

# **FINAL REGISTRATION REPORT**

## **Part B**

### **Section 5**

#### **Analytical Methods**

Detailed summary of the risk assessment

Product code: MIEDZIAN EXTRA 350 SC

Product names: **MIEDZIAN EXTRA 350 SC,**

**~~COBRESAL EXTRA 350 SC, KARES 350 SC~~**

Chemical active substance:

**Copper as a copper oxychloride, 350 g/l**

Central

Zonal Rapporteur Member State: **Poland**

#### **CORE ASSESSMENT**

(re-authorization according art. 43, Reg. 1107/2009)

Applicant: **Synthos Agro Sp. z o.o.**

Submission date: **07/2020**

MS Finalisation date: **05/2021; 08/2022**

## Version history

When	What
07.2020	Submission date
05.2022	zRMS finalised the dRR assessment
08/2022	The Final RR

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## 5 Analytical methods

### 5.1 Conclusion and summary of assessment

Sufficiently sensitive and selective analytical methods are available for the active substance and relevant impurities in the plant protection product Miedzian Extra 350 SC.

Noticed data gaps:

- none

### 5.2 Methods used for the generation of pre-authorization data (KCP 5.1)

#### 5.2.1 Analysis of the plant protection product (KCP 5.1.1)

##### 5.2.1.1 Determination of active substance and/or variant in the plant protection product (KCP 5.1.1)

An overview on the acceptable methods and possible data gaps for analysis of Copper oxychloride ~~and Copper oxychloride~~ in plant protection product is provided as follows:

Comments of zRMS:	The analytical method for the determination of active substance copper oxychloride in the plant protection product MIEDZIAN EXTRA 350 SC is suitable for the determination of the content of active substance.  The proposed analytical methods have been fully validated in terms of the interference, specificity, linearity and accuracy (recovery and repeatability). Proposed method fulfils the requirements of SANCO/3030/99 rev. 5 guidance.
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Reference: Karolina Stępień, MSc.

Report Miedzian Extra 350 SC Method development and validation for determination of the content of active substance in the formulation, Karolina Stępień MSc., 2019

Guideline(s): SANCO/3030/99 rev.5

Deviations: No

GLP: Yes

Acceptability: Yes

### Materials and methods

The content of active substance in the examined specimen was determined using potentiometric titration with platinum electrode method according to the analytical procedure.

#### Examined material:

Examined material: Miedzian Extra 350 SC  
Date of production: 01.05.2019  
Batch number: A1991051

Manufacturer: Synthos Agro Sp. z o.o.  
Test item code: 39/BF – 27/19

#### Reference material:

Copper oxychloride. IPO. batch no 14022701. purity 97.0%

#### Equipment:

- Titrometer Titroline 7750 - SI Analytics
- Analytical balance Mettler. AT26I DeltaRange
- Beaker. 150 mL volume
- Volumetric flask. 100 mL volume
- Pipette 10 mL volume

#### Reagents

- Sodium thiosulfate. standardized solution. (0.1M). POCh (the sodium thiosulfate ampoule for 1000 ml,  $c(\text{Na}_2\text{SO}_4) = 0,1 \text{ M/l}$  were introduced into a 1000 ml flask with a screw cap and water was added up to the volume)
- Sodium fluoride. pure for analysis. POCh (aqueous saturated solution - 48 g/l)
- Potassium iodide. pure for analysis. POCh
- Sulphuric acid. pure for analysis (water solution 1 M) - water solution of sulphuric acid. (5.5 mL of concentrated sulphuric acid in 100 mL solution of distilled water).
- Distilled water

#### Sample preparation

About 200 mg of sample was weighed with accuracy of 0.1 mg into the beaker (150 mL). Water (50 mL). 1 M sulphuric acid (8 mL). potassium iodide (1.5 g) and sodium fluoride (5 mL) were added. The solution was potentiometric titrated with 0.1 M sodium thiosulphate.

#### Calculations

The percentage content of copper was calculated using the following equation:

$$\% \text{ copper content} = (V * 6.355 * 100) / m$$

Where:

V – volume [ml] of sodium thiophosphate used in titration of the tested material,  
m – mass [mg] of the sample

1 ml 0.1 M sodium thiosulphate equals 6.355 mg Cu

As a result of examination the average from five determinations of Cu (II) content in examined sample not different more than 1% of average value. Results were calculated with accuracy of 0.01%.

#### Validation - Results and discussions

**Table 5.2-1: Methods suitable for the determination of active substances copper oxychloride in plant protection product Miedzian Extra 350 SC**

	Copper Oxychloride
Author(s), year	Karolina Stępień, MSc.
Principle of method	The content of active substance in the examined specimen was determined using potentiometric titration with platinum electrode method according to the analytical procedure.

	Copper Oxychloride
<b>Linearity</b> <b>Linear between</b>  <b>from 0.05189 g to 0.1374 g</b>  <b>Correlation coefficient = 1</b>	Five standard solutions were used at the concentration range between 0.05189 g to 0.1374 g  Correlation coefficient should be $r \geq 0.99$ . The obtained result is acceptable.  $y = 91.426 x + 0.0005$
<b>Precision – Repeatability Mean</b>  <b>n = 6</b> <b>0.20 %RSD</b> <b>Hr ≤ 1</b>	The repeatability of the method was assessed on the basis of six determinations of the copper oxychloride content in examined sample.  Acceptable relative standard deviation for main ingredient (~ 35%) is $RSDr \leq \pm 1.57\%$ . The obtained result 0.20% is acceptable. Hr = 0.18 0.13
<b>Accuracy</b>  <b>n = 12</b> <b>99.29% Recovery</b>	Accuracy of active substance determination in Miedzian Extra 350 SC was assessed by recovery value at two levels of concentration.  For the main ingredient at concentration of > 10% the average recovery value should be $100\% \pm 2\%$ . The obtained result of 99.29% is acceptable.
<b>Interference/ Specificity</b>	Iodometric determination of copper is hindered by the presence of substances that can liberate iodine from iodides – as, for example, iron (III). Sodium fluoride was added to mask small quantities of iron (III).
<b>Comment</b>	This study hasn't been evaluated yet

## Conclusion

It was confirmed that the above method of determination of the active substance copper oxychloride meets validation parameters as specificity, linearity, precision and accuracy stipulated in the current guideline of SANCO /3030 /99 rev.5.

### 5.2.1.2 Description of analytical methods for the determination of relevant impurities (KCP 5.1.1)

An overview on the acceptable methods and possible data gaps for analysis of relevant impurities in plant protection product is provided as follows:

Comments of zRMS:	The analytical method for the determination of relevant impurities (As, Cd, Pb) in plant protection product MIEDZIAN EXTRA 350 SC is suitable for the determination of the content of each of the relevant impurity in the presence of each other, active substance and other components.  The proposed analytical methods have been fully validated in terms of the interference, specificity, linearity, accuracy (recovery and repeatability) and LOQ values. Proposed method fulfils the requirements of SANCO/3030/99 rev. 5 guidance.
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Report	Determination of arsenic, cadmium and lead content in the Miedzian Extra 350 SC, Iwona Karczmarzyk., 2020, Study code: K389/MB/01
Guideline(s):	SANCO/3030/99 rev.5
Deviations:	No
GLP:	Yes
Acceptability:	Yes

## Materials and methods

### Examined material:

Examined material:	Miedzian Extra 350 SC
Batch number:	A1991025
Manufacturer:	Synthos Agro Sp. z o.o.

### Reference material:

- Arsenic standard for ICP, 1000 mg/L, Merck, batch no. HC98238703, exp. 28.02.2022
- Cadmium standard for ICP, 1000 mg/L, Merck, batch no. HC74539909, exp. 30.11.2020
- Lead standard for ICP, 1000 mg/L, Merck, batch no. HC85708928, exp. 31.03.2021

### Instruments:

- ICP Emission Spectrometer ICPE - 9820, Shimadzu, internal no. C16.ICP.003, exp. 23.07.2020
- Microwave Digestion System, internal no. C16.MN.001, exp. 01.07.2020
- Microwave Digestion System, internal no. C16.MN.002, exp. 22.10.2020
- Analytical balance with 0.01 mg readability, Sartorius, internal no. C17.SC.001, exp. 18.05.2020

### Reagents and materials

- Nitric acid 65%, Suprapur®, Merck, batch no. Z0604341949, exp. 21.12.2022
- Hydrochloric acid 33%, Merck, batch no. Z0572918926, exp. 30.06.2022
- Water Type I (18,2 MW) from Milli-Q, Millipore

### Measurement conditions

Before starting the measurement, the device should be prepared for work in accordance with the manufacturer's instructions. Take measurements after setting the spectrometer operating parameters in the ranges below.

