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Dr Mitchell A. Garber
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Oosterhout, 25 September 2001

Dear Dr Garber,

I hope all is well with you and that you get back to life after the terrible terrorists' attacks. My sympathy is with the victims and their families. I hope that people will come closer in order to improve our society instead of tear it down.

As I have announced in my e-mail of today, I enclose some materials that might be of interest in preparing the meeting in November. In case you need more information, please do not hesitate to contact me.

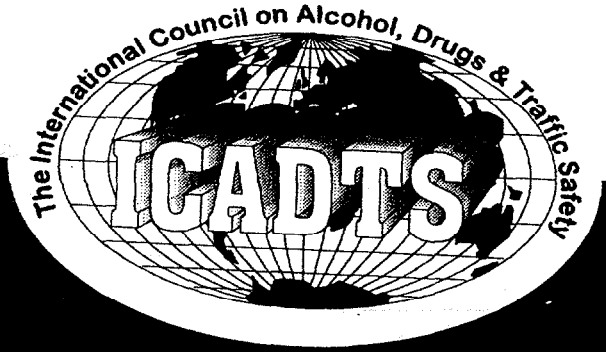
I look forward to meeting you soon.

Best regards,

Han de Gier

Encl: 5

PRESCRIBING AND DISPENSING GUIDELINES FOR MEDICINAL DRUGS AFFECTING DRIVING PERFORMANCE



International Council
on Alcohol, Drugs and Traffic Safety
(ICADTS)

Prescribing and Dispensing Guidelines for Medicinal Drugs Affecting Driving Performance

The ICADTS Working Group on
Prescribing and Dispensing Guidelines for Medicinal Drugs affecting Driving Performance

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March 2001

ICADTS is an independent nonprofit body whose goal is to reduce mortality and morbidity brought about by misuse of alcohol and drugs (licit and illicit) by operators of vehicles in all modes of transportation. To accomplish this goal, the Council sponsors international and regional conferences to collect, disseminate and share essential information among professionals in the fields of law, medicine, public health, economics, law enforcement, public information and education, human factors and public policy. The Council also publishes the proceedings of its conferences, reports of its working groups and a quarterly newsletter.

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1. BACKGROUND

At T97, the 14th International Conference on Alcohol, Drugs and Traffic Safety in Annecy, France the Chairman of the Road Safety Committee of the Parliament of Victoria (Australia) challenged delegates in his address to the closing ceremony with a clear message: "*Research has not been able to establish confidently for other drugs (than alcohol) the point at which a particular drug makes a driver unsafe on the road. Scientists disagree on what driving-related tasks are important to road safety or even how experiments should be conducted. No internationally agreed testing procedures exist for measuring the effects of drugs on driver performance*". In its report the Victorian Road Safety Committee recommended the development of international scientific guidelines (Parliament of Victoria, 1996). The speech called on experts in drugs and driving to step forward and use their knowledge to establish guide-lines that would underpin effective legislation and prevention.

The International Council on Alcohol, Drugs and Traffic Safety (ICADTS) Executive Board took up this challenge and decided to create a forum within the membership for where these problems could be examined and debated. The first step was the establishment of an ICADTS Working Group on *Standardisation of Impairment Levels for Licit and Illicit Drugs in Transportation*. That Working Group was later subdivided. One group was set up on illegal drugs and a second on prescribed medications. The report of the first group, *Illegal Drugs and Driving*, has been published by ICADTS (Walsh et al., 2000).

The first working group considered that management of drug issues in transportation was similar to the management of drug problems in the workplace as discussed in the report "*Management of Alcohol- and Drug-related Issues in the Workplace*" (ILO, Geneva, 1996). Aspects of the drug problem of relevance to the drugs and driving problem include: social issues, public education, identification and testing, intervention, and the linkage between alcohol and drug problems. The experience of dealing with these issues in the workplace should be more generally applicable and therefore benefit the discussion in respect to transportation.

However, the management of drug related issues in the transport system should not be limited to the regulation of impairment. Preventive approaches are known to effectively diminish or deter drug use by drivers. Early interventions, such as improving prescribing and dispensing medication for patients who drive, had the potential to be a more efficient approach to traffic safety than attempts to regulate active compounds in body fluids. An additional ICADTS Working Group was established to consider *Prescribing and Dispensing Guidelines for Medicinal Drugs Affecting Psychomotor Performance*. The members of this group have worked to prepare the current report to serve as an invitation to (inter)national organizations of physicians, pharmacists, drug manufacturers and patients to formulate joint statements on the need to develop criteria for better warning systems, guidelines for safe application of psychotropic drugs and systems for disseminating information on impairing properties of medi-cinal drugs.

2. OBJECTIVES

The primary objective of this report is to provide guidelines for safe prescribing and dispensing of medicinal drugs to patients who operate motor vehicles, or other transportation vehicles[1].

By developing recommendations for improving warning systems and effective dissemination of these guidelines the Working Group members have started an international debate aimed at making patients and their health care professionals more aware of their responsibilities in relation to transportation safety. The approach to medicines and safety must be shared between the health professionals and patients. The Working Group members believe that a multi-disciplinary approach is needed if prescribing guidelines are to be well accepted by the community.

The sharing of responsibility between patients and professionals implies the involvement of more actors than simply the prescribers and dispensers.

- The pharmaceutical industry and the drug regulatory authorities must be included. Their involvement is needed to improve warning statements for medicinal drugs affecting driving performance. If the warnings are to be meaningful they should be based on specific research conducted according to methodological guidelines accepted by the international scientific community (Vermeeren, et al. 1993; De Gier, 1998; Berghaus et al. 1999).
- Health educators play an essential role in raising awareness of traffic safety issues among those who eventually will guide patients who drive to adopt responsible behaviours pertaining to traffic safety. Obviously teachers in medical and pharmacy schools, driving instructors and those who educate law enforcement officers all need to be involved.
- Above all patients have a "right to know" about risks they may take when combining medication and driving. As users of potentially impairing medication they must be educated to demand better warning systems so that they can take appropriate safety precautions before operating their vehicles.

The Working Group hopes that this document will encourage the international acceptance of prescribing and dispensing guidelines by professional organizations and regulatory agencies. By informing their various memberships and starting discussions about the guidelines provided in this document, they will play a key role in solving problems related to the use of medicinal drugs by patients who want to receive treatments safe for driving.

[1] The term "driving" as used in this report is meant to refer to the operation of any transportation vehicle, not just motor vehicles and the term "motor vehicle" shall include all transportation vehicles.

3. SUMMARY

In the introduction of this report the Working Group describes how in general physicians update their knowledge about behavioural effects of medicinal drugs on driving performance. Most of the sources they use are not conclusive in explaining whether or not a particular patient will become an unsafe driver after using a specific psychotropic medication. The Working Group provides several recommendations how to improve the application of existing knowledge by using a graded level warning system (Chapter 5). Obviously the information to be disseminated should vary according to the target population (the patient-driver, physician, pharmacist, authorities with responsibilities in road safety and public health). Several key-messages to these respective subgroups are given (Chapter 6). The prescribing and dispensing guidelines allowing physicians and pharmacists to prescribe and dispense the least impairing medicinal drugs for drivers are presented in Chapter 7. Special attention has been given to include prescribing and dispensing information that will allow patients to be more aware of recognizing signs of impaired driving performance if drugs with little or no impairment cannot be used to treat their disorders. Chapter 8 describes the problem of ensuring that information concerning driving impairing properties of medicinal drugs is effectively communicated to physicians, pharmacists and patients. Several information 'tools', such as warning systems, package inserts, categorization of medicinal drugs and guidelines for good medical and pharmaceutical practice have been discussed along with the means of implementation (education, regulation, media, information and communication technologies). Conclusions and recommendations are summarized and presented in Chapter 9.

The Working Group assessed the available scientific knowledge regarding guidelines for the regulation of medicinal drugs and the operating of motor vehicles. As a result of this assessment, the following recommendations are made:

Regulatory authorities should

- **Implement warning systems that are effective and made clear in package inserts of medicinal drugs, all in accordance with present knowledge of the drug's effects on ability to drive.**
- **Discuss with health professionals, patients and drug manufacturers how a three-tier categorization system could be used as a practical reference in addition to present statements in package inserts, in order to improve warning systems for patients.**
- **Discuss new procedures for assigning label and insert warnings for medicinal drugs in order to develop a framework for drug manufacturers, physicians and pharmacists that will encourage them to apply a three-tier categorization system that identifies each drug's potential for affecting patient's driving ability.**
- **Improve the structure of guidelines to assist drug manufacturers in applying methodologies of drug testing that will allow categorization of drugs and reconsider the use of standardized information for the warning section in package inserts and drug information leaflets.**
- **Establish an independent international centre for maintaining a three-tier categorization system for drugs based on consensus among experts in the field of drugs and driving.**

Professional (national and international) organizations of physicians and pharmacists should

- **Discuss and propose joint efforts for improving their prescribing and dispensing practices concerning drugs with impairing potential for patients who drive or operate machines.**
- **Encourage their memberships to prescribe and dispense the least impairing or safe drug within each**

class as an alternative for more impairing ones.

- **Discuss the key-messages to be disseminated in order to improve knowledge and to change attitudes of their membership in respect to medication and transportation safety.**

- **Utilize information and communication technology (ICT) for encouraging the use of guidelines on prescribing and dispensing mediation and for documenting consultations with patients about their experiences with the driving impairing properties of the drug. The development of databases and software to support these activities should be encouraged.**

Authorities with responsibilities in transportation safety and public health should

- **Present recent evaluations on the quality of present warning systems (unique meaning, simple or complicated, readability, interpretation by the end-user, etc) and its effects on patients who drive.**

- **Review the present knowledge in their respective countries regarding the relative risks of injury-accidents by users of different types of psychotropic medication and facilitate the application of drug use and transportation accident data bases for extending their knowledge and further targeting their countermeasures.**

- **Discuss the development of new regulations with respect to medicinal drugs and driving with patient/consumer, and driver organizations in order to determine what new regulations should be applied in daily practice addressing the public and the individual patient who drives.**

- **Encourage physicians and pharmacists to implement prescribing and dispensing guidelines.**

- **Develop media campaigns to address relevant issues that will focus on changing roles of patients, drivers, health care professionals, police officers, educators and driving school instructors.**

Organizations and research institutes in the field of drugs and driving should

- **Disseminate information on the safe use of medicinal drugs by drivers via the internet, addressing both the public and professionals. Provide quality assurance for the users of this source of information.**

Driving licensing authorities should

- **Meet their obligation for assuring applicant's fitness to drive when issuing or renewing driving licences. Develop effective lines of communication with medical and pharmaceutical practitioners to acquire information on the driving fitness and medication history of applicants.**

Medical and pharmacy schools should

- **Develop their educational programs pertaining to drugs and driving and to update these, if needed, based on present knowledge for safe prescribing and dispensing.**

4. INTRODUCTION

In practice, physicians and pharmacists update their knowledge about the behavioural toxicity of medical drugs from three major sources:

i) Package inserts approved by the drug regulatory authorities provide some information about known impairment of driving ability caused by the relevant substances;

ii) Articles in scientific journals and drug bulletins which discuss impairment of psychomotor performance of healthy subjects and/or patients under various test conditions attributed to various substances or groups of substances;

iii) Product specific mailings by the pharmaceutical industry claiming that their products are safe for drivers, or giving general warnings.

Some jurisdictions have programs to study the prevalence of licit drugs in the general driving population and in (fatally) injured drivers. This data can be used to estimate the relative risk of involvement in traffic accidents attributable to certain drugs. However, in most countries such data is lacking or the available data does not allow reliable estimation of the impact of drugs due to methodological problems (De Gier, 1999). Even where epidemiological data exists, it describes population risk and not individual risk.

Physicians and pharmacists deal with individuals. They have to decide whether or not a particular patient will become an unsafe driver after using a specific psychotropic medication. Population studies are not easy to interpolate for the individual.

When clear statements are made about driving risk, the prescriber and dispenser may not know the scientific basis of this advice, and therefore cannot judge its validity for their patients. Although there is international consensus in the scientific community on the methodology that ought to be used in evaluating the risk of medication for driving, the regulatory authorities have not formally adopted any guidelines. Consequently there are no guidelines to ensure the pharmaceutical industry performs standardised research. Physicians and pharmacists erroneously assume that regulatory agencies 'know their jobs' and therefore reliable, standardised testing has been conducted.

A proposal to introduce a graded level warning system for medicinal drugs affecting driving performance was presented to the European Union in 1991. Such a system would allow prescribers to chose the least impairing medication within each therapeutic class of drugs (Wolschrijn et al., 1991). Although a framework has been proposed, no pan-European or national regulatory body is categorizing drugs on the basis of their hazard potential for driving (Alvarez and Del Rio, 1994; De Gier, 1998).

Consequently, many physicians find that the problem of drugs and driving remains such a complex one, and that no solution is evident. Clinicians know that medication can produce unpredictable effects on performance. Clinical experience teaches that drug side-effects vary from person to person and are compounded by polypharmacy and self-medication. Impairment is often worse when drugs are taken in combination with alcohol. The picture is further complicated by recognising that some medical conditions may themselves impair driving, if not treated properly with medication (e.g. epilepsy, allergic rhinitis, depression). The general principle is that it is usually best clinical practice to prescribe the least impairing member of a therapeutic class, where a suitable drug is available.

When physicians have doubts about the ability of a patient to drive safely when undergoing drug treatment, they need to advise the patient to avoid driving. The required counselling is time-consuming. The message that medication is necessary but makes driving hazardous is hard for the prescriber to give and the patient to hear. Proper explanation requires a clear understanding of the risks of accident involvement under different treatment conditions.

There are good examples of pharmacoepidemiology research, in which drug-use data in a given population is linked to accident data in the same population to estimate relative risk. These studies show that patients exposed to

various types of psychotropic medication, such as benzodiazepines, are at increased risk (Herings, 1994; Hemmelgarn et al., 1997: Neutel, 1998; Barbone et al., 1998). Table 1 presents data showing the overall risk of some particular benzodiazepines and one cyclopyrollone hypnotic used in therapeutic doses and comparable blood alcohol concentrations.

Table 1. Relative risks of injurious road traffic accidents associated with the use of particular hypnotic and anxiolytic drugs and comparable blood alcohol concentrations (from Borkenstein et al., 1974).

Drug	Relative Risk	Comparable to BAC (%)	Reference
Diazepam	3.1	0.075	Neutel, 1998
Flurazepam	5.1	0.095	Neutel, 1998
Lorazepam	2.4	0.070	Neutel, 1998
Oxazepam	1.0	0.050	Neutel, 1998
Triazolam	3.2	0.075	Neutel, 1998
Zopiclone	4.0	0.080	Barbone et al.,1998

The risk is highest during the first two weeks of treatment. Extremely high relative risks have been reported with certain benzodiazepines: for example a 5 to 6 fold increase in accident risk, which is comparable to a blood alcohol concentration of 0.1% (Neutel, 1995). This implies that patients who commence treatment with a benzodiazepine must be advised that they should not drive in the first two weeks of treatment. If physicians do not give this advise, their patients have an increased risk of being involved in accidents, but do not know that they are taking the risk. Patients have a right to receive adequate information to enable them to decide whether or not to drive.

The following chapters will provide information needed by those who have to be involved in improving the decision making process by drug prescribers, dispensers and users.

5. A GRADED LEVEL WARNING SYSTEM

The European Union (EU) has formally defined criteria that allow categorization of drugs according to their impairing properties. The EU's Committee for Proprietary Medicinal Products (CPMP) Operational Working Party stipulated in its Note for Guidance for the Summary of Product Characteristics (III/9163/90-EN, Final approval 16 October 1991) that all medicines registered after 1 January 1992 can be categorized within the 'Warning' section of package inserts with respect to 'Effects on ability to drive or operate machines'. Article 4.7 in the original Note for Guidance states the following:

On the basis of

- *the pharmacodynamic profile, reported ADR's (adverse drug reactions) and/or*
- *impairment of drug performance or performance related to driving,*

the medicine is:

1. *presumed to be safe or unlikely to produce an effect;*
2. *likely to produce minor or moderate adverse effects;*
3. *likely to produce severe effects or presumed to be potentially dangerous.*

For situations 2 and 3, special precautions for use/warnings relevant to the categorization should be mentioned.

The original Note for Guidance (III/9163/90-EN) has been included in the rules governing medicinal products in the EU (Note for Applicants, Volume 2A, Procedures for marketing authorization, July 1997). In the latest version the reference "relevant to the categorization" in the last sentence has been omitted and the numerals "1, 2 and 3" for the categories have been replaced by "a, b and c".

Although every national regulatory authority usually follows EU guidelines closely, the categorisation has not been implemented according to a recent survey (De Gier, 1998).

International scientists proposed this three-tier categorization as the most feasible approach for the most frequently used psychotropic drugs (Wolschrijn et al., 1991). Information on this categorization and suggested drug lists was published in 1997 by the German Pharmacists Association (ABDA) and sent out to all German pharmacists (ABDA, 1997).

In Belgium, new legislation for detecting and prosecuting illicit drug use by drivers was accompanied by a campaign to inform the public and health care professionals about problems arising from the use of medicinal drugs by drivers (Grenez et al, 1999). The reason for addressing this issue is obvious: the proportion of European drivers taking medicinal drugs that could impair driving is 5 to 10 times higher than the proportion taking illicit drugs (De Gier, 1995). The Belgian campaign produced two leaflets, one for physicians and pharmacists explaining the various drugs in each of the different categories and one for patients summarizing this information. Unfortunately the list of drugs within categories has not been regularly updated.

International concerted action is required to extend the categories of drugs and make the lists more specific for the effects of different doses of the same drug and duration of action (e.g. for hypnotics). It is the Working Group's belief that new initiatives are needed, first by approaching drug regulatory and health care authorities in Europe, the USA and Australia for funding an international documentation and information centre responsible for maintaining the drug categorization system.

The following recommendations should be considered by drug regulatory and health care authorities for implementing a graded level warning system:

5.1 Discuss with health professionals, patients and drug manufacturers how a three-tier categorization system could be used as a practical reference in addition to present statements in package inserts, in order to improve warning systems for patients.

5.2 Discuss new procedures for assigning label and insert warnings for medicinal drugs in order to develop a framework for drug manufacturers, physicians and phar-macists that will encourage them to apply a three-tier categorization system that

identifies each drug's potential for affecting patient's driving ability.

5.3 Improve the structure of guidelines to assist drug manufacturers in applying methodologies of drug testing that will allow categorization of drugs and reconsider the use of standardized information for the warning section in package inserts and drug information leaflets.

5.4 Establish an independent international centre for maintaining a three-tier categorization system for drugs based on consensus among experts in the field of drugs and driving.

6. DISSEMINATION OF INFORMATION REGARDING MEDICINAL DRUGS AND DRIVING PERFORMANCE / FITNESS.

Research efforts in drugs and driving over the last two decades have not resulted in the provision of adequate information to the key-players, such as the driver-patient, prescribing physician and dispensing pharmacist. There is a lag time of many years before standard medical and pharmaceutical practice has adopted new treatment guidelines. Therefore authorities with responsibilities in the field of health care and transportation safety should make every effort to disseminate new information regarding medicinal drugs and driving performance as it becomes available. This chapter will be dedicated to the question *what* information needs to be disseminated. The question *how* this information should be disseminated will be discussed in the following chapters.

One of the key-messages on *what* information needs to be disseminated is the application of the three-tier categorization system. In order to make physicians, pharmacists and patients aware of the meaning of each category a comparison to the impairing effects of alcohol, which are well known, is suggested. Data collected in experimental research, in which over-the-road driving tests have been applied with most frequently used medicinal drugs and alcohol (as "calibration"), have allowed researchers to interpret weaving effects by any drug as equivalent to that produced by a particular blood alcohol concentration (BAC) (Louwerens et al., 1987). It will be easier to understand the severity of impairment by medicinal drugs if this concept could be communicated as follows:

Category	Impairment description for medicinal drugs	Comparison with Blood Alcohol Concentration (BAC)
I	Presumed to be safe or unlikely to produce an effect	Equivalent to BAC < 0.2 g/l (< 0.02%)
II	Likely to produce minor or moderate adverse effects	Equivalent to BAC 0.2- 0.5 g/l (0.02-0.05%)
III	Likely to produce severe or presumed to be potentially dangerous	Equivalent to BAC > 0.5 g/l (>0.05%)

Obviously, the information to be disseminated should vary according to the target population. The following target groups are suggested:

i) The patient-driver,
ii) Physicians and pharmacists,
iii) Authorities with responsibility in the field of road safety and public health.

