

# Triphenyl phosphate, isopropylated (isopropylated phenyl phosphates, IPPhP) – Determination of isopropylated phenyl phosphates in the workplace air using gas chromatography (GC-MS)

## Air Monitoring Method – Translation of the German version from 2020

### Keywords

triphenyl phosphate; hazardous substances; air analysis; workplace measurement; gas chromatography; solvent desorption

W. Rosenberger<sup>1</sup>  
S. Schuchardt<sup>2</sup>  
R. Hebisch<sup>3,\*</sup>

T. H. Brock<sup>4,\*</sup>  
A. Hartwig<sup>5,\*</sup>  
MAK Commission<sup>6,\*</sup>

- <sup>1</sup> Institute of Occupational Medicine, Hannover Medical School (MHH), OE 5500, Carl-Neuberg-Str. 1, 30625 Hannover, Germany
- <sup>2</sup> Fraunhofer Institute for Toxicology and Experimental Medicine (ITEM), Head of Department of Bio- and Environmental Analytics, Nikolai-Fuchs-Str. 1, 30625 Hannover, Germany
- <sup>3</sup> Head of the working group "Air Analyses" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Federal Institute for Occupational Safety and Health (BAuA), Friedrich-Henkel-Weg 1–25, 44149 Dortmund, Germany
- <sup>4</sup> German Social Accident Insurance, Institution for the raw materials and chemical industry, Prevention – Department of Hazardous Substances, Biological Agents and Analytical Chemistry, Kurfürsten-Anlage 62, 69115 Heidelberg, Germany
- <sup>5</sup> Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute of Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany
- <sup>6</sup> Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

\* email: R. Hebisch ([luftanalysen-dfg@baua.bund.de](mailto:luftanalysen-dfg@baua.bund.de)), T. H. Brock ([analytik@bgrci.de](mailto:analytik@bgrci.de)), A. Hartwig ([andrea.hartwig@kit.edu](mailto:andrea.hartwig@kit.edu)), MAK Commission ([arbeitsstoffkommission@dfg.de](mailto:arbeitsstoffkommission@dfg.de))

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## Abstract

This analytical method is a validated measurement procedure for the determination of isopropylated triphenyl phosphate in workplace air in a concentration range of one tenth up to twice the currently valid OEL or MAK value of 1 mg/m<sup>3</sup> I. Isopropylated triphenyl phosphate is a complex isomeric mixture of variable composition. Sampling is performed by drawing a defined volume of air through a quartz filter spiked with triphenyl phosphate-d<sub>15</sub> (ISTD). The flow rate is set to 3.5 ml/min and sampling period can be 2 h up to 8 h, which correspond to a sampling volume of 420 to 1680 l. The collected isopropylated phenyl phosphates are extracted with ethyl acetate in an ultrasonic bath and a heated horizontal shaker. For purification, a solid phase extraction can be used. Analysis is performed by means of gas chromatography using a mass selective detector. The quantitative determination is based on a calibration function, whereby the quotients of the peak area of the isopropylated phenyl phosphates to triphenyl phosphates-d<sub>15</sub> are plotted against the peak areas of the organic phosphorus compounds. The relative limit of quantification (LOQ) is 0.050 mg/m<sup>3</sup> based on an air sample volume of approx. 420 l. The mean recovery of this method is 98,9% ± 6% and the expanded uncertainty for the overall measurement method 30.7%.

<b>Method number</b>	1
<b>Application</b>	Air analysis
<b>Analytical principle</b>	Gas chromatography/mass spectrometry (GC/MS)

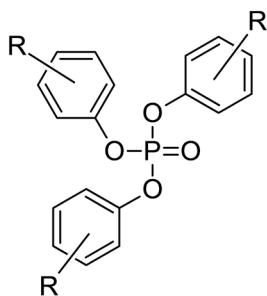
## 1 Characteristics of the method

Precision:	Standard deviation (rel.):	$s = 6\%$
	Expanded uncertainty:	$U = 30.7\%$
	for a concentration range of 0.05 to 0.49 mg/m <sup>3</sup> and $n = 24$ determinations (four concentration steps with 6 determinations in each case, sampling period of 2 h at 3.5 l/min)	
Limits of quantification:	Isopropylated phenyl phosphates (IPPhPs) 0.050 mg/m <sup>3</sup> for a sample volume of 420 l, a sample solution of 5 ml and an injection volume of 1 µl	
Recovery rates:	98.9 ± 6%	
Sampling recommendations:	Sampling period:	2 h
	Air sample volume:	420 l

## 2 Description of the substances

### Triphenyl phosphate, isopropylated (IPPhPs) [68937-41-7]

In the MAK value documentation it was noted that this is an isomer mixture of unknown or variable composition registered under REACH (see [Figure 1](#)) (ECHA 2020 b; Hartwig and MAK Commission 2016).



