

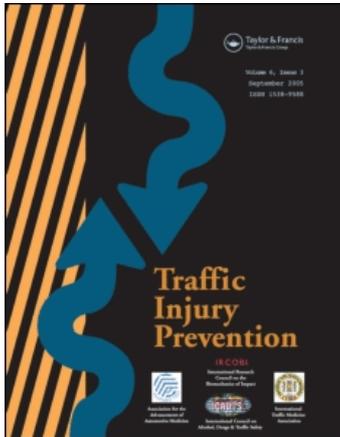
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Drugs and Driving

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Drugs and Driving

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The authors present a global overview on the issue of drugs and driving covering four major areas: (1) Epidemiology and Prevalence—which reviews epidemiological research, summarizes available information, discusses the methodological shortcomings of extant studies, and makes recommendations for future research to better define prevalence and epidemiology; (2) Effects of Medicinal and Illegal Drugs on Driving Performance—focuses on the six classes of drugs most often found in impaired and injured drivers, draws conclusions regarding the risk of these drugs to traffic safety and discusses the need for additional research; (3) Toxicological Issues—discusses ways to identify drug users via behavioral testing and analytical techniques, reviews the approaches used by different countries, screening and confirmation techniques, alternative specimens (e.g., urine, oral fluid, sweat), and how rapid roadside testing could be coupled with behavioral and laboratory testing in an effective approach to identifying and prosecuting drugged drivers; (4) Driving Under the Influence of Drugs [DUID] Laws—provides an overview of DUID laws in the United States and Europe, discusses the basic tenets of these laws, the various types of DUID statutes, the reasons why many existing laws hinder the prosecution of drugged drivers and the rationale for developing per se legislation as a strategy to more effectively manage the drugged driver problem.

Keywords Drugged Driving; Illegal Drugs; Driving; Toxicology; DUI; DUID; Drug Testing

PREVALENCE AND EPIDEMIOLOGY

In general, we have limited knowledge on the prevalence of drugs other than alcohol in road traffic due to methodological problems encountered with epidemiological studies of drugs and driving. Most of these problems can be categorized as problems with sample collection and data collection (Simpson & Vingilis, 1992). Epidemiological studies can provide strong evidence for drug-related crash-risk estimates where an increased frequency of drug use among drivers who sustained injuries compared with that by drivers who were not involved in accidents indicates a positive association and a higher odds-ratio. However, factors pertaining to study design and procedures, such

as misclassification of drug exposure, toxicological issues, confounding by drug treatment and drug concentration, and insufficient statistical power often result in discrepancies between experimental human psychopharmacological and epidemiological data (Ramaekers, 2003).

Population Under Examination

When conducting epidemiological research on illicit drugs and driving, the choice of population studied is critical and can make comparisons across countries problematic. Epidemiological research of illicit drugs and driving can be classified according to the population under examination:

1. General population
2. Offender populations
3. User/addict populations
4. Collision-involved drivers

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In surveys of illicit drug use in the *general population*, data gathering is generally through the use of questionnaires or interviews. Two of the most common observed problems relate to representativeness of the data and refusals. General population surveys include both drivers and non-drivers and do not allow extrapolation to the driver population. In roadside surveys, drivers are randomly or systematically selected to obtain information through self-reports on demographics, drug use, driving, and drug use through toxicological analyses of body fluids. Since roadside surveys tend to be executed during late-night hours on weekends, drivers tested are not representative of the total driving population. Refusal rates can have profound effects on inferences about illicit drug use derived from roadside surveys because those substances are detected with less frequency than alcohol where refusal rates of 15% are observed. Refusal rates can actually exceed the proportion of drivers who score positive for illicit drugs. An additional problem exists with the collection of body fluid samples for drug testing, when invasive procedures are unacceptable because of legal liability. A recent survey conducted by the Pompidou Group of the Council of Europe among 24 European countries revealed that with the exception of one country, The Netherlands, a random selection of the driver population can not be stopped and asked to provide a blood, saliva or urine sample to determine the prevalence of drugs other than alcohol due to legal or legislative barriers (De Gier, 2003).

In surveys of *offender populations* (i.e., those charged with driving under the influence of alcohol or drugs), drug screens are generally carried out if the blood alcohol level is below the legal limit, or if the police suspect drug use (Norway). This approach automatically excludes information on combinations of drugs with high levels of alcohol. Furthermore, the selection of drivers is initially determined by the arresting officer, which introduces a variety of biases.

In investigations of *user/addict populations* samples are generally drawn from treatment facilities. These surveys cannot be considered representative of the total user/addict population, since only a small proportion will seek formal treatment.

In surveys of *collision-involved populations* information is gathered on a wide range of variables (e.g., characteristics of crashes, psychological/behavioral characteristics, drug use problem). Documentation of drug impairment is based on different perceptions and decisions of officers, which can introduce biases. In accident fatalities, data are most of the time incomplete due to the fact that drug screens are not carried out on fatally—injured drivers found to be impaired by alcohol. In some European countries, legislation provides for collection of blood samples from all drivers involved in traffic accidents, causing injuries or death, or from drivers involved in accidents where at least one person is fatally injured (De Gier, 2003).

Data Collection

Sources of data and the methods by which they are collected can cause methodological problems. The first source of data is official records (police, coroner, medical, etc.) and has limita-

tions because data on illicit drug use are not routinely collected. Even when drug tests are carried out, generally only a select number of drugs are tested. In official records, underreporting is a serious problem because they tend to contain only the most extreme cases.

The second source of data is self-report instruments. Underreporting is also a problem in this approach since deviants tend to underreport.

Different methods of data collection used in surveys each have their own problems. The various methods of drug analyses in blood, sweat, saliva, or urine each have problems with respect to sample collection, handling, and transportation as well as toxicological assays used. The interpretation of drug levels detected can be difficult; for example cannabinoids can be detected in urine for days, after use and the relevance of this to traffic safety is ambiguous since the metabolites, primarily THCCOOH, only indicate prior exposure, whereas THC concentrations in the blood relate to pharmacological activity. Blood specimens are generally considered to be essential for surveys of illicit drugs and driving.

