

REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: GWN-10616

Product name: ELECTIS K-PLUS

Chemical active substances:

Zoxamide, 60 g/L

Potassium phosphonates, 755 g/L

Phosphonic acid equivalents, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: XXXX

Submission date: 31/10/2023 update 05/2024

zRMS evaluation date: 07/2024

MS Finalisation date: June 2025

Version history

When	What
May 2024	Initial RR
May 2024	The applicant's update: Table 7.1-1 correction 7.3.7 Other /special studies; A 2.3.6.1 Study 1 – Residue study in honey
July 2024	Revised initial RR
October 2024	RR Revision after comments; the updates are required from the applicant.
September 2024 October 2024	Update based on zRMS request of July 2024: Update based on zRMS request of October 2024 Chapter 7.3.1.1 and related A 2.3.6.1 and A 2.3.1.1.1.4 Chapter 7.3.3.2 Chapter 7.3.5.1 and related A 2.3.5.2.1 Table 7.3-10 Input values for consumer risk assessment A 2.5 IEDI calculation Appendix 3: MRL calculation in honey
October 2024	Update based on zRMS request of October 2024: Chapter 7.1.2 Chapter 7.3. Chapter 7.3.1.1 Chapter 7.3.8.1 Chapter 7.3.8.2 Appendix 1
November 2024	RR final Revision after comments; All the applicant's updates (blue and brown) were provided to the evaluator as a consequence of the comments (see reporting table), after commenting period, and they were applied by the evaluator for the finalisation of the RR.
June 2025	The accepted GAP update by zRMS

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7 Metabolism and residue data (KCA section 6)

It was stated by the zRMS in June 2025 as follows:

The update of the GAP registration recommendation for ELECTIS K-PLUS (GWN-10616) made below on light green background by the evaluator resulted from a request from the Polish Ministry of Agriculture and Rural Development sent to Eko-Futura by e-mail in Polish on 27 May 2025¹ due to the changes to the MRLs for zoxamide and phosphonic acid in the context of the residues evaluation already done on 06.11.2024. Below, we can see the relevant MRLs in force (as of 29 May 2025 on the EU WEB). The new MRL for zoxamide in honey is applicable from 19/08/2025.

In the case of apple, the MRL for zoxamide is still exceeded, preventing registration of this use (the measurement uncertainty estimated on the basis of the validation data does not allow rounding the value of 0.024 to the MRL level).

Taking into account the residue data for zoxamide and phosphonic acid for grapes, pome fruits and honey shown within the present report

(zoxamide in grapes 0.190, 0.208, 0.331, 0.340, 0.511, 0.591, 0.616, 0.905 phosphonic acid in grapes 1.439, 3.606, 70.039, 41.619, 69.545, 16.5, 18.9, 85.5; zoxamide in apples 6x <0.01, 0.024, phosphonic acid in apples 1.85, 11.6, 1.78, 2.63, 1.45, 2.38, 1.22, 0.687, 6.4; zoxamide in honey 3x <0.01, 0.078, phosphonic acid in honey 1.89 to 15.19),

the updated GAP in the table 7.1-1 can be approved and used as valid from 19/08/2025.

		Zoxamide	Phosphonic acid and its salts expressed as phosphonic acid
Code number	Groups and examples of individual products to which the MRLs apply	Applicable	Applicable
130010	Apples	0.02*	70
130020	Pears	0.02*	70
130030	Quinces	0.02*	70
130040	Medlars	0.02*	70
130050	Loquats/Japanese medlars	0.02*	70
130990	Others (pome fruits)	0.02*	70
151010	Table grapes	5	100
151020	Wine grapes	5	150
211000	Potatoes	0.02*	150
1040000	Honey and other apiculture products	0.05*	100
Code number	Groups and examples of individual products to which the MRLs apply (a)	Zoxamide (sum of isomers) applicable from 19/08/2025	
1040000	Honey and other apiculture products	0,2	

The use in grapes divided previously into 1a and 1b for technical reasons is now again the use number 1.

¹ A significant part of this e-mail in English is quoted here for the sake of order: "In reference to the letter of the Ministry of Agriculture and Rural Development dated 24 January 2024, reference number: DHR.rs1.8208.1.44.2023 regarding an assessment concerning the plant protection product ELECTIS K-PLUS (code name: GWN-10616) and in connection with the assessment of the product ELECTIS K-PLUS performed by EKO-FUTURA Sp. z o.o. and submitted to the Ministry in the letter dated 30 December 2024, I kindly ask you to update the part of the registration report concerning residues in connection with, among others, the change of:
- MRLs for zoxamide and phosphonic acid in honey,
- MRLs for phosphonic acid in grapevine for wine production.
The above update of the report should be made taking into account the findings from the harmonization meetings."

7.1 Summary and zRMS Conclusion

The applicant's dRR text was not rewritten by the zRMS except below paragraph 7.1 & 7.1.1. In the resulting RR all zRMS' comments /corrections/add-ons were placed on the grey background.

It is important to note that a part of zoxamide related studies presented in the Appendix 2 have been already submitted in May 2021 by XXXX. and its affiliates to the **RMS Latvia** and finalised in September 2023 as updated set of zoxamide data after the renewal. However, within the Appendix 2 of the present dRR B7 of GWN-10616, the applicant included "for a completeness" the summaries of these studies and added them in the list of "data submitted or referred to by the applicant and relied on". As a result, all these summaries had to be accompanied by the zRMS for the formal clarity with the original RMS Latvia assessment conclusions (grey boxes' content) taken from Circa from part B section 5 & 7 core assessments of the applicant products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG and GOW F113. The relevant list of studies was transferred to the list of studies "relied on but already evaluated". For all details please see the Appendix 1 and 2.

In zRMS opinion the dossier in the context of the authorisation request is overloaded which can be a suggestion for the applicant's future actions.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation GWN-10616 are presented in Table 7.1-1. They have been selected from the individual GAPs in the Central European Zone for grapes, pome fruits and potatoes. A list of all intended uses within the Central European Zone is given in Part B, Section 0.

Note: In the Southern European Zone the GAP for grapes, potatoes and pome fruits is the same as in the Central European Zone. The data sets performed in Northern and Southern Europe are statistically similar and were therefore merged for MRL setting and risk assessment. This is in accordance to SANTE/2019/12752.

Overall conclusion

Zoxamide:

The data available are considered sufficient for risk assessment.

An exceedance of the current MRL of 5 mg/kg for grapes (table and wine grapes) and 0.02* mg/kg for potatoes for Zoxamide as laid down in Reg. (EU) 2017/171 is not expected.

An exceedance of the current MRL of 0.02* mg/kg for pome fruits for Zoxamide as laid down in Reg. (EU) 2017/171 is expected. An MRL application for pome fruits will be submitted in parallel with the dossier. However, until the MRL is changed, the use in pome fruits cannot be registered.

Honey aspect:

Zoxamide is a non-systemic fungicide but according to SANTE/11956/2016 rev. 9 pome fruits and grapes are melliferous crops and the intended GAP does not exclude treatment during flowering.

Reg. (EU) 2017/171 set the current zoxamide MRL in honey for 0,05*. The data provided confirms the exceedance of the MRL (see report No. 19 48 BTR 0003: significant difference between 2 results from 2 trials in DE). Therefore, the use in pome fruits and grapes cannot be registered until the MRL is changed.

The applicant informs that for Zoxamide an MRL of 0.2 mg/kg (see also Appendix 3) for bee products is already proposed (EFSA RO is under preparation) and an exceedance of the proposed MRL is not expected.

Phosphonic acid:

The data available are considered sufficient for risk assessment.

An exceedance of the current MRL of 150 mg/kg for pome fruits and 200 mg/kg for potatoes for Fosetyl-Al (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl) as laid down in Reg. (EU) 2022/1324 is not expected.

In the Reg. (EU) 2022/1324, for wine grapes an MRL of 200 mg/kg and for table grapes an MRL of 100 mg/kg were set related to the existing residue definition for enforcement: Fosetyl-AI (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl). Based on the available residue data (old and new data), performed in Southern and Northern Europe, the calculated MRL for table grapes would be slightly exceeded. However, due to the highest residue level of 85 mg/kg (which was an exception) for Phosphonic acid, it is assumed that the existing MRLs are still appropriate and an MRL application for the use of GWN-10616 on table grapes is not needed.

Honey aspect:

The current fosetyl-AI MRL for honey is 0.5* mg/kg. Within the submitted dRR no phosphonic acid residues study report in honey. On pages e.g. 40, 45, 56, 68 it is written that the LoA for honey residue data is available. Therefore zRMS kindly recommends to make as soon as possible the missing data available within the present B7. EFSA reports e.g. phosphonic acid residue data (EFSA Journal 2022;20(1):6992) and this data shows HR 61,6 mg/kg which is a significant exceedance of the current MRL level. The EFSA data is as follows:

Commodity	Region ^(a)	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR ^(b) (mg/kg)	STMR ^(c) (mg/kg)
RD-Mo (existing): Fosetyl-AI (sum of fosetyl, phosphonic acid and their salts, expressed as fosetyl)						
RD-Mo (proposed (EFSA, 2021c)): Phosphonic acid and its salts, expressed as phosphonic acid						
RD-RA (EFSA, 2021c): Phosphonic acid and its salts, expressed as phosphonic acid						
Honey	EU	RD-Mo (existing)^(d): 0.95; 0.98; 26.8; 61.6 RD-RA=RD-Mo (proposed): 0.71; 0.73; 27; 46	Semi-field (tunnel) trials with buckwheat treated with potassium phosphonates (3 × 2.36 kg/ha) at BBCH 55–65 via foliar application. The number of trials is sufficient to derive an MRL in honey.	RD-Mo (existing): 150 RD-Mo (proposed): 100	RD-RA: 46	RD-RA: 10.37

The presented by the applicant phosphonic acid data also shows the exceedance of the currently adopted MRL in honey (see the Appendix 2 update in yellow).

According to ADI value TMDI was recalculated taking account new residue definition and input values consistent with it (see relevant paragraph and Appendix 3). The chronic and the short-term intakes of Zoxamide and Phosphonic acid residues are unlikely to present a public health concern.

Please, finally kindly note that to approve the use in pome fruits the following requirements must be fulfilled:

1. Taken in force the amended zoxamide MRLs in pome fruits.
2. Taken in force the amended zoxamide MRL in honey.
3. Taken in force the amended phosphonic acid MRL² in honey.

To approve 1a use (tab.7.1-1) in table and wine grapes the following requirements must be fulfilled:

1. Taken in force the amended zoxamide MRL in honey.
2. Taken in force the amended phosphonic acid MRL² in honey.
3. Taken in force the amended phosphonic acid MRL in table grapes (DE: according to the current residue definition for potassium phosphonates, an MRL exceedance for table grapes is expected, as the newly proposed enforcement residue definition has not entered into force yet).

After confirming by the zRMS the MRLs in force consistency with the applicant's residue data in honey and zoxamide in pome fruits, as well as an amending the report after commenting, the authorization of grapes (1a) and pome fruits may be granted without further action immediately once the above conditions are met.

The relevant residue data for phosphonic acid in honey should be completed in Appendix 1, 2 and in paragraph on magnitude of phosphonic acid residues (Table 7.3 6).

According to available data, no specific mitigation measures should apply.