**Fig. 1** General structure of isopropylated triphenyl phosphates (R = 0 to 3 isopropyl groups per ring)

The phosphoric acid esters described here are prepared from single or multiple isopropylated phenols in the meta, para and ortho positions by conversion with phosphorus oxychloride. Depending on the number of isopropyl groups, isomers with molar masses of among others 368.4 g/mol, 410.4 g/mol, 452.5 g/mol and 494.6 g/mol can occur. Generally, commercially available IPPhP consists of mixtures of variable composition (Brooke et al. 2009; Hartwig and MAK Commission 2016). Trade names for these substances are: Durad<sup>®</sup>, Lubad<sup>®</sup>, Phosflex 31L, Phosflex 41L, Reofos<sup>®</sup>, Reolube<sup>®</sup>, Roflex, Syn-o-ad 9578 (ECHA 2020 b). IPPhPs can be contaminated with triphenyl phosphate (TPP) [115-86-8], therefore, determination of this component is recommended using the method presented here (Rosenberger and Bader 2013). Important substance data are summarised in [Table 1](#).

**Tab. 1** Substance data for isopropylated phenyl phosphates (IPPhPs) (ECHA 2020 a)

Name	Isopropylated phenyl phosphates
Acronym	IPPhPs
CAS No.:	68937-41-7
Aggregate state at 20 °C	Liquid
Density at 20 °C [g/cm <sup>3</sup> ]	1.168
Octanol water partition coefficient log K <sub>ow</sub> at 20 °C	4.92...5.17
Vapour pressure at 20 °C [Pa]	2.5 × 10 <sup>-6</sup>
Melting point [°C]	< -20
Boiling point at 1013 hPa [°C]	> 400
Solubility in water at 20 °C [mg/l]	0.33
Bioconcentration factor (BCF) (Fent 2013) [l/kg]	776
PBT / vPvB substance (Fent 2013)	No / No
Classification and category of hazard	Toxic to reproduction 2 Specific target organ toxicity (repeated exposure) (adrenal gland) Chronic aquatic toxicity 1
Hazard information (H codes)	H 361, 373, 410
Precautionary information (P codes)	P 201, 202, 260, 273, 281, 308+313, 314, 391, 501
Limit values	
OEL, Germany (AGS 2020)	1 mg/m <sup>3</sup> (inhalable dust fraction)
MAK value, Germany (DFG 2019)	1 mg/m <sup>3</sup> (inhalable dust fraction)
MAK value, Switzerland (IFA 2020)	3.5 mg/m <sup>3</sup> (inhalable dust fraction)

### 3 General principles

The method enables the determination of the content of isopropylated phenyl phosphates (IPPhPs) in the workplace air as the inhalable dust fraction in the range of a tenth to twice the currently valid MAK value of 1 mg/m<sup>3</sup> I (inhalable dust fraction) (Hartwig and MAK Commission 2016). IPPhPs are complex isomer mixtures of variable compositions. At present, a maximum of nine individual components are available as calibration substances. The method was validated using eight standard substances. Therefore, as in the case of e.g. polychlorinated biphenyls (PCB), the entire IPPhP content cannot be directly quantified and is also currently not reported for practical reasons. However, the entire content of IPPhPs in the sample can be estimated. In this case, it must be calculated on the basis of a factor pertaining to the isomer proportions of the entire IPPhP content, which has been determined empirically or, if applicable, obtained from product information. Sampling is performed by drawing workplace air through a quartz filter spiked with D<sub>15</sub>-triphenyl phosphate (ISTD) using a suitable sampling pump. After sampling, the adsorbed IPPhPs and the ISTD are extracted with ethyl acetate in an ultrasonic bath as well as on a horizontal shaker. An optional purifying step in the form of solid phase extraction is available for heavily contaminated extracts. The components of the organic phase are subsequently separated by means of gas chromatography and determined using a mass-selective detector (GC-MS). The quantitative evaluation is carried out on the basis of a calibration function, whereby the quotients of the peak areas of the IPPhPs with respect to that of D<sub>15</sub>-triphenyl phosphate are plotted versus the corresponding IPPhP concentrations of the calibration standards used.

