	4	5
På litelighet av testen:	1	2	3	4	5
Bruksanvisning/opplæring:	1	2	3	4	5
Utseende/størrelse:	1	2	3	4	5
Generell vurdering	1	2	3	4	5

Fordeler og ulemper:

_____

_____

10. Estimater hvor lang tid en typisk test varte: _____ minutter.

11. Andre kommentarer:

_____

_____

_____

12. Vil du foretrekke en automatisk avleser? (I motsetning til manuell avlesning)

☐ Ja
☐ Nei
☐ Avhengig av situasjonen:_____

13. I fremtiden vil jeg bruke:

☐ Cozart Rapidscan ☐ Drugwipe
☐ En annen/bedre test ☐ Ingen test i det hele tatt

Kommentarer:

_____

_____
_____
_____
_____

TAKK FOR AT DU TOK DEG TID TIL Å SVARE!!!

Deliverable D4f - Spain

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: USDC.IML. Santiago de Compostela. Spain

Authors: M. LOPEZ-RIVADULLA, O. QUINTELA, A. CRUZ

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

In Spain there is no way of evaluating the influence of drugs and other chemicals on driving with devices applied at the roadside. Notwithstanding, there is legislation about this subject; it appears in articles in the Penal Code where "driving under the influence of drugs of abuse and psychoactive substances" is considered to be a crime. Despite this, no subsidiary norms have been developed that allow to establish and/or measure that influence. The case of alcohol is considerably different in the sense that the levels and procedures used to evaluate its influence on driving are perfectly delimited. The tests used to detect drugs and psychoactive substances appear very generically in the Traffic Law 13/1992 (January the 17th) and are established in the following terms:

1. The medical check-up and clinical analysis that the forensic surgeon or any other experienced scientific officer considers appropriate.
2. At the request of the person concerned or via judicial order.

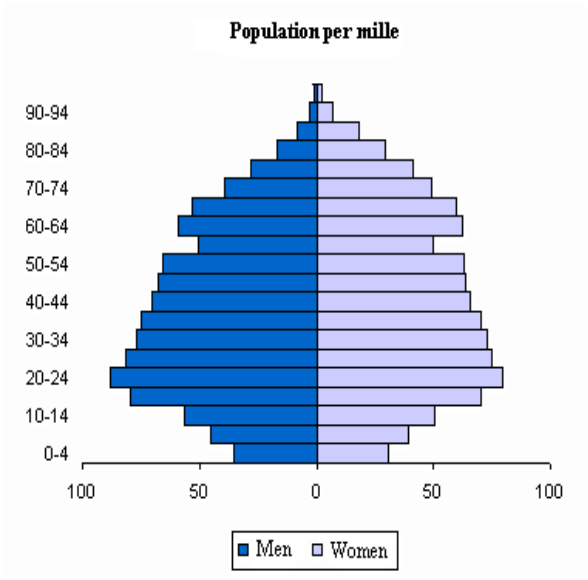
In this sense, it is necessary to indicate that there are noteworthy differences regarding this situation in other countries; in the big majority of the countries taking part in the project ROSITA, the suspicion of the Traffic Police that a driver is under the effects of drugs allows them to ask for biological samples such as urine and even blood. This measure is based on the agent's estimation of the clinical signs that the driver shows, and, logically, the test is performed warranting privacy and hygiene.
In addition, in Spain there are no precise epidemiological data about the incidence of drugs and chemicals in the road traffic, especially regarding the incidence on accidents, preventive controls and offences. Only the data provided by different investigators about the number of people killed in accidents and the number admissions of injured at hospitals have allowed to determine that the situation of the problem in Spain is similar to other surrounding countries.
Considering these circumstances, the organization of drug controls in road traffic in Spain -although with two limitations: restriction to a specific geographic area (NW Spain) and its voluntary nature has two important consequences:

1. The establishment of an awareness of the absolute need to control drugs and other chemicals in road traffic. A wide diffusion of the project in the mass media has contributed to it, as well as the information that was supplied to the drivers by the investigators and the police.
2. A good training of the traffic agents when assuming a task in the prevention of problems caused by the consumption of these substances and the accidents or infractions taking place in road traffic.

METHODS

Target Population

The Galician Autonomous Community has 2.800.000 inhabitants. The Institute of Legal Medicine (ILM), situate in the city of Santiago of Compostela, comprises an area of influence of 350.000 inhabitants.
The population that has been the object of the controls of the project ROSITA is located in a big area of the province of A Coruña. The group of the potential population reaches 700.000 inhabitants, with a slight dominance of the female sex over the male one. It is reckoned that 53,6% of all these inhabitants have driving licences and 38% of them are women whereas 62% are men.



Selection of subjects

The selection was done randomly and always carried out by the Traffic Police. The agents made vehicles stop and asked the driver to collaborate by undergoing always voluntarily and without any kind of adverse consequences for him or her- to the tests with the studied devices. On the other hand, the driver did not need to give his or her name and address, in order to ensure that the test was totally anonymous.
The conditions for the performance of the controls of ROSITA depended on the planning of the Traffic Police regarding the time range, the days of the week and the location of the police control.
So we obtain the following statistical data

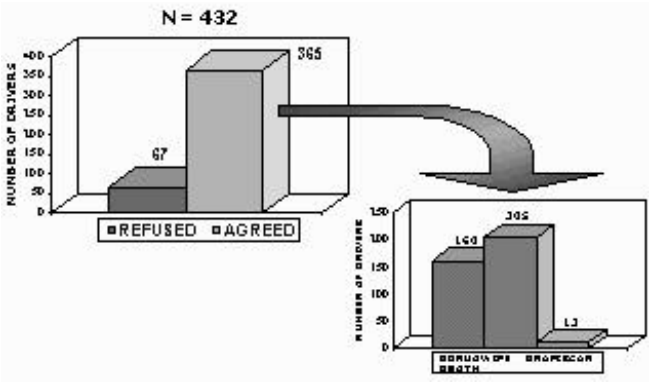


Fig. 1: The number of drivers who were asked

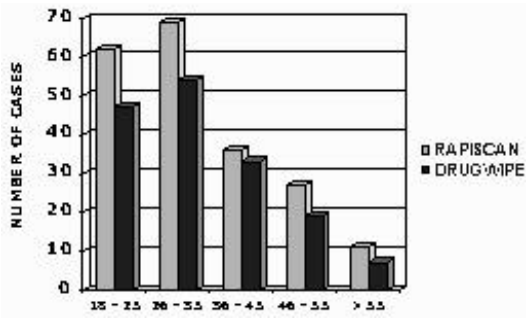


Fig. 2: Distribution according to age range

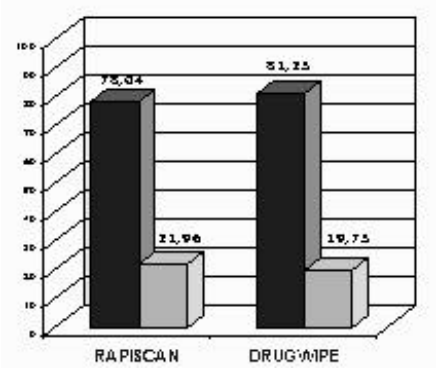


Fig. 3: Distribution according to sex

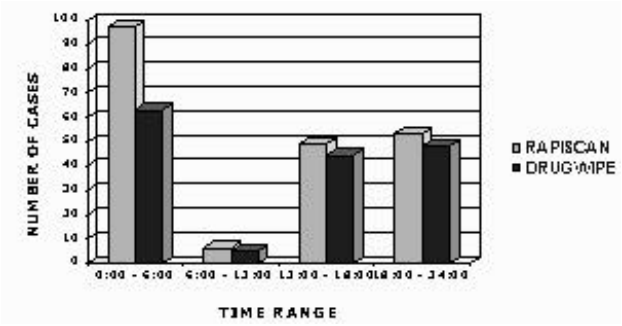


Fig. 4: Distribution according to time of day

Fig. 5: Distribution in days of the week

Fig. 6: Location of the road controls

Date or period of sampling
The fieldwork was carried out almost completely during February, March, April and May 2000.

Sampling: which samples were taken, how, how they were stored
The sample object of analysis in the project ROSITA in Spain was saliva.
The devices used for the tests were Rapiscan (COZART) and Drugwipe (SECURETEC). Such devices are used for drug detection in saliva. In addition to the correspondent saliva sample, those drivers whose results had been positive in saliva test were offered the possibility of giving -also voluntarily- a sample of urine. This way, we would be able to obtain complementary and interesting information for the project.
The collection of saliva was carried out by means of the kits of the devices. The urine, instead, was collected in plastic containers. The age and sex of the driver and the hour of collection were recorded to identify the sample.
Once the road control had finished, the samples of saliva were stored frozen conditions. In case of urine the storage was done by refrigeration.

Delay between sampling and analysis
In the case of saliva, the analysis was done with on-site devices immediately after collection.
The analysis of urine was done between 24 hours and a week after its collection.

