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Final Report

Independent Laboratory Validation for the Determination of Metamitron in Soil and Sediment

Data Requirements and Guidelines

SANCO/825/00 rev. 8.1
OCSPP 850.6100

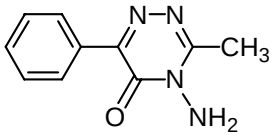
2 Study Objective

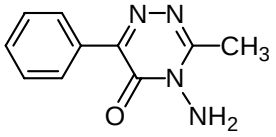
The objective of the study was to independently validate the “sponsor” method for the determination of Metamitron in soil and sediment in accordance to the guidance document SANCO/825/00, rev. 8.1 of the European Commission. The lowest tested limit of quantification is 0.01 mg/kg.

3 Materials and Methods

3.1 Test / Reference Item(s)

The test / reference item listed in the tables below may not be yet classified or has been identified as 'Toxic' or by the signal word 'Danger'. Appropriate personal protective measures should be taken in accordance to the test facilities SOPs and the MSDS, if available.

Reference Item			
Test item name	Metamitron	Batch number	2C/15
EAS Test item code	M-00001874	Appearance / colour	solid / white
Chemical name	4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one		
CAS number	41394-05-2	Purity analysed	99.9 % (w/w)
Chemical structure		Molecular weight	202.2 g/mol
Density	not applicable	Signal word(s)	warning
Issue date of certificate	Mar 2015	Expiry date	30 Jun 2022
		Storage conditions	cool (≤ 10 °C), dark, dry

Reference Item			
Test item name	Metamitron Technical	Batch number	201607228
EAS Test item code	M-00014997	Appearance / colour	solid / white
Chemical name	4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4*H*)-one		
CAS number	41394-05-2	Purity analysed	99.5 % (w/w)
Chemical structure		Molecular weight	202.2 g/mol
Density	not applicable	Signal word(s)	warning
Issue date of certificate	12 Dec 2017	Expiry date	31 Dec 2019
		Storage conditions	ambient (5 °C – 30 °C), dark, dry

Specifications essential for correct identification of the test / reference item(s) and for use under GLP are based on the information as provided by the study sponsor (e.g. certificate(s) of analysis). They have not been verified by the test facility and might have not been generated under GLP, except where this is explicitly claimed.

Additional specifications for test / reference item characterisation originate from (non-GLP) sources other than the study sponsor.

3.2 Test System(s), Sample Origin, Preparation and Storage

Test System (Commodity)	Preparation and Origin
Soil	Certified standard soil (loamy sand LUFA 2.2) was obtained from LUFA Speyer GmbH, Germany. A summary of characterization data was included in the final report (see Appendix G). The soil samples are in homogenised state and were stored at room temperature. The moisture content was determined in accordance with the test site's SOP.
Sediment	Artificial soil • 4.5 % (dry weight) sphagnum peat • 20 % (dry weight) kaolin clay (kaolinite content ≥ 30 %) • 75.28 % (dry weight) quartz sand (grain size ≤ 2 mm, but > 50 % of particles in the range of 50-200 µm) • 0.22 % lime (calcium carbonate) The dry constituents were blended in the correct proportions and mixed thoroughly in an electric mixer.

- Weighed sub-samples were stored at ≤ -18 °C in the dark until fortification and extraction.
- The moisture content of the matrices was determined in accordance with the test site's SOP by drying test portions in an oven at 105 °C overnight.

3.3 Method Summary

Method Reference(s)	Sponsor provided method: PTRL Europe Study, Report No. P/B 1355 G [4]
Validation Status	Validated according to SANCO/825/00 rev. 7 (17/3/2004)
Extraction	Acidification of a 25 g soil sample with 1 mL acetic acid, followed by addition of 50 mL methanol. Agitation on horizontal shaker and filtration over filter paper. Extraction is repeated twice.
Dilution	Sample dilution (1+9, v/v) with water
Storage	Final sample extracts were stored at 1 °C to 10 °C in the dark until analysis
Detection	Liquid chromatography with tandem mass spectrometry (LC-MS/MS)
Limit of Quantification (LOQ)	0.01 mg/kg (original LOQ 0.05 mg/kg)
Limit of Detection	20 % of the LOQ

Additions to the original method other than optimization of instrumental parameters were the addition of the test system sediment and the validation of an additional concentration level of 0.01 mg/kg (LOQ). No other addition or modification was done and no communication with the method developers or others familiar with the method was necessary in order to carry out the analysis.