#### Spectrometer technical parameters

- Radio Freq Power: 1.20 kW
- Plasma Gas: 10.0 L/min
- Auxiliary Gas: 0.60 L/min
- Carrier Gas: 0.70 L/min
- Exposure Time: 30 sec
- Sensitivity: Wide Range
- View Direction: Axial

#### Peristaltic pump

	Low speed	High speed
Solvent Rinse	20 sec	40 sec
Sample Rinse	40 sec	15 sec
Rotation Speed	20 r.p.m.	50 r.p.m.

### Analysis Element and Wavelength

Element $\lambda$	[nm]
As	228.812
Cd	226.502
Pb	220.353

## The preparation of standard and sample solutions

### Standard solutions

#### Lead Standard stock solution 10 mg/L – MIX 1

Into a 100 mL volumetric flask accurately transfer 1.0 mL of Lead Standard for ICP and 1 mL of nitric acid (65%). Dilute to volume with water and mix well.

#### Cadmium Standard stock solution 10 mg/L – MIX 2

Into a 100 mL volumetric flask accurately transfer 1.0 mL of Cadmium Standard for ICP and 1 mL of nitric acid (65%). Dilute to volume with water and mix well.

#### Cadmium Standard stock solution 1 mg/L – MIX 3

Into a 10 mL volumetric flask accurately transfer 1.0 mL of Cadmium Standard stock solution 10 mg/L and 1 mL of nitric acid (65%). Dilute to volume with water and mix well.

#### Arsenic Standard stock solution 10 mg/L – MIX 4

Into a 100 mL volumetric flask accurately transfer 1.0 mL of Arsenic Standard for ICP and 1 mL of nitric acid (65%). Dilute to volume with water and mix well.

#### Arsenic Standard stock solution 1 mg/L – MIX 5

Into a 10 mL volumetric flask accurately transfer 1.0 mL of Arsenic Standard stock solution 10 mg/L and 1 mL of nitric acid (65%). Dilute to volume with water and mix well.

### Calibration curve

Prepare calibration standard solutions containing arsenic, cadmium and lead at the concentration range:

Element symbol	STD 0 [mg/L]	STD 1 [mg/L]	STD 2 [mg/L]	STD 3 [mg/L]	STD 4 [mg/L]	STD 5 [mg/L]	STD 6 [mg/L]
As	0.0	0.0015	0.0017	0.0019	0.0022	0.0024	0.0031
Cd	0.0	0.0029	0.0032	0.0036	0.0041	0.0045	0.0059
Pb	0.0	0.090	0.1120	0.1280	0.1440	0.1600	0.2080

#### STD 6 – 0.0031 mg/L As, 0.0059 mg/L Cd, 0.2080 mg/L Pb,

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.31 mL of MIX 5, 0.59 mL of MIX 3, 2.080 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

#### STD 5 – 0.0024 mg/L As, 0.0045 mg/L Cd, 0.1600 mg/L Pb,

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.240 mL of MIX 5, 0.450 mL of MIX 3, 1.600 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

#### STD 4 – 0.0022 mg/L As, 0.0041 mg/L Cd, 0.144 mg/L Pb,



Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.22 mL of MIX 5, 0.41 mL of MIX 3, 1.440 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**STD 3 – 0.0019 mg/L As, 0.0036 mg/L Cd, 0.128 mg/L Pb,**

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.19 mL of MIX 5, 0.360 mL of MIX 3, 1.280 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**STD 2 – 0.0017 mg/L As, 0.0032 mg/L Cd, 0.1120 mg/L Pb,**

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.17 mL of MIX 5, 0.32 mL of MIX 3, 1.120 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**STD 1 – 0.0015 mg/L As, 0.0029 mg/L Cd, 0.090 mg/L Pb,**

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.15 mL of MIX 5, 0.29 mL of MIX 3, 0.9 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**STD 0 - Blank**

Into a 100 mL volumetric flask transfer about 30 mL water, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**Control standard 1: Sc – 0.0019 mg/L As, Sc – 0.0036mg/L Cd and Sc - 0.128 mg/L Pb**

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.19 mL of MIX 5, 0.360 mL of MIX 3, 1.280 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**Control standard 2: Sc - 0.0024 mg/L As, Sc - 0.0045 mg/L Cd and Sc - 0.1600 mg/L Pb**

Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.240 mL of MIX 5, 0.450 mL of MIX 3, 1.600 mL of MIX 1, 10 mL of nitric acid (65%) and 1 mL of hydrochloric acid. Dilute to volume with water and mix well.

**Sample preparation**

Accurately transfer about 0.204 mL of sample into a vessel, add 7 mL of Nitric acid 65 % and 1 mL of concentrated Hydrochloric acid. Let stand vessel for 30 minutes. After this time degasses a sample. Close the vessel and place it in the panels of the rotor. Perform sample digestion according to the program described below. Cool down, open, degas the sample and transfer into a 50 mL volumetric flask. Fill to volume with water and mix well..

**Blank preparation**

Into a vessel, add 7 mL of concentrated Nitric acid and 1 mL of Hydrochloric acid. Let stand vessel for 30 minutes. After this time degasses a sample. Close the vessel and place it in the panels of the rotor. Perform sample digestion according to the program described below. Cool down the vessels, open and degas the sample and transfer into a 50 mL volumetric flask. Fill to volume with water and mix well.

**Mineralization program**

Ramp time [min]	Temperature [°C]	Hold time [min]
30	230	20

## Procedure

The determination of arsenic, cadmium and lead content in Miedzian extra 350 S.C. was performed by ICP-OES detection. The amounts of the arsenic, cadmium and lead were calculated using the fit of the calibration model.

## Calculations

Sample concentrations:

$$X(\text{mg/kg}) = [(E-E_0)*V*DF]/Wt$$

where:

E – concentration of the element in sample solution [mg/L]

E<sub>0</sub> – concentration of element in blank solution [mg/L]

V – volume of sample solution [mL]

DF – dilution factor (if applicable)

Wt – sample weight [g]

δ – density [g/mL] = 1.472

## Validation - Results and discussions

**Table 5.2-2: Methods suitable for the determination of the relevant impurities in plant protection product (PPP) Miedzian Extra 350 SC**

	<b>As</b> <b>max 35 mg</b>	<b>Cd</b> <b>max 35 mg</b>	<b>Pb</b> <b>max 175 mg</b>
<b>Author(s), year</b>	Iwona Karczmarzyk, 2020	Iwona Karczmarzyk, 2020	Iwona Karczmarzyk, 2020
<b>Principle of method</b>	The determination of arsenic, cadmium and lead content in Miedzian Extra 350 SC was performed by ICP-OES detection. The amounts of the arsenic was calculated using the fit of the calibration model.	The determination of arsenic, cadmium and lead content in Miedzian Extra 350 SC was performed by ICP-OES detection. The amounts of the cadmium was calculated using the fit of the calibration model.	The determination of arsenic, cadmium and lead content in Miedzian Extra 350 SC was performed by ICP-OES detection. The amounts of the lead was calculated using the fit of the calibration model.
<b>Linearity</b>  <b><u>Arsenic</u></b>  <b>Linear between</b> <b>0.0015 mg/L and 0.0031 mg/L, corresponding to the following concentration range in the product from 0.368 mg/kg mg/L to 0.76 mg/kg mg/L)</b>  <b>Correlation coefficient = 0.9996</b>  <b><u>Cadmium</u></b>  <b>Linear between</b> <b>0.0029 mg/L and 0.0059</b>	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal concentration.  Standard solutions of arsenic was prepared at six (6) concentration levels in the range of the concentration from 0.0015 mg/L – 0.0031 mg/L (corresponding to 0.368 mg/L – 0.76 mg/L for sample product) for	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal concentration.  Standard solutions of cadmium was prepared at six (6) concentration levels in the range of the concentration from 0.0029 mg/L – 0.0059 mg/L (corresponding to 0.711 mg/L – 1.446 mg/L for sample	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal concentration.  Standard solutions of lead was prepared at six (6) concentration levels in the range of the concentration from 0.09 mg/L – 0.208 mg/L (corresponding to 22.059 mg/L – 50.98 mg/L for sample