Currently, as far as consumer health protection is concerned, Poland agrees with the authorization of the intended uses except grapes (1a) and pome fruits. The registered product must be MRL compliant. The use 1b in wine (acc. DE comment) grapes (with the flowering period excluded) can be authorised.

Data gaps

None

² 1040000 Honey and other apiculture products MRL 0,5 mg/kg (Fosetyl-AI (sum of fosetyl, phosphonic acid and their salts, expressed as fosetyl)) applicable from 18/08/2022 acc. to Reg. (EU) 2022/1324

Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)	Crop and/or situation **	Zone	Product code	F, Fn, Fpn G, Gn, Gpn or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment (Z) = Zoxamide (K) = Phosphonic acid			PHI (days)	Conclusion
						Type	Conc. Of as	method kind	growth stage & season	number min max	interval between applications (min)	g as/hL min max	water L/ha min max	g as/ha min max		
1, 2	Grapevine (table and wine) (VITVI)	CEZ	GWN-10616	F	Downy mildew <i>Plasmopara viticola</i> (PLASVI)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)	Broadcast foliar spray	BBCH 14-79	3	8	18-90 (Z) 10-50 g a.s./10000m ² tLWA (Z) 150-750 g a.s./10000m ² tLWA (K)	200-1000 111 – 557 L/10000 m ² tLWA	180 (Z); 1500 (K) 100 g a.s./ 10000 m ² tLWA (Z) 835 g a.s./ 10000 m ² tLWA (K)	28	
3,4	Pome fruit (NNNOK)	CEZ	GWN-10616	F	<i>Venturia sp.</i> (VENTSP)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)		BBCH 51-69	2	6	18-90 (Z) 10-50 g a.s./10000m ² tLWA (Z) 150-750 g a.s./10000m ² tLWA (K)	200-1000 111 – 557 L/10000 m ² tLWA	180 (Z); 1500 (K) 100 g a.s./ 10000 m ² tLWA (Z) 835 g a.s./ 10000 m ² tLWA (K)	NR	Pome fruits MRL exidance Treatments within the end of flowering Assuming max. 18000 m ² tLWA per ha ground area
5,6	Potato (SOLTU)	CEZ	GWN-10616	F	Potato late blight <i>Phytophthora infestans</i> (PHYTIN)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)		BBCH 21-89	3	7	30-75 (Z); 250-625 (K)	200-500	150 (Z); 1250 (K)	7	SANTE/10052/2018 Rev 2 23 March 2018

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)	Crop and/or situation	Zone	Product code	F, Fn, Fpn, G, Gn, Gpn or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment (Z)=Zoxamide (K)=Phosphonic acid			PHI (days)	Conclusion
						Type	Conc. Of as	method kind	growth stage & season	number min max	interval between applications (min)	g as/ha min max	water L/ha min max	g as/ha min max		
1a, 2	Grapevine (table and wine) (VITV)	CEZ	GWN-10616	F	Downy mildew <i>Plasmopara viticola</i> (PLASVI)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)	Broad-eat foliar spray	BBCH 14-79	3	8	18-90 (Z) 10-50 g a.s./10000m ² tLWA (Z) 150-750 g a.s./10000m ² tLWA (K)	200-1000 tLWA 111-557 L/10000 m ² tLWA	180 (Z); 1500 (K) 100 g a.s./10000 m ² tLWA (Z) 835 g a.s./10000 m ² tLWA (K)	28	Honey-MRL-exceeded Collateral effects on Botrytis cinerea Assuming max. 18000 m ² tLWA per ha ground area
1b	Grapevine (table and wine) (VITV)	CEZ	GWN-10616	F	Downy mildew <i>Plasmopara viticola</i> (PLASVI)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)		BBCH 14-57 & BBCH 71-79	3	8	18-90 (Z) 10-50 g a.s./10000m ² tLWA (Z) 150-750 g a.s./10000m ² tLWA (K)	200-1000 tLWA 111-557 L/10000 m ² tLWA	180 (Z); 1500 (K) 100 g a.s./10000 m ² tLWA (Z) 835 g a.s./10000 m ² tLWA (K)	28	GAP excluding flowering period
3,4	Pome fruit (NNNOK)	CEZ	GWN-10616	F	Venturia sp. (VENTSP)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)		BBCH 51-69	2	6	18-90 (Z) 10-50 g a.s./10000m ² tLWA (Z) 150-750 g a.s./10000m ² tLWA (K)	200-1000 tLWA 111-557 L/10000 m ² tLWA	180 (Z); 1500 (K) 100 g a.s./10000 m ² tLWA (Z) 835 g a.s./10000 m ² tLWA (K)	NR	Pome fruits and honey-MRL-exidance Treatments within the end-of-flowering Assuming max. 18000 m ² tLWA per ha ground area
5,6	Potato (SOLTU)	CEZ	GWN-10616	F	Potato late blight <i>Phytophthora infestans</i> (PHYTIN)	SC	Zoxamide 60 g/L K-phosphonate 755 g/L (500 g/L Phosphonic acid)		BBCH 21-89	3	7	30-75 (Z); 250-625 (K)	200-500	150 (Z); 1250 (K)	7	SANTE/10052/2018 Rev 2 23 March 2018

F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

NR: Not relevant

Explanation for Column 11 "Conclusion"

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

7.1.2 Summary of the evaluation

The preparation GWN-10616 is composed of Zoxamide and Phosphonic acid.

Table 7.1-2a: Toxicological reference values for the dietary risk assessment of Zoxamide and RH-150721

Reference value	Source	Year	Value	Study relied upon	Safety factor
Zoxamide					
ADI	EFSA	2017	0.5 mg /kg bw/day	dog, 1-year	100
ArfD	EFSA	2017	Not allocated – not necessary		
RH-150721					
ADI	EFSA	2023*	0.04 mg /kg bw/day	rat, 90 d	1000
ArfD	EFSA	2023*	0.22 mg/kg bw	rat, 14 d	300

* Proposed by EFSA following EU expert meeting conclusions on April 2023 and agreed by Latvia as RMS

Table 7.1-2b: Toxicological reference values for the dietary risk assessment of Phosphonic acid

Reference value	Source	Year	Value	Study relied upon	Safety factor
Phosphonic acid					
ADI	EFSA	2012 2018	2,25 1,0 mg /kg bw/day	2-year rat, with hydrated monosodium phosphonate, expressed as Phosphonic acid	100
ArfD	EFSA	2012 2018	Not relevant		

7.1.2.1 Summary for Zoxamide

Table 7.1-3: Summary for Zoxamide

Use-No.	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1,2	Grapevine (table and wine)	Yes	Yes (NEU: 8 trials: SEU: 8 trials)	Yes	Yes	Yes	No	No
3,4	Pome fruit	Yes	Yes (NEU: 9 trials: SEU: 10 trials)	Yes	Yes	No*		No
5,6	Potato	Yes	Yes	Yes	Yes	Yes		No

Use-No.	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
			(NEU: 8 trials; SEU: 8 trials)					

* An MRL application will be submitted together with the current dossier

For NEU there are 7 residue trials on apples and 2 trials on pears.

The effects of processing on the nature of Zoxamide residues and its metabolites have been investigated and have already been submitted to RMS Latvia.

Additional data on effects of processing on the amount of residue have been submitted.
These data were considered for risk assessment.

Residues in succeeding crops already have been submitted to RMS Latvia in the context of the interzonal evaluation of the confirmatory-like active substance data of Zoxamide after the AIR process taking into account the specific circumstances of the cGAP uses being considered here. It is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

7.1.2.2 Summary for Potassium phosphonates

Table 7.1-4: Summary for Potassium phosphonates

Use-No.	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for 11a calculated identified?	Acute risk for consumers identified?
1	Grapevine (table and wine)	Yes	Yes (NEU: 16 trials; SEU: 26 trials)	Yes	Yes	Yes*	No	No
3	Pome fruit	Yes	Yes (NEU: 9 trials; SEU: 8 trials)	Yes	Not required	Yes		No
5	Potato	Yes	Yes (NEU: 8 trials; SEU: 8 trials)	Yes	Study on-going	Yes		No

* In the joint MRL review for fosetyl and phosphonates a residue definition for potassium phosphonates in plant products as “Phosphonic acid and its salts, expressed as Phosphonic acid” for both enforcement and risk assessment has been proposed. EFSA Journal 2023;21(5):8033. Due to the highest residue level of 85 mg/kg for Phosphonic acid, it is assumed that the existing MRLs are still appropriate.

The effects of processing on the nature of Potassium phosphonate residues have been investigated (for details see 7.3.2.3).

Data on effects of processing on the amount of residue have been submitted.
These data were considered for risk assessment.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here (for details see 7.3.6). It is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

Honey

Different MRL proposals for honey have been derived in the joint MRL review (EFSA, 2021) and in the subsequent EFSA assessment of phosphonic acid residues in honey resulting from uses of potassium phosphonates as applied for in an MRL application (EFSA, 2022).

The joint MRL review proposed an MRL for honey of 0.3 mg/kg based on the available monitoring data (EFSA, 2021). Following the publication of the joint MRL review, on January 2022, EFSA issued a reasoned opinion on the modification of the existing MRLs for fosetyl/phosphonic acid in chards/beet leaves and honey resulting from the use of potassium phosphonates (EFSA, 2022). An MRL for honey of 100 mg/kg was proposed based on the treatment of buckwheat (selected as surrogate melliferous crop) with potassium phosphonates.

EFSA concludes it appropriate to set the MRL for honey at the level of 100 mg/kg on the basis of buckwheat residue field (tunnel) trials as assessed in the Article 10 reasoned opinion since in cases where both field trials and monitoring data are available, the data from field trials should prevail.

(From EFSA Journal 2022;20(7):7400: Scientific statement on the maximum residue levels for potassium phosphonates)

7.1.2.3 Summary for GWN-10616

Table 7.1-5: Information on GWN-10616 (KCA 6.8)

Crop	PHI for GWN-10616 proposed by applicant	PHI sufficiently supported for		PHI for GWN-10616 proposed by zRMS	zRMS Comments (if different PHI proposed)
		Zoxamide	Potassium phosphonates		
Grapevine (table and wine)	28	Yes	Yes	n/a	
Pome fruit	F*	NR (Yes)	NR (Yes)		
Potato	7	Yes	Yes		

NR: not relevant

* F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

Table 7.1-6: Waiting periods before planting succeeding crops

Waiting period before planting succeeding crops			Overall waiting period proposed by zRMS for GWN-10616
Crop group	Zoxamide	Potassium phosphonates	
<p>Zoxamide No waiting period needed, due to quick degradation in soil with a geometric mean DT₅₀ of 5.5 days (EFSA 2017). In addition, Zoxamide is not systemic. Therefore, residues of Zoxamide and its metabolites in rotational plants are very unlikely.</p> <p>Potassium phosphonates: In the RO on the joint review of MRLs for fosetyl, disodium phosphonate and potassium phosphonate according to Articles 12 and 43 of Reg. (EC) No. 396/2005 (EFSA Journal 2021; 19(8):6782), it was stated that the MRLs are expected to cover the possible uptake of Phosphonic acid in succeeding crops resulting from the use of fosetyl, potassium phosphonate and disodium phosphonates in compliance with the authorised GAPs and from the use of other products of agricultural relevance. As the GAP of the intended uses in grapes, apples and potatoes is covered by the already registered uses of the intended crops, no waiting period is needed.</p>			n/a

Re-entry period (in days) for livestock, to areas to be grazed:

Not applicable. GWN-10616 is not applied on areas intended to be grazed by livestock.