The key-messages to these respective subgroups are the following:

- To the patient-driver:
  i) Recognise that some medicinal drugs impair driving performance / fitness more than others, and this has not been disclosed in package inserts.
  ii) Ask for further information from health care professionals about how to detect a possible impairing effect and what to do about signs of impairment.
  iii) Avoid the increased risk of medicinal drug effect on driving performance in case of the use of more than one drug, the use of over-the-counter drugs, and the use of alcohol along with the drug by following instructions given by the physician and the pharmacist.

- To the physicians and pharmacists:
  i) Know the medicinal drugs that can impair driving performance/fitness, according to their categorization.
  ii) Know how to select the least impairing medicinal drugs within each therapeutic class and apply the lowest possible dose.

iii) Inform the patient properly concerning the potential hazardous effects of the prescribed medication on driving performance, and provide them with clear instructions such as an advice not to drive at the start (two weeks) of some treatments (for example a benzodiazepine treatment).

- To the authorities with responsibility in the field of transportation safety and public health:
  i) Inform and convince the public and healthcare professionals that driving under the influence of certain medicinal drugs poses a risk to transportation safety.
  ii) Facilitate new research efforts, such as case-controlled pharmacoepidemiological surveys based upon existing data bases to determine the relative risk of traffic accidents for users of all drugs identified as potentially hazardous and disseminate the outcomes.
  iii) Review the initiatives that have been undertaken in other countries to reduce driving under the influence of medicinal drugs and apply the results of these initiatives if possible.

The following recommendations should be considered for defining the information to be disseminated regarding medicinal drugs and driving performance:

6.1 National and international (professional) organizations of patients, physicians and pharmacists should discuss the key-messages to be disseminated in order to improve knowledge and to change attitudes of their membership in respect to medication and transportation safety.

6.2 Authorities with responsibilities in transportation safety and public health should review the present knowledge in their respective countries regarding the relative risks of injury-accidents by users of different types of psychotropic medication and facilitate the application of drug use and transportation accident data bases for extending their knowledge and further targeting their counter-measures.

7. GUIDELINES FOR PRESCRIBING PHYSICIANS AND DISPENSING PHARMACISTS

In medical care it is standard practice to apply protocols for diagnosing and treating various medical conditions. In cases where medication has been selected as the preferred treatment option, side effects of medication that could harm the patient or diminish the drug's action should be avoided. In pharmaceutical care it is becoming standard practice to follow up patients who have indicated drug related problems that cause treatment failure or harm to the patient (Cipolle et al., 1998; Van Mil, 2000). Special attention is normally given to patients receiving a drug for the first time. In cases in which pharmacists have built trusting relationships with patients it is feasible to extend their services to include a duty of care for safe use of medication. In many European countries, the USA and Australia such pharmaceutical care is being well received, not only by the pharmacists, but also by health care authorities. These authorities are aware that this valuable pharmaceutical knowledge has been under-utilised for many years.

Guidelines for prescribing and dispensing practice must ensure that patients will get the maximum benefit of this knowledge. Ideally, all advice given to patients will have the approval of the respective professional organizations of physicians and pharmacists. It makes sense to involve educators and trainers in this process, so that all graduates understand their responsibilities and the advice they should give. In addition present knowledge of drug categorization should be used to adjust the existing guidelines for all major complaints and illnesses for which psychotropic drugs are prescribed. In other words: if psychotropic medication is the selected treatment option, the guidelines must refer to the benefits of using the least impairing drug within that therapeutic class.

Patient education has to be a substantial part of the prescribing and dispensing guidelines. Patients need to be educated about how to detect any undesirable effects on psychomotor functioning at the start of treatment and at all follow-up visits if repeat medications are prescribed. The advice given should be presented orally and in writing for maximum effectiveness. In rational prescribing and dispensing the following key-messages can be defined as essential parts (general and drug specific) of the guidelines to be developed for some frequently used therapeutic drug classes (O'Hanlon, 1995; Taylor, 1995; Del Rio and Alvarez, 1995; Alvarez, 1997; De Gier, 1997):

Prescribing Guidelines	**Dispensing Guidelines**
1. Realize that the use of some psychoactive drugs has been associated with an increased risk of causing an injurious accident and that patients should receive this information.	1. Discuss with prescribing physicians what patient information (written and oral) should be provided at the first delivery of a particular impairing drug
2. Consider an alternative in the light of experimental research showing large differences between the effects on driving performance of various drugs within the same therapeutic class .	2. Inform the prescribing physician that alternative drugs exist in case a drug in class II or III has been prescribed, and inform the patient.
3. Start with the lowest doses of psychoactive medical drugs and whenever possible avoid multiple dosing over the day.	3. Advise the physician to prescribe the lowest effective dose of a particular psychoactive medicinal drug and to avoid multiple dosing over the day . Inform the patient.
4. Do not reflexively "double the dose" if patients fail to respond to psychoactive medication.	4. Advise the physician to try another drug if the patient reports a lack of efficacy after beginning of treatment and inform the patient. If higher doses are needed advise the patient to use the largest part before sleep.
5. Avoid prescribing different psychoactive drugs in combination.	5. Explain to the patient that poly-therapy with psychoactive drugs is always an experiment with the patient's safety and to avoid driving if treatment can not be adjusted.

Prescribing Guidelines	Dispensing Guidelines
6. Do not rely upon the manufacturers' advice for counselling patients about the effects of drug upon driving.	6. Explain to the patient why warnings provided by the manufacturer about their drug's effects on driving are vague, illogical and sometime misleading.
7. Advise patients concerning the ways they can minimize the risk of causing a traffic accident if it is impossible to avoid prescribing an obviously impairing drug or one with unknown impairing potential (see next Table).	7. Advise the patient the ways they can minimize the risk of causing a traffic accident if they have to use a drug with an impairing potential (see next Table).
8. Monitor the patient's driving experience with the drug.	8. Monitor the patient's driving experience with the drug (e.g. at the first refill) and report back to the physician or ask the patient to inform the physician.

The prescribing and dispensing guidelines need to include drug class-specific guidelines in which reference to the least impairing drugs within the class can be given, as well as risk factors, and additional prescribing and dispensing information. Although it is difficult to advise a safe drug in drug classes in which these are not really available (e.g. the hypnotics), safer alternatives for anxiolytics and antidepressants exist. For example selective serotonin reuptake inhibitors are safe with little or no impairment of driving performance, as shown in experimental and epidemiological studies (Ramaekers, 1998; Barbone et al., 1998). These drugs are also effective in the treatment of anxiety disorders (Ballenger, 1999). Another safer alternative in treating generalized anxiety disorders is venlafaxine, an antidepressant acting by selective serotonin and norepinephrine reuptake inhibition (O'Hanlon et al., 1998).

The information provided in the next table are examples of drug class specific guidelines.

Drug class	Drugs with little or no impairment	Risk factors	Prescribing information	Dispensing information
Hypnotics	> 10 h post dosing; taken at night: Temazepam 10 mg Lormetazepam 1 mg Zolpidem 10 mg	Combination with other psychoactive drugs Liver and/or renal dysfunction (elderly patients: half the normal dose)	Avoid prescribing for longer than 2-4 weeks	1. Avoid alcohol while taking this drug If drugs with little or no impairment can NOT be dispensed and/or at the beginning of treatment (also with least impairing one) focus on: 2. Recognize signs of impaired driving performance (stop for rest if any occur): • Blurred vision • Difficulty in concentrating or staying awake • Unusual surprise by ordinary traffic events • Not being able to remember how exactly you came at destination • Difficulty in holding steady course in traffic lane 3 Avoid taking longer than 2-4 weeks and more than one at night

Drug class	Drugs with little or no impairment	Risk factors	Prescribing information	Dispensing Information
Tranquillizers	Buspirone 10 mg b.d.s.	No specific risk factors known	Avoid combination with selective serotonin reuptake inhibitors (SSRIs) because of reduced therapeutic effect Consider combination for 1 week with oxazepam 10 mg t.d.s. if therapeutic response seems to be inadequate (forbid driving during the first week)	1. Avoid alcohol while taking this drug If drugs with little or no impairment can NOT be dispensed and/or at the beginning of treatment (also with least impairing one) focus on: 2. Recognize signs of impaired driving performance (stop for rest if any occur): • Blurred vision • Difficulty in concentrating or staying awake • Unusual surprise by ordinary traffic events • Not being able to remember how exactly you came at destination • Difficulty in holding steady course in traffic lane
	SSRI's are effective in more than 60% of patients with generalized anxiety disorders : Fluoxetine 20 mg OD Paroxetine 20 mg OD	No specific risk factors known	Avoid combined use of fluoxetine and nonselective MAOIs, tryptophan, selegiline, terfenadine (adverse drug interactions) Avoid combined use of paroxetine and nonselective MAOIs, (dex)fenfluramine and selegiline (adverse drug interactions)	
	Venlafaxine 75-150 mg q.d. (an SNRI effective in more than 80% of patients with generalized anxiety disorders)	No specific risk factors known	Avoid combined use of venlafaxine and nonselective MAOIs (adverse drug interactions)	

Drug class	Drugs with little or no impairment	Risk factors	Prescribing information	Dispensing Information
Anti-depressants	Fluoxetine 20 mg OD Moclobemide 200 mg b.d.s. Paroxetine 20 mg OD	No specific risk factors known	Avoid combined use of fluoxetine and nonselective MAOIs, tryptophan, selegiline, terfenadine (adverse drug interactions) Avoid combined use of moclobemide and dextromethorphan, (tricyclic) antidepressants, (pseudo)ephedrine (adverse drug interactions) Avoid combined use of paroxetine and nonselective MAOIs, (dex)fenfluramine and selegiline (adverse drug interactions)	1 Avoid alcohol while taking this drug. If drugs with little or no impairment can NOT be dispensed and/or at the beginning of treatment (also with least impairing one) focus on: 2 Recognize signs of impaired driving performance (stop for rest if any occur): • Blurred vision • Difficulty in concentrating or staying awake • Unusual surprise by ordinary traffic events • Not being able to remember how exactly you came at destination • Difficulty in holding steady course in traffic lane
	Venlafaxine 75-150 mg q.d. (an SNRI effective in more than 80% of patients with generalized anxiety disorders)	No specific risk factors known	Avoid combined use of venlafaxine and nonselective MAOIs (adverse drug interactions)	
Anti-histamines	Ebastine 20 mg OD Loratidine 10 mg OD Fexofenadine 60 mg b.d.s. or 120 mg/180 mg OD	Liver and/or renal dysfunction		1. Avoid alcohol while taking this drug If drugs with little or no impairment can NOT be dispensed and/or at the beginning of treatment (also with least impairing one) focus on: 2. Recognize signs of impaired driving performance (stop for rest if any occur): • Blurred vision • Difficulty in concentrating or staying awake • Unusual surprise by ordinary traffic events • Not being able to remember how exactly you came at destination • Difficulty in holding steady course in traffic lane

NOTE:
Driving licensing authorities in different countries will identify minimum standards of mental and physical fitness to drive with respect to the regular use of psychotropic agents by applicants for or holders of a driving

licence. Both physicians and licensing authorities need to be clear on the restrictions to be applied in the case of regular use of high therapeutic doses being prescribed when a patient holds a driving licence. In particular, drivers of heavy vehicles require specific medical examination according to some laws. The licensing authorities should know the actual drug use by the applicant before issuing or renewing driving licences and decide on possible adverse effect on driving based upon the quantity of the drug taken by the applicant. But, how do licensing authorities know when applicants are taking drugs that hamper their ability to drive? European directives call for knowledge that licensing authorities cannot have under the present system, where there is no direct communication with prescribing physicians.

The following recommendations should be considered for defining the guidelines for prescribing physicians and dispensing pharmacists:

7.1 **National professional organizations of physicians and pharmacists should discuss and propose joint efforts for improving their prescribing and dispensing practices concerning drugs with impairing potential for patients who drive or operate machines.**

7.2 **Authorities with responsibilities in transportation safety and public health should encourage physicians and pharmacists to implement prescribing and dispensing guidelines.**

7.3 **Driving licensing authorities should meet their obligation for assuring applicant's fitness to drive in issuing or renewing driving licences. Develop effective lines of communication with medical and pharmaceutical practitioners to acquire information on the driving fitness and medication history of applicants.**

8. IMPLEMENTATION STRATEGIES

The objective of this chapter is to describe the problem of ensuring that information concerning driving impairing properties of medicinal drugs is effectively communicated to physicians, pharmacists and patients.
For each topic we should ask ourselves "What has been published to show the impact of existing means of implementation?". Furthermore, it is important to mention what we don't know.

Information 'tools':
1. Warning systems
2. Package inserts
3. Categorization of medicinal drugs
4. Guidelines for good medical and pharmaceutical practice

Means of implementation:
1. Education
2. Regulation
3. Media
4. Information and Communication Technology (ICT)

Warning systems
The effect of warning systems, such as warning labels and pictograms affixed to drug packages, so far has not yet been shown to change attitudes of drivers. Only a few small scale studies are known in the Netherlands and Sweden, but these were carried out almost twenty years ago (Stout and de Gier, 1982). Present warning systems are dichotomous in nature and do not take into account
- the differences in impairing properties of different substances within one therapeutic class
- the dose of the psychotropic drug
- the time after administration (hypnotics)

Although information on these issues exists from experimental research, warning systems have not been changed to include this knowledge in the presentation of the system. Furthermore, as far as we know, prescribing physicians and dispensing pharmacists do not communicate the differences in impairing properties between members of a class of drugs to patients.

This question needs to be addressed by the responsible government bodies and professional organizations. They need to review the recent evaluations on the quality of the warning system (unique meaning, simple or complicated, readability, interpretation by the user, etc) and its effect on the patient who drives. The question should be addressed to:
- Health authorities responsible for market authorization of medicinal drugs, health care, and welfare.
- Pharmaceutical manufacturers
- Experts in patient education
- Politicians
- Consumer/patient organizations
- Professional organizations of physicians and pharmacists

Warning systems can be implemented if regulatory authorities decide to include the system as part of drug regulation. Media, education and ICT will be instrumental in the actual application of the warning system by physicians, pharmacists and patients who drive.

Package inserts
There is a legal requirement to provide package inserts with medicinal drugs written in lay language. However, there has been little evaluation of whether or not the information provided under the section "Effects on ability to drive", is clear and understandable. Information on what the patient has to do in order to decide whether he or she can drive is vague, illogical and sometimes misleading. It should be clear whether it is safe to drive or not and under what circumstances (e.g. in combination with alcohol and other drugs). There is little or no information on what a patient can do personally to detect serious impairing properties of the drug.

The need for implementation of more effective information related to driving should be stressed to the responsible organizations (see the list presented above under warning systems). The application of a warning system should be clear in the package insert and should be in accordance with descriptions of the drug's adverse side effects concerning impairment of the ability to drive.

Categorization system for medicinal drugs affecting driving performance
Experience in the Netherlands, Germany, Belgium and Spain indicates that a cate-

gorization system for medicinal drugs affecting driving performance can be used to sensitise healthcare professionals and the public. Although there is some debate about whether or not there is need for three or more categories, there is sufficient knowledge and expertise to develop more standardization in determining the categorization for each drug. The use of a categorization system as a practical method to interpret long lists of adverse effects and warnings in package inserts seems to be promising.

Data from experimental research shows that there are extremes at both ends: the least impairing and the most impairing drug within each therapeutic class. It makes no sense to wait till all available psychotropic drugs have been assigned to one specific category. The use of the least impairing or safe drug within each class as an alternative to the more impairing ones needs to be promoted among physicians and pharmacists. This is a first step of implementing the categorization system and should have great impact in reducing drug related accidents.

Guidelines

The medical guidelines for prescribing must not only focus on prescribing the least impairing drug but also on increasing knowledge about the actual experience patients have with the prescribed medication. This is of particular interest in the case of renal or liver dysfunction where combinations of drugs are known to cause adverse reactions due to drug-drug interactions and where there is increased susceptibility for specific side effects especially with alcohol. This is of importance both for professional drivers and private drivers. The support of dispensing pharmacists in providing pharmaceutical advice should be studied further in order to provide guidelines for the further development of integrated care in which the information flows are standardised and shared among the different health care providers involved in caring for the patient.

Recognising that the first two weeks of benzodiazepine use are associated with collision risks higher than blood alcohol concentrations greater than 1.0 g/l (0.1%), a physician should prohibit a patient from driving for two weeks after starting the benzodiazepine (or any other psychotropic drug) and ask for feedback before prescribing a refill . At all times patients should be advised not to drive the first 2-4 hours after drug intake. It should be stressed to national and international professional organizations of physicians and pharmacists that benzodiazepines currently are the most widely prescribed psychotropic drugs and therefore of particular relevance with respect to increasing accident risks of patients who drive. Professional support in constructing new guidelines is paramount.

Special attention should also be directed to patients who are multi-drug users, whether for therapeutic purposes or who combine prescribed medication with illicit drugs. Guidelines should allow physicians to prohibit patients from driving while using a combination of drugs known to impair driving.

Education

The Working Group believes that physicians and pharmacists have a responsibility to know all about drugs and driving Professional education about drugs and driving is not recognized as a special topic in most countries. Medical and pharmacy schools should be asked to develop specific educational programs covering the risks of drugs and driving Research is also required to determine whether education of driving instructors, police officers and teachers in primary and secondary schools deals with this topic adequately. A starting point would be to develop five relevant questions that all health care professionals, police officer or driving instructors should consider when discussing drug impairment with patients, drivers, or applicants for a driving licence.

Most traffic laws prohibit driving licenses from being issued or renewed for applicants or drivers who are dependent on or regularly abuse psychotropic substances. This can be made clear to drivers or applicants, as a specific reason to avoid drug dependence.

Regulation

It is obvious that national regulations should provide better warning systems, and package inserts based on a categorization system for drugs impairing driving performance. If the regulations were stronger, guidelines for health

care professionals and educational programs on how to apply this knowledge will follow naturally. Collaboration between regulators and professionals should be encouraged to facilitate the development of guidelines and educational programs. There has to be partnership instead of an attitude of 'wait and see what will happen'. Health authorities should provide drug information bulletins free of charge to all health care professionals to update their knowledge.

Special attention should be given to patients who use high doses of psychotropic drugs and/or multiple drug users. European directives (Second Council Directive 91/439/EEC, Annex III, Art. 15.1) state that "Driving licences shall not be issued to, or renewed for, applicants or drivers who regularly use psychotropic substances, in whatever form, which can hamper the ability to drive safely where the quantities absorbed are such as to have an adverse effect on driving. This shall apply to all other medicinal products or combinations of medicinal products which affect the ability to drive". The Working Group believes that standard medical practice should be in accordance with this regulation.

Acceptance of any new or proposed regulation by the public is important. Therefore, it is of paramount importance to involve patient and consumer organizations in discussing the development of new regulations and how they should be applied in daily practice.

Media

The specific impact of media campaigns concerning drugs and driving is generally not known. However, changes in regulations and professional activities in relation to patients who drive needs to be disseminated so that thoughtful individuals can alter their behaviour. Media campaigns will support this if they are clear and well constructed to address the relevant issues. The impact will be greater if health care professionals, police officers, educators and driving school instructors have accepted their changing roles. Changing the behaviour of patients and drivers requires the dissemination of good information and education before decisions are made about drug treatment and/or driving while taking medication. Therefore, timing and coordination of activities will be crucial in achieving safety objectives.

Information and Communication Technology (ICT)

There are two important developments in Information Technology that will facilitate dissemination of information on drugs and driving. First the Internet provides many sources of information for the public and professionals. The standard of the information is very variable. The major organizations involved in traffic safety, drugs and driving should be asked to to provide quality assurance so that the users know which sources are reliable.

The second development is the application of ICT in the practice of prescribing or dispensing. The implementation of guidelines, the documentation of consultations with patients about their experiences with the driving impairing properties of the drug and the communication of feedback to the prescriber are facilitated by computerization in daily practice. The development of quality databases and software to support these should be encouraged.

The following recommendations should be considered for defining strategies to increase awareness and implement knowledge concerning driving impairing properties of medicinal drugs:

8.1 Responsible governmental bodies and organizations in transportation and public health should present recent evaluations on the quality of present warning systems (unique meaning, simple or complicated, readability, interpretation by the end-user, etc) and its effects on patients who drive.

8.2 Regulatory authorities should implement warning systems that are effective and made clear in package inserts of medicinal drugs, all in accordance with present knowledge of the drug's effects on ability to drive.