	As max 35 mg	Cd max 35 mg	Pb max 175 mg
<p>mg/L, corresponding to the following concentration range in the product from 0.711 mg/kg mg/L to 1.446 mg/kg mg/L)</p> <p><b>Correlation coefficient = 0.9998</b></p> <p><u>Lead</u></p> <p><b>Linear between 0.09 mg/L and 0.208 mg/L, correspond to the following concentration range from 22.059 mg/kg mg/L to 50.98 mg/kg mg/L)</b></p> <p><b>Correlation coefficient = 0.9999</b></p>	<p>arsenic. In the linearity calculation also the blank solution was used.</p> <p>Correlation coefficient should be <math>R^2 \geq 0.99</math>. The obtained result is acceptable.</p> <p><math>y = 20584x + 2,9122</math></p>	<p>product) for cadmium. In the linearity calculation also the blank solution was used.</p> <p>Correlation coefficient should be <math>R^2 \geq 0.99</math>. The obtained result is acceptable.</p> <p><math>y = 18770x - 14,218</math></p>	<p>product) for lead. In the linearity calculation also the blank solution was used.</p> <p>Correlation coefficient should be <math>R^2 \geq 0.99</math>. The obtained result is acceptable.</p> <p><math>y = 1478,5x + 2,7982</math></p>
<p><b>Precision – Repeatability Mean</b></p> <p><u>Arsenic</u> n = 5 <b>4.63486 %RSD</b></p> <p><u>Cadmium</u> n = 5 <b>4.56750 %RSD</b></p> <p><u>Lead</u> n = 5 <b>5.04878 %RSD</b></p>	<p>Precision was established by analyzing five (5) samples of Miedzian Extra 350 SC</p> <p>Acceptable relative standard deviation RSDr <math>\leq 11.317\%</math>.</p> <p>The obtained result 4.63486% is acceptable. Hr = 0.410</p>	<p>Precision was established by analyzing five (5) samples of Miedzian Extra 350 SC</p> <p>Acceptable relative standard deviation RSDr <math>\leq 10.596\%</math>.</p> <p>The obtained result 4.56750% is acceptable. Hr = 0.431</p>	<p>Precision was established by analyzing five (5) samples of Miedzian Extra 350 SC</p> <p>Acceptable relative standard deviation RSDr <math>\leq 6.936\%</math>.</p> <p>The obtained result 5.04878% is acceptable. Hr = 0.728</p>
<p><b>Accuracy</b></p> <p><u>Arsenic</u> n = 18 (9 at LOQ level and 9 at level of 90% of nominal conc) <b>107 % Recovery at LOQ</b> <b>91 % Recovery at 90% of nominal concentration</b></p> <p><u>Cadmium</u> n = 18 (9 at LOQ level and 9 at level of 90% of nominal conc) <b>94 % Recovery at LOQ</b> <b>91 % Recovery at 90% of nominal concentration</b></p> <p><u>Lead</u> n = 18 (9 at LOQ level and 9 at level of 90% of nominal conc) <b>90 % Recovery at LOQ</b></p>	<p>Accuracy was established by analyzing sample the Miedzian extra 350 SC spiked with arsenic at the two (2) concentration levels.</p> <ul style="list-style-type: none"> <li>· LOQ level</li> <li>· 90 % of nominal concentration.</li> </ul> <p>The recovery rate for LOQ level must be in the range between 70 to 130 %</p> <p>The result 107% confirms the accuracy of the method.</p> <p>The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to</p>	<p>Accuracy was established by analyzing sample the Miedzian extra 350 S.C. spiked with cadmium at the two (2) concentration levels.</p> <ul style="list-style-type: none"> <li>· LOQ level</li> <li>· 90 % of nominal concentration.</li> </ul> <p>The recovery rate for LOQ level must be in the range between 70 to 130 %</p> <p>The result 94% confirms the accuracy of the method.</p> <p>The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to</p>	<p>Accuracy was established by analyzing sample the Miedzian extra 350 S.C. spiked with lead at the two (2) concentration levels.</p> <ul style="list-style-type: none"> <li>· LOQ level</li> <li>· 90 % of nominal concentration.</li> </ul> <p>The recovery rate for LOQ level must be in the range between 70 to 130 %</p> <p>The result 90% confirms the accuracy of the method.</p> <p>The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to</p>

	<b>As</b> <b>max 35 mg</b>	<b>Cd</b> <b>max 35 mg</b>	<b>Pb</b> <b>max 175 mg</b>
<b>95 % Recovery at 90% of nominal concentration</b>	125 %.  The result 91% confirms the accuracy of the method.	125 %.  The result 91% confirms the accuracy of the method.	125 %.  The result 95% confirms the accuracy of the method.
<b>Interference/ Specificity</b>	The specificity of the method was confirmed by blank analysis, Control Standard 1, Control Standard 2, and sample solution. The method showed no effect of the solvents used and no interference was observed between the tested element in the tested samples.	The specificity of the method was confirmed by blank analysis, Control Standard 1, Control Standard 2, and sample solution. The method showed no effect of the solvents used and no interference was observed between the tested element in the tested samples.	The specificity of the method was confirmed by blank analysis, Control Standard 1, Control Standard 2, and sample solution. The method showed no effect of the solvents used and no interference was observed between the tested element in the tested samples.
<b>LOQ</b>	The quantification limit of the method was defined as the lowest point in the calibration curve. The %RSD of intensity from ten (10) QL preparations was in the range of 1.6 – 2.6 % which fulfills acceptance criteria.  LOQ 0.0015 mg/L (corresponding to 0.368 mg/L for product)	The quantification limit of the method was defined as the lowest point in the calibration curve. The %RSD of intensity from ten (10) QL preparations was in the range of 1.6 – 2.6 % which fulfills acceptance criteria.  LOQ 0.0029 mg/L (corresponding to 0.71 mg/L for product)	The quantification limit of the method was defined as the lowest point in the calibration curve. The %RSD of intensity from ten (10) QL preparations was in the range of 1.6 – 2.6 % which fulfills acceptance criteria.  LOQ 0.09 mg/L (corresponding to 22.06 mg/L for product)
<b>Comment</b>	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU requirements given in SANCO/3030/99 rev.5.	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU requirements given in SANCO/3030/99 rev.5.	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU requirements given in SANCO/3030/99 rev.5.

## Conclusion

It was confirmed that the method of determination of relevant impurities as Arsenic, Cadmium and Lead is specific. No interference was observed. The validation parameters (specificity, linearity, limit of quantification (LOQ), repeatability (precision)) are within the acceptance range and fulfil EU requirements given in SANCO /3030 /99 rev.5. This is a new submitted method.

### 5.2.1.3 Description of analytical methods for the determination of formulants (KCP

### 5.1.1)

With respect to toxicological, eco-toxicological or environmental aspects Miedzian Extra 359 SC does not contain any relevant formulants. Therefore, a special analytical method and validation is not needed.

### 5.2.1.4 Applicability of existing CIPAC methods (KCP 5.1.1)

For copper in formulation, two methods are described in CIPAC Handbook E for wettable powder formulation (44WP/M) and dustable powder formulation (44/DP/M). Both methods are based on two possible procedures: titration or electrolytic. They are applicable on the different copper matrices and are considered applicable for the determination of total copper in the preparation (DAR, 2007).

Two methods for water-soluble copper are described in CIPAC Handbook F:

#### MT 98.1 Colorimetric method

The water soluble copper is extracted and reduced to the Cu<sup>+</sup> state. Bathocuproine is added and the absorbance of the coloured copper complex formed is measured at 465 nm. The method is suitable for the determination of water-soluble copper in copper oxychloride and other water-insoluble copper fungicides.

#### MT 98.2 Atomic absorption spectrophotometric method

The sample is dispersed in de-ionized water. The mixture is centrifuged, filtered and the copper determined by means of an atomic absorption spectrophotometer. The method is suitable for the determination of water-soluble copper in copper oxychloride and other water-insoluble copper fungicides.

### 5.2.2 Methods for the determination of residues (KCP 5.1.2)

An overview on the acceptable methods and possible data gaps for analysis of residues of copper oxychloride for the generation of pre-authorization data is given in the following table. For the detailed evaluation of new/ additional studies it is referred to Appendix 2.

**Table 5.2-3: Validated methods for the generation of pre-authorization data**

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Plants and plant products – Cherries	Primary	0.5 mg/kg	ICP/MS	Tomasz Peda, 2020a/ Synthos Agro Sp. z o.o.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be a specific method.		
Plants and plant products – Beans	Primary	1.0 mg/kg	ICP/MS	Tomasz Peda, 2020b/ Synthos Agro Sp. z o.o.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be a specific method.		
Plants and plant products – Grapes (Residues)	Primary	Grape fruit 5 mg/kg Grape wet pomace 5 mg/kg Grape must 1.5 mg/kg Grape dry pomace 25 mg/kg	AAS	Scibaldi, F. (2002a)/ DAR of copper compounds point B.5.2.1

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
		Grape stems 40 mg/kg Raisins 13 mg/kg Wine 0.28 mg/kg		
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be a specific method.		
Plants and plant products - Tomatoes (Residues)	Primary	Tomato fruit 2 mg/kg Tomato blanching water 0.3 mg/kg Tomato wet pomace 6 mg/kg Tomato juice 12 mg/kg Tomato puree 6 mg/kg Canned tomato 2 mg/kg	AAS	Scibaldi, F. (2002b)/ DAR of copper compounds point B.5.2.2
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be a specific method.		
Plants – Cucumber (Residues)	Primary	0.2 mg/kg	AAS	Scibaldi, F., Riccelli S. (2010)/ RAR of copper compounds point B.5.1.2.1.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be a specific method.		
Soil – Bioavailable copper (Environmental fate)	Primary	5 mg/kg	ICP-AAS	Kiefer, R. (2003)/ DAR of copper compounds point B.5.3.1
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Water (Ecotoxicology)	Primary	ISO medium: 0.01858 mg/l AAP medium: 0.01126 mg/l	ICP-OES	Marcin Świstak, (2020)/ Synthos Agro
	Confirmatory (if required)	Not required due to specific method to the analytes. According to SANCO/3029/99 rev. 4		
Soil (Ecotoxicology)	Primary	2.85755 mg/kg	ICP-OES	Patrycja Bielecka, 2020/ Synthos Agro
	Confirmatory (if required)	Not required due to specific method to the analytes. According to SANCO/3029/99 rev. 4		
Air (Residues)	Primary	0.3 ng/ m <sup>3</sup>	ICP-OES	Verein Deutscher Ingenieure (1997)/ DAR of copper compounds point B.5.3.3
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Body fluids and tissues – Plasma (Residues)	Primary	Plasma 3 mg/kg Bile 13.9 mg/kg Liver 371 mg/kg Feaces 832 mg/kg Carcass 46 mg/kg	ICP-AES	Himmelstein, M. W. (2003)/ DAR of copper compounds point B.5.4.