4 Validation Procedure, Results and Discussion

4.1 Selectivity

LC-MS/MS determination was conducted by monitoring two (2) mass transitions (203→175 *m/z* and 203→104 *m/z*). Mass transition 203→175 *m/z* is proposed to be used for quantification but both mass transitions are applicable interchangeably for quantification and confirmation.

A reagent blank and two (2) control samples per matrix were extracted and analysed according to the method to investigate the presence of residue and/or background interference at the retention time of Metamitron. For both mass transitions, the samples showed no significant interference (above 20 % of LOQ) at the retention time of Metamitron in any investigated matrix, therefore showing that the method is highly specific.

Blank correction was not performed.

4.2 Matrix Effects

The effect of matrix on the LC-MS/MS response was assessed by comparing peak areas of matrix-matched standards (90 % matrix amount) with solvent standards at identical nominal concentrations. Matrix effects were calculated as follows:

Matrix effect (%)	$= [(100 \cdot A_{Matrix\text{-}Std}) / (A_{Solv\text{-}Std})] - 100$
$A_{Solv\text{-}Std}$	Peak area of solvent standard
$A_{Matrix\text{-}Std}$	Peak area of matrix-matched standard

The matrix effects are summarised in the table below.

Matrix / Commodity	Standard Concentration (ng/mL)	Matrix Effect for Metamitron (%)	
		Quantification (203→175 m/z)	Confirmation (203→104 m/z)
Soil	10	(-) 2.4	(-) 3.4
	5	(-) 2.9	(-) 3.4
	2	(-) 4.0	(-) 4.3
	1	(-) 2.8	(-) 1.4
	0.5	(-) 2.7	(-) 4.0
	0.1	(-) 4.2	(-) 3.4
Sediment	10	(-) 4.6	(-) 5.6
	5	(-) 5.8	(-) 7.0
	2	(-) 8.6	(-) 8.6
	1	(-) 3.4	(-) 4.6
	0.5	(-) 4.1	(-) 6.2
	0.1	(-) 6.9	(-) 6.2

(+) matrix enhancement; (-) matrix suppression

Matrix suppression or enhancement was < 20 % for all investigated matrices and thus deemed to be insignificant. However, matrix-matched standards were used for quantification throughout the study.

4.3 Linearity

The linearity of the detector response was demonstrated by single determination of matrix-matched calibration standards at eight (8) concentration levels ranging from 0.025 ng/mL to 10 ng/mL. This range corresponds to a fortification level of 0.002 mg/kg to 0.8 mg/kg and thus covers the range from no more than 20 % of the limit of quantification (LOQ) and at least + 20 % of the highest analyte concentration detected in a (diluted) sample extract.

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4.4 Quantification

Quantification was performed using a calibration curve that fulfilled the above given criteria with additional correction for the mean response of standard injections bracketing the injections of the unknown specimen extracts.

4.5 Accuracy and Precision

Accuracy was determined by fortification of control samples with known amounts of the reference item and subsequent determination of the recoveries when applying the extraction procedure. Precision was determined by repeatability (relative standard deviation).

4.6 Limit of Quantification (LOQ) and Limit of Detection (LOD)

The LOQ of the method is defined as the lowest analyte concentration at which the methodology had been successfully validated. Thus, an LOQ of 0.01 mg/kg was confirmed for Metamitron in soil and in sediment. The LOQ was calculated on a wet weight basis.

The LOD was set at 20 % of the LOQ which is 0.002 mg/kg. As can be seen from representative chromatograms in Appendix D the chromatographic peaks at the LOD were equivalent to three times or more than the background noise.

4.7 Stability of Stock (and Fortification) Solutions

The stock solution prepared in methanol were stored at 1 °C to 10 °C for 7 days in the dark, which was sufficient to cover the length of time they were used in this study (*i. e.* 1 days). After this time freshly prepared dilution(s) of the stock solution(s) were compared to freshly prepared dilutions of freshly prepared stock solutions. One (1) mass transition was evaluated.

Results obtained are summarised in the table below.