Withholding period (in days) for animal feeding stuff:

Zoxamide:

A setting of a withholding period for animal feeding stuff is not needed due to low contribution to the exposure level.

Potassium phosphonates:

A setting of a withholding period for animal feeding stuff is not needed due to low contribution to the exposure level.

Waiting period (in days) between last application and sowing or planting succeeding crops:

Zoxamide:

Grapes, pome fruits:

A waiting period before sowing or planting succeeding crops is not needed, as grapes and pome fruits belong to permanent crops.

Potatoes:

A setting of a withholding period for planting succeeding crops is not needed due to low contribution to the exposure level.

Potassium phosphonates:

Grapes, pome fruits:

A waiting period before sowing or planting succeeding crops is not needed, as grapes and pome fruits belong to permanent crops.

Potatoes:

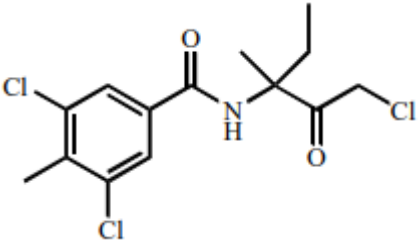
A setting of a withholding period for planting succeeding crops is not needed due to low contribution to the exposure level.

Assessment

7.2 ZOXAMIDE

General data on Zoxamide are summarised in the table below.

Table 7.2-1: General information on Zoxamide

Active substance (ISO Common Name)	Zoxamide
IUPAC	(RS)-3,5-dichloro-N-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-p-toluamide
Chemical structure	
Molecular formula	C ₁₄ H ₁₆ NO ₂ Cl ₃
Molar mass	336.65 g/mol
Chemical group	Benzamide
Mode of action (if available)	Inhibition of germ tube development and mycelium growth by inhibiting cell division.
Systemic	No
Company	XXXX
Rapporteur Member State (RMS)	Latvia
Approval status	Approved since 01/07/2018. Commission Implementing Regulation (EU) 2018/692 of 7 May 2018
Restriction (e.g. is restricted to use as "...")	None
Review Report	SANCO/10052/2018 – rev. 2 23/03/2018
Current MRL regulation	Regulation (EU) No 2017/171
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	EFSA Journal. 2023;21:e8427
EFSA Journal: Conclusion on the peer review	Yes, EFSA, 2017
EFSA Journal: Conclusion on Article 12	No
Current MRL applications on intended uses	EFSA-Q-2019-00404 Dry onion bulbs Status: Stop of clock (EFSA agreed with the EU COM to combine it with Art. 12 process) EFSA-Q-2008-649 Review of all existing MRLs Status: Ongoing (EFSA schedule anticipated Nov 2023)

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

Two freezer storage stability studies have been already provided to the RMS Latvia for evaluation of confirmatory-like active substance data. Results are summarised in the table below. The detailed assessment of these studies is presented in Appendix 2 only for completeness sake.

Table 7.2-2: Summary of stability data achieved at $\leq -18^{\circ}\text{C}$ (unless stated otherwise)

Matrix	Characteris- tics of the matrix	Acceptable Maximum Storage duration [months]						Reference
Data relied on in EU								
Plant products		Zox- amide	RH- 150721	RH- 141452	RH- 141455	RH- 24549	RH- 141288	
Potato tubers**	High starch content	24	--	24	24	--	--	EFSA, 2017
Grape berries**	High acid content	18	18	--	--	--	--	EFSA, 2017
Grape juice		24	--	--	--	--	--	EFSA, 2017
Wine		24	24	--	--	--	--	EFSA, 2017
Raisins*		24	--	--	--	--	--	EFSA, 2017
Animal Products								
--	--	--	--	--	--	--	--	--
Data – already submitted to RMS Latvia***								
Plant products		Zox- amide	RH- 150721	RH- 141452	RH- 141455	RH- 24549	RH- 141288	
Grape berries/bunches	High acid content	26	24	26	--	26	18	Report No. BPL- STUDY-18- 000038, Doc. No. 645-002, KCA 6.1/05
Grape juice		26	24	26	--	26	26	Report No. BPL- STUDY-18- 000038, Doc. No. 645-002, KCA 6.1/05
Wine		26	24	26	--	26	26	Report No. BPL- STUDY-18- 000038, Doc. No. 645-002,

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration [months]						Reference
								KCA 6.1/05
Grape berries/bunches, grape juice, wine	High acid content	Not stable for 3 months as first timepoint (RH-129151)						Report No. BPL-STUDY-18-000038, Doc. No. 645-002, KCA 6.1/05
Animal Products		Zoxamide	RH-150721	RH-141452	RH-141455	--	--	
Honey	High sugar content	2.8 (85 days)	--	--	--	--	--	Report No. 19 48 BTR 0003, Doc. No. 634-96001; KCA 6.1/06

* dry/high sugar content according to SANTE/2020/12830, Rev. 1

** -20°C

*** Data are summarised in the current dRR only for completeness sake.

Conclusion on stability of residues during storage

The freezer storage stability of Zoxamide in high starch commodity (potato tubers), high acid commodities (grape berries, grape juice, wine) and raisins has already been evaluated within the renewal procedure. In high acid commodities, Zoxamide was found to be stable in grape berries for 26 months and in grape juice, wine, and raisins for 24 months under deep frozen conditions. In high starch commodities (potato), Zoxamide residues were found to be stable under deep frozen conditions for 24 months.

RH-141452 was found to be stable in high starch commodity (potato tubers) for 24 months and for 26 months in grape berries and processed acidic commodities (grape juice and wine) under deep frozen conditions.

RH-150721 was found to be stable in high acid commodity for 18 months in grape berries and for 24 months in wine under deep frozen conditions.

In the honey residue study (report No. 19 48 BTR 0003, Doc. No. 634-96001, KCA 6.1/06) Zoxamide (racemate) has been demonstrated to be stable in frozen honey (high sugar content) samples for at least 85 days.

The freezer storage stability data for Zoxamide, RH-141452 and RH-150721 in high starch (potatoes), in high acid (grape berries, juice, wine and raisins) commodities and in honey are covering the max. storage periods within the residue and processing studies.

Freezer storage stability data in apples/pears are not needed, as Zoxamide and its metabolites have been analysed within 30 days.

No further data are needed.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

The stability of residues of Zoxamide and its metabolites in sample extracts was checked in fortification experiments (procedural recoveries) as part of the analytical phase of the individual supervised residue studies in case the extracts have been stored > 24 hours or within method validations.

This information is indicated below and in the study summaries presented in Appendix 2.

Matrix	Analyte	Temperature	Time period [days]	Reference
Grapes	Zoxamide	5 ± 3°C	3	Report No. GLP-STUDY-21-101; KCA 6.1/09; New method validation
	RH-141452	5 ± 3°C	3	Report No. GLP-STUDY-21-102; KCA 6.1/10; New method validation
Grapes, grape juice, wine, raisins	I-Zoxamide, (S)-Zoxamide, RH-141452, I-RH-150721, (S)- RH-150721	4°C	3	Report No. BPL-STUDY-18-000085; KCA 6.1/07 submitted to RMS Latvia
Apples	Zoxamide	5 ± 3°C	3	Report No. GPL-STUDY-21-53; KCA 6.1/11; New method validation
	RH-141452	5 ± 3°C	3	Report No. GLP-STUDY-21-54; KCA 6.1/12; New method validation
Potato tubers, potato flakes, fried potatoes	I-Zoxamide, (S)-Zoxamide, RH-141452	4°C	3	Report No. BPL-STUDY-18-000085; KCA 6.1/07; submitted to RMS Latvia

Conclusion on stability of residues in sample extracts

The stability of residues of Zoxamide and its metabolites in sample extracts was checked in fortification experiments (procedural recoveries) as part of the analytical phase of the individual supervised residue studies in case the extracts have been stored > 24 hours or within method validations.

Based on the available data, it was shown that Zoxamide and its metabolites (RH-141452, RH-150721) are stable in extracts of grapes (berries, juice, wine, raisins), apples and potatoes (tuber, flakes, fried potatoes) for at least 3 days at refrigerated temperature. No further data are needed.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-3: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (g a.s./ha)	No / interval	Sam-pling (DAT)	Remarks	
EU data								
Fruits and fruiting vegetable	Grape	¹⁴ C-phenyl ring labelled Zoxamide	foliar application, F	1867	3 / 26-28 days	1	only Zoxamide > 10 % AR (0.43 mg/kg)	EFSA, 2017
		¹⁴ C-phenyl ring labelled Zoxamide	foliar application, F	500	3 / 9-11 days	28	only Zoxamide > 10 % AR (3.67 mg/kg)	EFSA, 2017
	Tomato	¹⁴ C-phenyl ring labelled Zoxamide	foliar application, G	860	3 / 18-19 days	1	only Zoxamide > 10 % AR (0.22 mg/kg) in red tomato	EFSA, 2017
	Cucumber	¹⁴ C-phenyl ring labelled Zoxamide	foliar application, G	1344	3 / 7 days	1	only Zoxamide > 10 % AR (1.33 mg/kg)	EFSA, 2017
Leafy vegetables	--	--	--	--	--	--	--	--
Root and tuber vegetables	Potato	¹³ C- and ¹⁴ C-phenyl ring labelled Zoxamide	foliar application, F	900	3 / 21 and 17 days	14	RH-141452 (0.037 mg/kg) and RH-141455 (0.069 mg/kg) > 10 % AR	EFSA, 2017
Pulses and oilseeds	Peas	¹⁴ C-phenyl ring labelled Zoxamide	foliar application, F	145	2 / 7 days	7, 13, 30	only Zoxamide > 10 % AR (5.35 mg/kg in pods and 0.019 mg/kg in dry peas at a PHI of 30 days)	EFSA, 2017

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (g a.s./ha)	No / interval	Sampling (DAT)	Remarks	
			foliar application, F	725	2 / 7 days	7, 13, 30	only Zoxamide > 10 % AR (e.g. 36.52 mg/kg in immature whole plants at 7 days PHI; 10.01 mg/kg in pods at 13 days PHI; 0.04 mg/kg in fresh peas at 13 days PHI)	
Cereals	--	--	--	--	--	--	--	--
New data								
No new data submitted in the framework of this application.								

Summary of plant metabolism studies reported in the EU

The metabolism of Zoxamide in primary crops was investigated after foliar spray application in the categories fruit, pulses and oilseeds and root crops using Zoxamide ¹³C- and/or ¹⁴C-labelled in the phenyl ring. Zoxamide is not systemic, therefore following foliar application to crops, most of the applied material remains on the surface of the plants. In the metabolism studies conducted in grapes, tomato, cucumber and peas, the major component of the residue is unchanged Zoxamide (RH-7281/RH-117281). Degradation is by photolysis on the crop surface and hydrolysis or oxidation, and results in a number of minor metabolites.

Fruits

In total four metabolism studies are available on fruits (grapes) and fruiting vegetables (tomatoes and cucumber).

