STRICTLY CONFIDENTIAL

The THC Detector

Developed by The Ombra Group, Inc.

1.) **Fundamentals/Generals:**

Marijuana is one of the most widely used drugs, after alcohol. It is derived from the cannabis sativa plants and contains several hundred of chemical compounds. The Δ9-tetrahydrocannabinol (THC) is the most psychoactive of the various forms of THC.

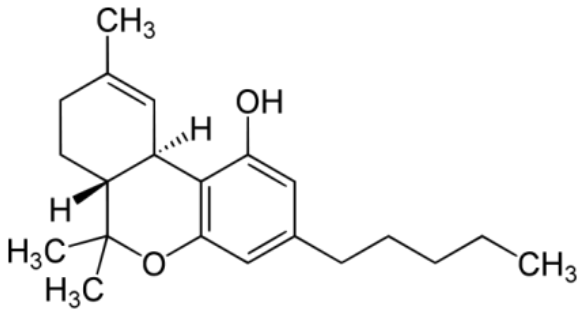
Traditionally, samples are screened for THC metabolites by immunoassay and confirmed using laboratory equipment such as GC-MS devices. The GC-MS, while the current standard for THC metabolite testing, requires time consuming sample derivatization prior to analysis. LC/MS provides the same specificity and sensitivity without the need for a derivatization process. These kinds of analysis of THC based on urine, blood and hair probes.

THC analytics

Under the analytic determination of drugs the correct detection of tetrahydrocannabinol is one of the most difficult methods because of the formation of many metabolites. ***Cannabinoids*** are a class of diverse chemical compounds that act on cannabinoid receptors on cells that repress neurotransmitter release in the brain. These cannabinoids are the following compounds: **Cannabidiol** (**CBD**) is one of at least 85 active cannabinoids identified in cannabis. **Cannabinol** (**CBN**) is a weak psychoactive cannabinoid found only in trace amounts in *Cannabis sativa* and *Cannabis indica.* It is mostly a metabolite of tetrahydrocannabinol (THC). **Cannabichromene** (**CBC**) is a cannabinoid found also in the *Cannabis* plant. It bears structural similarity to the other natural cannabinoids, including tetrahydrocannabinol, tetrahydrocannabivarin, cannabidiol, and cannabinol, among others. CBC has two stereoisomers. **Cannabigerol** (**CBG**) is a non-psychoactive cannabinoid found in the *Cannabis* genus of plants. **Tetrahydrocannabinol** (**THC**), or more precisely

its main isomer **(–)-*trans*-Δ^9-tetrahydrocannabinol** is the principal psychoactive constituent (or cannabinoid) of cannabis.

THC is metabolized mainly to 11-OH-THC (Hydroxy-THC) by the body. This metabolite is still psychoactive and is further oxidized to 11-nor-9-carboxy-THC (THC-COOH). In humans and animals, ***more than 100 metabolites*** could be identified, but 11-OH-THC and THC-COOH are the dominating metabolites. The conversion from THC into THC carbon acid depends also on temperature during the analytical procedure.



Structure of ?^{9}-THC

The analytical detection of THC is one of the most complicated procedures in drug laboratories. The analysis of THC is performed at samples of blood, hairs, urine and saliva (par example Dräger DrugTest 5000). Precise analytics of THC in blood samples by means of GC-MS demands much time because of matrix separation and sample preparation. Immunoassays can detect THC in a shorter time, but this method is disturbed by many matrix interferences. A new idea is to detect THC in exhaled breath. Exhaled breath can give also indications of diseases of test persons. It must be taking into account that THC is only detectable in exhaled breath 2 hours after THC-inhalation by smoke.

Results from the study of the 'Incidence of alcohol and drugs in road accident fatalities' have consistently shown a large increase in the incidence of drugs in fatal road casualties (drivers, riders, passengers and pedestrians). Therefore the consumption of THC of driver is of big interest.

