

Report	IIA 4.5/01 (OECD) / CA 4.1.2/09 (EU)	
Authors (year):	Janusch, F. (2014a)	
Title:	SL-573 and metabolite MT-2153: Validation of a residue analytical method for the determination of SL-573 and metabolite MT-2153 in drinking, ground and surface water	
PMRA no.	2522688	
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Owner:	Ishihara Sangyo Kaisha, Ltd., Japan	
Testing facility and address:	Harlan Laboratories Ltd., Zelgliweg 1, 4452 Itingen, Switzerland	
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Guideline(s) followed:	SANCO/825/00 rev. 8.1 (2010)	
Deviations from guidelines:	None	
GLP	Yes	Federal Office of Public Health (Switzerland)

Study Classification:

EPA: Acceptable

Summary written by: Katherine Keppel-Jones, PMRA, on November 25, 2015

Peer reviewed by: Kim Davis, PMRA, on January 26, 2016

Secondary review by: Marianne Mannix, EPA
Rochelle Bohaty, EPA

Marianne A. Mannix

Rochelle F. Bohaty

Digitally signed by MARIANNE MANNIX
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Executive summary

A method was validated to determine SL-573 and MT-2153 in drinking water, groundwater and surface water using LC-MS/MS. The LOQ was 0.01 µg/L. In samples fortified at 0.01 and 0.10 µg/L, mean recoveries were 70 - 110% with relative standard deviations ≤20%, demonstrating acceptable accuracy and precision of the analytical method. Storage of fortified matrices at refrigerator temperature (5°C) for four (drinking water) or seven days (groundwater and surface water) had no impact on recoveries of MT-2153; however there was an impact on recoveries of SL-573 and so samples should be analysed on the day of extraction.

Analyte / reference substance 1

ISO common name: Tolpyralate
Code no.: SL-573
CAS no.: 1101132-67-5
Lot/batch no.: 20120131
Purity: 99.9%
Description: Light yellow powder

Analyte / reference substance 2

Code no.: MT-2153
CAS no.: Not available
Lot/batch no.: 20120615
Purity: 99.5%
Description: White powder

Test matrices

1. Drinking water (from testing facility)
2. Groundwater (from fountain at 4460 Gelterkinden, Switzerland)
3. Surface water (from river Ergolz at 4415 Lausen, Switzerland)

Table 6. Characteristics of the water test matrices

Parameter	Drinking water	Groundwater	Surface water
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pH	6.87	8.15	8.23
Dissolved organic carbon (mg/L)	0.86	-	-
Total organic carbon (g/L)	-	0.0	0.0
Total hardness (°fr.H) ¹	38.4	18.0	39.6
Evaporation residue (g/L)	-	0.21	0.56
Filtration residue (mg)	-	1.0	0.6
¹ Presumed by the reviewer to mean French degree of hardness, where 1 °f means that 1 L of water contains dissolved hardness minerals equivalent to 10 mg of CaCO ₃ .			

Principle of the method

The analytical method involved passing the fortified matrix through a solid phase extraction cartridge, eluting with acetonitrile and then methanol. The eluate was evaporated to dryness under N₂ and the residue re-dissolved in methanol/water (20/80 v/v) containing 5 mM ammonium acetate prior to analysis by LC-MS/MS. Ion transitions monitored were *m/z* 485.3>383.3 (quantification) and *m/z* 485.3>409.3 (confirmation) (SL-573) and *m/z* 383.3>111.2 (quantification) and *m/z* 383.3>325.2 (confirmation) (MT-2153). Matrices were fortified at 0.01 and 0.1 µg/L (five replicates at each level).

Specificity

In control (untreated) samples, there was no apparent response (i.e. <30% of the LOQ) in the regions of the chromatogram at the retention times of SL-573 and MT-2153. As the chosen detection principle (LC-MS/MS with two transitions) was highly specific, no separate confirmatory method was required.

Linearity

The response of the LC-MS/MS system to standard solutions of SL-573 and MT-2153 was linear over the range 0.2 ng/mL to 7.5 ng/mL ($r \geq 0.9994$ for SL-573 and ≥ 0.9996 for MT-2153).

