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p-Chloroaniline – Determination of *p*-chloroaniline in workplace air using gas chromatography (GC-MS)

Air Monitoring Method

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Abstract

This analytical method is a validated measurement procedure for the determination of *p*-chloroaniline [106-47-8] after personal or stationary sampling. Sampling is performed by drawing a defined volume of air through two acid-impregnated glass fibre filters using a suitable flow-regulated pump. After liquid desorption, the *p*-chloroaniline retained on the filters is analysed using gas chromatography with mass spectrometry. The relative limit of quantification is 0.0037 mg/m^3 for an air sample volume of 240 l. The mean recovery for *p*-chloroaniline is 99.9%. The concentration-dependent expanded uncertainty is at most 27%. This analytical method has been accredited by the accident insurance companies for the detection in workplace air of substances that are carcinogenic, mutagenic or toxic to reproduction. This method has been tested and recommended for the determination of *p*-chloroaniline in work areas by the German

Social Accident Insurance (DGUV). Both personal and stationary sampling can be performed for measurements in order to evaluate work areas.

Name	CAS No.	Molar mass [g/mol]	Formula	Occupational exposure limit value [mg/m³]
p-Chloroaniline	106-47-8	127.57	C_6H_6ClN	0.3, EF 2(II) (AGS 2023)

EF: excursion factor (short-term value category)

1 Summary

This method involves the use of personal or stationary sampling procedures to determine the mean concentration of *p*-chloroaniline in the work area over the sampling period.

Measurement principle: A pump is used to draw a defined volume of air through two acid-impregnated filters. *p*-Chloroaniline is then desorbed from the filter using a mixture of acetonitrile and ammonia solution with *p*-propylaniline as internal standard (ISTD) and determined by mass spectrometry after separation by gas chromatography (GC-MS).

Limit of quantification: Absolute: 0.22 ng
0.89 µg per sample carrier
Relative: 0.0037 mg/m³ for an air sample volume of 240 l, 4 ml of desorption solution and an injection volume of 1 µl

Measurement range: 0.026 to 0.59 mg/m³

Selectivity: High selectivity through the use of a mass selective detector

Advantages: Personal and selective measurements are possible

Disadvantages: Does not detect concentration peaks

Apparatus: Sampling devices:
Pump and sampling head, filter cassette with acid-impregnated glass fibre filters
Volumetric flow meter
Gas chromatograph with mass spectrometer

2 Equipment and chemicals

2.1 Equipment

For sampling:

- Pump, suitable for a flow rate higher than 1 l/min (e.g. PP 5, from Gilian supplied by DEHA, Haan & Wittmer, 71296 Heimsheim, Germany)
- Volumetric flow meter (e.g. Gilibrator, from Gilian, supplied by DEHA Haan & Wittmer, 71296 Heimsheim, Germany)
- GSP sampling head, suitable for a flow rate of 1 l/min
- Filter holder for the GSP system
- Binder-free glass fibre filters, diameter 37 mm (e.g. type 85/90BF, from Macherey-Nagel GmbH & Co. KG, 52355 Düren, Germany)
- Watch glass

- Petri dishes

For analytical determination:

- Volumetric flasks 5 ml, 10 ml, 250 ml and 1000 ml
- Automatic piston pipette (e.g. Multipette pro, from Eppendorf SE, 22339 Hamburg, Germany)
- Sample vials, 5 ml
- Autosampler vials, 1.5 ml
- Flatbed shaker
- Gas chromatograph (e.g. Agilent 7890B, with mass selective detector and autosampler, from Agilent Technologies Deutschland GmbH, 76337 Waldbronn, Germany)
- Analytical balance

For validation:

- Filter cassette (e.g. Merck Millipore, from Merck KGaA, 64293 Darmstadt, Germany)
- Tube made of polytetrafluoroethylene (PTFE)

2.2 Chemicals

- *p*-Chloroaniline, purity 97% (e.g. Order No. C22415-100G, from Sigma-Aldrich Chemie GmbH, 64293 Darmstadt, Germany)
- Methanol, purity ≥ 99.9% (e.g. Order No. 1060022500, from Merck KGaA, 64293 Darmstadt, Germany)
- Ammonia solution (25% in water) (e.g. Order No. 1054321000, from Merck KGaA, 64293 Darmstadt, Germany)
- Sulphuric acid 0.5 M (e.g. Order No. 1090721000, from Merck KGaA, 64293 Darmstadt, Germany)
- *p*-Propylaniline, purity 98% (e.g. Order No. BL3H1F1CAD1A-5G, from Sigma-Aldrich Chemie GmbH, 64293 Darmstadt, Germany)
- Acetonitrile for chromatography (e.g. Order No. RD34851-2.5L, Riedel de Haën, from Honeywell Specialty Chemicals Seelze GmbH, 30926 Seelze, Germany)
- Polyethylene glycol Mn 400 (e.g. Order No. 8074850050, from Sigma-Aldrich Chemie GmbH, 64293 Darmstadt, Germany)
- Helium 5.0 (carrier gas)

2.3 Solutions

The following solutions were prepared using the chemicals listed in Section 2.2:

Solvent mixture: Solution of ammonia solution and acetonitrile
50 ml of ammonia solution (25% in water) are placed into a 1000-ml volumetric flask and the flask is filled to 1 l with acetonitrile. This mixture is stable for 6 months.

