Final report of the research
project carried out for the
Ministry of Economics, Small Business,
Technology and Transport of the
State of North Rhine-Westphalia

"Cannabis in road traffic"

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Synopsis

The basis of the research project was formed by 683 blood samples collected by the police during a two year period. These blood samples were tested in a pre-test procedure for cannabinoids, opiates, cocaine, amphetamine/amphetamine derivatives, benzodiazepines and alcohol. All samples that tested positive for cannabinoids were additionally tested to determine the exact concentration of THC (active ingredient of cannabis), 11-OH-THC and THC-COOH (THC metabolic products) using a sensitive procedure that was specifically invented for this purpose.

In only 8.63 % of the cases (59 cases), the initial suspicion of the consumption of drugs could not be confirmed. In 54 cases (7.91 %) only the consumption of alcohol could be proven. In all other 570 cases (83.46 %), other intoxicants were consumed. The consumption of cannabinoids was by far the most commonly observed. In 395 cases, the result was positive. The second largest group was the opiate consumers with 219 cases. Cannabis consumers who had consumed so-called 'hard drugs' (heroine or cocaine) were found in 250 incidences. One of the main purposes of this research was to determine the dangers posed by drivers under the influence of cannabis, therefore it was especially important to have a sufficient number of cases that showed sole consumption of cannabis. These persons, designated as cannabis-only users, were represented in a sufficient number (115 cases).

Determining the ratio of accumulated driving errors and behavioral disorders related to THC and THC metabolite concentrations was of particular interest in this group. For this purpose, the questionnaires specifically developed for this project, for which the police and the doctor taking the blood sample entered the observations and symptoms, were evaluated. It turned out that euphoric or talkative, lethargic or apathetic behavior increased depending on the amount of the concentration ratios of THC and metabolites in the blood; the same was observed regarding the test points of thick-wittedness, delayed perceptivity, tiredness, and widened pupils, as well as for drivers who weren’t able to keep their vehicle in their lane and attracted attention due to driving in a serpentine line. In 22 out of the 115 cannabis-only users, the police observed driving in a serpentine line. In 20 cases, the drivers who had consumed only cannabis caused an accident.

When comparing these results with data of accidents due to alcohol consumption (especially in terms of "driving off the road"), it became apparent that there were parallels in regard to the limit value of absolute unfitness to operate a vehicle due to alcohol consumption (BAC 1.10‰.) The results of this examination could be deduced. For this purpose, the cannabinoid concentrations in the blood were converted to a single value, the “Cannabis Influence Factor”, or short CIF, which could be used for further investigations. This is called a dimension-less value, which correlates much closer with the acute effect of cannabis than e.g. the THC concentration itself.

One of the characteristics of this substance is that it spreads quickly from the blood into the tissue, thus also the brain, therefore the blood concentration doesn't reflect the effect intensity of cannabis. If there is no acute effect, the CIF has a value of zero. On average, the cannabis-only users had a CIF of 20.
The CIF is calculated according to the following formula from the concentrations of THC, 11-OH-THC and THC-COOH, given in ng/mL.

$$CIF = \frac{\frac{[THC]}{314.5} + \frac{[11\text{-}OH\text{-}THC]}{330.5}}{\frac{[THC\text{-}COOH] * 0.01}{344.5}}$$

After the evaluation of all the data, it emerged that the cannabis consumers with a CIF of 10 or more became conspicuous as frequently as that of alcohol consumers with a BAC of 1.10‰ or more. Due to a lack of corresponding data, retrograde calculations, such as those known from alcohol, are not possible yet. The CIF value was determined using a collective, wherein the majority of blood samples were taken 1/2 to 1½ hours after the offence. Therefore the insights contained herein regarding the fitness to operate a vehicle and the CIF value applies to this time frame.
The following conclusion was drawn from the results of the research project "Cannabis in road traffic":

In drivers, whose blood was taken in between 0.5 hours and 1.5 hours after the drive, the cannabis active agent tetrahydrocannabinol (=THC) and its metabolites 11-OH-THC and THC-COOH were in concentrations such that the CIF (Cannabis Influence Factor) reached a value of 10 or more using the described method, and they must be viewed as absolutely unfit to drive due to cannabis consumption.

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Cannabis in road traffic

1. General

1.1 Cannabis

According to Appendix 1 of the Narcotics Act, cannabis (marijuana) or cannabis resin (hashish) are intoxicants leading to the inability to drive. If the consumed cannabis is industrial hemp, the Act contains exemption clauses (cf. 2. the Controlled Substances Act amending law of 04/04/1996).

The hemp plant, especially of the cannabis sativa kind, has been used and abused for centuries, as an intoxicant as well for the production of fibers . The book of herbs by Otto Brunfels (1489-1534), which appeared in 1536 and for the first time completely reproduced images of the domestic flora drawn to nature, refers to the intoxicating, psychotropic (i.e. influencing the human psyche) effect of the plant ("Is of an unpleasant taste / very unhealthy to sleep in it. Then it messes you up in the head.“ (Fig. 1 and 2). The psychotropic characteristics of cannabis are due to its active ingredient tetrahydrocannabinol (THC).


Kreüterbůchs Ander Teyl. xxix

Hanff.

Es Hanffs iſt zweyerley geſchlecht/nach der meynung Dioſcoridis. Eins ſo man ſäht. Dz ander wylder Hanff. Die Kryechen geben dem zammen Hanff diſen nammen Schenoſtrophon darũb/ das ſein wurtzel gar bräüchlich iſt ſeyl daruß zů machen. Iſt eins vnangenemen geſchmacks/ ſeer vngeſund darinn zů ſchlaffen. Dann er macht doll im kopff. Der wyld hanff hatt ſchwärtzer vnd horechter bletter.

Fig. 1: Excerpt from the treatise on hemp (cannabis) in Otto Brunfels' "Kreüterbuch" (Book of Herbs), published between 1532 and 1537 in Strasbourg.

The THC content of a plant can vary strongly from type to type, and depends on the climatic conditions during the growth phase. The highest THC content is found in the blossoms of the female plants; up to 5% THC. P l ants that grow under controlled conditions in greenhouses, i.e. in the Netherlands, have THC contents in the range of 10-15%, in some individual cases even higher.

Fig. 2: Cannabis plant: Woodcut by Hans Weiditz from the book of Otto Brunfels: “Contrafayt Kreüterbuch" (Contrafayt Book of Herbs). Part 2, Strasbourg, 1537.

In addition to the plant materials offered under the designation marijuana or grass, hashish, which contains a lot of resin and is obtained from the plant through an enrichment procedure, is preferentially consumed. In general, hashish contains 10-15% of THC. Top qualities reach even more than 30%. On rare occasions, one can find hashish oil on the illegal market, which is also obtained from the plant material through an extractive procedure. This oil can contain 60-80% of THC.

The common form of consumption is smoking a marijuana-tobacco mix or a hashish-tobacco mix in a joint, or smoking hashish in a pipe. Occasionally, food, so-called hashish cookies, is made of cannabis products and consumed.
THC is a highly effective compound. Just about 2 mg, directly introduced into the bloodstream, are sufficient for an intoxicating experience. When smoking a joint, the availability of THC is relatively low.

In most cases, only about 10% of the active ingredient of a joint gets into the body through the lungs. The largest part of the THC is destroyed or lost while smoking the joint. That value is different when hashish is smoked with a pipe (chillum) or water pipe (a so called hookah). In these cases, high availabilities are possible, especially if the hashish piece is smoked with only one or two deep drags. The effect is noticed immediately during the inhaling process so that the consumer is able to control the amount of THC he wants to use to a certain extent.

Due to the generally unknown THC content of cannabis products and the individually differing THC availabilities during consumption, it is impossible based solely on statements regarding the amount of consumed cannabis to draw conclusions about the amount of THC that entered the body. There are essential differences compared to alcohol where it is possible to determine what blood alcohol concentrations are likely to be achieved due to the consumption, based on the amount and the kind of alcohol consumed

1.2 Kinetics and dynamics of tetrahydrocannabinol

Through the enzyme systems, especially in the liver, Δ^9 – tetrahydrocannabinol is disintegrated or converted in the body into numerous metabolites. Of these metabolites, three are of unique importance. They are the 11-hydroxy-Δ^9 tetrahydrocannabinol (11-OH-THC), 11 -Nor-Δ^9 tetrahydrocannabinol-9 carboxylic acid (THC-COOH) and the glucuronide formed from this carboxylic acid (fig. 3).

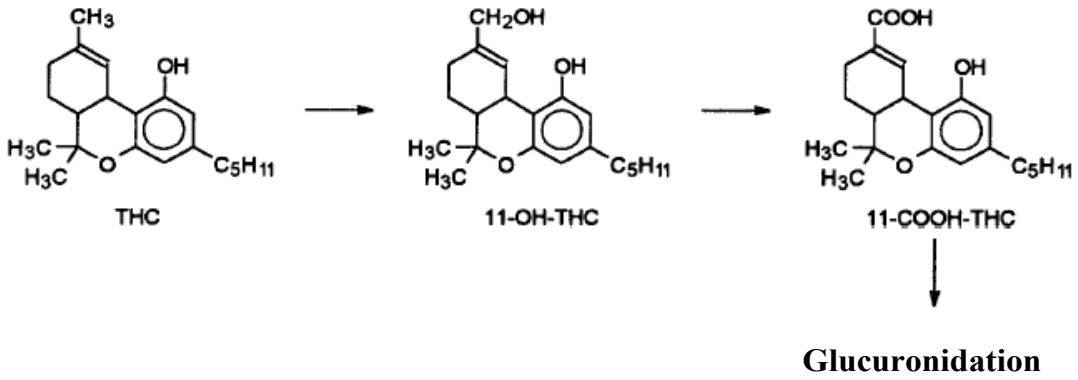

Fig. 3: Metabolism of tetrahydrocannabinol (THC).

THC and 11-OH-THC are psychotropically active, while THC-COOH and its glucuronide show no pharmacological effect. Due to its lipophilic characteristics, THC accumulates in adipose tissue and distributed in brain tissue. That results in a rapid decrease of the active ingredient concentration in the blood, and the THC concentration/time curve doesn't run parallel to the THC effect/curve (fig. 4).

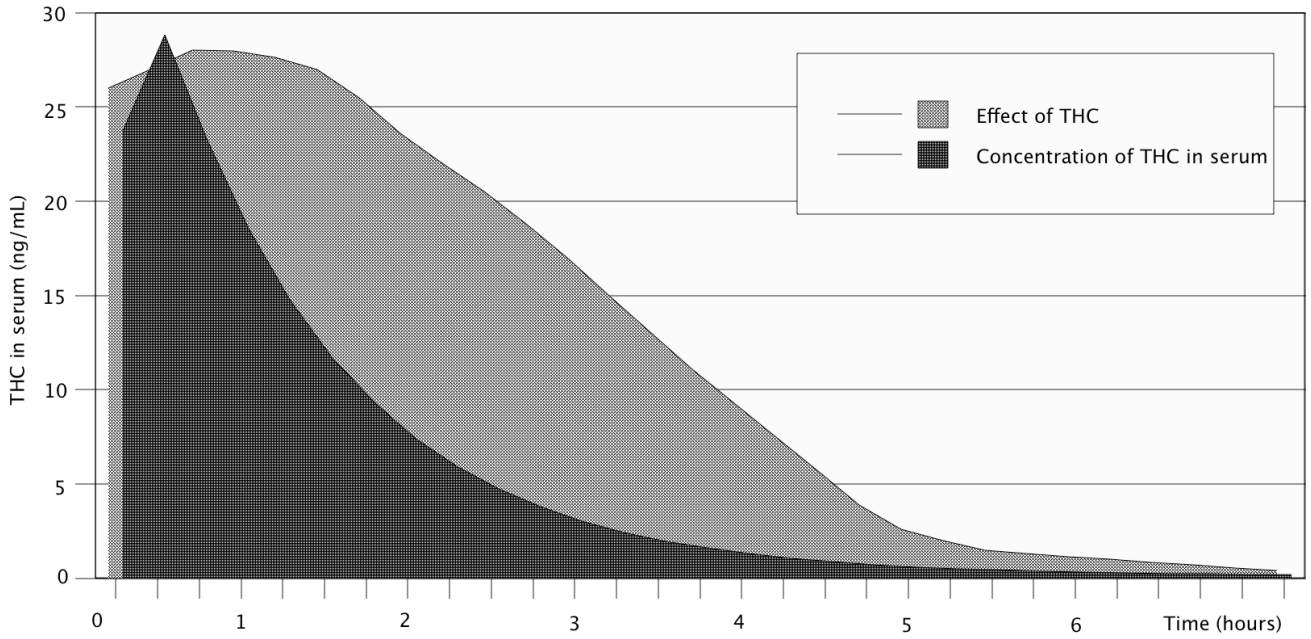

Fig. 4: THC serum concentration curve and THC effect curve, depending on time (hours) after the end of consumption.

In this respect, the metabolite 11-OH-THC behaves like the THC, even though it must be formed through metabolic steps from the THC first. Therefore, its concentration is generally much lower than the THC concentration. In the first 2 to 3 hours after the end of consumption, the half-life for the THC is relatively short, roughly about 30-60 minutes. However, they increase to values of about 24 hours, depending on the time frame that has passed since the consumption. In conclusion, high THC concentrations can only be found in the blood immediately after consumption, but very low THC concentrations can be found even many hours after consumption. The metabolite THC-COOH, and especially its glucuronide, show markedly longer half-lives, which in the end phase can be up to 8 days. As a result, these substances can accumulate in the body through regular consumption. Therefore, very high concentrations can always be found if people regularly consume cannabis products. These metabolites can possibly be detected in the blood and in the urine, even if the user stopped consumption about one to three months ago [22] (fig. 5).

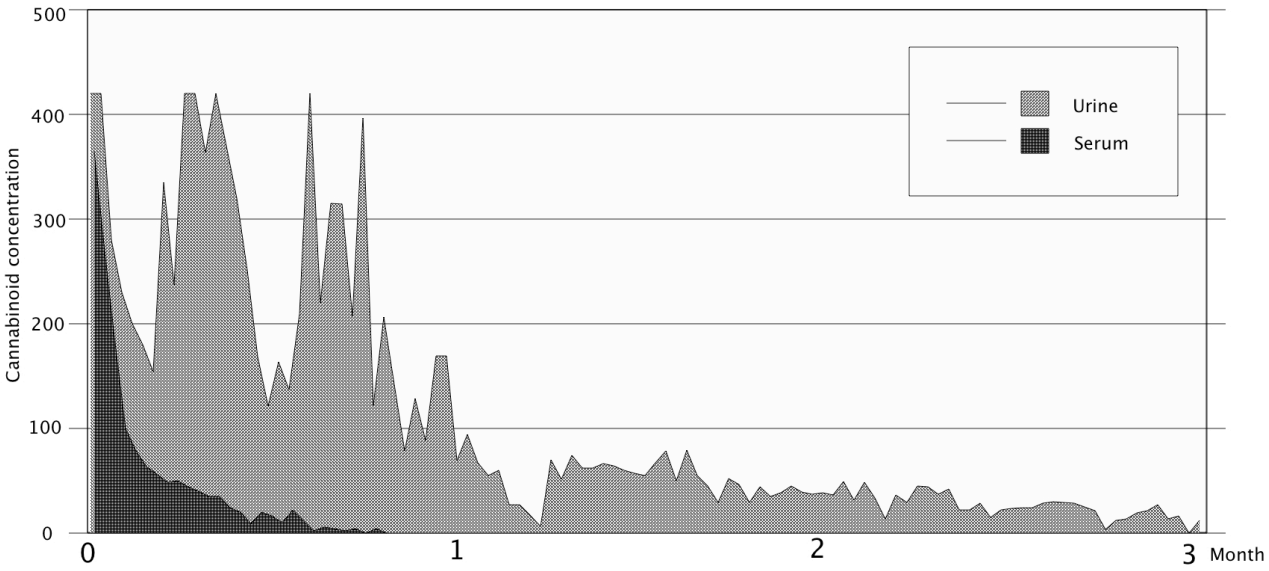

Fig. 5: Time-dependent proof of cannabinoids in serum and urine for a test person after finishing a phase of continuous cannabis consumption [22]

1.3 Acute effect

The subjective feeling after cannabis consumption depends not only on the dose, but also especially on the general mood of the consumer and on the environment, i.e. the location where the consumption takes place. This means that the positively and negatively experienced effects are also diverse. A survey of grammar school, middle school and vocational school students aged 14-20 of both sexes who had experienced the (desired) effect or the undesired side effect after the consumption of cannabis, produced the results shown in the table below [19].

Table 1: Effects of cannabis (n=659, multiple answers possible)

196	=	30%	Comfortable feeling
179	=	27%	Tiredness
120	=	18%	Euphoria
95	=	14%	Better musical feeling
69	=	10%	Reduced fear
64	=	10%	Floating
56	=	8%	Compulsive laughter
45	=	7%	Dancing mania or talkativeness
42	=	6%	More intense perception of colors
34	=	5%	Improved social connection
33	=	5%	Increased emotional perception
31	=	5%	Improved thinking faculty
28	=	4%	Intoxication as in the case of alcohol
26	=	4%	Dreamlike state
21	=	3%	Improved concentration
20	=	3%	Social withdrawal
17	=	3%	Hallucinations in the form of apparitions
17	=	3%	Reduced thinking and concentration faculties

14	=	2%	Sensitivity to noise
12	=	2%	Loss of self-control
11	=	2%	Hunger
11	=	2%	Increase of sexual arousal
8	=	1%	Thirst
7	=	1%	Increased fantasies
7	=	1%	Changed perception of time
7	=	1%	Impaired vision in the form of color formations
6	=	1%	Spatial hallucinations
6	=	1%	Delusions
5	=	1%	Delusions of grandeur
4	=	1%	Distorted vision
4	=	1%	Unclear vision
4	=	1%	Tremors

Table 2: Side effects (undesired effects) of cannabis (n=868, multiple answers possible).

155	=	18%	Nausea*
101	=	12%	Depression
60	=	7%	Impairment of vital functions*
60	=	7%	Headaches*
51	=	6%	Lack of drive
50	=	6%	Fear
49	=	6%	Dizziness*
43	=	5%	Vomiting or the urge to vomit*
25	=	3%	Lack of concentration
22	=	3%	Circulatory disorders*
20	=	2%	Nervousness
19	=	2%	Drop in performance
18	=	1%	Difficulty breathing
15	=	2%	Shaking, weakness in the knees*
13	=	1%	Stomach problems
12	=	1%	Heart disorders*
12	=	1%	Watery eyes
12	=	1%	Imbalance
11	=	1%	Sleep disorders
11	=	1%	Thinking disorders
10	=	1%	Cold sweat*
9	=	1%	Changing of the social experience
9	=	1%	Fainting*
8	=	1%	Aggression
8	=	1%	Disinhibition
8	=	1%	Visual disorders*
8	=	1%	Hallucinations
7	=	1%	Memory disorders
7	=	1%	Impotence
7	=	1%	Failure at school
7	=	1%	Throat and swallowing disorders
6	=	1%	Nightmares

It becomes apparent that, next to effects such as comfortable feelings and euphoria, tiredness and a reduction of fear are also mentioned relatively often.

In the cases of the side effects, the symptoms that can be combined under the term 'neurovegetative side effects' (effects of cannabis on the circulatory system) are prominent (these symptoms are marked with an asterisk *). These symptoms are nausea, impairment of the vital functions, headaches, dizziness, vomiting and the urge to vomit, and fainting. Zellmann [20] reports that in the case of a standing test with test subject who had smoked cannabis, almost every 5th subject had to abort the test after 4 minutes due to the risk of circulatory collapse. Schwarz and Beckenbach [19] report that according to their investigations, 49% of unique test subjects felt these undesired side affects after cannabis consumption.

1.4 Correlation of dosage and effect

Using smoking tests under controlled conditions, it is difficult to clearly prove the THC dosage and effect relationship. For example, Huestis et al . [1] carried out consumption tests with placebo and marijuana cigarettes with 1.75% or 3.55% THC. Subjectively, no differences regarding the psychotropic effect was detected by the test subjects between the low-dose cigarettes and the placebo. Regard the other test points, no significant differences were registered, with the exception of the heart rate. Since none of the test subjects showed mydriasis as a sign of effect of cannabis, it may be assumed that the THC amounts, which were ingested by the test persons during the tests, were too low to show a clear dosage and effect relationship.

However, this was achieved in a study by the local work group that was carried out in a Dutch coffee shop [21]. Herein, the number of joints or hashish pipes consumed in one evening by the individual visitors was compared with the effect visible on the outside. In several meetings, a total of 80 consumers were observed, of which 25 consumed one dose (joint or pipe), 39 consumed two doses, and 16 consumed up to a maximum of five doses during the observation period. There was a clear connection between the number of cannabis consumption units and their effect. This was particularly clear with regard to the test points mydriasis, unsteady gait, euphoria and conjunctivitis. Mydriasis was the most frequently detected conspicuous feature: 60% of the consumers had markedly widened pupils (table 3).