Based on clinical studies, the psychoactive cannabinoid THC is present in the breath of subjects who recently inhaled marijuana. Such a breath analysis offers an alternative for identifying recent driving under the influence of cannabis.

Governments in The US, Western Europe, and Australia have therefore introduced roadside drug testing for cannabis (and other drugs such as methylenedioxymethamfetamine and methamfetamine).

Legislators in countries that use roadside drug testing assume that it will substantially reduce road crash deaths in the same way that rapid breath testing did for alcohol related crashes.

Compound	Other names	sum formula	CAS No.
Tetrahydrocannabinol (THC)	• Delta-9-THC • Δ9-THC • (–)-Δ9-trans-Tetrahydrocannabinol • (6aR,10aR)-6,6,9-Trimethyl-3-pentyl-6a,7,8,10a-tetrahydro-6H-benzo[c]chromen-1-ol • Dronabinol	$C_{21}H_{30}O_2$	1972-08-3

THC	
Formula	$C_{21}H_{30}O_2$
Molecular mass	314.47 g/mol
Boiling point	157 °C (315 °F)
Solubility in water	0.0028 (23 °C) mg/ml
State of matter	liquid to solid
Vapor pressure	$4.63*10^{-8}$ mm Hg at 25 °C ➔ $6.17*10^{-8}$ mbar

2.) The Ombra GroupMedical approach

Principle

The physical principle of the THC-Analyzer is based on the different drift velocities of positive and negative ions in a homogen electrical field at atmospheric pressure. Ambient air arrives at an ion source and is ionized by means of a weak radioactive beta-source. In air the complex positive ions like are produced and originate the so called reaction ion peak RP^+ in the recorded spectrum. The negative reaction ion peak, RP^-, corresponds with the ions and $(H_2O)^-$ which are always present.

In the case that the compounds M are in ambient air charge transfers take place by means of the following simplified reactions:

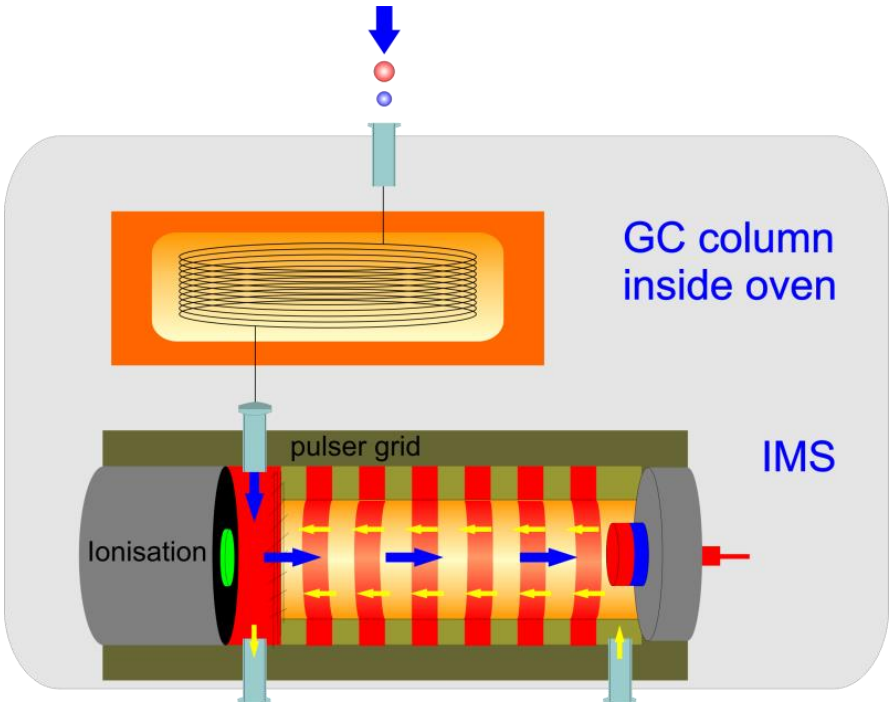
$RP^+ + M \rightarrow RP + M^+$ (positive mode)

$RP^- + M \rightarrow RP + M^-$ (negative mode)

Electrical pulses on a shutter grid push the produced ions into the drift region of the IM cell. In the homogen electrical field the ions move with various drift velocities due to their mobilities. They arrive at different times - their drift time - at the collector electrode and

produce an ion current. Drift times identify the specific molecule ions. The current is proportional to the concentration of this compound.