## 4 Equipment, chemicals and solutions

### 4.1 Equipment

- Pump for personal air sampling, output at least 120 l/h, e.g. SKC 224 DeLuxe, from SKIC, Dorset, UK, Gilian 5000, from Sensidyne, LP, St. Petersburg, USA, GSA-SG 5100, from GSA Messgerätebau, Ratingen, Germany
- Gas flow meter, e.g. Drycal, from DC-Lite M, Bios International Corporation, Butler, New Jersey, USA 07405
- Total dust sampling system (GSP), 3.5 l intake cone, from GSA Messgerätebau, Ratingen, Germany
- Quartz filter ( $\varnothing$  37 mm), pore width 2.2  $\mu\text{m}$ , Whatman™ 1851-037, QM-A grade quartz microfibre filter for air sampling
- Volumetric flasks (glass) with plastic stoppers: 2, 5, 10, 25, 50 and 100 ml, e.g. from Brand, Wertheim, Germany
- Piston pipettes (1–10  $\mu\text{l}$ ; 10–100  $\mu\text{l}$ , 100–1000  $\mu\text{l}$ , 1000–5000  $\mu\text{l}$ ), e.g. from Eppendorf, Hamburg, Germany
- GC sample vials, sealable, nominal volume 1.6 ml, 200- $\mu\text{l}$  microinserts, glass, with aluminium crimp caps/teflon-coated butyl rubber sealing disks, e.g. from MACHEREY-NAGEL, Düren, Germany
- Crimp-capped vials, sealable, nominal volume approx. 10 ml, with aluminium sealing caps with teflon-coated butyl rubber septa, e.g. from MACHEREY-NAGEL, Düren, Germany
- Centrifuge, e.g. Megafuge 1.0, from Heraeus, Hanau, Germany
- Ultrasonic bath, SONOR EX Super 10 P, e.g. from Bandelin electronic, Berlin, Germany
- Horizontal shaker, e.g. IKA HS 260 basic, from IKA Werke, Staufen, Germany
- Vacuum chamber for solid phase extraction, vacuum manifold, e.g. Vac Elut™ SPS 24, from Agilent, Waldbronn, Germany
- Membrane vacuum pump e.g. MZ 2 C, from Greiffenberger Antriebstechnik, Marktredwitz, Germany
- Solid phase extraction tubes (SPE), Supelclean™ ENVI-Florisil® SPE Tubes, 500 mg/3 ml, 57058 Supelco, from Merck, Darmstadt, Germany
- Soxhlet extraction apparatus, 30-ml Soxhlet extractor, 100-ml round-bottomed flask, Dimroth condenser, all from DURAN, Schott, e.g. from DWK Life Sciences, Wertheim, Germany or automatic solvent extractor e.g. ASE350, from ThermoFisher, Dreieich, Germany
- Laboratory heater, electrical heating, e.g. from C. Gerhardt, Königswinter, Germany
- Gas chromatograph with mass-selective detector MSD (e.g. Agilent 6890 and MSD 5973, from Agilent, Waldbronn, Germany)
- Capillary column: 30 m, inner diameter 0.25 mm, 0.25  $\mu\text{m}$  film thickness (e.g. Optima 5 MS accent, MACHEREY-NAGEL, Düren, Germany)

## 4.2 Chemicals

**Tab. 2** List of chemicals

Name	CAS No.	Purity specification	Available from	Article No.
<b>D<sub>15</sub>-Triphenyl phosphate (D<sub>15</sub>-TPP)</b>	no data	98 atom % D	Merck	615218 Aldrich
Triphenyl phosphate (TPP)	115-86-6	≥ 99%	Merck	241288 Aldrich
<b>Bis(2,4-diisopropylphenyl) phenyl phosphate</b>	no data	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>B24DIPPhPhP</b>
<b>2,4-Diisopropylphenyl diphenyl phosphate</b>	no data	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>24DIPPhDPhP</b>
<b>2-Isopropylphenyl diphenyl phosphate</b>	64532-94-1	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>2IPPhDPhP</b>
<b>4-Isopropylphenyl diphenyl phosphate</b>	55864-04-5	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>4IPPhDPhP</b>
<b>Bis(2-isopropylphenyl) phenyl phosphate</b>	69500-29-4	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>B2IPPhPhP</b>
<b>Bis(4-isopropylphenyl) phenyl phosphate</b>	no data	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>B4IPPhPhP</b>
<b>Tris(3-isopropylphenyl) phosphate</b>	72668-27-0	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>T3IPPhP</b>
<b>Tris(4-isopropylphenyl) phosphate</b>	2502-15-0	Solution in toluene (β = 50 µg/ml ± 5%)	Wellington Laboratories	<b>T4IPPhP</b>
Isopropyl phenyl phosphate mix, <b>IPPhP-Mix</b>	68937-41-7	High purity compound, 63.6% ± 0.2%	CPAchem	SB42460.100
Helium	7440-59-7	5.0, 99.999%	Linde	In-house delivery
Dichloromethane	75-09-2	for gas chromatography MS SupraSolv, ≥ 99.8%	Merck	1.00668 EMD Millipore
Ethyl acetate	141-78-6	for gas chromatography MS SupraSolv, ≥ 99.8% (GC)	Merck	100789
Nitrogen	7727-37-9		Central on-site gas supply	In-house delivery