Table 3: Connection between cannabis consumption unit (dosage) and affect

Case number Effect	1 Dose 25 %	2 Doses 39 %	3-5 Doses 16 %	All consumers 80 %
Mydriasis	36	56	88	60
Glassy eyes	32	28	56	49
Unsteady gait	16	38	100	41
Reduced drive	28	21	56	30
Euphoria	8	15	69	21
Conjunctivitis	8	28	56	16
Increased drive	0	21	0	10
Extroversion	0	13	19	10
Depression	0	8	6	8
Introversion	8	3	6	5
Reduced speed	8	0	0	3
Shaking	0	0	0	0
Aggression	0	0	0	0

Table 4: Observation criteria for the determination of effects

Mydriasis	Wide pupils in the brightly lit coffee shop
Glassy eyes	As if suffering from a fever
Unsteady gait	Staggering or unsteady gait
Reduced drive	Decrease of target-oriented activities
Euphoria	Exhilaration without reason
Conjunctivitis	Strong redness of the conjunctiva
Increased drive	Increase in target-oriented activities
Extroversion	Urge to laugh, talkativeness, increased social interaction
Depression	Sad mood or loss of interest in surroundings
Introversion	Decreased social interaction, loss of interest in surroundings, apathy
Reduced speed	Target-oriented motion at a markedly slower speed
Shaking	In the hands at rest, in the limbs in motion

1.5 Correlation of dosage and the THC concentration in the blood

The fact that it isn't possible to draw any conclusions regarding the THC concentration in the blood based on the statement of the consumed THC amount is also impressively shown by the very elaborate smoking study of Huestis et al. [2]. The tests were carried out with 6 test subjects who smoked standardized cigarettes with a THC content of 17.5 mg and 35.5 mg respectively. The measurements, which were carried out on blood samples taken 1.71 hours after the beginning of consumption, i.e. 1.5 hours after the end of consumption, showed the THC concentrations listed in the following table:

Table 5: THC concentration in the blood plasma of 6 test subjects 1.5 hours after the consumption of a cigarette with 17.5 mg or 35.5 mg of THC. (From [2])

Test subjects	Dose 17.5 mg THC THC concentration ng/mL	Dose 35.5 mg THC THC concentration ng/mL
B	2.6	8
C	2.8	6.2
E	3.4	3.4
F	5.3	9.4
G	3.0	11
H	4.5	10

We can see that the THC concentration in the blood samples of tests subjects who smoked the low-dose or the high-dose cigarette were in a range of 2.6-5.3 and 3.4-11 ng/mL respectively. Further considerable differences between the individuals are obvious; the consumption of a cigarette with twice the THC concentration by the same test subject doesn't usually lead to twice the THC concentration in the blood plasma.

1.6 Correlation of THC concentration in the blood and the effect

So far, there are only sufficient studies for alcohol that show the connection between the effect of alcohol on one's fitness to operate a vehicle and the amount of alcohol contained in the blood at the same time (blood alcohol concentration, BAC). On the basis of these studies, an abstract danger limit value of 0.80‰ (g of ethanol in 1000 g of blood) was legally set. In addition, a decision of the Federal Court of Justice determined that drivers who have 1.00‰ or more alcohol in their blood or

who have enough alcohol in their blood to lead to this blood alcohol concentration, must be considered as absolutely unfit to operate a vehicle due to the alcohol in the meaning of §§316 and 315c of the Criminal Code. Therefore, by taking into consideration a safety margin of 0.10‰, the limit value of the absolute unfitness to drive due to the influence of alcohol was set to 1.10‰.

It makes sense to use alcohol as the model for a concentration-effect relationship for other drugs, among them tetrahydrocannabinol. However, due to the considerable differences in the chemical and pharmacokinetic characteristics of ethanol and tetrahydrocannabinol, it's not possible in this case; the distribution as well as the elimination from the target location show considerable differences between the two substances.

Table 6: Comparison between the degrees of intoxication (minimum 0; maximum 10) stated by the cannabis consumers (n=11) and the THC concentrations available in the blood plasma at the same time (from [3])

Degree of intoxication	THC concentration ng/mL
0	2-190
1	2-6
2	3-317
3	3-240
4	2-251
5	2-250
6	3-210
7	4-112
8	4-215
9	7-196
10	5-160

All attempts to show direct correlations between the THC concentrations in the blood and the degree of intoxication stated by the consumers show considerable variations between individuals, so a universal rule of thumb cannot be established, as the investigations of Hollister's study group [3] impressively show. After the intravenous administration of THC or smoking cigarettes containing THC, the test persons were asked to state the degree of intoxication on a scale from 0 to 10 at various times during and after consumption. At the same time, blood sampling was carried out to

determine the THC concentration. Table 6 shows that high and low THC concentrations were found independently of the degree of intoxication. High THC concentrations and lower effects were found immediately after the intake of THC, i.e. before the corresponding concentrations were available at the target locations of the THC in the brain. A strong effect with a simultaneous low THC concentration in the blood was observed if some time had passed since the end of consumption. The effect of THC lags behind the concentration in the blood (cf. also fig. 4).

A direct proportionality between the THC concentration and the effect was only observed after the blood/tissue concentrations are in a state of balance, meaning that the distribution phase is largely completed (Cone, 1993, quoted according to [4]). Chiang [5] has also observed a direct proportionality between the medium THC concentration and the effect in a period of 1-4 hours after the start of consumption.

1.7 BAC vs. THC concentration

Despite the fundamental differences between THC and alcohol just shown, Berghaus [6] recently attempted to establish a relationship between the blood alcohol concentration and the THC concentration based on a meta-analysis of over 120 experimental studies.

He obtained the alcohol and THC performance curve shown in figure 6.

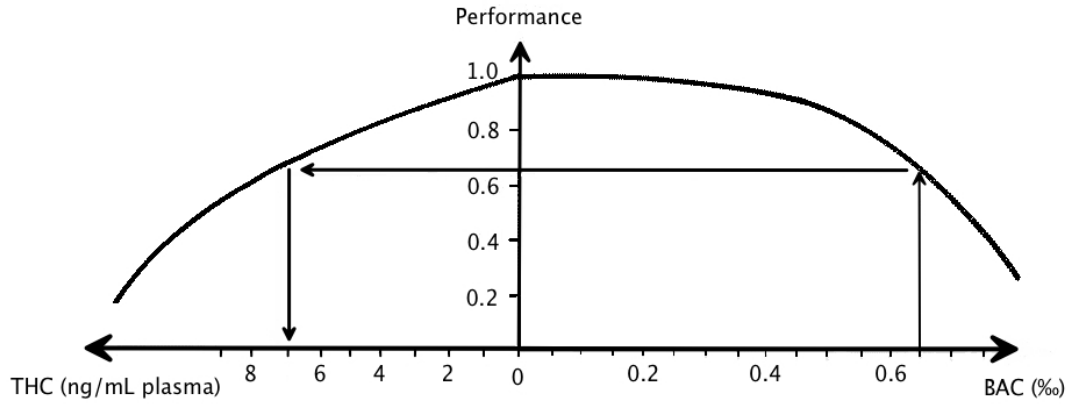

Fig. 6: Comparison of performance losses of people after cannabis and alcohol consumption (according to [6]).

From this curve, Berghaus deduced the following correlations between the performance losses:

The performance losses shown by people with 0.65‰ (or 1.00‰) alcohol in their blood would be equal to those individuals who have 7 ng (or 14 ng) of THC/mL plasma or serum. In the past, the local work group discussed a THC concentration of 15 ng/mL as a possible limit value of the absolute unfitness to drive (cf. AG Nettetal [7] and OLG (Higher Regional Court) Düsseldorf, [8, 9]).

This empirical value thus corresponds very precisely with the value worked out by Berghaus.

According to the above quote study, however, a direct comparison of the relationship effect of alcohol / BAC with the relationship THC effect / THC concentrations seems to be impossible. So how was it possible that Berghaus still found an [apparent] correlation between BAC and THC concentration? There are two essential reasons for this:

1. Since there had been only very few experimental studies about the effects of THC and simultaneous THC determination, Berghaus needed to calculate it using a pharmacokinetic curve to obtain the THC concentrations required for his evaluation. However, this calculation leads to theoretical (idealized) concentrations, which can be markedly differ from the actual concentrations, as was shown in the section "Correlation between dosage and THC concentration".
2. It was also not sufficiently taken into consideration that the THC effect of THC concentration changes in the blood might lack behind to a considerable extent. Nothing comparable was observed in the case of alcohol.

Through the data evaluation collected within the framework of the present research project it was found that the THC concentration by itself is no suitable measure of cannabis-related unfitness to drive.

1.8 Epidemiological studies

Epidemiological studies entailing the consumption of alcohol as well as other intoxicating substances consumed by traffic participants are available in large number. What remarkable is the largely consistent results that state that, next to alcohol, the consumption of cannabis products was most frequently proven, independently of whether the studies were conducted in North America, Europe or Australia. However, the majority of the studies aren't suitable to prove a factually existing concrete endangering of road safety due to the consumption of cannabis products. Especially questionable is the fact that blood samples in the majority of cases were only taken and investigated if alcohol consumption was also present, so that a distinction between the effect of cannabis and alcohol isn't possible. If one further checks the studies to find out how often only cannabis consumption was consumed, one will find that the number of cases is very low. Below, 4 larger studies of recent years from Germany, the US and Australia are mentioned representatively.

Table 7: Epidemiological studies (selection) regarding the frequency of the proof of drug consumption by road traffic participants

Authors	Country	Selection of the material to be analyzed	Year of publication	Case number	Cases only with cannabis consumption
Krüger [10]	Germany	general traffic	1995	1710	3
Möller [11]	Germany	conspicuous traffic participants	1994	660	15
Drummer [12]	Australia	Traffic	1994	1045	43
Terhune [13]	USA	deadly traffic accidents	1992	1882	25

Considering the low number of cases in which only cannabis was consumed, it is understandable that some are of the opinion that cannabis probably poses a rather negligible risk in road traffic. If one then uses the larger studies from Australia and the USA, where the evaluation of police files shows that people who had used only cannabis are supposed to have caused an accident due to culpable behavior just as rarely as drivers who hadn't taken any intoxicating substances, the question must be asked why we even talk of the fact that cannabis consumption can pose a risk to road traffic. The uniqueness surrounding cannabis is evident in the fact that experts have no doubts regarding the lessening of driving skills when consuming cannabis, yet the examination models used so far don't reflect this thesis when it comes to driving skills under the influence of cannabis, qualitatively and quantitatively.

In addition to the epidemiological studies, a series of laboratory tests as well as driving simulator tests were carried out [14, 15, 16]. While marked neurological deficits were detected in laboratory tests, especially during the attention test, the tracking test and the vigilance test, the reduction of the fitness to drive that was to be expected in driving tests wasn't observed to the extent that the lab tests lead one to expect. These tests, as they have been conducted so far, are thus also not suited to quantify the impairment of one's fitness to drive after the consumption of cannabis.

There are many reasons to believe that on the one hand, during these tests, the cannabis doses are too low in comparison to the cannabis amounts actually ingested by the consumers, and that additionally the disinhibiting, euphoric or other psychotropic effects of cannabis intoxication are suppressed by the test subjects during the driving tests, or that they cannot be experienced under test conditions, so driving errors don’t emerge clearly. The very extensive drive study carried out a

few years ago in Maastricht also didn't deliver any new results in this respect. Robbe, who was the leader of this study, wrote the following about it in his book [17]:

"The insights from this study, but also from previous studies, create the impression that alcohol stimulates risky road behavior and that THC lead to more caution, at least during the experimental examinations. Another qualitative difference between THC and other active ingredients is that people under the influence of THC seem to be better positioned to compensate the negative influences of this drug on the road behavior.
When testing so-called 'driving related skills', 'the negative effects of THC seem to be greater than on the road'.
Various reasons for these obvious discrepancies are discussed. On the one hand, very simple abilities are frequently tested in the lab, which certainly has a negative influence on the motivation of the test subjects because the test is not considered to be realistic. In addition, due to the simplification of the tests, there are fewer possibilities for compensation. Thirdly, the subjects who have a driver's license are so experienced driving that possible existing effects of the drugs on the fitness to drive only become apparent if one has to carry out 'real' driving tasks or tasks that come very close to such tasks.
However, it is also possible to imagine very simple situations in which the influence of marijuana can have extraordinarily dangerous effects, such as in emergency situations, which makes very high demands on the capacity of the driver to process information, long drives on a monotonous road (highway), and in cases where marijuana is combined with other psychotropic substances, especially with alcohol. Since these possibilities are no mere fantasy, the present study doesn't provide the final word on marijuana. For the time being, it should rather serve as a starting point for future studies, which must ultimately complete the image of the effect of marijuana on drivers' behavior." (Translation of the original Dutch text).

1.9 Objective of the present research project, among others

1. To show whether cannabis consumption by itself can really lead to an unfitness to drive, and
2. To determine whether there is a relationship between the concentration of the active ingredients in the blood and the unfitness to drive.

To answer these questions, a different starting point was chosen with regard to previous studies. All studies showed that only under real conditions is it possible to make assessments about the impairment of the fitness to drive under the influence of cannabis. It was necessary to obtain blood samples from drivers even if they were not under the influence of alcohol, but behaved conspicuously in road traffic in other ways, so that the measure of taking blood was justified. By means of corresponding toxicological examinations of the blood samples, it was also necessary to test which intoxicants were ingested in which amounts.

2 Methodological procedure

To show if and to what extent the consumption of cannabis leads to an unfitness to drive, a field test had to be carried out in close collaboration with the police. The police department of the administrative district of Düsseldorf agreed to this collaboration.
Before the field test, the situation was as follows: If a traffic participant was controlled by the police as a result of conspicuous behavior, a blood sample was taken only if there was a concrete suspicion of alcohol consumption. If the alcohol test was negative, no further police measures were taken in many cases to clarify the cause of the conspicuous behavior. The reason for this was that the police officers on site didn't have any clear standards as to how to proceed in such cases, when a blood sample may be taken, and what to do with such a blood sample.

2.1 Training of the police officers

Several informational events took place, the first one in March 1994. These events served the purpose of sensitizing the police officers to the problems of drugs in road traffic, and also to show what possibilities there are to recognize the influence of drugs in general, and regarding cannabis in particular. For this purpose, a checklist was made available as part of the police report (the so-called 'staggering sheet') (Appendix 2), which made it possible to detect the various neurological deficits typical for cannabis, but also for other intoxicating substances. The observations made by the police immediately after their intervention are of the greatest importance for an assessment of the fitness to drive because many other intoxicating substances, but especially cannabis, have a tendency to loose their effect very quickly, or to show changing effect images so that the doctors who takes blood samples and analyze them one hour later can no longer determine the symptoms available at the time the driver was checked.
In addition, the police officers received an informational document regarding the influence of the 4 most important drug groups (cannabis, heroin, cocaine and amphetamine) on the fitness to drive (Appendix 5).

2.2 Decree of the Ministry of Internal Affairs

On June 21, 1994, the Ministry of Internal Affairs of the state of North-Rhine Westphalia issued the following decree to the government of the administrative district Düsseldorf and to the police department of the administrative district Düsseldorf (ref.: -IV C4 - 2740 -):
In agreement with the Ministry of Justice and the Ministry for City Development and Traffic of North-Rhine Westphalia, the Institute for Legal Medicine of the Heinrich Heine University Düsseldorf will carry out a research project that intends to provide answers to the following questions:

- *How a traffic participant impaired by the influence of cannabis can securely be detected by police officers or doctors,*
- *Which amount of the active ingredient in the blood makes it safe to determine that a cannabis consumer is unfit to drive,*
- *Which method proves to be effective to determine the exact concentrations of the active ingredient in the blood serum.*

For this project, the cooperation of the police is very important. Until further notice, the procedure to be carried out should be as follows:

1. *All patrol officers should again be referred to the detection characteristics for the influence of drugs, listed in my brochure "Drugs in road traffic". The description of the research project attached as Appendix 1 is also suitable for this purpose. The influence of cannabis should always be assumed if a dangerous traffic situation / a traffic accident was caused by (younger, especially male) traffic participants, where (contrary to expectations) no, or only a little, alcohol was involved. The same applies in cases of concrete suspicion (e.g. additional infringements of the Narcotics Act, or if there is an initial suspicion of an unfitness to drive after checking for certain abnormalities, such as red eyes or widened pupils, delayed perspectivity, tiredness, presumptuousness etc. In all these cases, a blood sample under the requirements of § 81a of the Code of Criminal Procedure should be taken.*
2. *The officer who has detected the problem should add the additional police report, included as Appendix 2, to the procedure.*
3. *Aside from the medical report, the doctor taking the blood sample is required to fill out the additional document to B, included as Appendix 3, "Medical report". This report should also be added to the procedure.*
4. *The examination request, included as Appendix 4, should be sent exclusively to the Institute for Legal Medicine of Heinrich Heine University Düsseldorf together with the blood samples that were taken due to the suspicion of drug consumption.*
5. *After the return of the sample, the result of the examination should be made available to the officer who initiated the procedure. If important information is gained from the procedure, it should also be evaluated anonymously for service training. The report of the results must be included with the procedure.*

The participation of the police in the research project was checked regarding data protection laws. There were no objections.

On behalf of
Signed Dr. Möller

2.3 Collaboration with the blood-taking doctors

It was also an objective of the research project to gain new insights into the acute effects of cannabis detected during medical examinations. Therefore, a document (Appendix 3) was designed containing additional examination points, which are of special relevance for the evaluation of the influence of cannabis according to the current insights, among others from the test trials introduced in the literature. The goal was to check to what extent the neuro-vegetative and psychotropic effects of cannabis could be detected at all under the conditions of blood sampling and the medical examinations ordered by the police. Furthermore, the doctor should be given the option to evaluate the degree of cannabis influence, just like in the case of alcohol. A document, which individual police departments were to hand out to the respective doctors, was to inform them about the relevance of the different examination points. (Appendix 6)
Since the blood-taking doctors also need to gain experience recognizing the influence of drugs on individuals, we obtained the approval of sending them the results of the blood examinations and a copy of the additional examination documents in anonymized form (decrees of the Ministry of Justice of the state of North-Rhine Westphalia, June 15, 1994, ref.: 3003 E - II C. 3.128).

2.4 Working out a method for analyzing the blood samples

2.4.1 Pre-tests

2.4.1.1 Pre-test for cannabinoids, opiates, amphetamines, cocaine metabolite and benzodiazepines

The blood sample is immediately centrifugalized and a part of the serum is taken away and, in case a no fluoride-containing blood sampling system was used, mixed with 10 mg of NaF per milliliter. This sample is stored in glass tubes at -18 °C for future examinations. Then 300 µL of serum and watery calibration standards I to III (see Table 8) are each mixed with 300 µL of acetone on the vortex. Additionally, a blank value is produced (300 µL of water plus 300 µL of acetone). At the edge of the serum, the precipitate is then centrifuged (>10,000 rpm). 200 µL of the supernatant or of the respective calibration solutions and of the blank value are mixed with 20 µL of saturated saline solution, and then checked with the FPIA immunoassay (ADx system of the company Abbott) for the substances listed in the table, similarly to urine and according to manufacturer specifications. The resulting values of the calibration standards are graphically inserted after the deduction of the respective blank values.

Table 8: Immuno-chemical proof of cannabinoids, opiates, amphetamines, cocaine metabolites and benzodiazepines from serum

Active ingredient group	Standard substance	I ng/mL	II ng/mL	III ng/mL	Value of the quantitative results
Cannabinoids (SCK)	THC-COOH	20	50	100	meaningful
Opiates	Morphine	50	200	400	only for orientation
Amphetamines	d,l Amphetamine	100	200	500	only for orientation
Cocaine metabolites	Benzoyl-ecgonine	500	1000	1500	meaningful
Benzo-diazepines	Flunitrazepam	20	50	100	only for orientation

The calibration lines obtained in this way serve as the quantitative evaluation of the supernatant serum measurements. If the values from the serum are above the calibration line, a corresponding dilution (e.g. 1+4) must be produced with the still available supernatant, then measured again with the immunoassay.
The limit of detection for cannabinoids (SCK) is at about 10 ng/mL. If the value is lower than this, the examination is repeated. If the first result is confirmed, the analysis for cannabinoids is considered negative, and a corresponding result is sent to the police.
If a positive cannabinoid result is obtained with the pre-test, a confirmation analysis and a quantification of THC and its metabolites is carried out (see 2.4.2).

2.4.1.2 Testing for alcohol

50µL of serum together with 500 µL of watery internal standard (t-Butanol) are put into a Headspace sample glass and checked for ethanol via the automated gas chromatographic method approved for forensic blood alcohol determination.

2.4.2 Determination of THC, 11-OH-THC and THC-COOH in serum or blood

The psychotropic active ingredient of cannabis Δ^9-Tetrahydrocannabinol (THC) is metabolized in the body into, among others l1-Hydroxy-Δ^9-tetrahydrocannabinol (11-OH-THC) a nd l1-nor-Δ^9-Tetrahydrocannabinol-9 carboxylic acid (THC-COOH). THC-COOH is available both in free form and in the form of glucuronide. While THC and 11-OH-THC don't significantly accumulate even in cases of regular consumption, this is different for THC-COOH. Regular consumption leads to an

increase of the blood concentration of this metabolite. To prove an acute effect or an ingestion of cannabis that took place a relatively short time ago, the concentration of THC and 11-OH-THC istherefore decisive. Serum should preferentially be used for the analyses because THC and its two metabolites are basically distributed in this component of the blood. Another procedure for the analysis of blood or tissue is also described.