Desorption solution: Solution of approx. 36 mg *p*-propylaniline (ISTD)/l in solvent mixture
Several millilitres of solvent mixture are placed into a 250-ml volumetric flask before adding 10 µl of *p*-propylaniline (density 0.919 g/ml) by pipette. The flask is filled to the mark with solvent mixture and shaken.

Calibration stock solution: Solution of approx. 3.5 g *p*-chloroaniline/l of desorption solution
Approx. 36 mg of *p*-chloroaniline are weighed into a 10-ml volumetric flask to the nearest 0.1 mg. The flask is then filled to the mark with desorption solution and shaken.

Calibration solution:
Desorption solution is placed into separate 10-ml volumetric flasks before adding aliquots of the calibration stock solution by pipette. The flasks are then filled to the mark with desorption solution and shaken.

These calibration solutions are equivalent to the concentrations given in Table 1 at an air sample volume of 240 l.

Tab. 1 Calibration solutions

Volume of stock solution [µl]	*p*-Chloroaniline		
	[µg/ml]	[µg] absolute[a)]	[mg/m³][b)]
2.0	0.70	2.8	0.012
5.0	1.8	7.2	0.029
10	3.5	14	0.058
20	7.0	28	0.12
40	14	56	0.23
60	21	84	0.35
80	28	112	0.47
100	35	140	0.58

[a)] at a desorption volume of 4 ml
[b)] based on an air sample volume of 240 l

Validation solution: Solution of approx. 1.26 g *p*-chloroaniline/l in methanol
Approx. 6.5 mg of *p*-chloroaniline are weighed into a 5-ml volumetric flask to the nearest 0.1 mg. The flask is then filled to the mark with methanol and shaken.

2.4 Preparation of the impregnated filters

The glass fibre filters are immersed in 0.5 molar sulphuric acid mixed with 1 per cent by volume of polyethylene glycol Mn 400. The filters are placed on a watch glass and air-dried overnight. Polyethylene glycol Mn 400 is added to hold the moisture in the dried filters. The impregnated filters are stored in sealed petri dishes at room temperature. Under these conditions, the filters are stable for three months.

3 Sampling

A filter cassette fitted with two acid-impregnated filters is inserted into the GSP sampling head and connected to a pump (DIN 2023). A flow rate of 1 l/min is set. The pump and the filters are either worn by a person during working hours or placed into a stationary sampling device. The method was tested up to a sample volume of 240 l, which corresponds to a sampling time of 4 hours.

After sampling, the flow rate must be tested for constancy. If the deviation from the adjusted volumetric flow rate is greater than ± 5%, another sample should be taken (see DGUV Information 213-500 “General Part”, Section 3 (DGUV 2015)).

4 Analytical determination

4.1 Sample preparation

The two filters are placed into separate 5-ml sample vials. After adding 4 ml of desorption solution, the vials are immediately sealed and shaken for 30 minutes on a flatbed shaker. Approx. 1 ml of the solution is transferred into an autosampler vial. 1 µl of the sample is then injected into a gas chromatograph and analysed.

4.2 Operating conditions for chromatography

GC conditions

Apparatus:	Gas chromatograph Agilent 7890B with mass spectrometer and split/splitless injector		
Separation column:	Material:	quartz capillary	
	Length:	30 m	
	Stationary phase	DB-Wax	
	Inner diameter	0.25 mm	
	Film thickness	0.5 µm	
Injector temperature:	250 °C		
Split:	1 : 10		
Injection:	1 µl		
Temperature programme:	Initial temperature:	50 °C	
	Ramp rate I:	50 °C/min up to 180 °C	
	Ramp rate II:	5 °C/min up to 198 °C	
	Ramp rate III:	25 °C/min up to 240 °C	
	2 min isotherm		
Carrier gas:	Helium, 1.6 ml/min, constant flow		
MS conditions			
Temperatures:	Transfer line:	280 °C	
	Ion source:	150 °C	
Ionisation type:	Electron ionisation (70 eV)		
Mass range:	Full-scan measurement: 29–250 amu		
Evaluation mass:		Quantification (target ion)	Qualification (qualifier ion)
	p-Chloroaniline:	127 amu	129 / 65 amu
	p-Propylaniline:	106 amu	135 amu

5 Evaluation

5.1 Calibration

The calibration solutions prepared according to Section 2.3 are analysed as described in Section 4.