Analytes that were included
Saliva on-site:

- *Rapiscan device:* COCAINE, AMPHETAMINES, OPIATES, THC, BENZODIAZEPINES.
- *Drugwipe device:* COCAINE, AMPHETAMINES, OPIATES.
- *Laboratory analysis:* COCAINE, AMPHETAMINES, OPIATES, THC, BENZODIAZEPINES.

Performed by whom?
The tests were performed by the agents of the Traffic Police; the reading and interpretation of the results were done together by the members of the ILM present during the control and by the same traffic agents.

How many different people performed the tests?
Approximately twenty agents of the Traffic Police performed the tests. They had beforehand been trained to familiarised them with the working of the devices.

Where were the tests performed?
The tests were performed in roads of the province of A Coruña, particularly in black spots.

Screening analysis: method, cut-off,…for each biological fluid

SALIVA

RAPISCAN	
Compound	**Cut-off (ng/mL)**
Amphetamines	
Opiates	
Benzodiazepines	
Cannabis	
Cocaine	

DRUGWIPE	
Compound	**Cut-off (ng/mL)**
Amphetamine	300
MDA	250
MDMA	250
MDEA	750
Methamphetamine	300
THC	1,000
Morphine	200
Cocaine	200

URINE

TESTCUP	
Compound	**Cut-off (ng/mL)**
Amphetamine	1,000
MDA	2,000
MDMA	ND
Methamphetamine	ND
Cannabinoids	50
Benzoylecgonine	300
Morphine	300
PCP	25

DIP DRUGSCAN-ONE STEP	
Compound	**Cut-off (ng/mL)**
Amphetamine	500
Morphine	300
Benzoylecgonine	300
Methamphetamine	500
Cannabinoids	50

FPIA	
Compound	**Cut-off (ng/mL)**
Amphetamine/Methanphetamine II	300
Opiates	200
Benzodiazepines	200
Cannabinoids	25
Cocaine	35

Clinical or physiological evaluation used, by whom?

During the course of the saliva test, a questionnaire was filled in that contained two well-differentiated parts:

A first part contained several data of interest for the study, such as:

- Whether the driver wants voluntarily to take part in the test and whether she or he consents to give a sample of urine.
- The date and hour of the test
- The TIP (badge) identification of the agent performing the test.
- Age and sex of the driver, and
- the kind of device used, as well as the final result of the saliva test

In the second part of the questionnaire attention is paid to the external signs that are present in the driver subjected to the test. This physiological evaluation and the evaluation of other interesting parameters was done by the personnel of the ILM. The contents of the enquiry are the following : Physical constitution, Physical appearance, Clothes, Face, Look, Pupils, Alcoholic breath, Saliva, Speech, Verbal expression, Behaviour, Pulse, Other observations.

RESULTS

URINE: Analytical results

Number of samples: 37

- 22 samples from Rapiscan
- 19 samples from Drugwipe
- 4 samples tested with both devices

Screening procedures

Positive results				
ANALYTE	**IA (OSDS)**	**FPIA**	**EMIT**	**TEST CUP**
COCAINE	1	3	1	2
AMPHETAMINES	0	0	0	0
OPIATES	2	2	0	2
THC	2	6	0	6
BENZODIAZEPINES	0	0	0	0

OSDS: One Step Dip Drugscan

Confirmation procedures

Positive results			
ANALYTE	**GC-MS**	**HPLC-DAD (BZD)**	**RIA (THC)**
COCAINE	4	-	-
MORPHINE	2	-	-
MAM	2	-	-
CODEINE	4	-	-
THC	1	-	2
CBD	1	-	-
AMPHETAMINES	0	0	0
BENZODIAZEPINES	-	4	-

URINE: Practical results

The obtaining of urine, as has already been mentioned, was performed after the driver's voluntary consent, and always after having shown that the results of his or her saliva test-Rapiscan or Drugwipe- were positive. The major difficulties found when the driver subjected to the urine test was that there was no place ensuring his or her intimacy. In this sense, the personnel of the Traffic Police did not have vans , or something similar, with a separated room. It is significant that the rate of urine donors is superior in men (58,2%) than in women (23,1%). In this case we are not able to assure the potential adulteration of the sample, provided that the urine donation was not supervised by the agents nor by any of the members of the ILM.

In the majority of the cases the volume of sample was sufficient. There has to be mentioned that when the device used for the screening is the Ontrak Test-Cup ROCHE, we find that the minimal advisable volume for the test -30mL.- is problematic. Concretely, the Test-Cup was tested in the second stage of the project ROSITA carried out in our country, but it was always performed in the laboratory with the urine obtained on-site. Dealing more deeply with this device, and leaving aside what has been mentioned about the volume of the sample, we must say that its handling has proved to be simple for us. Besides, it does not require special qualification. The interpretation of the results is also easy and clear. Both things are no doubt essential if the test is to be performed on-site and by the traffic agents. The time spent in obtaining the results is approximately five minutes, which seems to us for on-site screening. In addition, the fact that there is no need to time the process simplifies everything.

SALIVA: Analytical results

Total tests done: 206 (Rapiscan) + 178 (Drugwipe) = **384**

Rapiscan

ANALYTE	*ON-SITE ASSAY*	*CONFIRMATION LAB*	*CONFIRMATION PROCEDURE*
COCAINE	6	2	GC-MS
AMPHETAMINES	9	-	
OPIATES	1	-	
THC	31	-	
BENZODIAZEPINES	21	4	HPLC-DAD

Drugwipe

ANALYTE	*ON-SITE ASSAY*	*CONFIRMATION LAB*	*CONFIRMATION PROCEDURE*
COCAINE	8		
AMPHETAMINES	9	No sample available	
OPIATES	12		

SALIVA: Practical aspects

In general terms, obtaining saliva has not been a complicated problem. The use of the Rapiscan has shown several advantages compared to the Drugwipe: at the same time that the test is being performed , the saliva is stored in a tube so that it can be analysed afterwards in the laboratory. In the case of the Drugwipe it is necessary to obtain the saliva via spitting or by using the Salivette®. The collection of sample was always supervised by the people who performed the test and no attempts at adulteration were observed. The samples were frozen two or three hours after having obtained them until their analysis in the laboratory. They were always kept in the right conditions for storing.

In the case of the Rapiscan, the final volume of saliva is small: approximately 120µL. that remain diluted in 2 mL. of buffer solution. This is the reason why the confirmation in GC-MS is carried out for just one analyte or two at most. This can cause some problem when more than one drug was positive in a subject.

In our investigation of the project ROSITA we only obtained samples of saliva to be analysed in the laboratory from the Rapiscan device. We obtained them owing to the reservoir of saliva that we kept after performing the road test. Such samples are stored in tubes which can be labelled with adhesives that make it easy to identify and later store them. The buffer solution that the saliva contains has a pH of approximately 8.0. This caused more difficulties than advantages when cocaine and its metabolites were to be analysed by GC-MS. The difficulties were due to the fact that the high values of pH in saliva are inversely correlated to the concentration of drugs in the saliva (pHsaliva 5,8-7,6). The buffer solution caused hydrolysis of cocaine to benzoylecgonine. Anyway, we could detect a small quantity of cocaine owing to the use of a derivative agent that improved its chromatographic characteristics. Finally, ecgonine methylester was not detected in any of the samples. This could be due to way of administration of the drug or to the time elapsed since the administration took place.

The use of HPLC-DAD for detection and confirmation of benzodiazepines in saliva samples was very useful. Seven types of benzodiazepines were detected in this way : Alprazolam, Lorazepam, Desmethyldiazepam, Tetrazepam, Diazepam, Flunitrazepam and 7-Aminoflunitrazepam. The UV spectra of benzodiazepines in derivative mode were used in order to confirm each benzodiazepine. The detection limit (LOD) was the criteria used to confirm the positive analysis.

CRITERIA OF POSITIVE RESULTS	
Compound	**LOD (µg/mL)**
Alprazolam	0.05
Lorazepam	0.05
Desmethyldiazepan	0.01
Tetrazepam	0.08
Diazepan	0.05
Flunitrazepam	0.10
7-Aminoflunitrazepam	0.50

In summary, the saliva seems to be an appropriate biological sample for the detection of recent drug consumption. It would be important to have an additional aliquot of saliva to be analysed in the laboratory. In case the saliva was diluted in a buffer, that buffer should have a pH very similar to that of the saliva. This way, it would allow high levels of extraction of drugs and it would avoid their degradation, with which the chromatographic characteristics of the analytes would improve considerably.
In relation to the devices that are object of our study -Rapiscan and Drugwipe-, we can highlight their most relevant aspects, both positive and negative, in the following way:

Rapiscan

ADVANTAGES	***INCONVENIENCES***
• Multitest (5 drugs test) • Existence of reference band • Very good reading	•Difficult to take samples •Excessive manipulation •Excessive time during performance •Van essential •No printed report •Difficult to use at accidents