## 4.3 Solutions

The following solutions, which can be stored in the refrigerator at +4 °C for at least 6 months, are prepared from the substances listed in Table 2. The specified solutions containing TPP are optional and only required, if triphenyl phosphate is to be determined at the same time.

### IPPhP-8 calibration stock solution:

Eight IPPhP individual standards (see Table 2) that are available as solutions in toluene with a volume of 1.2 ml in snap-off ampoules (IPPhP-8 calibration starting solutions) are used for the calibration. First the ampoules are opened and a piston pipette is used to transfer the contents into GC vials made of amber glass. Then the stock solution is prepared and the GC vials are sealed with crimp caps. 200 µl of each individual standard are added into a 2-ml volumetric flask using a pipette and the flask is filled to the mark with toluene ( $\beta_{\text{IPPhP}} = 5 \mu\text{g/ml}$  per component).

### IPPhP-mix stock solution:

10.08 mg of IPPhP-mix (purity = 63.6%) are weighed exactly into a 1-ml volumetric flask, dissolved in ethyl acetate and the flask is filled to the mark ( $\beta_{\text{IPPhP-mix}} = 6.87 \text{ mg/ml}$ ).

### Triphenyl phosphate, TPP stock solution:

113.2 mg of TPP (purity ≥ 99%) are weighed exactly into a 10-ml volumetric flask, dissolved in ethyl acetate and the flask is filled to the mark ( $\beta_{\text{TPP}} = 11.2 \text{ mg/ml}$ ).

Internal standard: D<sub>15</sub>-Triphenyl phosphate (D<sub>15</sub>-TPP)

**D<sub>15</sub>-TPP stock solution:**

102.4 mg of D<sub>15</sub>-TPP (purity = 98%) are weighed exactly into a 10-ml volumetric flask, dissolved in ethyl acetate and the flask is filled to the mark ( $\beta_{D_{15}\text{-TPP}} = 10.04 \text{ mg/ml}$ ).

**D<sub>15</sub>-TPP standard solution and spiking solution for the quartz filters:**

100  $\mu\text{l}$  of the D<sub>15</sub>-TPP stock solution are diluted exactly to 10 ml with ethyl acetate in a 10-ml volumetric flask ( $\beta_{D_{15}\text{-TPP}} = 100 \text{ }\mu\text{g/ml}$ ).

**IPPhP calibration standards:**

Two calibration series can be prepared from the IPPhP-8 calibration stock solution, whereby calibration series 1 is recommended for the practical application. As part of the validation of the method it is advisable to also use calibration series 2. The respective pipetting schemes are shown in [Tables 3 and 4](#).

**Tab. 3** Calibration series 1 for IPPhPs in the range of 0.050 to 0.50  $\mu\text{g/ml}$ 

Calibration standard No.	Volume of IPPhP-8 calibration stock solution	Concentration per IPPhP	Volume of D <sub>15</sub> -TPP standard solution	Final volume
	$\mu\text{l}$	$\mu\text{g/ml}$	$\mu\text{l}$	ml
Indoor-8-IPPhP-Cal-1	0	0.00	20	2
Indoor-8-IPPhP-Cal-2	20	0.05	20	2
Indoor-8-IPPhP-Cal-3	40	0.10	20	2
Indoor-8-IPPhP-Cal-4	80	0.20	20	2
Indoor-8-IPPhP-Cal-5	120	0.30	20	2
Indoor-8-IPPhP-Cal-6	160	0.40	20	2
Indoor-8-IPPhP-Cal-7	200	0.50	20	2

A quadratic fit of the calibration function is recommended for calibration series 2 shown in [Table 4](#).