8.3 **Professional organizations of physicians and pharmacists should encourage their memberships to prescribe ands dispense the least impairing or safe drug within each class as an alternative for more impairing ones.**

8.4 **Medical and pharmacy schools should develop their educational programs pertaining to drugs and driving and to update these, if needed, based on present knowledge for safe prescribing and dispensing.**

8.5 **The development of new regulations with respect to medicinal drugs and driving should be discussed with patient/consumer, and driver organizations in order to determine what new regulations should be applied in daily practice addressing the public and the individual patient who drives.**

8.6 **Media campaigns should be clear and well constructed to address relevant issues that will focus on changing roles of patients, drivers, health care professionals, police officers, educators and driving school instructors.**

8.7 **Organizations in the field of drugs and driving should disseminate information on the safe use of medicinal drugs by drivers via the internet, addressing both the public and professionals. Provide quality assurance for the users of this source of information.**

8.8 **Professional organizations of physicians and pharmacists should utilize information and communication technology (ICT) for encouraging the use of guidelines on prescribing and dispensing medications and for documenting consultations with patients about their experiences with the driving impairing properties of the drug. The development of databases and software to support these activities should be encouraged.**

9. CONCLUSIONS AND RECOMMENDATIONS

A challenge was issued to the International Council on Alcohol, Drugs and Traffic Safety at the 14th International ICADTS Conference in Annecy, France (1997), to recommend international guidelines to assist in the regulation of medicinal drugs and driving. A Working Group was formed to consider the scientific basis for recommendations.

The Working Group concludes that the major problem is the lack of clear statements made about driving risk after taking psychotropic medication. This is surprising since there is now a vast body of evidence based on results from experimental and epidemiological research that shows that clear statements are feasible. Some drugs within a therapeutic class are considered as incompatible with driving (likely to produce severe adverse effects or presumed to be potentially dangerous), whereas others have minor effects or are presumed to be safe. These messages have not reached the prescribing physicians and dispensing pharmacists to an extent that they have improved their practices. Regulatory bodies should play a more defining role in changing this situation. The Working Group members conclude that a multidisciplinary approach is needed if prescribing and dispensing guidelines are to be well accepted by the community.

The sharing of responsibility between patients and professionals implies the involvement of more actors than simply the prescribers and dispensers.

- The pharmaceutical industry and the drug regulatory authorities must be included. Their involvement is needed to improve warning statements for medicinal drugs affecting driving performance. If the warnings are to be meaningful they should be based on specific research conducted according to methodological guidelines accepted by the international scientific community.
- Health educators play an essential role in raising awareness of traffic safety issues among those who eventually will guide patients who drive to adopt responsible behaviours pertaining to traffic safety. Obviously teachers in medical and pharmacy schools, driving instructors and those who educate law enforcement officers all need to be involved.
- Above all patients have a "right to know" about risks they may take when combining medication and driving. As users of potentially impairing medication they must be educated to demand better warning systems so that they can take appropriate safety precautions before operating their vehicles.

The Working Group members believe that an international debate aimed at making patients and their health care professionals more aware of their responsibilities in relation to transportation safety is just a first step. The proposed guidelines in this report are a second step and show how scientific knowledge can be applied for establishing practical guidelines to improve medical and pharmaceutical care. It is concluded that more collaboration between authorities in transportation safety and public health pertaining to the drugs and driving issues will eventually lead to more acceptance of these practice guidelines by the community. The Working Group therefore recommends that

Regulatory authorities should

9.1 Implement warning systems that are effective and made clear in package inserts of medicinal drugs, all in accordance with present knowledge of the drug's effects on ability to drive.

9.2 Discuss with health professionals, patients and drug manufacturers how a three-tier categorization system could be used as a practical reference in addition to present statements in package inserts, in order to improve warning systems for patients.

9.3 Discuss new procedures for assigning label and insert warnings for medicinal drugs in order to develop a framework for drug manufacturers, physicians and pharmacists

that will encourage them to apply a three-tier categorization system that identifies each drug's potential for affecting patient's driving abi-lity.

9.4 Improve the structure of guidelines to assist drug manufacturers in applying methodologies of drug testing that will allow categorization of drugs and reconsider the use of standardized information for the warning section in package inserts and drug information leaflets.

9.5 Establish an independent international centre for maintaining a three-tier categorization system for drugs based on consensus among experts in the field of drugs and driving.

Professional (national and international) organizations of physicians and pharmacists should

9.6 Discuss and propose joint efforts for improving their prescribing and dispensing practices concerning drugs with impairing potential for patients who drive or operate machines.

9.7 Encourage their memberships to prescribe and dispense the least impairing or safe drug within each class as an alternative for more impairing ones.

9.8 Discuss the key-messages to be disseminated in order to improve knowledge and to change attitudes of their membership in respect to medication and transportation safety.

9.9 Utilize information and communication technology (ICT) for encouraging the use of guidelines on prescribing and dispensing medication and for documenting consultations with patients about their experiences with the driving impairing properties of the drug. The development of databases and software to support these activities should be encouraged.

Authorities with responsibilities in transportation safety and public health should

9.10 Present recent evaluations on the quality of present warning systems (unique meaning, simple or complicated, readability, interpretation by the end-user, etc) and its effects on patients who drive.

9.11 Review the present knowledge in their respective countries regarding the relative risks of injury-accidents by users of different types of psychotropic medication and facilitate the application of drug use and transportation accident data bases for extending their knowledge and further targeting their countermeasures.

9.12 Discuss the development of new regulations with respect to medicinal drugs and driving with patient/consumer, and driver organizations in order to determine what new regulations should be applied in daily practice addressing the public and the individual patient who drives.

9.13 Encourage physicians and pharmacists to implement prescribing and dispensing guidelines.

9.14 Develop media campaigns to address relevant issues that will focus on changing roles of patients, drivers, health care professionals, police officers, educators and driving school instructors.

Organizations and research institutes in the field of drugs and driving should

9.15 Disseminate information on the safe use of medicinal drugs by drivers via the internet, addressing both the public and professionals. Provide quality assurance for the users of this source of information.

Driving licensing authorities should

9.16 Meet their obligation for assuring applicant's fitness to drive when issuing or renewing driving licences. Develop effective lines of communcation with medical and pharmaeutical practitioners to acquire information on the driving fitness and medication history of applicants.

Medical and pharmacy schools should

9.17 Develop their educational programs pertaining to drugs and driving and to update these, if needed, based on present knowledge for safe prescribing and dispensing.

The Working group hopes that this document will encourage the international acceptance of prescribing and dispensing guidelines by professional organizations and regulatory agencies. By informing their memberships and starting discussions about the guidelines provided in this document, they can play a key role in solving problems related to the use of medicinal drugs by patients who want to receive treatments safe for driving.

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Drugs and Driving Research: Application of Results by Drug Regulatory Authorities

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This paper describes the use of data about the effects of medicinal drugs on driving that are submitted by applicants for product licensing in the European Union. Existing European guidelines and directives are discussed in order to illustrate the need to review the requirements of data pertaining to the effects of psychotropic drugs on driving. The impact of results from experimental human psychopharmacological research on these guidelines and directives is reviewed briefly to show that some progress has been achieved in improving regulatory processes. Specific interest is focused on the graded warning system that can appear on official package inserts and which was adopted by the Committee for Proprietary Medicinal Products in 1991. This paper concludes with a discussion of ways by which regulatory authorities can implement an improved warning system for patients who are likely to engage in potentially dangerous activities like driving. © 1998 John Wiley & Sons, Ltd.

KEY WORDS — drug labelling; accident liability; evaluation; drug regulation

INTRODUCTION

The European drug regulatory system allows for the evaluation of the effects of drugs on driving. Since 1 November 1985, drug manufacturers are required under European Directive 83/570/EEC to submit a Summary of Product Characteristics (SPC) of each product, including a statement about the effects of the product on the ability to drive and operate machinery. Before this date, data concerning the effects of a drug on driving ability were not routinely provided. Isaacs reviewed 56 product licence applications for new active substances received in 1984 and 1985 by the UK Licensing Authority (Isaacs, 1988). In five applications the agents could be considered as being psychoactive, but only one application addressed the issue of whether the product affected driving ability. Isaacs clearly indicated the need to review data requirements in connection with the effects of drugs on driving. He concluded his paper by stating that specific topics for future consideration should include the precise methodology used to validate the effects of psychoactive drugs on driving.

DRIVING AND DRUG REGULATION

During the First International Symposium on Prescription Drugs and Driving Performance, held in the Netherlands, 25–28 June 1984, O'Hanlon *et al.* (1986) presented arguments for incorporating one particular driving test into procedures required for new drug registration. They clearly indicated the need to adjust regulations if a test or test battery was found to discriminate between safe and unsafe drugs with respect to their effects on driving. They suggested that the adverse effects of new psychoactive drugs should be monitored more thoroughly in order to make it possible for regulatory authorities to issue specific warnings. For example, when to prohibit driving for specified periods after last administration of the drug (e.g. a hypnotic) or when beginning regular use of a drug. The authors suggested that the most realistic test would be a real driving test. One performance measure which has most consistently discriminated between the effects of different drugs or doses is the standard deviation of lateral position (SDLP, see also Brookhuis, this issue). The authors recommend that this test be used in the final stage of screening for the CNS effects of drugs, after laboratory testing has been completed. They discussed construct and content validity. Validation of the driving test against the criterion of actual accident involvement is virtually unattainable, so they validated the test against alcohol as a secondary criterion that is highly

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correlated with accident risk. This approach has proved to be successful in calibrating performance changes produced by prescription drugs to changes brought about by increasing blood alcohol concentrations (BACs). These comparisons of drug- and alcohol-produced changes in performance have had a significant impact on communication of the issue of drugs and driving to the public, health care providers, and policy makers. For the first time it was possible to replace warnings about classes of drugs by more specific information. By relating the changes in SDLP produced by any drug to the same changes produced by a given BAC, it has been possible to categorize impairment as severe (BAC > 100 mg/dl), moderate (BAC 50–100 mg/dl), and slight (BAC < 50 mg/dl) or none (comparable to placebo).

It is largely thanks to the research efforts of O'Hanlon and co-workers over the last decades that standard on-the-road drug tests are considered appropriate to determine whether hypnotics or anxiolytics may impair psychomotor functions, but this is not yet the case for antidepressants. EC guidelines on psychotropic drugs help applicants in the interpretation of Directive 91/507/EEC with respect to specific problems arising from clinical investigations (Guidelines on Psychotropic Drugs for the EC, 1994, 1995). Unfortunately these guidelines do not specifically describe the methodologies that should be used for drug screening. Methodological diversity is still responsible for the relatively small influence of drugs and driving research on regulatory bodies. Researchers in this field have expressed the need for more standardized methodologies and have developed a set of guidelines based on a consensus of scientific opinion (Vermeeren *et al.*, 1993). These guidelines for experimental research on drugs affecting driving performance have not yet been adopted by drug regulatory authorities, which is unfortunate because without these quality control guidelines it is hard to reach firm conclusions about the degree of behavioural impairment attributable to particular drugs. The time has come for drug regulators to realize that they must play a meaningful role in supporting higher standards of psychopharmacological research. The undefined behavioural toxicity of medicinal products is a major threat to patients' quality of life. Now that public and health care providers have become more aware of the causal relationships between drug use and accident involvement, drug regulatory authorities can no longer ignore the need to improve drug warnings.

DRUG CATEGORIZATION AND WARNING SYSTEMS

Over the past decade increasingly more research has focused on the behavioural side-effects of drugs. Moreover, advances in pharmaceutical research have led to the development of medications with fewer or no sedative effects (i.e. the new antihistamines and the selective serotonin reuptake inhibitors, new antidepressants). As a result of these developments, health care providers and governmental agencies in the Netherlands have expressed a need to be able to distinguish between drug effects on behaviour on the basis of dosage and/or form of administration. The need for more specific warnings in package inserts, as well as symbols on drug packages has resulted in the development of a new categorization system for drugs that affect driving performance (Wolschrijn *et al.*, 1991). A survey among international experts has led to a proposal for a new classification of a number of frequently used potentially hazardous drugs (in traffic). This new classification was discussed by the Committee for Proprietary Medicinal Products of Directorate General III and was finally introduced in the Final Note for Guidance on the SPC (III/9163/90-EN, final approval 16 October 1991). This Note stipulated that all new medicines (New Chemical Entities) registered after 1 January 1992 should include a statement in the warning section of package insert leaflets about the effects of the drug on the ability to drive and use machines on the basis of:

(a) the pharmacodynamic profile, reported adverse drug reactions and/or
(b) impairment of driving performance or performance related to driving, categorized as
    (i) presumed to be safe or unlikely to produce an effect;
    (ii) likely to produce minor or moderate adverse effects;
    (iii) likely to produce severe adverse effects or presumed to be potentially dangerous.

For situations (ii) and (iii), special precautions for use/warnings relevant to the categorization should be mentioned in the SPC.

However, there is no evidence that pan-European or national regulatory bodies are categorizing drugs on the basis of their hazard potential for driving. This was first noted by Spanish pharmacologists in 1994, who expressed

the hope that categorization in the SPC would be accomplished within the near future (Alvarez and Del Rio, 1994). That period has now elapsed, but the same lack of implementation is still apparent. The unanswered question 'why?' is becoming urgent. When interviewing national regulatory authorities about their procedures for determining the drugs and driving warning, it often transpires that the normal procedure is to consider the pharmaceutical manufacturer's specific warning and the data supporting that statement. In a case-by-case assessment without specific algorithms for reviewing specific data, the company's statements are generally accepted. Disagreement is unlikely to occur about the text of a warning, and the drugs and driving issue never holds up licensing. In general, there seems to be no great priority for the articles of the SPC concerning the effects of drugs on the ability to drive and use machines. There seems to be more interest in discussing statements such as those on a drug's undesirable effects and its use in pregnancy.

Pharmaceutical manufacturers will not change these procedures unless they are forced to do so by the regulatory authorities. This, however, will not occur because there seems to be a trend to apply one general statement for all drugs within a chemical or therapeutical class, e.g. for benzodiazepines used as anxiolytics or hypnotics (III/3653/91-EN, Final approval by the CPMP, October 1994). This kind of harmonization prevents the introduction of more specific warnings according to a drug's behavioural toxicity. In discussions with representatives from industry it is always made clear that they do not see this issue as a priority in today's regulatory context. However, some companies do appreciate that there is growing interest in patients' quality of life issues and pharmacoeconomic evaluations of treatment outcomes.

Scenarios for implementing improved warning systems

It is a difficult and certainly discouraging exercise to look into the future of drug regulatory development in Europe, given the experience to date with respect to the drugs and driving issue. This experience, however, has led to the appreciation that no single actor in the process of drug screening, drug regulation, or drug treatment can change the whole process. Yet someone has to take the initiative. For this reason, a couple of scenarios for implementing an improved warning system for the effects of drugs on the ability to drive and use machines are presented. The first scenario is to carry on with the current registration procedures. There will be no fundamental change in the procedure for establishing these warnings in the SPC. This means that patients and health care providers will not receive information that allows them to select the least impairing drug for treatment. Nothing will change until large pharmacoepidemiological studies reveal that specific drugs within a therapeutic class of psychotropic medication constitute a higher risk for accident involvement than other comparable drugs. Uncertainty will exist about the impact of such results if studies are not funded by responsible governmental agencies in the first place. It is expected that these studies will be conducted within 5 years; in Canada, the USA, and the Netherlands researchers have already shown the power of this methodological approach (Ray *et al.*, 1992; Herings, 1994; Neutel, 1995).

A second scenario envisages that the European authorities responsible for drug regulation, public and environmental health, transport safety and consumer affairs together decide that a joint action program is required to implement, maintain, and evaluate a new warning system for drugs that affect driving ability based on categorization. New partners, in particular the pharmaceutical industry, organizations of physicians, pharmacists and patients, and insurance companies, should be invited to take part. These new partners have a greater awareness of health issues as a result of health education campaigns and publicity in journals, and they realize that the health care industry is changing. Prevention and health-related quality of life issues are becoming determining factors for both policy makers and payers of health care costs. A first and essential step is for the responsible Directorates General in the European Union to respond to these initiatives and to promote this joint effort to develop a new warning system. The next step is to prepare a work plan which will focus on issues or problems raised in different EU surveys and by experts, the possibilities for involving the new partners in the development of strategies for implementing a new warning system, and strategies for continuing efforts to maintain the most appropriate use of this system. Education will be another important issue for discussion, including basic education and academic training, the latter in particular for physicians and pharmacists.

CONCLUSIONS

Drug regulatory authorities are key players in the process of restructuring drug screening programs to assess a drug's potential for impairing psychomotor and driving performance. Experts in the field of human psychopharmacology who have assessed the effects of drugs on driving have provided the relevant information needed to perform this task. The impact of these efforts on drug regulation has been noticed, but it has not had a significant effect on improving warning systems for patients who drive. Experts should be more effective in disseminating their research data to the public, health care providers, and policy makers. Physicians and pharmacists can contribute to the use of safer drugs by monitoring patient outcomes with respect to behavioural impairment. By selecting the least impairing drug in their prescribing and dispensing practices, they play a significant role in enhancing public safety. In order to be able to do this, they have to know how to assess the level of impairment of each individual drug. This information is already available for many new and 'old' medicines. The time has come for patient and consumer organizations to ask who is responsible for not applying this knowledge.

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Review of investigations of prevalence o
illicit drugs in road traffi
in different European countrie

Review of investigations of prevalence of illicit drugs in road traffic in different European countries

Study conducted with the support of the Council of Europe (Pompidou Group)

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CONTENTS

SUMMARY

The specific focus of this survey has been the prevalence of illicit drug use in road traffic in thirteen European counties. The literature search conducted to accomplish this survey included the relevant scientific journals, institutes' reports published over the last decade and the proceedings of the last two conferences organized by the International Council on Alcohol, Drugs and Traffic Safety in 1995 and 1997.

A total of thirty studies have been critically reviewed in order to present the prevalence of illicit drug use alone and in combination with alcohol as well as multiple drug use. The prevalence of licit drug use is also presented, since this has been frequently reported in most studies. The different scope of the various studies entails prevalence being presented in different driver populations, such as 'general driver population', 'drivers suspected of driving under the influence of alcohol and/or drugs' and 'collision-involved drivers'.

Different methodological problems arise with sample collection and data collection in many studies, thus most study outcomes do not allow comparisons across different European countries. Differences may occur especially in selecting the sample of drivers if police forces in one country focus more on detecting drugged drivers than in other countries. One general problem for all categories of driver populations is the representativeness of the sample under examination, which is also a problem if small sample sizes are included and or selection criteria are not clear.

Only four large scale studies have been published, one German study focusing on the general driver population, one Norwegian study involving drivers suspected of driving under the influence of drugs, and two studies, from Belgium and Italy, in which collision-involved drivers were screened for drugs. The results from these studies are not expected to completely reflect the situation in other countries, for one thing because of societal and cultural differences that determine drug use patterns (licit and illicit drug use) and the impact of public campaigns, which is mostly unknown. Consequently the conclusions from these studies are intended to be indicators for further discussion.

In the *general driver population* the prevalence of *illicit* drug use will probably fall in the range of 1%-5% (cannabis and opiates being most frequently observed), whereas *licit* drug use will fall in the range of 5%-15% (with benzodiazepines being most frequently detected). The prevalence of the combination of illicit drugs with alcohol reflects much more of a problem than the combination of licit drugs with alcohol, probably because patients tend to be much more aware of impairing effects of this combination. The prevalence of multiple drug use in the general driver population is very low if the German results are taken as an indicator.

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. 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. Cocaine has been detected with a very low prevalence (0.5%-0.7%) in Belgium and Italy, whereas in Spain a high prevalence (5%-7%) has been reported. 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 to 36% in a Norwegian study in drug positive cases. 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.

It should be stressed that knowledge about the prevalence of drug positive drivers in different driver populations cannot 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 (except for Germany) there is a lack of data on the prevalence of drugs among the normal driver population. The high prevalence of drugs found in representative samples of collision-involved drivers supports the assumption that there is a serious road safety problem. However, Europe does not have 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 should be embarked upon and that national laws prohibiting roadside surveys should be abolished or modified to permit the same surveys to be conducted on a pan-European basis.

1. PURPOSE

The purpose of this report is to give a review of investigations in different European countries that show the prevalence of illicit drugs in road traffic with special regard to multiple abuse, which means a combination of various drugs, including alcohol and licit drugs. The literature search conducted to accomplish this review included the relevant scientific journals, institutes' reports published over the last decade, and the proceedings of the last two conferences organized by the International Council on Alcohol, Drugs and Traffic Safety in 1995 and 1997. After summarizing the results of the different reports for each country, discussion will follow in order to combine the relevant data and to provide a general conclusion and define the problem that will allow those responsible for traffic safety throughout Europe to determine the necessary steps for developing counter-measures. The results of this review will be complementary to the overview of the legal systems, analysis of difficulties faced by the police, the prosecutors and the courts with respect to illicit drugs in road traffic, and of preventive attempts to control the problem. These aspects will be covered by a report written by Prof H-P Krüger (Centre for Traffic Sciences, University of Würzburg, Germany).