Two metabolism studies are available on grapes (Reibach & Spencer, 1998, see RAR 2017) with a PHI of 1 day and Staffa & Möndel (2014) with a PHI of 28 days. Both studies were performed outdoors. The grape metabolism study with a PHI of 1 day does not reflect the intended GAP of Zoxamide products with a PHI of 28 days and is therefore only regarded as supportive.

In a metabolism study on cucumber, Zoxamide was applied to the foliage at nominally 3 x 1344 g a.s./ha with an interval of 7 days and a PHI of one day.

In the metabolism study on tomato (Sharma, 1999) Zoxamide was applied to the foliage at a 1-day PHI at a nominal rate of 3 x 860 g a.s./ha. The study was performed in the greenhouse.

In fruits, Zoxamide was the main component of the total radioactive residue (TRR) with 48 % and 44 % in green and red tomatoes and 92 % in both cucumber and grape. The remaining TRR was extensively metabolised to a range of metabolites representing less than 10 % TRR in these commodities, except for RH-141452 which was observed only in tomato and constituted with 15 % TRR (0.044 mg/kg) and 11 % (0.056 mg/kg) a major metabolite in green and red tomatoes, respectively.

The residue definition has been discussed within Art. 12 and Art. 10 for IT in bulb onions with Latvia and EFSA and during the Pesticide Peer Review Meeting TC 100 (17-21 April 2023)

Root crops (i.e., potatoes)

After foliar application of [¹⁴C]-Zoxamide to potatoes with a 14-days PHI at a nominal rate of 3 x 900 g a.s./ha, the total radioactive residue (TRR) in potato tubers (RAC) determined by combustion was

0.178 mg/kg. Two major metabolites, RH-141452 and RH-141455, were observed in potato tubers at 21 % and 39 % TRR, respectively. Parent Zoxamide was not found.

The GAP used in the potato metabolism study was 3 x 900 g a.s./ha (total of 2700 g a.s./ha/year), applied with a spray interval 17-21 days and a PHI 14 days. For GWN-10616 the intended GAP of Zoxamide for potatoes is at max 3 x 150 g a.s./ha, applied at 7-8 days interval with a PHI 7 days. Thus, the metabolism study in potato tubers represents a worse-case in terms of higher single and seasonal application rate and longer PHI – which allows more time for the formation and accumulation of metabolites in the edible part of potatoes.

However, supervised potato residues trials in compliance to the GAP of GWN-10616 confirmed that no residues of Zoxamide, RH-141455 and RH-141452 above the LOQ (i.e. 0.01 mg/kg) is detected when GWN-10616 is applied according to the GAP.

Summary of new plant metabolism studies

No new data were submitted in the framework of this application.

Conclusion on metabolism in primary crops

In the EFSA conclusion (2017), the following provisional residue definitions were set:

Plant residue definition for monitoring	Zoxamide (fruit, pulses and oilseeds) Metabolites RH-141455 and RH-141452 (root crops) pending data gap for RH-141455 and RH-141452
Plant residue definition for risk assessment	Zoxamide and RH-141452 (fruit) pending data gap on RH-141452 Zoxamide (pulses and oilseeds) Metabolites RH-141452 and RH-141455 (root crops) pending data gap on RH-141452

Following the Pesticide Peer Review Meeting TC 100 the following has been decided:

Metabolite RH-141452 was considered covered by the toxicological profile of the parent compound.

EMS proposes following RDs for all primary crops:

RD-Mo = parent only

RD-RA= parent + RH-141452, expressed as the parent.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

From the intended uses potatoes can be grown in rotation.

Available data

No new data submitted in the framework of this application.

Table 7.2-4: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Fruits and fruiting vegetable	--	--	--	--	--	--	--	--
Leafy vegetables	Mustard	¹³ C- and ¹⁴ C- Zoxamide, uniformly ring labelled	F	4 x 0.5 kg a.s./ha	30, 145, 210, 365	Immature, mature	After 30 days PBI max. 0.009 mg/kg RH-141452 as only relevant residue in immature mustard leaves	EFSA, 2017
Root and tuber vegetables	Radish, turnip	¹³ C- and ¹⁴ C- Zoxamide, uniformly ring labelled	F	4 x 0.5 kg a.s./ha	30, 137, 210, 365	Immature, mature	After 30 days PBI max. 0.006 mg/kg RH-141452 in immature radish tops	EFSA, 2017
Pulses and oilseeds	Soybean	¹³ C- and ¹⁴ C- Zoxamide, uniformly ring labelled	F	4 x 0.5 kg a.s./ha	30, 137, 210, 365	Immature, mature	After 30 days PBI max. 0.023 mg/kg RH-141452 in immature soybean forage	EFSA, 2017
Cereals	Sorghum	¹³ C- and ¹⁴ C- Zoxamide, uniformly ring labelled	F	4 x 0.5 kg a.s./ha	30, 137, 210, 365	Immature, mature	After 30 days PBI max. 0.001 mg/kg RH-141452 in immature sorghum forage	EFSA, 2017
New data								
No new data submitted in the framework of this application.								

* Outdoor/field application (F) or glasshouse/protected/indoor application (G); PBI = Plant back interval; DAT = days after treatment

Summary of metabolism studies in rotational crops reported in the EU

Zoxamide degrades quickly in soil with a DT_{50} of 5.5 days. In addition, Zoxamide is not systemic. Therefore, residues of Zoxamide and its metabolites in rotational plants are very unlikely.

In the rotational crop study, ^{14}C -Zoxamide was applied directly to bare soil at a rate of 4 x 0.50 kg a.s./ha. Leaf (mustard), root (radish/turnip), small grain (wheat/sorghum), and oilseed (soybean) crops were planted into the soil at 30, 137/145, 210 or 365 days after the last application (DALA), and the crops grown to maturity. The results indicate that following application to bare soil, Zoxamide residues are minimally translocated to crop samples and will not result in any detectable levels of parent compound or parent related metabolites in rotational crops. The highest TRR observed was 0.189 mg/kg in 30 DALA soybean hay and 0.127 mg/kg in immature radish and no mature crop except soybeans contained \geq 0.05 mg/kg of TRR in any sample at any plant back interval.

The major portion of the observed residue was not extractable except by hydrolytic processes. Parent Zoxamide was not present in any crop sample at any plant back interval. No organic solvent extractable compound was present at \geq 0.01 ppm in any crop sample at any plant back interval. The crop metabolite RH-141452 was found only in traces (at max. of 0.023 mg/kg in immature soybean forage), a highly degraded soil metabolite, also occurring at low levels in potato tubers.

The metabolism in rotational crop and primary crop is considered to be similar.

Summary of new metabolism studies in rotational crops

No new data submitted in the framework of this application.

Conclusion on metabolism in rotational crops

A confined crop rotation study was previously evaluated for renewal. Study showed minimal translocation of Zoxamide residues from soil into crops. Parent Zoxamide was not detected in following crops. The crop metabolite RH-141452 was found at trace levels in following crops. No detectable residues of Zoxamide or related metabolites are expected in rotational crops.

No further data are needed.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

Simulated processing studies have been already provided to the RMS Latvia within the interzonal evaluation of the confirmatory-like data. Results are summarised in the table below. The detailed assessment of these studies is presented in Appendix 2 only for completeness sake.

Table 7.2-5: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Pasteurisation (20 minutes, 90°C, pH 4)		
Baking, boiling, brewing (60 minutes, 100°C, pH 5)		
Sterilisation (20 minutes, 120°C, pH 6)		
Other conditions	Identified compound(s) (%)	
Winemaking ...	Radiolabelled vinification study showed that the major residue in wine is the metabolite RH-150721.	EFSA, 2017
Data – derived with Zoxamide as test item*; already submitted to RMS Latvia**		
Pasteurisation (20 minutes, 90°C, pH 4)	Parent Zoxamide (35.3 %) RH-24549 (9.7 %) RH-150721 (46.7 %)	Report No. RB66JN, Doc. No. 638-018, KCA 6.5.1/01
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Parent Zoxamide (1.2 %) RH-24549 (62.7 %) RH-150721 (11.0 %) RH-129151 (13.1 %)	
Sterilisation (20 minutes, 120°C, pH 6)	Parent Zoxamide (0.8 %) RH-24549 (43.0 %) RH-129151 (20.8 %) RH-141288 (27.3 %)	
Data – derived with RH-141455 as test item*; already submitted to RMS Latvia**		
Pasteurisation (20 minutes, 90°C, pH 4)	Parent RH-141455 (99.39 %)	Report No. BPL- STUDY-19-000009, Doc. No. 638-009, KCA 6.5.1/03
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Parent RH-141455 (98.95 %)	
Sterilisation (20 minutes, 120°C, pH 6)	Parent RH-141455 (99.75 %)	
Data– derived with RH-141452 as test item*		
Pasteurisation (20 minutes, 90°C, pH 4)	Parent RH-141452 (99.22 %)	Report No. BPL-STUDY-18- 000092, Doc. No. 638-008, KCA 6.5.1/02
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Parent RH-141452 (100.8 %)	
Sterilisation (20 minutes, 120°C, pH 6)	Parent RH-141452 (99.29 %)	
Data– derived with RH-129151 as test item*; already submitted to RMS Latvia**		
Pasteurisation (20 minutes, 90°C, pH 4)	Parent RH-129151 (3.4 %) RH-24549 (13.6 %) RH-150721 (70.8 %)	Report No. GOW-004/5-42, Doc. No. 638-016, KCA 6.5.1/04
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Parent RH-129151 (26.8 %) RH-24549 (73.2 %)	
Sterilisation (20 minutes, 120°C, pH 6)	Parent RH-129151 (53.9 %) RH-24549 (13.8 %) RH-141288 (26.7 %)	

* compounds appearing ≥ 10 % of applied are considered

**Data are summarised in the current dRR only for completeness sake.

Conclusion on nature of residues in processed commodities

Based on the above, the following residue definition for processed commodities is proposed:

Plant residue definition for monitoring in processed commodities:	Zoxamide
Plant residue definition for risk assessment in processed commodities:	Zoxamide, RH-150721

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2-6: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Fruits and fruiting vegetables (grapes, tomatoes, cucumber) Root and tuber vegetables (potatoes) Pulses and oilseeds (peas)
Rotational crops covered	Yes
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	a.s. is not stable under standard hydrolysis conditions RH-129151 is not stable under hydrolysis conditions, it reveals the same metabolism paths as Zoxamide RH-141455 and RH-141452 are stable under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	No Other residue definition in processed commodities: RD for monitoring (M) – Parent only RD for risk assessment (RA1) – Parent only RD for risk assessment (RA2) – RH-150721
Plant residue definition for monitoring	RD for monitoring (M) – Parent only zoxamide (sum of constituent isomers)
Plant residue definition for risk assessment	Residue definition EFSA (2017) revised + RD for risk assessment (RA) – Parent + RH-141452 (calculated as Zoxamide equivalents) Raw commodities: sum of zoxamide and RH-141452, expressed as zoxamide; Processed commodities: RD-1: sum of zoxamide and RH-141452, expressed as zoxamide; RD-2 metabolite RH-150721
Conversion factor from enforcement to RA	None, due to residues < 0.01 mg/kg for metabolite RH-141452 in 51 trials except for one trial in grapes

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

Table 7.2-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	¹⁴ C-Zoxamide labelled in the phenyl ring	2	2.82 mg/kg bw/d (60.7 mg/kg)	7	Milk	twice daily	EFSA, 2017
						Urine and faeces	Daily	
						Tissues	at sacrifice	
Laying poultry	--	--	--	--	--	Eggs	--	--
						Excreta	--	
						Tissues	--	
Pig	Not required, as the metabolic patterns in the goat and the rat are similar.							EFSA, 2017
New data								
Lactating ruminants	No new data were submitted in the framework of this application.							
Laying poultry	No new data were submitted in the framework of this application.							
Pig	Not required, as the metabolic patterns in the goat and the rat are similar.							
Fish	From the intended uses only potatoes might be fed to fish. However, residues of Zoxamide and RH-141452 in fish feed arising from the uses on potatoes are < 0.1 mg/kg feed (dry matter basis), and therefore a fish metabolism study is not required.							