**Tab. 4** Calibration series 2 for IPPhP in the range of 0.10 to 5.00  $\mu\text{g/ml}$ 

Calibration standard No.	Volume of IPPhP-8 calibration stock solution	Concentration per IPPhP	Volume of D <sub>15</sub> -TPP standard solution	Final volume
	$\mu\text{l}$	$\mu\text{g/ml}$	$\mu\text{l}$	ml
APM-8-IPPhP-Cal-1	0	0.00	20	2
APM-8-IPPhP-Cal-2	40	0.10	20	2
APM-8-IPPhP-Cal-3	100	0.25	20	2
APM-8-IPPhP-Cal-4	200	0.50	20	2
APM-8-IPPhP-Cal-5	400	1.00	20	2
APM-8-IPPhP-Cal-6	1000	2.50	20	2
APM-8-IPPhP-Cal-7	200 $\mu\text{l}$ per Sl <sup>a)</sup>	5.00	20	2

<sup>a)</sup> SL: IPPhP-8 calibration starting solutions (see [Section 4.3](#))

For the practical application it is advisable to calibrate up to 0.50  $\mu\text{g/ml}$  ([Table 3](#)) and to suitably dilute the sample measurement solutions so that the measurement signals of the respective concentrations are in the range of the calibration.

## 5 Sampling and sample preparation

### 5.1 Preparation of the sample carriers

To avoid blank values the glassware, sample holders and support screens that are used for the determination of the IPPhPs are cleaned in a commonly used laboratory dishwashing machine and rinsed with dichloromethane. Then the glassware is heated at 250 °C in the drying cabinet (preferably overnight). The filters are cleaned with ethyl acetate

in a 30-ml Soxhlet extractor for at least 60 cycles and then dried before being used for sampling. The filters are then spiked with 50 µl of the D<sub>15</sub>-TPP standard solution and placed into the holders of the GSP after the ethyl acetate has evaporated. Packed in aluminium foil the sampling systems thus prepared can be used directly for sampling or stored in the refrigerator for at least two weeks at +4 °C.

## 5.2 Sampling

Before sampling the sampling system is connected to the pump, the flow rate is adjusted to the desired rate of approx. 3.5 l/min and is checked using a gas flow meter. Depending on the investigation and the expected concentrations, the sampling time can be selected between 2 and 8 h. At 3.5 l/min this is equivalent to an air sample volume of 420 to 1680 litres. On completion of sampling the flow rate is checked again and the sampling system is sealed with the designated sealing caps. The samples should be stored in a cool and dark place (e.g. in the refrigerator at +4 °C) until further preparation is carried out. The important data and parameters for the determination of the concentrations of IPPhPs in air are documented in the sampling record.

## 5.3 Sample preparation

For sample preparation the filter is transferred into a 10 ml headspace vial using tweezers and immersed in 5 ml of ethyl acetate. After sealing the vials with crimp caps, the samples are extracted first in the ultrasonic bath and then on a horizontal shaker (210 vibrations per min) for one hour in each case. If particles are present, they are separated by centrifugation at 2000 × g if necessary. 100 µl of the supernatant clear sample solution are transferred into a GC microvial and then analysed. The content of D<sub>15</sub>-TPP in the measurement solutions thus prepared is identical to that in the calibration standards. If immediate analysis of the sample is not possible, then it is stored at +4 °C in a refrigerator until GC measurement. Long-term storage of the sample at –28 °C is also possible.

A field blank value that undergoes the entire sampling procedure is also analysed.

## 6 Operating conditions

Apparatus: Gas chromatograph with autosampler (e.g. Agilent 6890) and mass-selective detector MSD (e.g. Agilent 5973)

### Operating conditions for gas chromatography:

Column:	Material:	Fused silica
	Stationary phase:	e.g. Optima 5 MS accent
	Length:	30 m
	Inner diameter:	0.25 mm
	Film thickness:	0.25 µm
Injector:	Programmed temperature vaporising injector (PTV):	60 to 320 °C (12 °C/s)
	Split ratio:	Splitless (1 min)
Carrier gas:	Helium 5.0	1.0 ml/min
Temperatures:	Column:	60 °C (1 min) $\xrightarrow{10\text{ °C/min}}$ 320 °C (13 min)
	Transfer line:	300 °C