In pharmacoepidemiological studies for risk assessment, the use of drugs among injured drivers is generally ascertained from prescription records (Ray et al., 1992; Leveille et al., 1994; Neutel, 1995; Barbone et al., 1998). Many of these studies successfully established elevated odds-ratios for benzodiazepine users, where risk estimates equal or exceed the risk of accidents associated with a blood alcohol concentration of 0.05%. Misclassification of drug exposure might easily occur due to the absence of non-prescription drugs, such as sedating antihistamines that are being sold over-the-counter, leading to an underestimation of crash risk. Confounding by drug treatment duration and concentration in epidemiological studies can be expected if certain drug groups are considered, such as tricyclic antidepressants, where complete tolerance to the initial impairing effects after one or two weeks of repeated dosing can occur (Ramaekers, 2003). A failure to find a positive association between tricyclic antidepressants and traffic accidents merely reflects the occurrence of tolerance in drivers after prolonged treatment. A positive association might have been found in drivers, however, during the first weeks of treatment with these drugs.

Another method for determining illicit drug use among drivers relies on the use of clinical and psychophysical tests. The usefulness of the last method is still unclear. Self-report tools for the assessment of drug use and driving show different problems with respect to accuracy (reliability of recall information).

Finally, comparisons across studies are often difficult because of the lack of conventions used in reporting findings. For example, there is no consistency in reporting percentages (all drivers in the sample or only those who were tested for drugs).

Statistical Power

In many epidemiological studies, the power to detect significant proportional differences between injured drivers and controls seems low given the small samples used. Given the low

prevalence of illicit and licit drug use among drivers the problem of limited sample sizes becomes most relevant. If the prevalence rates are low, the sample under study should be relatively high.

Prevalence in European Countries, Australia, and Quebec. A survey conducted for the Pompidou Group of the Council of Europe focus has examined the prevalence of illicit drug use in road traffic in thirteen European countries (De Gier, 1998). Since illicit drug use other than alcohol has been frequently reported in most studies, the prevalence of licit drugs has been reported as well. Most study outcomes do not allow comparisons across different European countries due to the different methodological problems as discussed above. However, one can estimate that the prevalence of illicit drug use in the *general* driver population will fall (at least in Europe) in the range of 1–5%, whereas the prevalence of *licit* drugs affecting driving performance will be higher (5–10%). The drugs of interest at this moment in Europe seem to be cannabis and opiates (not in particular cocaine as found in many studies in the US), followed by amphetamines, if looking at the illicit drugs. For the *licit* drugs, benzodiazepines are predominantly found, whereas tricyclic antidepressants are much less detected. The distribution of alcohol and other drugs among 5,931 drivers who participated in two roadside surveys in August 1999 and 2000 in Quebec and provided a urine sample showed similar results (Dussault et al., 2002). Drugs other than alcohol were found in 11.8% of urine samples in the following proportions: cannabis 6.7%, cocaine 1.1%, benzodiazepines 3.6%, opiates 1.2%, PCP 0.03%, amphetamines 0.1%, and barbiturates 0.5%. Alcohol was found in 5.9% of all drug cases. In a recent Danish study among 1,000 randomly stopped car drivers, laboratory analyses of saliva samples confirmed that 2% were positive for benzodiazepines or illegal drugs (amphetamine, cannabis, cocaine, or opiates): 1.3% were positive for illegal drugs and 0.7% for benzodiazepines (Behrensdoerff & Steentoft, 2003). Looking at the data for populations of drivers suspected of driving under the influence of drugs and collision-involved drivers there are no clear differences reported.

In *populations of drivers suspected of driving under the influence of drugs* high prevalences of *licit* drug use (primarily benzodiazepines) are reported ranging from 14–74%. The prevalence of *illicit* drug use is lower than for illicit drugs (9–57% for cannabis, 8–42% for opiates, and 1–20% for amphetamines). These findings depend on the perception and awareness of police officers in the different countries who decide on the inclusion of a driver in the sample. For example, in Norway the police force seems to be focused very much on drugs other than alcohol, which causes large differences in prevalences of drug use among drivers in comparing the results from various Nordic countries. Remarkable differences between countries are observed, for example the prevalence of the use of amphetamines in Norway is relatively high, while in contrast the use of opiates is rather low. The combination of licit and/or illicit drugs and alcohol is expected to be high in samples selected for suspicion of driving under the influence of drugs/alcohol. However, in most studies the data for separating the prevalence of combinations of drugs (including alcohol) are lacking. The prevalence in drug positive

cases is 25% in Norway, whereas the prevalence in all drivers in the sample in two Swiss studies ranged from 18–28%. The prevalence of multiple drug use is reported in a few studies for all licit and illicit drug use together. A high prevalence (62%) has been observed by Swiss researchers.

In *collision-involved drivers* the prevalence of *illicit* drug use ranged from 10–25% in the different studies. Cannabis and opiates are about equally divided among the samples (6% and 7.5% respectively) and are detected about two to three times more frequently than amphetamines. In a more recent French study the main active substance of cannabis (delta 9 THC) was found in 10% of drivers injured in road accidents, whereas morphine in 2.7% and benzodiazepines in 9.4% of these drivers (Mura et al., 2003). Cocaine has been detected with a very low prevalence (0.5–0.7%) in Belgium and Italy, whereas in Spain a high prevalence (5%) has been reported. Illicit and medicinal drugs found additionally among 5,745 Spanish drivers killed in road accidents from January 1999 to December 2000 were opiates 3.2%, cannabis 2.2%, benzodiazepines 3.4%, antidepressants 0.6%, and narcotic analgesics 0.4% (Del Rio & Alvarez, 2002).

The prevalence of the combination of drugs (licit and illicit together) and alcohol use in drug positive drivers ranged from 27–65% in most studies. The prevalence of multiple drug use is also reported in most studies for licit and illicit drugs together and ranged from 20% in the Belgian study and 80–90% in drug positive cases in Norway. When considering the complete driver sample in some other studies, the prevalence is lower, from 5% in the study in the United Kingdom to 17.5% in an Italian study.

In a more recent publication, the incidence of drugs in 3,398 fatally injured drivers was determined in three Australian states: Victoria, New South Wales, and Western Australia for the period of 1990–1999 (Drummer et al., 2003). Drugs other than alcohol were present in 26.7% of the cases and comprised cannabis (13.5%), opioid (4.9%), stimulants (4.1%), benzodiazepines (4.1%), and other psychotropic drugs (2.7%). Almost 10% of the cases involved both alcohol and drugs. The prevalence of drugs increased over the decade, particular cannabis and opioids, while alcohol decreased. The prevalence of alcohol, cannabinoids, benzodiazepines and stimulants amongst 2,500 injured drivers and their role in driver culpability was studied by Longo et al. (2000) in Adelaide, Australia. There was no significant increase in culpability when THC was used alone. For those drivers with benzodiazepines at therapeutic concentrations and above, there was a significant increase in culpability. The prevalence of alcohol and other drugs among 482 fatally injured drivers who deceased between April 1999 and November 2001 in Quebec was presented by Dussault et al. (2002). Drugs other than alcohol were found in 30.2% of urine samples in the following proportions: cannabis 19.5%, cocaine 6.8%, benzodiazepines 8.5%, opiates 1.4%, PCP 1.1%, amphetamines 0.8%, and barbiturates 0.3%. Alcohol was found in 41.1% of all drug cases.