2. INTRODUCTION

Background to the problem

Road accidents in countries of the European Union, resulting in 50,000 fatalities and 1.5 million injuries every year, cost society over 70 billion ECU (White Paper on Transport Policy, COM 92/494, European Commission). It has been suggested that if all the Member States were to compile their statistical data according to the criteria used in those countries that prepare the most accurate estimations, then the real number of people injured in road accidents would probably exceed 3 million annually (Gil-Robles, 1998). The figures have reached a level that the European Union can no longer accept.

Since transport safety and public health are interrelated, road accidents caused by drugs other than alcohol have become an important public health issue. It is widely recognized that alcohol use is a causal factor in 20-40% of fatal road accidents, but many licit and illicit drugs are also known to impair driving ability. Available data allow one to conclude that use of the most frequently prescribed benzodia-zepine tranquillizers more than doubles the risk of injurious accidents (comparable to the risk of 0.5 g/l BAC or blood alcohol concentration), while the use of tricyclic antidepressants increases the risk even more (Ray et al., 1992). One more recent epidemiological investigation revealed an extremely high relative risk (5 to 6 - fold increase, comparable to 1.0 g/l BAC) within a large population of benzodia-zepines users during the first two weeks of using their initial prescription (Neutel, 1995).

Epidemiological studies on the most widely used illicit drug cannabis indicate the presence of tetrahydrocannabinol (THC) in roughly 4-12% of drivers injured or killed in traffic accidents, even if the population at risk is probably less than 4%. The THC incidence among injured or killed drivers is not conclusive evidence for establishing its role as a causal factor, since alcohol was present in the majority of THC positive accident victims (Robbe, 1994). It has been suggested that cannabis and alcohol in combination carry a greater risk potential than either of them alone (Terhune et al., 992). The independent contribution of cannabis use in impairing road safety is still dubious.

Estimations of the percentage of illicit drug use in driving licence-holders varies from 1-2% in the various EU Member States, whereas an average of 10% of the adult population drives under the influence of impairing medicinal drugs (De Gier, 1995). Comparisons across Member States on the prevalence of illicit drug use in road traffic are, however, difficult to achieve. The data from the studies reviewed show major discre-pancies, depending on the method and scale of data collection (last year or lifetime prevalence), the scope of the survey (nationwide general population, regional data, or selected populations who seek professional treatment for drug dependence). In most cases the accuracy of the records in various countries is not known. It is impossible to draw any conclusions to demonstrate the relationship between illicit drug use and accidents because of a lack of sound epidemiological studies. There is a need for actions to standardize research methodologies and to provide the relevant data.

A complete understanding of the problem of illicit drugs and driving will only be achieved in two complementary approaches: experimentation and epidemiology (Simpson and Vingilis, 1992). Experimental studies focus on drug effects on psychomotor performance, in particular the types of skills affected and the dosages used. However, it is fairly impossible to translate these effects into road crashes. Questions on the extent or magnitude of this problem, as well as the determination of which drugs are risk factors for collision

involvement, can be answered in sound epidemiological research.

Descriptive epidemiology provides insight into the relative importance of different types of drugs. In other words, which drugs are detected that contribute to a significant traffic safety problem. If repeated evaluations are performed in time, insight can be provided into changing patterns of drug use and driving within society.
Analytic epidemiology determines which drugs are overrepresented in persons involved in road accidents. Involvement of control groups allows researchers to provide relative risk data. The relationship established through the risk factors approach is one of association, not of causation. Experimental research into the causal links between drug levels and behavioral impairment remains necessary to draw conclusions on causation potentials of different drugs.

Generally speaking, the application of epidemiological research to drugs (other than alcohol) and driving can only permit meaningful cross-cultural comparisons if standardized data-gathering methods are used However, several factors (such as political, legal, social, economic) deter-mine the research capabilities of re-searchers in different countries and will result in different approaches to sample selection and data collection. A review of investigations of prevalence of illicit drugs in road traffic in selected countries will therefore include studies in which numerous methodological problems are to be encountered This review for the Council of Europe, includes more recent studies, some of them have adopted improved methodological designs

3. METHODOLOGICAL ISSUES

In general most methodological problems encountered with epidemiological studies of drugs and driving can be categorized as problems with sample collection and data collection (Simpson and Vingilis, 1992).

Population under examination

The choice of population studied is critical and can give rise to problems in comparisons across countries. Epidemio-logical 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

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 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.

In surveys of *offender populations* (charged with driving under the influence of alcohol or drugs), drug screens are carried out if the blood alcohol level is below the legal limit. 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.

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 limitations because data on illicit drug use are not routinely collected. Even when drug tests are carried out 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 have their own problems. The method of drug analyses in blood, sweat, saliva or urine has problems with respect to sample collection, handling and transportation as well as toxicological assays used. Interpretation of drug levels detected is difficult; for example cannabinoids can be detected in urine many days, even weeks, after use and the relevance of this to traffic safety is obscure. Blood specimens are considered to be essential for surveys of illicit drugs and driving. 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).

4. SURVEYS OF ILLICIT DRUG USE IN ROAD TRAFFIC IN DIFFERENT EUROPEAN COUNTRIES

4.1 AUSTRIA

In a pilot study of the 'Bundespolizeidirektion' in Vienna urine samples of 27 drivers with extremely conspicuous behavior in road traffic and negative breathalyzer results for the presence of alcohol were analyzed using the Abbott ADx-analyzer (a fluorescence polarization immunoassay) for cocaine metabolites, cannabinoids and opiates (Fous, 1995). Gas Chromatography/MassSpectrometry (GC/MS) was used to confirm positive results obtained with the immunoassay technique. In 8 cases (32%) these analyses confirmed the use of one drug, in 13 cases (52%) two drugs, and in 4 cases (16%) all three drugs tested for could be found positive. Without exception all 25 samples found positive in the ADx-analyzer were taken from young drivers (22 males, 3 females), 48% of them born between 1968 and 1970. 84% of tested drivers had previous convictions and 68% had drug addiction records. The results of GC/MS confirmed samples are given in Table 1.

The author indicated that his findings could be considered the 'tip of the iceberg'. However, it is impossible to draw conclusions from only a small sample and to demonstrate the prevalence of illicit drug use in road traffic in Austria since the sub-sample of drivers was not representative of the driving population. No other examples of recent surveys could be obtained from the 'Kuratorium für Verkehrssicherheit'.

TABLE 1 RESULTS OF GC/MS CONFIRMED SAMPLES

Substance	Negatives	Positives		
		<100 ng/ml	<500 ng/ml	<1500 ng/ml
Cannabinoids (THC)	7	9	6	3
		<1000 ng/ml	<5000 ng/ml	<40000 ng/ml
Opiates	8	5	8	4
		<1000 ng/ml	5000 ng/ml	<36000 ng/ml
Cocaine metabolites	13	7	2	3

4.2 BELGIUM

The Belgian Toxicology and Trauma Study (BTTS) was conducted as a prospective, multi-centre survey in six hospital emergency departments sufficiently spread over the country (Meulemans et al., 1997). Inclusion criteria were: all drivers, at least 14 years of age, of bicycles or motor vehicles involved in a traffic accident on a public road, directly admitted to one of the selected emergency departments for at least one day or dying upon or after admission. During the registration period (January 16th 1995 till June 15th 1996) blood and urine samples were taken from 2,143 patients.
Blood alcohol concentration was assessed first by screening in whole blood on fluoride-oxalate, using Radiative Energy Attenuation (REA; Abbott). Positive samples were confirmed by Gas Chromatography/Flame Ionisation Detec-tion. Toxicological screening was per-formed on the urine samples, using Fluorescence Polarisation Immuno-Assay FPIA) on ADx-analyzing equipment (Abbott). The screening battery consisted of 8 tests and searched for amphetamines, barbiturates, benzodiazepines, canna-binoids, cocaine metabolites, methadone, opiates, and propoxyphene.

In addition the presence of benzodiazepines in serum was searched for using the same technique. Confirmation for most substances was performed on urine by Gas Chroma-tography/Mass Spectrometry (GC-MS). The confirmation of benzodiazepines in serum was carried out by High Pressure Liquid Chromatography (HPLC) and Gas Chromatography with Electron Capture Detection (GC-ECD). For barbiturates in serum confirmation was performed by Gas Chromatography with Nitrogen Phosphorus Detection (GC-NPD). Analytical cut-off values for the different drugs are presented in Table 2.

Although a total of 2,143 patients were included during the collection period of the study, a final sample size of 2,053 patients could be used for analyses. This was due to inappropriate handling of the methodological protocol by two of the collaborative centers. The study population consisted of 1514 men (74%) and 539 women (26%). A majority of younger people could be observed: more than one third (34.7% men, 33.8% women), whereas fewer than 10% were 65 years of age or older. Very young drivers (below 20 years) and elderly drivers (over 60 years) were slightly more represented in the female group compared to the male group (18% and 12% versus 12% and 9% respectively).

TABLE 2 SUBSTANCES, TEST METHODS AND CUT-OFF VALUES USED IN THE BTTS

Substance	Screening	Cut-off	Confirmation
Alcohol	REA, serum	0.10 g/l	GC-FID in total blood
Amphetamines	EPIA, urine	300 ng/ml	GC-MS in urine
Barbiturates	EPIA, urine	200 ng/ml	GC-NPD in serum
Benzodiazepines	EPIA, urine	50 ng/ml	HPLC/GC-ECD in
	EPIA, serum	12 ng/ml	serum
Cannabis	EPIA, urine	25 ng/ml	GC-MS in urine
Cocaine	EPIA, urine	300 ng/ml	GC-MS in urine
Methadone	EPIA, urine	300 ng/ml	GC-MS in urine
Opiates	EPIA, urine	200 ng/ml	GC-MS in urine
Propoxyphene	EPIA, urine	300 ng/ml	GC-MS in urine

In 1,959 cases from the final sample information on recent medication use could be obtained as reported by the patients. In 35% of those cases patients admitted having used some kind of medication during the week preceding the accident. If focus is given to psychotropic medication, it turned out that 10% of the study population reported the use of a medicine known to impair driving performance.

The consumption of more than 30 'standard units' of alcohol during the last week preceding the accident was reported by 7% of the injured drivers. This was noticed more often in men (8,3% versus 1,7% in women) and most frequently in the 40-49 age group (13,8%). Eighty-six percent of the patients reported their alcohol consumption during the last week as representative for their normal drinking habits, in 7% it had been lower and in 5.4% it had been higher than usual.

The use of illicit drugs during the three months preceding the accident was admitted by 5.1% of the patients. The major classes reported were cannabis (3.7%) and amphetamines (1.4%).

The toxicological analyses showed the following results. In 35 cases (1.7%) neither blood nor urine samples had been obtained, while from another 139 patients (6.8%) only blood samples had been collected. Blood alcohol concentration (BAC) could be assessed in 1871 patients (91%), 1342 of which (72%) were presented with an analytical result not reaching the legal limit (0.5 g/l). Of the remaining 529 'positive' patients (28%), two thirds (65.6%) had a BAC exceeding 1.5 g/l, and more than one third (37.6%) even exceeded 2 g/l. Of the patients with both self-reported information on recent alcohol consumption and blood samples, 17 (3.3%) of the 521 claiming they had not imbibed any alcohol during the last week were nevertheless shown to have a BAC exceeding 0.5 g/l, 11 of whom (65%) showing 1.5 g/l or more. In the group admitting recent alcohol consumption these figures reached 37% and 61% respectively. In patients reported with higher alcohol consumption habits (more than 30 'standard units' in the week before the accient), 70% exceeded the legal limit and three quarters even showed more than 1.5 g/l.

The results on medication and illicit drugs were obtained in samples of patients who did not receive (potentially interfering) medication before sampling. In total 391 cases (19%) were confirmed positive on one or more of the following substances: amphetamines, benzodiazepines (in blood), barbiturates (in blood), cannabis, cocaine, opiates, methadone, or propoxyphene. Of these, 107 (27%) also had a BAC exceeding the legal limit of 0.5 g/l, the latter being seen significantly more often in men (32% of the positives, versus 15% in women). The prevalence of the detected substances is summarized in Table 3.

TABLE 3 TOXICOLOGICAL RESULTS OBTAINED IN PATIENTS INCLUDED THE BTTS

Substance (sample)	N analyzed	Screening positive	Confirmation positive	Prevalence (%)
Amphetamines (urine)	1879	60	56	3.0
Barbiturates (urine)	1879	37	25	1.3
Benzodiazepines (blood)	1871	232	160	8.5
Benzodiazepines (urine)	1879	278	*	*
Cannabis (urine)	1879	114	113	6.0
Cocaine (urine)	1879	14	14	0.7
Methadone (urine)	1879	6	5	0.4
Opiates (urine)	1879	149	141**	7.5
Propoxyphene (urine)	1879	6	4	0.2

* Positive screening results were confirmed in blood only.

** 103 (73%) resulted from analgesics, antitussives, and 38 (27%) from the use of morphine/heroine.

The highest scores by far were noticed for benzodiazepines (8.5%), opiates (7.5%), and cannabis (6%), followed by the other substances (amphetamines 3%, barbiturates 1.3%, and cocaine, metha-done, and propoxyphene each less than 1%). Of those found positive on amphetamines, only 22% had reported the use of this substance during admission. For cannabis and cocaine positive cases these figures were 36% and 21% respectively. For propoxyphene one out of the four patients mentioned the use of this substance. None of the five patients who were found positive for use of methadone had mentioned this upon anamnesis on illicit drug use and only two had mentioned it on medication use

Multiple drug use was observed in 80 patients, or in 20% of the positives (64 on two substances, 13 on three, 2 on four, and 1 on five). In 24 of these multi-substance (ab)users BAC levels exceeded 0.5 g/l. In general, teenagers had a positive rate of 20% for the toxicological analysis, 15% of them combining this with a BAC exceeding the legal limit. In the age group 20-30 years these figures reached 24% and 29% respectively, for 30-40 years 19% and 38%, for 40-50 years 27% and 38%, for 50-60 years 19% and 23%, and in the age group of 60 and over 21% and 10%.

One interesting finding that gives weight to the concern of higher accident risk by multiple drug use is a clear synergistic interaction for alcohol and medication/illicit drugs, if mortality was taken as the outcome variable. The results of the BSST indicate a relative risk of 2.56 in the combined positive group, in which a mere additive effect would theoretically have led to a relative risk of 1.60.

The Belgian Toxicology and Trauma Study (BSST) is one of the very few good examples of descriptive epidemiological research that provides insight into the relative importance of different types of drugs in collision involved drivers. By combining the data from self-reported drug use with data from toxicological analyses the relative usefulness of self-report instruments could be illustrated in a very comprehensive way.

4.3 DENMARK

In a Danish study by Worm et al. (1996) the occurrence of drugs and narcotics in violators of the Danish Road Traffic Act during the year 1993 was determined according to the request by the police. These requests are not frequently received if the blood alcohol concentration (BAC) is above the legal limit of 0.8 g/l. In 1993 the central laboratory (Department of Forensic Chemistry at the University of Copenhagen) received 425 cases, of which only 317 were analyzed for the presence of drugs (legal) or narcotics. In 256 cases drugs or narcotics were found present with in total 531 positive findings. In 40% of the cases only one substance was found present. The most frequently detected substances were benzodiazepines, morphine, methadone, canna-binoids and amphetamine with 239, 52, 42, 32, and 28 positive findings, respectively. Radioim-munoassays or receptor methods were used for screening the samples. Quantitative determinations were carried out by using liquid chromatography with UV- and electrochemical detectors and capillary gaschromatography with nitrogen and electron capture detectors. Only findings confirmed by two different methods were included in the results.

In 58 of the 108 cases that were not analyzed for drugs the BAC was below the legal limit. In 61 of the 317 cases analyzed for drugs and/or narcotics no positive findings could be detected. In 28 of these drug negative cases the BAC was lower than the legal limit. In 44% of the drug positive cases only one compound was found present, alcohol not included. In about half of these cases the BAC was higher than 0.8 g/l.

The authors compared their results with outcomes of a similar investigation in Norway (Kruse, 1994). Denmark and Norway are both Scandinavian countries with approximately the same size of population, about four million in Norway and five million in Denmark. In the Norwegian study 2371 samples were analyzed compared to the 317 in the Danish study. Interestingly, the drug use patterns in both countries are quiet different looking at the five most frequently detected substances (Table 4). In Norway cannabis was the most frequently observed drug, whereas this was only rated number five in Denmark. Methadone was probably more frequently used in Denmark, while codeine and ethylmorphine were seen quite often in Norway. The authors do not attempt to explain these differences, but it is clearly shown that drug use patterns differ substantially among European countries. It once again underlines the complex nature of licit and illicit drug use in general while discussing trends in European countries. Many factors influence drug use, most of them poorly understood, such as the effectiveness of public campaigns and rational prescribing of medicines by doctors.

In order to illustrate the development of drug use patterns in traffic cases the authors presented the results for the years 1989 and 1995 (Steentoft et al., 1997). Once again they emphasize that in Denmark the police decide for what drugs screening and analyses have to be performed. In about half of the cases only analyses for single drugs are requested, often directly related to information gathered from the person under suspicion. This practice introduces a variety of biases and will result in inconsistency in reporting percentages of drug use. The authors however detect a trend towards increased use of benzodiazepines, in particular of flunitrazepam, morphine and cocaine, but the numbers of the latter are limited (Table 5).

TABLE 4 **COMPARISONS OF FREQUENTLY OBSERVED DRUGS OR NARCOTICS IN TRAFFIC CASES IN NORWAY AND DENMARK (WORM ET AL., 1996)**

Country	N analyzed samples	N positives in %	Drug name	N positives	In % of samples analyzed
Norway	2372	60	Cannabinoids	842	35.5
			Benzodiazepines	802	33.8
			Amphetam-ines	391	16.0
			Morphine	107	4.5
			Codeine, ethylmorphine	86	3.6
Denmark	317	81	Benzodiazepines	239	75.4
			Morphine	52	16.4
			Methadone	42	13.3
			Cannabinoids	32	10.1
			Amphetam-ines	28	8.8

TABLE 5 **TRAFFIC CASES INVESTIGATED FOR DRUGS OTHER THAN ALCOHOL (1989 VS 1995)**

Selection of cases	**1989**	**1995**
Cases investigated for alcohol	26363	16432
Cases received for investigating drugs other than alcohol	391	314
Of these cancelled by police	119	93
Cases analyzed for drugs other than alcohol	272	221
Drug names		
Benzodiazepines	123 (45%)	118 (53%)
Diazepam	85 (31%)	57 (26%)
Flunitrazepam	33 (12%)	62 (28%)
Cannabis	33 (12%)	38 (17%)
Amphetamine	31 (11%)	21 (10%)
Morphine	28 (10%)	59 (27%)
Methadone	29 (11%)	29 (13%)
Ketobemidone	12 (4%)	13 (6%)
Cocaine	2 (1%)	14 (6%)
No drugs detected	70 (26%)	31 (14%)

The data are difficult to apply in presenting the prevalence of illicit drug use in offender populations in road traffic in Denmark. Drug screening is carried out if the blood alcohol level is below the legal limit or if the police have specific information on potential drug use from the offender. This approach automatically excludes information on combinations of drugs with high levels of alcohol. Since the police determine the selection of drivers and decide on the screening for drugs other than alcohol, a variety of biases has been introduced. It is not possible to speak of anything more than 'possible trends in illicit drug use in Denmark'.

4.4 FRANCE

The prevalence of psychotropic licit drugs, opiates and alcohol in fatally - injured drivers during the period from 1 September 1991 till 31 August 1992 has been investigated in northern France (Region Nord-Pas de Calais) by Deveaux et al. (1995). Blood samples were taken from 103 fatally - injured drivers. Screening for benzodiazepines, tricyclic antidepressants and barbiturates was performed by fluorescence polarization immunoasssays (FPIA) using ADX equipment (Abbott). Each positive result was confirmed using Gas Chromatography/Mass Spectrometry (GC/MS). Opiates were determined using a radioimmunoassay technique (RIA-Coat a Count Morphine, Behring), whereas alcohol was determined using Gas Chromatography.
Blood samples were taken from 88 males with an average age of 37.5 years (range 15 - 80), and 15 females with an average age of 38.9 years (range 14-81). Blood alcohol concentrations (BACs) were above the legal limit (> 0.7 g/l) in 45.7% of all cases (46.6% males, 40.0% females). For screening for drugs only 97 samples contained sufficient quantities of blood to perform analyses. The results are presented in Table 6.