Summary of animal metabolism studies reported in the EU

A goat metabolism study has been evaluated within the EU review. Zoxamide was not detected in the goat study and the metabolites RH-141452 and RH-141455 were observed as terminal compounds of a minor metabolic pathway.

Summary of new animal metabolism studies

No new data are submitted in the framework of this application.

Conclusion on metabolism in livestock

From the intended uses for GWN-10616 on grapes, pome fruits and potatoes, only pome fruits (wet apple) and potatoes will be fed to livestock. However, the intended uses for GWN-10616 on potatoes and pome fruits (wet apple) do not result in residues above 0.1 mg/kg total diet (dry matter basis) in the diet of poultry, ruminants and fish, therefore no data on livestock metabolism are required.

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2-8: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	--
Time needed to reach a plateau concentration	2 days in milk
	--
Animal residue definition for monitoring	None/not relevant (see also Regulation (EU) n° 2017/171)
Animal residue definition for risk assessment	Pending (EFSA 2017) However, no change to Regulation (EU) n° 2017/171 regarded applicable based on the available data.
Conversion factor	--
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Yes (potentially), log Pow 3.76 for Zoxamide. However, as Zoxamide is extensively metabolised and total residue levels in fat were low and not significantly different from other edible tissues, it is proposed that Zoxamide should be listed as not fat soluble. Data gap identified by EFSA (2017) for RH-141288 and RH-127450 have been addressed in dRR provided to Lativa (Art 43).
Fish	Zoxamide in fish feed arising from the intended uses on potatoes are < 0.1 mg/kg feed (dry matter basis), and therefore a fish metabolism study is not required.
Bee product	Residue data on honey are provided. Proposed residue definition: Zoxamide

7.2.3.1 Summary of European data and new data supporting the intended uses

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of GWN-10616 and conformity to existing MRL

Commod- ity	Source	Resi- due zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition: Zoxamide RA = according to risk assessment residue defini- tion: Zoxamide + RH-141452, calculated as Zoxamide equivalents	STMR (mg/kg) RD: Zoxamide	STMR (mg/kg) RD: Zoxamide + RH- 141452, 27alcul- ate as Zoxamide equiva- lents Input data for RA	HR (mg/kg) RD: Zox- amide	HR (mg/kg) RD: Zoxamide + RH- 141452, calculated as Zox- amide equiva- lents Input data for dietary burden	Rounded OECD cal- culator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL com- pliance
Grapevine (table and wine)	EFSA, 2017	N-EU	Not relevant (not GAP compliant; overdosed; higher LOQ)		N/A					
	EFSA, 2017	S-EU	Not relevant (not GAP compliant; overdosed; higher LOQ)							
	New trials	N-EU	Trials GAP: 3 x 180 g Zoxamide/ha, PHI 28 days, outdoor E: 0.190, 0.208, 0.331,0.340, 0.511, 0.591, 0.616, 0.905 RA: 0.200, 0.218, 0.341, 0.350, 0.521, 0.601, 0.627, 0.915							
	New trials	S-EU	Trials GAP: 3 x 180 g Zoxamide/ha, PHI 28 days,							

[illegible]

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition: Zoxamide RA = according to risk assessment residue definition: Zoxamide + RH-141452, calculated as Zoxamide equivalents	STMR (mg/kg) RD: Zoxamide	STMR (mg/kg) RD: Zoxamide + RH-141452, 27alculated as Zoxamide equivalents Input data for RA	HR (mg/kg) RD: Zoxamide	HR (mg/kg) RD: Zoxamide + RH-141452, calculated as Zoxamide equivalents Input data for dietary burden	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
			E: 8x <0.01, 0.024 RA: 8x <0.02, 0.034 (7x apple, 2x pear)							
	New trials	S-EU	Trials GAP: 2 x 180 g Zoxamide/ha, BBCH 51-69, outdoor E: 9x <0.01, 0.0183 RA: 9x <0.02, 0.0283 (8x apple, 2x pear)							
	Overall supporting data for cGAP	N-EU + S-EU	E: 17x <0.01, 0.0183, 0.024 RA: 17x <0.02, 0.0283, 0.034 Populations from S-EU and N-EU are similar (Mann-Whitney U-test).	E: <0.01	RA: <0.02	E: 0.024	RA: 0.034	0.03	0.02*	No; an MRL application will be submitted with the current dossier.
Potato	EFSA, 2017	N-EU	Not relevant.		N/A					
	EFSA, 2017	S-EU	Not relevant.							

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition: Zoxamide RA = according to risk assessment residue definition: Zoxamide + RH-141452, calculated as Zoxamide equivalents	STMR (mg/kg) RD: Zoxamide	STMR (mg/kg) RD: Zoxamide + RH-141452, 27% calculate as Zoxamide equivalents Input data for RA	HR (mg/kg) RD: Zoxamide	HR (mg/kg) RD: Zoxamide + RH-141452, calculated as Zoxamide equivalents Input data for dietary burden	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
	New trials	N-EU	Trials GAP: 3 x 150 g Zoxamide/ha, PHI 7 days, outdoor E: 8x <0.01 RA: 8x <0.02							
	New trials	S-EU	Trials GAP: 3 x 150 g Zoxamide/ha, PHI 7 days, outdoor E: 8 x <0.01 RA: 8x <0.02							
	Overall supporting data for cGAP	N-EU + S-EU	E: 16x <0.01 RA: 16x <0.02	E: <0.01	RA: <0.02	E: <0.01	RA: <0.02	0.01*	0.02*	Yes
Honey	Overall supporting data for cGAP	EU	Trials GAP: 2 x 180 g Zoxamide/ha E: 3x <0.01, 0.078 RA: 3x <0.01, 0.078 The above presented residue data are related to Zoxamide only. Residue levels for RH-141452 are not relevant, as not observed during pasteurisation.	E: <0.01	RA: <0.01	E: 0.078	RA: - (not required)	0.2	0.05* (0.2 ^{###})	Yes Currently no

* indicated residue levels below the level of quantification (LOQ)

Source of EU MRL: Reg. (EU) 2017/171^{###} EFSA RO under preparation

7.2.3.2 Conclusion on the magnitude of residues in plants

In the Southern European Zone, the GAP for grapes, potatoes and pome fruits is the same as in the Central European Zone. The data sets performed in Northern and Southern Europe are statistically similar and were therefore merged for MRL setting and risk assessment. This is in accordance to SANTE/2019/12752.

Grapes (NEU, SEU, GAP: 3 x 180 g Zoxamide/ha, PHI 28 days)

According to SANTE/2019/12752, residue data on wine grapes can be extrapolated to table grapes and *vice versa*.

As the intended GAP on grapes is in line with the GAP considered for MRL setting, the available residue data on grapes (NEU: 8 trials; SEU: 8 trials) sufficiently support the intended use of GWN-10616 on grapes (table and wine grapes) in the Central European Zone.

The data submitted show that no exceedance of the MRL will occur.

The use on grapes (table and wine grapes) is considered acceptable.

Pome fruits (NEU, SEU, GAP: 2 x 180 g Zoxamide/ha, BBCH 51-69)

According to SANTE/2019/12752, residue data on apples and pears (minimum 4 apple trials) can be extrapolated to the whole group “pome fruits”.

As the intended GAP on apples and pears is in line with the GAP considered for MRL setting, the available residue data on apples (NEU: 7 trials on apples; 2 trials on pears; SEU: 8 trials on apples; 2 trials on pears) sufficiently support the intended use of GWN-10616 on pome fruits in the Central European Zone.

The data submitted show that an exceedance of the MRL will occur. An MRL application will be submitted in parallel with the current dossier. The use on pome fruits is considered acceptable. The relevant MRL should be raised.

Potatoes (NEU, SEU, GAP: 3 x 150 g Zoxamide/ha, PHI 7 days)

As the intended GAP on potatoes is in line with the GAP considered for MRL setting, the available residue data on potatoes (NEU: 8 trials; SEU: 8 trials) sufficiently support the intended use of GWN-10616 on potatoes in the Central European Zone.

The data submitted show that no exceedance of the MRL will occur. The use on potatoes is considered acceptable.

Honey

As the intended GAP on honey is in line with the GAP considered for MRL setting, the available residue data on honey (EU: 4 trials) sufficiently support the intended use of GWN-10616 on honey in the Central European Zone.

The above presented residue data are related to Zoxamide only. Residue levels for RH-141452 are not relevant, as not observed during pasteurisation.

For Zoxamide the current MRL is 0,05 mg/kg. An exceedance is expected.

An MRL of 0.2 mg/kg for bee products is proposed (EFSA RO is under preparation.). An exceedance of this MRL is not expected.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

Table 7.2-10: Input values for the dietary burden calculation (considering the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Zoxamide + RH-141452 (calculated as Zoxamide equivalents)				
Root & tubers				
Potato – tuber/cull	0.02	STMR _{RA} (Table 7.2 9)	0.02	HR _{RA} (Table 7.2 9)
By-products				
Apple - pomace, wet	0.10	0.02 mg/kg * 5 ^(a) (STMR _{RA} x PF, Table 7.2 9)	0.10	0.02 mg/kg * 5 ^(a) (STMR _{RA} x PF, Table 7.2 9)
Potato – process waste	0.02	0.02 mg/kg * 1 ^(a) (STMR _{RA} x PF, Table 7.2 9)	0.02	0.02 mg/kg * 1 ^(a) (STMR _{RA} x PF, Table 7.2 9)
Potato – dried pulp	0.02	0.02 mg/kg * 1 ^(a) (STMR _{RA} x PF, Table 7.2 9)	0.02	0.02 mg/kg * 1 ^(a) (STMR _{RA} x PF, Table 7.2 9)

^(a)PF = Processing Factor; for apple pomace, a processing factor of 5 is considered in the dietary burden calculation.

For potato -process waste and potato -dried pulp, a processing factor of 1 has been considered, due to residues in RAC < LOQ for Zoxamide and RH-141452.

Table 7.2-11: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Risk assessment residue definition: Zoxamide + RH-141452 (calculated as Zoxamide equivalents)					
Beef cattle	0.0023	0.002	process waste	0.10	N
Dairy cattle	0.0031	0.003	process waste	0.08	N
Ram/ewe	0.0032	0.003	process waste	0.10	N
Lamb	0.0023	0.002	process waste	0.05	N
Breeding swine	0.002	0.002	process waste	0.08	N
Finishing swine	0.002	0.002	process waste	0.05	N
Broiler poultry	0.001	0.001	culls	0.01	N
Layer poultry	0.001	0.001	culls	0.01	N
Turkey	0.001	0.001	culls	0.02	N

Conclusion:

A metabolism study in lactating ruminants, pig and poultry is not triggered.