The use of the combination of drugs and alcohol in the general driver population revealed major differences while looking at licit and illicit drug use in one large-scale German roadside survey (Krüger et al., 1995). The prevalence of the combination

of licit drugs and alcohol was extremely low (only one case), whereas considerably high prevalence was detected for the combination with illicit drugs (44%). Similarly, a high prevalence of combined use was found in other driver populations (drivers suspected of DUI of drugs and collision-involved drivers) in a few other large scale European studies. Although they do not all separate for licit and illicit drug use, one has to conclude that the combination of drugs with alcohol is one of great concern in terms of traffic safety. The significant importance of the synergistic interaction for alcohol and drugs has been stressed by several experts both in the field of epidemiology and experimental human psychopharmacology. If mortality was taken as the outcome variable, Belgian researchers indicated a relative risk of 3.56 in the combined positive group, in which a mere additive effect would theoretically have led to a relative risk of 1.60 (Meulemans et al., 1997). Furthermore, it has been suggested that alcohol and cannabis use in combination carry a greater risk potential than either of them alone (both in epidemiological research, Terhune et al. (1992) and experimental research, Robbe & O'Hanlon, 1998).

Prevalence in North America

A recent review of North American studies that have examined the presence of drugs in crash-involved drivers, non-crashed on-the-road drivers and drivers stopped or arrested for traffic violations has been published by Jones et al. (2003).

The mean prevalences that have been presented and compared with the data from foreign studies (see Figure 1) do not reflect the significant variance in the data for the various drugs other than alcohol, and do not take into account the different methodological problems that have been described above. In particular, the results from some recent studies in Canada and Australia show that cannabis and cocaine are detected more frequently in fatally injured drivers than suggested in the report on the comparison with North American studies. It should be stressed that knowledge about the prevalence of drug positive drivers in different driver populations does not prove that the use of drugs is

a serious safety problem. Ideally, a study to determine accident risks needs to match collision-involved drivers for case-control comparisons. In most countries, there is a lack of data on the prevalence of drugs among the normal driver population. However, the high prevalence of drugs found in representative samples of collision-involved drivers supports the assumption that there is a serious road safety problem. Unfortunately, neither Europe nor the United States has an approach in which standardized methodologies are applied in repeated studies during a given period of time in each country for cross-national comparisons. It is recommended that such studies be embarked upon and that national laws prohibiting roadside surveys be abolished or modified to permit the same surveys to be conducted on a global basis.

There is a clear need for better data, more harmonization of data collection techniques, and a standardization of core data variables.

EFFECTS OF MEDICINAL AND ILLEGAL DRUGS ON DRIVING PERFORMANCE

In recent years, several non-alcoholic drugs have been increasingly recognized as hazards to road traffic safety. Review articles summarizing results from numerous studies have been published recently (Vingilis & Macdonald, 2000; Mørland, 2000). In spite of comprehensive research, several problems persist in establishing legal limits for drugs other than alcohol based on scientific documentation of their associated accident risks. Theoretically, all psychoactive compounds, including illegal and medicinal drugs, depending of dose, may have detrimental effects on psychomotor performance that is important for driving skills. For some drugs, the effect may be evident for acute use, while reduced after tolerance has developed (Mørland, 2000). For large groups of patients, the use of psychoactive drugs is necessary for coping with daily life. In terms of accident risks, the problem is compounded by the fact that multi-drug use is common among patients and particularly drug abusers.

Two major sources of complementary research have contributed to the present knowledge of the effects of medicinal illegal drugs on driver performance: (1) Controlled experimental studies, including performance tests, simulated driving, driving in closed road circuits and in "real" traffic; and (2) Analytical epidemiological studies, including case-controlled accident studies. Descriptive epidemiological studies give valuable information, however, reliable values for accident risk cannot be estimated, as the prevalence of drug use in the general driving population is almost unknown. Results from different accident studies often show large variability with regard to the different drugs detected. Some of this variability may be related to the protocol used for the studies (e.g., drugs included in the tox analysis) their cut-off limits and biological matrix used for analyses (blood, urine). The time between accident and sampling also may be critical for some drugs due to instability, especially in autopsy blood samples.

While many drugs/medicines may impair skills for driving, the available literature on drugs, driving performance and

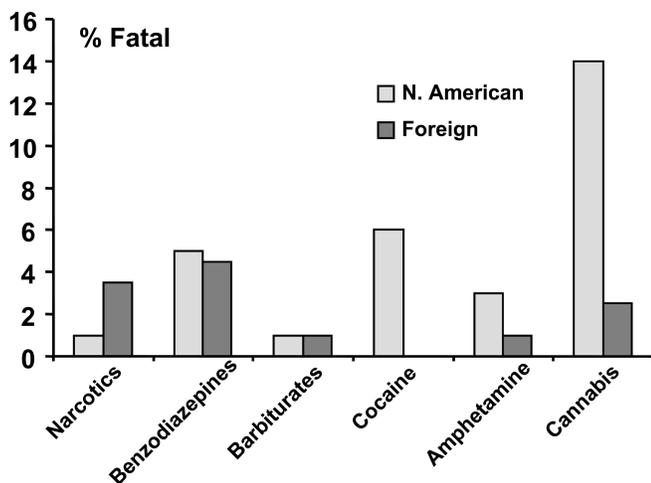


Figure 1 Mean % of fatally injured drivers testing positive for various drugs in North American and Foreign reviewed studies (Jones et al., 2003).

accident risks, has focused mainly on six different drugs or drug groups, which will be briefly summarized in this report with reference to some selected studies, and with conclusions based on an earlier published review (Mørland, 2000).

