ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Analytical methods for air

Development and Validation of an Analytical Method for the Determination of Imiprothrin TG in Air –Certification of cis- and trans- isomers and of TGAI, Study I.D. PTRL Europe ID [redacted], Bendig P., 2016

Analyte (type of analyte e.g. active substance)	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)			Limit of quantification (LOQ) or other limits	Reference
					Range	Mean	RSD		
m/z = 123 → 81									
Imiprothrin (active substance)	GC-MS/MS	0.83 µg/m³ (ambient air)	1.18 – 942 ng/ml r^2 = 0.9997 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9990 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	87 78 88	[redacted]	0.83 µg/m³	Bendig P, 2016 ([redacted])
		8.4 µg/m³ (ambient air)	1.18 – 942 ng/ml r^2 = 0.9997 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9990 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	94 84 97	[redacted]	0.83 µg/m³	

		0.82 µg/m³ (warm, humid air)	1.18 – 942 ng/ml r^2 = 0.9997 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9990 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	80 74 82	[redacted]	0.82 µg/m³	
		8.5 µg/m³ (warm, humid air)	1.18 – 942 ng/ml r^2 = 0.9997 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9990 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	83 77 85	[redacted]	0.82 µg/m³	
m/z = 123 → 79									
Imiprothrin (active substance)	GC-MS/MS	0.83 µg/m³ (ambient air)	1.18 – 942 ng/ml r^2 = 0.9998 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9993 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	98 78 102	[redacted]	0.83 µg/m³	Bendig P, 2016 ([redacted])

		8.4 µg/m³ (ambient air)	1.18 – 942 ng/ml r^2 = 0.9998 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9993 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	99 91 105	[redacted]	0.83 µg/m³	
		0.82 µg/m³ (warm, humid air)	1.18 – 942 ng/ml r^2 = 0.9998 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9993 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	98 82 102	[redacted]	0.82 µg/m³	
		8.5 µg/m³ (warm, humid air)	1.18 – 942 ng/ml r^2 = 0.9998 (cis-imiprothrin) 5.0-1008 ng/ml r^2 = 0.9993 (trans-imiprothrin)	Chromatograms showed no interference. Quantification by MS/MS at m/z 123→81 and confirmation at m/z 123→79.	[redacted]	83 77 89	[redacted]	0.82 µg/m³	

An air sampling cartridge (ORBO-43 XAD) containing XAD adsorbent material was fortified with 10 µL of imiprothrin (sum of isomers of known geometrical purity) fortification solution to result in fortification levels of approximately 0.30 µg and 3.0 µg per absorption tube representing the LOQ and 10 x LOQ. To this cartridge, treated air of temperature 35°C and relative humidity of ≥80% was passed through the cartridge at a constant rate of approximately 1.0 L/min for a period of approximately 6 hours equating to an approximate total air sampling volume of 0.36 m^3. On the basis of this air sampling volume, the fortification levels of imiprothrin (sum of isomers) equate to approximately 0.83 µg/m^3 and 8.4 µg/m^3 (ambient air) and 0.82 µg/m^3 and 8.5 µg/m^3 (warm, humid air).

The adsorbent material is then subsequently extracted with ethyl acetate – an aliquot is then taken and evaporated to dryness prior to being re-dissolved in toluene for analysis via GC-MS/MS using lindane as an internal standard. This is considered to be an appropriate internal standard as it is never found in imiprothrin and is well resolved via the analytical parameters used. It is noted however that it elutes before imiprothrin but the retention times are not vastly different. A Thermo TG-5MS column (60m x 0.32mm i.d., 0.25µm film thickness) was used with helium carrier gas and oven temperatures 60°C to 300°C and using m/z 123→81 (for quantification) and m/z 123→79 (for confirmation). No matrix effects were noted.

The extraction efficiency of the adsorbent material and storage stability of extracts was investigated at fortification rates of 10 x LOQ and acceptable results were achieved relevant to the periods of storage used in this study. . In addition, the retention efficiency of the adsorbent material was investigated at a fortification rate of 10 x LOQ via investigation of breakthrough determination. No breakthrough at levels greater than approximately 30% of the LOQ was observed.

