FINAL REGISTRATION REPORT
Part B
Section 5
Analytical Methods
Detailed summary of the risk assessment

Product code: MIEDZIAN 50 WP

Product names: **MIEDZIAN 50 WP,**

COBRESAL 50 WP, DALION 50 WP, SPATOR 50 WP

Chemical active substance:

Copper as a copper oxychloride, 500 g/kg

Central Zone

Zonal Rapporteur Member State: **Poland**

CORE ASSESSMENT

(re-authorization according art. 43 and art. 51, Reg. 1107/2009)

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

Submission date: **07/2020**

Finalisation date: 05.2021; 08/2022

Version history

When	What
07/2020	Renewal of registration of plant protection product according art. 43, Reg. 1107/2009
05/2021	Assessment by expert
08/2022	The Final RR

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5   Analytical methods

5.1   Conclusion and summary of assessment

zRMS conclusions and corrections are marked in grey.

Sufficiently sensitive and selective analytical methods are available for the active substance and relevant impurities in the plant protection product.
Noticed data gaps are:
- none

Sufficiently sensitive and selective analytical methods are available for all analytes included in the residue definitions.
Noticed data gaps are:
- none

Applicant has presented letters of accesses to the protected data of copper compounds from:
Industrias Quimicas Del Valles, SA (IQV) and Cinkarna metalursko-kemicna industrija Celje, d.d. (members of European Union (EU) Copper Task Force for the renewal of approval of the active substance copper compounds)

Commodity/crop	Supported/ Not supported
Pome fruit	Supported
Stone fruit	Supported
Fruiting vegetables	Supported
Berries and small fruits	Supported
Legume vegetables	Supported
Nuts	Supported

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:

Reference: Anna Kiełczewska, MSc.

Report   Development and validation of the method of determination of active
                        ingredient content in Miedzian 50 WP formulation, Anna Kiełczewska

MSc., 2011, Study code: BA-11/11

Guideline(s):	No, but meets the requirement of SANCO/3030/99 rev.5
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

The content of active ingredient was evaluated by determination of copper (II) in the tested material. The method used was potentiometric titration performed by Scott Titroline Alpha with platinum electrode, Pt 48 A.

Examined material:
Examined material: Miedzian 50 WP
Date of production: 01.2011
Batch number: 4/W
Manufacturer: „Organika-Azot" S.A. (former owner of the dossier)

Reference material:
Copper oxychloride, purity 95+%

Equipment:
- Titrometer TitroLine alpha, SCHOTT
- Analytical balance Mettler, AT261 DeltaRange
- Beaker, 150 ml volume
- Volumetric flask, 100 ml volume
- Pipette, 10 ml volume

Reagents
- Sodium thiosulphate, standardized solution, (0,1M), POCh
- 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

Test performance
About 150 mg of sample was weighed with accuracy of 0.1 mg into the five beaker (150 ml). Add water (50 ml), 1 M sulphuric acid (8 ml), potassium iodide (1.5 g) and sodium fluoride (5 ml). The solution was potentiometric titrated 0.1 M sodium thiosulphate

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

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

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 50 WP**

	Copper Oxychloride
Author(s), year	Anna Kiełczewska, MSc.
Principle of method	The content of active ingredient was evaluated by determination of copper (II) in the tested material
Linearity **Linear between** **from 100.2 mg to 201.1 mg, correspond to the following concentration range 70% to 130%** **Correlation coefficient = 0.9992**	Five standard solutions were used at the concentration range between 100.2 mg to 201.1 mg, which correspond to the concentration range of 70% to 130% of Coppercontent in te preparation. Correlation coefficient should be $r \geq 0.99$. The obtained result is acceptable.
Precision – Repeatability Mean **n = 5** **0.82 %RSD** **Hr $\leq$ 1**	The repeatability of the method was assessed on the base of five determinations of the copper oxychloride content in examined sample. Acceptable relative standard deviation for main ingredient ($\sim 50\%$) is RSDr $\leq 1.49\%$. The obtained result 0.82% is acceptable. Hr = 0.55
Accuracy **n = 10** **100.575 % Recovery**	Accuracy of the method was assessed by determination of copper (II) in fortified samples. Known amount of copper oxychloride standard was added to Miedzian 50 WP sample. The accuracy was determined by fortification done at two levels. For the main ingredient at concentration of $> 10\%$ the average recovery value should be $100 \pm 2\%$. The obtained result of 100.575% is acceptable.
Interference/ Specificity	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).
Comment	This study has already been favourable evaluated during the evaluation of the dossier for Miedzian 50 WP in Poland

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. This study has already been favourable evaluated during the evaluation of the dossier for Miedzian 50 WP in Poland.