Benzodiazepines and Related Drugs

Comprehensive research related to benzodiazepines (BZDs) and traffic safety has been published. Berghaus and Grass (1997) summarized more than 500 experimental studies in which the effects of one or more BZDs on driving-related performance were assessed. They found an almost linear correlation between serum BZD concentrations and performance deficit for most of the BZDs investigated. "Real" driving tests on different BZDs and zopiclone have demonstrated adverse effects on the standard deviation of lateral position (SDLP). Some of the BZDs tested the morning after use as hypnotics caused impairment comparable to BACs of 0.05–0.1% (O'Hanlon, 1986). Comparable studies on the acute impairing effects of BZDs in therapeutic or higher doses, have shown that some BZDs are more likely to adversely affect performance than others at equivalent doses. However, at high doses almost all BZDs may cause severe impairment (EMCDDA, 1999). Combined use of BZDs with alcohol increases psychomotor impairment compared to the effects when the drugs are used alone (Linnoila, 1990). It has been postulated that anxious patients (who probably were unsafe drivers), could improve their driving ability after BZD treatment. However, some studies have documented adverse effects, in spite of significantly reduced anxiety symptoms (O'Hanlon et al., 1995).

Several analytical epidemiological studies on BZDs combined with accidents have been reported. In a study by Honkanen et al. (1980), the prevalence of BZDs was found to be 5% among accident drivers, compared to 2% in a control group. From an Australian study including 2880 fatally injured drivers, the odds ratio (OR) for BZDs was found to be 1.8, after comparing culpable to non-culpable groups of drivers (Drummer, 2001). Increased risk was found when BZDs were apparently used above therapeutic doses or combined with alcohol, and significantly higher when alcohol was used alone. Another accident study comparing responsible drivers to a non-responsible group of patients, showed that BZDs were present in blood samples from 10% and 1.5%, respectively (Currie et al., 1995). From other case-controlled studies, similar findings have been reported (Barbone et al., 2000). In pharmacoepidemiological studies, patients using BZDs and related compounds have been linked to accident data for the same population and compared with control groups not using BZDs. Neutel (1995) studied the risk for hospitalization after traffic accidents based on large groups of patients having their first BZD prescription. Depending on the drug and time after the prescription, the odds ratios (OR) varied from 2.4 to 13.5 compared to the control groups. The highest risks were found during the first two weeks after the prescription.

From descriptive epidemiological studies, BZDs seem to represent the most frequently detected drugs after alcohol, varying

from 8% to more than 40% among fatal and non-fatal accident drivers (Gjerde et al., 1993; Christophersen et al., 1995; Meulemans et al., 1996). BZDs also represented the most commonly detected drugs after alcohol among drivers apprehended due to erratic or dangerous driving (Christophersen, 2000).

Conclusions. Based on the present knowledge, BZDs constitute a considerable risk to traffic safety, both in therapeutic doses and to a much greater degree at higher doses. The high prevalence among drivers involved in accidents shows that BZDs represent a major traffic safety problem.

Opioids

The opioid-group includes both medicinal and illegal drugs. An overview published by Zacny (1995), summarizing approximately 200 experimental studies, showed large variations with regard to responses, probably due to different sensitivities of the tests. It was concluded that opioids can impair performance, with the degree of impairment dependent of the particular opioid, dose, former use, and possible tolerance. More studies are needed on subjects using high doses of opioids (pain treatment, methadone for substitution therapy, high-tolerance heroin users). A report on methadone and driving has recently been published by the Pompidou Group (de Gier, 2003). This includes discussion of the best practice for patients in substitution programs and possibility for driving, that may in turn depend on the time in the program and any changes of dose. Control studies on opioids among accident drivers are inconclusive. The responsibility analysis performed by Drummer (2001) on fatally injured drivers, documented an OR of 1.2 for opioids. A study on drivers above 65 years of age who were involved in accidents, demonstrated a relative risk of 1.8, with codeine being the most frequently detected opioid (Leveille, 1994). From descriptive epidemiological studies, the presence of opioids in single-vehicle fatal or non-fatal accidents has varied from approximately 1% to 7% (Gjerde et al., 1993; Christophersen et al., 1995; Meulemans et al., 1996).

Conclusions. Based on our present knowledge, opioids do represent a risk to traffic safety, especially for patients with no drug use experience. The prevalence of opioids among drivers involved in accidents indicates a traffic safety problem.

Amphetamines, Cocaine, and Other Stimulant Drugs

The most important drugs in this group are the amphetamines, amphetamine-dioxy derivatives ("ecstasy") and cocaine. The effects of amphetamine on driving have recently been summarized by Logan (2002), concluding that methamphetamine increases the likelihood of performance deficits on complex psychomotor tasks such as driving. In some studies, increased risk taking seemed to be documented (Logan, 2002). Several laboratory investigations on stimulants have failed to document negative effects on traditional performance tests (Koelega, 1993). However, the amphetamine doses used by abusers are generally 5–10 times higher than therapeutic doses, which have not been tested in controlled experimental studies.

Epidemiological studies have demonstrated responsibility rates above unity for amphetamine in fatally injured drivers compared to controls (Terhune et al., 1992). In the responsibility study carried out by Drummer (2001), the OR for stimulants was calculated to be 2.1. The frequency of amphetamines detected in different descriptive accident studies have varied from approximately 1 to 4 % (Gjerde et al., 1993; Christophersen et al., 1995; Meulmans et al., 1996). Some studies from North America have demonstrated a high frequency of cocaine use among accident drivers (Dussault et al., 2002).

Conclusions. Based on present knowledge, it can be stated that amphetamine, cocaine, and other stimulants appear to constitute a risk to traffic safety, at least at high doses. The prevalence of stimulants, mainly amphetamines and cocaine among different groups of accident drivers, indicates an important traffic safety problem.

Cannabis

In 1995, Berghaus et al. published a meta-analysis based on more than 120 experimental studies, including laboratory, driving simulator, and on-road experiments. Impaired performance, directly related to increasing tetrahydrocannabinol (THC) blood levels, was demonstrated. The results from other studies using "real" driving, have also documented dose-related effects on SDLP and performance (Ramaekers et al., 2000). In several studies, pharmacodynamic interactions between THC and ethanol have been documented with enhanced impairment greater than the effects of cannabis or ethanol alone (Ramaekers et al., 2000). Inconclusive results have been obtained from studies investigating a possible link between THC and fatal accidents, which may possibly be connected to the instability of THC in post-mortem blood. From the Australian culpability study on fatal accident drivers, an OR of 4.3 for THC was calculated (Drummer, 2001). Results from descriptive studies on fatal and non-fatal accidents have demonstrated frequencies of cannabis ranging from few percent and up to 50% (Mørland, 2000). In some studies, urine samples have been used for the detection for THC-acid, which can be detected for days (and possibly weeks at very low concentrations) after drug use.

Conclusions. Based on present knowledge, it can be stated that cannabis use constitutes a risk to traffic safety at least for the first few hours after use. The prevalence of cannabis among drivers involved in accidents indicates a substantial quantitative traffic safety problem.