Appropriate validation data are shown above – the method is considered acceptably validated for the determination of imiprothrin (in respect to the sum of isomers and the individual cis- and trans- isomers). The supported LOQ of 0.82-0.83 µg/m^3 of air (based on the sum of isomers) is considered acceptable on the basis of the lowest relevant exposure level of 0.1 mg/kg bw/day which results in a concentration level of 0.03 mg/m^3 air (i.e. 30 µg/m^3 air).

No validation data are available to demonstrate that the method can acceptably quantify the levels of the 1R and 1S isomers individually – indeed this is not expected as it does not appear that a chiral column is employed. This therefore represents a worse-case scenario – levels of 1S isomer are expected to be very low in comparison to the levels of 1R isomer present and there is not considered to be a toxicological differential therefore this is not considered to be of undue concern and the method can be considered acceptable.

Analytical methods for water Development and Validation of the Residue Analytical Method for S-41311 TG in Surface Water, RCC Project No. 763481, Wais, A. 2000										
Analyte (type of analyte e.g. active substance)	**Medium**	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
						Range	Mean	RSD		
Imiprothrin (active substance)	Water (Surface – river)	GC-NPD Confirmed by GC-MS	0.1 µg/L 1 µg/L	0.01 – 1.0 µg/ml (r^2 = 0.997)	Chromatograms showed no interference. Confirmation via MS (m/z 151)	[redacted] [redacted]	101.58 97.1	[redacted] [redacted]	0.1 µg/L	Wais, A (2000), [redacted]

Samples of surface water were fortified with imiprothrin – sodium chloride was then added and the imiprothrin was extracted with dichloromethane. The dichloromethane extracts were dried with sodium sulphate and then evaporated to dryness. The resulting residue was then dissolved in acetone/0.02% polyethylene glycol prior to determination via GC-NPD using a 20m x 0.25mm DB5 column (Rtx-5 for GC-MS) with helium carrier gas. Oven temperature 60°C raising to 180°C (for 3 mins) then to 280°C for 6 minutes. Injector temperature 270°C, detector temperature 300°C.

Appropriate chromatograms were supplied and are acceptable. The method appears acceptably validated for determination of imiprothrin (R and S isomers) in surface (river) water with a LOQ of 0.1 µg/L.

Only one sample of river water has been validated within the supporting study. Details regarding the water sample used have been provided – key information is summarised below:

Type	**Surface water**
Source	River Wiese, Mambach, Germany
Total organic carbon (TOC)	2.0 mg C/L
pH	5
Residue of evaporation	100 mg/L
Hardness (°dH)	2

It is considered that this sample of surface water is of typical composition and is acceptable. No samples of drinking water have been evaluated under this study, however this is not considered to be of concern given that a LOQ of 0.1 µg/L (which complies with the EU drinking water limit as specified within the Drinking Water Directive) has been acceptably validated.

The predicted no effect concentration level (PNEC) as detailed within Document I, Section 2.2.2.2 for surface water is calculated as 3.8×10^{-5} mg/L (0.038 µg/L) which is lower than the limit of quantification for the method which is 0.1 µg/L. Consequently, it is considered that further validation data will be required to support a lower LOQ in surface water to accommodate the calculated PNEC. **DATA GAP**

Analytical methods for animal and human body fluids and tissues										
Analyte (type of analyte e.g. active substance)	**Matrix**	**Analytical method**	**Fortification range / Number of measurements***	**Linearity**	**Specificity**	**Recovery rate[1] (%)**			**Limit of quantification (LOQ) or other limits**	**Reference**
						Range	Mean	RSD		
No method has been provided for determination of imiprothrin within animal and human body fluids and tissues. Under Regulation 528/2012, such a method is only a requirement in situations such that the active substance is classified as toxic or very toxic. Such a classification is not proposed for imiprothrin and hence a validated method is not considered necessary.										