Principle of the method

THC, 11-OH-THC and THC-COOH (only the free form) are eluted with acetonitrile under slightly acidic conditions after the application of the serum to a C18 solid phase. If only blood is available, an acetonitrile precipitation is first used to remove interfering proteins. To avoid THC losses due to unspecified glass bindings, the extract is constrained in silanized vials and examined after methylation [18] in a gas chromatographic, mass fragmentometric way (GC-MS). Deuterated THC and THC-COOH serve as internal standards.

The processing of the samples is carried out manually, while the GH-MS analysis with the subsequent evaluation is carried out automatically with a special computer program on the basis of a table calculation.

Material to be analyzed

Serum, 2 mL

If the analyses cannot be carried out immediately, the serum is mixed with 10 mg of sodium fluoride per mL, and stored at -18 °C.

Alternatively, blood or tissue (e.g. brain) can also be used.

Tools

Equipment

Gas chromatograph: Hewlett Packard 5890 Series II with split-splitless injector, glass line with glass wool HP 5062-3587, Merlin Microseal Septum HP 5181-8833, Fused Silica capillary column HP-5MS (30m x 0.25 mm inner diameter, df = 0.25 µm).

Sampler: Hewlett Packard 7673 GC/SFC injector and Controller with special support sleeve for 1.1 mL rolled edge bottle for sample carousel (own manufacturing) and support sleeves type TTS-313 in the sample plate, WGA, Pfungstadt.

Mass spectrometer: Hewlett Packard 5972 Series Mass Selective Detector.

Computer: Hewlett Packard Vectra 486/33N with HP MS DOS 5.00-E.00.02 (Engl.), MS Windows 3.1 (Engl.), HP ChemStation B.02.02, Samson-Top Gl034C Version C.01.05 and MS Excel 4.0 (Engl.). *Vacuum device:* Baker spe-l 2G System.

Consumables

Sampler bottles: Rolled edge bottle type 1.1-CTVG (1.1 mL) with flange cap 11-AC-TST (PTFE/Silicon/PTFE, 1mm) WGA, Pfungstadt.

Vibration mixer (Vortex).

Microman M 50 capillary pipette, ABIMED.
Sample flasks wrapped in black paper to store the light-sensitive solutions and extracts that contain THC.
Vials (2 mL).
Centrifuge glasses (10 mL) with ground-glass stoppers.

Required chemicals (analytical grade)
Δ^9-Tetrahydrocannabinol (THC), ethanol solution (Makor or Radian) 11-Hydroxy-Δ^9-tetrahydrocannabinol (11-OH-THC), 1 mg/mL (Radian)
11-nor-Δ^9-Tetrahydrocannabinol-9 carboxylic acid (THC-COOH) (Radian or HSPC)
Δ^9-Tetrahydrocannabinol-D 3 (THC-D3) (Radian)
11-nor-Δ^9-Tetrahydrocannabinol-9-carboxylic acid-D3 (THC-COOH-D3) (Radian or HSPC)
Tetramethylammonium hydroxide pentahydrate (TMAH)
Dimethylsulfoxide (DMSO)
Acetic acid (10%)
Acetic acid, 0.1 mol/L
Methyleneiodide
Hydrochloric acid, 0.1 mol/L
Ethanol
Methanol
Acetonitrile
Ethylacetate
Isooctane
Toluene
Dichlordimethylsilan
Sodium fluoride
Extraction columns BAKERBOND spe Octadecyl (C18), J.T. Baker B.V., Deventer, Holland
Helium, purity 6.0

Reagents and solutions

Silanization solution

10 mL dichlormethylsilane are added to 190 mL of toluene. The solution is stored in the refrigerator in a bottle with a ground-glass stopper. The seal is additionally protected against humidity with parafilm.

TMAH/DMSO solution

Mix 0.2 mL of T solution (2.49 g of TMAH ad 5 mL water, kept in a refrigerator) with 3.8 mL of DMSO. Prepare the mix anew daily.

Loading solutions

THC loading solution, 0.1 mg/mL

10 mg THC (40 µL of a 250 mg/mL solution) ad 10 mL with ethanol. When protected from light at -18°C, this solution can be kept for several years. 100 µL ad 1 mL of this solution is diluted with methanol. Store the solution protected from light at -18°C.

11-OH-THC loading solution, 0.1 mg/mL

Dilute 1 mL 11-OH-THC ad 10 mL with methanol. When protected from light at -18°C, the loading solution can be kept for months.

THC-COOH loading solution, 0.1 mg/mL

Commercially available (e.g. Sigma). When protected from light at -18°C, the solution can be kept for months.

THC-D3 loading solution, 0.1 mg/mL

Commercially available (e.g. Radian). When protected from light at -18°C, the solution can be kept for months.

THC-COOH-D3 loading solution, 0.1 mg/mL

Commercially available (e.g. Radian). When protected from light at -18°C, the solution can be kept for months.

D_3 mix

Solution A: 0. Mix 1 mL THC-D3 loading solution ad 1 mL with methanol.

Solution B: 0. Mix 1 mL THC-COOH-D3 loading solution ad 1 mL with methanol.

Mix 0.2 mL solution A, 0.4 mL solution B and 3.4 mL methanol. Store the solution protected from light at -18°C.

Comparison standard

Solution A: 0.1 mL THC loading solution ad 10 mL with methanol. Store the solution protected from light at -18°C.

Solution B: 0.1 mL11-OH-THC loading solution ad 10 mL with methanol. Store the solution protected from light at -18°C.

Solution C: 0.1 mL THC-COOH loading solution ad 1 mL with methanol. Store the solution protected from light at -18°C.

Dilute 0.2 mL solution A + 0.2 mL solution B + 0.2 mL solution C ad 2 mL with methanol. This comparison standard contains 5 ng THC, 5 ng 11-OH-THC and 50 ng THC-COOH in 50 µL. When protected from light at -18°C, the solution can be kept for a few days.

Controls

20 mL of cannabinoid-free human serum is mixed with 200 mg of sodium fluoride and with 0.1 mL each of solutions A, B and C that have been produced according to section 6.5. The serum is stirred

mechanically for 30 minutes and then mixed again for 1 minute on the vortex. Sampler bottles are filled with 2 mL each and are stored at -18°C until the analysis.
A commercially available control agent (Medichem , Stuttgart) can also be used. However, this doesn't contain any 11-OH-THC.

Silanization of the vials

The vials are filled in the exhaust hood with 1 mL of silanization solution and briefly shaken on the vortex. The solution is left to rest for about 5 minutes in the vial. The silanization solution is poured back into a supply bottle (can be used repeatedly, and can still be used if, during the overcoating of the opening of the filled vial, hydrochloric acid mists are formed). After that, flush the vials twice in a row with 1 mL of Toluol and 1 mL of methanol each. Store the vials in a dry cabinet at a temperature of 80°C for 20 minutes, then cool and seal them.

Sample preparation

Serum samples: 1.0 mL or 0.5 mL (where only little examination material is available) of serum are mixed with 40 µL of D_3 mix and brought to pH4 with about 150 or 75 µL of acetic acid (10%).
Blood samples (tissue homogenate): 1 mL or 1 g of sample are mixed with 40 µL D_3 mix and mixed intensively and completely with 2 mL of acetonitrile (if necessary, using ultrasound) and centrifuged for 3 minutes at about 10,000 rpm. 2 mL of the clear supernatant are diluted with 3 mL of water.

Carrying out the analysis

Extraction and derivatization

The C18 extraction columns are conditioned through washing with 2 mL of methanol, followed by 2 mL of water and 1 mL of acetic acid (0.1 mol/L). The prepared solutions of serum or blood are applied to the columns in a vacuum with a flow rate of about 1 mL/min. The columns are washed with 1 mL of acetic acid (0.1 mol/L), followed by 1 mL of 40% acetic acid (v/v) in water, and are then dried through centrifugation of the column (5 min., 1,000 g). The cannabinoids are eluted in an silanized vial with two times 0.75 ml of acetonitrile. The eluate is evaporated at 50°C under nitrogen. The methyl derivatives are obtained by having the residue absorbed in 0.2 mL of TMAH/DMSO solution and then incubated at room temperature for 2 minutes; this is followed by the addition of 50 µL of methyl iodide and further incubation for 15 minutes at room temperature; after the addition of each component, mixing is carried out on the vortex. The mixture is acetified with 0.2 mL of hydrochloric acid and then extracted with 1 mL of isooctane. 0.8 mL of the organic supernatant is transferred into a sampler bottle and evaporated at 50°C under nitrogen. The residue is reconstituted in 50 mL of ethyl acetate, and an aliquot is subjected to a GC/MS analysis.
The control is processed analogously to the serum samples.

50 µL of the comparison standard is mixed in a silanized vial with 40 µL of D_3 mix, evaporated at 50°C under nitrogen, and derivatized and further processed like the sample extract residues.

GC-MS analysis

The sample plate is loaded with the flasks as follows: Position 1: ethyl acetate (=empty), Position 2: comparison standard. The additional positions are loaded with the samples or the control. The sampler is programed to inject ethyl acetate (empty) after each sample in order to exclude substance carryover. After every 5 samples, the comparison standard is carried out.

Injection volume: 2 µL

Temperature program: 100°C for 2 min, 40°C/min to 275°C for 5 min, 40°C/min to 290°C for 5 min; split/splitless injector at 270°C.

Carrier gas: Helium, 0.9 mL/min

MS Acquisition Parameter:

Solvent Delay: 8 minutes

SIM parameter:

Group 1: THC; 8.00 minutes; dwell time 15 msec; m/z 285, 313, 316, 328, 331

Group 2: 11-OH-THC; 9.00 minutes; dwell time 45 msec; m/z 9.00, 45, 313, 314, 358

Group 3: THC-COOH; 10.00 minutes; dwell time 55 msec; m/z 313, 316, 357, 360, 372, 375

Calibration

The following 3 solutions are needed for the calibration of the GC-MS device:

Calibration solution I: 0.1 mL THC loading solution + 0.1 mL 11-OH-THC loading solution ad 1 mL with methanol. 0.12 mL of this solution + 0.06 mL THC-COOH loading solution ad 2 mL with methanol.

Calibration solution II: 1 mL calibration solution I + 1 mL methanol.

Calibration solution III: 0.5 mL calibration solution II + 1 mL methanol.

50 µL of each of the calibration solutions I to III are pipetted with 40 µL D_3 mix into a silanized vial and further processed for the comparison standard as described under 9.1.

For the generation of the calibration line, the following values are inserted on the X-axis (concentrations apply if 1 mL of sample has been processed): Calibration solution I: 30 ng/mL THC, 30 ng/mL 11-OH-THC and 150 ng/mL THC-COOH;

Calibration solution II: 15 ng/mL THC, 15 ng/mL 11-OH-THC and 75 ng/mL THC-COOH;

Calibration solution III: 5 ng/mL THC, 5 ng/mL 11-OH-THC and 25 ng/mL THC-COOH. For the rest, the calibration takes place according to the information of the manufacturer of the GC/MS device.

Evaluation

The following peak height ratios are used for quantification (fig. 7 und 8): For THC: m/z 313 (THC)/ m/z 316 (THC-D3)

For 11-OH-THC: m/z 313 (11-THC-OH) / m/z 316 (THC-COOH-D3)
For THC-COOH: m/z 313 (THC-COOH) / m/z 316 (THC-COOH-D3).

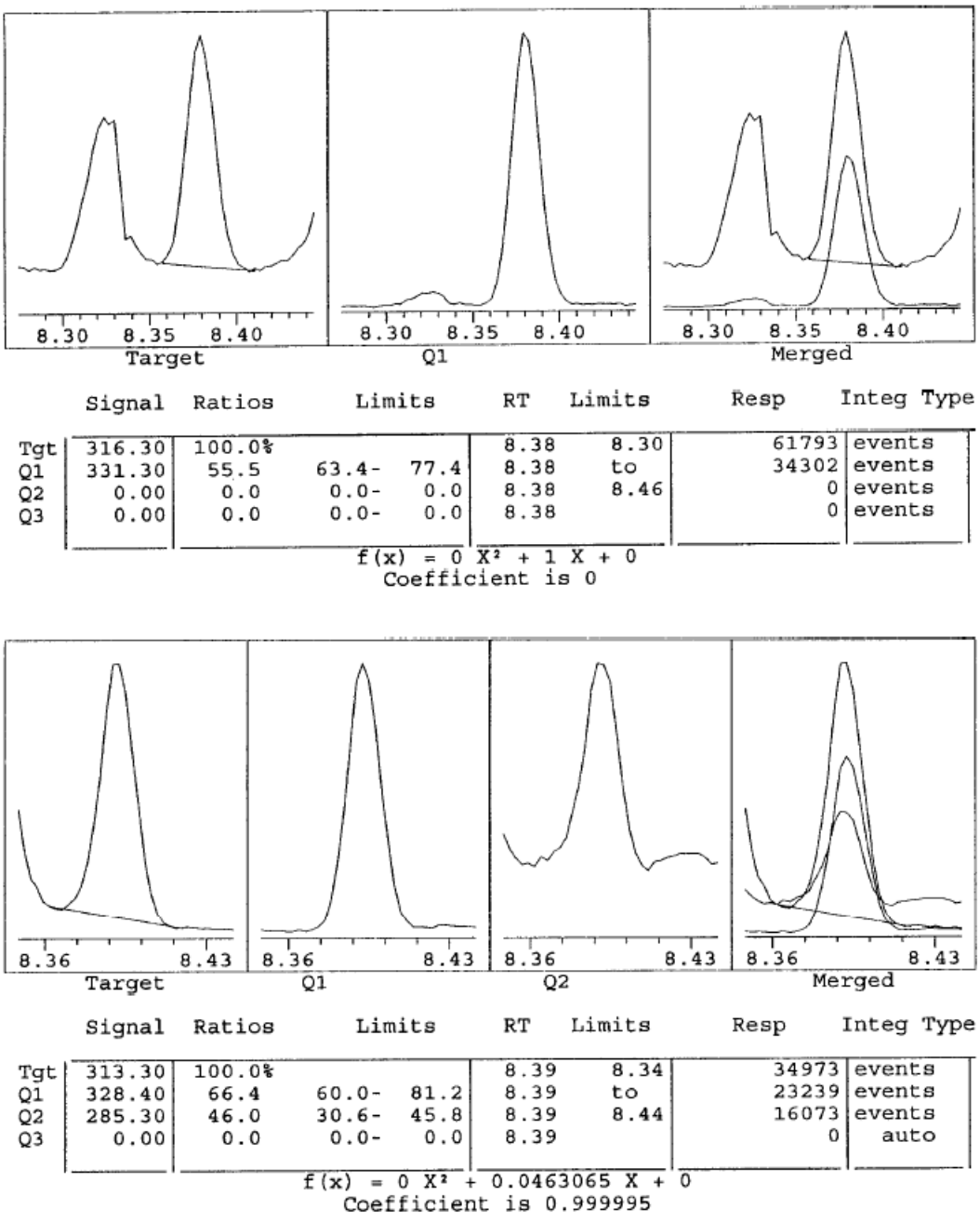

Fig. 7: Pilot ring test 1995 of the Society for Toxicological and Forensic Chemistry (GTFCh) for proving the availability of THC and THC-COOH in the serum. Original ion chromatogram of THC-D3 (above) and THC (below). The ring test serum sample was contaminated. The determined THC concentration was 12.65 ng/mL (see fig. 9).

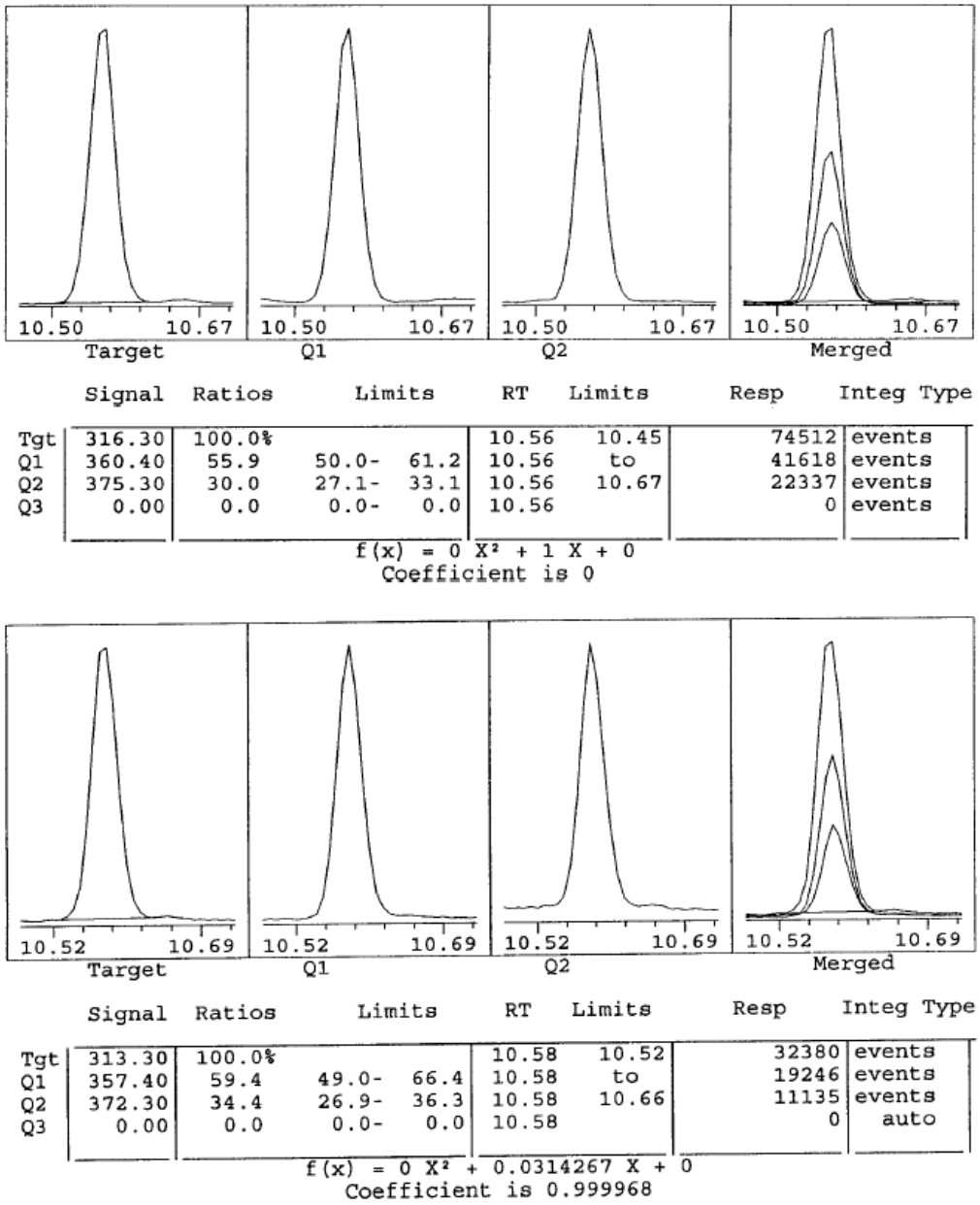

Fig. 8: Pilot ring test 1995 of the Society for Toxicological and Forensic Chemistry (GTFCh) for proving the availability of THC and THC-COOH in the serum. Original ion chromatogram of THC-COOH-D 3 (above) und THC-COOH (below). The determined THC-COOH concentration was 14.70 ng/mL (see fig. 9).

Version of: Feb. 28, 95
Methode: THC
RM D'dorf

File:	VGL1.D	RIMO1.D	RIMO2.D
date	Mar. 6, 95	Mar. 9, 95	Mar. 9, 95

Substance	Spec. inf.	Type:	Ion:	5/5/50 ng/m	rimo 1	rimo 2
THC		Tgt.-Ion	313.30	7014	34973	29029
ng/µl in comp.	0.1	Q1	328.40	5576	23239	18559
Resp.-F	4.63E-02	Q1	285.30	2684	16073	11878
11-OH-THC		Tgt.Ion	313.30	13218	0	0
ng/µl in comp.	0.1	Q1	314.40	3143	0	0
Resp.-F	3.59E-02	Q2	358.40	1184	0	0
COOH-THC		Tgt.-Ion	313.30	111684	32380	31645
ng/µl in comp.	1.0	Q1	357.40	63972	19246	18767
Resp.-F	3.14E-02	Q2	372.30	35573	11135	10932
D3-COOH-THC		Tgt.-Ion	316.30	74218	74512	70267
ng/µl in comp.	0.8	Q1	360.40	40295	41618	41144
		Q1	375.30	21243	22337	22123
D3-THC		Tgt.-Ion	316.30	30809	61793	49563
ng/µl in comp.	0.4	Q1	331.30	21791	34302	27387

Substance	(Reference:)	(Qual:)	Target:	Actual:	Actual:	Actual:
THC	Ret.-time	In min	8.43	8.36	8.39	8.39
conc.:	NG=0.3	ng/ml	5.00	4.92	12.43	12.86
Height ratio	313.30	328.40	76.71	79.49	66.45	63.93
Height ratio	313.30	285.30	39.95	38.26	45.96	40.92
11-OH-THC	Ret.-time	In min	9.47	9.38	0.00	0.00
conc.:	NG=0.3	ng/ml	5.00	4.95	negative	negative
Height ratio	313.30	314.40	24.67	23.78	0.00	0.00
Height ratio	313.30	358.40	9.58	8.96	0.00	0.00
COOH-THC	Ret.-time	In min	10.69	10.57	10.58	10.57
conc.:	NG=0.3	ng/ml	50.00	47.88	14.44	14.96
Height ratio	313.30	357.40	57.97	57.28	59.44	59.31
Height ratio	313.30	372.30	30.97	31.85	34.39	34.55
D3-COOH-THC	Ret.-time	In min	10.66	10.55	10.56	10.55
Retrieval	In	%	[100]	comp.	100.40	94.68
Height ratio	316.30	360.40	52.48	54.29	55.85	58.55
Height ratio	316.30	375.30	30.09	28.62	29.98	31.48
D3-THC	Ret.-time	In min	8.43	8.35	8.38	8.37
Retrieval	In	%	[100]	Comp.	200.57	160.87
Height ratio	316.30	331.30	77.78	70.73	55.51	55.26
Height ratio						

Peak1/2:	Ion 1:	Ion 2:	Target:	Actual:	Approach:	Approach:
COOH/D3-C	313.30	316.30	1.57	1.50	1000	1000
11-OH/D3-C	313.30	316.30	0.18	0.18	µl sample	µl sample
THC/D3-THC	313.30	316.30	0.23	0.23	40.00	40.00
THC/COOH	313.30	313.30	0.13	0.06	µl std	µl std

Fig. 9: Evaluation protocol.