### Operating conditions for mass spectrometry:

Ionisation type:	Electron impact ionisation (EI)
Ionisation energy:	70 eV

Measuring time per ion:	25 to 50 ms	
Temperatures:	Quadrupole:	150 °C
	Ion source:	230 °C
SIM mode:	selected masses (see Table 5)	
Solvent delay:	10 min	
Injection volume:	1 µl	

**Tab. 5** SIM masses and time intervals

Time until minute	Components	Quantifier ion m/z	Qualifier ion	Dwell time ms/ion	Ion/interval	Multiplier voltage V
10.00	Solvent delay					
20.00	D <sub>15</sub> -TPP	341	243	50	2	
	TPP	326	215	50	2	
22.00	Mono-IPPhPs	368				e.g. 1800 (after autotuning)
	Di-IPPhPs	410	118, 145, 160,	25	10	
	Tri-IPPhPs	452	251, 395, 437			
	Tetra-IPPhPs	494				

## 7 Analytical determination

To analyse the samples prepared as described in Section 5.3, in each case 1 µl of the sample solution is injected into the gas chromatograph and analysed under the conditions stated in Section 6. If the measured concentrations are above the calibration range, then a suitable dilution of the sample must be prepared and the analysis must be repeated.

## 8 Calibration

The calibration solutions (see Table 3) described in Section 4.3 are used to obtain the calibration functions. In each case 1 µl of the calibration solutions is injected into the gas chromatograph and analysed in the same manner as the sample solutions. The quotients calculated from the peak areas of the individual IPPhPs with respect to that of D<sub>15</sub>-TPP are plotted versus the respective IPPhP concentrations. A control sample should be analysed each working day to check the calibration functions.

## 9 Calculation of the analytical results

The concentrations of the selected eight IPPhPs in the air at the workplace are calculated on the basis of calibration functions. Equation 1 shows the relationship between the signal intensity and the concentration of an IPPhP in the calibration functions obtained by means of linear regression:

$$A_Q = m \times x_{IPPhP} + b \quad (1)$$

where:

$A_Q$	is the quotient of the peak area of the respective IPPhP with respect to the internal standard D <sub>15</sub> -triphenyl phosphate
$m$	is the gradient of the graph of the calibration function
$x_{IPPhP}$	is the concentration of the respective IPPhP in µg/sample
$b$	is the intercept with the y axis



Equation 2 is obtained by transposition as follows:

$$x_{IPPhP} = \frac{A_Q - b}{m} \quad (2)$$

Sample evaluation is carried out by the evaluation software of the analytical instrument or by another suitable data evaluation program.

When the sample volume is taken into account, the concentrations of selected IPPhPs can be calculated in  $\mu\text{g}/\text{m}^3$  according to Equation 3:

$$\rho_{IPPhP} = \frac{x_{IPPhP}}{V} \quad (3)$$

Calculation of the entire content of IPPhPs:

At present, only eight IPPhPs are available as pure substances. Therefore, the entire content of IPPhPs in the sample can only be estimated. In this case it is advisable to analyse the substance used at the workplace as a material sample and determine the content of the eight IPPhPs and to put it in proportion to the amount used. The entire content can be calculated (Equation 4) using factor “F” calculated in this manner.

$$\rho_G = \rho_{8-IPPhP} * F \quad (4)$$

where:

$\rho_G$  is the entire content of IPPhPs in the working material  
 $\rho_{8-IPPhP}$  is the content of the eight IPPhPs in the working material  
 $F$  is the correction factor to be empirically determined

Example: In an analysed mass of 100 mg of the working material 25 mg are determined as the sum of the 8 individual standards after analysis. A factor “F” of 4 for the air samples to be investigated is obtained.

## 10 Reliability of the method

The characteristics of the method were calculated as stipulated in DIN EN 482 (DIN 2015), DIN EN ISO 22065 (DIN 2021), DIN EN ISO 21832 (DIN 2020) and DIN 32645 (DIN 2008) from the calibration functions of the respective IPPhPs in the concentration range from 0.1 to 2.5  $\mu\text{g}/\text{ml}$  (equivalent to 0.2 to 5.3  $\mu\text{g}/\text{m}^3$  at a sample volume of 480 l).

### 10.1 Recovery, precision and expanded uncertainty

The precision of the entire method and the expanded uncertainty are determined based on the recovery experiments.