Accuracy

The method was validated at 0.01 µg/L and 0.10 µg/L. Results obtained were within guideline requirements (mean recoveries 70 - 110%).

Precision (repeatability)

Results obtained were within guideline requirements (relative standard deviations $\leq 20\%$).

Table 7. Validation data for tolpyralate (SL-573) in water

Fortification level (µg/L)	Matrix	Number of replicates	Mean recovery (%)	Relative standard deviation (%)
Quantification transition (<i>m/z</i> 485.3>383.3), retention time ~3.7 min				
0.01	Drinking water	5	86	8
0.10		5	85	10
		Total = 10	Overall mean = 85	Overall = 8
0.01	Groundwater	5	87	6
0.10		5	89	12
		Total = 10	Overall mean = 88	Overall = 9
0.01	Surface water	5	83	7
0.10		5	78	6
		Total = 10	Overall mean = 81	Overall = 7
Confirmatory transition (<i>m/z</i> 485.3>409.3)				
0.01	Drinking water	5	88	5
0.10		5	85	9
		Total = 10	Overall mean = 87	Overall = 7
0.01	Groundwater	5	88	7
0.10		5	88	11
		Total = 10	Overall mean = 88	Overall = 8
0.01	Surface water	5	85	5
0.10		5	78	5
		Total = 10	Overall mean = 82	Overall = 7

Duplicate control samples were analysed and no residues were detected

Table 8. Validation data for MT-2153 in water

Fortification level ($\mu\text{g/L}$)	Matrix	Number of replicates	Mean recovery (%)	Relative standard deviation (%)
Quantification transition (m/z 383.3>111.2), retention time ~1.9 min				
0.01	Drinking water	5	86	4
0.10		5	94	6
		Total = 10	Overall mean = 90	Overall = 7
0.01	Groundwater	5	91	5
0.10		5	101	6
		Total = 10	Overall mean = 96	Overall = 8
0.01	Surface water	5	94	15
0.10		5	96	10
		Total = 10	Overall mean = 95	Overall = 12
Confirmatory transition (m/z 383.3>325.2)				
0.01	Drinking water	5	89	4
0.10		5	95	5
		Total = 10	Overall mean = 92	Overall = 6
0.01	Groundwater	5	96	7
0.10		5	100	6
		Total = 10	Overall mean = 98	Overall = 7
0.01	Surface water	5	94	12
0.10		5	97	9
		Total = 10	Overall mean = 96	Overall = 10

Duplicate control samples were analysed and no residues were detected

Limit of quantification (LOQ) and limit of detection (LOD)

The limit of quantification is defined as the lowest fortification level with mean recoveries ranging from 70% to 120% at a relative standard deviation of $\leq 20\%$. These criteria were fulfilled for SL-573 and MT-2153 in all three matrices with an LOQ of 0.01 $\mu\text{g/L}$.

Based on the lowest calibration standard (0.2 ng/mL), the limit of detection was equivalent to 0.003 $\mu\text{g/L}$.

Storage stability

The stability of fortified matrices was examined for drinking water over a period of four days and for groundwater and surface water over a period of seven days. Samples were stored at $5 \pm 3^\circ\text{C}$ before LC-MS/MS measurement. The results showed that, while there was no impact on MT-2153 recovery due to the storage period in drinking, ground and surface water, there was an impact for SL-573; thus the samples should be analysed on the day of extraction.

Conclusion

An analytical method for the determination of SL-573 and MT-2153 in drinking water, groundwater and surface water was validated at 0.01 $\mu\text{g/L}$ (the LOQ) and 0.10 $\mu\text{g/L}$ in terms of specificity, linearity, accuracy and precision. Residues were quantified using the LC-MS/MS ion transitions of m/z 485.3>383.3 (quantification) and m/z 485.3>409.3 (confirmation) (SL-573) and m/z 383.3>111.2 (quantification) and m/z 383.3>325.2 (confirmation) (MT-2153). Samples should be analysed on the day of extraction.

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