Psychotropic drugs were detected in 36.4% of all cases. Alcohol and psychotropic drugs were found in 19.8% of the samples, whereas the combination with alcohol > 0.7 g/l was present in 15.6% of all cases

In a study by Pélissier et al. (1996) urine samples of young adult injured drivers involved in road accidents were tested for opiates, cannabinoids, cocaine and amphetamines. This multi-center study was conducted in emergency units of three hospitals following a prospective case controlled design including injured drivers aged 18-35 years. A first screening was carried out using the Abbott ADx-analyzer (a fluorescence polarization immunoassay, FPIA). Positive samples were confirmed by gaschromatography/ mass spectrometry (GC/MS). The analyses of urine samples revealed that 10% of the injured drivers (6 out of 60) showed positive values for cannabinoids, 5% (3 out of 60) showed positive opiates values, while one sample was detected positive for amphetamines. Positive cocaine could not be observed. Only one sample indicated multiple drug use (cannabinoids and amphetamines used together). In 60 samples obtained from control patients (admitted to the hospital for other reasons than accidents) only five positive cannabinoids could be confirmed. Cocaine, opiates and amphetamines could not be detected at levels higher than the cut-off values. The results show no significant differences in the prevalence of illicit drugs between the two groups of relatively small sample size. Determination of alcohol and legal drugs was not involved in this study.

In a recent collaborative case-control study the prevalence of opiates, cocaine metabolites, cannabinoids, and amphetamines in the urine of drivers injured in road accidents was compared with the values of non-accident subjects (Marquet et al., 1998). Recruitment was performed nationwide in the emergency departments of five hospitals (Lille, Limoges, Marseille, Paris, and Toulouse) and comprised 296 drivers aged 18 to 35 (males or females, recruited consecutively, night and day) and 278 non-traumatic patients (admitted during the same period to the same emergency units for any non-traumatic reason) in the same age range. The whole study was strictly anonymous, no consent had to be requested and no information on the aim of the study was provided, leading to no refusals. Screening for drugs in urine was performed by fluorescence polarization immunoasssays (FPIA) using ADX or TDX equipment (Abbott).

TABLE 6 PREVALENCE OF PSYCHOTROPIC DRUGS IN 97 FATALLY INJURED DRIVERS

Substance	Number of positives in males (n=35)	Number of positives in females (n=3)	Total number of positives
Benzodiazepines > 50 ng/ml	11	1	12
Tricyclic antidepressants > 75 ng/ml	19	1	20
Barbiturates > 2 µg/ml	1	0	1
Opiates >1.6 ng/ml	4	1	5

Each positive results was confirmed using Gas Chromatography/ Mass Spectrometry (GC/MS), in one single laboratory. Statistical analyses to assess potential differences in prevalence of drugs comprised single-step logistic regression. Confounding factors (age, sex, centers) between the two populations were simultaneously analyzed.
The mean age of the drivers and patients was 25.5 ± 5.2 and 26.5 ± 5.2 years, respectively (p<0.02). Females represented 28.4% of the drivers and 44.2% of the patients (p=0.0001). The prevalence of drugs in urine of drivers and patients is presented in Table 7. The respective prevalences for drivers and patients were: 13.8% and 7.6% for cannabinoids; 10.5% and 10.4% for opiates; 1.35% and 2.52% for amphetamines;and 1.10% and 1.08% for cocaine metabolites.

After adjustments for differences in age and sex distribution, the apparent difference in the prevalence of cannabinoids between drivers and patients was not statistically significant (p=0.054), except in females for whom the prevalence in drivers' urine was significantly higher than in patients (p=0.020). A higher prevalence of cannabinoids was found in urine samples of males, both in drivers (p<0.05) and patients (p<0.0001). No difference between drivers and patients was found for the prevalence of urinary opiates. However, a significantly higher prevalence of opiates was found in males positive for cannabinoids compared to cannabinoid-negative drivers (p=0.003) or patients (p=0.001). In female drivers and patients this difference was not significant. Because of the limited numbers of positives, no statistical comparison could be made between drivers and patients with regard to cocaine and amphetamines.
The authors discuss the limitations of their study. Firstly, the opiates found in about 10% of all samples. These results can correspond to either illicit or to therapeutic use. Secondly, there was no access to police records, thereby leaving out the determination of the control population as being a group of non-accident drivers. Thirdly, the lack of alcohol and licit drug testing. The probability of drivers being responsible for the accident increases with the combination of cannabis, alcohol and benzodiazepines (Schermann et al., 1992). Therefore the present results cannot be applied for determining the causal involvement of drugs in road accidents. They rather indicate the representation of drug users among injured drivers compared to a group of patients.

TABLE 7 PREVALENCE OF DRUGS IN 296 DRIVERS AND 278 PATIENTS

Substances	Positives (%) in drivers		Positives (%) in patients	
	males	females	males	females
Cannabinoids	16.0	8.3	12.3	1.6
Opiates	10.4	11.0	10.7	9.8
Cocaine	0.0	3.6	1.3	0.8
Amphetamines	0.5	3.6	1.9	3.3

4.5 GERMANY

In Germany several investigations have been published that allow some insight in to the prevalence of illicit drug use in road traffic. The first two studies were based on the screening of blood samples from drivers stopped for suspicion of driving under the influence of alcohol (DUI). In the study by Rittner et al. (1991) 650 randomly selected blood samples were taken from all samples submitted for blood alcohol in 1987 in Rheinland-Pfalz. It was found that 7.7% of male and 2.7% of female drivers aged between 18 and 35 who were suspected of DUI had also consumed cannabis, while 3.4% of males and 13.3% of females had taken benzodiazepines in addition to alcohol.

In another study by Möller (1994) 660 blood samples of randomly selected DUI cases were analyzed for licit and illicit drugs. Toxicological screening was performed with Radio-Immuno Assay (RIA) and Fluorescence Polarisation Immuno-Assay (FPIA). The confirmation of benzodiazepines was carried out with use of Gas Chromatography with Electron Capture Detection (ECD). The other drugs were confirmed by Gas Chromatography/Mass Spectrometry (GS-MS)
In 570 (86.4%) of the 660 cases, only alcohol could be detected. In 65 cases (9.8%) licit and illicit drugs alone were found in addition to alcohol. In 22 cases (3.3%) licit and illicit drugs were found alone. Nearly two thirds (64.4%) of the positive cases (licit and illicit drugs) contained illicit drugs (amphetamines, cannabinoids, opiates). Cannabinoids were found in 54 cases, opiates in 12 cases and amphetamines in three. No cocaine was found. Benzodiazepines were found in 36 cases and barbiturates in seven. No tricyclic antidepressants were found (Table 8). Ten of the benzodiazepine positive cases (30.6%) and eighteen of the cannabinoids positive cases (33%) were found negative for alcohol use. The average blood alcohol concentration (BAC) of all drug positive cases (0.103%) was 0.06% lower than the average BAC of the drug negative ones (0.163%). Despite the fact that the average BAC was below 0.11% in 47.1% of the drug positive cases, the frequency of traffic accidents involving injuries was almost doubled in this group compared with the drug negative cases.
Multiple drug use was most prominently found in the amphetamine cases (all three cases were also positive for cannabinoids) and opiates cases (eight out of twelve were found positive for cannabinoids). Only 11% of cannabinoid positive cases were found positive for other drugs.
The average age of the drug positive drivers was 28.7 years, whereas that of drivers with only alcohol positive findings was 33.8. The average age in the cannabis positive cases was 24.9 years. A breakdown by sex revealed a relatively high proportion of females in drug positive cases.

The most recent large scale study was conducted by Krüger et al. (1995, 1996) to determine the prevalence of psychotropic drugs (licit and illicit) among the German general driving population. During the German Roadside Survey from 1992 to 1994, breath alcohol measurements were collected from more than 21,000 drivers in two regions: Unterfranken and Thueringen. In addition, 13,122 drivers were asked for a saliva sample, and 12,213 (93.1%) agreed to participate. In 1992, 3,027 samples were obtained for drug analyses (cannabinoids, amphetamines, opiates, cocaine, benzodiazepines, and barbiturates). Of the samples collected, 32,6% were essentially dry prior to analysis (volume less than 0.1 ml), therefore eventually 2,234 samples were actually analyzed. Toxicological screening was performed on 0.3 ml of the saliva sample, using Fluorescence Polarisation Immuno-Assay (FPIA) on ADx-analyzing equipment (Abbott).

TABLE 8 DRUG AND ALCOHOL POSITIVE CASES IN 660 RANDOMLY SELECTED DUI BLOOD SAMPLES

Substance	Positive cases (n=)
Cannabinoids	54
Benzodiazepines	36
Opiates	12
Barbiturates	7
Amphetamines	3
Cocaine	0
Antiepileptic drugs	(1)
Tricyclic antidepressants	0
Alcohol	635

TABLE 9 PREVALENCE OF ALCOHOL AND DRUGS IN A SAMPLE OF GERMAN DRIVERS (N=3,027)

Substance	Positive cases (%)
BAC > 0%	5.50
BAC > 0.03%	2.01
BAC > 0.05%	1.20
BAC > 0.08%	0.56
BAC > 0.11%	0.43
Benzodiazepines 3 ng/ml cut-off	3.64
Benzodiazepines 5 ng/ml cut-off	2.60
Barbiturates 100 ng/ml cut-off	0.53
Cannabinoids 20 ng/ml cut-off	0.61
Opiates (including Codeine) 100 ng ml cut-off	0.70
Opiates (excluding Codeine) 100 ng ml cut-off	0.15
Amphetamines 100 ng ml cut-off	0.08
Cocaine 200 ng/ml cut-off	0.01

Another 1.0 ml of the saliva sample was needed for confirmation by Gas Chromatography/Mass Spectrometry (GC-MS) Alcohol was determined using a Gas Chromatographic method on 0.2 ml of the sample.

After adjustments of the results to reflect a representative driving population, the following positives were found benzodiazepines, 2.7%; opiates (including codeine), 0.7%; cannabinoids, 0.6%, barbiturates, 0.6%; amphetamines, 0.08%, cocaine, 0.01%. Alcohol was found in 5.5% of the saliva samples (Table 9).

The benzodiazepines are the most prominent drugs other than alcohol. In fact these drugs had the same prevalence as alcohol in a BAC higher than 0.03%. Cannabis was the most frequently used illicit drug. Most samples could be analyzed for more than one drug. Only one sample could be detected with multiple drug use (positive for benzodiazepines and opiates). None of the samples tested positive for benzodiazepines or barbiturates tested positive for alcohol as well. The combined use of illicit drugs and alcohol was tested with the following re-

spective ratios: cocaine, 0 alcohol positives out of 2; opiates, 3 out of 9; cannabinoids, 2 out of 5; and amphetamines, 1 out of 2. The authors also discuss the concentrations of the various drugs found in their survey. Although concentration measures only provide rough estimates of psychotropic activity, some information on interpreting the meaning of their findings is provided.

The results of the last two studies show important differences in the prevalence of benzodiazepines in combination with alcohol. In the German Roadside Survey 3.64% of the saliva samples were found positive for benzodiazepines, but none of these samples was tested positive for alcohol, whereas in the study by Möller benzodiazepines were found in 36 cases (=5.45%), of which 26 cases tested positive for alcohol use. These findings illustrate that prevalence in a normal driver population can differ substantially from prevalence in a population of drivers stopped for suspicion of driving under the influence of alcohol.

4.6 HUNGARY

In Hungary there are no systematic research efforts published that allow presentations of prevalence of illicit drug use by drivers, although interest in the topic of drugs (other than alcohol) and driving is present (Nyiri, 1997).

4.7 ITALY

A large survey to determine drug usage of drivers, involving 5,910 injured drivers and pedestrians hospitalized in Padua from July 1978 - December 1988, was carried out by Ferrara et al. (1990). Patients under the age of 14, examined two hours after the accident, from whom no blood or urine samples were available or for whom a complete drug screening was not feasible were excluded from the survey. Urine and saliva samples from 4,350 drivers (3,002 males; 1,348 females) and 650 pedestrians (403 males; 247 females) included in the survey were used for screening on 72 different drugs (anti - inflammatory drugs, antiepileptics, barbiturates, benzodiazepi-nes, meprobamate, methaqualone, tricyclic antidepressants, phenothiazines, analge-sics, narcotics, stimulants, psychomimetics and cannabinoids). Enzyme Immuno-Assay techniques (EMIT) were used for screening, while Chromatographic techniques (HPLC, GC/MS) were used for confirmation in blood. Any detectable concentration of psychotropic drugs (including alcohol) in blood plasma, was considered positive, whereas a positive drug level in urine existed with concentrations higher than 0.2 mg/l. A control group of drivers not involved in road accidents consisted of 500 non-violating drivers enlisted at two checkpoints in Padua on every last Friday of the week from 7:00 pm to 00:30 am for a three months period during the years 1981 till 1988.

Results indicate a total prevalence of drugs in plasma and urine in respectively 28.6% and 40.7% of all cases (Table 10). The total prevalence of alcohol was 49.0% and 53.3%, respectively. Anti - inflammatory drugs (9.8%) and benzodiazepines (8.5%) were the drugs most prominently found in blood plasma (Table 11). Fifty one percent of all BACs were in a lower range (< 0.1 g/l), whereas 31.8% were in the range between 0.1 and 0.5 g/l, the remainder was above 0.5 g/l. For the comparison group 85% was below 0.1 g/l, 7% in the 0.1 to 0.5 g/l range.

TABLE 10 PREVALENCE (%) OF ALCOHOL AND DRUGS IN PLASMA AND URINE

Substance	Plasma	Urine
Drugs alone	15.0	23.2
Alcohol and drugs	13.6	17.5
Alcohol alone	35.4	35.8
Total prevalence of drugs	28.6	40.7
Total prevalence of alcohol	49.0	53.3
No alcohol, no drugs	36.0	23.5

TABLE 11 DRUGS IN PLASMA SAMPLES OF 5,000 CASES

Substance	Number	%
Antiinflammatory drugs	490	9.8
Benzodiazepines	425	8.5
Barbiturates	170	3.4
Phenothiazines	150	3.0
Tricyclic antidepressants	75	1.5
Antiepileptics	60	1.2
Narcotics	25	0.5
Amphetamines/cocaine	25	0.5
Meprobamate	10	0.2
Total	1430	28.6

Cannabis was the most prominently found illicit drug in urine, in 5.5% of all cases. Narcotics was found in 3.5% and stimulants in 2.7% of all samples (n=5,000). Multiple drug use is presented as a result of analyses in a subset of the samples (Table 12).

TABLE 12 MULTIPLE DRUG USE AS A PERCENTAGE OF POSITIVES IN PLASMA AND URINE

Substance	Plasma (n=940; 18.8%)	Urine (n=1534; 30.7%)
One drug	11.6	13.2
- drug only	6.1	7.8
- with alcohol	5.5	5.4
Two or more drugs	7.2	17.4
- drugs only	3.1	9.4
- with alcohol	4.1	8.0

The prevalence of psychoactive drugs alone or with alcohol in the subset of plasma and urine samples is about the same. Consumption of a combination of psychoactive substances is slightly more frequently observed if only urine samples are considered. If plasma samples are taken into consideration single drug use is observed more frequently.

The authors did not attempt to conclude on causation potentials of different drugs, obviously because of the limitations of the comparison group (e.g. samples collected on Friday nights only).

The study presents the methodology and results of a ten - year epidemiological survey carried out at the University of Padua. It provides guidelines for adequately presenting the epidemiological data in order to allow comparisons across studies performed by different teams of investigators.

A project involving a roadside survey in 1994-1995 to determine drug usage of drivers in northeast Italy is described by Zancaner et al. (1995). The study involved 1,237 drivers, including 265 who were suspected of driving under the influence of drugs. Data were collected in collaboration

with the police who stopped the drivers on Sunday mornings between the hours of 1:00 a.m. and 7:00 a.m. during the months of July, August, and December 1994 and January 1995, and asked them to participate in the study. The subject selection, however, was not described. The authors indicated that 'rapid clinical screening' was performed on 1537 car drivers, and that 309 were subjected to 'complete clinical and toxicological ascertainment'. They do not describe, however, what this means nor how these drivers were selected. Of these 309 drivers, 14 refused to provide a blood or urine sample, leaving 295 (94.2% males; 5.8% females) who were tested for drugs. Of these 249 supplied a blood sample and 221 a urine sample.

The results show that 51.4% of the drivers who were subjected to complete toxicological ascertainment had a measurable BAC, and 30.9% of the entire driver sample was legally drunk (BAC > 0.8 g/l). The study concluded that 10.2% (n=30) of the subjects were driving under the influence of psychoactive substances (Table 13)

Most of the 30 drug positive drivers had used either cannabis or cocaine or both. Table 14 presents the multiple drug intake by the subjects.

The results of this study do not allow any conclusions about the drug use of drivers in general. because of the failure to describe sample selection. Obviously the study focussed on drivers suspected of drunk or drugged driving, and allows for comparisons only if the same methods were to be used in a follow-up study carried out in the same region.

TABLE 13 PSYCHOACTIVE SUBSTANCES IN BIOLOGICAL FLUIDS

Substances	Number of subjects
Cannabinoids	18
Cocaine	9
Amphetamines	6
Opiates	3
Benzodiazepines	1

TABLE 14 MULTIPLE INTAKE OF PSYCHOACTIVE SUBSTANCES

Substances	Number of subjects
Psychoactive substances without alcohol	30
Alcohol and psychoactive substances	18
Two or more psychoactive substances without alcohol	11
Alcohol and two or more psychoactive substances	6

The project described above is probably an ongoing one since a second report was published by Ferrara et al in 1997. The period of sample collection was extended and included the months August, September, and December 1995. Rapid clinical screening was carried out on 2,779 drivers, including 480 who were suspected of driving under the influence of drugs. The results indicate that 52.3% of the drivers who were subjected to complete toxicological ascertainment had a measurable BAC, and 31.7% of the entire driver sample were legally drunk (BAC > 0.8 g/l). The study concluded that 11.7% of the subjects were driving under the influence of psychoactive substances. Since the drivers were stopped early on Sundays morning (between 1:00 a.m. and 7:00 a.m.) it was obvious that many drivers came from discos and other public places (about 70%). It was clear that stimulants were taken primarily by drivers coming from discos, whereas cannabis was found to be used by drivers coming from various places (Table 15).

TABLE 15 USE OF PSYCHOACTIVE SUBSTANCES ACCORDING TO PLACES VISITED BEFORE DRIVING

Setting	Cannabinoids	Amphetamines	Cocaine	Opiates
Disco	15	6	6	2
Other public place	11	0	3	2
Private house	8	1	3	1
Other	7	0	2	0
Total	**41**	7	**14**	**5**

4.8 NETHERLANDS

The prevalence of drug and/or alcohol use by drivers during weekend nights has recently been investigated in the Netherlands (Mathijssen, 1998). In the autumn of 1997 roadside tests were conducted in nine selected research areas (cities, nationally distributed) on Friday or Saturday nights between 10:00 p.m. and 4:00 a.m. In one area (Amsterdam), measurements were carried out on both Friday and Saturday night. The main objective of the study was to obtain insight into possibilities for reliably determining the use of drugs (whether or not in combination with alcohol) among motorists. In particular the occurrence of non-responders was of interest to the investigators. A second objective of the study was to assess the practical application as well as the reliability of rapid drug screening tests, such as the Drugwipe® for detecting amphetamines and cannabinoids in sweat. Subsequently, urine samples were tested afterwards for the detection of amphetamines, cannabinoids, cocaine, opiates, methadone, benzodiazepines, barbiturates and tricyclic antidepressants using the Triage® and Accusign® systems. Confirmative analyses were conducted by using Gas Chromatography/Mass Spectrometry (GC/MS), or, in the case of cannabinoids, with High Pressure Liquid Chromatography (HPLC-DAD).

A total of 402 motorists were requested by the police to participate in the study. Of them, 47 (11.7%) refused to participate. From 62 subjects (15.4%) it was not possible to obtain a urine sample, although sweat tests could be taken. No clear indications were found to suggest that drug use characteristics of these subjects differed from those who were able to produce a urine sample.

The results of the study indicated that 8.5% of the samples tested positive for drugs other than alcohol (Table 16). Especially among male drivers in the age of 18 to 25, the prevalence of illicit drugs was found to be high: 17.5% tested positive. The vast majority of these involved the use of cannabis.

The Drugwipe® for the rapid detection of amphetamines in sweat turned out to be an extremely insensitive test; none of the subjects who tested positive in urine had tested positive with the sweat test. No clear conclusions could be drawn from the results with the Drugwipe® for the detection of cannabinoids. Triage® and Accusign®, however, did appear to be reasonably reliable screening tests.