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
Body fluids and tissues – Receptor fluid (Residues)	Primary	0.1 µg/L	HR-ICP-MS	Shouten, A., de Haan H.P.M. (2016)/ RAR of copper compounds point B.5.1.2.6.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Body fluids and tissues – Receptor/ Donor wash (Residues)	Primary	0.25 µg/L	HR-ICP-MS	Shouten, A., de Haan H.P.M. (2016)/ RAR of copper compounds point B.5.1.2.6.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Body fluids and tissues – Skin membrane, Tape strip (Residues)	Primary	0.02 µg/L	HR-ICP-MS	Shouten, A., de Haan H.P.M. (2016)/ RAR of copper compounds point B.5.1.2.6.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Body fluids and tissues – Skin wash (Residues)	Primary	0.05 µg/L	HR-ICP-MS	Shouten, A., de Haan H.P.M. (2016)/ RAR of copper compounds point B.5.1.2.6.
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		

### 5.3 Methods for post-authorization control and monitoring purposes (KCP 5.2)

#### 5.3.1 Analysis of the plant protection product (KCP 5.2)

Analytical methods for the determination of the active substance and relevant impurities in the plant protection product shall be submitted, unless the applicant shows that these methods already submitted in accordance with the requirements set out in point 5.2.1 can be applied.

#### 5.3.2 Description of analytical methods for the determination of residues of Copper oxychloride (KCP 5.2)

##### 5.3.2.1 Overview of residue definitions and levels for which compliance is required

Compared to the residue definition proposed in the Draft Assessment Report (incl. its addenda) the current legal residue definition is identical.

**Table 5.3-1: Relevant residue definitions for monitoring/enforcement and levels for which compliance is required**

Matrix	Residue definition	MRL / limit	Reference for MRL/level Remarks
Plant, high water content	Copper	5 mg/kg	Regulation (EC) No 149/2008, annex III part A
Plant, high acid content		5 mg/kg	Regulation (EC) No 149/2008, annex III part A
Plant, high protein/high starch content (dry commodities)		5 mg/kg	Regulation (EC) No 149/2008, annex III part A
Plant, high oil content		20 mg/kg	Regulation (EC) No 149/2008, annex III part A
Plant, difficult matrices (hops, spices, tea)		1000 mg/kg	Regulation (EC) No 149/2008, annex III part A
Muscle	Copper	5 mg/kg	Regulation (EC) No 149/2008, annex III part A
Milk		2 mg/kg	Regulation (EC) No 149/2008, annex III part A
Eggs		2 mg/kg	Regulation (EC) No 149/2008, annex III part A
Fat		5 mg/kg	Regulation (EC) No 149/2008, annex III part A
Liver, kidney		30 mg/kg	Regulation (EC) No 149/2008, annex III part A
Soil (Ecotoxicology)	total copper	20-60 mg/kg (protection level for soils in accordance with Federal Soil Protection and Contamination Ordinance (BBodSchV))	average background values of copper content in soil: 6 - 25 mg/kg; in agricultural used soil up to 1280 mg/kg; EFSA Scientific Report (2008) 187, 1-101, ASB2012-3573
Drinking water (Human toxicology)	soluble copper	2 mg/L	general limit for drinking water Directive 98/83/EC, annex 1, part B, 1998-11-03
Surface water (Ecotoxicology)	soluble copper	1.7 µg Cu (dissolved)/L	NOEC <i>O. mykiss</i> EFSA Scientific Report (2008) 187, 1-101, ASB2012-3573
Air	total copper	22 µg Cu/m <sup>3</sup>	AOEL sys: 0.072 mg/kg bw/d



Matrix	Residue definition	MRL / limit	Reference for MRL/level Remarks
			EFSA Scientific Report (2008) 187, 1-101, ASB2012-3573
Tissue (meat or liver)	not residue relevant	Not required	notclassified as T / T+
Body fluids		Not required	notclassified as T / T+

### 5.3.2.2 Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of Copper in plant matrices is given in the following tables. For the detailed evaluation of new/ additional studies it is referred to Appendix 2.

**Table 5.3-2: Validated methods for food and feed of plant origin (required for all matrix types, “difficult” matrix only when indicated by intended GAP)**

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
High water content	Primary	LOQ 2 mg/kg	AAS	Scibaldi, F. (2002b)/ DAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
	Primary	LOQ 0.2 mg/kg	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
High acid con-	Primary	LOQ 5 mg/kg	AAS	Scibaldi, F. (2002a)/ DAR of

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
tent				copper compounds point B.5.2.1
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
	Primary	LOQ 0.2 mg/kg	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
High oil content	Primary	LOQ 0.2 mg/kg Not fully validated	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
High protein/high starch content (dry)	Primary	LOQ 0.2 mg/kg Not fully validated	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types.		

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing / EU agreed
Difficult (if required, depends on intended use)		<b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
	Primary	LOQ 0.2 mg/kg Not fully validated	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compounds point B.5.2.2
	ILV	The European standard EN 13805, developed by the CEN/TC275 committee has been adopted in most European countries, including France and Germany. It is one standard of the official methods for the determination of heavy metals in feed and food, as approved by the European Union Reference Laboratory. These standards have been validated in ring tests (e.g. EN 13805 by 12 laboratories) and are used by accredited laboratories to monitor copper in all feed and food types. <b>Therefore the method should be considered fully validated and no ILV is required.</b>		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		

For any special comments or remarkable points concerning the analytical methods for the determination of residues in plant matrices, please refer to Appendix 2.

**Table 5.3-3: Statement on extraction efficiency**

	Method for products of plant origin
Required, available from:	Not required
Not required, because:	All standard methods analyse copper after an acid digestion. Whether this is done under microwave assistance, under pressure, after dry ashing or any other standard procedure, it will always completely dissolve the copper present in the matrix. Therefore the extraction efficiency is 100%.

### 5.3.2.3 Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of Copper oxychloride in animal matrices is given in the following tables. For the detailed evaluation of new/ additional studies it is referred to Appendix 2.

**Table 5.3-4: Validated methods for food and feed of animal origin (if appropriate)**

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Milk	Primary	The EN 14082 method using AAS can be used for the determination of cop-		

Component of residue definition: Copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
	ILV	per in foodstuff of animal origin.		
	Confirmatory (if required)	It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices.		
Eggs	Primary	The EN 14082 method using AAS can be used for the determination of copper in foodstuff of animal origin.		
	ILV			
	Confirmatory (if required)	It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices.		
Muscle	Primary	The EN 14082 method using AAS can be used for the determination of copper in foodstuff of animal origin.		
	ILV			
	Confirmatory (if required)	It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices.		
Fat	Primary	The EN 14082 method using AAS can be used for the determination of copper in foodstuff of animal origin.		
	ILV			
	Confirmatory (if required)	It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices.		
Kidney, liver	Primary	The EN 14082 method using AAS can be used for the determination of copper in foodstuff of animal origin.		
	ILV			
	Confirmatory (if required)	It should be noted that for the representative uses evaluated, there is no need for monitoring methods in animal matrices.		

For any special comments or remarkable points concerning the analytical methods for the determination of residues in animal matrices, please refer to Appendix 2.

#### 5.3.2.4 Description of methods for the analysis of soil (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of copper in soil is given in the following tables. For the detailed evaluation of new/additional studies it is referred to Appendix 2.

**Table 5.3-5: Validated methods for soil (if appropriate)**

Component of residue definition: Copper			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	5 mg/kg	ICP-AAS	Kiefer, R. (2003)/ DAR of copper compounds point B.5.3.1
Confirmatory	ICP-AES method is considered as inherently selective for copper and, therefore, no additional confirmation method is required.		

For any special comments or remarkable points concerning the analytical methods for soil please refer to Appendix 2.