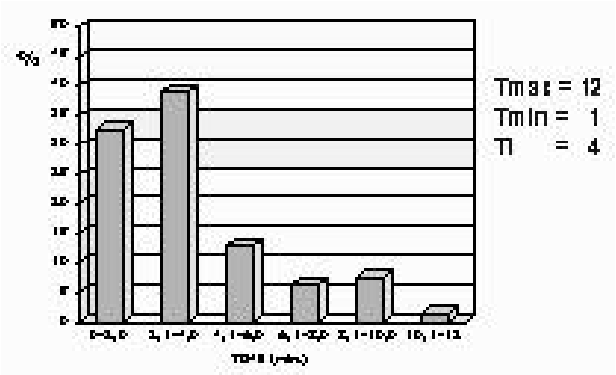
Drugwipe

ADVANTAGES	***INCONVENIENCES***
• Easy to use and transport • Easy to take sample • Quick results • Possibility to do the test for motorcyclist	• Single panel one drug • No light display in lector • No reference band • No printed report • Water required • Difficult to use at accidents

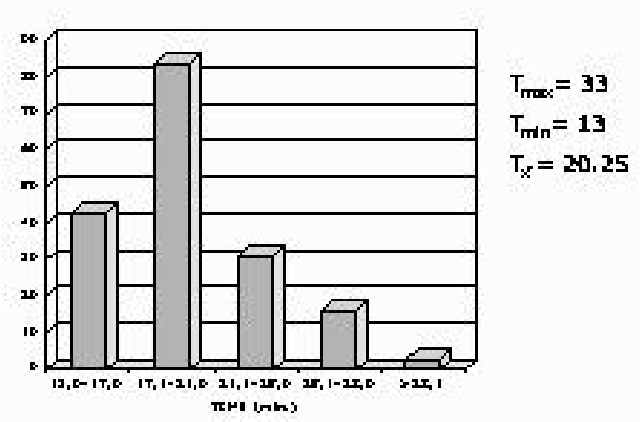
DISCUSSION AND CONCLUSIONS

According to our experience, the Rapiscan device shows certain aspects that make it appropriate for the drugs control roadside, at the same time that it shows aspects advising against it. It has an equipment that, though not very complex, shows a considerable level of labor intensive. In addition, a van -or something the like- is necessary; this van should have a flat surface where to place the required elements used in the test performance: cartridges, a pack with pipette, a tube with preservative buffer solution, a separator filter tube and a sterile saliva collection pad, and also the Rapiscan reading instrument. We must bear in mind that there is a substantial difference in the way the devices were handled by the scientific personnel and the Police Agents.

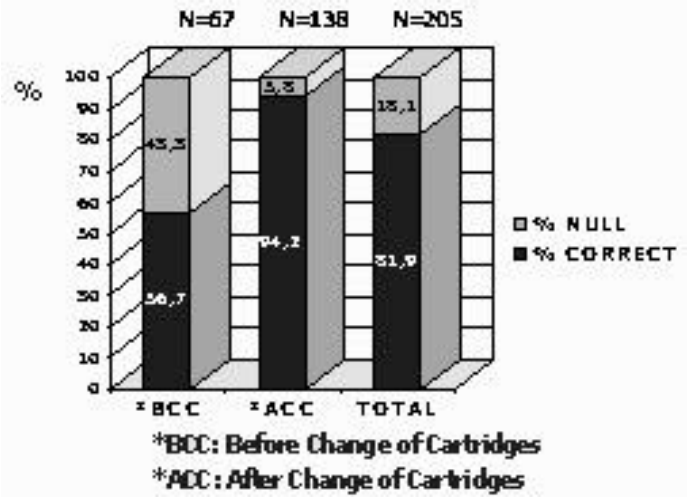
Generally, the collection of samples has been well accepted by the drivers who to take part in the test with the Rapiscan device. However, there were few cases in which the drivers found it annoying to keep the sterile saliva collection pad inside their mouth. This was even worse when the person had little saliva in that moment, which, also made the collection of sample take longer. It is more important that a certain number of people were not able to soak the sterile saliva collection pad; this occurred either because they did not have enough saliva in their mouths or because they did not accept to do it. This last possibility makes reference to the fact that a driver who voluntarily refuses to soak the sterile saliva collection pad, will not have to do it , since he or she can swallow his or her saliva and never do the test.



Between the beginning of sample collection and the moment the results are obtained, approximately twenty minutes pass (as an average). With regard to time takes to give a sample, most drivers took between 1-4 minutes, the overall average being 4 minutes. The minimum value was 1 minute and the maximum 12 minutes.



The total time taken to carry out the test ranged in most cases from 13 to 21 minutes with an average time of 20.25 minutes, and minimum and maximum times of 134 and 33 minutes respectively. According to the traffic agents, this time is too long and our opinion coincides with theirs.



In the first stage of the study we got a high rate of null results due probably to the bad conditions of the cartridges that we were given. This problem was solved by changing those cartridges. Another difficulty found when performing the test with the Rapiscan device is the fact that the traffic agents added four exact drops.

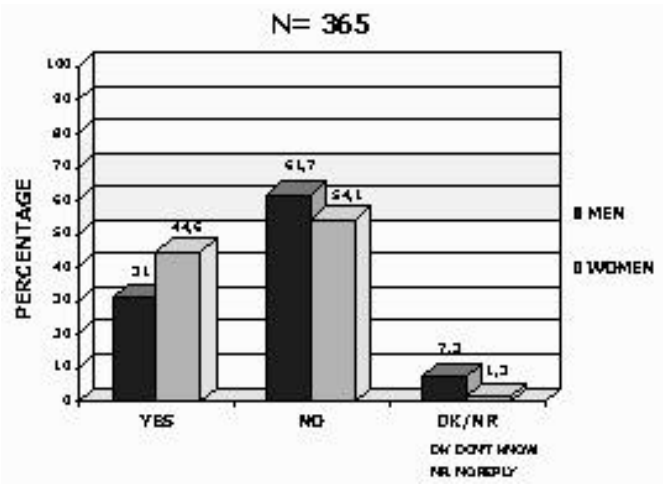
The tests that were performed together by the members of the ILM and traffic agents consisted of preventive controls. Therefore, the performance conditions of these tests can be considered as ideal. This way, the driver accepted voluntarily, and the staff performing the tests showed great interest. However, we, as scientific personnel, have not taken part in cases in which accidents or offences took place because these specific cases could not be foreseen. We consider that the conditions that surround an accident, even without damage, or an offence (although to a minor extent) make the performance more difficult when dealing with this device: the driver may be in an unfavourable state of mind, and all the instructions to collect the sample may be complicated to be executed precisely. Thus, in our opinion, the application of the Rapiscan in these situations shows serious difficulties. In fact, in our study we present the low number of cases by accident or offence in which the traffic police performed the test without any member of the scientific personnel.

As far as the Drugwipe device is concerned, it has the advantage that it can be used much more easily and in situations that are more awkward for the Rapiscan: its use in the driver's own vehicle and the possibility of test performance for the motorcyclists of the traffic police.

We consider it a disadvantage not to have devices for benzodiazepines and THC. Another disadvantage is the absence of a referential band that assures the good conditions of the stick and that the test has been perfectly performed.

In addition, it would be more appropriate for the controls on-site to have a multitest device in order not to have to perform a test per every drug that we wish to detect. In this sense, the situation could be softened by means of training adequately the traffic police to make them able to know which device is to be used by just doing a physical exploration. But despite this ideal situation, we concluded that multitest controls would be more appropriate.

On the other hand, once the results of the test have been positive, the Drugwipe entails the necessity to collect an extra saliva sample to be confirmed in the laboratory. In order to get to these ideal conditions it would be convenient to have appropriate recipients for the collection of another sample; notwithstanding, this would go against the simplicity of the Drugwipe test on-site.



The survey made it possible to ascertain the use of therapeutic drugs and this is shown in the figure. It is noteworthy that 31% of the male drivers were taking some kind of medication, whilst amongst women the figure rose to 44.6%. In some cases people did not remember what medication they were taking.

The more common therapeutic drugs used among drivers were:

- Antibiotics
- Antidepressants
- Antidiabetics
- Antihypertensives
- Antithyroid agents
- Anxiolytics and neuroleptics
- Antihistamines
- Anti-ulcer agents
- Cough suppressants Expectorants and Mucolytics
- Analgesics and Anti-inflammatory agents
- Oral contraceptives
- Vitamins
- Oral antiseptics

However, these contributions must be completed, in our opinion, with a series of measures that entail a standard development regarding the way in which they must be carried out. In this sense, the conclusions of the file will be distributed to the Parliaments of the Galician Autonomous Community and to the Spanish Parliament, as well as to the authorities in charge of traffic in Spain. On the other hand, and provided that the Traffic Police shows a high grade of availability, it is very necessary to increase the information related to the use of the devices, as well as training sessions and formation for their correct use. Besides, it should be completed with a description of the most evident clinical signs that allow the traffic agents to obtain reasonable traces of the driver's recent consumption of these substances.

The Drugwipe devices which were used during the first phase were read with the naked eye, whilst during the second phase an electronic reader was available. With regard to Drugwipe we looked the results according to the type of drug we can appreciate an increase in the number of positive results for cocaine once the electronic reader was available, whilst remaining practically the same in the case of opiates. It is noteworthy that in the case of amphetamines a very high level of uncertain results was obtained with a visual reading. For the Police Forces the use of an electronic reader was very useful and they preferred to use it.