The first quantitative evaluation based on the stored calibration and the generation of the report takes place according to the instructions of the GC-MS software manufacturer. However, in a second step, all data required for the evaluation is automatically written into the defined fields of a spreadsheet.

We used the Excel program supplied by HP. On this data sheet, up to 7 results are shown next to each other in 7 columns. In addition, all the marginal conditions are given as variables. This includes especially the concentration of cannabinoids in the comparison standard, the amount of examination material that was processed, the limits of detection and the amount of internal standard (D3 mix) added to the sample. The data sheet further contains information about the kind of examination material (serum, blood, etc.) and the target vales for the retention times, for the peak height ratios of the qualifier ions and for the height ratios (m/z 313 or 316) of THC-COOH/THC-COOH-D 3, 11-OH-THC/THC-COOH-D3, THC/THC-D3 and THC/THC-COOH of the comparison standard.

From the data (peak heights, retention times, calculated concentrations, analysis data and analysis ID) acquired from the GC-MS software, the peak height ratios and the absolute retrievals of the two deuterated internal standards were calculated, among others. In addition, the concentrations of THC, 11-OH-THC and THC-COOH provided by the GC-MS software were newly calculated by taking into consideration the actually used sample amount, the selected proof limit (if the calculated concentration was below the numbers for the proof limits that are stated in the fields, a "negative" result is output) and the comparison standard that was always running at the beginning of an analysis series. Hereby, an adjustment of the saved calibration curve to the actual condition of the analysis system was carried out before each series.

Figure 9 shows the evaluation protocol with the calculation of peak height ratios, absolute yields and concentrations of the pilot ring test 1995 of the Society for Toxicological and Forensic Chemistry (GTFCh) for the detection of THC and THC-COOH in the serum. VGL 1 = Comparison (5 ng/mL THC, 5 ng/mL 1 1-0H-THC and 50 ng/mL THC-COOH); RIMO 1 and RIMO 2 are the ring test samples (double determination). The lower left shows the peak height ratio of the comparison: Target/Actual serves for checking the right quantitative composition. Since the results of up to 7 analyses, which were conducted consecutively, are listed on the A4 size data sheet – of which the first and the last are always the comparison standard – one can quickly gain an overview of the quality of the individual analyses compared with the other analyses in the series, and can thus be able to reliably recognize whether the analysis series as a whole is OK or if an individual analysis or the whole series might have to be repeated. Since this data sheet is part of the case-related lab documents, it is possible even after many years to quickly and comprehensively obtain the information about the condition of the analysis system and the quality of the analysis series at the time.

Analytical assessment

Precision

To determine the precision in the series, human serum was extracted after the addition of 3 different amounts of THC, 11-OH-THC and THC-COOH. To determine the day-to-day precision, a control serum that contained THC and THC-COOH was processed on 10 different days. The precision data can be found in table 9.

Table 9: Precision data of the determination of THC, 11-OH-THC and THC-COOH in serum.

	n	$X_{average}$	X_{min}	X_{max}	s	VK
		(ng/mL)	(ng/mL)	(ng/mL)	(ng/mL)	(%)
Precision in the series	6	2.05	1.88	2.20	0.13	6.51
THC	5	4.84	4.58	5.10	0.21	4.41
	5	9.31	8.48	10.06	0.72	7.71

	n	$X_{average}$	X_{min}	X_{max}	s	VK
		(ng/mL)	(ng/mL)	(ng/mL)	(ng/mL)	(%)
Precision in the series	6	2.10	1.93	2.24	0.11	5.43
11-OH-THC	5	4.72	4.22	5.11	0.35	7.46
	5	10.19	9.77	10.91	0.44	4.28

	n	$X_{average}$	X_{min}	X_{max}	s	VK
		(ng/mL)	(ng/mL)	(ng/mL)	(ng/mL)	(%)
Precision in the series	6	19.12	18.29	20.51	0.94	4.93
THC-COOH	5	49.76	47.97	51.79	1.74	3.49
	5	105.15	99.97	109.54	4.19	3.99

	n	$X_{average}$	X_{min}	X_{max}	s	VK
		(ng/mL)	(ng/mL)	(ng/mL)	(ng/mL)	(%)
Day-to-day precision						
THC	10	3.01	2.60	3.65	0.37	12.25
THC-COOH	10	12.36	9.59	13.58	1.24	10.02

Validity

Linearity

The test of linearity was carried out by means of increased serum samples and methanolic control. The calibration curves are linear in the range of 1 to 50 ng/mL (THC and 11-OH-THC) and l to 150 ng/mL (THC-COOH), respectively.

Limit of detection

The following limits of detection (LOD) were
calculated: THC: 0.5 ng/mL
11-OH-THC: 0.3 ng/mL
THC-COOH: 0.3 ng/mL
As a proof limit, a general value of 0.3 ng/mL is preset in the evaluation program (see Fig. 9). If a concentration below this value is calculated, the result is automatically output as "negative". The amount of deuterated standard is set so low that the contained amount of non-deuterated THC or THC-COOH is not verifiable with the procedure any more.

Possibilities of interference

Depending on the column used in the gas chromatograph, there can be errors in the substance peaks of THC, 11-OH-THC and THC-COOH due to contaminations of the samples. This is especially true for samples that have been store for a longer period of time. Hereby, errors in the quantitative determination may occur. To avoid such errors, the chromatographic conditions must be optimized to such an extent that the interfering substances are completely separated from the cannabinoids.
A marked loss, especially of THC, during processing cannot be excluded if the extracts are exposed to light for a long period of time or if the extracts are not constrained in glass containers before the derivatization.
Before the deuterated standards may be added to the samples of the test subjects, the non-deuterated share must be determined (it is about 1 to 2 %!). The absolute amount of the deuterated standard must be so low that even in the range of the LOD no wrongly positive results are possible.

3 Results

3.1 Specimen

Since July 1, 1994, the police have regularly ordered the taking of blood samples if they suspect that a traffic participant is under the influence of drugs, and the blood samples were sent in for examination. Up until June 30, 1996, blood samples of a total of 683 people (hereafter called test subjects) could thus be examined within the framework of the research project, and the finding sheets (blood sampling protocol, supplementary medical report and the so-called 'staggering sheet') as well as the traffic offence charges or accident reports could be evaluated.

3.2 Sender

The senders were the police departments from the administrative district Düsseldorf. Listed below are the senders (only submissions until the end of 1995 were taken into consideration) and the case numbers per sender, as well as the respective population:

Table 10: Sender of blood samples until the end of 1995

Sender	Population	Blood samples	Blood samples per 100,000 inhabitants
PP Essen	622,380	100	16
PP Duisburg	536,797	69	13
OKD Wesel	459,109	44	10
OKD Mettmann	506,262	44	9
OKD Kleve	281,921	25	9
PP Düsseldorf	574,936	44	8
OKD Neuss	430,913	35	8
PP Krefeld	249,565	19	8
PP Wuppertal	679,320	32	5
OKD Viersen	282,091	15	5
PP Mönchengladbach	265,312	10	4
PP Mülheim	177,175	7	4
PP Oberhausen	226,025	5	2
Motorway police	-	50	-

3.3 Frequency proof of intoxicating substances

In 624 of the 683 cases (= 91.4%), the use of an intoxicating substance could be proven. Of these, 54 cases were related to alcohol use only, while 570 persons had used other intoxicating substances, as shown in the following table.

Table 11: Frequency of positive results

	Number	Percent
Negative	59	8.63
Only alcohol	54	7.91
Other intoxicating substances	570	83.46
Total number	683	100

The next table breaks down the overall positive results. Since many test subjects had used more than one intoxicating substance, the number of positive results is 1,205. On average, this means that each test subject had taken 2 (exactly 1.93) intoxicating substances

Table 12: Number of consumed intoxicating substances

Substance/Substance group	Positive results
Cannabinoids	395
Alcohol	227
Opiates	219
Cocaine	151
Amphetamines	60
Benzodiazepines	149
Others	4

3.4 Primary incident leading to taking a blood sample

According to the documents made available for us by the police, we tried to find out what the primary reason for checking a traffic participant was. In many cases, during a general traffic check it was noted that the driver may have taken drugs. Here, it can be seen that the training of the police officers for recognizing the effect of drugs is very important. In many other cases, the impairment due to drug consumption was found while recording a traffic accident. The following table breaks down the individual primary results.

Table 13: Reasons for the police measures

Reason	Number	Percent
Traffic check	231	33.8
Accident	213	31.2
Conspicuous driving	116	17.0
Infringement of Traffic Regulations	57	8.3
Other cases	66	9.7
Total	683	100

3.5 Accidents

213 of the 683 test persons were involved in a traffic accident. 61 had left the location of the accident without permission. Based on the available documents, the accidents were subdivided into three categories: minor, serious and very serious accidents.

Table 14: Number of and types of accidents

	Number	Percent
Minor accident	130	61.0
Serious accident	72	33.8
very serious accident	11	5.2

3.6 Conspicuous driving/Infringements of Traffic Regulations

In 173 cases, traffic participants were taken notice of due to driving errors or serious violations of the Traffic Regulations. Some relevant findings, or findings that seem relevant regarding the assessment of one's fitness to drive are listed in table 15:

Table 15: Conspicuous driving

Type	Number
Driving in a serpentine line	108
Failure to yield	25
Driving too fast	39
Driving very slowly	16
Other conspicuous driving	48
Other violations of the Traffic	50

3.7 User groups

Based on the consumption patterns, the test subjects can be divided into 5 groups:

Alcohol users:	No intoxicating substances other than alcohol were used.
Medication users:	No illegal drugs, but centrally active medication were used; possible alcohol consumption.
Cannabis users:	No heroin or cocaine, but cannabis was used, also possibly alcohol, amphetamine or centrally active medication.
Cannabis only users:	Only cannabis was consumed.
Opiate users:	Consumption of opiates, and possible consumption of all other intoxicating substances.
Cocaine users:	No heroin, but cocaine was used, possibly together with other intoxicating substances.

If the 624 test subjects who had consumed intoxicating substances are divided into the 5 or 6 user groups, the following image emerges (table 16):

Table 16: Distribution of user groups

	Number	Percent
Cannabis users	250	40.0
(Cannabis only user)	(115)	(18.4)
Opiate users	219	35.1
Cocaine users	64	10.3
Alcohol users	54	10.3
Medication users	37	5.9
Total	624	100

This means that the cannabis users are the largest group among the total number.

3.8 **Times of the offences** (evaluation period until the end of 1995)

In the majority of cases, the time of the offence was at night. Figure 10 shows that the maximum number was between midnight and 2:00 a.m., while the minimum number was in the morning hours between 9:00 and 10:00 a.m. If we select only the cannabis users, we find an additional maximum around 11:00 p.m. Drivers under the influence of cannabis can already be found in traffic earlier in the evening. This is especially true for cannabis only users, who very rarely appear conspicuous as drivers between 10:00 a.m. and 2:00 p.m. (Fig. 10).

3.9 **Age structure** (evaluation period until the end of 1995)

As was to be expected, the age of the consumers was the relatively low. Especially numerous were users between the ages of 20 and 22. While the frequency decreases relatively uniformly with increasing age (tailing), among cannabis users, and even more markedly among the cannabis only users, there is a clear concentration on the ages from 18 to 22, even if there are consumers of this drug who are older than 40. However, none of the cannabis users were over 50 years old (Fig. 11).

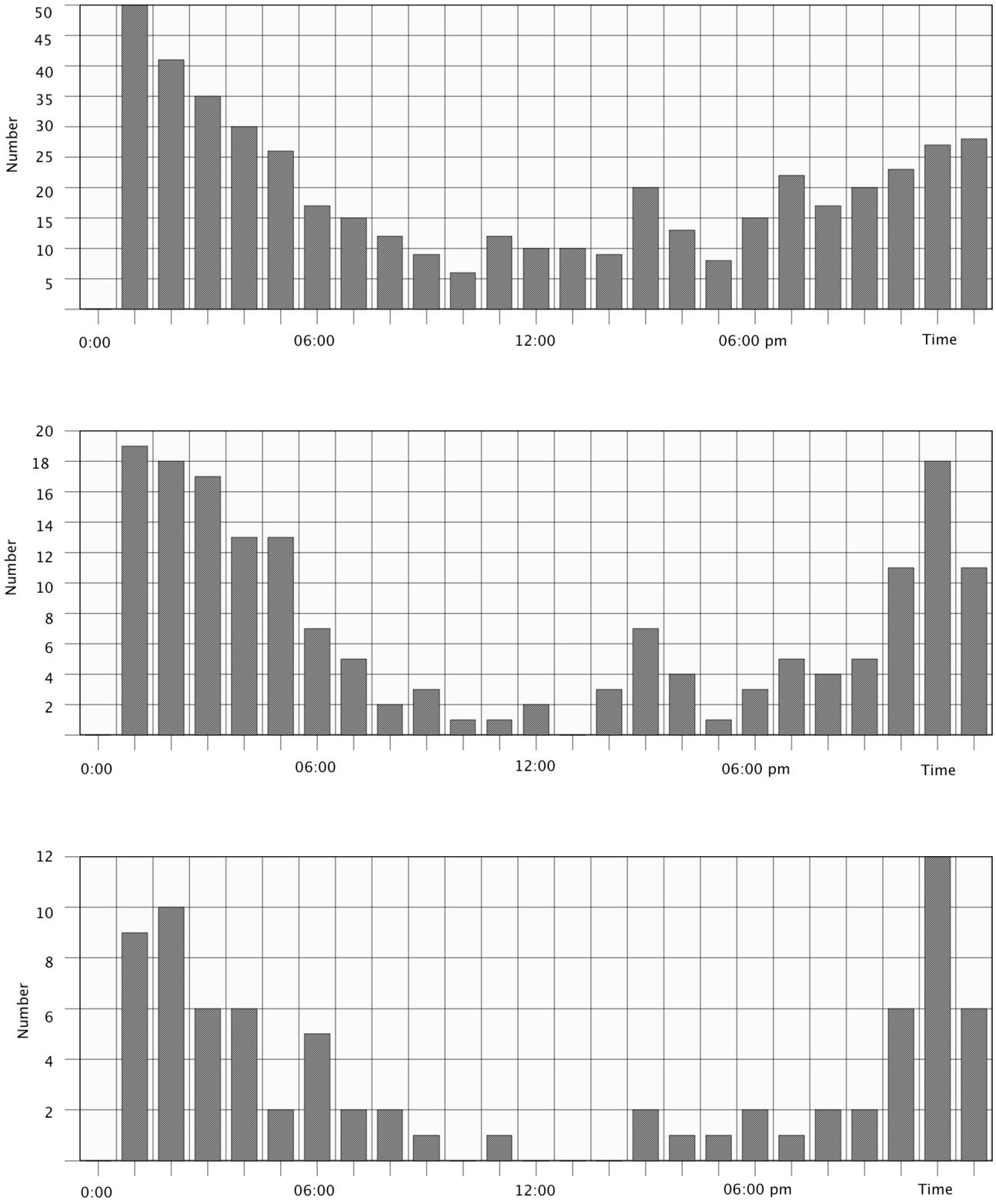

Fig. 10: Distribution of the time of offence. Top: Overall; Middle: Cannabis users; Bottom: Cannabis only users.

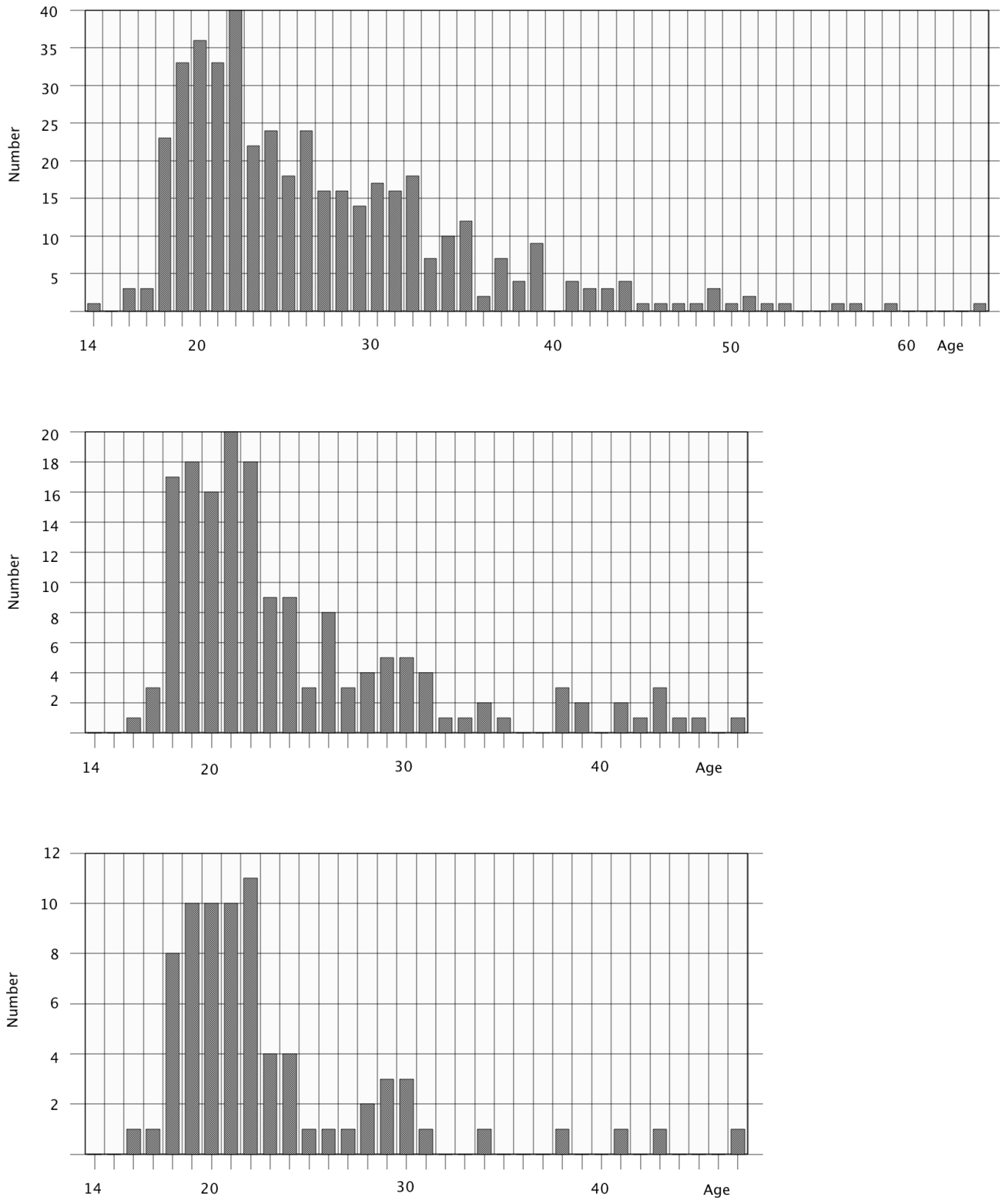

Fig. 11: Age distribution. Top: Overall; Middle: Cannabis users; Bottom: Cannabis only users.

3.10 User type and driving peculiarities

3.10.1 User type and accidents

We checked whether particular peculiarities in driving or in behavior were found especially frequently among certain user groups. First, we compared the user types with the accident results (Fig. 17).

Table 17: User type and accidents

Consumer group	Number	Number of accidents	Share in accidents (%)	Accident frequency within the group (%)
Cannabis users	250	66	31.0	26.4
Opiate users	219	66	31.0	30.1
Cocaine users	64	22	10.3	34.4
Only alcohol	54	19	8.9	35.2
Other substances	37	21	9.9	56.8
negative	59	19	8.9	32.2
Total	683	213	100	31.2

Here, we can detect no clear differences between the individual user groups. This only means that drivers who had consumed only alcohol or other substances were involved in traffic accidents somewhat more frequently.