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 50 WP 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.

Reference:	Iwona Karczmarzyk
Report	Determination of arsenic, cadmium and lead content in the Miedzian 50 WP, Iwona Karczmarzyk., 2020, Study code: K388/MB/01
Guideline(s):	SANCO/3030/99 rev.5
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

Examined material:
Examined material: Miedzian 50 WP
Batch number: 287385/04
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
- Millex® Syringe driven filter unit, 0.45 μm

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 manufac-

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turer'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 λ	[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]
As	0.0	0.0051	0.0058	0.0065	0.0072	0.0094
Cd	0.0	0.0091	0.0104	0.0117	0.0130	0.0169
Pb	0.0	0.1550	0.1770	0.1990	0.2210	0.2880

STD 5 – 0.0094 mg/L As, 0.0169 mg/L Cd, 0.2880 mg/L Pb,
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.94 mL of MIX 5, 1.690 mL of MIX 3, 2.880 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 – 0.0072 mg/L As, 0.0130 mg/L Cd, 0.2210 mg/L Pb,
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.72 mL of MIX 5, 1.300 mL of MIX 3, 2.210 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 – 0.0065 mg/L As, 0.0117 mg/L Cd, 0.1990 mg/L Pb,
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.65 mL of MIX 5, 1.170 mL of MIX 3, 1.990 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 – 0.0058 mg/L As, 0.0104 mg/L Cd, 0.1770 mg/L Pb,
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.58 mL of MIX 5, 1.04 mL of MIX 3, 1.770 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 – 0.0051 mg/L As, 0.0091 mg/L Cd, 0.1550 mg/L Pb,
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.51 mL of MIX 5, 0.91 mL of MIX 3, 1.550 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 – 0.0058 mg/L As, Sc – 0.0104 mg/L Cd and Sc - 0.177 mg/L Pb
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.58 mL of MIX 5, 1.04 mL of MIX 3, 1.770 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 - 0.0072 mg/L As, Sc - 0.0130 mg/L Cd and Sc - 0.2210 mg/L Pb
Into a 100 mL volumetric flask accurately transfer about 30 mL water, 0.72 mL of MIX 5, 1.300 mL of MIX 3, 2.210 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 weigh about 300 mg 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. Filter the solution using a plastic syringe and filter 0.45 μm.

Blank preparation

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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, open, degas the sample and transfer into a 50 mL volumetric flask. Fill to volume with water and mix well. Filter the solution using a plastic syringe and filter 0.45 μm.

Mineralization program

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

Procedure
The determination of arsenic, cadmium and lead content in Miedzian 50 WP 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:

$$X_{(mg/kg)} = [(E-E_o)*V*DF]/Wt$$

where:
E – concentration of the element in sample solution [mg/L]
E_0 – concentration of element in blank solution [mg/L]
V – volume of sample solution [mL]
DF – dilution factor (if applicable)
Wt – sample weight [g]

Validation - Results and discussions

Table 5.2-2:   **Methods suitable for the determination of the relevant impurities in plant protection product (PPP) Miedzian 50 WP**

	As 50 mg	Cd 50 mg	Pb 250 mg
Author(s), year	Iwona Karczmarzyk, 2020	Iwona Karczmarzyk, 2020	Iwona Karczmarzyk, 2020
Principle of method	The determination of arsenic, cadmium and lead content in Miedzian 50 WP 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 50 WP 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 50 WP was performed by ICP-OES detection. The amounts of the lead was calculated using the fit of the calibration model.
Linearity **Arsenic** **Linear between** **0.0051 mg/L and 0.0094 mg/L, corresponding to**	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal	The linearity range was cover range about ± 30% of nominal concentration thereby are in the acceptable range extending of at least ± 20% of nominal