With the coupling of a GC column with an IMS to a so called GC-IMS, the two dimension info (drift time and concentration) is extended to a three dimension info (drift time and concentration plus the retention time of the GC column), as shown in figure 2 and 3.



Goal of development

The goal of the Ombra Group Medial development of such a THC-Analyzer is the fast identification of traces of cannabinoids in breath, with minimal sample preparation. The THC-Analyzer is being developed to give law enforcement and employers the ability to test for recent consumption of the THC component of marijuana.
The mobile Analyzer is based on the proven technology of ion mobility spectrometry (IMS), which operates under atmospheric pressure conditions. It is highly sensitive with typical detection limits of less than 1 ppb without prior enrichment. With this trace-gas analyzer THC can be detected and identified without any enrichment directly in situ already at a very low concentration level. For the further enhancement of the selectivity and further reduction of cross sensitivities the THC-Analyzer will be coupled with a gas chromatographic column, the so called GC-IMS approach. There the IMS is coupled with a gas chromatographic column (GC) for pre-separation.

3.) IMS-Spectra

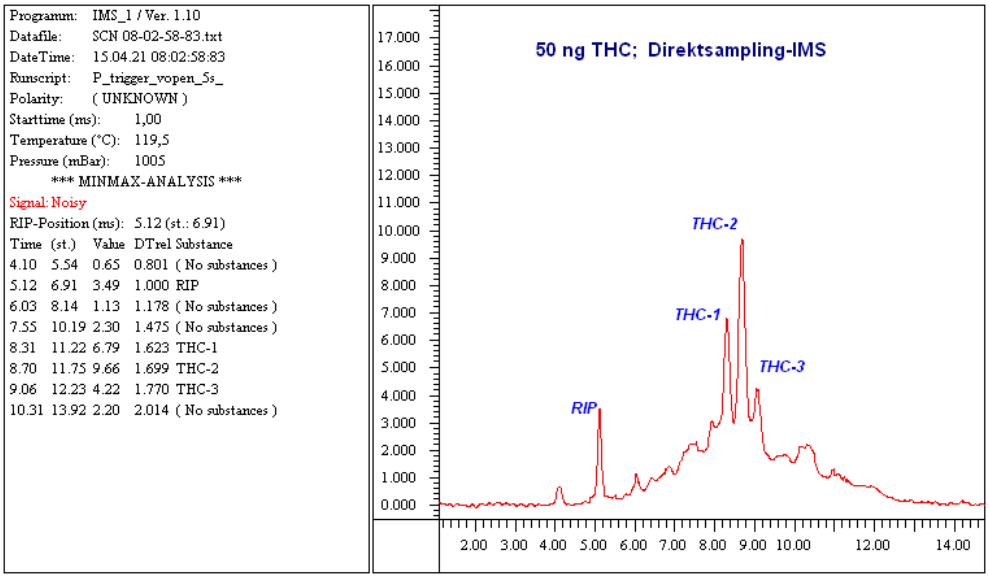


Figure 1: Measured THC spectrum. Worldwide first results.