Analyte	Solvent of stock solution	Standard conc. of diluted stock solution (ng/mL)	Storage period (Days)	Difference (%) of stored stock solution compared to freshly prepared stock solution
Metamitron (203→175 m/z)	Methanol	1	7	+ 6

The peak area of the stored diluted stock solution was within ± 20 % of the mean peak areas of the freshly prepared diluted stock solution indicating that stock solutions are stable when stored at 1 °C to 10 °C in the dark for 7 days. Fortification solutions were prepared in the same solvent as the stock solutions and were also stored at 1 °C to 10 °C in the dark. Therefore, investigation of the stability of fortification solutions was not necessary.

4.8 Stability of Solvent Calibration Solutions

The calibration solutions prepared in the respective solvent were stored at 1 °C to 10 °C for 7 days in the dark, which was sufficient to cover the length of time they were used in this study (*i. e*. 1 days). After this time two (2) solvent standard solutions were compared to freshly prepared solvent standard solutions of the same concentration. One (1) mass transition was evaluated. Results obtained are summarised in the table below.

Analyte	Solvent for calibration solutions	Standard conc. (ng/mL)	Storage period (Days)	Difference (%) of stored solution compared to a freshly prepared solution
Metamitron (203→175 m/z)	Water/acetonitrile (1/1, v/v)	1	7	+ 18
		5	7	+ 20

The peak areas of the stored solutions were within ± 20 % of the peak areas of the freshly prepared solutions indicating that solvent standards solutions are stable when stored at 1 °C to 10 °C in the dark for 7 days.

Matrix-matched calibration standards were used for quantification throughout the study. The investigation of extract stability demonstrates the stability of the matrix-matched calibration standards.

4.9 Extract Stability

Following the first analysis, the final extracts fortified at the 10x LOQ level together with one (1) control sample extract were stored at 1 °C to 10 °C in the dark for 7 days. After this period, the final extracts were re-analysed against freshly prepared calibration standards. One (1) mass transition was evaluated.

4.10 Storage Stability

Storage stability testing with fortified or incurred samples as mentioned in the guidance document SANCO/825/00, rev. 8.1 was not conducted as part of this study.

4.11 Extractability

Testing of extraction efficiency as mentioned in the guidance document SANCO/825/00, rev. 8.1 was not conducted as a part of this study.

5 Conclusion

The method was successfully validated for the determination of Metamitron in/on soil and sediment from the tested LOQ of 0.01 mg/kg up to 0.5 mg/kg according to the guidance document SANCO/825/00, rev. 8.1.

Additions to the original method other than optimization of instrumental parameters were the addition of the test system sediment and the validation of an additional concentration level of 0.01 mg/kg (LOQ). No other addition or modification to the original method Bacher, R. (2007) was done. Primary validation and independent laboratory validation were carried out at different locations, by different study personnel, and using different instrumentation and stocks of chemicals. No communication with the method developers or others familiar with the method was necessary to carry out the analysis.

Appendix A

Analytical Method

I. Reagents and Materials

Information pertaining to the identity and source of reagents is summarised in Table I. Alternative, equivalent reagents and materials may be used, unless specifically stated otherwise.

Table I: Identification of Reagents and Materials

- Acetic acid p.a.
  (Prolabo, Art. No. 20104.298)
- Acetonitrile HPLC grade
  (VWR, Art. No. 83639.320)
- Formic acid p.a.
  (Prolabo, Art. No. 20318.320)
- Methanol LCMS grade
  (Honeywell, Art. No. 34966-2.5L))
- Water HPLC grade
  (Merck, Art. No. 1.15333.2500)
- Demineralized water
  (prepared at laboratory)
- Folded Filters
  (Whatman, Art. No. 10311644)

II. Instrumentation and Apparatus

Information pertaining to the identity of instruments and apparatus is summarised in Table II. Alternative, equivalent reagents and materials may be used, unless specifically stated otherwise.