### 5.3.2.5 Description of methods for the analysis of water (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of copper in surface and drinking water is given in the following tables. For the detailed valuation of new/ additional studies it is referred to Appendix 2.

**Table 5.3-6: Validated methods for water (if appropriate)**

Component of residue definition: copper				
Matrix type	Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Drinking water	Primary	0.1 mg/L	ICP-AES	Heintze, A. (2000 and 2001)/ RAR of copper compounds point B.5.2.4
	ILV	No ILV has been provided.		
	Confirmatory	ICP-AES method is considered as inherently selective for copper and, therefore, no additional confirmation method is required.		
Surface water	Primary	0.1 mg/L	ICP-AES	Heintze, A. (2000 and 2001)/ RAR of copper compounds point B.5.2.4
	Confirmatory	ICP-AES method is considered as inherently selective for copper and, therefore, no additional confirmation method is required.		

For any special comments or remarkable points concerning the analytical methods for water please refer to Appendix 2.

### 5.3.2.6 Description of methods for the analysis of air (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of copper in air is given in the following tables. For the detailed evaluation of new/ additional studies please refer to Appendix 2.

**Table 5.3-7: Validated methods for air (if appropriate)**

Component of residue definition: copper			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	0.5-0.8 µg/m <sup>3</sup>	GF-AAS	Anon. (1999)/ DAR of copper compounds point B.5.3.3
Primary	0.3 µg/m <sup>3</sup>	ICP-OES	Anon. (1997)/ DAR of copper compounds point B.5.3.3

For any special comments or remarkable points concerning the analytical methods for air it is referred to Appendix 2.

### 5.3.2.7 Description of methods for the analysis of body fluids and tissues (KCP 5.2)

An overview on the acceptable methods and possible data gaps for analysis of copper in body fluids and tissues is given in the following table. For the detailed evaluation of new/ additional studies it is referred

to Appendix 2.

**Table 5.3-8: Methods for body fluids and tissues (if appropriate)**

Component of residue definition: copper			
Method type	Method LOQ	Principle of method (i.e. GC-MS or HPLC-UV)	Author(s), year / missing
Primary	3.0 mg/kg (Plasma) 359 mg/kg (Liver)	ICP-AES	Himmelstein, M. W. (2003)/ RAR of copper compunds point B.5.2.6
Confirmatory	ICP-AES method is considered as inherently selective for copper and, therefore, no additional confirmation method is required		

For any special comments or remarkable points concerning the analytical methods for body fluids and tissues please refer to Appendix 2.

### 5.3.2.8 Other studies/ information

No other studies or information.

## Appendix 1 Lists of data considered in support of the evaluation

### List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 5.1.1	Karolina Stępień MSc.	2019	Miedzian Extra 350 SC Method development and validation for determination of the content of active substance in the formulation. Łukasiewicz Research Network - Institute of Industrial Organic Chemistry in Warsaw GLP Unpublished	N	Synthos Agro Sp. z o.o.
KCP 5.1.1	Iwona Karczmarzyk	2020	Determination of arsenic, cadmium and lead content in the Miedzian 50 WP. Study code: K388/MB/01 Selvita Services Sp. z o.o. in Cracow GLP Unpublished	N	Synthos Agro Sp. z o.o.
KCP 5.1.2	Tomasz Peda	2020a	Magnitude of the residue of copper oxychloride in cherry (raw Agricultural Commodity) after three application of Miedzian 50 WP – two harvest trials and two decline curve trials in Poland – 2019. Study code: 19SGS16 SGS Polska Sp. z o.o. in Warsaw GLP Unpublished	N	Synthos Agro Sp. z o.o.
KCP 5.1.2	Tomasz Peda	2020b	Magnitude of the residue of copper oxychloride in French bean (openfield) Raw Agricultural Commodity after two applications of Miedzian 50 WP – two harvest trials in Poland – 2019. Study code: 19SGS19 SGS Polska Sp. z o.o. in Warsaw GLP Unpublished	N	Synthos Agro Sp. z o.o.
KCP 5.1.2	Marcin Świstak	2020	Validation of analytical method for the determination of test item Miedzian Extra 350 SC in the media for breeding aquatic organisms. Study code: 0030/0001/FA	N	Synthos Agro Sp. z o.o.

<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
			SORBOLAB Research Laboratory – Poznań (Poland) GLP: Yes Unpublished		
KCP 5.1.2	Patrycja Bielecka	2020	Validation of analytical method for the determination of test item Miedzian Extra 350 SC in soil for breeding earthworms. Study code: 0030/0002/FA SORBOLAB Research Laboratory – Poznań (Poland) GLP: Yes Unpublished	N	Synthos Agro Sp. z o.o.

**List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review**

<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
KCP 5.1.2	Scibaldi, F.	2002a	Analytical method validation for the determination of copper in/on grapes and their processed fractions. Report No.: 00123 Isagro Ricerca S.r.l GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)
KCP 5.1.2	Scibaldi, F.	2002b	Analytical method validation for the determination of copper in/on tomatoes, their processed fractions and leaves. Report No.: 00119 Isagro Ricerca S.r.l	N	EUCuTF  In DAR (2007)



Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP: Yes Unpublished		
KCP 5.1.2	Scibaldi, F., Riccelli S.	2010	Method validation for the reduction of the Limit of Quantification for copper in representative matrices of plant origin. Report No.: RA.09.23 Isagro Ricerca S.r.l GLP: Yes Unpublished	N	EUCuTF  RAR
KCP 5.1.2	Kiefer, R.	2003	Validation of an analytical method for the determination of bioavailable copper in soil samples Report No.: 20031084/02-UVX GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)
KCP 5.1.2	Verein Deutscher Ingenieure	1997	Determination of suspended matter in ambient air. Determination of the mass concentration of Be, Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb, Sb, V, Zn by optical emission spectrometry (ICP-OES) after sampling on filters and digestion in an oxidizing agent. VDI/DIN Manual Reinhaltung der luft (Air Pollution Prevention). Method No. VDI 2267, Part 5. GLP: No Published	N	Public
KCP 5.1.2	Himmelstein, M. W.	2003	Five copper substances: Absorption, distribution, and excretion in male rats. Report No.: DuPont-11784 E.I. du Pont de Nemours and Company GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)
KCP 5.1.2	Shouten, A., de Haan H.P.M.	2016	Validation of the determination of <sup>65</sup> Cu in receptor fluid, stripped skin, tape strips, receptor/donor wash solution and skin wash used in the 'In vitro percutaneous absorption test of cop-	N	EUCuTF

<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
			per through human and rat skin', using a double-focusing high resolution inductively coupled plasma mass spectrometer (HR-ICP-MS). Report No.: V20801 GLP: Yes Unpublished		RAR
KCP 5.2	Scibaldi, F.	2002a	Analytical method validation for the determination of copper in/on grapes and their processed fractions. Report No.: 00123 Isagro Ricerca S.r.l GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)
KCP 5.2	Scibaldi, F.	2002b	Analytical method validation for the determination of copper in/on tomatoes, their processed fractions and leaves. Report No.: 00119 Isagro Ricerca S.r.l GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)
KCP 5.2	Scibaldi, F., Riccelli S.	2010	Method validation for the reduction of the Limit of Quantification for copper in representative matrices of plant origin. Report No.: RA.09.23 Isagro Ricerca S.r.l GLP: Yes Unpublished	N	EUCuTF  RAR
KCP 5.2	Kiefer, R.	2003	Validation of an analytical method for the determination of bioavailable copper in soil samples Report No.: 20031084/02-UVX GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)

<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
KCP 5.2	Heintze, A.	2000	Assessment of side effects of URA-08740-F-0-WP on the larvae of the midge, Chironomous riparius with the laboratory test method. Report No.: 99507/01-ASCr GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH GLP: Yes Unpublished		EUCuTF  In DAR (2007)
KCP 5.2	Heintze, A.	2001	Assessment of side effects of URA-13900-F-0-WP on the larvae of the midge, Chironomous riparius with the laboratory test method. Report No.: 99520/01-ASCr GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH GLP: Yes Unpublished		EUCuTF  In DAR (2007)
KCP 5.2	Anon.	1999	Determination of suspended matter in ambient air. Measurement of the concentration by mass of As, Be, Cd, Co, Cr, Cu, Mn, Ni, Pb, Sb, Tl, Zn by atomic absorption spectrometry (AAS) after sampling on filters and digestion in an oxidising acid mixture. VDI 2267, Part 1, VDI/DIN Manual Reinhaltung der Luft (Air Pollution Prevention). GLP: No Published		Public
KCP 5.2	Himmelstein, M. W.	2003	Five copper substances: Absorption, distribution, and excretion in male rats. Report No.: DuPont-11784 E.I. du Pont de Nemours and Company GLP: Yes Unpublished	N	EUCuTF  In DAR (2007)

## **Appendix 2 Detailed evaluation of submitted analytical methods**

### **A 2.1 Analytical methods for Copper oxychloride**

#### **A 2.1.1 Methods used for the generation of pre-authorization data (KCP 5.1)**

##### **A 2.1.1.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.1)**

###### **A 2.1.1.1.1 Analytical method 1 (Residues in Cherries)**

###### **A 2.1.1.1.1.1 Method validation**

Reference: Validation included in the following report:

Tomasz Peda, 2020a

Report Magnitude of the residue of copper oxychloride in cherry (raw Agricultural Commodity) after three application of Miedzian 50 WP – two harvest trials and two decline curve trials in Poland – 2019, Tomasz Peda, 2020a, Study code: 19SGS16

Guideline(s): SANCO/3029/99 rev.4  
SANCO/825/00 rev. 8.1

Deviations: No

GLP: Yes

Acceptability: Yes

### **Materials and methods**

#### **Examined materials:**

Cherry fruits from test sites.