Antihistamines

The review by EMCDDA, (1999) on controlled experimental studies concludes that dose-dependent impairment of performance is associated with the use of first generation antihistamines (e.g., diphenhydramine). The newer generation antihistamines do not have such negative effects, except in higher doses. Controlled epidemiological accident studies on antihistamines have shown none or minor risk effects for antihistamines (Mørland, 2000). In descriptive accident studies, the prevalence

of antihistamine use has varied from zero to approximately 2%.

Conclusion. Based on current knowledge, the use of first generation antihistamines may constitute a risk to traffic safety. Results from epidemiological accident studies, indicate that antihistamines do not represent a serious traffic safety problem.

Antidepressants

Conclusions from controlled experimental studies (EMCDDA, 1999) have demonstrated impaired performance associated with the use of the most sedative tricyclic antidepressants. New generation antidepressants do not seem to interfere with performance, except when used in higher doses. Analytical epidemiological studies, mainly on older drivers, have documented increased accident risks with a RR of 2.3 (Leveille, 1994). A comparison of responsible and non-responsible accident drivers demonstrated a higher incidence of antidepressant use among the responsible group (Currie et al., 1995). In descriptive epidemiological studies, antidepressants have either not been detected or detected only at low levels (approximately 1%) except in a French study (Mørland, 2000; Deveaux, 1996).

Conclusion. Tricyclic antidepressants might represent a risk to traffic safety, especially during early treatment periods. The prevalence of antidepressant among accident drivers, indicates that these drugs do not represent a major traffic safety problem, except possibly in some countries.

Conclusions—Further Research

Based on the present information, there is a need for further studies to increase our knowledge of the association between the use of certain non-alcoholic drugs and road traffic safety. Further research is needed both for frequently used drugs, new drugs that will appear on the market, and different drug combinations and alcohol. It is recommended that such experimental studies should be more standardized according to proposed guidelines (de Gier, 1995). Within the field of epidemiology, more knowledge is needed about the effects on traffic safety by using medicinal drugs at therapeutic doses. Future accident studies where the cause or culpability is related to drug findings should be prioritized. As a background for risk factor calculations, larger roadside studies to evaluate the occurrence of drug use among the general driving population would be important. The use of saliva combined with reliable on-site tests covering the most important drugs, offers tremendous potential in this type of study. For the examination of drug impairment, the comparison of simpler easy performing tests, with the more complex test batteries would be of great importance. Last, but not least, international collaboration between different countries would be most welcome and is highly recommended.

TOXICOLOGICAL ISSUES—WAYS TO IDENTIFY DRUG USERS, METHODS/STANDARDS, ETC.

The suspicion that a driver is under the influence of drugs can be based on specific symptoms of drug use, like mydriasis,

Table I Steps in the detection of driving under the influence, showing the parallelism between alcohol and drugs

	Alcohol	Drugs
Initial screening	Smell of alcohol	Signs of recent drug use
Test (roadside or police station)	Breath test	Roadside drug test in urine, oral fluid, or sweat
Evidentiary analysis (lab)	Breath or blood analysis	Quantitative analysis of drugs in blood

bloodshot eyes or trembling, or on the fact that the driver is obviously impaired while a breathalyzer test is negative. The initial screening can be very short, or it can be elaborate, for example checklists are used in Belgium (Verstraete & Maes, 2000), and Germany (Steinmeyer, Ohr et al., 2001) or the more elaborate Drug Evaluation and Classification system (DEC) that is used in the United States (Page, 2002). Following the initial behavioral screening, the second step (in many parts of the world, although not in the U.S.) is becoming a roadside rapid drug test. The third step is the analysis of a body fluid, most often blood (or serum or plasma) by a reference chromatographic technique, in a certified laboratory. Irrespective of the legislation, a combination of the three steps described in Table I is very often used. We will review the present status of these three steps in the detection process in the paragraphs to follow.

Behavioral Testing

Signs of recent drug use or impairment are important, either to give the police officer initial suspicion, or, in impairment legislation, to document that the driver was impaired. Typically, a checklist will be used that includes a collection of different symptoms of impairment or recent drug consumption shown by drivers. For example, in Germany, the checklist includes observations on driving style and observations when the driver is stopped or encountered. In the latter group, one observes: speed of reaction, appearance, unusual physical signs (sweating, shaking, vomiting), speech, orientation, mood and behavior, mode of walking, smell of alcohol, appearance of the eyes and pupils, and the evolution of the behavior (normalization or worsening). In the U.S. DEC program, there are twelve steps (Page, 2002):

1. blood (or breath) alcohol concentration
2. interview of the arresting officer
3. preliminary examination (includes the first of three pulses)
4. eye examinations (horizontal and vertical nystagmus, lack of convergence)
5. divided attention tests (modified Romberg, walk and turn, one-leg stand, finger to nose)
6. vital signs examinations (includes the second of three pulses, blood pressure, temperature)
7. darkroom examinations of pupil size (includes an examination of the nasal and oral cavities)
8. muscle tone

9. examination of injection sites (includes the third pulse)
10. statements, interrogation
11. opinion of the DRE (drug recognition expert)
12. toxicology: obtaining a specimen and subsequent analysis

There have been several evaluations of the DEC program. When Drug Recognition Experts [DREs] concluded that impairment was due to drugs other than ethanol, their opinions were consistent with toxicology in 44% of cases after intake of ethanol, cocaine, and marijuana (Heishman, Singleton et al., 1996). In a second study, the ability of the DEC evaluation to predict the intake of alprazolam, d-amphetamine, codeine, or marijuana was optimal when using two to seven variables from the evaluation. DREs' decisions of impairment were consistent with the administration of any active drug in 76% of cases, and their drug class decisions were consistent with toxicology in 32% of cases, according to standards of the International Association of Chiefs of Police (Heishman, Singleton et al., 1998).

Further research is needed on the most sensitive and specific behavioral tests, so the procedure can be simplified and tests that give little additional information can be avoided.

Roadside Drug Screening

Because blood sampling is invasive, requires medical personnel, analysis of the sample takes time and is relatively expensive, there is a need for a rapid screening test that can give a result in minutes. Such a rapid screening test is necessary in order to take immediate measures, in particular a temporary driving ban, or to order a blood test. During the Rosita project, an investigation in 16 countries determined the needs of the police forces (Moeller, Steinmeyer et al., 2001). The needs differed across countries, but there was a general desire to have a multi-drug test that provided an unambiguous result within five minutes for the detection of cannabis, amphetamines, cocaine, opiates, and benzodiazepines. Saliva was regarded as the best matrix to carry out the tests; sweat was regarded as acceptable, and analysis of urine was considered to be unacceptable in certain countries.