Fish

The fish dietary burden was calculated with the DietaryBurdenCalculator 3.0.2 from Fraunhofer Institute for Molecular Biology and Applied Ecology IME.

Input values are summarised in Table 7.2-12.

The estimated maximum animal intakes are provided in Appendix 4.

Table 7.2-12: Input values for the dietary burden calculation for fish

Category	Crop	Commodity	Residue input value	Residue (mg/kg)	Comment
Plant By-Products	Potato	protein	STMR-P	0.02	(STMR _{RA} : 0.02) * (PF: 1) ^(a)

^(a)PF = Processing Factor; due to residue levels in RAC < LOQ for Zoxamide and RH-141452, a processing factor of 1 was considered for the calculation of the dietary burden.

Table 7.2-13: Results of the dietary burden calculation for fish

	Maximum dietary burden in mg/kg (dry matter)
Common carp	0.001
Rainbow trout	0.000
Atlantic salmon	0.000

Conclusion:

A fish metabolism study is not triggered.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

No new data were submitted in the framework of this application.

Conclusion on feeding studies

From the intended uses only apples (wet pomace) and potatoes (culls, process waste and dried pulp) are fed to livestock. However, based on the available residues on apples/pears and potatoes, livestock feeding studies are not triggered. Therefore, respective studies on residues of Zoxamide in livestock were not conducted. No further data are needed.

Accepted.

7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

Data/information on processing studies were reviewed during the approval of Zoxamide and were considered acceptable.

Additional studies have been performed and are reported below and summarised in A 2.1.5.2.1 till A 2.1.5.2.8

7.2.5.1 Available data for all crops under consideration

Processing studies have been already provided to the RMS Latvia. Results are summarised in the table below. The detailed assessment of these studies are presented in Appendix 2 only for completeness sake.

Table 7.2-14: Overview of the available processing studies

Processed commodity	Number of studies	Individual PF	Median CF *	Comments	Reference
EU data					
Enforcement residue definition: Zoxamide					
Grapes, juice (unclarified)	2	0.10 0.16 Mean: 0.13	--	-	RAR, 2017
Grapes, juice (clarified)	2	0.05 0.05 Mean: 0.05	--	-	RAR, 2017
Grapes, dried (raisins)	2	2.2 3.5 Mean: 2.85	--	-	RAR, 2017
Grapes, pomace	9	1.53 3.09 0.01 0.07 0.02 1.13 0.05 0.13 0.79 Median: 0.13	--	-	RAR, 2017
New data (but already submitted to RMS Latvia)					
Enforcement residue definition: Zoxamide					
Grapes					
Grapes, dried (raisins)	2	1.11 1.73 Mean: 1.42	1	-	BPL-STUDY-19-000058 , Doc. No. 638-0012, KCA 6.5.3/01; 18097-03R , Doc. No. 638-005, KCA 6.5.3/02
Grapes, juice before pasteurisation	2	0.032 0.042 Mean: 0.037	1	-	18097-03R , Doc. No. 638-005, KCA 6.5.3/02
Grapes, juice after pasteurisation	8	<0.01 <0.01 0.019 ^{##} /0.018 ^{###} 0.010 ^{##} /0.012 ^{###} 0.083 0.405 0.063 <0.04 Median: 0.030 ^{##} /0.029 ^{###}	1	-	AB2-18-35355 , Doc. No. 638-007, KCA 6.5.3/03; BPL-STUDY-19-000041 , Doc. No. 638-0010, KCA 6.5.3/04, 19200-01R , Doc. No. 638-006, KCA 6.5.3/10, BPL-STUDY-19-000051 , Doc. No. 638-011,

Processed commodity	Number of studies	Individual PF	Median CF *	Comments	Reference
					KCA 6.5.3/06
Must	6	1.06 0.385 1.09 0.846 0.060 0.116 Median: 0.616	1	-	AB2-18-35355 , Doc. No. 638-007, KCA 6.5.3/03; 19200-01R , Doc. No. 638-006, KCA 6.5.3/10, CREG2117/CREG2120 , Doc. No. 638-013/638-014, KCA 6.5.3/11/KCA 6.5.3/12
Young wine	10	0.074 0.148 0.034 [#] /0.032 ^{###} 0.016 [#] /0.020 ^{###} <0.01 <0.02 <0.05 0.196 0.069 0.077 Median: 0.060	1	-	AB2-18-35355 , Doc. No. 638-007, KCA 6.5.3/03; BPL-STUDY-19-000041 , Doc. No. 638-0010, KCA 6.5.3/04, BPL-STUDY-19-000051 , Doc. No. 638-011, KCA 6.5.3/06; 19200-01R , Doc. No. 638-006, KCA 6.5.3/10, CREG2117/CREG2120 , Doc. No. 638-013/638-014, KCA 6.5.3/11/KCA 6.5.3/12
Bottled wine	12	0.048 0.123 0.033 [#] /0.032 ^{###} <0.01 [#] / <0.01 ^{##} <0.01 <0.02 <0.05 0.165 0.05 <0.04 0.068 <0.03 Median: 0.044	1	-	AB2-18-35355 , Doc. No. 638-007, KCA 6.5.3/03; BPL-STUDY-19-000041 , Doc. No. 638-0010, KCA 6.5.3/04, BPL-STUDY-19-000051 , Doc. No. 638-011, KCA 6.5.3/06; GLP-STUDY-20-30 , Doc. No. 638-015, KCA 6.3.1/01; CREG2117/CREG2120 , Doc. No. 638-013/638-014, KCA 6.5.3/11/KCA 6.5.3/12

* The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

The mean value of the two Pf is calculated to give the processing factor. In case of three or more processing tests, the processing factor is the median of the single factors from each test
The resulting processing factor is indicated with a "<". For the calculation of the mean/median processing factor, a residue factor of <0.01 is considered as 0.01.

mean of 3 analytical determinations were calculated: 2 grape samples analysed just before processing phase start and 1 grape sample from the field was analysed.

mean of 2 grape samples analysed just before processing phase start was calculated.

7.2.5.2 Conclusion on processing studies

According to Commission Regulations (EU) No 283/2013 and 284/2013, processing studies are required, if residues ≥ 0.1 mg/kg occur. In case of residues < 0.1 mg/kg, processing studies are still required, if the

contribution of the crop under consideration to the dietary risk assessment is $\geq 10\%$ ADI.
As residues on pome fruits and potatoes are < 0.1 mg/kg in all trials and ADI utilization is much less than 10% , no processing study is triggered for pome fruits and potatoes.
Processing studies on grapes have been already evaluated during the renewal process. New processing data have been conducted, confirming that a concentration of Zoxamide can be only expected in raisins.
Based on the available processing data for Zoxamide the following overall processing factors can be derived:

Processed commodity	Number of studies	Mean/median PF
Grapes, juice (unclarified)	2	Mean: 0.13
Grapes, juice (clarified)	2	Mean: 0.05
Grapes, juice before pasteurisation	2	Mean: 0.037
Grapes, juice after pasteurisation	8	Median: 0.030
Grapes, dried (raisins)	4	Median: 1.97
Grapes, pomace	9	Median: 0.13
Must	6	Median: 0.616
Young wine	10	Median: 0.060
Bottled wine	12	Median: 0.044

7.2.6 Magnitude of residues in representative succeeding crops

From the intended uses, only potatoes are grown in rotation.
Considering available data dealing with nature of residues (see 7.2.2), no study dealing with magnitude of residues in succeeding crops is needed.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

From the intended uses, only potatoes are grown in rotation.

Available data

No new data submitted in the framework of this application.

Table 7.2-15: Summary of available studies in field rotational crops

Primary crop	Rate (kg a.s./ha) (GS at application or PHI)	Residue levels in succeeding crops			
		Succeeding crop group	Succeeding crop	Sowing intervals (DAT)	Reference / Remarks
EU data					
Low residues were found in the rotational crop metabolism study using an exaggerated application rate. Residues are not expected to exceed the LOQ in practice.					EFSA, 2017
New data					
No new data submitted in the framework of this application.					

Conclusion on rotational crops studies

In the confined rotational crop metabolism study, the only crops to contain total radioactive residues greater than 0.1 mg/kg were immature radish (0.127 mg/kg) and soybean hay (0.189 mg/kg). Both crops were

planted 30 days after bare soil was treated (4 applications at 18 day-intervals) at a rate of 500 g Zoxamide/ha. The application rate was equivalent to 4.4 N rate (total rate) for potato. Therefore, residues in succeeding crops are not considered to be of concern. Thus, rotational crop studies are not required.

7.2.7 Other / special studies (KCA6.10, 6.10.1)

From the intended uses, pome fruits and grapes are melliferous and based on the GAP, the application during flowering cannot be excluded.

Thus, data dealing with the magnitude of residues in honey have been submitted and are summarised in A 2.1.7.1.

No further data are needed.

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

As ARfD was not deemed necessary, acute risk assessment is not relevant.

7.2.8.1 Input values for the consumer risk assessment

Table 7.2-16: Input values for the consumer risk assessment for unprocessed commodities - Zoxamide

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Risk assessment residue definition: Zoxamide + RH-141452 (calculated as Zoxamide equivalents)		
Grapes (table and wine)	0.355	STMR _{RA} (Table 7.2-9)
Pome fruits	0.02	STMR _{RA} (Table 7.2-9)
Potatoes	0.02	STMR _{RA} (Table 7.2-9)
Honey	0.01	STMR _{RA} (Table 7.2-9)

Table 7.2-17: Input values for the consumer risk assessment for processed commodities - RH-150721

Commodity	Acute risk assessment	
	Input value (mg/kg)	Comment
Risk assessment residue definition: RH-150721		
Grapes (table), raisins	0.73	HR (Zoxamide) * CF * PF 0.905 * 0.41 * 1.97 (Table 7.2-9, Table A 64, 7.2-14)

Commodity	Acute risk assessment	
	Input value (mg/kg)	Comment
Risk assessment residue definition: RH-150721		
Grapes (wine), bottled	0.03	HR (Zoxamide) * CF * PF 0.905 * 0.76 * 0.044 (Table 7.2-9, Table A 64, 7.2-14)
Grapes (wine), juice pasteurised	0.01	STMR (Zoxamide) * CF * PF 0.345 * 0.90 * 0.03 (Table 7.2-9, Table A 64, 7.2-14)

CF: Conversion factor; for wine, the conversion factor for wine is based on young and bottled wine; the conversion factor for juice is based on pre- and post-pasteurised juice.
PF: Processing factor

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in A 2.4.

For the calculation of the chronic dietary risk assessment (IEDI), the proposed STMR of the intended uses are taken into account.

Table 7.2-18: Consumer risk assessment


Unprocessed commodities	
Zoxamide	
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	0.2 % (based on PT general)
Processed commodities	
RH-150721	
IESTI (°%ARfD) according to EFSA PRIMo rev. 3.1	0.2 % (wine grapes / juice) – children 0.4°% (table grapes / raisins) – adults 0.1 % (wine grapes / wine) – adults 0.09 % (wine grapes / juice) – adults

The proposed uses of Zoxamide in the formulation GWN-10616 do not represent an unacceptable acute and chronic risk for the consumer.