These results do not provide insight in the prevalence of drug use by the total driving population. The Dutch survey includes a subset of drivers stopped at road side blocks during late-night hours on weekends. The sample of motorists is too limited to conclude on the prevalence of drugs in drivers during weekend nights. Furthermore, the refusal rate exceeds the total prevalence, which might have a profound effect on inferences about drug use from this study. The limited number of drivers tested positive for licit drugs is probably due to the selection of the periods during which drivers were stopped. At these hours drivers tend to be younger and are generally not being treated for anxiety, sleep disorders or depression.

TABLE 16 THE PREVALENCE OF DRUG USE WITH OR WITHOUT ALCOHOL IN 293 CASES

Region	N (urine samples)	Number of positives	% Positives
Utrecht	22	1 x benzodiazepines 1 x cannabinoids + BAC 1.53g/l	9.1
Amsterdam	40	1 x cannabinoids 1 x cocaine + BAC 1.10 g/l 1 x amphetamine + methamphetamine	7.5
Terneuzen	30	1 x codeine 1 x cannabinoids 1 x cocaine + cannabinoids	10.0
Oostburg	33	1 x codeine 1 x cannabinoids 1 x amphetamines	12.1
Noordwijk	30	1 x cannabinoids + BAC 0.45 g/l	3.3
Rotterdam	34	3 x cannabinoids 1 x amphetamines + cannabinoids	11.8
Sittard	28	1 x codeine + BAC 0.47 g/l 1 x cannabinoids 1 x morphine	10.7
Kerkrade	36	3 x cannabinoids 1 x amphetamine + BAC 0.28 g/l	11.1
Maastricht	40	1 x cannabinoids	2.5
Total	293	25	8.5

4.9 NORWAY

In a Norwegian study published by Skurtveit et al. (1996), blood samples from 2,819 drivers for suspicion of driving under the influence of drugs were received (as a subset of a total of 8,429 samples) by National Institute of Forensic Toxicology in 1994 were screened for the most commonly abused drugs. The screening was carried out if the BAC was below 0.15 percent (1.5 g/l). Samples with BACs above 0.15 percent, were analyzed for drugs other than alcohol only after special requests by the police. Hence, drug analyses were completed on 2,529 samples. Screening on cannabinoids, amphetamines, benzodiazepines, opiates, cocaine and barbiturates was performed by using immunological methods. Positive results were confirmed by Gas Chromatography/ Mass Spectrometry (GC/MS).

The results show that about 47% of thesuspected drunken drivers had a BAC above 0.15 percent, being more than three times the legal limit in Norway of 0.5 g/l. This percentage was 25% for drugged drivers (Table 17).

Drugs were found in 59% (n=1,495) of all cases. In 30% (n=753) alcohol was the only psychoactive substance found. In 11% of the cases neither alcohol nor drugs were detected. The most frequently detected drugs were benzodiazepines (n=775; diazepam, n=577; flunitrazepam, n=198), cannabinoids (n=660), amphetamine (n=533), morphine (n=193), and codeine (n=104). Cocaine was found in only one case, whereas methylenedioxymetamphe-tamine (MDMA or Ecstacy) could not be detected. Benzodiazepines were most frequently detected in female drivers, whereas cannabinoids were less frequently detected in this group, compared to male drivers (Table 18).

The authors emphasized that during the last ten years the number of drivers suspected for drugged driving in Norway has shown a three-fold increase. The largest increase since 1990 has been found for amphetamines (more than 145%). The authors further indicated that Norway has a higher frequency of cases from suspected drugged drivers compared to other Nordic countries. The ratio of frequencies varied from 3.9 (Finland) to 8.2 (Denmark). It is unclear whether this statement can be made in general, since the sample selection procedures by the police and road traffic laws might not be the same in the various Nordic countries. This explanation was suggested by the authors as well, since epidemiological studies revealed that the

TABLE 17 DISTRIBUTION OF BAC'S OF DRIVERS SUSPECTED FOR DRUNK AND DRUGGED DRIVING

Blood Alcohol Concentration (g/l)	Suspicion of driving under the influence of alcohol	Suspicion of driving under the influence of drugs other than alcohol
	Number (%)	Number (%)
0.0 - 0.5	767 (13.7)	1,575 (55.9)
0.5 - 1.5	2,229 (39.7)	538 (19.1)
> 1.5	2,614 (48.6)	706 (25.0)
Total	5,610 (100)	2,819 (100)

TABLE 18 DISTRIBUTION OF DRUGS OTHER THAN ALCOHOL IN 267 FEMALE AND 2,262 MALE DRIVERS

Substance	Number of positives (f)	Percentage (f)	Number of positives (m)	Percentage (m)	Significance p<
Benzodiazepines	103	38.6	672	29.7	0.005
Cannabinoids	47	17.6	613	27.1	0.001
Amphetamines	50	18.7	483	21.4	NS
Morphine	28	10.5	165	7.3	NS

f = females; m = males

prevalence of drugs other than alcohol in fatal crashes in Norway was similar to that found in other countries. One possible explanation for the apparent high prevalence of drugged driving in Norway may be that the Norwegian police force is more focused on detecting these problems. Some countries do not have legislation that that applies to drug control in drivers as easily as for alcohol control. The results further indicate a high prevalence of benzodiazepine use in drugged drivers. It is unclear how the use of these drugs in the general population has been changed over the last few years.

An update of the Norwegian data has been given by Christophersen and Morland (1997). They report an increase in the total number of drivers suspected of driving under the influence of drugs other than alcohol, from 33% in 1994 to about 40% in 1995. The highest increase was noted for cannabinoids and amphetamines, the increase of the latter being recorded from 216 cases in 1991 to 937 cases in 1995 (more than 300%). Some other findings are of interest as trends in drug abuse. An increasing misuse of clonazepam (medicinal drug for the treatment of epilepsy) among drivers has been observed, often found in combination with other drugs and/or in concentrations above therapeutic levels. Only 3% (n=3) of the clonazepam positive samples (n=91) could be referred to medical treatment. A closer look at the samples analyzed in 1995 revealed that benzodiazepines were often not taken according to recommended therapeutic standards. According to the authors' interpretation of the blood levels they indicated that only 5% of the benzodiazepine positive samples could represent normal therapeutic use. A correlation has been documented between the number of prescriptions for benzodiazepines in the different provinces and the frequency of benzodiazepines detected in blood samples of drugged drivers (Skurtveit et al. 1995). The normal prescribing and dispensing practices therefore are found responsible for the use of these drugs in the driver population.

In an attempt to estimate the prevalence of drugs in drivers injured in traffic crashes in Norway Christophersen et al. (1995) analyzed the blood samples of drivers involved in non-fatal accidents. The study included all blood samples of injured drivers (n=394) received by the Norwegian Institute of Forensic Toxicology during a five - month period (August through December 1993). The samples were analyzed by using the methods described above both for alcohol and drugs independently of the primary suspicion by the police. The total number of blood samples included 206 drivers suspected of driving under the influence of alcohol, and 188 suspected of driving under the influence of drugs other than alcohol.

Alcohol only, drugs only and alcohol combined with drugs were found in 51.8 (n=204), 12.9 (n=51), and 11.2% (n=44) of the samples respectively. The most prevalent drugs besides alcohol were benzodiazepines (13.7%), cannabinoids (7.5%) and amphetamines (4.1%). The number of positive cases and multiple drug use are summarized in Tables 19 and 20.

All samples with blood alcohol concentration (BAC) above 0.01% were recorded as positive. Alcohol was detected with a prevalence of more than 50% among accident drivers. Alcohol was also found in 46% of the samples positive for drugs other than alcohol. More than one drug was detected in 36% of the drug positive samples (alcohol not included). The distribution of BACs in samples positive for alcohol and samples positive for both alcohol and drugs was not significantly different ($p>0.05$; χ^2-test). This finding indicates that alcohol consumption by drivers combining alcohol and drugs, is similar to the consumption by drivers using alcohol only.

The Norwegian data presented by Christophersen et al. are most likely to be conservative for injured drivers in general, since samples entered the study as a result of police suspecting alcohol or drug involvement. As a concluding remark Christophersen and Mørland (1997) indicate that Norwegian authorities have decided that all blood samples from drivers suspected by the police of driving under the influence will be analyzed for both alcohol and drugs, independent of the primary suspicion from the police. This new routine started from October 1996.

TABLE 19 ALCOHOL AND DRUG USE AMONG INJURED DRIVERS (N=394)

Substance	Number of cases (%)
No alcohol, no drugs	95 (24.1)
Alcohol only	204 (51.8)
Drugs only	51 (12.9)
Alcohol and drugs	44 (11.2)
Alcohol- total	248 (62.9)
Drugs - total	95 (24.1)
Drugs and alcohol - total	299 (75.9)

TABLE 20 SINGLE AND MULTIPLE DRUG USE AMONG INJURED DRIVERS (N=394)

Substances	Number of cases (%)
Benzodiazepines only	12 (3.1)
Benzodiazepines only or combined with other drugs	28 (7.4)
Benzodiazepines - total	54 (13.7)
Cannabinoids only	5 (1.3)
Cannabinoids only or combined with other drugs	15 (3.8)
Cannabinoids - total	30 (7.6)
Amphetamines only	6 (1.5)
Amphetamines only or combined with other drugs	13 (3.3)
Amphetamines - total	16 (4.1)
Opiates only	5 (1.3)
Opiates only or combined with other drugs	13 (3.3)
Opiates - total	17 (4.3)

4.10 SPAIN

A driver population based survey carried out by the University of Valladolid and the National Traffic Agency revealed that about 5% of Spanish drivers are taking regularly (at least for 1 month duration) medication which can impair driving performance (Del Rio & Alvarez, 1996). The medicines involved are characterized as known to impair driving ability according to the drug's official summary of product characteristics and package insert. Furthermore, the same study revealed that driving after taking illicit drugs is reported by 3% of the driver population included in the survey (Del Rio & Alvarez, 1995).

The prevalence of licit and illicit drug use in fatally - injured drivers was investigated in two separate studies conducted with support of the National Traffic Agency (Alvarez et al., 1997).
The first study was carried out by the University of Valladolid. Between January 1994 and October 1996 in total 322 blood samples could be obtained from drivers killed in road traffic accidents. The authors did not provide any information on selection procedures. However, they stated that research purposes instead of legal objectives were involved. In 37 cases analytical procedures could not be carried out (reason not mentioned), resulting in 285 cases in the final sample (from 255 male and 30 female drivers). Age distribution was as follows: 33.7% (n=96) between 16 and 25 years, 43.3% (n=129) between 26 and 45, and 21.0% (n=60) over 45. The average age (± SD) was 34.1 ± 13.2, 33.9 ± 13.1 for men and 36.0 ± 14.7 for women. Most accidents occurred during weekend hours (60.3%), whereas 39.6% of the drivers were killed on week days (Monday to Friday). Blood samples were analyzed for alcohol by head space Gas Chromatography. Screening for drugs other than alcohol was carried out by immunoassay techniques or chroma-tographic methods. Positives were confirmed and analyzed for quantitative determinations by Gas Chromatography/ Mass Spectrometry (GC/MS), High Pressure Liquid Chromatography or Gas Chromatography.

In the second study 979 blood samples of drivers killed in road crashes and suspected by the police to be influenced by drugs or alcohol were taken by forensic doctors and sent to the National Toxicological Center in Madrid. Samples could be obtained from 887 male drivers, whereas 86 were females (the sex was not known in six cases). The average age of the fatally injured drivers was 35 years. In 42% of all cases accidents occurred during weekends (Saturday and Sunday). Analytical procedures were the same as those described above in the first study. Statistical analyses in both studies were carried out by means of SAS (version 6.7) and p-values < 0.05 were considered to show significant differences.

The prevalence of alcohol, licit and illicit drugs in fatally - injured drivers in both studies are summarized in Table 21. Different types of illicit drugs found in the samples are given in Table 22.

Alcohol was detected in more than half of the drivers killed in road traffic accidents. The combination of illicit drugs with alcohol was more frequently found than the combination of medicines and alcohol.

TABLE 21 PREVALENCE OF ALCOHOL AND DRUG USE IN FATAL ROAD ACCIDENTS

Substances	Study 1 (n=285) Number of cases (%)	Study 2 (n=979) Number of cases (%)
Alcohol only	126 (44.2)	434 (44.3)
Alcohol with other substances	18 (6.3)	68 (6.9)
Alcohol with BAC's 0.01-0.79 g/l	43 (15.1)	136 (13.9)
Alcohol with BAC's >0.8 g/l	101 (35.4)	366 (37.4)
Medicines only	12 (4.2)	31 (3.9)
Medicines with alcohol	4 (1.4)	23 (2.3)
Medicines with illicit drugs	8 (2.8)	16 (1.6)
Medicines with alcohol and illicit drugs	2 (0.7)	4 (0.4)
Illicit drugs only	7 (2.5)	20 (2.0)
Illicit drugs with alcohol	12 (4.2)	41 (4.1)
Medicines - total	26 (9.1)	74 (7.5)
Illicit drugs - total	29 (10.2)	81 (8.3)
Any substance - total	45 (15.8)	135 (13.8)
No substance detected	114 (40.0)	410 (41.6)

TABLE 22 DIFFERENT ILLICIT DRUGS FOUND IN DRIVERS INVOLVED IN FATAL ROAD ACCIDENTS

Substances	Study 1 (n=285) Number of cases (%)	Study 2 (n=979) Number of cases (%)
Any illicit drug	46 (100.0)	109 (100.0)
Amphetamine	4 (8.7)	9 (8.3)
Cocaine	21 (45.6)	49 (44.9)
Cannabinoids	4 (8.7)	15 (13.8)
Opiates	14 (30.4)	30 (27.5)
Other substances	3 (6.5)	6 (5.5)

Cocaine and opiates were the drug most frequently found in fatally - injured drivers The most recent information on the prevalence of drugs other than alcohol in drivers killed in road accidents is presented in Table 23. These data are the extension of the second study for the year 1996 (Sancho, 1997). The total number of samples sent to the National Toxicological Center was 383, compared to the number of 1995 (279) an increase by 37%. The samples were obtained from forensic doctors in ten different regions of Spain. The majority of the samples were taken from male drivers (90.6%), whereas about half of the total samples were collected during weekends and holidays (52%). Alcohol was found positive (>0.2 g/l) in 186 blood samples (48.5%); 35% of all positives were found with BACs > 0.8 g/l.

TABLE 23 PREVALENCE OF LICIT AND ILLICIT DRUG USE, WITH OR WITHOUT ALCOHOL, IN FATALLY INJURED DRIVERS (1996)

Substance	Number of positives cases with alcohol	Number of positives cases without alcohol
Medicines:	11	11
Benzodiazepines	(5)	(4)
Antidepressants	(0)	(4)
Barbiturates/antiepileptics	(4)	(2)
Analgesics	(1)	(1)
Antiemetics	(1)	(0)
Illicit drugs:	23	12
Cocaine	(14)	(10)
Cannabinoids	(7)	(2)
Amphetamines	(7)	(2)
Benzodiazepines	(2)	(4)
Heroin	(2)	(5)
Multiple drug use:	7	11
Cocaine, cannabinoids	(1)	(1)
Cocaine, amphetamines	(3)	(1)
Cocaine, benzodiazepines, heroin	(2)	(0)
Amphetamines, cannabinoids	(1)	(1)
Benzodiazepines, heroin	(0)	(1)
Benzodiazepines, cocaine	(0)	(3)
Heroin, cocaine	(0)	(4)

Although the number of the positive cases is too small to draw any conclusions, it is clear that the trend shown in the previous years is still apparent. Cocaine is the most frequently detected illicit drug, whereas the use of illicit drugs in combination with alcohol is more prominent than the use without alcohol consumption.

It is unclear how these data relate to the prevalence of drug use in Spain, since the selection of cases and blood samples is determined by forensic doctors and the selection procedures are unknown. However, the data are collected and analyzed within the last five years using those procedures and methods and can provide reasonable insight into the trends in licit and illicit drug use in Spanish drivers killed in road accidents.

4.11 SWEDEN

A number of studies on the prevalence of drugs other than alcohol were carried out in the 1970s and early 1980s. A Swedish study done in the late 1970s revealed that drugs were found in 4% of road accident victims (motor vehicle occupants, pedestrians, and cyclists) treated at the emergency ward (Jacobson et al. 1983). An other study done in the late 1970s in Southern Sweden showed that 32% of fatally injured drivers had drugs and/or alcohol (Krantz and Wannerberg, 1981). A more recent study was undertaken by Sjögren et al. (1997a) to determine the prevalence of drug and alcohol use in motor vehicle drivers. Injured motor vehicle drivers (n=130; 104 men, 26 women) who were hospitalized in Umeå (Northern Sweden) and fatally injured drivers who were autopsied (in Umeå: n=111: 91 men, 20 women; and in Gothenburg, Western Sweden: n=136, 104 men, 32 women) from May 1991 through December 1993 were tested for alcohol and both licit and illicit drugs. Because Swedish law strongly recommends that police authorities request postmortem examination of all fatally injured drivers, almost all traffic fatalities are autopsied in Sweden. Since official statistics in Sweden on alcohol and drug use by injured victims are based on police assessments of inebriation the authors also compared the rate of police detection by comparing blood analyses. Blood samples were tested for the presence of alcohol, licit drugs (including all drugs that are officially regarded as traffic hazardous in Sweden, e.g. benzodiazepines and barbiturates), and illicit drugs such as amphetamines, heroin, cocaine, and cannabinoids. Nineteen percent of the Umeå-hospitalized drivers (UHDs), 28% of the Umeå fatally injured drivers (UFDs), and 21% of the Gothenburg fatally injured drivers (GFDs) tested positive for drugs and/or alcohol (Table 24). Ten percent of the UHDs, 8% of the UFDs and 6% of the GFDs tested positive for drugs. Almost 5% of the UHDs had illicit drugs, and 5% had licit drugs. Only 3% of the GFDs and none of the UFDs had illicit drugs. Twelve percent of the UHDs, 24% of the HFDs, and 17% of the GFDs tested positive for alcohol. Two percent of the UHDs, 6% of the UFDs, and 2% of the GFDs had a combination drugs and alcohol (Sjögren et al., 1997b)

Benzodiazepines were the most commonly found licit drugs in the UHDs (Table 25). Five percent of the UHDs had opiates such as codeine, dextropropoxyphene, and morphine. These drugs were less common among the GFDs. The most commonly found illicit drug was cannabis, followed by amphetamines.

TABLE 24 PREVALENCE OF DRUG/ALCOHOL USE IN (FATALLY) INJURED DRIVERS

Substance	UHDs ; n=130 (%)	UFDs; n=111 (%)	GFDs; n=136 (%)
Drugs	10 (8)	2 (2)	6 (4)
Alcohol	13 (10)	21 (19)	20 (15)
Drugs and alcohol	2 (2)	6 (6)	3 (2)
Missing data	5 (4)	-	-
Negative test	100 (77)	82 (74)	107 (79)

TABLE 25 DRUGS FOUND IN (FATALLY) INJURED DRIVERS

Substance	UHDs ; n=130 (%)	UFDs; n=111 (%)	GFDs; n=136 (%)
Benzodiazepines	8 (6)	3 (3)	4 (3)
Opiates	6 (5)	5 (5)	3 (2)
Cannabinoids	4 (3)	-	3 (2)
Amphetamines	3 (2)	-	-
Barbiturates	2 (2)	1 (1)	-
Antiepileptics	2 (2)	-	-
Central muscle relax.	-	2 (2)	3 (2)
Sedatives	-	1 (1)	3 (2)

Drivers who tested positive for drugs and/or alcohol were more likely to be involved in single vehicle crashes than those who were tested negative ($p<0.0005$).
One-fifth of the injured hospitalized drivers had taken drugs and/or alcohol. There are no comparable reports in Sweden. The present figures for the fatally - injured drivers (26% in Northern Sweden and 21% in Western Sweden) are lower than those found (32%) in the study carried out in the late 1970s. The authors indicate that this discrepancy may be due to a change in drug and/or alcohol consumption in the last 20 years or due to a geographical variation in substance use in the different areas in Sweden or due to a combination of these factors.

The findings of the blood analyses were compared with police reports on intoxication by alcohol and/or drugs in the second study (Sjögren et al., 1997b). In the injured hospitalized drivers the police suspected intoxication in 13%, whereas blood analyses showed drug and/or alcohol in 18% of the drivers. In the fatally injured drivers these figures were 7% and 23%, respectively. The sample size was too small and too limited to be considered as representative of the entire Swedish population. But the findings are important indicators of the disparity between assessments on intoxications made by the police and blood analyses. Therefore the authors conclude that official statistics on these prevalences should be based on blood analyses only. An important final finding was the fact that 17% of the reports on hospitalized drivers were missing. The most likely reason for this is that the crash was not reported to the police. It is estimated that in Sweden, only 51% of crashes in which drivers are inured will be reported to the police (Official Statistics of Sweden. Traffic Injuries, 1992).