During the field evaluations of the Rosita project, the need for a rapid drug test was confirmed. Rapid drug tests facilitate law enforcement and save time (by avoiding the need to take the suspect driver to the police station) and money (by avoiding the more expensive blood analysis when the chance of a positive result is low). The use of a rapid test increases the confidence of the police officer (because it immediately confirms his initial suspicion) and encourages him to pursue the case. The study also showed that police officers did not have objections to taking samples and to performing the tests. The drivers were often impressed by the result of test, and if at the beginning they denied having taken the drug, a positive result often made them confess. The use of roadside tests and the publicity associated with their use can have a deterrent effect, because the subjective risk of getting caught increases (Verstraete & Puddu, 2001a; Verstraete & Puddu, 2001b).

Matrices that could be used for roadside drug testing are urine, oral fluid and sweat. Their respective advantages and

Table II Advantages and disadvantages of the different matrices for roadside drug testing

	Advantages	Disadvantages
Urine	<ul style="list-style-type: none"> • Availability of several reliable on-site tests • High concentrations of drug metabolites present • Robust and well-known technology 	<ul style="list-style-type: none"> • Delayed appearance of drugs in urine • No correlation with impairment • Sampling difficult at the roadside • Risk of sample adulteration
Oral fluid (saliva)	<ul style="list-style-type: none"> • Presence of parent drug • Sampling can be performed without embarrassment • Some correlation with impairment 	<ul style="list-style-type: none"> • No reliable on-site test presently available • Little and very viscous oral fluid after recent intake of drug • Very low concentrations of THC and benzodiazepines • Still much research needed
Sweat	<ul style="list-style-type: none"> • Presence of parent drug • Sampling can be performed without embarrassment 	<ul style="list-style-type: none"> • Few on-site tests available • No standardization of sampling • Delayed appearance of drugs in sweat • Very low concentrations of THC and benzodiazepines • Possibility of environmental contamination • Still much research needed

disadvantages are given in Table II. In Belgium, a fast urine test is included in the legal procedure (Verstraete & Maes, 2000). In other countries like Germany, urine tests are often used (Steinmeyer, Ohr et al., 2001). In the Australian State of Victoria, very recent legislation will permit random roadside drug testing in oral fluid in 2004.

A combination of a first behavioral screening followed by a roadside urine drug test seems to work well. The evaluation of the Belgian procedure showed that drugs were found in the blood of 85% of the cases that were preselected by a positive checklist and a urine drug test (Maes, Samyn et al., 2003). Similar results were found in Sweden (Ahlner J., communication at the 40th TIAFT meeting in Paris, August 2002).

In the Rosita study, it was shown that if a urine test is applied after selection of the drivers suspect to be under influence of drugs, urine analysis (by GC-MS) correctly predicted the presence or absence of drugs in blood in 94% of the cases for the amphetamines, 89% for benzodiazepines, 86% for cannabis, 97% for cocaine and 86% for opiates (Verstraete & Puddu, 2001a). In oral fluid these percentages were 95% Amphetamines, 29% Benzodiazepines (explained by the insufficient sensitivity of the confirmation method), 89% Cannabis, 99% Cocaine, and 91% Opiates.

The Rosita study showed that the reliability of the oral fluid tests available at the time (Avitar Oralscreen, Cozart Rapiscan, and Securetec Drugwipe) was insufficient for police work, with many false positives and false negatives (Verstraete & Puddu, 2001a). A lot of progress has been made in this area, but in 2004, there is still no reliable salivary test for all classes of drugs (Walsh, Flegel, Crouch, et al., 2003). To our knowledge, there are currently 10 rapid oral fluid tests, of which several exist only as prototypes. The major problems that remain to be solved are the sensitivity for cannabis and benzodiazepines, and the collection and sampling from subjects who have little saliva or very viscous saliva.

More research is needed to increase the reliability and sensitivity of on-site oral fluid drug tests. Moreover, the newer tests must be evaluated in the field in order to establish their value.

Efforts should also be targeted to training of police officers in recognizing driving under the influence of drugs.

Evidentiary Analysis of Drugs in Blood

With an analytical or *per se* legislation, the presence of drugs in blood (above a certain cut-off) corresponds to an offense of driving under the influence.

In all the countries that have introduced analytical legislation, there have been serious discussions on the cut-offs to use. At this time, no "danger cut-offs" (i.e., drug concentrations in blood or oral fluid above which the crash risk has been shown to increase) exist. Moreover, to choose danger cut-offs is equivalent to condoning the use of drugs, which remains illegal in almost all countries. Indeed, if one puts a danger cut-off in the law, one will have very quickly questions like: Can I smoke a half joint without being positive during a road control?

In Germany the cut-offs are established by the Grenzwertkommission, and they are the concentrations that can be reliably determined by the analytical labs, based on the results of the proficiency testing. In some other countries (Sweden, France), no cut-offs have been established, and the limits of quantitation of the individual labs are applied. Table III gives an overview of the cut-offs that are used in these countries.

For the analysis of drugs in blood, the French Society for Analytical Toxicology (SFTA) has recommended various methods by gas chromatography-mass spectrometry, which are largely used (Gaillard, Pepin et al., 1996; Kintz, Cirimele et al., 1996; Marquet, Lachâtre et al., 1996). There are also some very recent exhaustive reviews on this subject, such as for example that of Moeller and Kraemer (2002) which take stock since a former review (Moeller, Steinmeyer et al., 1998).

GC-MS is still the most widely used method for confirmation analysis of the serum, plasma, or blood samples, but liquid chromatography-mass spectrometry (LC-MS) procedures have also been introduced for different classes of drugs for confirmatory analyses or even for screening and confirmation in one step (Marquet, 2002; Wood, De Boeck et al., 2003). Some laboratories make an initial screening by immunoassay (ELISA)

Table III Analytical cutoffs (ng/mL, except Sweden: ng/g) used in four European countries

	Germany		Belgium	France	Sweden
	1998	2002*			
Amphetamine	50	25	50	LOQ	30
MDMA	50	25	50	LOQ	20
MDEA	50	25	50	LOQ	20
MDA	—	—	—	LOQ	20
MBDB	—	—	50	LOQ	20
Cocaine	—	—	50	LOQ	20
Benzoylcegonine	150	75	50	LOQ	20
Morphine (free)	20	10	20	LOQ	5
THC	2	1	2	LOQ	0.3

LOQ: limit of quantitation, *: (Grenzwertkommission, 2002).

before confirming the positive ones. Various authors validated these tests (Kemp, Sneed et al., 2002; Kupiec, DeCicco et al., 2002; Moore, Werner et al., 1999). For saliva, several laboratories now have a method by liquid chromatography coupled with tandem mass spectrometry, which allows them to quantify the main drugs on a sample of 250 μ L. The method of Mortier allows the sensitive determination of amphetamines, opiates and cocaine with a limit of detection of 2 ng/mL on a sample of 200 μ L, after extraction by a solid phase method (Mortier, Maudens et al., 2002). The method of Wood, limited to amphetamines, lasts only 20 minutes and has a limit of detection of 2 ng/mL (Wood, De Boeck et al., 2003).