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APPENDIX 1

PROYECTO ROSITA

(**Ro**ad **Si**de **T**esting **A**ssesment)

Comisión Europea FP4DGVII Project Task 11.7

EVALUACION DE DISPOSITIVOS POR LA GUARDIA CIVIL DE TRAFICO PARA DETECTAR PRESENCIA DE DROGAS EN SALIVA

La participación en esta prueba es **VOLUNTARIA**. Las pruebas realizadas y los resultados obtenidos **NO TENDRÁN NINGUNA REPERCUSIÓN LEGAL**, ni podrán ser usadas por tanto para acusar al que someta a ellas de ningún ilícito penal ni administrativo. Se trata de obtener información con fines **EXCLUSIVAMENTE DE INVESTIGACION**

El conductor sometido a la prueba expresa su consentimiento para someterse a la prueba en saliva para el panel completo de drogas :

SI **NO**

El conductor sometido a la prueba expresa su consentimiento para donar una muestra de sangre y/o orina en un Centro hospitalario:

SI **NO**

Hora de recogida de las muestras biológicas suministradas:

Agrupación de tráfico de
Prueba realizada con ocasión de : Accidente Infracción. Preventivo
Fecha dd/mm/aa **Hora.....**
Edad_____; Sexo Hombre Mujer
Identificación TIP del agente que hace la prueba
Signos que presenta el conductor (veáse anexo I)
Tipo de dispositivo usado: **Drugwipe**
Cozart
Resultados: **Positivo** **Cannabis** **Anfetaminas** **Opiáceos**
Cocaína **Bzd**
Negativo

SIGNOS EXTERNOS QUE PRESENTA EL CONDUCTOR SOMETIDO A LA PRUEBA

En el lugar de la prueba, a las.....horas del día.....de.....de....., por medio de la presente diligencia se procede a reseñar los signos externos que presenta.

CONSTITUCION FISICA

Estatura aproximada (cm)

Sexo V H

Peso aproximado (Kg.)

Atlético ☐ Obeso ☐ Delgado ☐

ASPECTO EXTERNO.

- ☐ Normal
- ☐ Dinámico
- ☐ Cansado
- ☐ Agotado
- ☐ Apático
- ☐ Estuporoso
- ☐ Heridas
- ☐ Contusiones
- ☐ Otros

VESTIDOS

- ☐ Sin peculiaridades
- ☐ Desarreglados
- ☐ Sucios
- ☐ Olor a alcohol

ROSTRO:

- ☐ Ningún detalle destacable
- ☐ Pálido
- ☐ Sudoroso
- ☐ Ligeramente congestionado
- ☐ Muy congestionado.

MIRADA

- ☐ Normal
- ☐ Ojos apagados
- ☐ Ojos velados(humedecidos)
- ☐ Ojos brillantes (muy humedecidos)
- ☐ Conjuntiva ligeramente enrojecida
- ☐ Conjuntiva muy enrojecida
- ☐ Nistagmus (movimiento ocular e incapacidad de fijar la mirada)

PUPILAS

- ☐ Normales
- ☐ Contraídas
- ☐ Algo dilatadas
- ☐ Muy dilatadas
- ☐ Anisocóricas (desiguales)
- ☐ Reactivas a la luz

HALITOSIS ALCOHOLICA

- ☐ Ausente
- ☐ Muy marcada de cerca
- ☐ Notoria a distancia

SALIVA

- ☐ Normal
- ☐ Escasa
- ☐ Abundante

HABLA

- ☐ Clara
- ☐ Pastosa
- ☐ Balbuceante

EXPRESION VERBAL

- ☐ Normal, con respuestas claras y lógicas
- ☐ Repetición de frases e ideas
- ☐ Incoherencias
- ☐ Falta de conexión lógica en las expresiones
- ☐ Volumen elevado de voz
- ☐ Gritos

COMPORTAMIENTO

- ☐ Normal
- ☐ Tranquilo y educado
- ☐ Arrogante
- ☐ Amenazador
- ☐ Insultante
- ☐ Agresivo
- ☐ Nada colaborador
- ☐ Desinhibido
- ☐ Eufórico
- ☐ Locuacidad extrema
- ☐ Exaltado

DEAMBULACION

- ☐ Correcta, con completa estabilidad
- ☐ Titubeante
- ☐ Movimiento oscilante de la verticalidad del cuerpo
- ☐ Dificultad para mantenerse erguido
- ☐ Total incapacidad para mantenerse erguido
- ☐ Signo de Romberg positivo(no acierta a emplazar el dedo índice sobre la nariz con los ojos cerrados)
- ☐ Incapaz de caminar de modo recto sobre una línea de 3 m.
- ☐ No desea realizar ninguna de las 2 últimas pruebas.

RESPIRACION

- ☐ Normal
- ☐ Lenta
- ☐ Agitada

PULSO

- ☐ Normal
- ☐ Lento
- ☐ Acelerado

OTRAS OBSERVACIONES.....

Deliverable D4g - France

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

Coordinator: Alain VERSTRAETE

Partners: IMLS, Institut de Médecine Légale, 11 rue Humann, F-67000 Strasbourg, France

Authors: Pascal KINTZ and Vincent CIRIMELE

Date: 30 November 2000

PROJECT FUNDED BY THE EUROPEAN COMMISSION UNDER THE TRANSPORT RTD PROGRAMME OF THE 4th FRAMEWORK PROGRAMME

INTRODUCTION

The goal of Rosita evaluation in our country was the comparison in term of positivity, practicability, rapidity, cost and scientific interpretation (particularly for legal applications, i.e. judges, court cases, acceptability, discussion with attorneys ...) of results obtained from 4 different matrices.
Blood, urine, sweat and saliva will be collected from drivers admitted in emergency rooms following an accident during a 9-months period in the Strasbourg area. As it is forbidden by the French law, it is not possible to perform roadside tests. Therefore, this study was focused on the comparison of alternative specimens (saliva, sweat) with conventional specimens (blood, urine).

METHODS

During a 9-months period (March 99 to November 99), 198 injuried drivers (car, bicycle, motorcycle, truck …) were included in the ROSITA study. All of them were admitted at the Emergency unit of the "Centre de Traumatologie", an hospital of Strasbourg, France.

Simultaneously, 7.5 ml of blood (Sarstedt monovette), 10-20 ml of urine (sterile cup), saliva (Sarstedt salivette, without stimulant) and sweat (cosmetic pad, spiked with 500 ml of water-isopropanol, 1:1) were anonymously collected by the medical staff. Only the sex, age and delay between the accident and specimens sampling were noted. All the subjects gave their verbal consent.

Saliva, about 1 ml, was collected by chewing the cotton roll for about 2 min. Sweat was collected by wiping the forehead for 10 sec. After collection, all the biological specimens were stored at + 4 °C.

When present, urine was screened by FPIA (Abbott ADx). In all cases, blood was screened by GC/MS (Hewlett Packard 5973), LC/DAD (Waters Alliance) and LC/MS (PE Sciex API 100) for cannabis, amphetamines, opiates, cocaine, narcotics, buprenorphine and psychoactive pharmaceuticals, including benzodiazepines, barbiturates, neuroleptics, antidepressants and antiepileptics, using previously published procedures (1-3). Ethanol was analyzed by headspace GC/FID. Due to a lack of a large volume of specimen, saliva and sweat were only analyzed for the corresponding drug(s) that were screened in blood or urine. The cotton rolls and the cosmetic pads were extracted in the specific organic mixture of each pharmacological class of drugs in presence of deuterated internal standards by horizontal agitation for 20 min. Then, the target compounds were analyzed under classic conditions (liquid/liquid extraction at specific pH, derivatization by silylation or acylation, GC/MS) (3-4). No cut-off was used, in respect with our forensic procedures.

In the laboratory, 3 specific devices, American Biomedica Rapid Drug Screen (ABM), Syva Rapid test (SRT) and Cortez DipDrugScanOnestep (CORT) have been tested on urine specimens.

RESULTS

During the 9-months period, 198 drivers were screened. There was 162 men (81.8 %) and 36 women (18.2 %), aged 13 to 57 (mean 29.5) and 19 to 54 (mean 33.5) years for men and women, respectively. The delay between the accident and the specimens collection was in the range 45 minutes to 7 hours, with a mean value of 2 hours 21 minutes.

URINE

Analytical results

198 drivers were tested during the study and 23 were positive for THC-COOH in urine using FPIA with a cut-off at 25 ng/ml. In urine, THC-COOH concentrations were in the range of 7 to 813 ng/ml.
Two urine samples were positive for amphetamine derivatives:
- Amphetamine (380 ng/ml), MDMA (1806 ng/ml), MDA (432 ng/ml)
- MDMA (180127 ng/ml), MDA (10118 ng/ml)

Twelve specimens were positive for opiates including 6-monoacetylmorphine (65 ng/ml, n=1), morphine (24 to 12226 ng/ml, n=), codeine (14 to 33659 ng/ml, n=) and one for cocaine (cocaine 665 ng/ml, benzoylecgonine 11744 ng/ml, ecgoninemethylester 3678 ng/ml).
The 3 specific on-site devices, American Biomedica Rapid Drug Screen (ABM), Syva Rapid test (SRT) and Cortez DipDrugScanOnestep (CORT) have been tested on urine specimens. Results, when compared with GC/MS, are summerized in the following table.