7.3 POTASSIUM PHOSPHONATES

General data on potassium phosphonates are summarised in the table below.

Table 7.3-1: General information on potassium phosphonate

Active substance (ISO Common Name)	Potassium phosphonates
IUPAC	Potassium hydrogen phosphonate Dipotassium phosphonate
Chemical structure	
Molecular formula	KH_2PO_3 [$\text{HPO}(\text{OH})(\text{O}^-\text{K}^+)$] and K_2HPO_3 [$\text{HPO}(\text{O}^-\text{K}^+)_2$]
Molar mass	Monopotassium phosphonate: 120.1 g/mol Dipotassium phosphonate: 158.2 g/mol
Chemical group	Inorganic phosphonate
Mode of action (if available)	Potassium phosphonate acts in two ways, first within the fungus inhibiting fungus growth, and second by changing the nature of the fungal cell walls by activating the plants own immune defense mechanisms.
Systemic	Yes
Company	Luxembourg Industries (Pamol) Ltd. *
Rapporteur Member State (RMS)	France
Approval status	Approved Commission Implementing Regulation (EU) No 369/2013 of 22 April 2013
Restriction (e.g. is restricted to use as "...")	No
Review Report	SANCO/10416/2013 rev 2 of 15 March 2013
Current MRL regulation	Commission Regulation (EU) 2022/1324
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal: Conclusion on the peer review	Yes, EFSA, 2013
EFSA Journal: Conclusion on Article 12	Yes, EFSA, 2021
Current MRL applications on intended uses	No

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data

A brief summary of the storage stability data on potassium phosphonates is given in the following table.. New stability data in apples have been submitted by the applicant in the framework of this application. One

new study in potatoes is ongoing. Results are summarised in the table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.3-2: Summary of stability data achieved at $\leq -18^{\circ}\text{C}$ (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Grapes	High acid content	12 months	EFSA, 2013
Potatoes	High starch content	25 months	EFSA 2018, mended 2019
Animal Products			
--	--	--	--
New data			
Plant products			
Grapes, processed commodities	LoA for storage stability data is available. (See A 2.3.1.1.1.4) Definitely instead of the LoA the applicant have to provide the relevant data.		
Apples	High water content	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Apple juice	High water content	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Apple, wet pomace	High water content	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Apple compote	High water content	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Apple, canned	High water content	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Apple, dried	-	6 months	Report No. LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13
Potatoes (tuber)	High starch content	3 months, ongoing	Report No. IF23-06197326 Doc. No.645-004, KCA 6.1/14 (interim report)
Potatoes, peel (wet)	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Potatoes, protein	-	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Potatoes, fried potato	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004,

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
			KCA 6.1/14 (interim report)
Potato, crisps	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Potato, flakes	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Potato, starch	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Potato, dried pulp	--	3 months, ongoing	Report No. IF23-06197326 Doc. No. 645-004, KCA 6.1/14 (interim report)
Animal Products			
Honey	LoA for storage stability data is available. Therefore the data should be definitely presented within the dRR Storage stability data in honey are presented in A 2.3.6.1.		

* according to SANTE/2020/12830, Rev. 1

Conclusion on stability of residues during storage

Residues of Phosphonic acid are stable in grapes under deep frozen conditions for at least 12 months covering the longest storage period in residue and processing studies.

Freezer storage stability for Phosphonic acid in apples and related processed commodities (apple juice, wet pomace, compote, canned apples, dried apples) has been shown for 6 months covering the longest storage period in residue and processing studies.

In addition, the storage stability in potatoes and related processed commodities (wet peel, protein, fried potatoes, crisps, flakes, starch and dried pulp) is expected to cover the longest storage period in residue and processing studies.

zRMS: The applicant to include also the storage stability data presented in the RAR. The dRR should be amended.

7.3.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

The stability of residue of Phosphonic acid in extracts of grapes was already addressed during the Annex I inclusion. In addition, the stability of residues of Phosphonic acid in sample extracts was checked in fortification experiments (procedural recoveries) as part of the analytical phase of the individual supervised residue studies in case the extracts have been stored > 24 hours.

Furthermore, the stability of Phosphonic acid in sample extracts was tested within the method validations. This information is indicated below and in the study summaries presented in Appendix 2.

Matrix	Analyte	Temperature	Time period [days]	Reference
Grapes	Phosphonic acid	5 ± 3 °C	3	Report No. GLP-STUDY-21-103; KCA 6.1/15 New method validation
Apples Apple juice, apple wet pomace, apple compote, canned apple and dried apples	Phosphonic acid	5 ± 3 °C	4 3	Report No. GLP-STUDY-21-55; KCA 6.1/16 New method validation
Potato tuber, potato waste, potato dried pulp	Phosphonic acid	5 ± 3 °C	3	Report No. GLP-STUDY-21-52; KCA 6.1/17 New method validation

Conclusion on stability of residues in sample extracts

Storage stability of Phosphonic acid in sample extracts from grapes, apples (RAC and processed commodities: apple juice, apple wet pomace, apple compote, canned apple and dried apples) and potatoes (RAC and processed commodities: potato waste and potato dried pulp) was shown for a period of 3 – 4 days at refrigerated temperature. The stability of residues in sample extracts is considered as sufficiently proven and no additional data are needed.

7.3.2 Nature of residues in plants, livestock and processed commodities

7.3.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

No new data submitted in the framework of this application.

Conclusion on metabolism in primary crops

EFSA concluded in its Conclusion on the peer review (EFSA, 2013) that phosphonates are translocated through the entire plant after soil or foliar application and that phosphonates are not significantly oxidised to phosphate in plants. Only transformation of the potassium phosphonate salts into Phosphonic acid is expected in plants.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Table 7.3-3: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Fruits and fruiting vegetable	--	--	--	--	--	--	--	--
Leafy vegetables	Lettuce	--	F	4.9 mg Phosphonic acid/kg soil corresponding to 14 kg Phosphonic acid/ha	na	32	Due to problems radiolabelling Phosphonic acid, the study was performed with a non-radiolabelled phosphonic acid	EFSA, 2005, revised 2013
Root and tuber vegetables	Radish	--	F		na	31		
Pulses and oilseeds	--	--	--	--	--	--	--	--
Cereals	Barley	--	F	4.9 mg Phosphonic acid/kg soil corresponding to 14 kg Phosphonic acid/ha	na	32, 182	Due to problems radiolabelling Phosphonic acid, the studywas performed with a non-radio-labelledPhos-phonic acid	EFSA, 2005, revised 2013
New data								
Fruits and fruiting vegetable	--	--	--	--	--	--	--	--
Leafy vegetables	--	--	--	--	--	--	--	--
Root and tuber vegetables	--	--	--	--	--	--	--	--
Pulses and oilseeds	--	--	--	--	--	--	--	--
Cereals	--	--	--	--	--	--	--	--

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Conclusion on metabolism in rotational crops

The nature of Phosphonic acid (because fosetyl-Al degrades rapidly in the soil to Phosphonic acid) in rotational crops was investigated in the peer review of fosetyl-Al and indicates that Phosphonic acid is the main metabolite in rotational crops (EFSA, 2005).

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data submitted in the framework of this application.

The effect of processing on the nature of Phosphonic acid, which is the main product produced from the metabolism of potassium phosphonates, was investigated in the framework of the EU pesticides peer reviews for potassium phosphonates and fosetyl (EFSA, 2012, 2018). These studies showed that Phosphonic acid is hydrolytically stable under standard processing conditions representative of pasteurisation, baking/brewing/boiling and sterilisation.

7.3.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.3-4: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	<p>The behaviour of potassium phosphonate was described in several studies in open literature. The major conclusions drawn from these studies were:</p> <ul style="list-style-type: none"> – Potassium phosphonate readily penetrates both bark and cuticle of <i>Betula pendula</i> trees. – Following trunk injection, phosphonate is bipetally translocated in phloem and in xylem. – Following foliar application, phosphonate is detected in the plant roots, confirming its mobility in the plant phloem. – Distribution of phosphonate to both roots and leaves is more rapid after foliar application than after trunk injection. – Phosphonate can be actively taken up into the symplast of castor bean plants and sugar beet leaves and transported through the phloem. The involvement of an active transport system is evidenced by the effect of metabolic inhibitors. <p>Information on phosphonate residues can also be extracted from studies with Fosetyl-Al, since phosphonate, the biologically active substance in potassium phosphonate is also the main metabolite and the biologically active substance of Fosetyl-Al, and the relevant residue in both cases. The major conclusions from these studies are as follows:</p> <ul style="list-style-type: none"> – Levels of phosphonate residues are related to the total dose applied, and to the route of application. – In aerial plant parts, residue levels increase rapidly after foliar application but decline within 4-6 weeks after treatment. <p>Phosphonate is not readily oxidised in the plant to phosphate, evidenced by the fact that phosphate levels in plant tissues are not raised upon phosphonate applications, but sometimes even reduced. Thus, phosphonate bound phosphorus does not serve as an immediate P source in plants</p>
Rotational crops covered	<p>DT₉₀ of Phosphonic acid is > 365 d.</p> <p>Confined study: outdoors, incorporation of Phosphonic acid (no radio-label) into bare soil, rotational crops radish, lettuce and barley, PBI 30 days, application rate 4.9 mg/kg soil (based on an application rate of 14 kg Phosphonic acid/ha which corresponds to 15 kg fosetyl-Al/ha, the cGAP in the EU)</p> <p>Levels of Phosphonic acid in some of the harvested products were above the LOQ of 0.5 mg/kg (0.80 mg/kg in radish and 0.76 mg/kg in lettuce leaves) for the investigated PBI of 30 days.</p>
Metabolism in rotational crops similar to metabolism in primary	Yes

Endpoints	
crops?	
Processed commodities	Not required. The chemistry of Phosphonic acid is well understood. Apart from acid-base conversion, no further modification of the residue has to be expected.
Residue pattern in processed commodities similar to pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Potassium phosphonate forms Phosphonic acid. Thus it is covered by the already existing residue definition “Fosetyl-Al (sum fosetyl + Phosphonic acid and their salts, expressed as fosetyl)” which is established in Reg. (EC) No 396/2005.
Plant residue definition for risk assessment	Phosphonic acid and its salts, expressed as Phosphonic acid (EFSA, 2013)
Conversion factor from enforcement to RA	1.34

7.3.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

Conclusion on metabolism in livestock

This point has already been evaluated during 91/414/EEC process (DAR, 2005).

Inorganic phosphonate compounds are biologically inert and do not interfere with enzymatic reactions and upon ingestion and phosphonate undergoes rapid urinary excretion.

In the RO on the joint review of MRLs for fosetyl, disodium phosphonate and potassium phosphonate according to Articles 12 and 43 of Reg. (EC) No. 396/2005 (EFSA Journal 2021; 19(8):6782), it was concluded that the metabolism of fosetyl-Al, potassium and disodium phosphonates in livestock is adequately elucidated, and Phosphonic acid can be considered as the most relevant component of the residues in commodities of animal origin for both enforcement and risk assessment.

No fish metabolism study is triggered due to log Pow <3 (-4.96).