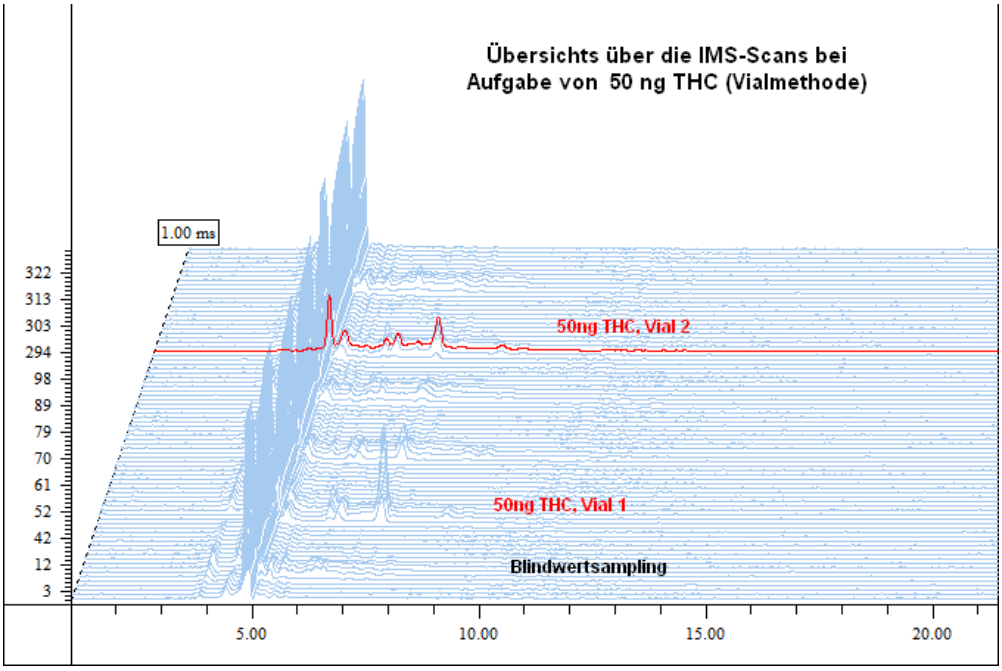


Figure 2: 3D-spectrum of GC-IMS with 50 ng THC in the air sample.