Devices	*Number False Positive*	*Number False Negative*
FPIA (n = 166)	Benzodiazepines: 1 Amphetamine: 2 Cannabis: 2	Benzodiazepines: 1 Opiates: 1
ABM (n = 98)	Benzodiazepines: 1	Benzodiazepines: 2
Syva (n = 97)	Benzodiazepines: 7	Benzodiazepines: 2
Cortez (n = 69)	-	Benzodiazepines: 2

Practical results

Even in the Emergency Unit, urine was missing in 32 cases (16.2%), being an omen of numerous difficulties for road-side collection.
As the window of detection of cannabis is long in urine, several days after the last exposure, this biological specimen is not suitable to demonstrate direct influence of the drug at the moment of the accident.

SALIVA

Analytical results

Drugs	*Saliva (ng/salivette)*
Cannabis	THC: 1 to 103 (n=14)
Ecstasy (n=1)	MDMA: 2032
Cocaine (n=1)	COC: 2, BZE: 69 and EME: 41
Heroin (n=1)	MOR: 26 and COD: 8
Codeine (n=3)	COD: 102 to 4028 MOR: ND to 37

ND : not detected
About 1 ml of saliva is collected by the salivette

Practical aspects

Saliva was missing in 1 case. The analyses of saliva confirmed that the parent drug is the major analyte that is found in this specimen.
In saliva, the parent cocaine and 6-acetylmorphine were not detected, probably due to hydrolysis.
11-hydroxy-THC and THC-COOH were never detected in saliva. Cannabinol and cannabidiol were occasionally identified. From the 19 positive blood cases (recent cannabis exposure), 14 tested positive in saliva for THC. The THC concentrations were in the range 1-103 ng/salivette (mean 16 ng/salivette) for saliva. Saliva/blood concentration ratios vary over a wide range, from 0.5 to 147, being < 1 in 5 cases. A high ratio is rather indicative of oral cavity contamination.
There was no difficulties to identify opiates, cocaine or amphetamines derivatives in saliva. In all cases, the saliva to blood ratios were > 1. For example, this ratio was 2.6 for morphine in case of heroin abuse, 5.4 to 26.4 for codeine or 5.6 for MDMA.
Unfortunately, this favorable situation was not observed for benzodiazepines, irrespective of the compound. Saliva concentrations were always low, in the range 5 to 40 ng/salivette.

SWEAT

Analytical results

Drugs	*Sweat (ng/pad)*
Cannabis	THC: 4 to 152 (n=16)
Ecstasy (n=1)	MDMA: 930, MDA : 18
Cocaine (n=1)	COC: 121, BZE: 19 and EME: 13
Heroin (n=1)	6-MAM: 256, MOR: 64 and COD: 5
Codeine (n=3)	COD: 36 to 1239 MOR: ND to 19

ND : not detected

Practical aspects

Sweat specimen was missing in 1 case. The analyses of sweat confirmed that the parent drug is the major analyte that is found in this specimen. In sweat, it was possible to detect cocaine (121 ng/pad) and its metabolites, such as benzoylecgonine (19 ng/pad) and ecgonine methylester (13 ng/pad) or 6-acetylmorphine (256 ng/pad), the heroin primary marker and its metabolites, morphine (64 ng/pad) and codeine (5 ng/pad). In cases where urine is missing, sweat appears as an excellent alternative to document heroin exposure by the identification of 6-acetylmorphine.
11-hydroxy-THC and THC-COOH were never detected in sweat. Cannabinol and cannabidiol were occasionally identified. From the 19 positive blood cases (recent cannabis exposure), 16 were positive in sweat for THC. The THC concentrations were in the range 4-152 ng/pad (mean 51 ng/pad) for sweat.
The potential external contamination of sweat (smoking cannabis by another subject in a closed room) was observed in 1 case. The subject was negative for cannabis in blood, but THC was identified in sweat at 68 ng/pad.
There was no difficulties to identify opiates, cocaine or amphetamines derivatives in sweat. Unfortunately, this favorable situation was not observed for benzodiazepines, irrespective of the compound as it was not possible to detect any drug in sweat.

BLOOD

Analytical results:

Ethanol was detected in 27 cases (13.6 %) in the range 0.11 to 3.19 g/l, with a mean value of 1.49 g/l. BAC was > 0.5 g/l in 21 cases (10.6 %).
Toxicological findings in the blood of 198 injured drivers are the following:

Class of drug	*Analyte*	*Number of cases*	*Concentrations (ng/ml)*
Cannabis	THC	19	0.4 – 5.4
Norephedrine	norephedrine	1	162
Ecstasy	MDMA + MDA	1	361 + 18
Cocaine	BZE + EME	1	122 + 18
Opiates	Heroin ** (morphine)	1	10
	codeine	3	5 - 747
Benzodiazepines *	nordiazepam	7	90 - 9890
	clobazam	1	160
	bromazepam	3	46 – 330
	diazepam	1	580

*: parent compound
**: identification of 6-acetylmorphine in urine

Cannabis tested positive in 19 cases (9.6 %), clearly indicating that this is the major problem. Ecstasy, heroin and cocaine were only detected in 1 case for each drug. Benzodiazepines were identified in 12 drivers (6.1 %). This is lower then the expected value, but is probably due to the rather young population that was tested. Phenytoïn, hydroxyzine, clomipramine, fluoxetine and buprenorphine were identified each one time, at therapeutic concentrations.
Regarding the biological specimens, it was always possible to collect blood. As pointed out by other authors, cannabis tested positive in a higher range in urine than in blood, 23 cases versus 19, due to slow release into the bladder.

DISCUSSION

Saliva and sweat have been proposed as an alternative to blood and/or urine to document drug exposure. Saliva and sweat provide an easily available, non-invasive medium (unlike blood) without the intrusion of privacy (unlike urine), that can be collected under close supervision, but very few data seems available in the literature on the identification and quantitation of illicit drugs in alternative specimens. Saliva and sweat were strongly promoted for road-side testing (5), but until now, saliva collection is not uniformed, leading to controversial results. Drug concentrations are highly variable, and there is a need of test sensitivity covering the broad concentration ranges.

Immunoassays that are available for urine are not suitable for the analysis of saliva. The antibodies are designed for metabolites and they only poorly cross-react with the parent drug, that is the major salivary analyte. Moreover, the positive cut-off levels are too high for saliva testing, leading to a weak sensitivity in drug detection. Manufacturers must propose new devices, that are specific for these specimens.

Excepted the Drugwipe, there is no specific device to test for sweat (3). All the road-side experiments have been achieved using home-made collectors, as the sweat patch cannot be used in such a situation, as there is a need to wear it for several hours before collecting a sufficient amount of sweat. Again, there is a lack of homogeneity among the active researchers.

Moreover, there is a risk of external contamination of skin, that can produce false positive response, when compared with blood. After drug administration, there is a variable time delay (1-12 hours) until the drug will be excreted in sweat. As the skin acts as a drug reservoir, sweat is less appropriate than saliva to detect recent drug exposure (impairment).

CONCLUSION

Although saliva appears as a promising specimen for large epidemiological studies, the market lacks of suitable on-site devices, particularly for cannabis. Based on these observations, it is hard to believe that any immunoassay devoted to the identification of THC-COOH would be suitable for oral fluid and forehead wipe testing. In order to propose on-site tests for cannabis in these specimens, manufacturers, will definitively have to change their kits to target the parent THC. These devices will have to be able to give a positive response for THC in concentrations equivalent to 2 ng/ml. It is obvious, at least for forensic purposes, that impairment due to drug consumption must be documented by a reliable blood analysis, performed by GC/MS.

ACKNOWLEDGEMENTS

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Deliverable D4h - Italy

Evaluation of different roadside drug testing equipment

Status P
ROSITA Contract No DG VII PL98-3032

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INTRODUCTION

Since 1992, a specific legislation on driving under the influence (DUI) of alcohol and psychoactive substances is existing in Italy (Art. 186 and 187 respectively of Law 285/1992, the New Highway Code). It covers alcohol, with a Blood Alcohol (BAC) limit of 80 mg/100 ml, and stupefying and psychotropic substances, without mentioning specific substances or legal limits.

The procedure for DUI ascertainments may be initiated by Police in case of road accidents or when physical and psychic alteration is suspected, on the basis of circumstantial or subjective clinical signs. Sanctions are imposed against drivers who have a documented impaired driving performance or drivers involved in traffic accidents and found positive for alcohol and drugs.

As regards DUI of psychoactive substances, the Police, in case of road accidents or suspicion of physical and psychic alteration may accompany the driver to health structures where samples of biological fluids will be taken. Art. 187 does not state which kind of biological fluids must be taken. Nevertheless, medical examinations should be made in conditions of clinical safety excluding recourse to invasive techniques. Therefore, a driver informed consent for clinical ascertainments and sampling of biological fluids is needed. In any case, refusal to cooperate with Police is punished with the same administrative and penal sanctions deriving from positive ascertainments. The basis for a conviction for drugs and driving is the Police report which usually contains the documentation of clinical and analytical data or the driver refusal.