#### **Reference materials:**

Copper standard solution 1000 µg/ml (Plasma HIQU), 1 g Cu/2-5% HNO<sub>3</sub>, Chem-Lab, Belgium  
ICP-MS Internal Std Mix, Agilent Part Number: 5188-6525, Lot Number: 50-025CRY2  
Certified Reference Material, NCS ZC73031 Carrot, Approved by China National Analysis Center for Iron and Steel (Beijing, China)  
Certified Reference Material, NCS ZC73032 Celery, Approved by China National Analysis Center for Iron and Steel (Beijing, China)  
Rye grass, ERM-CD281, Institute of Reference Materials and Measurements IRMM (Belgium)  
Standard Reference Material 1570a, Trace Elements in Spinach Leaves, NIST (Gaithersburg)

#### **Apparatus:**

- Electronic balance Class I

- Electronic balance Class II
- Freezer – storage of:
  - Analytical samples before the analytical part
  - Archived analytical samples
- Fridge – storage of analytical samples extracts until the end of the instrumental analysis
- Cutter (knife grinder)
- Volumetric flasks, 50 – 100 ml
- Automatic pipettes, 10 µl – 10 ml
- Disposable glass test tubes with caps, 20 ml
- UltraWAVE, Microwave Digestion System
- Inductively coupled plasma – mass spectrometer (ICP/MS), Model 7800 (Agilent)

#### Reagents and materials:

- Deionized Water
- Nitric Acid, HNO<sub>3</sub>, 65%, for analysis (max 0.01 ppm Cu) J.T. Baker

#### The preparation of standard solutions

Intermediate solutions of analytical standard were prepared by diluting a stock solution (1000 ppm) of analytical standard in appropriate solvent.

#### Sample solution

About 0.50 g of sample was weighed into a reaction vessel. 4 ml of concentrated nitric acid was added to the reaction vessels. Two matrix blank (P0) samples, two fortified samples at LOQ level (0.50 mg/ kg) and two fortified samples (5.00 mg/kg) were prepared in parallel for each series of samples. After the acid was added, the sample rack was placed in the mineralizer and the previously set mineralization program was started. The mineralization program consisted of two stages:

- (I) Heating the samples to 230°C for 30 minutes
- (II) Maintaining the temperature of 230°C for 15 minutes

After the mineralization was complete, the reaction vessels were removed from the mineralizer and allowed to cool. Then the contents were quantitatively transferred to 50 ml volumetric flasks and make up to the mark with distilled water (if necessary the samples were filtered). The final extract was directly employed for ICP/MS analysis. Quantification was performed using an internal standard (Rh<sup>103</sup>), which was added to the during analysis. Analysis was performed for each sample in one replicate.

#### Calculations

The detector signals (CPS = counts per second) were registered using the software data system (Agilent). The signal intensity was taken into account to determine the amount of active substance. The calibration curves were calculated from the CPS signal of the calibration solutions with their corresponding concentrations of active substances.

The initial standard method was used for the calculation. The calculation process was as follows:

$$X = [(a - 0) * V * r] / m$$

where:

- x – result of determination
- a – reading from ICP
- m – sample mass [g]
- r – dilution
- V – the volume of the volumetric flask [ml], 50 ml

0 – blank value (the reading of the blank sample in the calibration of the final result can be omitted when its reading is so low that it has no significant effect on the final result)

## Results and discussions

**Table A 1: Recovery results from method validation of copper using the analytical method**

Matrix	Analyte	Fortification level (mg/kg) (n = x)	Mean recovery (%)	RSD (%)	Comments
Cherries	Copper	n = 10 0.5000 5.0000	97.4 97.0	5.15 3.58	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Carrot	Copper	n = 10 4.10	98.1	6.68	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Celery	Copper	n = 10 8.20	97.2	3.38	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Rye Grass	Copper	n = 10 10.20	105	1.06	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Spinach	Copper	n = 10 12.22	101	1.37	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4

**Table A 2: Characteristics for the analytical method used for validation of copper residues in cherries**

	Copper
Specificity	ICP/MS method was used during the study. One atomic mass was evaluated and used for quantification. The specificity of the method was evaluated on the basis of the analysis of spectra recorded for the matrix blank samples.
Calibration (type, number of data points)	The coefficient of determination ( $R^2$ ) was determined.  $R^2$ was 0.9996  The curve is described as $y = 5.7476x + 0.0031$
Calibration range	The linearity of the detector response was demonstrated by single determination of calibration standards at six concentration levels ranging from 0.10 to 20.0 mg/kg.

	<b>Copper</b>
Specificity	ICP/MS method was used during the study. One atomic mass was evaluated and used for quantification. The specificity of the method was evaluated on the basis of the analysis of spectra recorded for the matrix blank samples.
Assessment of matrix effects is presented	Yes In all cases of control sample analysis, a certain copper content (copper naturally occurring in nature) was determined. To show actual recovery of the method, this amount was subtracted from fortified samples at both levels 0.50 and 5.00 mg/kg
Limit of determination/quantification	The LOQ is the lowest validated fortification level for which an average recovery in the range of 70 – 110% and RSD ≤ 15% is achieved.  For Cu <b>LOQ</b> was successfully established at <b>0.50 mg/kg</b> for cherry  <b>Limit of detection (LOD)</b> was established at <b>0.15 mg/kg</b> as ±30% LOQ

## Conclusion

The validation parameters (specificity, linearity, accuracy, recovery and precision) are within the acceptance range and fulfil EU requirements given in SANCO /3029/99 rev.4. The same method as for Miedzian 50 WP can be used in order to determine copper in plant matrices.

### A 2.1.1.1.2 Analytical method 2 (Residues in French bean)

#### A 2.1.1.1.2.1 Method validation

Reference: Validation included in the following report:

Tomasz Peda, 2020b

Report Magnitude of the residue of copper oxychloride in French bean (openfield) Raw Agricultural Commodity after two applications of Miedzian 50 WP – two harvest trials in Poland – 2019, Tomasz Peda, 2020b, Study code: 19SGS19

Guideline(s): SANCO/3029/99 rev.4  
 SANCO/825/00 rev. 8.1

Deviations: No

GLP: Yes

Acceptability: Yes

## Materials and methods

### Examined materials:

French beans from test sites.

### Reference materials:

- Copper standard solution 1000 µg/ml (Plasma HIQU), 1 g Cu/2-5% HNO<sub>3</sub>, Chem-Lab, Belgium
- ICP-MS Internal Std Mix, Agilent Part Number: 5188-6525, Lot Number: 50-025CRY2
- Certified Reference Material, NCS ZC73031 Carrot, Approved by China National Analysis Center for Iron and Steel (Beijing, China)
- Certified Reference Material, NCS ZC73032 Celery, Approved by China National Analysis Center for Iron and Steel (Beijing, China)
- Rye grass, ERM-CD281, Institute of Reference Materials and Measurements IRMM (Belgium)
- Standard Reference Material 1570a, Trace Elements in Spinach Leaves, NIST (Gaithersburg)

#### **Apparatus:**

- Electronic balance Class I
- Electronic balance Class II
- Freezer – storage of:
  - Analytical samples before the analytical part
  - Archived analytical samples
- Fridge – storage of analytical samples extracts until the end of the instrumental analysis
- Cutter (knife grinder)
- Volumetric flasks, 50 – 100 ml
- Automatic pipettes, 10 µl – 10 ml
- Disposable glass test tubes with caps, 20 ml
- UltraWAVE, Microwave Digestion System
- Inductively coupled plasma – mass spectrometer (ICP/MS), Model 7800 (Agilent)

#### **Reagents and materials:**

- Deionized Water
- Nitric Acid, HNO<sub>3</sub>, 65%, for analysis (max 0.01 ppm Cu) J.T. Baker

#### **The preparation of standard solutions**

Intermediate solutions of analytical standard were prepared by diluting a stock solution (1000 ppm) of analytical standard in appropriate solvent.