Further research is needed to determine danger cut-offs, which would make communication of the risk clearer to the public, to simplify the analytical techniques in order to reduce the costs, and to harmonize methods between different countries.

DRIVING UNDER THE INFLUENCE OF DRUG [DUID] LAWS

Driving under the influence of drugs is generally covered in existing legislation in most nations around the globe. In the United States, DUID statutes are predominately found in the Transportation or Motor Vehicle Codes or Titles of the respective states' Codes or Statutes. In only three states (Idaho, Minnesota, and Texas) do you find the state's DUID statutes in the Penal Code or Criminal Title (Walsh, Danziger, et al. 2002). In Europe, some nations codify the DUID statutes within Traffic Law, or Public Health Code, and many countries (Czech Republic, Finland, Germany, Ireland, Norway, Poland, and Spain) also have provisions within the penal or criminal codes (Moeller, Steinmeyer, & Aberl, 2001).

In general practice, there are two approaches used to identify a drugged driver: (a) Impairment (Behavioral approach)—which involves documenting the behavior of the driver; and (b) The Analytical approach that involves the chemical testing of biological fluids for drugs. All DUID laws involve one or both of these approaches. There are three main types of DUID statutes: (1) Statutes requiring that drugs render a driver "incapable of driving safely"; (2) Statutes requiring that the drug "impair" the

driver's ability to operate safely or require a driver to be "under the influence" or "affected by an intoxicating drug"; and (3) "Zero Tolerance" per se laws which make it a criminal offense to have a drug or metabolite in the body while operating a motor vehicle.

DUID Laws in the United States

All of the states, except Texas and New York, use the phrase "under the influence" in their DUID statutes. A total of 14 states (Alabama, Arkansas, Illinois, Kansas, Nevada, Maryland, New Mexico, North Dakota, Oklahoma, Pennsylvania, South Dakota, Vermont, Wisconsin, and Wyoming) define the standard that constitutes "under the influence" within the body of the statute as "incapacity" (i.e., the influence of the drug "renders the driver incapable of safely driving"). Incapacity to drive safely is thus linked to the drug ingested and the prosecutor must show a connection between drug ingestion and the incapacity of the driver.

Eight states (Arizona, Florida, Hawaii, Indiana, Kentucky, Montana, South Carolina, and Virginia) use the standard of impairment to define "under the influence" so that the influence is such that the driver's abilities are impaired. This suggests a requirement of proof that is less stringent than one that renders the driver "incapable" of safely driving; nevertheless, the prosecutor must still prove that the impairment is directly related to the drug ingested.

In contrast to alcohol, the interpretation of drug concentrations in biological fluids, especially with regard to behavioral effect, requires some knowledge about the dose, the route of administration, the pattern or frequency of drug use, and the dispositional kinetics (distribution, metabolism, and excretion) of the drug. Interpreting the meaning of either drug/metabolite concentration in a single biological specimen with reference to impaired driver performance is therefore an extremely difficult task for a scientist and even more difficult for a prosecutor. The variables involved create a sufficiently great range of possible interpretations to render any specific interpretation questionable, other than to conclude the individual has used a specific drug in the immediate past (days) (Hawks & Chang, 1987). These complicated pharmacokinetic relationships have prevented the establishment of specific levels of drug concentrations, which could be interpreted as evidence of impairment either in blood, urine, or other bodily substance (Consensus Development, 1985). As a result, these factors make it very difficult for prosecutors to prove that a specific drug "caused" the driving impairment which is required under most state laws. Consequently, there is limited enforcement of DUID laws that require prosecutors to prove that drug consumption caused the driving impairment.

There are a total of 18 states that have variations of zero tolerance type "per se" legislation with regard to DUID. Five states (California, Colorado, Idaho, Kansas, and West Virginia) make it illegal for any drug addict or habitual user of drugs to drive a vehicle in their states. Two states (North Carolina, South Dakota) make it illegal for any person under the age of twenty-one to drive with any amount of a prohibited drug or

substance in their bodies. One state (Nevada) has determined that driving with specific cutoff levels of certain prohibited drugs or substances other than alcohol is a per se violation of its DUI statute. However, only ten states (Arizona, Georgia, Indiana, Illinois, Iowa, Minnesota, Rhode Island, Utah, and Wisconsin) will not tolerate any presence of a prohibited drug or substance in a driver's body while he/she is driving. In these states any amount of prohibited drug found in the blood or urine of drivers while operating a motor vehicle is a per se violation of those states' DUI statutes.

In most of these per se states the compelling argument for adoption of the per se statute was that a driver was far less likely to be prosecuted for impaired driving if he/she were under the influence of an illegal substance than if he/she were under the influence of a legal substance (alcohol). This dilemma existed because there was a per se level for alcohol but no practical or legal way to establish an impairment linked per se level for controlled substances. The per se strategy creates an important legal distinction between having to prove a nexus between the observed driver impairment and drug use (causal relationship) and simply demonstrating that observed impaired driving behavior was associated with specified concentrations of drug/metabolite in the individuals body while operating the motor vehicle. In essence, the per se drug statute attempts to remedy the inequality of dealing with alcohol and other drugs by making the per se drug limit "any amount" of a controlled substance, and by making this offense equivalent to the per se alcohol offense. Officials from the states with per se statutes indicate they are working well but to date there are no scientific studies to demonstrate effectiveness.