Daytime roadside ascertainments for alcohol and psychoactive substances are usually made in Italy by Highway Police, Local Traffic Police and Carabinieri from Armed Forces, in occasion of road accidents or when driver physical and psychic alteration is suspected. Nevertheless, the prevalence of alcohol and psychoactive substances in the driving population, not involved in road accidents, has never been investigated on a regular basis in Italy. The only continuative initiative in this field was taken by the Centre of Behavioural and Forensic Toxicology (CBFT) of Padova University in collaboration with the Highway Police of North-East Italy and Italian Red Cross (1-8).

Due to the lack and/or limitations of specific legislation (indications of specific substances, kind of biological fluids to be taken, necessities of clinical safety, etc.), roadside drug tests have been up to now sporadically carried out in some regions of Italy. The ROSITA project can be considered the first comprehensive experience in this field carried out in Italy with full cooperation between scientific institutions and Police forces.

METHODS

Evaluation of on-site devices (WP4 protocol) were obtained in occasion of police checks with clinical and toxicological ascertainments organized by the Centre of Behavioural and Forensic Toxicology (CBFT) of the University of Padova in collaboration with the Highway Police of North-East Italy and Italian Red Cross.

These checks were carried out mainly during week-end nights on the main roads of the 7 Provinces of the Veneto Region, Italy (about 4 million people population). Some additional day and night midweek checks were organized too.

The study period was October 1999 – May 2000.

Police personnel was equipped with speed checking equipment and breathalyser. Medical teams (1 forensic doctor and 3 Red Cross volunteers) worked inside ambulances equipped for emergency intensive care and ordinary health care.

Police personnel stopped and identified drivers, evaluated their physical and psychic conditions and eventually performed a breathalyser test. On selected drivers, medical teams obtained the consent to clinical ascertainments and sampling of biological fluids (eventually including the consent to road-side testing their saliva or collect a sample for laboratory analyses, in both cases for research purposes only). Then, they obtained rapid (optical and neurological) and/or specialized clinical assessments and samples of biological fluids. At this time, on-site devices were tested by police personnel or ambulance volunteers, including filling in suitable forms for recording of analytical results and general evaluation of devices. One of the devices for urine samples was tested on a permanent place (CBFT) by trained technicians.

The total number of tested drivers was 302.

Road-side collection of both blood and urine samples by medical personnel, for later laboratory screening and confirmation analyses and counter-analyses, was obtained from 302 drivers. In addition saliva samples from 57 drivers were also collected.
Suitable amounts of the collected urine samples were placed in separated tubes and police or ambulance personnel tested two different types of on-site devices for urine analysis : Syva Rapid Test and Biosite Diagnostics Triage. In some cases the above on-site devices were tested on a permanent place (CBFT) by trained technicians.
100 urine samples were selected among the above 302 and, on a permanent place (CBFT), tested with American Bio Medica Rapid Drug Screen devices.
On the same subjects, and in a time as close as possible of that of blood sampling, on-site devices for saliva were tested by police or medical personnel. In particular, 302 Securetec Drugwipe devices (99 for Opiates, 100 for Cocaine and 103 for Amphetamines) were tested. Among the above subjects, 57 were asked to supply a suitable amount of saliva (about 2.5 – 3 ml collected by means of Teflon chewing) for later laboratory analyses.
Evaluation of on-site devices for urine at the permanent place, as well as laboratory screening analyses, were carried out on collected samples within few hours. Urine, blood and saliva samples were stored at –20 °C and confirmation analyses were carried out within 1-2 weeks. Evaluation of results from on-site devices was obtained by at least two persons and positivity was assigned on the basis of coincident opinions.

Laboratory analytical criteria

Urine
Positive samples by on-site devices or instrumental immunoassay (EMIT) were confirmed by GC-MS. About 10% (n = 20) samples of the remaining negative ones were confirmed by GC-MS for the classes of Cannabinoids, Cocaine, Opiates and Amphetamines.

Blood
Samples from subjects positive by Drugwipe devices on saliva or corresponding to urine samples positive by at least one immunoassay test (on-site or instrumental) were analysed by GC-MS. Remaining blood samples were tested by EMIT after pre-treatment with N,N-Dimethylformamide (9,10).

Saliva
All collected samples were analysed by GC-MS for Opiates, Cocaine and Amphetamines.

Analytical conditions (cut-off concentrations in ng/ml) for laboratory immunoassay tests (EMIT)

Urine
Cannabinoids 50, Cocaine 300, Opiates 300, Amphetamines (monoclonal assay) 1000, Amphetamines (polyclonal assay) 300, Methadone 300, Benzodiazepines 200, Barbiturates 200.

Blood
Cannabinoids 10, Cocaine 30, Opiates 40, Amphetamines (monoclonal assay) 150, Methadone 20.

Analytical conditions (analytes included and cut-off concentrations in ng/ml for target analytes of each class, if any) for confirmation analyses (GC-MS)

Cannabinoids
THC, THC-COOH; Urine 10 (THC-COOH), Blood/Saliva 2 (THC).

Cocaine
Cocaine, Benzoylecgonine, Ecgonine methylester; Urine 150 (Benzoylecgonine), Blood/Saliva 5 (Cocaine/ Benzoylecgonine).

Opiates
Morphine, Codeine, 6-Acetylmorphine, 6-Acetylcodeine, Ethylmorphine, Dihydrocodein, Heroin; Urine 200 (Morphine), Blood/Saliva 5 (Morphine).

Amphetamines
Amphetamine, Phenylpropanolamine, Methamphetamine, MDA, MDMA, MDEA, MBDB; Urine 250, Blood/Saliva 30.

Methadone
Methadone, EDDP; Urine 250 (Methadone), Blood/Saliva 10 (Methadone).

Benzodiazepines
Lorazepam, Temazepam, Flunitrazepam, 7-Aminoflunitrazepam, Triazolam, Alpha-OH-triazolam, Lormetazepam, Oxazepam, Flurazepam, Desalkylflurazepam, Alprazolam, Alpha-OH-alprazolam, Clonazepam, 7-Aminoclonazepam, Bromazepam, 3-OH-bromazepam, Diazepam, Nordiazepam; Urine 50, Blood/Saliva 50.

Barbiturates
Butalbital, Butabarbital, Phenobarbital, Secobarbital ; Urine 50, Blood/Saliva 50.
Internal standards used for GC/MS confirmation analyses were: D_3-THC and D_3-THC-COOH (Cannabinoids), D_3-Benzoylecgonine (Cocaine), D_3-Morphine (Opiates), Methylendioxypropylamphetamine (Amphetamines), Benzexol (Methadone), Pinazepam (Benzodiazepines), Ethyl-tolylbarbituric acid (Barbiturates).

RESULTS

URINE

Analytical results

The total number of collected and processed urine samples was 302.
According to the reference method, the total number of positive samples was 54 (out of 302, 17.9%), the total number of positive results for drugs was 68 and the positive results for each class of drugs were as follows.
Cannabinoids 42 (32 Cannabinoids only, 7 with Cocaine, 2 with Cocaine and Amphetamines, 1 with Benzodiazepines)
Cocaine 18 (8 Cocaine only, 7 with Cannabinoids, 2 with Cannabinoids and Amphetamines, 1 with Opiates)
Amphetamines 2 (2 with Cannabinoids and Cocaine)
Opiates 2 (1 with Cocaine, 1 with Methadone)
Benzodiazepines 2 (1 Benzodiazepines only, 1 with Cannabinoids)
Methadone 1 (1 with Opiates)
Barbiturates 1 (1 Barbiturates only)
None of the 20 samples negative by on-site tests and/or instrumental immunoassay, and tested by GC-MS for the classes of Cannabinoids, Cocaine, Opiates and Amphetamines, resulted positive.

According to the **BioSite DiagnosticsTriage** on-site test, the total number of positive samples was 46 (out of 302, 15.2%), the total number of positive results for drugs was 59 and the positive results for each class of drugs were as follows.
Cannabinoids 34
Cocaine 17
Amphetamines 2
Opiates 2
Benzodiazepines 2
Methadone 1
Barbiturates 1
Tricyclics 0

According to **the Syva Rapid Test** on-site test, the total number of positive samples was 45 (out of 302, 14.9%), the total number of positive results for drugs was 58 and the positive results for each class of drugs were as follows.
Cannabinoids 36
Cocaine 18
Amphetamines 2
Opiates 2

According to the **American BioMedica Rapid Drug Screen** on-site test, the total number of positive samples was 15 (out of 100, 15.0%), the total number of positive results for drugs was 16 and the positive results for each class of drugs were as follows.
Cannabinoids 8
Cocaine 6
Benzodiazepines 2
Amphetamines 0
Opiates 0

Accuracy results were as follows (samples were defined as true negatives on the basis of negative immunoassay results).