Table II: Identification of Instrumentation and Apparatus

- Adjustable pipettes
  (Eppendorf: Research 10-100 µL, Research 100-1000 µL)
- Common laboratory glassware
- Balances
  (Sartorius CPA224S, Kern PFB 2000-2)
- Dispenser
  (Brand Dispensette 10-100 mL)
- Horizontal flatbed shaker
  (Bühler SM 25 A)
- Drying chamber
  (Memmert, VWR DL115)
- Laboratory centrifuge
  (Hettich Rotina 380)
- Vortex mixer
  (Scientific Industries Genie 2, VWR Analog Vortex Mixer)
- HPLC-MS/MS
  (Applied Biosystems API5000 with Agilent 1290 Infinity HPLC)

III. Reagent Solutions and Mobile Phases

Mobile Phase A: Water + 0.1 % formic acid

Mobile Phase B: Acetonitrile + 0.1 % formic acid

IV. Preparation of Standard Solutions

Stock solutions of the analyte are prepared by dissolving a weight of the test / reference item. Each stock solution is allocated a reference number.

The stock solutions are further diluted for use as fortification solutions in the recovery process and as (intermediate) standard solutions for subsequent use as solvent calibration solutions and preparation of matrix-matched calibration solutions.

Matrix-matched calibration solutions are prepared using final sample extracts of control (untreated) samples of a respective matrix which are then fortified with (intermediate) solvent standard solutions.

All solutions are stored 1 °C to 10 °C (target) in a brown glass vial in the dark.

A summary of the typical dilutions to be carried out is presented in the following tables.

Table III: Preparation of a Stock Solution of Metamitron in Methanol

Purity of reference item* (%)	Weighed amount of reference item (mg)	Amount of analyte corrected for purity (mg)	Final volume (mL)	Equivalent concentration (µg/mL)	Reference of standard solution produced
99.9	10.2	10.19	10.19	1000	S1000
99.5	10.1	10.05	10.05	1000	S1000

* to be taken from the Certificate of Analysis

Table IV: Preparation of Fortification Solutions of Metamitron in Methanol

Reference of standard solution used	Concentration (µg/mL)	Volume taken (mL)	Final volume (mL)	Equivalent concentration (ng/mL)	Reference of standard solution produced
S1000	1000	0.625	5	125000	S125
S125	125	1.00	10	12500	S12.5
S100	100	0.250	10	2500	S2.5

Table V: Preparation of Intermediate Standard Solutions of Metamitron in Methanol

Reference of standard solution used	Concentration (ng/mL)	Volume taken (mL)	Final volume (mL)	Equivalent concentration (ng/mL)	Reference of standard solution produced
S125	125	0.08	10	1000	S1

Table VI: Preparation of Solvent Calibration Solutions of Metamitron in Acetonitrile/Water (1/1, v/v)

Reference of standard solution used	Concentration (ng/mL)	Volume taken (µL)	Final volume (mL)	Equivalent concentration (ng/mL)	Reference of standard solution produced
S1	1000	100	1.0	100	Std 100 ng/mL
S1	1000	50	1.0	50.0	Std 50 ng/mL
S1	1000	20	1.0	20.0	Std 20 ng/mL
Std 100 ng/mL	100	100	1.0	10.0	Std 10 ng/mL
Std 100 ng/mL	100	50	1.0	5.0	Std 5 ng/mL
Std 10 ng/mL	10.0	100	1.0	1.0	Std 1 ng/mL
Std 10 ng/mL	10.0	50	1.0	0.50	Std 0.5 ng/mL
Std 10 ng/mL	10.0	25	1.0	0.25	Std 0.25 ng/mL

Table VII: Preparation of Mixed Matrix-matched Calibration Solutions of Metamitron in Matrix Soil or Sediment

Reference of standard solution used	Concentration (ng/mL)	Volume of solvent standard solution taken (µL)	Volume of control matrix extract taken (µL)	Equivalent concentration (ng/mL)	Reference of standard solution produced
Std 100 ng/mL	100	100	900	10.0	mStd 10 ng/mL
Std 50 ng/mL	50.0	100	900	5.0	mStd 5 ng/mL
Std 20 ng/mL	20.0	100	900	2.0	mStd 2 ng/mL
Std 10 ng/mL	10.0	100	900	1.0	mStd 1 ng/mL
Std 5 ng/mL	5.0	100	900	0.50	mStd 0.5 ng/mL
Std 1 ng/mL	1.0	100	900	0.10	mStd 0.1 ng/mL
Std 0.5 ng/mL	0.50	100	900	0.050	mStd 0.05 ng/mL
Std 0.25 ng/mL	0.25	100	900	0.025	mStd 0.025 ng/mL

V. Laboratory Specimen Preparation

Specimen preparation as done in this independent laboratory validation study is described in section 3.2 of this report.