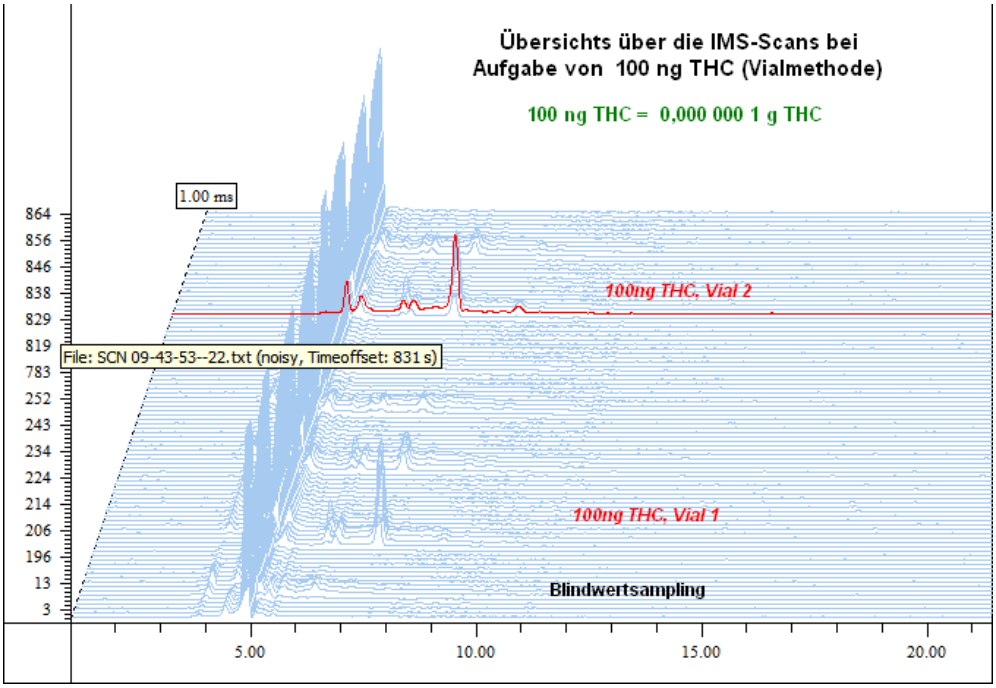
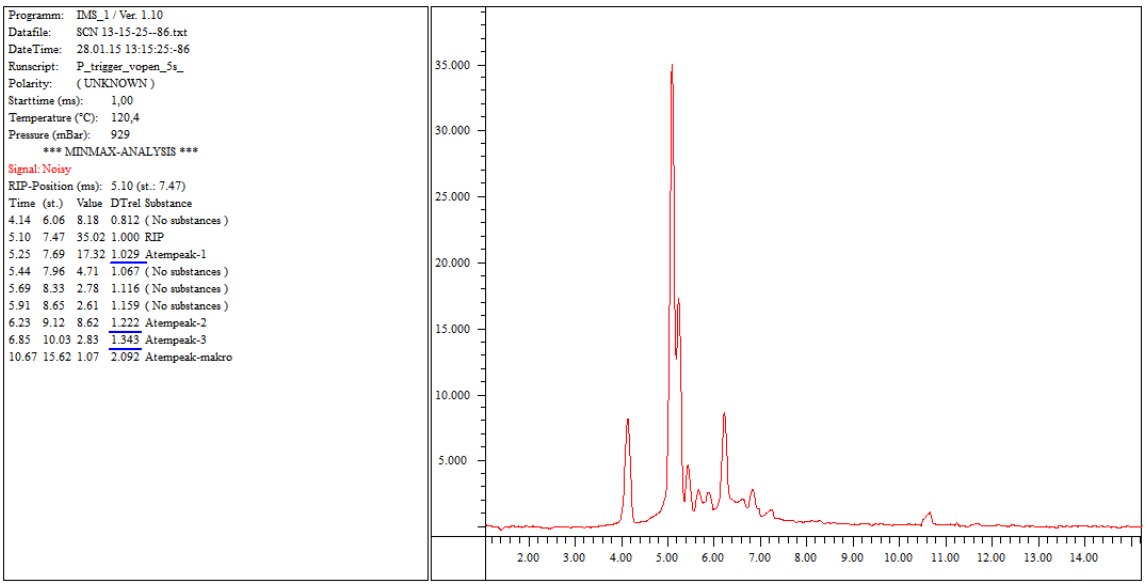


Figure 3: 3D-spectrum of GC-IMS with 100 ng THC in the air sample.

4.) **Common Breath Air Spectra**

During the last weeks we have investigated exhaled breath of some test persons to understand how the IMS detects VOCs in breath air and if one can see distinctions between the tested people.