BioSite DiagnosticsTriage.
True Positives (TP):
Cannabinoids 34 (100%), Cocaine 17 (100%), Amphetamines 2 (100%), Opiates 2 (100%), Benzodiazepines 2 (100%), Barbiturates 1 (100%), Methadone 1 (100%).
False Positives (FP):
Cannabinoids 0 (0%), Cocaine 0 (0%), Amphetamines 0 (0%), Opiates 0 (0%), Benzodiazepines 0 (0%), Barbiturates 0 (0%), Methadone 0 (0%).
True Negatives (TN):
Cannabinoids 260 (98%), Cocaine 284 (99.6%), Amphetamines 300 (100%), Opiates 300 (100%), Benzodiazepines 300 (100%), Barbiturates 301 (100%), Methadone 301 (100%).
False Negatives (FN):
Cannabinoids 8 (3.0%), Cocaine 1 (0.4%), Amphetamines 0 (0%), Opiates 0 (0%), Benzodiazepines 0 (0%), Barbiturates 0 (0%), Methadone 0 (0%).
Sensitivity:
Cannabinoids 81.0%, Cocaine 94.4%, Amphetamines 100%, Opiates 100%, Benzodiazepines 100%, Barbiturates 100%, Methadone 100%.
Specificity:
Cannabinoids 100%, Cocaine 100%, Amphetamines 100%, Opiates 100%, Benzodiazepines 100%, Barbiturates 100%, Methadone 100%.

Syva Rapid Test.
True Positives (TP):
Cannabinoids 36 (100%), Cocaine 18 (100%), Amphetamines 2 (100%), Opiates 2 (100%).
False Positives (FP):
Cannabinoids 0 (0%), Cocaine 0 (0%), Amphetamines 0 (0%), Opiates 0 (0%).
True Negatives (TN):
Cannabinoids 260 (97.7%), Cocaine 284 (100%), Amphetamines 300 (100%), Opiates 300 (100%).
False Negatives (FN):
Cannabinoids 6 (2.2%), Cocaine 0 (0%), Amphetamines 0 (0%), Opiates 0 (0%).
Sensitivity:
Cannabinoids 85.7%, Cocaine 100%, Amphetamines 100%, Opiates 100%.
Specificity:
Cannabinoids 100%, Cocaine 100%, Amphetamines 100%, Opiates 100%.

American Biomedica Rapid Drug Screen.
True Positives (TP):
Cannabinoids 8 (100%), Cocaine 6 (100%), Amphetamines 0 (100%), Opiates 0 (100%), Benzodiazepines 2 (100%).
False Positives (FP):
Cannabinoids 0 (0%), Cocaine 0 (0%), Amphetamines 0 (0%), Opiates 0 (0%), Benzodiazepines 0 (0%).
True Negatives (TN):
Cannabinoids 92 (100%), Cocaine 94 (100%), Amphetamines 100 (100%), Opiates 100 (100%), Benzodiazepines 98 (100%).
False Negatives (FN):
Cannabinoids 0 (0%), Cocaine 0 (0%), Amphetamines 0 (0%), Opiates 0 (0%), Benzodiazepines 0 (0%).
Sensitivity:
Cannabinoids 100%, Cocaine 100%, Benzodiazepines 100%.
Specificity:
Cannabinoids 100%, Cocaine 100%, Amphetamines 100%, Opiates 100%, Benzodiazepines 100%.

Practical results

No particular problems were encountered roadside to obtain urine samples from stopped drivers. All drivers actively collaborated with Police in this respect. Privacy issues were overcome by obtaining biological samples inside an ambulance equipped for emergency intensive care and ordinary health care. Urine was obtained under the direct observation of medical personnel, so no adulteration

problems were experienced. The obtained volume of urine was in all cases sufficient for roadside tests and laboratory analyses. Samples with the largest volume were selected for AMerican Biomedica Rapid Drug Screen testing.

Advantages and disadvantages of all the on-site devices used

Training requirements:
The easiest device was considered to be the Syva Rapid Test, whereas the worst the Triage due to the high number of analytical steps required. ABM was judged sufficiently easy in this respect.

Manipulation requirements:
ABM and Syva Rapid Test were considered quite easy to handle, whereas the Triage was judged difficult to handle due to the high number of analytical steps required.

Biological fluid amount:
Syva Rapid Test and Triage require only few drops of urine and this was judged quite easy to obtain roadside. ABM requires several milliliters of urine, a volume sometimes difficult to obtain roadside or, if obtained, likely needed mainly for laboratory analyses.

Measurement time:
Triage requires a relatively long measurement time that can pose some problems roadside. Syva Rapid Test and ABM are considerably faster in this respect, thus considered more useful roadside.

Result interpretation:
Results from all devices for urine testing resulted quite easy to interpretate. The best however was judged to be the Triage (clearer coloured bands).

Positive/Negative control system:
All devices for urine testing have control lines very useful for result interpretation.

Data storage/Documentation:
All devices for urine testing show no possibilities to store data, an unhelpful characteristic for roadside testing.

SALIVA

Analytical results:

The total number of saliva samples tested on-site with Securetec Drugwipe devices (99 for Opiates, 100 for Cocaine and 103 for Amphetamines) was 302. 57 drivers supplied a suitable amount of saliva (about 2.5 – 3 ml collected by means of Teflon chewing) for later laboratory analyses.
As agreed with the project coordinator, on-site results for amphetamines are not reported and discussed in this document. This is due to notification by manufacturer, after completion of WP4 protocol, of production of altered devices for Amphetamines in a limited time range, that were sent to CBFT for the above protocol. However, results from GC/MS analyses of corresponding blood and saliva samples are reported all the same.
Positive/negative results with Drugwipe devices were obtained roadside by visual reading in a limited number of cases. Most of the results were obtained by means of a prototype electronic reader supplied by manufacturer and positivity/negativity were assigned according to recommended electronic cut-offs (number of digits).

According to the Securetec Drugwipe on-site test, the total number of positive samples for Opiates was 9 (out of 99, 9.1%), the total number of positive samples for Cocaine was 8 (out of 100, 8%).
As compared to corresponding blood results, saliva on-site results for Opiates were as follows:
Saliva positive and blood positive: 0 (0%);
Saliva positive and blood negative: 9 (100%);
Saliva negative and blood negative: 90 (100%);

Saliva negative and blood positive: 0 (0%).
As compared to corresponding blood results, saliva on-site results for Cocaine were as follows:
Saliva positive and blood positive: 4 (50%);
Saliva positive and blood negative: 4 (50%);
Saliva negative and blood negative: 86 (93.5%);
Saliva negative and blood positive: 6 (6.5%).

According to the reference method, the total number of positive samples for Cocaine and Opiates, of the collected saliva samples, was 2 (out of 57, 3.5%), the total number of positive results for the above drugs was 2 and the positive results for each class of drugs were as follows.
Cocaine 2, Opiates 0.

Accuracy results for the **Securetec Drugwipe** with respect to the collected saliva samples were as follows.
True Positives (TP):
Cocaine 0 (0%), Opiates 0 (0%).
False Positives (FP):
Cocaine 1 (100%), Opiates 1 (100%).
True Negatives (TN):
Cocaine 13 (100%), Opiates 18 (100%).
False Negatives (FN):
Cocaine 0 (0%), Opiates 0 (0%).
Sensitivity:
Results not obtainable.
Specificity:
Cocaine 92.9%, Opiates 94.7%.

Practical results

No particular problems were encountered roadside to test stopped drivers with the on-site device for saliva and to obtain saliva samples from selected drivers. All drivers actively collaborated with Police and medical personnel in this respect. Privacy issues were overcome by obtaining biological samples inside an ambulance equipped for emergency intensive care and ordinary health care. Saliva was tested and/or obtained under the direct observation of medical personnel, so no particular problems were experienced. The obtained saliva samples had in all cases a volume sufficient for laboratory analyses.

Advantages and disadvantages of the Securetec Drugwipe device used

Training requirements:
Drugwipe was judged sufficiently simple for training purposes.

Manipulation requirements:
Drugwipe was considered quite easy to handle, despite the number of analytical steps required.

Biological fluid amount:
Drugwipe requires only few drops of saliva (wiping of the tongue) and this was judged quite easy to obtain roadside.

Measurement time:
Drugwipe requires a relatively short measurement time that can be useful roadside.

Result interpretation:
Results from Drugwipe devices resulted often difficult to interpretate by visual reading and, on the other hand, extremely easy to read by using the electronic reader.

Positive/Negative control system:
Drugwipe devices do not have control lines, thus being the results difficult to interpretate by visual reading. However, the electronic cut-offs of the electronic reader represent an effective control system.

Data storage/Documentation:

Drugwipe show no possibilities to store data, an unhelpful characteristic for roadside testing.

BLOOD

Analytical results:

The total number of collected and processed blood samples was 302.
According to the reference method, the total number of positive samples was 36 (out of 302, 11.9%), the total number of positive results for drugs was 40 and the positive results for each class of drugs were as follows.
Cannabinoids 20;
Cocaine 16;
Amphetamines 2;
Opiates 1;
Benzodiazepines 0;
Methadone 1;
Barbiturates 0.