The area quotients of *p*-chloroaniline and the ISTD are plotted against the mass quotients of *p*-chloroaniline and the ISTD of the respective calibration solutions. The calibration function is determined by linear regression analysis.

The calibration function is linear in the examined concentration range and is regularly checked during routine analysis. For this purpose, a reference standard of known concentration is analysed as part of each analytical series.

5.2 Calculation of the analytical result

The chromatograms are used to determine the peak areas of *p*-chloroaniline and of the ISTD and to obtain their quotient. The respective calibration function is used to calculate the corresponding concentration (c) in the sample solution in µg/ml.

The corresponding mass concentration (ρ) is calculated using Equation 1:

$$\rho = \frac{c \times V_d}{V_{air} \times \eta} \quad (1)$$

where:

ρ is the mass concentration of *p*-chloroaniline in the air in mg/m³

c is the concentration of *p*-chloroaniline in the analytical sample in µg/ml

V_d is the desorption volume in ml (4 ml)

V_{air} is the air sample volume in litres

η is the recovery (see Section 6.1)

6 Reliability of the method

6.1 Precision and recovery

The precision in the lowest measurement range as well as the recovery for 3 concentrations (see Table 2) were determined according to DIN EN 482 (DIN 2021). The validation solution prepared in Section 2.3 was used for this purpose.

To determine the precision of the method, Millipore cassettes were loaded with filters, one non-impregnated filter in front of two filters impregnated with sulphuric acid. A spacer was placed to separate the acid-impregnated filters from the non-impregnated filter. The non-impregnated glass fibre filters were spiked with 5 µl, 50 µl and 100 µl of the validation solution. Laboratory air was drawn through the loaded cassettes for 4 hours at a flow rate of 1 l/min (temperature approx. 23 °C, relative humidity between 50% and 55%). The experiment was repeated six times for each spike. The preparation and analytical determination were carried out as described in Section 4.

Tab. 2 Precision and recovery

Mass of *p*-chloroaniline [µg]	Concentration of *p*-chloroaniline[a)] [mg/m³]	Relative standard deviation [%]	Recovery [%]
6.3	0.026	1.0	101
63	0.262	1.9	97.3
126	0.525	3.6	101

[a)] based on an air sample volume of 240 l

The mean recovery is 99.9%.

6.2 Breakthrough volume

Two Millipore cassettes were connected to one another by a tube made of PTFE. The tube was kept as short as possible. The second sampling system served as a control layer. After spiking with 50 µl of the validation solution, 240 l of laboratory air was drawn through the systems. No evidence of breakthrough was found during analysis.

6.3 Limit of quantification

The limit of quantification was determined according to DIN 32645 (DIN 2008) using the calibration line method with 10 calibration solutions covering the lower concentration range.

Tab. 3 Limit of quantification (P = 99% and k = 3)

Mass range [µg]	Limits of quantification	
	Absolute per sample carrier [µg]	Relative[a)] [µg/m³]
2.8–7.0	0.89	3.7

[a)] based on an air sample volume of 240 l

The absolute limit of quantification is 0.22 ng for an injection volume of 1 µl.

The experiments demonstrated that signals that are suitable for analysis are produced by concentrations in the range of the determined limit of quantification.

6.4 Storage stability

Storage stability was determined using three loaded sample carriers per run. The sampling systems were spiked with 50 µl of the validation solution, which is equivalent to 0.262 mg/m³. After spiking with the solution, 240 l of laboratory air (23 °C, between 50 and 55% relative humidity) were drawn through each sample. The sampling systems were sealed and stored at room temperature in dry and dark conditions. The experiments were carried out over periods of 3, 7 or 14 days. The samples remain stable over a period of 14 days if stored in the dark at room temperature (recovery 99%).

6.5 Selectivity

Interfering components may lead to excessively high readings. Substances with the same dwell time may interfere with the measurements. Interference is largely eliminated through the use of a mass selective detector.

6.6 Uncertainty

The expanded uncertainty was determined taking all relevant influencing parameters into consideration (IFA 2023). The main sources of uncertainty in the results obtained by the method as a whole and thus also in the results of the measurements are uncertainties in the sampling procedure (e.g. air sample volume) and in the analytical procedure (e.g. complete desorption, scatter of the calibration function, fluctuations in recovery and reproducibility). The expanded uncertainty was at most 27% over the entire measurement range.

6.7 Comments

The method is also suitable for sampling times of 2 hours. To date, breakthroughs have not been observed.

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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