- **Healthy persons, no smoker**



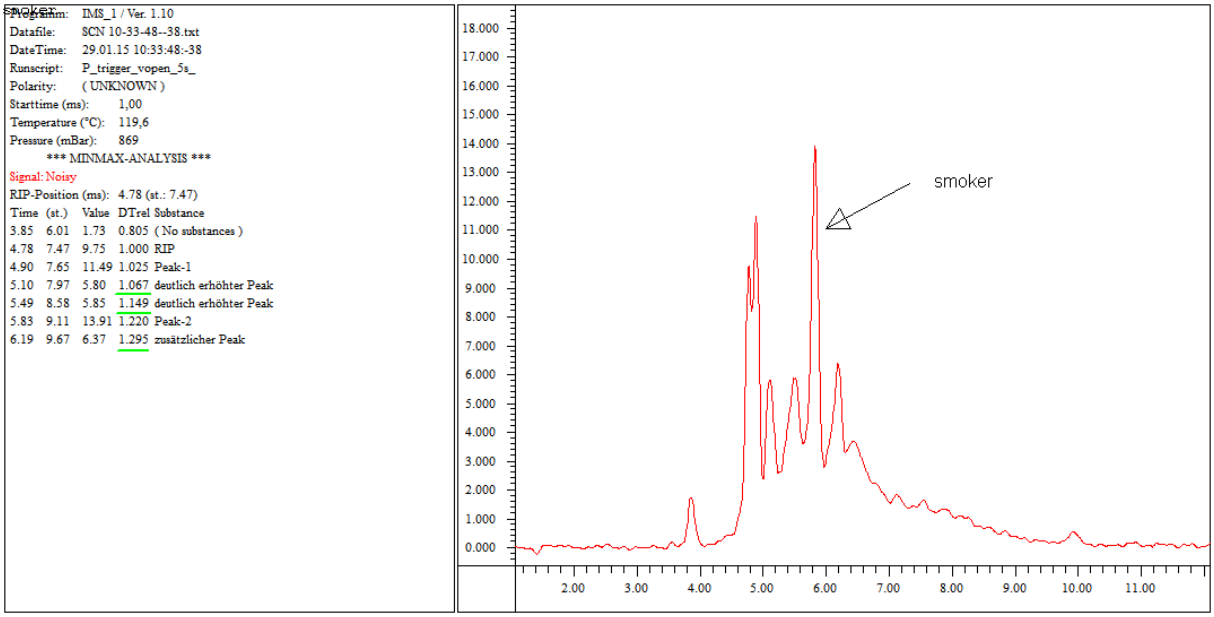
Programm: IMS_1 / Ver. 1.10
Datafile: SCN 13-15-25--86.txt
DateTime: 28.01.15 13:15:25:-86
Runscript: P_trigger_vopen_5s_
Polarity: (UNKNOWN)
Starttime (ms): 1,00
Temperature (°C): 120,4
Pressure (mBar): 929
*** MINMAX-ANALYSIS ***
Signal: Noisy
RIP-Position (ms): 5.10 (st.: 7.47)

Time (st.)		Value	DTrel	Substance
4.14	6.06	8.18	0.812	(No substances)
5.10	7.47	35.02	1.000	RIP
5.25	7.69	17.32	1.029	Atempeak-1
5.44	7.96	4.71	1.067	(No substances)
5.69	8.33	2.78	1.116	(No substances)
5.91	8.65	2.61	1.159	(No substances)
6.23	9.12	8.62	1.222	Atempeak-2
6.85	10.03	2.83	1.343	Atempeak-3
10.67	15.62	1.07	2.092	Atempeak-makro

The IMS spectra of no smoking people show three peaks in Exhaled breath with relative drift times about 1.03 (very near at RIP), 1.22 and 1.34. A drift time window of 1.22 corresponds to Acetone, which is well known as a VOC in exhaled air.