Comparison of blood results with those of the corresponding urine samples shows that:
42 drivers had urine positive for Cannabinoids and 20 of them had blood with the same positivity;
18 drivers had urine positive for Cocaine and 15 of them had blood with the same positivity, whereas 1 driver had blood positive for Cocaine and urine negative;
2 drivers had both urine and blood positive for Amphetamines;
2 drivers had urine positive for Opiates and 1 of them had blood with the same positivity;
2 drivers had urine positive for Benzodiazepines and blood negative;
1 driver had both urine and blood positive for Methadone;
1 driver had urine positive for Barbiturates and blood negative.

Practical results:

No particular problems were encountered roadside to obtain blood samples from stopped drivers. All drivers actively collaborated with Police and medical personnel in this respect. Clinical safety was ensured by obtaining blood samples inside an ambulance equipped for emergency intensive care and ordinary health care and with the direct intervention of medical personnel, so no particular problems were experienced. The obtained volume of blood was in all cases sufficient for laboratory analyses and no storage and/or analytical problems were encountered.

DISCUSSION AND CONCLUSION

In conclusion, on the basis of our experience, urine was considered a biological fluid easy to collect and to analyze and, considering the toxicokinetics of drugs, it can be very useful for the roadside screening of drivers. Saliva was considered quite easy to test roadside, at least by using the tested device. Blood is considered to be the most important biological fluid for the evaluation of driving impairment. From a general point of view, its roadside collection can pose some problems (e.g. refusal of subjects). These problems, in our experience, were practically absent as all stopped drivers showed a good level of collaboration, probably due to the constant presence of a physician for blood taking. A negative aspect is that the use of roadside tests on blood is precluded.
Acceptability by police officers of roadside use of on-site devices was quite good for the ROSITA project, but it could be not so good on a national scale, considering the limited experiences with on-site devices done up to now in Italy.
Finally, on the basis of the obtained results, cut-offs of on-site devices for urine seemed to be adequate for roadside screening of drivers, whereas the sparse results obtained on saliva preclude an estimation of the corresponding on-site device.

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Deliverable D5

General conclusions and recommendations

Status P
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CONCLUSIONS AND RECOMMENDATIONS

The Rosita project studied 2968 subjects and compared 15 different urine on-site drug tests and 3 on-site saliva tests (one of which was used on sweat as well) in 8 countries.
From this experience, the following conclusions can be drawn:

Place/Status/Significance/Role of roadside drug tests in EU Traffic Safety

- There is a need for roadside drug tests.
- Roadside drug tests are useful under both types of legislation: impairment type and *per se* type.
- Roadside drug tests will increase the confidence of police officers when prosecuting drugged driving. Without an on-site tool to confirm the suspicion, a police officer will be more reluctant to prosecute.
- Roadside drug tests can save time and simplify the enforcement procedure, e.g. by avoiding the need to take the subject to a police station or health care facility for testing.
- Roadside drug tests can save money, by excluding a drug as cause of the impairment and thus avoiding more expensive laboratory analysis. In addition, they can help to reduce the inconvenience experienced by people who did not take drugs by allowing them to continue on their way more rapidly.
- Subjects are impressed by the result (even more so if the procedure was complex or if the result is read electronically) and often confess when confronted with a positive result, sometimes after a long and vehement denial before the test result.
- Roadside tests and the publicity made around them can have a deterrent effect, because the subjective risk of being caught increases
- The use of on-site tests will be more targeted and economical if it is based on a suspicion by a trained police officer. Training in recognition of recent drug use or impairment is also essential to an effective enforcement of drug-driving laws.
- Users of on-site tests have shown great creativity in overcoming some of the encountered problems.
- The need for on-site tests is so great that in some countries, police officers would rather use an imperfect device than wait for a more suitable one.
- Roadside tests are, and should always remain, preliminary tests, that allow the police officer to take immediate measures on-site. A legal sanction should only be based on the result of a reference method in a certified laboratory and/or on the signs of impairment of the subject (depending on the type of legislation in force).
- Those countries which do not permit roadside testing at present (e.g. the UK, apart from alcohol) should consider legislative changes which would in future permit the use of on-site tests of proven validity.

Choice of the sample to be tested

- In all countries, blood is considered the best fluid for confirmation analysis, because the presence of drugs in blood corresponds best with recent use and impairment. On the basis of the comparison between the results of reference analysis in blood, urine, oral fluid and sweat, the following fluids seem suitable for on-site analysis (i.e. there is a good agreement between the results in this fluid and in blood).
  - *Amphetamines*: excellent agreement between urine, oral fluid and blood; for sweat, the low numbers of samples do not allow a conclusion
  - *Benzodiazepines*: urine gives moderately good results, for oral fluid, the sensitivity needs to be improved and sweat was not tested
  - *Cannabinoids*: better agreement with oral fluid than with urine. Urine has a better sensitivity, but not a good specificity. Oral fluid has a sensitivity and specificity of approximately 90 %
  - *Cocaine*: excellent for urine and oral fluid; for sweat, the low numbers of samples do not allow a conclusion
  - *Opiates*: slightly better agreement with oral fluid than with urine. Urine has a better sensitivity (97 %), but a lower specificity (85 %). Oral fluid has a sensitivity and specificity of approximately 90%

- When the necessary facilities are available (e.g. a sanitary van), urine can be obtained relatively easily at the roadside.
- When the facilities are not available, obtaining a urine sample is a problem and it can be time-consuming if the driver has to be brought to a suitable facility.
- In some cases, the volume of urine obtained is low, and tests should require a small sample volume.
- Some countries clearly stated that sampling urine at the roadside was unacceptable.
- A clear majority of countries prefer oral fluid as the matrix for roadside testing, while one country favoured sweat and one favoured urine.
- The methods for obtaining saliva need further improvements. Wiping over the tongue seems to be a well accepted technique, but in this case the analytical detection technique needs to be very sensitive. Sampling oral fluid with dedicated devices gave the following problems:
    - It was sometimes messy;
    - It was sometimes uncomfortable for the subject;
    - In some cases it took a long time;
    - The co-operation of the subject was needed (in some cases, intentionally or not, the subject swallowed the collection device);
    - Oral fluid is sometimes viscous, which can give problems with some devices;
    - Literature data have shown variable oral fluid concentrations for codeine, according to the sampling method used (with or without stimulation, …) with spitting giving the highest concentrations;
    - There are indications that tetrahydrocannabinol (THC) binds to the material of some sampling devices;

- Dry mouth is a frequently encountered problem in drug users. Sampling is then more difficult and time-consuming, but in the evaluation it was possible to obtain oral fluid in nearly all cases.
- In all, sweat and saliva sampling seemed very well accepted by the subjects, much better than urine or blood sampling.

Evaluation of the on-site urine drug tests

- For each type of drug, several urine drug tests satisfied our analytical criteria for a good test (accuracy > 95%, sensitivity > 90%, specificity > 90%, when compared with a reference method in urine), but none scored highly for all the drug categories.
- In general, on-site tests for methamphetamine have a better sensitivity for XTC and related compounds. However their sensitivity for samples that only contained amphetamine was much lower.
- Use of a combination of an amphetamine test with a methamphetamine test gave very good results in the detection of amphetamine and ecstasy.
- On-site urine tests are relatively easy to use after some training.
- Appropriate training in the use and reading of on-site tests is essential.
- There is no clear majority for dip- or pipette-type devices. Cup-type devices would be preferred if they did not leak and required less sample.
- A preference exists for blue lines (easier to read at night under street-lighting) and multi-analyte tests.
- In some countries, ‘aggressive’ tests (more false positives than false negatives) are preferred.

Evaluation of the on-site oral fluid and sweat tests

- With possibly one exception, the presently available on-site devices for oral fluid are too complex, and take too much time.
- The present-generation of on-site tests for oral fluids are insufficiently sensitive and/or specific to give reliable results for most classes of drugs.
- There are several new versions of the evaluated tests and new on-site tests for oral fluid, some of which look very promising in terms of sensitivity, which should be evaluated when they become available.
- On-site tests for oral fluid should be targeted to the parent molecule and not to the urinary metabolite, e.g. to THC, 6-acetylmorphine, cocaine.

- The significance of the much higher concentrations of THC found when extracting a Salivette®, compared to the concentrations in liquid saliva, needs further study.
- One device for testing sweat was evaluated. Sweat as a roadside specimen looks promising but needs further evaluation and dedicated studies

Optimal cut-offs for oral fluid

- Our evaluation was performed on a too limited set of samples to permit firm recommendations for the cut-offs to be used in oral fluid. Some data are given in WP4, but they need further validation.

International co-operation

- The ROSITA project has shown that there is a strong desire amongst forensic scientists, police officers and manufacturers in the EU to co-operate in technical developments in the field of traffic safety. This should be encouraged by the EU, perhaps by setting up an EU-wide technical review committee to keep a watching brief on emergent technology and developments in other regions (for example the USA) which might be adopted within the EU. Some of the principal aims of this committee might be to harmonise technical procedures and produce EU guidelines for roadside tests, including impairment tests by police officers, and laboratory confirmatory methods used subsequent to impairment tests and/or on-site drug tests.
- It would be desirable if a move could be made within the EU to a single set of regulations for driving under the influence, given the removal of barriers to movement within the EU. The committee could perhaps work on this also. We accept that this is likely to be a long-term aim, but at least the trend would be determined on a scientific rather than a political basis.