3.10.2 User type and hit and run

Among 213 accidents, there were 61 hit-and-run cases; this offence was committed disproportionately frequently (27 of the 61 cases = 44.3%) by drivers that must be counted among the cannabis users. (Fig. 18).

Table 18: User type and hit and run

Consumer group	Number	Number of incidents	Frequency (%)	Frequency among the group (%)
Cannabis users	250	27	44.3	10.8
Opiate users	219	17	27.9	7.8
Cocaine users	64	2	3.3	3.1
Only alcohol	54	7	11.5	13.0
Other substances	37	5	8.2	13.5
negative	59	3	4.9	5.1
Total	683	61	100	8.9

3.10.3 User type and driving errors

Driving a vehicle in a serpentine line occurs in all groups in equal frequency. What is conspicuous among our test persons is that this driving error was less frequently observed among those who had only drunk alcohol (Fig. 19).

Table 19: User type and driving error (serpentine lines)

Consumer group	Number	Number of incidents	Frequency (%)	Frequency within the group (%)
Cannabis users	250	38	35.2	15.2
Opiate users	219	37	34.3	16.9
Cocaine users	64	8	7.4	12.5
Only alcohol	54	5	4.6	9.3
Other substances	37	9	8.3	24.3
negative	59	11	10.2	18.6
Total	683	108	100	15.8

The situation isn't much different if we compare the test point "high-speed driving" with the consumer groups. This peculiarity was observed relatively more frequently in persons whose blood analyses delivered only negative results (Table 20).

Table 20: User type and "high-speed driving"

Consumer group	Number	Number of incidents	Frequency (%)	Frequency within the group (%)
Cannabis users	250	15	38.5	6.0
Opiate users	219	10	25.6	4.6
Cocaine users	64	5	12.8	7.8
Only alcohol	54	3	7.7	5.6
Other substances	37	0	0	0
negative	59	6	15.4	10.2
Total	683	39	100	5.7

Regarding the test point “failure to yield”, we found no differences between the user groups (Table 21).

Table 21: User type and failure to yield (“red traffic light”, stop sign)

Consumer group	Number	Number incidents	Frequency (%)	Frequency within the group (%)
Cannabis users	250	8	32.0	3.2
Opiate users	219	6	24.0	2.7
Cocaine users	64	1	4.0	1.6
Only alcohol	54	2	8.0	3.7
Other	37	3	12.0	8.1
negative	59	5	20.0	8.5
Total	683	25	100	3.7

3.10.4 Conclusion

As already mentioned above, a blood sample was only taken if the checking police officers had the impression that the driver was unfit to drive due to the consumption of a narcotic substance. Thus, a selection took place. However, the selection didn't bear on the type of narcotic substance or the other intoxicating substances (except alcohol), which possibly had an influence on the driver. This means that, if the cannabis users are in first place among the comparisons carried out here, seen absolutely, this group is also very frequently unfit to drive in road traffic. The fact that, in absolute numbers, the opiate consumers closely follow the cannabis group, also means that the individual opiate consumers (there are many more cannabis consumers than opiate consumers) obviously pose a much greater risk to road traffic safety than the individual cannabis consumers.

4 Calculating a limit value to determine the inability to operate a vehicle as a result of cannabis consumption

4.1 General

It has already been mentioned that there is no (or doesn't seem to be any) absolute relationship between the dosage, THC concentration in the blood and the effect, and that there are large fluctuations between different individuals as well as for particular individuals. This could also be confirmed by the present research project. Every attempt to compare the THC concentrations and the assessments of the police and blood-sampling doctor regarding conspicuous behavior and driving errors hasn't led to any discernable relationships. Independently of the degree of conspicuous behavior or the gravity of the driving errors, both low and high THC concentrations were found in the blood (see the results for the group of cannabis only users printed in tabular form in Appendix 8). In this respect, the experimental studies with volunteers were confirmed.

On the other hand, experimental studies have also shown that, after the distribution of the active ingredient between blood and tissue, there is a direct proportionality between the THC concentration and the effective strength for the individual consumer. In addition, different authors have noted that there seems to be a relationship between the concentration ratio of THC and its metabolite THC-COOH on the one hand and the time interval between consumption and blood sampling on the other hand. This relationship was made tangible in 1992 by the work group lead by Huestis [5]. They describe calculation models, which can be used to calculate the time of cannabis consumption with relative precision from the THC and the THC-COOH concentrations and the time of the blood sampling. The correctness of the calculations was verified through the data we collected and with the published data. However, no test based on authentic blood samples collected by the police had yet taken place. This was carried out later by Daldrup [23], based on 368 serum samples of cannabis consumers, who in most cases had consumed cannabis products in Dutch coffee shops and against whom preliminary proceedings had taken place because of a suspicion of violating the Narcotics Act. Using the calculation models, the theoretical consumption time was calculated and compared with the time of the offence, but also with the statement of the concerned persons regarding the time of consumption. It could be seen that with one calculation model, about 50% of the answers obtained were correct, while another 15% of the results were obviously wrong; in these cases, the calculated time of consumption was a time during which the police measures were already being carried out. In this respect, the calculation models were considered unsuitable

for forensic purposes. However, since the calculation models could always be used to determine the time interval between consumption and blood sampling quite accurately when cannabis was smoked once under controlled conditions, it can be assumed that there are some principles that can possibly also be used for a procedure to determine the limit value for the absolute unfitness to drive. The calculation also takes into consideration, as already explained, that for smoking tests under controlled conditions, there are considerable individual fluctuations. However, the calculation also uses the concentration of the THC metabolite THC-COOH. Hereby, individual fluctuations can obviously be harmonized.

4.2 Introduction of the ”Cannabis Influence Factor” (ClF)

The present study has now checked whether it's possible to harmonize the considerable fluctuations between different individuals and among the same individual regarding the relationship between the concentration of the active ingredient in the blood and its effect. Therefore, the concentration of THC and its effective metabolite 11-OH-THC were compared with the concentration of the ineffective metabolite THC-COOH. The result of this calculation was called the “Cannabis Influence Factor", abbreviated CIF. For the calculation of the CIF, the usually obtained mass concentrations (measurement unit ng/mL) are converted into substance quantity concentrations (measurement unit nmol/mL). The CIF is calculated using the following formula:

$$CIF = \frac{\frac{[THC]}{314.5} + \frac{[11\text{-}OH\text{-}THC]}{330.5}}{\frac{[THC\text{-}COOH] * 0.01}{344.5}}$$

where for [THC], [11-OH-THC] and [THC-COOH], the respective concentrations of these substances in the measurement units ng/mL are used.
The obtained result is rounded to an integer. This means that the CIF is an integer and non-dimensional. However, the prerequisite for the use of this formula of the calculation of the CIF is that the total THC and 11-OH-THC concentrations are at least 1 ng/mL. If the concentrations are lower than that, a value of 0 is input for their concentration, so that the value of the CIP will also be zero.

4.2.1 Examining the relationship CIF / driving error

Various driving errors recorded by the police were then compared with the CIF determined from the blood examination. For this purpose, a cumulative representation was chosen. This allows us to see directly with what accumulation a certain driving error, such as driving in serpentine lines, was detected at a certain CIF.

In tables 22 and 23, the CIF value ranges (CIF = O; CIF = 1 to 9; CIF = 10 or larger) for peculiarities of driving style 3 are compared. The CIF values are valid for the time of blood sampling. Table 22 shows the results of the cannabis user group (of the 250 cases, the results of the confirmation analysis were also available for 239 cases), and table 23 shows the cannabis only users.

Table 22: CIF and fitness to drive (cannabis user group)

Type of incident	n	CIF 0	CIF 1 to 9	CIF >/= 10
Total	239	18.0%	18.8%	63.2%
Minor accidents	41	23.5%	35.3%	41.2%
Serious accidents	22	18.2%	27.3%	54.5%
Veering off the road	18	16.7%	33.3%	50.0%
Total accidents	63	20.6%	28.6%	50.8%
Hit and run	26	15.4%	42.3%	42.3%
Accidents (without running)	37	24.3%	18.9%	56.6%
“Serpentine lines”	37	16.2%	16.2%	67.2%
“high speed”	14	7.1%	21.4%	71.5%
“too slow”	9	11.1%	0.0%	88.9%
“red traffic light”, “stop sign”	7	28.6%	14.3%	57.1%

It becomes apparent that there is a positive correlation between the accumulation of driving errors and the CIF value. This applies to cannabis users who, in part, had additionally consumed alcohol, amphetamines or centrally active medication, as well as for cannabis only consumers, who weren't under the influence of alcohol (BAC below 0.1‰). Based on a blood examination, this allows us to conclude that the CIF seems to be a suitable value to prove an unfitness to drive after the consumption of cannabis.

Table 23: CIF and fitness to drive (group of cannabis only users)

Type of incident	n	CIF 0	CIF 1 to 9	CIF >/= 10
Total	115	12.2%	18.3%	69.5%
Minor accidents	9	22.2%	33.3%	44.4%
Serious accidents	11	27.3%	27.3%	45.4%
Veering off the road	3	0.0%	33.3%	66.7%
Total accidents	20	25.0%	30.0%	45.0%
Hit and run	8	25.0%	50.0%	25.0%
Accidents (without running)	12	25.0%	16.7%	58.3%
“Serpentine lines”	22	9.1%	9.1%	81.8%
“high speed”	8	0.0%	25.0%	75.0%
“too slow”	8	12.5%	0.0%	87.5%
“red traffic light”, “stop sign”	4	25.0%	0.0%	75.0%

4.3 Correlation of BAC and CIF

We searched for a method to set a limit value for the CIF that could be directly compared with the currently valid BAC limit value for the absolute unfitness to drive due to alcohol consumption. Based on the accident data of 1994 for the administrative district Düsseldorf, we tried to confirm the limit value of the absolute unfitness to drive due to alcohol consumption.

4.3.1 Absolute unfitness to drive due to alcohol consumption

A decree of the Federal Court of Justice (BGH) on June 28, 1990 [24] stated that drivers are absolutely unfit to drive at a blood alcohol content of 1.10‰. A base value of 1.00‰ was used as the starting point. This base value of the blood alcohol concentration serves as a threshold value at which the ability of an individual to operate a vehicle can't be determined anymore. By a decree in 1990, the base value was decreased from 1.10‰ to 1.00‰. One of the reasons for this was based on a 1966 report of the Federal Health Office that stated: “Alcohol in traffic offences” [25] with regard to the number traffic accidents with fatalities, the risk posed by inebriated drivers with a blood alcohol concentration between 0.6‰ and 0.7‰ increased threefold, while for blood alcohol

concentrations of 1.0‰ to 1.1‰ it increased six-fold compared to that of a sober driver. The first value was the basis for setting the risk limit value of 0.8‰ in 24a of the Road Traffic Act.

Driving tests subsequently carried out have confirmed the base value of 1.0‰. In addition, when setting the base value, the fact that since 1966 the traffic conditions have changed so much that the performance requirements of individual drivers have increased markedly had to be taken into consideration. This is reflected especially in increases in traffic density and in the fact that the average drive speed, especially on the Autobahn and on roads, has increased greatly. But if performance requirements on drivers are raised as a result of the road traffic, the reduction of the driver's psycho-physical performance due to alcohol poses a risk to other traffic participants more quickly, so the danger of a driver under the influence of alcohol is principally increased [24].

The basis of the basic value of 1.0‰ alcohol in the blood at which one is unfit to drive and that leads to the known limit value of absolute unfitness to drive if one adds a safety value of 0.1‰ was formed by the results of statistical examinations in which the number of traffic fatalities was compared with the detected blood alcohol concentrations of the involved drivers. We have tested whether the same results can still be achieved today if the model from the 1960s is used, and if this or another model is suitable for setting the limit value of one's absolute unfitness to drive due to the consumption of cannabis.

Therefore, all traffic accidents that occurred in 1994 in the administrative district Düsseldorf which were included in the police statistics NRW [32] were examined with regard to accident type, accident category and alcohol involvement. A total of 158,253 accidents were recorded in the administrative district Düsseldorf in 1994. In 4,158 accidents (=2.6%), alcohol was involved. Table 24 shows the accidents with or without the influence of alcohol with regard to the different accident categories. Thus, the accumulation of serious accidents (category 1 to 4) under the influence of alcohol (per 100 accidents) was twofold (category 3) to fourfold (category 4).

Table 24: Traffic accidents with or without the influence of alcohol in the administrative district Düsseldorf in 1994

Accident category	Traffic accidents without alcohol		Traffic accidents with alcohol	
	n	n per 100 Accidents	n	n per 100 Accidents
Cat. 1: Accidents with fatalities	245	0.2	27	0.6
Cat. 2: Accidents with serious injuries	4,848	3.1	483	11.6
Cat. 3: Accidents with slight injuries	16,045	10.4	850	20.4
Cat. 4: Accidents with heavy damage	8,404	5.5	936	22.5
Cat 5: Minor accidents	10,3048	66.9	-	-
Cat. 6: Minor accidents under the influence alcohol or with hit and run	21,505	14.0	1,862	44.8
Number of fatalities	270	0.2	28	0.7
Number of seriously injured	5379	3.5	543	13.1
Number of slightly injured	19,594	12.7	1,080	26.0

These accident statistics show that the number of traffic accidents with fatalities that didn't involve alcohol were 245, while those that involved alcohol were 'only' 27.

The number of people who died in traffic accidents decreased by 60% between 1970 and 1990 in the old Federal Republic of Germany in spite of increased vehicle density. The passive and active safety of modern automobiles and the general introduction and improvement of restraint systems for car passengers as well as airbag systems have substantially contributed to this reduction [26, 27]. Due to this technical progress, the chance of fatal accidents occurring was much lower than in the 1960s with regard to driving under the influence of alcohol. Therefore, the criterion “Traffic accident resulting in death” doesn’t seem suitable today to statistically prove the limit value of the absolute unfitness to drive.

It is a different matter if one analyzes so-called alcohol-typical accidents statistically. Rudolf [28] showed that the most frequent causes of accidents involving traffic participants under the influence of alcohol differ from the most common general causes according to the accident statistics. The accidents weren't occuring while overtaking or passing, or due to failures to yield when it came to driving under the influence of alcohol; instead, most motorcycle and bike accidents fell into the category “Falls without external cause”, while for automobile drivers it was mostly ‘veering off the road' and ‘driving into obstacles in standing traffic’. Mueller et al. [29] found that, among drivers under the influence of alcohol, an increased non-compliance with driving in the correct lane without any obvious reason, hit-and-run cases, spinning out of a bend that is actually harmless, veering off of a straight line, driving in serpentine lines and skidding without an obvious reason.

Mallach and Stein [30] found that accidents in bends are very frequent among drivers under the influence of alcohol, while Bürkle [31] found that veering off the road is a frequent cause.

In the police statistic NRW, there were statements regarding the accident type in 55,115 of the 158,253 registered accidents (table 25).

Table 25: Types of accidents with or without the influence of alcohol in the in the administrative district Düsseldorf in 1994

Type of accident Collision with another vehicle, which	Traffic accidents without alcohol (n = 51047)		Traffic accidents with alcohol (n = 4068)	
	n	n per 100 accidents	n	n per 100 accidents
(1) started, stopped or was standing in stationary traffic	5095	10.0	1119	27.5
(2) drove ahead or waited	18372	36.0	438	10.8
(3) drove laterally in the same direction	5300	10.4	113	2.8
(4) approached	2154	4.2	196	4.8
(5) turned or crossed	1817	3.6	400	9.8
(6) collision between cars and pedestrians	10276	20.1	185	4.5
(7) collision with an obstacle on the road	3236	6.3	32	0.8
(8) leaving the road to the right	205	0.4	646	15.9
(9) leaving the road to the left	2582	5.1	486	11.9
(0) Accident of another kind	2010	3.9	453	11.1

As described in the literature, it becomes apparent that veering off the road to the left and more so to the right were observed remarkably often in drivers under the influence of alcohol. If the dependency of the increase of this alcohol-typical accident occurrence on the BAC of the driver is examined, it becomes apparent that drivers with a BAC between 0.6 and 0.7‰ veer off the road with their vehicle to the right or to the left about 3 times more often than mostly sober drivers (BAC up to a maximum of 0.1‰); when the BAC is between 1.00 and 1.10‰, this number almost doubles.

(Fig. 12). The same increases of danger at the stated BACs were also statistically detected in the previously mentioned report “Alcohol in traffic offences”. This means that an evaluation of the alcohol-typical accidents, such as veering off the road, can statistically prove the increased perilousness of drivers under the influence of alcohol with the same result as the one achieved by Freundenberg in 1966 [25] in the report regarding the evaluation of traffic accidents with fatalities.

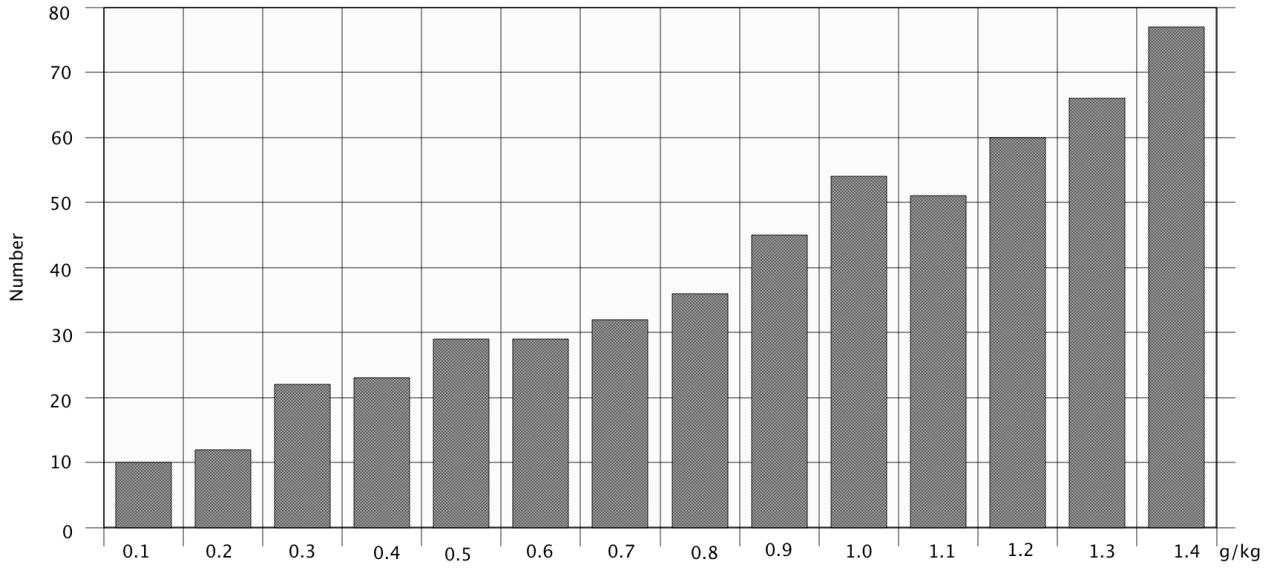

Fig. 12: BAC up to 1.40‰ and alcohol-typical accident (veering off the road). Evaluation of all accidents registered in the administrative district Düsseldorf in 1994 which were due to the influence of alcohol (Accident type 8 or 9; police statistic NRW).

4.3.2 The “26% value"

Therefore, for this research project we selected the total number of accidents on the one hand, and the accident type “Veering off the road” on the other, depending on the BAC of the person involved in the accident, to determine the connections between the BAC value and the accumulated appearance of driving errors. Of special interest was the question of the percentage of drivers under the influence of alcohol who had BACs of under or over 1.10‰.

To determine this, all traffic accidents recorded in the administrative district of Düsseldorf in which alcohol was involved were counted out and assigned to BAC classes (up to 0.1‰; up to 0.2‰, up to 0.3‰, etc.). The results are shown in figures 13 and 14. It can be seen that the overall accidents and for the accident type 'Veering off the road', about 26% of the drivers had BACs under 1.10‰. This “25% value” indicates that 74% of the accident drivers had a BAC of at least 1.10‰ and thus were absolutely unfit to drive due to the influence of alcohol. As for the remaining 26% of the drivers, the blood alcohol value alone isn’t sufficient as proof of the absolute unfitness to drive.