4.12 SWITZERLAND

The objective of a survey by Augsburger and Rivier (1997) was to investigate the nature of drugs used among drivers suspected of driving under the influence of drugs (DUID) in the Canton of Vaud during a 13 years period ranging from 1982 to 1994. In a retrospective evaluation 641 cases were selected using the following criteria: drivers still alive 24 hours after the event with age over 18 years, availability of specimens (urine and/or blood) suitable for analyses and documentation to support DUID. Analytical procedures were kept unchanged over the period of 13 years and included several immunological screening tests and different Gas Chromatographical methods for confirming the presence of various drugs. Drugs included in the analytical screening were several drugs of abuse such as amphetamines, cannabinoids, cocaine, LSD-25, opiates and medicinal drugs such as antiepileptics, barbiturates, benzodiazepines, phenothiazines, and tricyclic antidepressants. Police controls (273 of 641, 42.6%) and accidents (254 of 641, 39.6%) were the most frequent circumstances for requesting toxicological analyses. Erratic driving was less frequently found (95 of 641, 14.8%), whereas in the remaining cases circumstances were not indicated. The population of the sample consisted of 551 males (86%) and 90 females (14%), and the average age was 27 $\pm$ 7 years (range: 18-74).
Only 46 cases (7.2%) were concluded drug free (alcohol included), to be considered as false positive observations by the police. Among these cases 27 (58.7%) were accidents, situations in which identification of drug influence is not easy, because of state of shock or injuries. The prevalence of detected drugs in urine or blood among 641 drivers suspected of DUID is presented in Table 26.

Benzodiazepines were the most frequently present licit drugs. Methadone and methaqualone were never found alone. Methadone is frequently used as heroin substitute for narcotic maintenance treatment in former opiate addicts, but the drug is also used illegally. In the case of treatment methadone is often prescribed in combination with benzodiazepines. Methaqualone is commercially available in a combined preparation with diphenhydramine.

TABLE 26 PREVALENCE OF DRUG USE AMONG 641 DRIVERS SUSPECTED OF DUID

Substance	Number of positives (%)
Alcohol only	50 (7.8)
Drugs only	365 (56.9)
Alcohol with drugs	180 (28.1)
Alcohol - total	230 (35.9)
Drugs - total	545 (85.0)
Cannabinnoids	(57.3)
Opiates	(36.3)
Benzodiazepines	(14.8)
Cocaine	(10.5)
Methadone	(10.3)
Amphetamines, methaqualone others	(<5%)

TABLE 27 PREVALENCE OF MULTIPLE DRUG USE IN 641 CASES

Multiple use	Number of positives (%)
Cannabinoids with alcohol	132 (20.6)
Cannabinoids with opiates	123 (19.2)
Opiates with methadone	50 (7.8)
Opiates with cocaine	46 (7.2)
Opiates with alcohol	45 (7.0)
Opiates with benzodiazepines	44 (6.9)
Cannabinoids with benzodiazepines	35 (5.5)
Cannabinoids with cocaine	32 (5.0)
Cannabinoids with methadone	30 (4.7)
Benzodiazepines with alcohol	26 (4.1)

Combinations of drugs were most frequently observed with cannabinoids (132 cases with alcohol; and 123 cases with opiates), both found in approximately 20% of the drivers suspected of DUID. Multiple drug use is presented in Table 27.

There was a remarkable increase in the number of positive cases for amphetamines. During 1982 - 1989 only one case was found positive, whereas eight cases were found for the period 1990-1992, and eighteen cases for the1993-1994 period.

The authors focus their results on discussing the risk of combinations of drugs. The use of cannabis without any other drug seems to be less common, since 70.3% of the cannabinoids positives also contain at least one other drug, and 36% of cannabinoids positives also contain alcohol. They stress the fact that the adverse effects from interactions of drugs on driving ability have still not been investigated to an extent that allows simple interpretations of results by toxicological experts. They strongly suggest that educational programs should be developed to prevent drivers from driving after polydrug consumption and abuse.

In a study by Staub et al. (1994) the prevalence of psychotropic drugs of 383 drivers being responsible for car accidents and had taken alcohol as well, was investigated in the Canton of Geneva. During the period of 1st November 1990 till 31st October 1991 blood analyses were requested by the police in 476 cases (out of in total 4592 traffic accidents). Only the cases in which the driver was responsible for the accident were included in this study. The average age of the drivers included in the study was 36 years (range 18-72). In 88% of all samples blood alcohol concentrations (BACs) above the legal limit of 0.8 g/l were detected, whereas about half of the samples (51.2%) contained BACs between 1.0 and 2.0 g/l. In 58% of all cases (n=222) accidents occurred between 8:00 p.m. and 4:00 a.m. Drugs included in the analytical screening were several drugs of abuse such as amphetamines, cannabinoids, cocaine, opiates and medicinal drugs such as barbiturates, benzodiazepines, methadone and tricyclic antidepressants. Blood samples were first screened by using the Abbott ADx-analyzer (a fluorescence polarization immunoassay). For screening on benzodiazepines the immunological technique developed by DPC (Diagnostic Product Corporation) was used in order to achieve more sensitivity. Different Chromatographic techniques and detectors as well as Gas Chromatography/Mass Spectrometry (GC/
MS) were used to confirm positive results obtained with the immunoassay technique.

The prevalence of psychotropic drugs in the 383 cases is presented in Table 28.
It was shown that multiple drug use could be observed in 20% of the drug positive cases. Benzodiazepines and cannabinoids were the drugs most frequently detected in the blood samples of the drivers. In comparing the users of both drugs it was further shown that in 21% of the benzodiazepine positive cases no alcohol was detected, whereas this was the case in only 11% of the cannabinoids positives. The average age of drivers using benzodiazepine was 41 years, with 18% above 55. In this age category no cannabinoids postive driver could be detected, while the average age of cannabinoids positive cases was 32 years.
The time of accident in the benzodiazepine positive cases was between 12.00 hrs and 16.00 hrs, whereas 40% of the cannabinoids positives were detected in drivers involved in accidents between 24.00 hrs and 4.00 hrs. These results are not representative for all drivers taking psychotropic drugs, but indicate the different types of drug users among those drivers who are found responsible for a car accident while having consumed alcohol.
In a study conducted by the Institute of Forensic Medicine of the University of Zurich (Canton of Zurich) all cases of drivers suspected of driving under theinfluence of drugs other than alcohol submitted from 1989-1991 were used for toxicological and medical evaluations (Friedrich-Koch and Iten, 1994). Blood and urine samples were screened with different immunoassays (RIA and EMIT) for opiates, cocaine, cannabinoids, methadone, benzodiazepines, barbiturates and amphetamines. Different Chromatographic techniques and detectors as well as Gas Chromatography/Mass Spectrometry (GC/MS) were used to confirm positive results obtained with the immunoassay technique. In 160 of the 243 cases included (65.8%) at least one substance possibly affecting driving performance could be confirmed in blood (or urine for cannabis). Of these 160 positive drug cases 105 resulted from accidents and 55 from police controls, whereas one third of these were registered while making routine controls. Only 137 of the 160 cases allowed complete toxicological and medical evaluations and were included for final analyses. Most of the drivers were male (87.5%). The majority of the drivers were between 20-29 years (67.5%), whereas the next most frequent group were drivers between 30-39 (18.1%). Most drivers belonged to the so - called 'drug scene'. The prevalence of drugs in blood and urine samples of 137 cases is presented in Table 29.

TABLE 28 PREVALENCE OF DRUG POSITIVES IN 383 DRIVERS RESPONSIBLE FOR CAR ACCIDENTS

Substance	Number of positives (%)
Alcohol only	285 (74.4)
Alcohol with drugs	70 (18.3)
Drugs only	15 (4.0)
Benzodiazepines	52 (13.6)
Cannabinoids	31 (8.9)
Barbiturates	11 (2.9)
Opiates	5 (1.3)
Tricyclic antidepressants	2 (0.5)
Cocaine	2 (0.5)
Methadone	2 (0.5)
Amphetamines	1 (0.3)

Flunitrazepam (a hypnotic also very popular as a drug of abuse) was detected in 35 of the 54 benzodiazepine positives (64.8%).

When examining the consumption pattern of the drivers included in this study, it was shown that multiple drug occurred in two thirds of all cases (62%). In 38% of drug positive cases only one substance could be detected (Table 30).

The most frequently used combinations of drugs were all drugs/alcohol (30x), cannabis/alcohol (12x), opiates/cannabis (9x), opiates/cocaine (7x), benzo-diazepines/ cannabis (7x). Cannabis use in combination with alcohol was more frequently found than any other licit or illicit drug. The results of this study provide an estimate of drug presence in drivers suspected of driving under the influence of drugs other than alcohol in the Canton of Zurich. The percentages reported are most likely conservative for drivers in general due to the way in which samples entered the study, that is, as a result of police suspecting drug involvement particularly in accident situations.

TABLE 29 PREVALENCE OF DRUGS IN 137 DRIVERS SUSPECTED OF DRIVING UNDER THE INFLUENCE OF DRUGS OTHER THAN ALCOHOL

Substance	Number of positives (%)
Cannabinoids	64 (46.7)
Opiates	58 (42.3)
Benzodiazepines	54 (39.4)
Cocaine	38 (27.7)
Alcohol	30 (21.9)
Methadone	7 (5.1)
Codeine	3 (2.2)
Phenobarbital	2 (1.5)
Clomethiazol	1 (0.7)

TABLE 30 MULTIPLE DRUG USE IN 137 DRUG POSITIVE CASES

Multiple drug use	Number of positives (%)
One drug	52 (38.0)
Two drugs	55 (40.1)
Three drugs	25 (18.2)
Four drugs	5 (3.6)

4.13 UNITED KINGDOM

In a survey by the Road Safety Division of the Department of the Environment, Transport & the Regions findings were reported from 619 road user fatalities during the first 15 months of the study (up to 7th January 1998) of a 3 year study on the incidence of drugs in road accident fatalities (DETR, 1998). These 619 fatalities represented a sample of about 20% of all road fatalities aged 16 years and over, including passengers and pedestrians, who died within 12 hours of being injured in a road traffic accident in England, Scotland and Wales. Pathologists had been asked to take samples at random. Blood and urine samples were taken in all cases, whether the presence of drugs was suspected or not. The following classes of drugs were screened for in the urine samples by immunoassay techniques: alcohol, amphetamines, cannabis, cocaine, opiates, methadone, LSD, benzodiazepines, tricyclic antidepressants. The percentages of those testing positive for licit and illicit drugs by road user group are given in Table 31.

All these figures indicate a considerable increase in cannabis taking and multiple illicit drug use compared with a previous study in 1985-1987. The prevalence of licit drugs likely to affect driving has not changed significantly in comparing the results of both surveys.

The results of the recent study are based on a representative sample of the incidence of drugs amongst various road user groups. There was a wide geographical distribution, both urban and rural. Furthermore, the distribution of cases which had alcohol above the 0.8 g/l limit was almost identical to that found in national data for each of the road user groups.

Analysis of the data found by age show that cannabis use is confined largely to the under 40s, particularly the under 25, whereas licit drug use is mainly found in the drivers over 40 (Table 32)

TABLE 31 **PERCENTAGES OF VARIOUS ROAD USER GROUPS TESTING POSITIVE FOR LICIT AND ILLICIT DRUGS**

Substance	Percentage positives				
	Drivers (n=284)	Riders (n=125)	Passengers (n=126)	Pedestrians (n=84)	Total (n=619)
Licit drugs	4	6	9	8	6
Illicit drugs: of which	18	14	21	8	16
Cannabinoids	10	5	13	1	8
Amphetamines	2	2	2	2	2
Opiates	1	1	2	1	1
Cocaine	0	0	0	0	0
Methadone	1	0	0	0	0
Multiple drugs	4	6	4	4	5
Alcohol (> 0.8 g/l)	22	15	29	31	23

TABLE 32 DRUG USE BY ROAD USERS IN DIFFERENT AGE GROUPS

	Number of positives						
Substance	**Age groups**						
	16-19	20-24	25-39	40-59	60+	Not known	Total
No drugs	44	71	159	109	66	31	480
Cannabis	17	15	13	3	2	1	51
Amphetamines	0	2	4	4	1	1	12
Opiates	0	3	3	4	5	3	18
Cocaine	1	0	0	0	0	0	1
Methadone	0	0	1	0	1	1	3
LSD	0	0	0	0	0	0	0
Benzodiazepines	0	1	2	4	6	0	13
Tricycl. Antidepr	0	0	0	1	2	0	3
Multiple drugs	3	12	6	6	8	3	38
Total	65	104	188	131	91	40	619

The results represent a realistic picture of the change in the drug use pattern amongst road users since the last study, 10 years ago. There has been a noticeable increase in the number of fatalities, particularly among drivers and riders, who had taken two or more different types of illicit drugs. Only a few drivers and riders (19%) had taken both an illicit drug and alcohol over the legal limit.

5. DISCUSSION

In surveys of illicit drug use in the driver population several problems are encountered such as problems with sample collection and data collection (see also Chapter 3). As a result comparisons across studies from different European countries are often very difficult. Furthermore the lack of conventions used in reporting of the findings may result in significant differences as well. For example, there is no consistency in reporting percentages (all drivers in the sample or only those who were tested for drugs). In the following tables the prevalences of different drugs other than alcohol are presented for each country based upon the research findings gathered in this survey. The overview in each table does not allow the reader to conclude on the prevalence with reference to different populations of drivers. It will only serve as a global description of what has been published and caution is required in presenting an average prevalence.

In the tables for each drug class or substance the following categories of driver populations have been included general driver population, driver population (during late-night hours on weekends), drivers suspected of driving under the influence of drugs, and collision-involved drivers, including (fatally) injured drivers. Different problems exist with each of these categories of drivers. One general problem for all categories is the representativeness of the sample under examination, which in addition is a problem if small sample sizes are included and/or selection criteria are not clear.

In surveys of drug use in the *general driver population* data - gathering is generally through the use of questionnaires or interviews. One major problem observed here involves refusals. Refusal rates can be expected among those drivers who anticipate being confronted with driving under the influence of a drug in a possible contact with the police. This will have profound effects on the results presented if substances are detected with less frequency than alcohol where refusal rates of 15% are observed. For example, if refusal rates of 10% are observed when the expected proportion of drivers who are positive for a given drug is below this percentage, caution has to be given to the interpretation of the research findings.

With *driver populations during late-night hours on weekends* it is clear that the drivers tested are not representative of the total driving population. In general younger drivers are observed, while older drivers are underrepresented. This may cause serious problems if the prevalence of medicinal drugs is determined. For example tranquillizers are expected among a population over 40.

In surveys of *drivers suspected of driving under the influence of alcohol or drugs* drug screens are generally carried out if the blood alcohol level is below the legal limit. This approach automatically excludes information on combinations of licit and illicit drugs with higher blood alcohol levels. Furthermore, the selection of drivers is initially determined by the arresting officer which will undoubtedly introduce biases. Depending upon what variables (e.g. behavioral, signs of drug use) are taken into consideration, if there is suspicion of driving under the influence of drugs other than alcohol, high prevalences can be reported. If drug screening has been carried out in randomly - selected blood samples of drivers suspected of driving under the influence of alcohol-low prevalences will be observed.

In investigations on *collision-involved drivers* documentation of drug impairment is based on different decisions of police officers, doctors and coroners, which can introduce biases. Furthermore, it is known from several studies that only about one half of accidents with injured drivers are reported to the police. It is likely that drivers who have consumed illicit drugs or

large doses of alcohol will avoid contact with the police if possible. Consequently, the prevalence of drug use among drivers in accidents reported to the police is probably lower than among drivers involved in (fatal) injury accidents. In fatally - injured drivers who are found to be impaired by alcohol, data are incomplete most of the time due to the fact that screening for drugs other than alcohol is often not carried out. Previous studies have shown that the police only detects a part of drug positive drivers involved in accidents, which results in the reporting of lower prevalences than actually exist.

Benzodiazepines (Table 33)
The most frequently detected licit drugs in all driver populations are the benzodiazepines. It is expected that these drugs will only show with low prevalences in the general driving population compared to drivers suspected of driving under the influence of drugs other than alcohol. These drugs are normally observed in the older age categories above 40. In Germany a large roadside survey allows one to conclude that for this country the prevalence is about 3%. In Italy and the Netherlands the reported data from roadside surveys were collected during weekend nights and therefore will probably lack a representation of the population of users, since primarily younger drivers were included. In most studies on drivers suspected of driving under the influence of drugs other than alcohol, benzodiazepines are the most predominantly found licit drug class with high prevalences (13% - 75 %) In collision-involved drivers lower prevalences are found (2%-13%) The high prevalence found in Norwegian studies has been explained by the authors as a result of the fact that the Norwegian police force is more focused on detecting drugged driver problems.

Barbiturates (Table 34)
These drugs are known to cause severe drowsiness and sedation. For that reason physicians frequently will not prescribe these 'old' medicines, unless a barbituarate has been selected for the treatment of epilepsy. Users of these drugs will be less frequently detected in all samples of driver population than users of benzodiazepines. Concequently, compared to the latter drugs barbiturates are less of a safety problem in all European countries.

TABLE 33 PREVALENCE OF BENZODIAZEPINES IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	8.5
Denmark Worm (1996) Steentoft (1997)			 n = 317 n = 221		 75 53
France Deveaux (1995)				n = 97	12
Germany Möller (1994) Krüger (1995)	 n = 3,027		 n = 660		 5 3.6
Italy Ferrara (1990) Zancaner (1995)		 n = 972	 n = 265	 n = 5,000	 8.5 <1
Netherlands Mathijssen (1998)		n = 293			0.3
Norway Skurtveit (1996) Christophersen (1995)			 n = 2,529	 n = 394	 31 13.7
Spain Sancho (1997)				n = 383	2
Sweden Sjögren (1997)				n = 377	4
Switzerland Augsburger (1997) Staub (1994) F-Koch (1994)			 n = 641 n = 383 n = 137		 14.8 13.6 39.4
United Kingdom DETR (1998)				n = 619	2

*NOTE: Prevalence data from different countries are not comparable due due to differences in the set-up of the studies!

TABLE 34 PREVALENCE OF BARBITURATES IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
France Deveaux (1995)				n = 97	1
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		1 0.5
Italy Ferrara (1990)				n = 5,000	3.4
Netherlands Mathijssen (1998)		n = 293			0
Spain Sancho (1997)				n = 383	1.6
Sweden Sjögren (1997)				n = 377	1.5
Switzerland Staub (1994) F-Koch (1994)			n = 383 n = 137		2.9 1.5

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies!

TABLE 35 PREVALENCE OF TRICYCLIC ANTIDEPRESSANTS IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
France Deveaux (1995)				n = 97	21
Germany Möller (1994)			n = 660		0
Italy Ferrara (1990)				n = 5,000	1.5
Spain Sancho (1997)				n = 383	1
Sweden Sjögren (1997)				n = 377	4
Switzerland Staub (1994)			n = 383		0.5
United Kingdom DETR (1998)				n = 619	0.5

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies!

Tricyclic antidepressants (Table 35)

Over the last decade the use of antidepressants has increased in some European countries where data on medicinal drug consumption are available (De Gier, 1995). For example in Germany a 50% increase was observed in 1993 compared to 1984. By contrast the consumption of benzodiazepines has been cut virtually by half during that same period. An increase in the use of antidepressants has also been reported in the Netherlands. An increase in use of antidepressants caused by the introduction of the so-called 'second generation' antidepressants (such as serotonin reuptake inhibitors) does not necessarily mean an increase in the use of drugs that cause driving impairment. These newer antidepressants are known to be less impairing than the 'older' ones such as the tricyclic antidepressants.

The prevalence of tricyclic antidepressants in the general driver population is unknown due to the lack of screening data in the reported surveys. The remarkable high prevalence of 21% in fatally - injured drivers in the French study cannot be explained. This high figure even exceeds the prevalence of benzodiazepines. Similar findings are not known in the available literature and may have to do with the prescribing practices of physicians in northern France (Region Nord- Pas de Calais).

The impairing properties of tricyclic antidepressants (in contrast to 'second generation' drugs) are well know from experimental research. On the other hand, users of tricyclic antidepressants are probably at lower increased risk of experiencing a road traffic accident than users of benzodiazepines, based on some epidemiological data. (Barbone et al., 1998). Therefore, the problems with respect to traffic safety based on the findings in various European countries in this survey (excluding France) are less servere than expected for benzodiazepines and of the same magnitude as those reported for barbiturates.