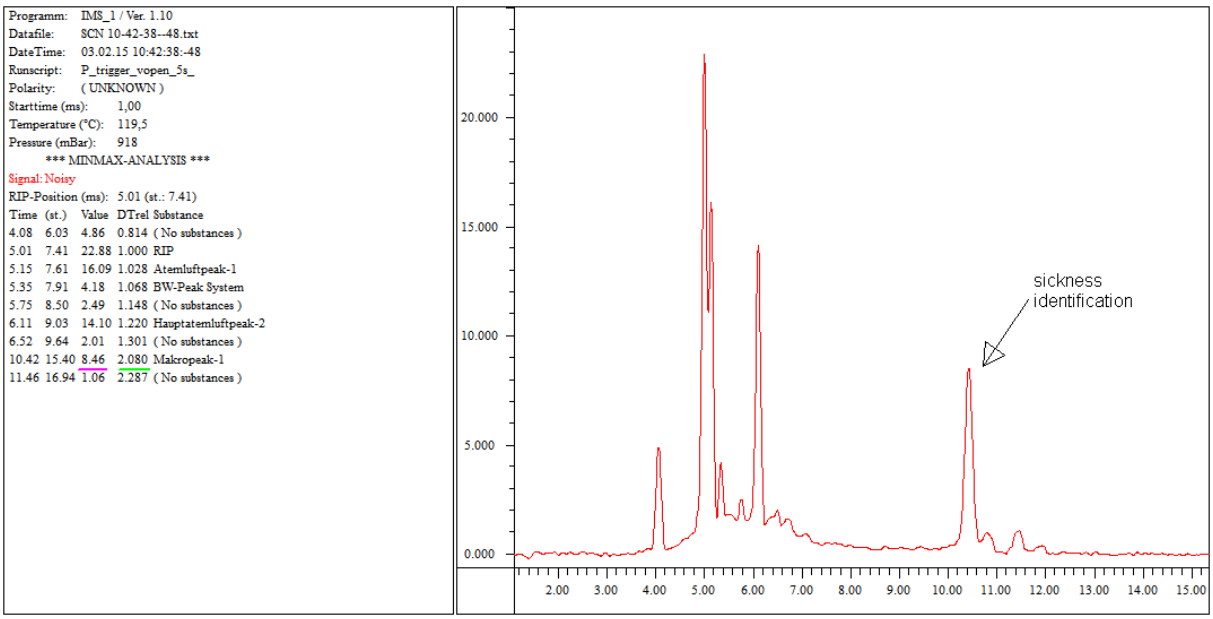
- **Healthy persons, smoker**

The exhaled breath of healthy smokers shows a new peak at a relative drift time of 1.30. Furthermore the peaks at a value of 1.06 and 1.15 are significant higher than the peaks of no smoking persons. The peaks of nonsmokers at these relative drift times are so small that they marginally differ from noise or the blank IMS spectrum.