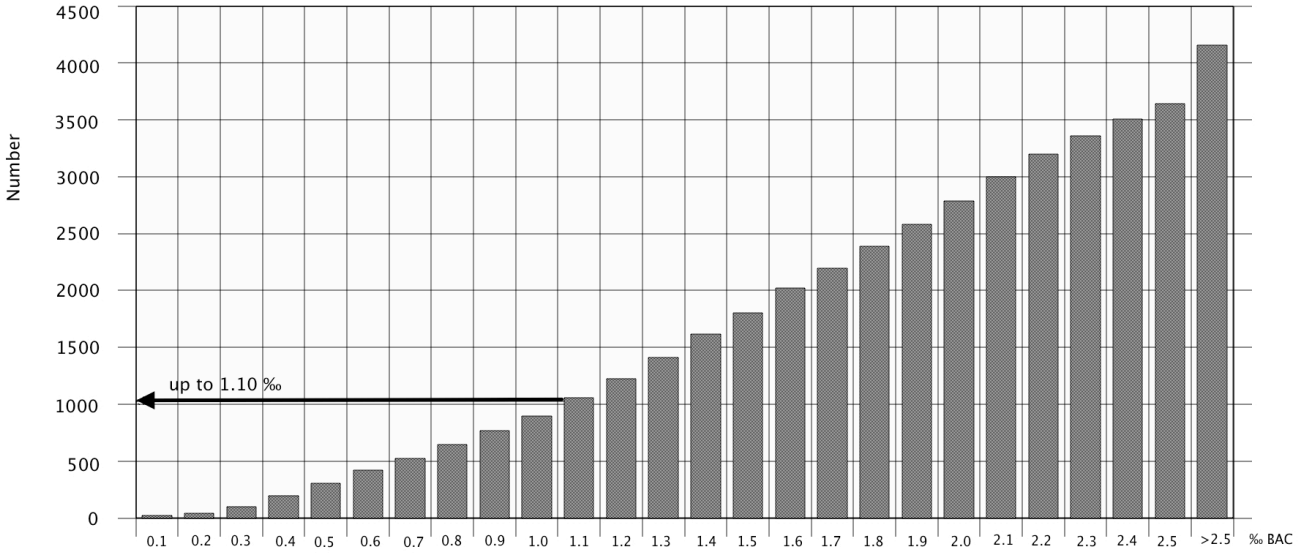

Fig. 13 BAC and accidents in 1994 in the administrative district Düsseldorf (total number of accidents in which alcohol was involved: 4158; of these, the number of accidents with BACs of up to 1.10‰: 1059 (=25.5%).

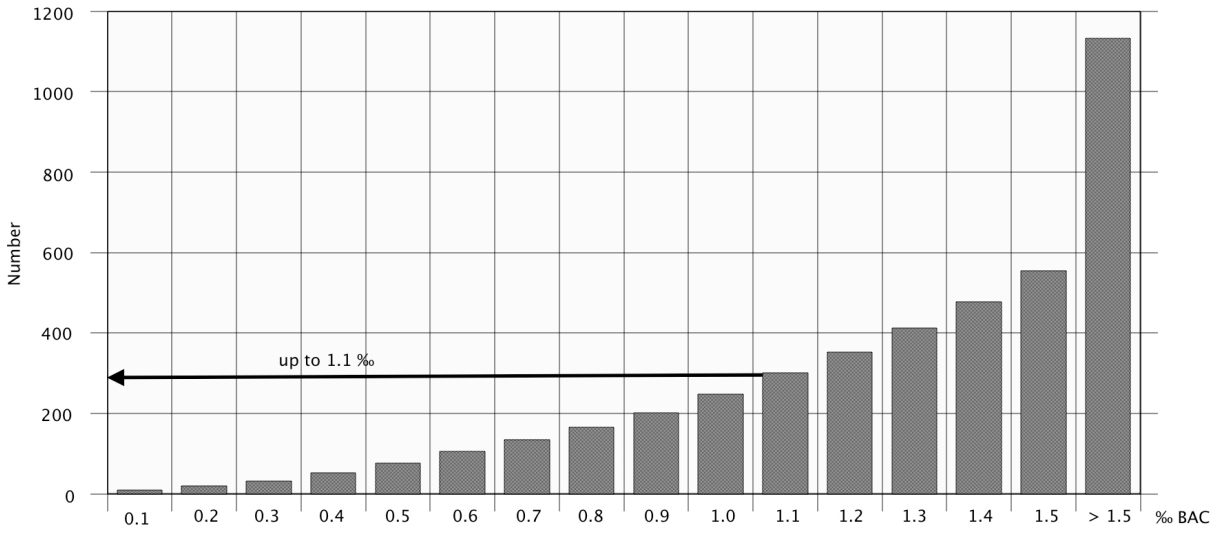

Fig. 14: BAC and accidents in which alcohol and veering off the road were involved in 1994 in the administrative district Düsseldorf (total number: 1132; of these the number of incidents with BACs of up to 1.10‰: 301 (=26.6%).

This 26% value was subsequently selected to establish a limit value between the relative absolute unfitness to drive due to the consumption of cannabis. For different types of conspicuous behavior and driving errors that were detected, especially by the police, in cases of cannabis consumers who didn't use any other drugs and who weren't under the influence of alcohol (BAC under 0.1‰), from what CIF the 26% value was exceeded was checked

4.4 CIF, conspicuous behavior and driving errors

The peculiarities recorded in the police report (staggering sheet) with regard to driving a motor vehicle, and the behavior while checking cannabis only users, were assigned to the following CIF groups: CIF 0 to 4, CIF 5 to 9, CIF 10 to 14, CIF 15 to 19, CIF 20 to 24, CIF 25 to 29 and CIF over 29.

4.4.1 CIF and aggression or agitation

The results are shown in figure 15. It becomes apparent that aggressive and agitated behavior during police measures were observed more easily in the cases of cannabis consumers with a low CIF. Above a CIF of 9, such behavior is only rarely found; the total case numbers hardly increase with a growing CIF. The present results show that this cannabis effect can come to the foreground after the acute effect subsides. Accordingly, the 26% value is just above a CIF of 4.

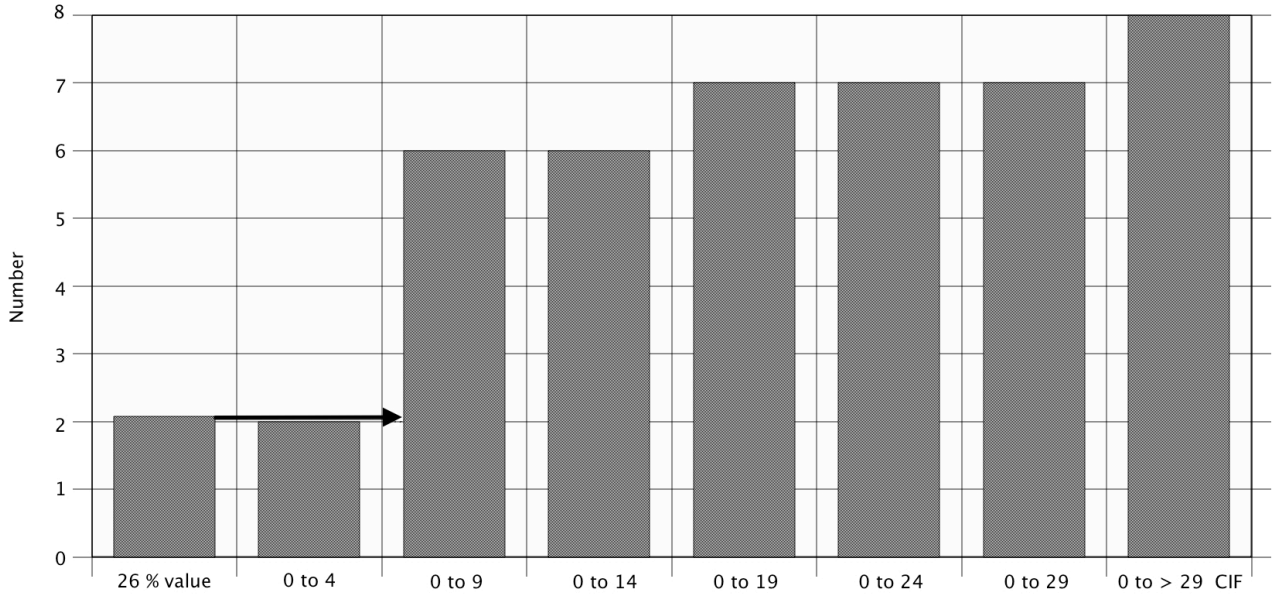

Fig. 15: CIF and accumulation of aggressive or agitated behavior.

4.4.2 CIF and euphoria or talkativeness

Euphoric or talkative behavior is a known typical effect of cannabis. This is also reflected in the CIF. If the CIF increases, a continuous increase in the total number of cases is observed, for which the police made the corresponding findings (Fig. 16). The 26% value corresponds to the CIF range up to 9, i.e. 26 percent of the affected people have already shown this behavior if a CIF between 5 and 9 was determined in a blood sample.

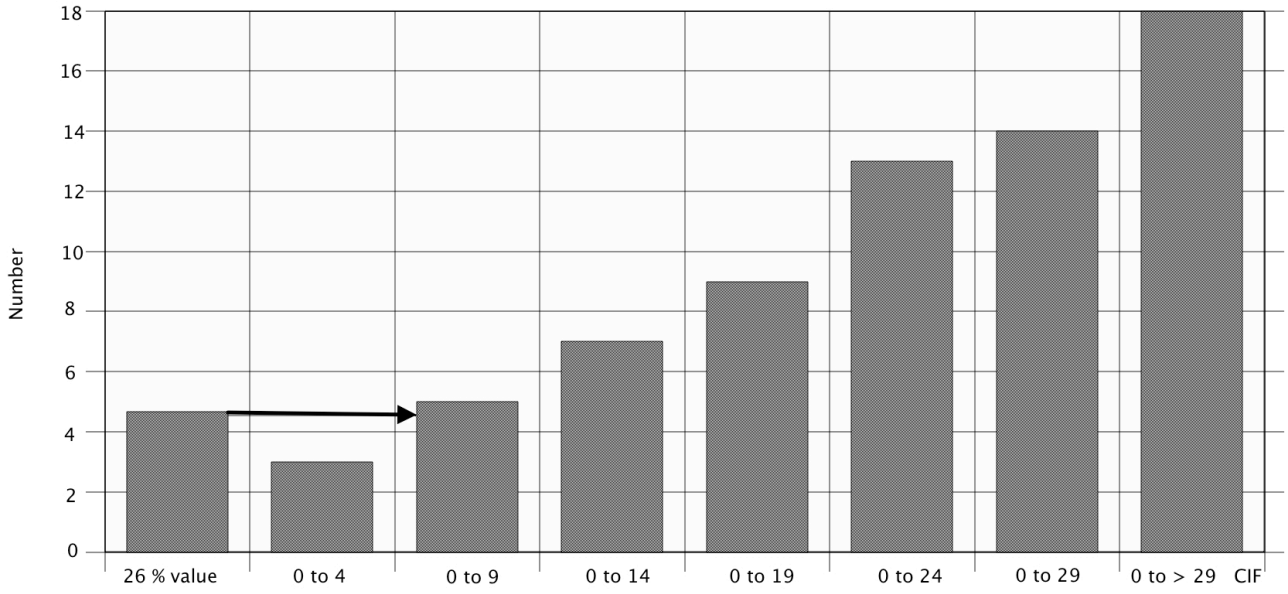

Fig. 16: CIF and the accumulation of euphoric or talkative behavior.

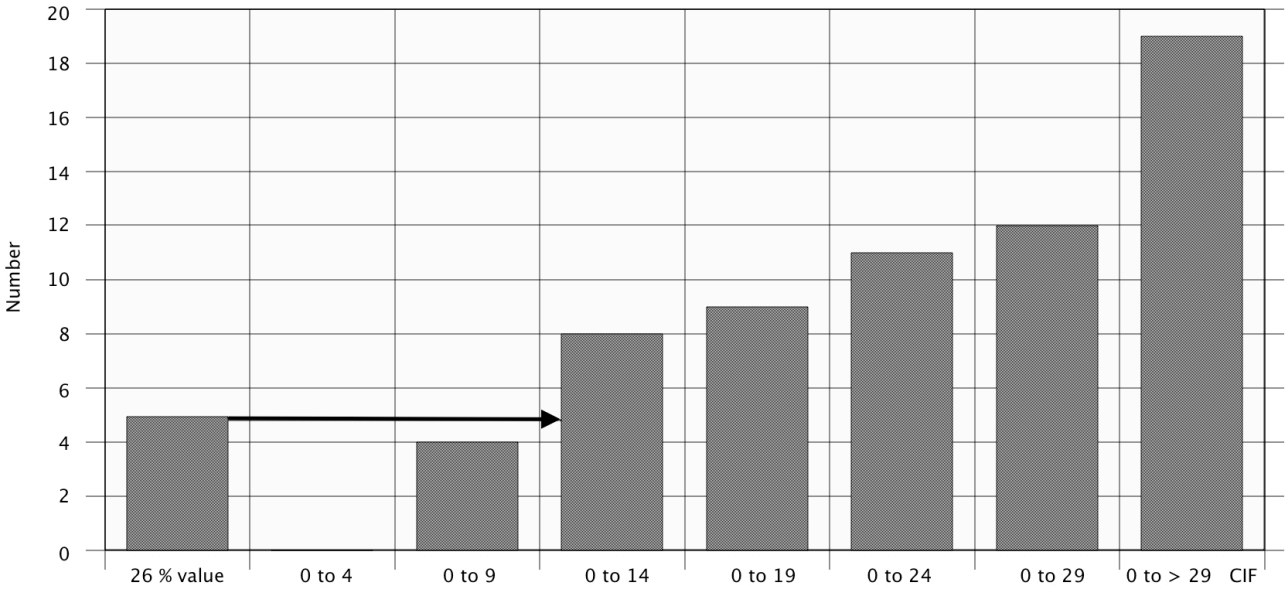

Fig. 17: CIF and the accumulation of lethargic or apathetic behavior.

4.4.3 CIF and lethargy or apathy

The compiled results clearly show that lethargic and apathetic behavior go hand in hand with a high CIF. None of the people stopped by the police with this type of behavior showed a CIF under 5. The 26% value was reached at a CIF between 10 and 14 (Fig. 17)

4.4.4 CIF and tiredness

It is known that cannabis has a tiring effect. The evaluation of the documents regarding this point shows that the total number of cases in which the police officers had the suspicion that the concerned individual was tired when they carried out the inspection increased continuously as CIF increased. The 26% value was reached at a CIF between 10 and 14 (Fig. 18).

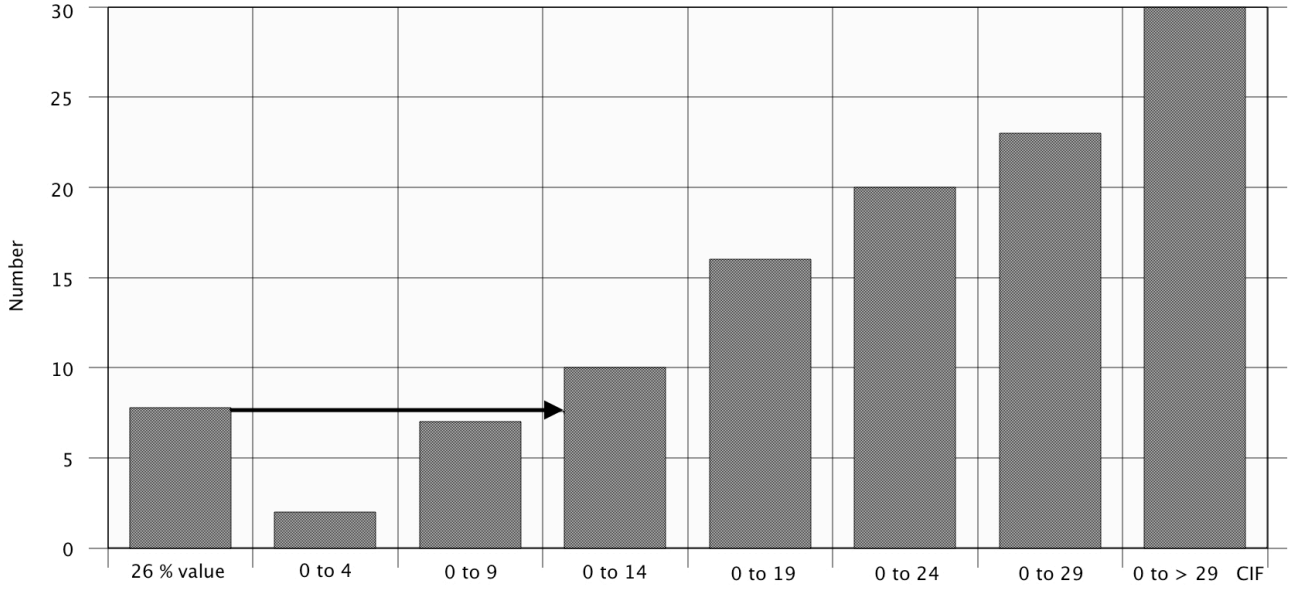

Fig. 18: CIF and the accumulation of tiredness.

4.4.5 CIF and thick-wittedness or delayed perceptivity

An increasing CIF also means a continuous increase in the total number of cases in which the concerned people gave off the impression of being thick-witted or of having delayed perceptivity during the police inspection (Fig. 19). From a CIF of 10 to 14, these types of behavior, which is a typical effect of cannabis, were increasingly observed.

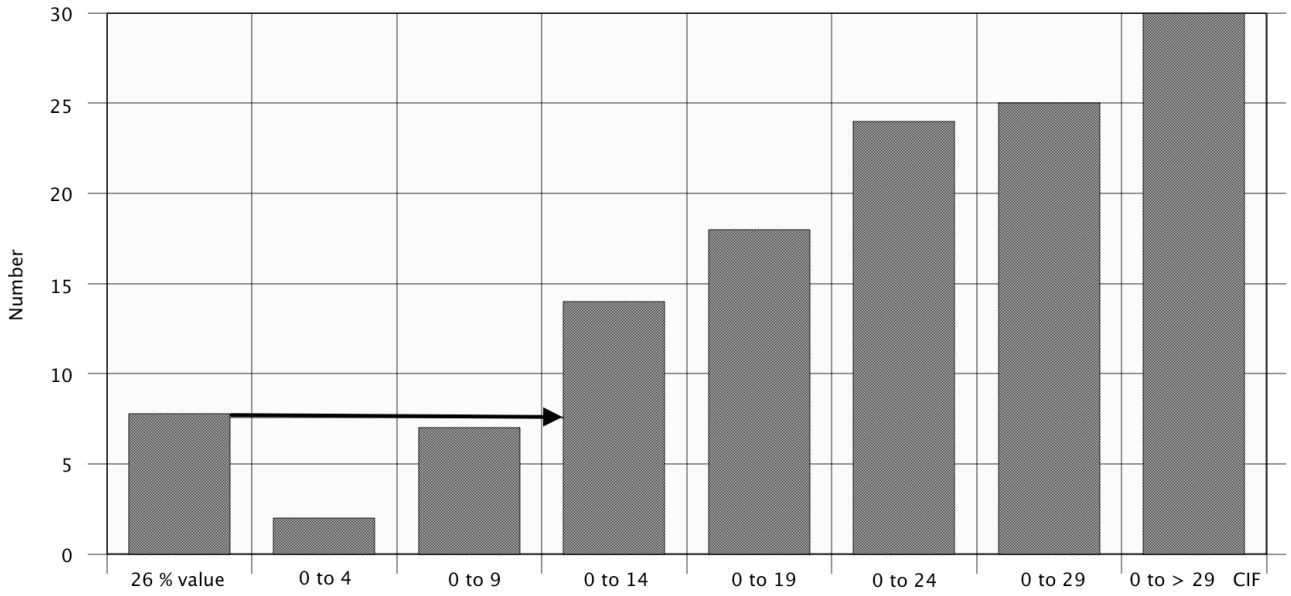

Fig. 19: CIF and the accumulation of thick-wittedness or delayed perceptivity.

4.4.6 CIF and wide pupils

Checking one's pupils' reaction with a flashlight is a suitable means of confirming the initial suspicion of drug consumption. Widened pupils with slow reactions to light stimulation observed in particular after stronger cannabis consumption. The comparison CIF/wide pupils shows that this symptom appears more frequently at a higher CIF. Correspondingly, the 26% value of this test point is between 10 and 14 (Fig. 20).

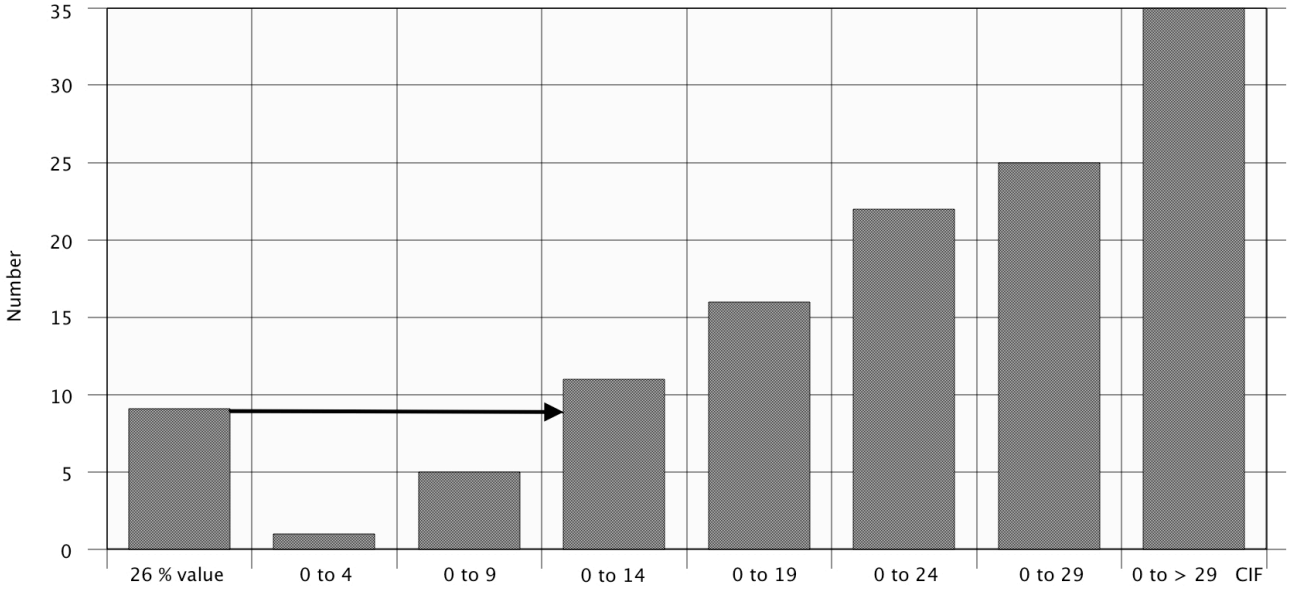

Fig. 20: CIF and the accumulation of widened pupils (mydriasis).