#### **Sample solution**

About 0.50 g of sample was weighed into a reaction vessel. 4 ml of concentrated nitric acid was added to the reaction vessels. Two matrix blank (P0) samples, two fortified samples at LOQ level (1.00 mg/ kg) and two fortified samples at 10LOQ (10.0 mg/kg) were prepared in parallel for each series of samples. After the acid was added, the sample rack was placed in the mineralizer and the previously set mineralization program was started. The mineralization program consisted of two stages:

- (I) Heating the samples to 230°C for 30 minutes
- (II) Maintaining the temperature of 230°C for 15 minutes

After the mineralization was complete, the reaction vessels were removed from the mineralizer and allowed to cool. Then the contents were quantitatively transferred to 50 ml volumetric flasks and make up to the mark with distilled water (if necessary the samples were filtered). The final extract was directly employed for ICP/MS analysis. Quantification was performed using an internal standard (Rh<sup>103</sup>), which was added to the during analysis. Analysis was performed for each sample in one replicate.

#### **Calculations**

The detector signals (CPS = counts per second) were registered using the software data system (Agilent). The signal intensity was taken into account to determine the amount of active substance. The calibration curves were calculated from the CPS signal of the calibration solutions with their corresponding concentrations of active substances.



The initial standard method was used for the calculation. The calculation process was as follows:

$$X = [(a - 0) * V * r] / m$$

where:

x – result of determination

a – reading from ICP

m – sample mass [g]

r – dilution

V – the volume of the volumetric flask [ml], 50 ml

0 – blank value (the reading of the blank sample in the calibration of the final result can be omitted when its reading is so low that it has no significant effect on the final result)

## Results and discussions

**Table A 3: Recovery results from method validation of copper using the analytical method**

Matrix	Analyte	Fortification level (mg/kg) (n = x)	Mean recovery (%)	RSD (%)	Comments
French beans	Copper	n = 10 1.00 10.0	96.7 94.4	2.96 3.09	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Carrot	Copper	n = 10 4.10	98.1	6.68	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Celery	Copper	n = 10 8.20	97.2	3.38	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Rye Grass	Copper	n = 10 10.20	105	1.06	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4
Spinach	Copper	n = 10 12.22	101	1.37	Mean recovery on each fortification levels are in the ideally range 80-100% according to SANCO/3029/99 rev.4

**Table A 4: Characteristics for the analytical method used for validation of copper residues in cherries**

	<b>Copper</b>
Specificity	ICP/MS method was used during the study. One atomic mass was evaluated and used for quantification. The specificity of the method was evaluated on the basis of the analysis of spectra recorded for the matrix blank samples.
Calibration (type, number of data points)	The coefficient of determination ( $R^2$ ) was determined.  $R^2$ was 0.9997  The curve is described as $y = 5.7542x + 0.0017$
Calibration range	The linearity of the detector response was demonstrated by single determination of calibration standards at six concentration levels ranging from 0.10 to 20.0 mg/kg.
Assessment of matrix effects is presented	Yes In all cases of control sample analysis, a certain copper content (copper naturally occurring in nature) was determined. To show actual recovery of the method, this amount was subtracted from fortified samples at both levels 1.00 and 10.00 mg/kg
Limit of determination/quantification	The LOQ is the lowest validated fortification level for which an average recovery in the range of 70 – 110% and $RSD \leq 15\%$ is achieved.  For Cu <b>LOQ</b> was successfully established at <b>1.0 mg/kg</b> for bean  <b>Limit of detection (LOD)</b> was established at <b>0.30 mg/kg</b> as $\pm 30\%$ LOQ

## Conclusion

The validation parameters (specificity, linearity, accuracy, recovery and precision) are within the acceptance range and fulfil EU requirements given in SANCO /3029/99 rev.4. The same method as for Miedzian 50 WP can be used in order to determine copper in plant matrices.

#### **A 2.1.1.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.1)**

No new or additional studies have been submitted

#### **A 2.1.1.3 Description of Methods for the Analysis of Soil (KCP 5.1)**

##### **A 2.1.1.3.1 Analytical method 1 – Soil (Ecotoxicology)**

##### **A 2.1.1.3.1.1 Method validation**

Reference: Validation included in the following report:

Patrycja Bielecka, MSc

Report Validation of analytical method for the determination of test item  
Miedzian Extra 350 SC in soil for breeding earthworms. Patrycja Bielecka,  
MSc 2020, Study code: 0030/0002/FA

Guideline(s): SANCO/3029/99 rev.4

Deviations: No

GLP: Yes

Acceptability: Yes

#### **Materials and methods**

Optical emission spectrometry (OES) with inductively coupled plasma induction (ICP) technique was used to determine the concentration of the test item in soil. The study was based on a determination of the copper content and then calculating determined concentration into the content of the test item in the soil. Identification of copper was performed based on the characteristic analytical line (emission) at a wavelength of 327.395 nm and the quantitation was performed by external standard method, using peak intensities.

##### **Preparation of copper oxychloride standard**

42.90 mg of copper oxychloride standard was weighed into the 10 mL volumetric flask. 0.1 mL of nitric acid was added, then the contents of the flask were made up to the nominal volume with solution for dilution (blank). The whole was placed in an ultrasonic bath for 20 minutes. The prepared standard solution was diluted with solution for dilution (blank) to the concentration of 4,290 mg/L. 1.25 mL of copper oxychloride standard solution was taken into the mineralization vessel and mineralized. The final concentration of the copper standard solution is 0.24 mg/L.

##### **Preparation of copper standard**

The 1000 mg/L copper standard solution was diluted with solution for dilution (blank) to 0.2 mg/L.

##### **Preparation of the samples of test item in soil**

The solution of the tested item in ultrapure water was added to the soil as below.  
The sample was mineralized. The final concentration of the copper is 1.13 mg/L.

### Preparation of soil for testing

10 g of dry soil was weighted with an accuracy 0.01 g. Then was added the test item solution in ultrapure water in the volume resulting from the WHC (maximum water capacity) soil.

### Conditions of the chemical determinations

#### Reagents:

- copper ICP standard at concentration 1000 mg/L, ROTH, lot number: 665209 (quality certificate Appendix 2)
- copper oxychloride standard, Santa Cruse biotechnology, lot number H1418 (quality certificate Appendix 3)
- ultrapure water
- hydrochloric acid 30%, ultrapure, Chempur, lot number 19/10/03
- nitric acid 65%, ultrapure, Chempur, lot number 200309056
- solution for dilution (blank): 2% (v/v) nitric acid solution in ultrapure water
- soil prepared by the Laboratory of Ecotoxicology according to the procedure SPT-E/81

#### Equipment:

- emission spectrometer with inductively coupled plasma ICP-OES Varian Vista Pro
- microwave reaction system Mars 6
- system for obtaining ultrapure water Millipore Synergy UV
- deionizer Solpure 78
- analytical balance Radwag XA 82\_220.4Y.A
- ultrasonic washer Sonic-10
- adjustable automatic pipettes: Acura Manual 826 XS, Transferpette S 1000 µL, Transferpette S 5 mL, Transferpette S 10 mL
- syringes and syringe filters 0.22 µm

#### Analysis conditions:

- |                                 |            |
|---------------------------------|------------|
| • Carrier gas                   | Argon      |
| • Power                         | 1.00 kW    |
| • Flow rate of carrier gas      | 15 L/min   |
| • Flow rate of additional gas   | 1.5 L/min  |
| • Flow of gas through nebulizer | 0.75 L/min |
| • Reading time replicates       | 1 s        |
| • Stabilization                 | 15 s       |
| • Pump speed                    | 15 rpm     |
| • Washing time                  | 10 s       |
| • Torch orientation             | horizontal |
| • Analytical wavelength         | 327.395 nm |

### Mineralization

1 g of soil was weighed into the mineralization vessel with an accuracy of 0.01 mg prepared according to section 4.4. The 5 mL of hydrochloric acid and 5 mL of nitric acid were added.

The whole was mineralized according to the following parameters:

- |                                |            |
|--------------------------------|------------|
| • Power                        | 1200 W     |
| • Temperature                  | 180°C      |
| • Rise to temperature of 180°C | 20 minutes |
| • Temperature maintenance      | 10 minutes |

After mineralization, the sample was filtered through a syringe filter. Then 2 mL of the solution was added to a 10 mL flask and were made up to the nominal volume with solution for dilution (blank).