Specimen amount to be taken for preparation of a representative sample has to be in compliance with EU Guidance document 7029/VI/95, rev. 5. Specimen preparation should be in compliance with the test facilities/sites standard operation procedures (SOPs). In case of any conflict between the requirements of SOPs and study plan, the study plan would take priority.

VI. Sample Weight(s) and Fortifications

Sample weights as done in this study are described in section 3.3 of this report.

Control (untreated) specimens of soil and sediment are fortified prior to extraction with the fortification solutions as described below. The solvent is allowed to evaporate before starting the extraction procedure.

Table VIII: Summary of Sample Weights and Fortifications

Fortified analyte(s)	Matrix	Sample weight (g)	Reference of fortification solution used	Concentration of fortification solution (ng/mL)	Volume of fortification solution added (mL)	Fortification level (mg/kg)
Metamitron	Soil	25	S2.5	2500	0.10	0.01
		25	S12.5	12500	0.10	0.05
		25	S125	125000	0.10	0.5
	Sediment	25	S2.5	2500	0.10	0.01
		25	S12.5	12500	0.10	0.05
		25	S125	125000	0.10	0.5

The LOQ is calculated on a wet weight basis.

VII. Sample Work-Up Procedure

Extraction

Extraction of soil and sediment:

1) Each 25 g ± 0.25 g homogenised specimen of lettuce soil or sediment is weighed into a 250-mL screw-capped PE bottle.
2) Recovery specimen are fortified with Metamitron**.**
3) Specimen are acidified using 1.0 mL of concentrated acetic acid.
4) For extraction, 50 mL of methanol is added.
5) The PE bottle is capped and shaken on a horizontal shaker for 30 min at 270 rpm**.**
6) The sample bottle is centrifuged for 2 minutes at about 4000 rpm.
7) Supernatant is filtered through a folded filter into a measuring cylinder.
8) Residue is re-extracted twice using 50 mL portions of methanol (for details see point 4 to 7)
9) Raw extracts are combined in a measuring cylinder.
10) Raw extract volume is adjusted to V_{Ex} = 200 mL using methanol.
11) An aliquot of the raw extract (V_1 = 0.10 mL) is transferred into an autosampler vial.
12) 0.90 mL of purified water is added to establish a final volume V_{End} of 1.0 mL.

VIII. Chromatographic and Mass Spectrometric Conditions

A summary of the typical chromatographic and mass spectrometric conditions used for quantification is included in the following table:

Table IX: Summary of chromatographic and mass spectrometric conditions

Chromatographic conditions for Metamitron in Matrices Soil and Sediment						
HPLC system	1290 Infinity Binary LC System, Agilent Technologies					
Pre-column	HPLC guard column (KJ0-4282, Phenomenex) with 4 mm C18 cartridge (AJ0-4287, Phenomenex)					
Column	Thermo AQUASIL C18, (150 mm x 3.0 mm, 3 µm, Thermo Part. No. 77503-153030)					
Column oven temperature	30 °C					
Injection volume	20 µL					
Mobile phases	Eluent A: Water containing 0.1 % (v/v) formic acid Eluent B: Acetonitrile containing 0.1 % (v/v) formic acid					
Gradient	Time [min]	% Eluent A	% Eluent B	Flow [µL/min]		
	0.00	85	15	500		
	1.00	85	15	500		
	1.01	35	65	500		
	6.00	35	65	500		
	6.01	0	100	500		
	8.00	0	100	500		
	8.01	85	15	500		
	11.00	85	15	500		
Divert valve	0.0 min to 2.5 min to waste; 2.5 min to 4.5 min to MS; 4.5 min to 11.0 min to waste					
Retention time	Metamitron: approx. 3.3 min					
Mass spectrometric conditions for Metamitron in Matrices Soil and Sediment						
MS system	SCIEX TripleQuad 5000 System, SCIEX (Triple quadrupole mass spectrometer)					
Ionisation type	Electrospray ionisation (ESI, TurboIon Spray)					
Polarity	Positive ion mode					
Scan type	MS/MS, Multiple Reaction Monitoring (MRM)					
Capillary voltage (IS)	5000 V		Ionspray turbo heater (TEM)		550 °C	
Curtain gas (CUR)	40 (arbitrary units)		Gas flow 1 (GS1)		40 (arbitrary units)	
Collision gas (CAD)	5 (arbitrary units)		Gas flow 2 (GS2)		70 (arbitrary units)	
Analyte monitored	Mass transition monitored *(m/z)*	Declustering potential (DP) [V]	Entrance potential (EP) [V]	Collision energy (CE) [V]	Cell exit potential (CXP) [V]	Dwell time [ms]
Metamitron	203 → 175[#]	50	10	25	12	250
	203 → 104	50	10	35	20	250