4.4.7 CIF and driving a vehicle in a serpentine line

If a driver is no longer able to keep their vehicle in the lane, this is a clear sign of the presence of an alcohol-related unfitness to drive. Driving in serpentine lines after the consumption of intoxicating substances in general, but also for drivers consuming only cannabis, was observed relatively often, especially if a high CIF was determined based on the blood examination (Fig. 21). The 26% value, which was derived from the BAC limit value of 1.10‰ (see chapter 4.3), appears at a CIF that is higher than 9 for this type of driving error. This means that three quarters of the drivers going in serpentine lines had a CIF of 10 or more.

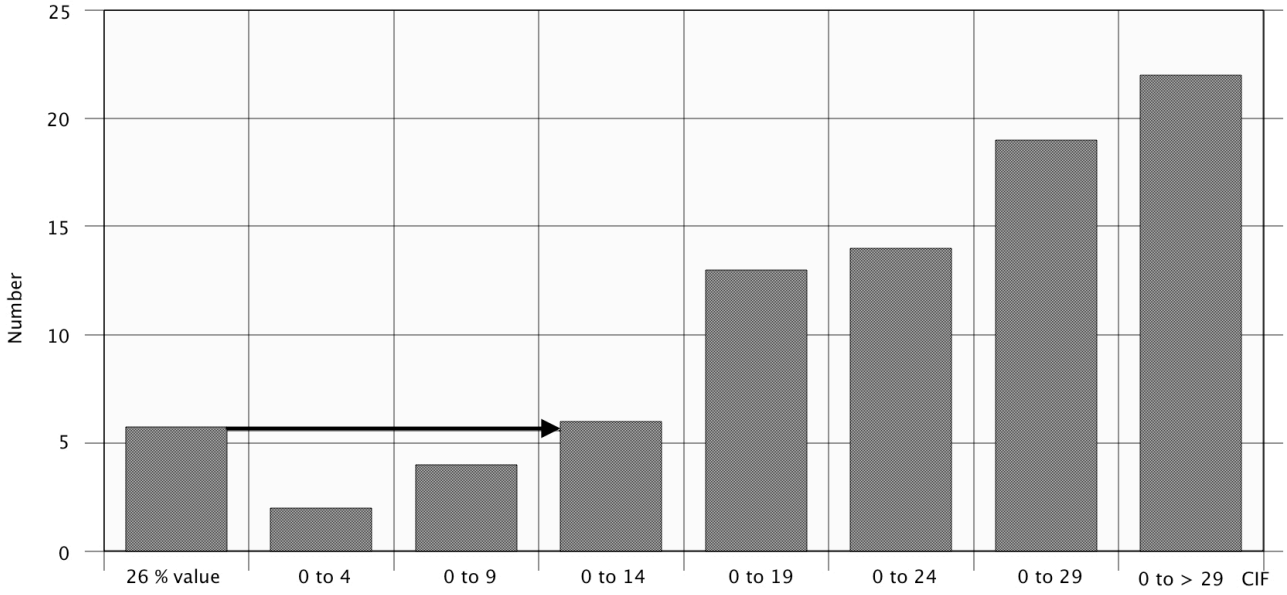

Fig. 21: CIF and the accumulation of driving in serpentine lines.

4.4.8 CIF and accidents

The evaluation showed that a large number of accidents were caused by drivers with a relatively low CIF. However, it must be taken into consideration that in the evaluation of these results the cannabis consumers remarkably often left the place of the accident without permission. This means that there was a time delay before the blood sampling can be ordered and carried out. However, during this delay the cannabinoids can be broken down; this accounts for the fact that for drivers who had an accident, the CIF values and therefore the 26% values, are relatively low. 22).

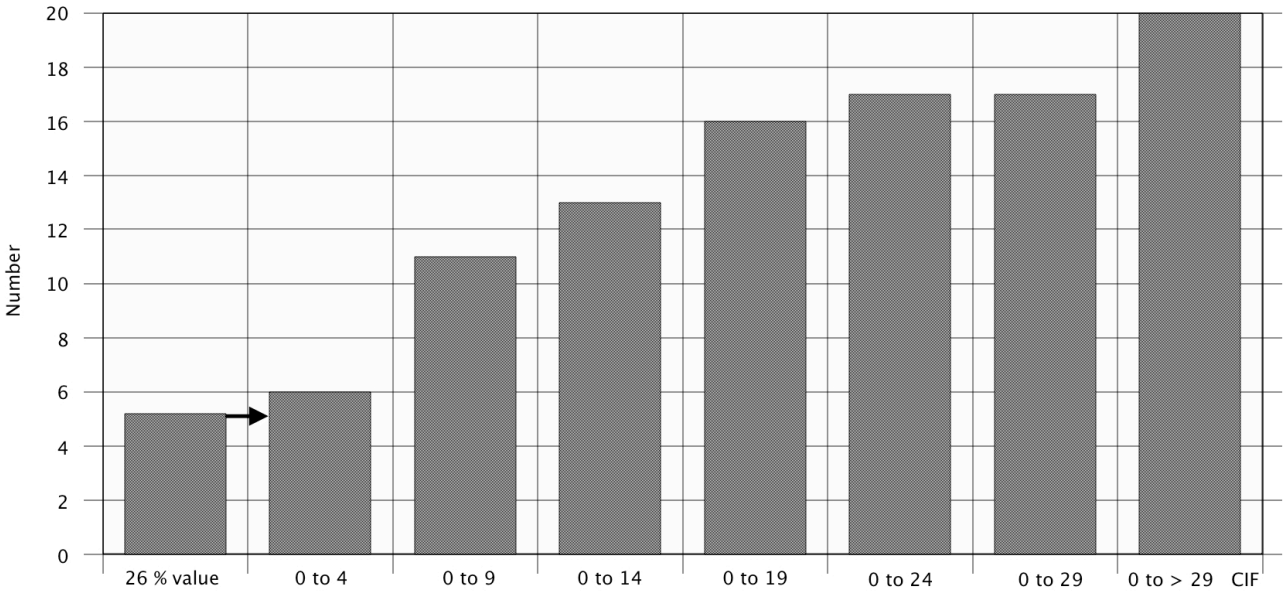

Fig. 22: CIF and the accumulation of accidents.

4.5 CIF and retrograde calculations to the time of the offence

A time-dependent CIF decrease was noticed after the consumption of cannabis and the conclusion of the resorption. For the usual consumption type (smoking), the resorption time is negligibly small and may be disregarded; however, this isn't the case for the rather rare cases of oral consumption of cannabis products. The determined CIF is therefore only valid for the time of the blood sampling. If cannabis was smoked and there was no later consumption, a higher CIF will be present in every case at the time of the consumption, depending on the length of time between the consumption and the blood sampling.

A retrograde calculation is currently not possible due to a lack of the corresponding empirical values. Such empirical values must first be gained through corresponding test trials. A first analysis of the results of the blood samples of 6 tests persons (published by Huestis et al. [2]) who had taken part in a cannabis smoking trial, showed that the median half-life for the CIF was 1.5 hours, 1 to 6 hours after the end of consumption. This first result may serve as the starting point for future cannabis smoking trials.

Table 26: Comparison of the CIF and the concentrations of THC and its metabolites, taking into consideration the time between consumption and blood sampling. All cannabis only users who were conspicuous due to driving in serpentine lines were selected (cf. also Fig. 21).

No	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Time difference between consump-tion and blood sampling (hours)
9420	0	0	1.2	0	
9421	0.4	0	5.8	0	0.33
9178	2.4	0.7	57.2	5	0.8
9605	2.6	0.5	38.3	8	
9028	1.8	2	38	10	1
9123	2.7	1.3	32.3	13	1.08
9367	2	2	27	15	
9089	4.7	1.4	42.7	15	1.8
9433	12.1	2.9	102	15	0.92
9200	3.1	1.9	32.2	16	1.41
9345	5.8	2.9	56.6	16	0.75
9514	3.7	1.7	32.9	17	0.5
9002	1.53	1.31	16	18	2.17
9343	3.7	1.2	24.2	21	0.78
9011	3.2	2	20	27	
9249	25.5	8.7	136.1	27	0.67
9052	5.3	1.4	25.8	28	1.25
9003	6.8	2.9	35	29	0.42
9334	3.3	1.1	16.1	29	0.67
8656	2.8	0.8	12.7	30	0.75
9015	1.1	1.2	5	49	1.66
9501	27	4.9	68.7	50	1
Median	5.52	1.95	37.54	20	1
SD	7.01	1.82	31.16	13	0.48
Maximum	27	8.7	136.1	50	2.17
Minimum	0	0	1.2	0	0.33
n	22	22	22	22	18

4.6 Time frame between offence and blood-drawing

The time interval was calculated for all cases for which information about the consumption time and the time of the blood sampling were available. This time interval is stated in the table printed as Appendix 8 with the important results for all cannabis only users, as well as in table 26, which by way of example compares the concentrations of THC and its metabolites with the calculated CIF for the cannabis only users who became conspicuous due to driving in serpentine lines. After ignoring individual extreme values it became apparent that the time period between consumption and blood sampling for the determination of the CIF limit value of the cannabis only users who became conspicuous due to driving in serpentine lines was an average of 1.24 hours (= 1 hour 15 minutes) with a standard deviation of 35 minutes or 1 hour ±0.5 hours. Therefore, it can be said that the detected connections between the value of the CIF and the peculiarities or driving errors are applicable to other events if no more than 1.5 hours has passed between consumption and blood-sampling. The same applies to the proposed limit value for the absolute unfitness to drive due to cannabis consumption (see below). If this period is exceeded and if a CIF below the limit value is found, an individual test of the fitness to drive must be carried out.

4.7 CIF and blood sample

The active agent of cannabis, THC, and its metabolites have the characteristic of accumulating much more in the blood serum than in the red blood cells. This means that different THC concentrations can be found for one unique blood sample depending on whether the serum or the whole blood sample was examined. The concentration difference is even more obvious if the so-called residual blood is examined, from which the serum was removed for alcohol detection. In such blood samples, only a low amount of the previously present THC will remain. This anomaly is little known outside of circles of experts. If we want to set limit values based solely on THC concentrations, we must clearly define whether this value is for the whole blood or the serum. A limit value for the residual blood would not be possible because it has different qualities depending on how many parts of the serum were taken from it.
This is much simpler in the case of the CIF. Since we determine the concentration ratio of THC and THC metabolites, this ratio not significantly different in the whole blood compared to the serum, as was shown by the tests carried out so far. The blood quality doesn't matter. However, it is recommended that the blood samples be examined as soon as possible because

after storing them in the refrigerator for several weeks, losses, especially with regard to THC, may occur, so that a CIF that is too low cannot be excluded. Deep-freezing and storing part of the blood sample immediately after it is received has proven successful. Stored under these conditions, it is possible to carry out a perfect quantitative analysis even after many months.

5 Proposal to set a limit value to determine the inability to operate a vehicle after cannabis consumption

During the two-year study, in a close cooperation between the corresponding ministries and the police, over 680 blood samples of those who were suspected by the police of being under the influence of drugs at the time of their inspection were examined. This initial suspicion was subsequently confirmed in most of the cases. All samples were checked for the availability of cannabinoids, opiates, cocaine, amphetamine and amphetamine derivatives, benzodiazepine and alcohol. In addition, the reports of the police and the blood-sampling doctor that were submitted together with the blood sample were also evaluated. Using the documents and the lab results, about 100 different types of information were queried and anonymized and saved in a database. The approximately 68,000 data items collected this way were used for the current report.
In 395 cases (see chapter 3.3), cannabis consumption was clearly confirmed by an additional specific GC/MS analysis for the active agent THC and two of its main metabolites. Of these 395 suspects, 145 had also consumed opiates or cocaine, so they were not included in the group of cannabis only users.
In order to determine a limit value for a certain intoxicant, it is especially important to show that one works with a group, where no (relevant) consumption of other intoxicating substances takes place. Therefore, all cannabis users who consumed another intoxicating substances were removed, which means that 115 cannabis only users were left.
These 115 cannabis only users showed peculiarities in various degrees or driving errors with different frequencies. To obtain a measure for the statistical connection between the cannabis concentration in the blood in the form of the CIF and the danger posed to other traffic participants by a driver under the influence of cannabis, the insights from alcohol research regarding this topic were used. The number of alcohol-related accidents, which were registered by the police for the same period (1994) in the same region (the administrative district Düsseldorf) for the present research project were evaluated. Starting from the known BAC limit value of 1.10‰, the number of drivers with a BAC above or below this limit value showing driving peculiarities was checked. The accident types ‘Veering off the road to the right or to the left' (based on the data, the limit value of 1.10‰ could be substantiated (chapter 4.3. 1)) proved to be very useful for this evaluation. It became apparent that about 26% of the drivers involved in accidents who were under the influence of alcohol, as well as about 26% of those who veered off the road, had BACs of under 26%. About three quarters of drivers with a BAC of 1.10‰ had consumed more alcohol at the time of the accident.

The same benchmark was then also used for the drivers under the influence of cannabis. The 26% value corresponded to the 1.10‰ value for the individual test points. Since the number of cases with a total of 115 of cannabis only users isn't very high, CIF classes were formed and compared with the individual peculiarities or driving errors, and the respective 26% value was determined. Depending on the test criterion, this value was found in the CIF class of 5 to 9 as well as in 10 to 14

(chapter 4.4.1 to 4.4.7). A lower value was found only for accidents. However, as described above, this was due to the high number of hit-and-run drivers (over 40%, see Table 23), and the related delayed blood sampling, and therefore this value is distorted (see also chapter 4.6). As a result of that, we propose using the results of the criterion “Driving a vehicle in serpentine lines" as the main criterion for setting a limit value. Herein, the 26% value is found in the range of the CIF classes of 10 to 14 (Fig. 21). We therefore propose the following suggestion as the conclusion of the research project:

> **Drivers whose blood, taken between 0.5 hours and 1.5 hours after the drive, for which the cannabis active agent tetrahydrocannabinol (=THC) and its metabolites 11-OH-THC and THC-COOH were in such concentrations that the CIF (Cannabis Influence Factor) reached a value of 10 or more using the described method, have to be viewed as absolutely unfit to drive due to cannabis consumption.**

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APPENDICES

Appendix 1

INFORMATION ABOUT THE RESEARCH PROJECT

1. General

It is well known that buying cannabis products (hashish or marijuana) is very easy, not least since the opening of the border to the Netherlands. Many younger traffic participants drive to our neighboring country to buy and consume this drug in coffee shops. However, it's generally not difficult for a young people to obtain cannabis because they are often approached directly in broad daylight by respective dealers, or they knows someone among their acquaintances who consumes hashish.
Due to the inhibiting effect of this drug, which reduces the critical faculties and produces euphoric states, the consumer may not recognize, or may not recognize correctly, their objectively given unfitness to drive, thus driving on the road in this unsuitable condition. So far it is unknown how many cannabis consumers drive cars daily in a condition unfit to drive, thereby endangering themselves and others. They don't attract attention during police checks because police officers aren't trained properly and don't have the expertise to recognize the typical, often hidden symptoms caused by the consumption of cannabis. The same is true when recording traffic violations, accidents etc. Cannabis consumers are mostly let go, and no blood samples are taken unless they have also consumed alcohol. But even in these cases, it is rarely checked if, in addition to alcohol, there was also impairment due to the consumption of cannabis present. Different investigations have shown that blood samples sent to the centers for blood alcohol examination originated on average from 10 to 20% of the persons who had consumed alcohol and cannabis, in other words, substances that potentiate their effects. This additional consumption was generally not detected by police investigations. In the rare cases in which a "cannabis drive" is detected, the evaluation of the reduction in the fitness to drive is relatively difficult because so far there are neither limit values for blood serum-agent concentrations nor studies that would show - analogously to alcohol - how the frequency of accidents increases depending on the consumed amount of cannabis.
It is the objective of the present research project to show for the first time, based on a comprehensive field trial, what kind of connections exist between the cannabis agents in the blood serum and the fitness to drive. The results of this study can then be used to formulate concrete danger limit values for cannabis. Once the design of this study has proven successful, the study can also be used to work out corresponding values for other drugs.

2 Study design

2.1 Police investigations:

One should always think of the involvement of cannabis every time a traffic violation / traffic accident was committed by a younger, especially male, driver and in which (contrary to expectations) either no amount or a minor amount of alcohol was involved. The same is true in cases of a concrete suspicion (e.g. an additional violation of the Controlled Substances Act) after checking certain peculiarities, such as red eyes or widened pupils, delayed perceptivity, tiredness, presumptuousness etc., whenever there's an initial suspicion of an unfitness to drive.
In all these cases, blood sampling should be ordered. The police officers should record their observations using the form designed for this purpose and send the completed form together with the blood sample, a copy of the police protocol (with the usual information regarding the event) and the examination report of the doctor taking the blood sample to the address listed above. The result of the blood test is promptly sent to the police officer in charge (our goal is 1 to 2 days after the receipt of the blood sample). Connected with this quick information of the test result (until now it took usually 4 weeks) is the hope that the police officers experience a learning effect ("I had the right hunch"), which leads to an increase in the "hit rate". The experiences to be gained by all police officers are made available after anonymization and evaluation as a training means, to each of the officers participating in the project. We hope to find the optimal procedure for police officers this way, in order to bring a traffic participant under the influence of cannabis to justice.

2.2 The blood samples

Blood sampling should only be carried out by doctors who are willing to carefully carry out additional examinations that make it possible to objectify an impairment due to cannabis consumption. These doctors will also receive the result of the blood tests of their "patients" so that they too have the chance to optimize their research methods and sharpen their "diagnostic vision."

2.3 Research lab

Blood samples are examined for cannabinoids in research labs with a pre-test. If this test is positive, the confirmation analysis takes place using a procedure (extraction, derivatization, and gas-chromatographic / mass spectrometric determination, computer-based correctness test), that corresponds to the quality standard of the current blood alcohol regulations with regard to correctness and precision, even though the concentration of the cannabis agents in the blood are lower than those

of alcohol by a factor of 100,000. In this test, the concentration of the active cannabis component THC and its metabolites THC-OH as well as THC-COOH in the serum will be determined. Should further examinations be desired or necessary (alcohol, other intoxicants, etc.), a blood sample is forwarded to the corresponding centers, such as blood alcohol examination center or a chemical-toxicological lab.

2.4 The results of the research project

After evaluation the police investigations, medical examinations of the blood samples and the analyses, statements should be made, especially with regard to the following questions:

- How can a traffic participant impaired due to cannabis consumption be recognized by a police officer or a doctor with sufficient certainty?
- What concentration level of the cannabis agent in the serum is sufficient to determine that a cannabis consumer is absolutely unfit to drive?
- Which method can be used to determine accurate concentrations of the active ingredient the blood serum?

Appendix 2

Research project: Cannabis in road traffic • Institute for Legal Medicine, Heinrich Heine University, Düsseldorf

Police report

Police station _____ Crime reference number _____

1. Incident

Type: _____
_____
Location: _____
Time: _____

2. Driving style
☐ normal ☐ uncertain gear change
☐ stalling/revving the engine
☐ serpentine lines (description under 6.)