	As 50 mg	Cd 50 mg	Pb 250 mg
the following concentra-tion range from 0.85 mg/kg to 1.567 mg/kg **Correlation coefficient = 0.9999** **Cadmium** **Linear between** **0.0091 mg/L and 0.0169 mg/L, corresponding to the following concentra-tion range from 1.517 mg/kg to 2.817 mg/kg** **Correlation coefficient = 0.9999** **Lead** **Linear between** **0.155 mg/L and 0.288 mg/L, corresponding to the following concentra-tion range from 25.833 mg/kg to 48 mg/kg** **Correlation coefficient = 0.9997**	concentration. Standard solutions of arsenic, cadmium and lead was prepared at five (5) concentration levels in the range of the concentration from 0.0051 mg/L – 0.0094 mg/L (0.85 mg/kg – 1.567 mg/kg) for arsenic. In the linarity calculation also the blank solution was used. Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable. y = 18868x + 3,5986	concentration. Standard solutions of arsenic, cadmium and lead was prepared at five (5) concentration levels. The concentration from 0.0091 mg/L – 0.0169 mg/L (1.517 mg/kg – 2.817 mg/kg) for cadmium. In the linarity calculation also the blank solution was used. Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable. y = 17553x + 6,0196	concentration. Standard solutions of arsenic, cadmium and lead was prepared at five (5) concentration levels. The concentration from 0.155 mg/L – 0.288 mg/L (25.833 mg/kg – 48 mg/kg) for lead. In the linarity calculation also the blank solution was used. Correlation coefficient should be $R^2 \geq 0.99$. The obtained result is acceptable. y = 1438,8x + 0,497
Precision – Repeatability Mean **Arsenic** **n = 5** **0.50175 %RSD** **Cadmium** **n = 5** **0.83718 %RSD** **Lead** **n = 5** **1.04994 %RSD**	Precision was established by analyzing five (5) samples of Miedzian 50 WP. Acceptable relative standard deviation RSDr $\leq$ 15.712% 10.527% The obtained result 10.527% 0.50175% is acceptable. Hr = 0.048	Precision was established by analyzing five (5) samples of Miedzian 50 WP. Acceptable relative standard deviation RSDr $\leq$ 14.729% 9.869%. The obtained result 9.869% 0.83718% is acceptable. Hr = 0.085	Precision was established by analyzing five (5) samples of Miedzian 50 WP. Acceptable relative standard deviation RSDr $\leq$ 10.518% 7.047%. The obtained result 7.047% 1.04994% is acceptable. Hr = 0.149
Accuracy **Arsenic** **n = 18** **102 % Recovery at LOQ** **93 % Recovery at 90% of nominal concentration** **Cadmium** **n = 18** **98 % Recovery at LOQ** **86 % Recovery at 90% of nominal**	Accuracy was established by analyzing sample the Miedzian 50 WP spiked with arsenic at the two (2) concentration levels. Accuracy was determined by comparing the theoretical amount of elemental impurities to the measured level determined with the use of the validated method.	Accuracy was established by analyzing sample the Miedzian 50 WP spiked with cadmium at the two (2) concentration levels. Accuracy was determined by comparing the theoretical amount of elemental impurities to the measured level determined with the use of the validated method.	Accuracy was established by analyzing sample the Miedzian 50 WP spiked with arsenic, cadmium and lead, at the two (2) concentration levels. Accuracy was determined by comparing the theoretical amount of elemental impurities to the measured level determined with the use

	As 50 mg	Cd 50 mg	Pb 250 mg
concentration <u>**Lead**</u> **n = 18** **96 % Recovery at LOQ** **82 % Recovery at 90% of nominal concentration**	The recovery rate for LOQ level must be in the range between 70 to 130 % The result 102% confirms the accuracy of the method. The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to 125 %. The result 93% confirms the accuracy of the method.	The recovery rate for LOQ level must be in the range between 70 to 130 % The result 98% confirms the accuracy of the method. The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to 125 %. The result 86% confirms the accuracy of the method.	of the validated method. The recovery rate for LOQ level must be in the range between 70 to 130 % The result 96% confirms the accuracy of the method. The recovery rate for the level of 90% of nominal concentration must be in the range between 75 to 125 %. The result 82% confirms the accuracy of the method.
Interference/ Specificity	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.
LOQ	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 0.5 – 0.7 % which fulfills acceptance criteria. LOQ 0.0051 mg/L LOQ 0.85 mg/L	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 0.5 – 0.7 % which fulfills acceptance criteria. LOQ 0.0091 mg/L LOQ 1.517 mg/L	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 0.5 – 0.7 % which fulfills acceptance criteria. LOQ 0.155 mg/L LOQ 25.83 mg/L
Comment	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU	The determined validation parameters such as specificity, linearity, limit of quantification (LOQ), repeatability (precision) and accuracy are compliant with EU