DUID Laws in the Europe

As in the United States, the DUID laws in Europe are generally similar across nations but each country has some unique nuances. Comprehensive reviews of the DUID statutes in most European countries can be found in the reports by Moeller, Steinmeyer, and Aberl (2001), Krueger, Perrine, Huessy, and Mettke (2000) and in the document on drugs and driving in the European legal database on drugs (EMCDDA 2003). These reports indicate that most European countries use a combined impairment and analytical approach. The Krueger et al., review indicates that most countries provide sanctions for drugged driving only in the case of actual impairment. In contrast with European alcohol laws, the mere analytical presence of drugs in the driver is not subject to punishment in these countries. However, as in the United States it is widely recognized in Europe that evidence of impairment due to drug consumption is difficult to gather and to prove. In recognition of these problems and the lack of data to define specific levels of drugs, some European countries have introduced an analytical zero limit. At this time five countries (Belgium, Germany, and Sweden, and more recently Finland and France) have enacted zero tolerance per se laws. In Sweden, in the first six month period that the per se law was applicable (the second half of 1999), the number of prosecuted cases increased

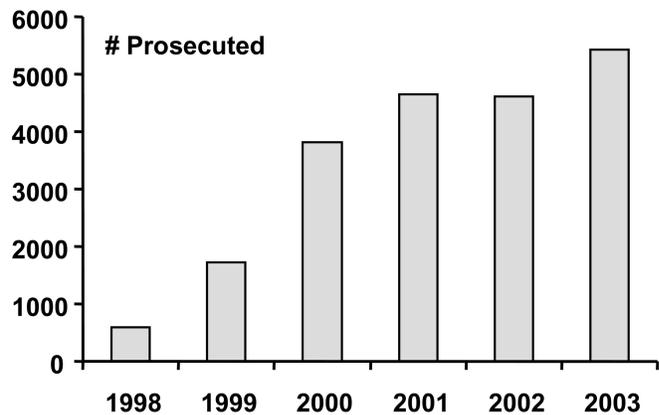


Figure 2 Number of suspects prosecuted for Drugged Driving in Sweden, 1998–2003. Source: Swedish Police Board.

five-fold. In 1999, 1700 drivers were arrested, while in 2000, there were 3800 cases, and by the end of 2003 over 5000 cases (see Figure 2). In Belgium, there were nearly no cases that were prosecuted before the per se law. In 2000–2001, 896 samples were analyzed by the National Institute for Criminalistics and Criminology in Brussels (Maes, 2003) and in 2003, there were 790 cases. In Germany, a study on the effect of the zero-tolerance law is underway, but the results are not yet known.

DUID Laws in Australia

The Parliament of Victoria Australia has recently amended the Road Safety Act of 1986 to focus enforcement efforts on drugged driving. The Road Safety (Drug Driving) Act 2003 allows police and other authorized officers to require oral fluid samples from drivers at the roadside for the purpose of drug testing. The act specifically authorizes testing for cannabis and methamphetamine and prohibits a driver from testing positive within three hours of driving. This legislation extends the existing enforcement system relating to drink-driving to the new drug-driving offences, such as requirements to cooperate in tests, power for police to prevent drivers who test positive to the target drugs from continuing their journey, and proof of offences through use of certificate evidence. This law is scheduled to take effect in 2004.

Globally, drugged driver legislation is very complex. Judge Roderick Kennedy (State of New Mexico, Court of Appeals) has written about the complexities of interpreting U.S. DUID law from a legal perspective:

Alcohol is a substance which affects the brain in a broad, non-specific fashion. That is, alcohol acts on the entire brain when it is present, in a pretty much uniform, predictable fashion. Drugs often (if not usually) don't act as broadly. Drugs act on specific areas, functions or receptors in the brain, and often with different results in different persons. Poly-drug abuse only increases the possibilities. In a "normal" drug case like possession or sale the problem pertaining to a drug is *what it is*. In DUI/DRUG cases, the issue is *what the drug does* Both cases can deal with amount of a drug, but in the first instance, the problem is purely

quantitative (how many units?), where the latter blends quantitative considerations with qualitative—is the amount of drug enough to impair this person at the time the person is driving? Lawyers familiar with the vagaries of alcohol effects can expect the effects and symptomatology of alcohol to look very stable compared to what happens when drugs, humans and vehicles hit the road. Quantifying driving behavior, quantifying drug doses which are sufficient to cause a decreased ability to drive a car, and then relating them all is challenging, to say the least. Add to this the differing statutory schemes nationwide (worldwide) concerning driving while under the influence of drugs, and the universal facts become merely that drivers ingest drugs that impair driving abilities, and drug-impaired drivers cause accidents. How these things are handled is not universal.

For a variety of reasons, existing laws often hinder the prosecution of drugged drivers. Notwithstanding sufficient evidence, it is often very difficult to prove a nexus between the observed impairment and a drug as required by most statutes. In addition, in most U.S. states, there is no incentive for police to look for drugs if alcohol is present above the legal limit because the law doesn't provide for additional penalties.

In a recent consensus development process (Walsh et al., 2002) experts agreed that per se DUID laws are an acceptable extension of DUI laws and represent a reasonable strategy to deal with the increasing problem of drugged driving. However, a critical point made repeatedly by police, prosecutors, and judges was that from a practical point, a per se DUID law is a good concept but not a panacea. Legal requirements and practicality tell us that reasonable suspicion, and ultimately, probable cause is required to obtain toxicological evidence of drugs in the person's body. Generally, judges will require that the state present some evidence of impairment, and have some reasonable suspicion that drugs have been used. If the state cannot meet these prerequisites, the analytical data may not be admissible in court. The consensus was that a per se DUID law could arguably facilitate or at least assist in the prosecution of drugged drivers and could produce real improvements in traffic safety.

SUMMARY

While we have limited knowledge of the prevalence of drugs other than alcohol in road traffic, it appears that drugged driving is a significant problem worldwide. There is a clear need for better data, more harmonization of data collection techniques, and a standardization of core data variables to establish a better epidemiological database. Further research is needed both for frequently used drugs, new drugs that will appear on the market, and different drug combinations and alcohol. It is recommended that such experimental studies should be more standardized according to proposed guidelines (de Gier, 1995). Accident studies where the cause or culpability is related to drug findings should be prioritized. As a background for risk factor calculations, larger roadside studies to evaluate the occurrence of drug use among the general driving population would be extremely valuable. The use of saliva combined with reliable on-site tests covering the most important drugs, offer tremendous potential

in this type of study. More research is needed to increase the reliability and sensitivity of on-site oral fluid drug tests. Moreover the newer drug-tests must be evaluated in the field in order to establish their value. Efforts should also be targeted to training of police officers in recognizing driving under the influence of drugs. Globally, there is a lack of uniformity in the way in which nations approach the drugged driver problem. Efforts to support standardization or harmonization of laws through the development of "model" legislation should be encouraged. There is a recent trend to adopt per se type statutes, which make it illegal to operate a motor vehicle with illicit drugs in the body but data to demonstrate the effectiveness of this strategy is still in development. Last, but not least, international collaboration between different countries would be most welcome and is highly recommended.

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