3. Weather
☐ dry ☐ rain ☐ ice/snow
☐ strong wind/storm

4. Road condition
☐ good ☐ bad (description under 6)

5. Road lighting
☐ good ☐ bad

6. Special notes

7. Suspicion of the consumption of:

8. Statements of the consumer of ingestion of cannabis/narcotic substances after instruction:
Type: _____
Amount: _____
Time: _____

9. Alcohol test
☐ yes, on (date)_____at (time)_____
Result:_____Device no.:_____
☐ refused ☐ cannot be carried out

Reason: _____

10. Understands German:
10. Understands German:
☐ yes ☐ no ☐ partly

11. Gait
☐ secure ☐ halting
☐ swaying ☐ staggering

12. Eyes
☐ inconspicuous ☐ red conjunctiva
☐ shiny ☐ unsteady

13. Pupils
☐ inconspicuous ☐ very narrow
☐ very wide (checked with:
)

14. Behavior / Mood
☐ controlled ☐ communicative
☐ calm ☐ tired
☐ aggressive ☐ agitated
☐ depressive ☐ cheerful
☐ talkative ☐ quiet
☐ apathetic ☐ whiny
☐ indifferent ☐ lethargic
☐ _____

15. Perceptivity
☐ good ☐ delayed
☐ thick-witted ☐ changeable
☐ disoriented ☐ cannot be assessed

16. Other characteristics
☐ Shivering ☐ Unrest
☐ Sleepiness ☐ Attack of sweating
☐ Nervousness ☐ _____

17. Other

Determined by:

Name and Signature

Appendix 3

Research project: Cannabis in road traffic • Institute for Legal Medicine, Heinrich Heine University, Düsseldorf

Additional sheet to B "Medical report" – Protocol and application for determining the availability of alcohol in the blood

Last Name:_____
First Name:_____
Age:
Blood sampling on (date) at (time)

1. Mood
☐ inconspicuous ☐ euphoric
☐ depressive ☐ maladjusted

2. Sense of time/Short-term memory
☐ normal ☐ impaired

3. Self-assessment / Critical faculty / Evaluation the current situation:

4. Motor skills / Fine motor skills:

5. Blood pressure: mmHg

6. Pulse: per minute

7. Breathing rate: per minute

8. Pupils
☐ inconspicuous
☐ very wide ☐ very narrow
Width:_____mm
Reaction to light in_____seconds

9. Redness of the conjunctiva
☐ none ☐ slight
☐ obvious ☐ strong

10. Facial look
☐ pale ☐ reddened
☐ swollen ☐ inconspicuous

11. General condition:
11. General condition:

12. Anamnestic data:

13. Tobacco consumption:
☐ yes ☐ no

14. Urine sample
☐ yes ☐ no

15. Patient seems to be under the influence of
☐ centrally dulling substances
☐ centrally stimulating substances
☐ hallucinogenic substances
☐ _____

16. Patients seems to be
☐ unnoticeably ☐ slightly
☐ markedly
under the influence of
☐ cannabis ☐ cannabis + alcohol
☐_____

17. Notes:

Name, address of the examining doctor (Stamp):

Signature_____

Appendix 4

Research project: Cannabis in road traffic • Institute for Legal Medicine, Heinrich Heine University, Düsseldorf

Sender (stamp)

Prof. Th. Daldrup
Institute for Legal Medicine,
Heinrich Heine University, Düsseldorf
Moorenst. 5
40225 Düsseldorf

Request for examination

The attached blood sample of

Last Name:_____ **First Name:**_____ **Date of Birth:**_____

Address:_____ ☐ male ☐ female

should be examined for cannabis agents.

☐ The blood sample should be additionally examined for alcohol.

The following are attached:

☐ Blood sampling protocol
☐ Blood sample
☐ Medical report (additional sheet to B)
☐ Copy of the accident report
☐ Copy of the criminal charge
☐ Urine sample
☐ Police report
☐ Copy of the traffic violation charge
☐ Notes / Other documents

Please send the result of the examination to:

Person in charge _____ Telephone _____
Reference number

Date _____ Signature _____

Appendix 5

Drug-influenced traffic participants

Appearance, effects, typical driving errors
Compiled by Prof. Th. Daldrup, Düsseldorf

General problem: Mixed consumption

Almost all drug consumers use tobacco products and alcohol, and additionally also cannabis. Sleeping pills and sedatives are regularly taken by heroin, cocaine and amphetamine consumers, either to increase the effect (in the case of heroin) or to reduce the stimulating, exciting effect of cocaine and amphetamine.

The cannabis consumer

Only cannabis is consumed, possibly combined with alcohol. Other drugs, mainly amphetamines, are sometimes tried out. The consumer prefers the joint first and later, especially in cases of dependency, the pipe.

Three phases of the effects must be distinguished:

- the acute phase; shortly after consumption (duration about **1** to 2 hours, and if a high amount was consumed, even longer): Sluggish walk, difficulty speaking, overall slow, thick-witted, eyes reddened, glassy look, pupils wide and with a slow response to light.

- Typical driving peculiarities: changing speed for no reason, low speeds, difficulty staying in the same lane followed by steering correction, easily distracted, lacking concentration and thus has no adequate reactions to unexpected events; failure to yield, or the "overlooking" of red traffic lights or pedestrians crossing the street, and no immediate reaction to the request of the police to stop.

- the sub-acute phase follows immediately after the acute phase and is applicable only if a low amount of cannabis was consumed (duration about 4 to 6 hours, possibly longer): The sluggishness of the acute phase is over. The basic mood is exuberant and carefree (euphoria, general feeling of wellbeing). The critical faculties are reduced, one's own capabilities and abilities are overestimated, eyes red to normal, and the pupils are widened or normal.

- Typical driving peculiarities: risky driving at high speeds; after an accident occurs, leaving the scene is not infrequent; still easily distractible and lacks concentration; this may lead to inadequate reactions to unexpected events; failure to yield or the "overlooking" of red traffic lights.

-the post-acute phase; lasts about 12 to 24 hours, until the cannabis consumer has the feeling of being "clear in the head" again. After regular chronic consumption, this time is much longer. It is

marked by a lack of concentration, easy distractibility, and dreaming. If there is a traffic check, it will be difficult to notice inconspicuous behavior.

- Typical driving peculiarities: not known. It can be assumed that they are making driving errors due to a lack of concentration.

Other frequent symptoms after cannabis consumption are: **circulatory lability**, nausea, dizziness, headaches, shivering, cold sweat, and even fainting (while standing). Individuals driving their cars in spite of these side effects become conspicuous due to a generally very insecure and uneven way of driving (e.g. frequent stops, seemingly without any reason, very slow speeds, etc.), which results directly from the above-stated symptoms).

Additionally, in cases of regular consumption, **cannabis psychosis** with hallucinations may be expected. Those indivituals act bewildered and disoriented.

Heroin consumers

A heroin addict is never fit to drive. Whether it's during the acute intoxication or in the withdrawal phase. Since this type of consumer generally also consumes centrally active medications (e.g. Valium® or Rohypnol®) or other opiates / opioids (codeine, dihydrocodeine, methadon, etc.) or alcohol, the fitness to drive is also not given during the individual heroin applications as a result of the above listed intoxicants.

The popular combination of cocaine and heroin is even more dangerous. Since the stimulating effect of cocaine subsides faster than the dulling effect of heroin (and the other possibly consumed substances), a sudden clouding of consciousness may occur. If a driver has consumed this mix, serious accidents are almost guaranteed to happen.

The **driving peculiarities** depend on the stage of the heroin's effect.

In the acute phase, the centrally dulling effect is predominant: generally slow, halting, insecure walking; unclear speech. Even under poor lighting conditions, the pupils are very narrow (check the pupils where the light isn't strong!) .

Once the effect of the heroin subsides and the first withdrawal symptoms appear, nervousness, unrest, shivering and a lack of concentration become predominant. The pupils aren't narrow any more, but rather widened.

The way of driving depends on the current state of the driver and the current effect of the heroin and the other consumed intoxicants. The following is possible: a slow, very insecure way of driving with a veering of the road or the lane or rear-end collisions can be predominant (e.g. shortly after consumption, possibly also in cases of strong withdrawal symptoms); an uninhibited, aggressive way of driving, with the coercion of other traffic participants, dangerous overtaking, failures to yield, etc. (this is noticed when a relatively small amount of heroin is consumed, or after the strong hypnotic effect subsides).

Consumers of stimulants (cocaine, amphetamine)

After the consumption of stimulants, the power of concentration increases and the signs of tiredness are suppressed. Thus, it is difficult to notice that someone is under the acute effects of these substances just by examining their way of driving.

In cases of traffic checks, the widened pupils, the unexplainable unrest or nervous behavior and talkativeness may be some clues to the effects of cocaine or amphetamine. If driving peculiarities are noticed, these would be an uninhibited way of driving at an unsuitably high speed, e.g. in curves, in construction areas, in bad weather etc. Drivers under the influence of such substances overestimate their own capabilities as well as those of their vehicles.

This consumer group often becomes conspicuous in the phase of the subsiding effect of cocaine or amphetamine, especially if higher doses were consumed over the course of many hours or days. In the withdrawal phase there is often a pathological need to sleep and a depressive mood due to physical **exhaustion.** Not infrequently, one also might appear disoriented and confused. Even psychoses, or **psychosis-like states** with hallucinations, especially with the feeling of being constantly observed, may occur. These marked peculiarities are easily recognized if a consumer is checked.

This conspicuous way of driving is caused by strong tiredness (slow and fluctuating drive speeds, difficulties staying in the lane, etc.) and by disorientation (no longer knowing where one is and how one can reach one's destination; considerable insecurities at intersections, possibly stopping the vehicle in the middle of the road, etc.).

Appendix 6

Effect of cannabis

1. Mood

The consumption of cannabis regularly leads to a generally pleasant feeling of wellbeing so that the mood is high to euphoric. The consumer is talkative, communicative and often very cooperative. On the other hand, after the consumption of cannabis, the following symptoms may appear: passivity, apathy, lethargy and depressive behavior, or aggressive and unreasonable behavior.

2. Sense of time/short-term memory

The sense of time seems to be off under the acute effect of cannabis, probably because stimulations from the outside, impressions, thoughts etc. are experienced more intensively, and therefore time intervals seem to be perceived as longer than they are. The increased distractibility and changed openness to stimuli leads to a deterioration of the short-term memory.

3. Self-assessment/critical faculty/evaluation of the current situation

Under the influence of cannabis, the following symptoms can be noticed: a more or less pronounced lack of judgment or a misjudgment of one's own capabilities as well as frequently erroneous (delayed) perceptivity.

4. Motor skills/fine motor skills

The consumption of cannabis using a “normal” dosage commonly leads to a minor reduction in motor skills. Higher dosages, however, seem to lead to difficulties walking.

5. Blood pressure / pulse / breathing rate

In cases of allergic reactions due to cannabis, there can be considerable circulatory problems. Otherwise, one may notice a slight increase in the user's pulse under the acute effects of the drug.

6. Eyes

Under the influence of cannabis, a clearly noticeable, centrally effected mydriasis can be observed. Clearly widened pupils can be noticed after the consumption of cocaine or amphetamine, as well as after intermediate alcohol consumption. Additionally, there is often a feverish look in the eyes. Conjunctivitis is one of the typical signs of the acute effects of cannabis. Some researchers claim to have found a direct correlation between the degree of redness of the conjunctiva and the degree of the acute cannabis effect. Frequently, a nystagmus cannot be triggered.

7. Typical cannabis consumer

The average user is a younger male aged 16 to 30 years. In addition, it can be assumed that in the predominant number of cases, hashish consumers or drug consumers are smokers. Only rarely can one find a non-smoker among drug consumers. Regular consumption leads to a general reduction in determination and performance, a lack of social interest, and a preoccupation with oneself (a-motivational syndrome = AMS), and thus a change in personality.

Appendix 7

INSTITUTE FOR LEGAL MEDICINE
HEINRICH HEINE UNIVERSITY DÜSSELDORF
Research project: Cannabis in road traffic
Project leader: Prof. Th. Daldrup

Prof. Daldrup, Institute for Legal Medicine, P.O. Box 101007, D-40001 Düsseldorf

Düsseldorf, July 24, 95
P.O. Box 101007 • D-40001 Düsseldorf
Address: Moorenstr. 5, D-40225 Düsseldorf
Telephone: (0211) 311-2375 / 2385

Ch. ID no.: A-0000

Please specify this number in writing

Police station Musterdorf
PI 1, POK Müller
Am Dorfweiher 22
12345 Musterdorf

Expert report

The serum sample of "John Doe"
Venule control number: 1234

was checked for cannabinoids after special preparation of the sample by means of immunoassay and GC / MS (with deuterated standards). The following forensically important results were found:

THC:	2.1	ng/ml	(Method: GH / MS)
11-OH-THC:	1.3	ng/ml	
THC-COOH:	26.0	ng/ml	
SCK:	6.5	ng/ml	(Method: Immunoassay)

Evaluation (applicable items are marked)

The results indicate:

☐ low/one-time ☐ stronger/possibly multiple ☐ stronger/possibly regular £ regular/habitual consumption of cannabis.

The cannabinoids are in a concentration ratio (CIF = 12), as is for found for people who are:

☐ strongly ☐ mildly ☐ unrecognizably under the acute influence of cannabis.

Furthermore, using the pre-test (immunoassay), we found additional indications for the consumption of the following intoxicating substances*:
(amphetamine), benzodiazepine, cocaine, opiates.
* Positive results need to be confirmed.

Prof. Th. Daldrup

A request for the confirmation analysis has already been made. The expert report will follow.

Abbreviations: ng/mL = nanograms per milliliter, THC = tetrahydrocannabinol (cannabis agent), 11-OH-THC = active THC metabolite, THC-COOH = ineffective THC metabolite, available in free form, SCK = serum cannabinoid concentration, CIF = factor to determine the influence of cannabis agents.

Appendix 8

Concentration of THC and metabolites, CIF, type of incident*, impairment according to the police report and the doctor's report*, and the time difference between consumption and the blood sampling of the cannabis only users. Sorted ascendingly according to the THC concentration.

No.	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Type of incident*	Impairment according to the police report*	Impairment according to the doctor's report*	Time difference Consumption - blood sampling Hours
9651	0	0	19.6	0	12	3	0	(9.5)
9588	0	0	4.3	0	11	0	2	
9536	0	0	5	0	43	3	3	
9031	0	0	0.4	0	11	1	2	1.25
9304	0	0	0.3	0	12	1	2	1.5
9420	0	0	1.2	0	21	2	0	(6.83)
9206	0	0	2.1	0	50	3	2	1..25
9479	0	0	13.9	0	12	2	2	2.34
9225	0	0	2.9	0	43	2	2	0.67
9256	0	0	30	0	43	0	2	1.25
9421	0.4	0	5.8	0	21	0	0	0.33
9172	0.5	0	4.4	0	42	3	1	0.91
9087	0.7	0	5.9	0	43	0	2	2.25
9570	0.8	0.4	7.4	17	34	2	0	1.15
9422	0.9	0	10.2	0	50	3	1	(9.34)
9427	1	0	13.3	8	23	0	0	1.2
9557	1.1	0.7	19	10	34	2	2	3.2
9377	1.1	0.6	39.8	4	12	0	0	(14.35)
9086	1.1	0.6	32.8	5	43	0	2	2
9015	1.1	1.2	5	49	21	1	1	1.66
9461	1.4	0.5	11.9	17	11	2	2	
9155	1.5	0.6	24.3	9	11	1	1	1.08
9002	1.5	1.3	16	18	21	3	0	2.17
9295	1.6	0.9	21.4	12	41	2	2	0.92
9602	1.7	0.4	19.1	11	50	0	2	(5.25)
9642	1.7	0.8	12	22	43	1	2	
9033	1.7	0.7	7	37	31	3	3	
9679	1.8	0	12.9	13	50	0	0	1.5
9028	1.8	2	38	10	22	1	2	1
9214	1.8	0.5	10.9	22	25	1	2	1.13
9092	1.9	2	71.7	5	43	0	0	1.17
9328	1.9	1	15	20	11	3	2	1.63
9613	2	0.6	37.6	7	12	3	0	(4.08)

APPENDICES

No.	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Type of incident*	Impairment according to the police report*	Impairment according to the doctor's report*	Time difference Consumption - blood sampling Hours
9128	2	1	47	6	43	0	0	
9143	2	1	38.6	8	50	3	2	（4.42）
9489	2	1.3	41.4	8	43	1	2	1
9367	2	2	27	15	21	2	0	
9035	2	2.6	28	17	11	2	0	1.87
9173	2.1	1	32	10	12	2	2	2.25
9178	2.4	0.7	57.2	5	11	2	0	0.8
9144	2.5	0.7	38.3	9	11	3	2	（4）
9605	2.6	0.5	38.3	8	22	1	2	
9123	2.7	1.3	32.3	13	22	1	0	1.08
9627	2.8	1.9	17.5	28	34	0	1	1.17
8656	2.8	0.8	12.7	30	22	3	2	0.75
9468	2.9	0.9	22.2	18	43	0	2	
9298	3	1.7	51.3	9	43	1	0	1.08
9007	3	1.3	35．1	13	33	3	3	2.75
9200	3.1	1.9	32.2	16	21	0	0	1.41
9011	3.2	2	20	27	21	3	3	
9071	3.3	2.9	122	5	36	3	3	0.75
9334	3.3	1.1	16.1	29	21	1	2	0.67
9530	3.4	2.4	27．8	22	43	2	2	1.17
9577	3.5	2.1	44.2	13	11	1	2	1.08
9088	3.5	1.7	34.4	16	43	0	2	1.96
9514	3.7	1.7	32.9	17	21	0	0	0.5
9211	3.7	1.8	50.6	11	36	0	2	1.47
9343	3.7	1.2	24.2	21	22	2	2	0.78
9554	3.8	0.6	10.7	44	12	0	2	1.5
9169	3.8	1.6	60.1	9	43	0	0	
9189	3.8	1.9	26.9	22	25	0	2	0.67
9621	4.1	1.2	31.6	18	25	1	2	0.84
9036	4.1	3.2	25	31	41	1	2	0.67
9213	4.3	1.9	48.8	13	43	1	2	0.67
9571	4.5	1.6	27.5	23	50	3	0	2.17
9021	4.5	1.5	15	43	43	0	2	0.54
9455	4.7	3.8	99.5	9	43	0	0	1
9089	4.7	1.4	42.7	15	21	0	2	1.8

No.	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Type of incident*	Impairment according to the police report*	Impairment according to the doctor's report*	Time difference Consumption - blood sampling Hours
9664	4.9	1.4	21.4	31	41	0	2	
9259	4.9	2.4	50.6	15	23	0	2	0.8
9254	5.2	2.6	74.1	11	43	3	2	1.5
9052	5.3	1.4	25.8	28	22	0	2	1.25
9637	5.6	1.5	30.1	25	34	0	2	1.16
9548	5.8	1.3	15.8	48	43	3	3	
9345	5.8	2.9	56.6	16	21	2	2	0.75
9618	5.9	2.9	102.2	9	33	1	2	1.41
9280	5.9	4.1	14.1	70	43	1	1	1.21
9562	6	3.2	81	12	50	3	0	2.63
9507	6	3	78.9	12	41	1	0	
9130	6	4.6	51	22	43	0	0	0.58
9034	6	3.2	21	47	43	2	3	0.67
9482	6.4	2.7	42.7	23	43	1	0	1
9406	6.5	1.5	36	23	43	0	2	0.83
9053	6.4	4.4	29.2	39	12	0	2	1.75
9003	6.8	2.9	35	29	21	2	2	0.42
8015	7	2.9	129	8	43	1	2	（7.16）
8016	7.2	2.4	68.6	15	42	1	1	2.41
9358	7.3	2	46.5	21	36	0	0	0.58
9294	7.7	6.7	116.1	13	50	3	2	
9244	7.7	6.2	55.5	26	36	0	0	2.5
9306	8.1	2.7	21.5	54	43	0	2	0.67
9402	8.2	2.1	157.4	7	33	2	2	1.58
9612	8.3	1.9	30.4	36	43	2	2	1.38
9054	9.6	4.2	26	57	34	0	0	0.83
9568	10	2.7	31.4	43	36	0	2	1.25
9476	10.7	3.6	300.6	5	12	2	0	1.09
9549	12	2.3	40.4	38	43	3	3	
9433	12.1	2.9	102	15	21	0	0	0.92
9485	12.2	4.4	123.3	14	42	0	1	1.25
9492	12.5	6.3	46.2	43	43	3	0	1
9308	12.7	5.5	82.5	23	43	0	1	0.84
9593	12.9	3.1	52.9	32	43	0	2	1.03
9097	13.7	9.8	190.4	13	23	2	2	1.42
9370	13.7	3.2	115.7	15	12	0	0	1.34
9442	15.3	5	244.9	8	43	1	1	

No.	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Type of incident*	Impairment according to the police report*	Impairment according to the doctor's report*	Time difference Consumption - blood sampling Hours
9006	15.4	8	107.5	23	33	0	0	
9407	18.5	4.5	105.9	23	43	2	1	1
9565	20	5.5	113.9	24	41	3	2	1.58
9540	23.3	9.1	156.5	22	43	0	0	0.92
9249	25.5	8.7	136.1	27	21	2	0	0.67
9501	27	4.9	68.7	50	21	0	0	1
9558	29.1	5.7	22.4	168	43	2	2	
9396	33.3	8.2	146.1	30	12	0	0	
9483	40.7	7.9	55.9	94	43	1	1	1
9508	57	15.2	235.4	33	43	2	0	0.42

Statistics

	THC ng/mL	11-OH-THC ng/mL	THC-COOH ng/mL	CIF	Time difference Consumption - blood sampling Hours
MW	6.46	2.39	49.8	20.32	1.24
SD	8.5	2.47	52.09	21.02	0.58
Min	0	0	0.3	0	0.33
Max	57	15.2	300.6	168	3.20
n	115	115	115	115	86

*Abbreviations:

Type of incident

11 minor accident	12 serious accident	13 very serious accident
21 slight serpentine lines	22 strong serpentine lines	23 stalling of the engine
24 wrong lights	25 other driving peculiarity	
31 driving through a red light	32 driving through a stop sign	33 too fast
34 too slow	35 dangerous overtaking	36 other
41-43 traffic controls		50 others

Impairment

According to the police/doctor's report: 0: none 1: strong 2: moderate to low 3: cannot be evaluated