**Tab. 6** Precision in the series, standard deviation (rel.) and expanded uncertainty *U* for *n* = 24 determinations

	Theoretical value µg/ml	Actual mean value µg/ml	Relative standard deviation %	Recovery %	U
<b>Low concentration 1 a</b>					
Σ of the 8 IPPhPs	4.0	3.87	3.7	<b>96.8</b>	<b>21.5</b>
<b>Low concentration 1 b</b>					
Σ of the 8 IPPhPs	9.0	8.13	3	<b>90.4</b>	<b>23.5</b>
<b>Medium concentration</b>					
Σ of the 8 IPPhPs	15.2	16.1	6.3	<b>106</b>	<b>22.5</b>
<b>High concentration</b>					
Σ of the 8 IPPhPs	40.0	41.1	2.4	<b>103</b>	<b>21.4</b>
Mean value				<b>98.9 ± 6</b>	<b>22.2 + 8.5<sup>a)</sup> = 30.7</b>

<sup>a)</sup> Plus the error of 8.5% for the efficiency of the sampler with respect to the inhalable fraction (Möhlmann 2012).

## 10.2 Limit of quantification

The limits of quantification of the individual IPPhPs were determined according to DIN 32645 from a 10-point calibration for an air sample volume of 480 litres, a sample solution of 1 ml and an injection volume of 1 µl (DIN 2008). In this case the calibration series from 0.05 to 0.5 µg of IPPhPs per ml was investigated. The analytical limits of quantification are summarised in Table 7.

**Tab. 7** Limit of detection (LOD) and limit of quantification (LOQ) of the IPPhPs

Sample material	Limit of detection (LOD) <sup>a)</sup>			Limit of quantification (LOQ) <sup>a)</sup>		
	Measurement solution µg/ml	Air after 1/4 h mg/m <sup>3</sup>	Air after 2 h mg/m <sup>3</sup>	Measurement solution µg/ml	Air after 1/4 h mg/m <sup>3</sup>	Air after 2 h mg/m <sup>3</sup>
2IPPhDPhP	0.14	0.003	0.0003	0.48	0.01	0.0012
B2IPPhPhP	0.14	0.003	0.0003	0.48	0.01	0.0012
4IPPhDPhP	0.15	0.003	0.0003	0.52	0.01	0.0013
24DIPPhDPhP	0.14	0.003	0.0003	0.51	0.01	0.0012
B4IPPhPhP	0.13	0.002	0.0003	0.45	0.01	0.0011
T3IPPhP	0.11	0.002	0.0003	0.38	0.01	0.0009
B24IPPhPhP	0.14	0.003	0.0003	0.51	0.01	0.0012
T4IPPhP	0.14	0.003	0.0003	0.48	0.01	0.0012
<b>Σ of the 8 IPPhPs</b>	<b>1.06</b>	<b>0.020</b>	<b>0.0025</b>	<b>3.80</b>	<b>0.07</b>	<b>0.0091</b>
<b>Total IPPhPs (if the 8 account for approx. 1/5 of the total content)<sup>b)</sup></b>	<b>5.30</b>	<b>0.10</b>	<b>0.02</b>	<b>19.00</b>	<b>0.36</b>	<b>0.05</b>

<sup>a)</sup> In the case of data for air samples after sampling at a flow rate of 3.5 l/min the following applies: short-term sampling = 15 min ≈ 52.5 l and time-weighted average sampling = 2 h ≈ 420 l