Cannabinoids (Table 36)

In most surveys reported in different European countries cannabinoids are the most frequently detected illicit drug. The prevalence in the driver population as derived from a German study is rather low (0.6%). Higher prevalences are observed in the 'late-night weekend-drivers' (e.g. 5% in the Netherlands), whereas drivers suspected of driving under the influence of alcohol and/or drugs show results with great variation: from 8% in Germany in randomly - selected blood alcohol samples to 57% in samples of drivers suspected of driving under the influence of drugs in Switzerland. In collision-involved drivers results are observed with similar variation (from 1.3% in fatally-injured drivers in Spain to 12% in injured drivers in France). These differences are partly explained by differences in selecting the population under examination. However, another contributing factor might be the differences in drug use pattern among European countries. For example, Denmark and Norway are both Scandinavian countries with approximately the same size of population. Looking at the five most frequently detected substances in similar investigations, it is shown that in Norway cannabis was most observed, whereas in Denmark this drug only rated number five. This once again underlines the complex nature of cannabis use when discussing trends in European countries.

Opiates (Table 37)

In general the use of opiates is less frequently observed in driver populations than the use of cannabis. In investigating the general driver population in Germany a low prevalence was presented (0.7%). A slightly higher prevalence was detected in drivers screened in the late-night hours (<1% in Italy and 1.3% in the Netherlands). Data derived from drivers suspected of driving under the influence of alcohol or drug, once again show great variations (from 1.3% in a Swiss study among drivers responsible for car accidents and having

taken alcohol as well, to 42.3% in another Swiss study among drivers suspected of driving under the influence of drugs other than alcohol). A ten-fold variation has been observed in collision-involved drivers (from 1% in the United Kingdom in fatally-injured drivers to 10.7% in injured drivers in France). The differences in drug use patterns among drivers in the different European countries will once again contribute to the great variation in prevalence of drug use observed in this survey.

TABLE 36 PREVALENCE OF CANNABINOIDS IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	6
Denmark Worm (1996) Steentoft (1997)			n = 317 n = 221		10 17
France Pélissier (1996) Marquet (1998)				n = 60 n = 296	10 12
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		8 0.6
Italy Ferrara (1990) Zancaner (1995)		n = 972	n = 265	n = 5,000	5.5 1.5
Netherlands Mathijssen (1998)		n = 293			5
Norway Skurtveit (1996) Christophersen (1995)			n = 2,529	n = 394	26 7.6
Spain Alvarez (1997) Alvarez (1997) Sancho (1997)				n = 285 n = 979 n = 383	1.3 1.5 2
Sweden Sjögren (1997)				n = 377	3
Switzerland Augsburger (1997) Staub (1994) F-Koch (1994)			n = 641 n = 383 n = 137		57 8.9 46.7
United Kingdom DETR (1998)				n = 619	8

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies[1]

TABLE 37 PREVALENCE OF OPIATES IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	7.5
Denmark Worm (1996) Steentoft (1997)			n = 317 n = 221		16.4 40
France Pélissier (1996) Marquet (1998)				n = 60 n = 296	5 10.7
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		2 0.7
Italy Ferrara (1990) Zancaner (1995)		n = 972	n = 265	n = 5,000	3.5 <1
Netherlands Mathijssen (1998)		n = 293			1.3
Norway Skurtveit (1996) Christophersen (1995)			n = 2,529	n = 394	8 4.3
Spain Alvarez (1997) Alvarez (1997) Sancho (1997)				n = 285 n = 979 n = 383	4.6 3 2
Sweden Sjögren (1997)				n = 377	4
Switzerland Augsburger (1997) Staub (1994) F-Koch (1994)			n = 641 n = 383 n = 137		36.3 1.3 42.3
United Kingdom DETR (1998)				n = 619	1

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies'

Amphetamines (Table 38)

The prevalence of amphetamines in different driver populations compared to opiates is lower. One remarkable exception is the Norwegian study by Skurtveit (1996) in which blood samples from drivers suspected of driving under the influence of drugs were received in 1994. Amphetamines were detected in 21% (compared to 8% for opiates) of the samples, whereas methylenedioxy-metamphetamine (MDMA or Ecstasy) could not be detected.

The authors emphasized that during the last ten years the number of drivers suspected of drugged driving has shown a three-fold increase in Norway. The largest increase since 1990 has been found for amphetamines (more than 145%). In non-fatal accidents the prevalence of amphetamines (4.1%) in Norway is also the highest com-

pared to data from non-fatal accidents in other countries. The authors indicate that one explanation for this increase may be that the Norwegian police force is more focused to detect drugged driving than in other countries.

TABLE 38 PREVALENCE OF AMPHETAMINES IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	3
Denmark Worm (1996) Steentoft (1997)			n = 317 n = 221		8.8 10
France Pélissier (1996) Marquet (1998)				n = 60 n = 296	2 2
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		0.5 0.08
Italy Ferrara (1990) Zancaner (1995)		n = 972	n = 265	n = 5,000	2.7 0.5
Netherlands Mathijssen (1998)		n = 293			1.3
Norway Skurtveit (1996) Christophersen (1995)			n = 2,529	n = 394	21 4.1
Spain Alvarez (1997) Alvarez (1997) Sancho (1997)				n = 285 n = 979 n = 383	1.3 1.0 2
Sweden Sjögren (1997)				n = 377	2
Switzerland Augsburger (1997) Staub (1994)			n = 641 n = 383		<5 0.3
United Kingdom DETR (1998)				n = 619	2

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies'

Cocaine (Table 39)

The prevalence of cocaine among drivers is among the lowest compared with other il licit substances. In the Norwegian study by Skurtveit (1996) only one sample of the

2,529 blood samples was detected positive for cocaine (not included in Table 39). A high prevalence among drivers suspected of driving under the influence of drugs other than alcohol has been found in the Swiss study by Friedrich-Koch and Iten (1994). In 27.7% of the samples cocaine could be detected. In fatally-injured drivers the prevalence of cocaine in Spain is remarkably high (6%) compared to other countries such as the United Kingdom where cocaine use by (fatally-injured) drivers is not observed.

TABLE 39 PREVALENCE OF COCAINE IN DIFFERENT DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	0.7
Denmark Worm (1996)			n = 221		6
France Marquet (1998)				n = 296	1.8
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		0 0.01
Italy Ferrara (1990) Zancaner (1995)		n = 972	n = 265	n = 5,000	0.5 0.7
Netherlands Mathijssen (1998)		n = 293			0.7
Spain Alvarez (1997) Alvarez (1997) Sancho (1997)				n = 285 n = 979 n = 383	7 5 6
Switzerland Augsburger (1997) Staub (1994) F-Koch (1994)			n = 641 n = 383 n = 137		10.5 0.5 27.7
United Kingdom DETR (1998)				n = 619	0

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies'

Combination of drugs with alcohol (Tables 40 and 41)

The prevalence of drug use in combination with alcohol is frequently reported in the different studies included in this survey. Although the available data do not allow a general figure to be presented, some of the studies have shown results that need further

discussion. In studies in which the combination of drugs with alcohol has been reported as observation in a selection of drug positive cases (Table 40), the prevalence is higher than the percentage of the total sample (Table 41). The variation caused by characteristics of driver populations seem to be less extensive than presented in the previous discussion on the prevalences of various types of drugs. Among drivers found positive for drug use other than alcohol, 20%-65% show positive levels of alcohol in the blood or urine samples. However, differences do exist, especially if the prevalence in a normal driver population is compared to prevalence in a population of drivers stopped for suspicion of driving under the influence of alcohol. In the German Road Side Survey (Krüger et al., 1995), it was shown that none of the samples that were found positive for benzodiazepines (3.64%) was tested positive for alcohol. In contrast, in the study by Möller (1994) benzodiazepines were found in 36 cases (= 5.45%), of which 26 cases tested positive for alcohol use. These findings illustrate that caution is required in drawing conclusions on the use of the combination of drugs with alcohol.

One interesting finding that gives weight to the concern about higher accident risks in the event of multiple drug use is a clear synergistic interaction for alcohol and licit/illicit drugs, if mortality is taken as the outcome variable. The results of the Belgian Toxicology and Trauma Study indicate 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.

In the presentation of data obtained from studies in which the combination of drugs and alcohol among all drivers in the sample has been reported the prevalences are obviously lower and vary from 3% in a Swedish survey to 28% in a Swiss study (Table 41). The latter has reported higher prevalences because the drivers involved were suspected of driving under the influence of drugs other than alcohol. In fatally- injured drivers the prevalence ranges from 3% in Sweden to 19.8% in France.

TABLE 40 PREVALENCE OF THE COMBINATION OF DRUGS WITH ALCOHOL IN DRUG POSITIVE CASES AMONG DRIVER POPULATIONS IN EUROPE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of drug use in combination with alcohol in percentages *
Belgium Meulemans (1997)				n = 2.143	27
Germany Krüger (1995)	n = 3.027				44
Netherlands Mathijssen (1998)		n = 293			20
Norway Skurtveit (1996) Christophersen (1995)			n = 2.529	n = 394	25 46
Spain Sancho (1997)				n = 383	65

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies!

TABLE 41 PREVALENCE OF THE COMBINATION OF DRUG AND ALCOHOL USE AMONG ALL DRIVERS IN THE SAMPLE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, include (fatally) injured	Prevalence of drug use in combination with alcohol in percentages *
France Deveaux (1995)				n = 97	19.8
Italy Ferrara (1990)				n = 5,000	17.5
Norway Christophersen (1998)				n = 394	11.2
Spain Alvarez (1997) Alvarez (1997)				n = 285 n = 979	6.3 6.8
Sweden Sjögren (1997)				n = 377	3
Switzerland Augsburger (1997) Staub (1994)			n = 641 n = 383		28.1 18.3

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies!

Multiple drug use (Tables 42 and 43)

The multiple use of drugs has been reported in different studies. In some studies it is unclear whether or not alcohol is included as a drug. Multiple drug use in drug positive cases is presented without alcohol (Table 42). In a general driver population the prevalence of multiple drug use is zero in the German roadside survey.

In another German study involving randomly - selected samples of drivers suspected of driving under the influence of alcohol the prevalence of multiple drug use among drug positive cases was 25%. In the driver population screened at the weekend during late-night hours in the Netherlands the prevalence of multiple drug use in drug positive cases is 12% (3 out of 25 drug positive cases). In collision-involved drivers with positive tests on drugs other than alcohol the prevalence of multiple drug use tends to be somewhat higher (ranging from 20%-36%).

Multiple drug use among all injured drivers in the Italian study has been reported with a prevalence of 17.4% (two or more drugs, alcohol included) for urine samples. The prevalence for drugs only has been given as 9.4%. In fatally - injured drivers in Spain and the United Kingdom the prevalence is almost similar, 3% and 5% respectively. In drivers suspected of driving under the influence of drugs other than alcohol the prevalence of multiple drug use is higher. In two Swiss studies these prevalences were 62% and 85%, although alcohol was included as a drug.

TABLE 42 MULTIPLE DRUG USE IN DRUG POSITIVE CASES

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of multiple drug use in percentages *
Belgium Meulemans (1997)				n = 2,143	20
Germany Möller (1994) Krüger (1995)	n = 3,027		n = 660		25 nil
Netherlands Mathijssen (1998)		n = 293			12
Norway Christophersen (1995)				n = 394	36
Spain Sancho (1997)				n = 383	32

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies!

TABLE 43 MULTIPLE DRUG USE AMONG ALL DRIVERS IN THE SAMPLE

Country (References)	General driver population	Driver population (during weekend nights)	Drivers suspected of Driving Under the Influence	Collision-involved drivers, incl (fatally) injured	Prevalence of multiple drug use in percentages *
Italy Ferrara (1990)				n = 5,000	17.5
Norway Christophersen (1995)				n = 394	15
Spain Alvarez (1997) Alvarez (1997)				n = 285 n = 979	2.8 1.6
Switzerland Augsburger (1997) F-Koch (1994)			n = 641 n = 137		85 62
United Kingdom DETR (1998)				n = 619	5

* NOTE: Prevalence data from different countries are not comparable due to differences in the set-up of the studies'

6. CONCLUSIONS

In this survey specific focus has been given to the prevalence of illicit drug use in road traffic in different European countries. Information could be gathered from literature and other sources concerning research findings in twelve countries. The provision of data from countries in eastern Europe turned out to be a problem. As a result no review on drug use in traffic could be included in this survey. It is not clear whether relevant data on illicit drug use by motorists exist, although interest is growing in countries such as Hungary.

The results presented in the foregoing chapters are based on recent research efforts by scientists and experts in the field of drugs and driving. The identification of issues previously described as 'methodological issues' (Chapter 3) is crucial in order to draw further conclusions from each individual research effort. These 'methodological issues' have been discussed again in reviewing the combined results as presented in Chapter 5 (Discussion). Only four large scale studies have been published, one German study focusing on the general driving population, one Norwegian study involving drivers suspected of driving under the influence of drugs and two studies (from Italy and Belgium) in which collision-involved drivers were screened for drugs. The results derived from these studies are not expected to reflect the situation in other European countries with respect to the different driver populations mentioned above, especially if in those countries the drug use patterns (for illicit drugs), the prescribing practices of physicians with respect to licit drugs, and the impact of public campaigns are not known. However, if one wishes to describe the magnitude of a problem, it is defensible to make reference to sound epidemiological investigations and discuss the contributions of societal and cultural differences that can have an effect on drug use in general in each individual country. If these aspects are considered to be significantly different to those in the four countries mentioned above, it will be a problem to apply the results presented in this survey.

The following conclusions are meant to be used as indicators for further discussion and will be presented with reference to the comments discussed in the last Chapter. Although the terminology relating to 'drugs other than alcohol' differs from one country to another, the following definitions have been used to achieve a common nomenclature:

Licit or medicinal drugs are medications which might impair functions of the central nervous system and which are prescribed for patients by doctors or obtained as OTC -over the counter- drugs.
Illicit drugs are sometimes described as 'drugs' or 'narcotics' in lay language.

General driving population:

1. In the *general driving population* the prevalence of *licit* drug use will fall in the range of 5%-15%, depending upon the inclusion of classes of drugs known to impair driving performance and drug use patterns. Benzodiazepines are the most frequently detected drugs. Tricyclic antidepressants and barbiturates will be used by a very small proportion of the driving population, but cannot be ignored in defining countermeasures (e.g. programs to promote the use of 'safer' alternatives).

2. The prevalence of *illicit* drug use will fall in the range of 1%-5%. Cannabis (in the majority of cases) and opiates are most frequently observed, but the use of amphetamines (especially by younger drivers) is increasing in some countries (e.g. Norway). The detection of cocaine is a rare event according to the findings in the German roadside survey.

3. The combination of *licit* drugs and alcohol is not well-established in the general driving population. The German roadside survey revealed that the prevalence of this combination was extremely low. Probably most patients are aware of the detrimental effects of the combination on driving.

4. The combination of *illicit* drugs and alcohol is much more of a problem. In the German roadside survey the prevalence of this combination in drug positive cases was 44%. However, the number of cases was limited and caution should be given to drawing any conclusions.

5. The prevalence of multiple drug use in the general population is probably very low. In the German roadside survey only one sample was detected as positive for a combination of benzodiazepines and opiates.

Population of drivers suspected of driving under the influence of drugs:

1. In *drivers suspected of driving under the influence of drugs* high prevalences of *licit* drug use are reported. However, the selection of this sample of the driving population is completely dependent on the perception and awareness of police officers who decide on the inclusion of a driver in the sample. The procedures they use and the focus they give to detect drugged drivers is different in the various countries. With this restriction in mind the prevalence of benzodiazepine use is rather high in Denmark (53%-75%), Norway (31%), and Switzerland (14%-39%). The prevalence of tricyclic antidepressants and barbiturates is very moderate, ranging from 0.5%-3%.

2. The prevalence of *illicit* drug use is lower than for licit drugs. For cannabinoids the prevalence is 10%-17% in Denmark, 26% in Norway, and 9%-57% in Switzerland. For opiates these prevalences are 17%-40% in Denmark, 8% in Norway and 1%-42% in Switzerland, whereas for amphetamines these figures are 9%-10%, 21%, and 1%-5% in the respective countries. For cocaine the prevalence is 6% in Denmark, and ranges from 0.5%-28% in Switzerland. Remarkable differences between countries are observed, for example the prevalence of use of amphetamines in Norway is relatively high, while in contrast the use of opiates rather low.

3. The combination of *licit* and/or *illicit* drugs and alcohol is expected in samples selected for the suspicion of driving under the influence of alcohol/drugs. In most studies the data for separating prevalences of combinations of alcohol with licit and illicit drug 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%.

4. The prevalence of multiple drug use is reported in a few studies for the total of licit and illicit drug use. A high prevalence (62%) has been observed by Swiss researchers.

Collision-involved drivers:

1. The prevalence of *licit* drug use in different surveys ranged from 6%-21%. The two large studies from Belgium and Italy both show a prevalence of benzodiazepine use of 8.5%, whereas in Spain and Sweden these figures are 2% and 4% respectively. In France and Norway the prevalence of benzodiazepine use is 12% and 14% respectively. The prevalence of barbiturates show lower figures, 1.5% in Sweden and Spain, and 3.5% in Italy. The prevalence of tricyclic antide-pressants in most studies was similarly low from 0.5%-4%. One exception has been reported in a French study: 21%.

2. The prevalence of *illicit* drugs in (fatally) injured drivers ranged from 10%-25% in the different studies. Cannabinoids and opiates are about equally divided among the samples and are detected about two to three times more frequently than amphetamines. Cocaine has been detected with low prevalences (0.5%-0.7%) in Belgium and Italy, whereas in Spain relatively high prevalences (5%-7%) have been reported. The two largest studies from Belgium and Italy reported with fairly similar prevalences for cannabinoids, opiates and amphetamines: 6%, 7.5% and 3%.

3. The prevalence of the combination of drugs and alcohol use has been reported for licit and illicit drugs together in most studies. In the Belgian study the prevalence in drug positive drivers was 27%, whereas in a Norwegian study and a Spanish study the prevalences were 46% and 65%, respectively. In some other studies the prevalences are reported including the whole sample of drivers. The figures presented are lower ranging from 3%-20%.

4. 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 to 36% in a Norwegian study in drug positive cases. When considering the complete driver samples in some other studies, the prevalences are lower, from 5% in the study from the United Kingdom to 17.5% in an Italian study.

Knowledge about the prevalence of drug positive drivers in different driver populations cannot 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 all studies (but one, the German roadside survey) there is a lack of data on the prevalence of drugs among the normal driving population in respective countries. It is obvious that if the prevalence of drug positive drivers is negligible in collision-involved drivers, there will be no serious traffic safety problem. A high prevalence of drug positive drivers will support the assumption that there will be a serious road safety problem.

This survey shows significant prevalences of cannabinoids, opiates, amphetamines, and for the licit drugs this will also counts for benzodiazepines. The combination with alcohol and multiple drug use are issues to be considered as well. In monitoring the prevalence of (multiple) drug use, either licit or illicit, and in combination with alcohol, the best approach would be to repeat studies with standardized methodologies over a given period of time in different European countries. These studies need to be conducted in representative samples of collision-involved drivers with matched controls in the normal driving population. This approach will allow the accident risk of drugged drivers to be determined. In addition trends in drug use and drug use patterns among drivers will become apparent in studies involving any driver population under investigation provided that the methodologies are standardized with respect to sample selection and data collection. It is recommended that roadside surveys in different European countries should be devised to define the relative risk of accident involvement for the users of various drugs, alone or in combination. National laws prohibiting roadside surveys should be abolished or modified to permit the same surveys to be conducted on a pan-European basis.

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8. APPENDIX

Work plan

The following steps have been taken in order to conduct this survey:

1. Literature survey (IRRD, ICADTS)
2. Approaching national traffic safety organizations, experts ('ICADTS Network') and research institutes.
3. Evaluation of research findings and other responses received.
4. Seeking clarification for those findings where single and multiple use was not specified.
5. Preparation of the first draft or preliminary version of (most parts of) the report (not later than June 1998).
6. Preparation of the final report (not later than August 1998).

Resources used in the survey

The review of investigations was be based on the availability of research data published in both scientific journals and institute's reports. The first resource was covered by the International Road Research Documentation (IRRD) database (an OECD database). Reports provided by an European Network of experts (members of the International Council on Alcohol, Drugs and Traffic Safety, ICADTS) were screened to reveal information on the prevalence of illicit drugs and driving with specific regard to multiple drug abuse, comprised the second resource to be applied in this survey. In addition proceedings of ICADTS conferences in the last five to seven years were included.

Valuable information could be obtained from various national traffic safety organizations in the different countries as indicated by the Pompidou Group Permanent representatives of some European countries have been approached with requests to send relevant reports. Their support has been gratefully acknowledged.