[#] proposed/used for quantification but any of the ions listed can be used for quantification

IX. Special Precautions

None

X. Calculation of Results

Quantification is performed using calibration plots with a minimum of five (5) different concentration levels covering the required calibration range.

A calibration curve is injected prior to analysis of the samples with additional correction for the mean response of standard injections bracketing the injections of the unknown samples (typically not greater than five (5)).

The linearity of the detection system is demonstrated by use of standard solutions covering a working range which is equivalent no more than 20 % of the LOQ and at lea

st + 20 % of the highest analyte concentration level in a sample extract.

A linear regression is performed with 1/x weighting. The correlation coefficient (R) must be greater or equal to 0.995 meaning that the coefficient of determination (R^2) must be greater or equal to 0.990.

A linear calibration function (y = a + b·x) as determined by software Analyst 1.6.3, SCIEX is used to calculate the analyte concentration in final extracts as follows:

C_A =	$\frac{A_A - a}{b}$
C_A	Concentration of analyte in final extract (ng/mL) (x)
A_A	Peak area of analyte in the final solution (counts) (y) as obtained by integration with software Analyst 1.6.3, SCIEX
a	y -axis Intercept of the calibration curve (counts)
b	Slope of calibration curve (counts mL/ng)

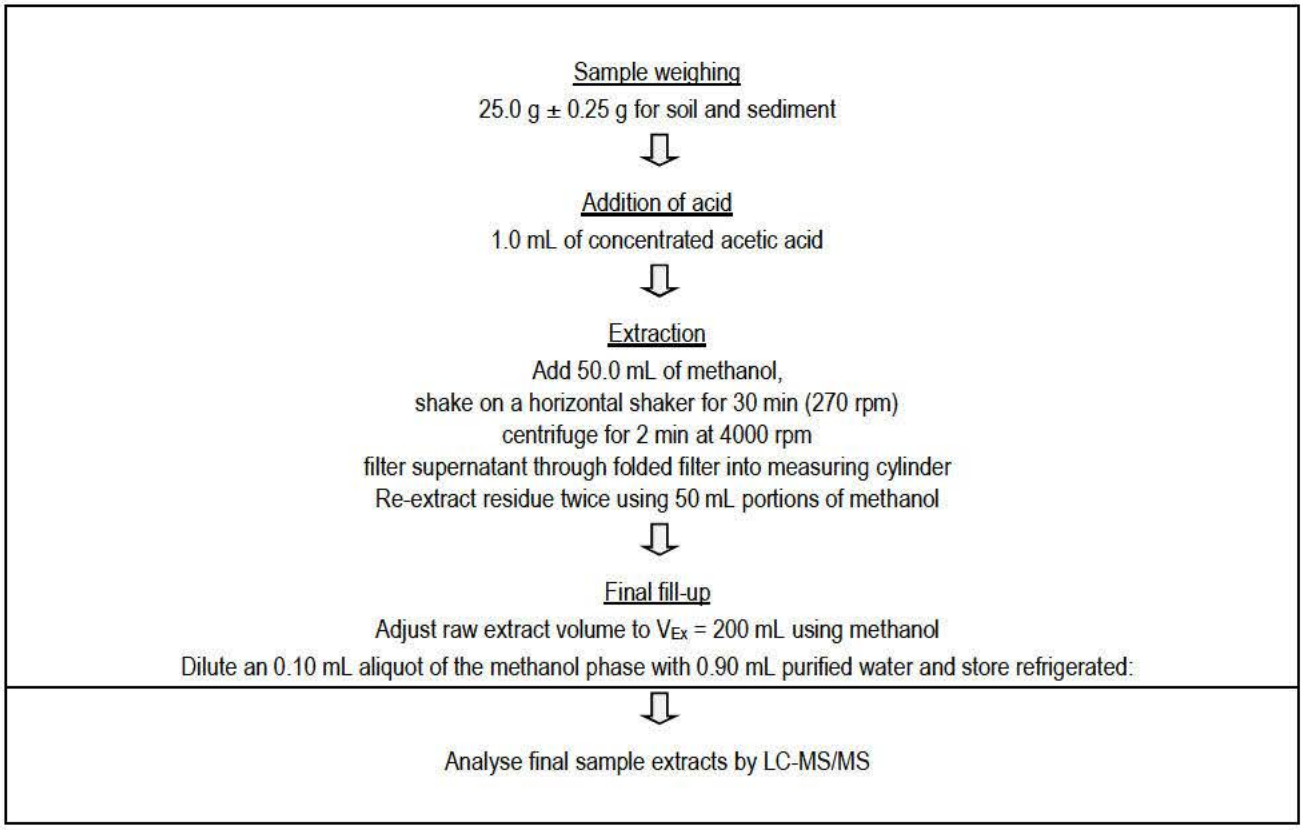
The residues are calculated by reference to the mean response of the appropriate bracketing matrix standards as follows:

R =	$\frac{C_1}{C_2} \times C_A \times \frac{V_{Ex} \times V_{End} \times DF}{W \times V_{Ali} \times CF}$
R	Analyte Residue (mg/kg)
C_1	Nominal concentration of bracketing matrix standards (ng/mL)
C_2	Average calculated concentration of matrix standards bracketed between samples, obtained from the matrix calibration function (ng/mL)
C_A	Analysed concentration of the sample, as calculated from the matrix calibration function (ng/mL)
V_{Ex}	Extraction volume (200 mL)
V_{End}	Final volume (1 mL)
V_{Ali}	Aliquot of the extract (0.1 mL)
W	Sample weight (25 g)
DF	Dilution factor
CF	Conversion from ng into µg (1000)

The recovery of a fortification experiment is calculated as follows:

Recovery (%) =	$\frac{R}{F} \times 100$
R	Analyte residue (mg/kg)
F	Nominal fortification level (mg/kg)

XI. Method Flow Chart



XII. Safety Information

Equipment	Hettich centrifuge – ensure all 4 buckets are equally balanced

Reagents	H- and P-Codes	H- and P-Phrases
Methanol	H225 H301+H311+H331 H370	• Highly flammable liquid and vapour. • Toxic if swallowed, in contact with skin or if inhaled. • Causes damage to organs
	P210	• Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
	P280	• Wear protective gloves/protective clothing/eye protection/face protection.
	P302+P352+P312	• IF ON SKIN: Wash with plenty of soap and water, and call a POISON CENTER/doctor/… if you feel unwell.
	P304+P340+P311	• IF INHALED: Remove person to fresh air and keep comfortable for breathing and call a POISON CENTER/doctor/…
	P370+P378	• In case of fire: use extinguishing powder or dry sand.
	P403+P235	• Store in a well-ventilated place. Keep cool.
Acetonitrile	H225 H302, H312, H332 H319	• Highly flammable liquid and vapour. • Harmful if swallowed, in contact with skin, if inhaled. • Causes serious eye irritation.
	P210	• Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
	P280	• Wear protective gloves/protective clothing/eye protection/face protection.
	P305+P351+P338	• IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
	P309+P311	• IF exposed or if you feel unwell: call a POISON CENTER or doctor/physician.
Formic acid	H314	• Causes severe skin burns and eye damage.
	P280	• Wear protective gloves/protective clothing/eye protection/face protection.
	P305+P351+P338	• IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
	P301+P330+P331	• IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
	P309+P311	• IF exposed or if you feel unwell: call a POISON CENTER or doctor/physician.

Acetic acid	H226 H290 H314 P210 P280 P305+P351+P338 P301+P330+P331 P308+P310	• Flammable liquid and vapour. • May be corrosive to metals. • Causes severe skin burns and eye damage. • Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking. • Wear protective gloves/protective clothing/eye protection/face protection. • IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. • IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. • IF exposed or concerned: Immediately call a POISON CENTER/doctor/…