## Calculations

The concentration of the tested material in the soil was calculated from the formula:

$$C_{\text{mg/kg}} = (C_{\text{mg/l}} * v) / m_g$$

where:

$C_{\text{mg/kg}}$  concentration of the tested material in the soil [mg/kg]

$C_{\text{mg/l}}$  concentration of the aqueous solution [mg/L]

$v$  volume of the aqueous solution added to the soil [mL]

$m_g$  mass of soil [g]

## Validation - Results and discussions

**Table 5.3-1: Characteristics for the analytical method used for validation of copper ox-  
 ychloride residues in soil (Ecotoxicology)**

<b>Linearity</b>	<p>The copper standard solution at concentration 1000 mg/L was diluted with solution for dilution (blank) to concentration: 0.1000 mg/L; 0.2000 mg/L; 0.4000 mg/L, 0.8000 mg/L; 1,6000 mg/L.</p> <p>A calibration curve was described by equation:  <math>f(x) = 15183.748 x + 375.7</math>                      Correlation coefficient was equal: <math>r = 0.999</math>                      Criterion of acceptance <math>r \geq 0.99</math> was fulfilled.</p>
<b>Precision – Repeatability Mean</b>	<p>In the method used, precision in the analyzed concentration levels were not exceed the value of RSD [%] <math>\leq 20\%</math>.</p>
<b>Accuracy</b>	<p>To accuracy determination of method solution of test item in soil in five replications at two concentration levels in range of linearity of method were prepared</p> <p>Accuracy of method was:                      90.0% (level I – 89.4%, level II – 90.4%)</p> <p>Acceptance criteria are 70-110%</p>
<b>Interference/ Specificity</b>	<p>In samples of copper standard, test item and copper oxychloride standard there are a copper peak at wavelength 327.395 nm.</p> <p>In samples of the solution for dilution (blank) there are no peaks interfering with the copper under the analysis conditions.</p> <p>Copper is present in the control samples, therefore the value of the copper concentration in the control sample is subtracted from the samples of the test item in the soil.</p>
<b>Limit of determination/quantification</b>	<p>Limit of detection equal:                      0.95252 mg/kg of test item in soil</p> <p>Limit of quantification equal:                      2.85755 mg/kg of test item in soil</p>

## Conclusion

The linearity of response of the analytical method, its specificity, precision, recovery, limit of quantification and detection were assessed in the process of the analytical method validation. The validated analytical methods was performed according to SANCO/3029/99 rev.4 and fulfil its requirements.

#### **A 2.1.1.4 Description of Methods for the Analysis of Water (KCP 5.1)**

##### **A 2.1.1.4.1 Analytical method 1 – Water (Ecotoxicology)**

##### **A 2.1.1.4.1.1 Method validation**

Reference: Validation included in the following report:

Marcin Świstak, MSc

Report Validation of analytical method for the determination of test item Miedzian Extra 350 SC in the media for breeding aquatic organisms. Marcin Świstak, MSc 2020, Study code: 0030/0001/FA

Guideline(s): SANCO/3029/99 rev.4

Deviations: No

GLP: Yes

Acceptability: Yes

#### **Materials and methods**

Optical emission spectrometry (OES) with inductively coupled plasma induction (ICP) technique was used to determine the concentration of the test item in aqueous media (ISO and AAP). Determination was based on a determination of the copper content and then calculating determined concentration into the content of the test item in the medium. Identification of copper was performed based on the characteristic analytical line (emission) at a wavelength of 327.395 nm and the quantitation was performed by external standard method, using peak intensities.

#### **Preparation of copper oxychloride standard**

42.90 mg of copper oxychloride standard was weight to the 10 mL volumetric flask. 0.1 mL of nitric acid was added, then the contents of the flask were made up to the nominal volume with solution for dilution (blank). The whole was placed in an ultrasonic bath for 20 minutes. The prepared standard solution was diluted with solution for dilution (blank) to the concentration of 0.4290 mg/L. The solution was mineralized.

#### **Preparation of copper standard**

The 1000 mg/L copper standard solution was diluted with solution for dilution (blank) to 0.4 mg/L.

#### **Preparation of the test items**

The weight of the test item was dissolved in a volumetric flask using an appropriate medium (ISO, AAP). Samples were diluted with medium to the concentrations: 1.02984 mg/L (ISO medium) and 1.12700 mg/L (AAP medium). Samples was mineralized.

#### **Conditions of the chemical determinations**

Reagents:

- copper ICP standard at concentration 1000 mg/L, ROTH, lot number: 665209 (quality certificate Appendix 2)
- copper oxychloride standard, Santa Cruse biotechnology, lot number H1418 (quality certificate Appendix 3)
- ultrapure water

- hydrochloric acid 30%, ultrapure, Chempur, lot number 19/10/03
- nitric acid 65%, ultrapure, Chempur, lot number 200309056
- solution for dilution (blank): 2% (v/v) nitric acid solution in ultrapure water
- ISO medium prepared by the Laboratory of Ecotoxicology according to the procedure SPT-E/59
- AAP medium prepared by the Laboratory of Ecotoxicology according to the procedure SPT-E/12

**Equipment:**

- emission spectrometer with inductively coupled plasma ICP-OES Varian Vista Pro
- microwave reaction system Mars 6
- system for obtaining ultrapure water Millipore Synergy UV
- deionizer Solpure 78
- analytical balance Radwag XA 82\_220.4Y.A
- ultrasonic washer Sonic-10
- adjustable automatic pipettes: Acura Manual 826 XS, Transferpette S 1000 µL, Transferpette S 5 mL, Transferpette S 10 mL

**Analysis conditions:**

- Carrier gas Argon
- Power 1.00 kW
- Flow rate of carrier gas 15 L/min
- Flow rate of additional gas 1.5 L/min
- Flow of gas through nebulizer 0.75 L/min
- Reading time replicates 1 s
- Stabilization 15 s
- Pump speed 15 rpm
- Washing time 10 s
- Torch orientation horizontal
- Analytical wavelength 327.395 nm

**Mineralization**

20 mL of the mineralized solution was taken into the mineralization vessel. Then 2 mL of hydrochloric acid and 2 mL of nitric acid were added. The whole was mineralized according to the following parameters:

- Power 1200 W
- Temperature 180°C
- Rise to temperature of 180°C 20 minutes
- Temperature maintenance 10 minutes

**Validation - Results and discussions**

**Table 5.3-2: Characteristics for the analytical method used for validation of copper ox-ychloride residues in water (Ecotoxicology)**

<b>Linearity</b>	<p>The copper standard solution at concentration 1000 mg/L was diluted with solution for dilution (blank) to concentration: 0.01200 mg/L; 0.02800 mg/L; 0.06000 mg/L, 0.16000 mg/L; 0.40000 mg/L.</p> <p>A calibration curve was described by equation:  <math>f(x) = 25362.236x + 93.8</math>                      Correlation coefficient was equal: <math>r = 0.999</math>                      Criterion of acceptance <math>r \geq 0.99</math> was fulfilled.</p>
<b>Precision – Repeatability Mean</b>	<p>In the method used, precision in the analyzed concentration levels were not exceed the value of RSD [%] <math>\leq 20\%</math>.</p>

<b>Accuracy</b>	<p>To accuracy determination of method solution of test item in medium ISO and AAP in five replications at two concentration levels in range of linearity of method were prepared.</p> <p>Accuracy of method was:                      98% (level I – 95.7%, level II – 99.5%) for ISO medium                      98% (level I – 98.2%, level II – 98.6%) for AAP medium</p> <p>Acceptance criteria are 70-110%</p>
<b>Interference/ Specificity</b>	<p>In samples of copper standard, test item and copper oxychloride standard there is a copper peak at wavelength 327.395 nm.</p> <p>In samples of ISO medium, AAP medium and the solution for dilution (blank) there are no peaks interfering with the copper under the analysis conditions.</p>
<b>Limit of determination/quantification</b>	<p>Limit of detection:                      ISO Medium 0.00619 mg/L                      AAP Medium 0.00375 mg/L</p> <p>Limit of quantification:                      ISO Medium 0.01858 mg/L                      AAP Medium 0.01126 mg/L</p>

## Conclusion

The linearity of response of the analytical method, its specificity, precision, recovery, limit of quantification and detection were assessed in the process of the analytical method validation. The validated analytical methods was performed according to SANCO/3029/99 rev.4 and fulfil its requirements.

### A 2.1.1.5 Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.1)

No new or additional studies have been submitted

### A 2.1.1.6 Other Studies/ Information

No new or additional studies have been submitted

### A 2.1.2 Methods for post-authorization control and monitoring purposes (KCP 5.2)

#### A 2.1.2.1 Description of analytical methods for the determination of residues in plant matrices (KCP 5.2)

No new or additional studies have been submitted

#### A 2.1.2.2 Description of analytical methods for the determination of residues in animal matrices (KCP 5.2)

No new or additional studies have been submitted



**A 2.1.2.3            Description of Methods for the Analysis of Soil (KCP 5.2)**

No new or additional studies have been submitted

**A 2.1.2.4            Description of Methods for the Analysis of Water (KCP 5.2)**

No new or additional studies have been submitted

**A 2.1.2.5            Description of Methods for the Analysis of Air (KCP 5.2)**

No new or additional studies have been submitted

**A 2.1.2.6            Description of Methods for the Analysis of Body Fluids and Tissues (KCP 5.2)**

No new or additional studies have been submitted

**A 2.1.2.7            A.2.A.9    Other Studies/ Information**

No new or additional studies have been submitted