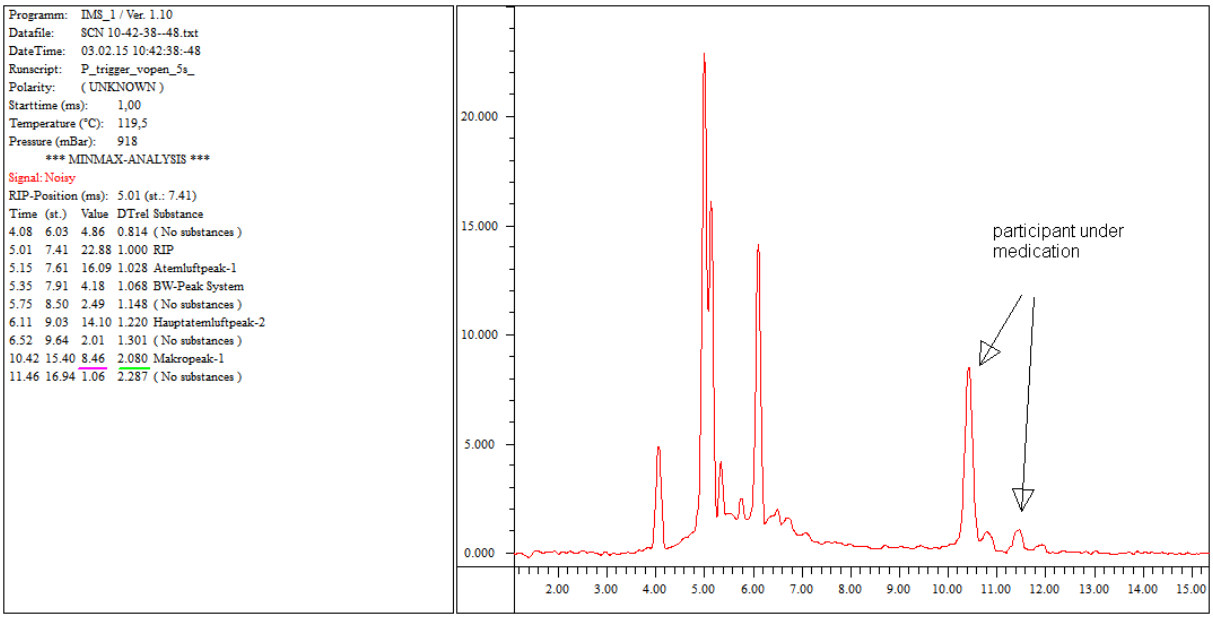


- **Sick (Flue)**

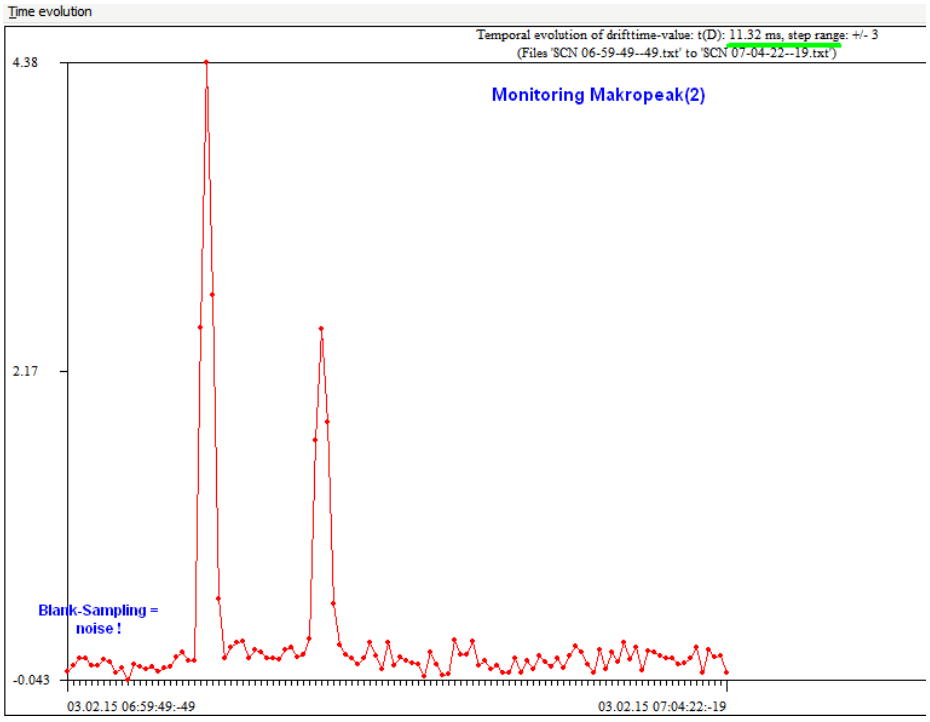
We have also measured the breath air of two ill persons, one man continuously use medicaments and the other study participant had a tracheal cough since some weeks. Both participants show increased peaks at relative drift times ***above 2.0***, the so called macro peaks, because such high drift times caused by complex molecules within the drift field of IMS.



IMS spectrum of test participant with long time tracheal cough



IMS spectrum of test participant under medication



Peak monitoring at the peak with a relative drift time of 2.29 in breath air of the participant under medication

5.) Next Steps

- **New designs for handheld devices**
- **New electronic/ basic design**
- **Test series with German Police, Canada, US Law Enforcement**
- **Continued testing of persons (THC smoker)**
- **Test at Maryland University**
- **Submit to NTSB for Testing**

6.) Features of THC-Analyzer

- Mobile / handheld
- Lightweight device (< 10 kg)
- Real-time analysis of THC in breath
- High sensitivity in lower ppb-range
- Superior selectivity and cross sensitivity rejection
- Enhancement with GC-column coupling (GC-IMS)

- Analysis directly in situ (No Tedlar bag sampling / no lab analysis)
- Operation under ambient air pressure
- Low operations costs, no consumables, no carrier gas required
- Operation with rechargeable battery