	As 50 mg	Cd 50 mg	Pb 250 mg
	requirements given in SANCO/3030/99 rev.5.	requirements given in SANCO/3030/99 rev.5.	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 50 WP 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^+ state. Bathocurproine 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)			
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 Grape stems 40 mg/kg Raisins 13 mg/kg Wine 0.28 mg/kg	AAS	Scibaldi, F. (2002a)/ DAR of copper compunds point B.5.2.1
	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 compunds 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 compunds 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 compunds point B.5.3.1
	Confirmatory (if required)	Not required. Due to the method itself, it can be considered to be enough specific.		
Air (Residues)	Primary	0.3 ng/ m^3	ICP-OES	Verein Deutscher Ingenieure (1997)/ DAR of copper compunds 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	Primary	Plasma 3 mg/kg Bile 13.9 mg/kg	ICP-AES	xxx (2003)/ DAR of copper compunds 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
(Residues)		Liver 371 mg/kg Feaces 832 mg/kg Carcass 46 mg/kg		
	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 compunds 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 compunds 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 compunds 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 compunds 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.

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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 *O. mykiss* EFSA Scientific Report (2008) 187, 1-101, ASB2012-3573
Air	total copper	22 µg Cu/m$_3$	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 compunds 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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 compunds 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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 copper compunds 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**
tent				
	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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 compunds 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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 compunds 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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 compunds 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. **Therefore the method should be considered fully validated and no ILV is**		

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**
		required.		
	Confirmatory (if required)	Not required. Determination of Copper by ICP/AES is inherently specific.		
Difficult (if required, depends on intended use)	Primary	LOQ 0.2 mg/kg Not fully validated	AAS	Scibaldi, F., Riccelli, S. (2010)/ RAR of copper compunds 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. **Therefore the method should be considered fully validated and no ILV is required.**		
	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 copper in foodstuff of animal origin.		
	ILV			

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**
	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 compunds 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 compunds 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 compunds 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 $\mu g/m^3$	GF-AAS	Anon. (1999)/ DAR of copper compunds point B.5.3.3
Primary	0.3 $\mu g/m^3$	ICP-OES	Anon. (1997)/ DAR of copper compunds 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	xxx (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	Anna Kiełczewska, MSc.	2011	Development and validation of the method of determination of active ingredient content in Miedzian 50 WP formulation. Study code: BA-11/11 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.

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

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 5.1.2	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 GLP: Yes Unpublished	N	EUCuTF In DAR (2007)
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	N	Public

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
			(Air Pollution Prevention). Method No. VDI 2267, Part 5. GLP: No Published		
KCP 5.1.2	xxx	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 65Cu in receptor fluid, stripped skin, tape strips, receptor/donor wash solution and skin wash used in the 'In vitro percutaneous absorption test of copper 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	N	EUCuTF 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)

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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 5.2	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)
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).		Public

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: No Ppublished		
KCP 5.2	xxx	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 5.2)

A 2.1.1.1.1   Analytical method 1 (Residues in Cherries)

A 2.1.1.1.1.1   Method validation

Evaluator's comment:
Study is accepted

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_3, 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, Instidude 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_3, 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^{103}), 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 coeficient 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

	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.
	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 occuring 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 **LOQ** was successfully established at **0.50 mg/kg** for cherry **Limit of detetion (LOD)** was established at **0.15 mg/kg** 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.

A 2.1.1.1.2   Analytical method 2 (Residues in French bean)

A 2.1.1.1.2.1   Method validation

Evaluator's comment:
Study is accepted

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_3, 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_3, 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^{103}), 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

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Table A 4:   **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 coeficient 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 occuring 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 ≤ 15% is achieved. For Cu **LOQ** was successfully established at **1.0 mg/kg** for bean **Limit of detetion (LOD)** was established at **0.30 mg/kg** 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.

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 2.1.2.1.1.1   Confirmatory method (if required)

No confirmatory method is required

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