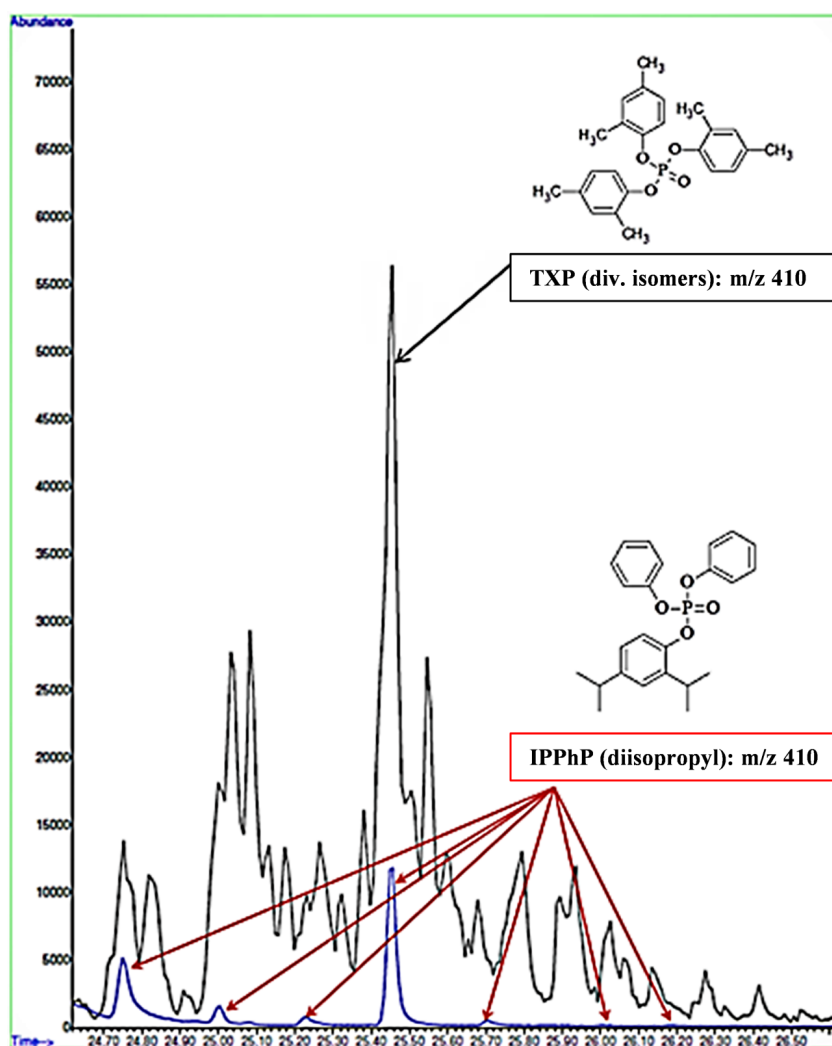
<sup>b)</sup> Applies to the IPPhP mixture investigated in this validation. Calculated from the linear calibration functions by means of B.E.N. 2.03 as stipulated in DIN 32645 (DIN 2008)

## 10.3 Storage stability

The storage stability was determined by spiking 15 sample carriers (quartz filters) with standard solution and then drawing air through them for 2 hours at a flow rate of 3.5 l/min. The sample carriers were sealed with the plastic caps designated for the purpose, stored for 14 days at +4 °C in a refrigerator and subsequently processed and analysed according to Sections 5.3, 6 and 7. The recovery rate over this time period for the sum of IPPhPs is 112%, whereby there were inaccuracies for Bis-4-IPPhPhP and Bis-2,4-DIPPhPhP in the form of increased findings (152 and 139%). Conversely reduced recovery rates were determined for T3IPPhP and T4IPPhP (70 and 77%).

## 10.4 Interference

The analytical procedure by means of GC-MS is specific and robust under the conditions stated here. On principle, reliable identification of the target substances is ensured by using a mass-selective detector. As is widely known, only the signals of previously defined mass fragments are registered during sensitive measurement in the SIM mode, not complete spectra. Both the selection of the ions as well as the optimisation of the chromatographic separation were designed to ensure a definite differentiation of mono-isopropylated phenyl phosphates from tricresyl phosphates (both  $m/z$  368). However, di-isopropylated phenyl phosphates can be determined at  $m/z$  410, only if no trixylyl phosphates (TXPs) are present, as these also have a  $[M]^+$  of 410 u and otherwise hardly fragment. TXPs are a complex mixture of numerous positional isomers, which cannot be separated under the given gas chromatographic conditions. A characteristic chromatogram (Figure 2) shows that qualitative differentiation of Di-IPPhPs is possible on principle; however, there is overlapping, therefore rendering quantification based on the mass fraction of  $m/z$  410 impossible. In such cases, it is necessary to revert to evaluation of  $m/z$  395 or  $m/z$  251, as these fragments are not generated by TXPs.



**Fig. 2** Overlapping of the signals of diisopropyl phenyl phosphates (blue line) by TXP at comparable amounts (black line at  $[M]^+$  410)

## 11 Discussion

The concentrations of selected IPPhPs in the workplace air can be selectively and sensitively determined with the analytical method presented here. The use of an isotope-labelled internal standard for spiking the filters prior to sampling compensates for sampling-related and preparation-related influencing factors.

The entire content of IPPhP in the sample can currently only be estimated. A calibration with 8 IPPhPs is possible at present, so that the entire content can be estimated by the multiplication of the sum of these 8 IPPhPs by a factor derived from the original substance or, if necessary, also from other information on hazardous substances.

The possible exposure to a mixture with triphenyl phosphate (TPP) should be taken into consideration when monitoring the MAK value for IPPhPs, depending on the composition of the commercial product. Triphenyl phosphate can be measured simultaneously using this method.

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