7.3.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.3-5: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	-
Time needed to reach a plateau concentration	-
Animal residue definition for monitoring	Existing: Fosetyl-Al (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl) Proposed: Phosphonic acid (EFSA RO: EFSA Journal 2021; 19(8):6782)

	Endpoints
Animal residue definition for risk assessment	Existing: Fosetyl-Al (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl) Proposed: Phosphonic acid (EFSA RO: EFSA Journal 2021; 19(8):6782)
Conversion factor	1
Metabolism in rat and ruminant similar	--
Fat soluble residue	No
Fish metabolism	Not relevant, due to log Pow < 3.
Bee products	LoA for honey residue data is available. Existing: Fosetyl-Al (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl) Proposed residue definition: Phosphonic acid Definitely instead of the LoA the applicant have to provide the relevant data.

7.3.3 Magnitude of residues in plants (KCA 6.3)

7.3.3.1 Summary of European data and new data supporting the intended uses

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. These studies are summarised in the table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.3-6: Summary of EU reported and new data supporting the intended uses of GWN-10616 and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) of Phosphonic acid E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
Grapes	EFSA, 2012	N-EU	GAP on which MRL/EU a.s. assessment is based: 6 x 2904 g Potassium phosphonates/ha, PHI 60 days, outdoor <u>Phosphonic acid</u> E and RA: 19.9, 16.7, 21, 23.4, 26.8, 35.2, 36, 37 <u>Fosetyl (x 1.34)</u> ** E and RA: 26.7, 22.4, 28.1, 31.4, 35.9, 47.2, 48.2, 49.6	N/A				
	EFSA, 2012	S-EU	GAP on which MRL/EU a.s. assessment is based: 6 x 2904 g Potassium phosphonates/ha, PHI 60 days, outdoor <u>Phosphonic acid</u> E and RA: 4, 4.4, 9.9, 12, 14, 22.5, 23.5, 25.5, 3.5, 4.4, 4.9, 5.1, 6.4, 18, 20, 22.5, 23.5, 25.9 <u>Fosetyl (x 1.34)</u> ** E and RA: 5.4, 5.9, 13.3, 16.1, 18.8, 30.2, 31.5, 34.2, 4.7, 5.9, 6.6, 6.8, 8.6, 24.1, 26.8, 30.2, 31.5, 34.7					
	New trials	N-EU	Trials GAP: 3 x 1500 g Phosphonic acid/ha, PHI 28 days,					

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) of Phosphonic acid E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
			outdoor <u>Phosphonic acid</u> E and RA: 1.439, 3.606, 70.039, 41.619, 69.545, 16.5, 18.9, 85.5 <u>Fosetyl (x 1.34)</u> ** E and RA: 1.9, 4.8, 93.9, 55.8, 93.2, 22.1, 25.3, 114.6					
	New trials	S-EU	Trials GAP: 3 x 1500 g Phosphonic acid/ha, PHI 28 days, outdoor <u>Phosphonic acid</u> E and RA: 5.818, 29.112, 25.403, 35.345, 16.374, 4.67, 30.5, 12.7 <u>Fosetyl (x 1.34)</u> ** E and RA: 7.8, 39, 34, 47.4, 21.9, 6.3, 40.9, 17					
	Overall supporting data for cGAP	N-EU+ S-EU	<u>Phosphonic acid</u> E and RA : 19.9, 16.7, 21, 23.4, 26.8, 35.2, 36, 37, 1.439, 3.606, 70.039, 41.619, 69.545, 16.5, 18.9, 85.5, 4, 4.4, 9.9, 12, 14, 22.5, 23.5, 25.5, 3.5, 4.4, 4.9, 5.1, 6.4, 18, 20, 22.5, 23.5, 25.9, 5.818, 29.112, 25.403, 35.345, 16.374, 4.67, 30.5, 12.7 <u>Fosetyl (x 1.34)</u> ** E and RA: 26.7, 22.4, 28.1, 31.4, 35.9, 47.2, 48.2, 49.6, 1.9, 4.8, 93.9, 55.8, 93.2, 22.1, 25.3, 114.6, 5.4, 5.9, 13.3, 16.1, 18.8, 30.2, 31.5, 34.2, 4.7, 5.9, 6.6, 6.8, 8.6, 24.1, 26.8, 30.2, 31.5, 34.7, 7.8, 39, 34, 47.4, 21.9, 6.3, 40.9, 17					
	Overall supporting data	N-EU+ S-EU	Normalised to total rate: 3 x 1500 g Phosphonic acid/ha (= 3 x 2265 g Potassium Phosphonate/ha) = 6795 g Potassium	Fosetyl: E and RA:	Fosetyl E and RA:	Fosetyl: 150	Fosetyl: 100	Fosetyl: MRL for

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) of Phosphonic acid E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
	for cGAP		phosphonate/ha (see below) <u>Phosphonic acid</u> E and RA: 11.4, 9.2, 14.3, 13.2, 15.0, 22.7, 24.1, 24.8, 1.4, 3.6, 68.1, 39.0, 70.5, 16.1, 20.6, 85.0, 2.7, 2.5, 6.8, 8.2, 9.6, 12.3, 13, 14.4, 1.6, 2.5, 2.2, 2.3, 2.9, 12.2, 13.7, 12.3, 13, 14.7, 5.8, 29, 25.1, 33.5, 16, 4.7, 30.2, 12.6 <u>Fosetyl (x 1.34) **</u> E and RA: 15.3, 12.3, 19.1, 17.7, 20.1, 30.4, 32.3, 33.2, 1.9, 4.8, 91.3, 52.3, 94.5, 21.5, 27.6, 113.9, 3.6, 3.3, 9.2, 10.9, 12.9, 16.5, 17.4, 19.3, 2.1, 3.3, 3.0, 3.1, 3.9, 16.4, 18.4, 16.5, 17.4, 19.7, 7.7, 38.8, 33.7, 44.9, 21.5, 6.3, 40.4, 16.9	17.4 Phosphonic acid: E and RA: 13.0	113.9 Phosphonic acid: E and RA: 85.0	Phosphonic acid: 100	(Table grapes) 200 (Wine grapes) Proposed MRL Phosphonic acid; EFSA Journal 2021;19(8):6782: 100 (Table grapes) 150 (Wine grapes)	table grapes would be exceeded but not for wine grapes. Phosphonic acid: Yes
Apples/pears → extrapolated to pome fruits	EFSA, 2021 (EFSA Journal 2021;19(8):6782)	EU	Not relevant	N/A				
	New trials	N-EU	Trials GAP: 2 x 1500 g Phosphonic acid/ha, BBCH 51-69, outdoor <u>Phosphonic acid</u> E and RA: 1.85, 11.6, 1.78, 2.63, 1.45, 2.38, 1.22, 0.687, 6.4 <u>Fosetyl (x 1.34) **</u> E and RA: 2.48, 15.54, 2.39, 3.52, 1.94, 3.19, 1.63, 0.92, 8.58 (7x apple, 2x pear)					
	New trials	S-EU	Trials GAP: 2 x 1500 g Phosphonic acid/ha, BBCH 51-69, outdoor <u>Phosphonic acid</u> E and RA: 2.85, 5.18, 3.32, 4.33, 7.93, 1.02, 5.92, 4.72					

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) of Phosphonic acid E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
			Fosetyl (x 1.34) ** E and RA: 3.82, 6.94, 4.45, 5.80, 10.63, 1.37, 7.93, 6.32 (8x apple, 2x pear)					
	Overall supporting data for cGAP	N-EU+ S-EU	<u>Phosphonic acid</u> E and RA: 1.85, 11.6, 1.78, 2.63, 1.45, 2.38, 1.22, 0.687, 6.4, 2.85, 5.18, 3.32, 4.33, 7.93, 1.02, 5.92, 4.72 <u>Fosetyl (x 1.34) **</u> E and RA: 2.48, 15.54, 2.39, 3.52, 1.94, 3.19, 1.63, 0.92, 8.58, 3.82, 6.94, 4.45, 5.80, 10.63, 1.37, 7.93, 6.32 Populations from S-EU and N-EU are similar (Mann-Whitney U-test).	Fosetyl: E and RA: 3.82 Phosphonic acid: E and RA: 2.85	Fosetyl E and RA: 15.54 Phosphonic acid: E and RA: 11.6	Fosetyl: 20 Phosphonic acid: 15	Fosetyl: 150 Phosphonic acid: 70	Yes
Potato	EFSA, 2021 (EFSA Journal 2021;19(8):6782)	EU	Not relevant	N/A				
	New trials	N-EU	Trials GAP: 3 x 1250 g Phosphonic acid/ha, PHI 7 days <u>Phosphonic acid:</u> E and RA: 20.7, 53.9, 7.3, 14, 7.3, 26, 12, 26 <u>Fosetyl (x 1.34) ##</u> E and RA: 27.7, 72.2, 9.8, 18.8, 9.8, 34.8, 16.1, 34.8					
	New trials	S-EU	Trials GAP: 3 x 1250 g Phosphonic acid/ha, PHI 7 days <u>Phosphonic acid:</u> E and RA: 7.14, 11.6, 2.8, 28, 65, 37, 4.2, 13 <u>Fosetyl (x 1.34) ##</u>					

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) of Phosphonic acid E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Rounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) #	MRL compliance
			E and RA: 9.6, 15.5, 3.8, 37.5, 87.1, 49.6, 5.6, 17.4					
	Overall supporting data for cGAP	N-EU + S-EU	<u>Phosphonic acid:</u> E and RA: 20.7, 53.9, 7.3, 14, 7.3, 26, 12, 26, 7.14, 11.6, 2.8, 28, 65, 37, 4.2, 13 <u>Fosetyl (x 1.34) ##</u> E and RA: 27.7, 72.2, 9.8, 18.8, 9.8, 34.8, 16.1, 34.8, 9.6, 15.5, 3.8, 37.5, 87.1, 49.6, 5.6, 17.4 Populations from S-EU and N-EU are similar (Mann-Whitney U-test).	Fosetyl: E and RA: 18.1 (Phosphonic acid: E and RA: 13.5)	Fosetyl E and RA: 87.1 (Phosphonic acid: E and RA: 65.0)	Fosetyl: 150 (Phosphonic acid: 100)	Fosetyl: 200 Proposed MRL Phosphonic acid; EFSA Journal 2021;19(8):6782: Phosphonic acid: 150	Yes

Source of EU MRL: Reg. (EU) 2022/1324

Individual residue values measured as Phosphonic acid were recalculated to express them as fosetyl by a molecular weight (MW) conversion factor of 1.34 - MW Fosetyl (110 g/mol)/MW Phosphonic acid (82 g/mol).

Normalisation of residue levels in grape trials to total rate:

Residue data, evaluated at EU level

No of applications	Application rate [kg Potassium Phosphonates/ha]	Total application rate [kg Potassium Phosphonates/ha]	Residue level Phosphonic acid [mg/kg]	Residue level fosetyl [mg/kg] (x 1.34)	Residue level Phosphonic acid [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphonate/ha) = 6.795 kg Potassium phosphonate/ha	Residue level fosetyl [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphonate/ha) = 6.795 kg Potassium phosphonate/ha	Reference
NEU							
6	1.97	11.82	19.9	26.7	11.4	15.3	DAR; Report No. 20011174/E1-FPVI
6	2.06	12.36	16.7	22.4	9.2	12.3	DAR; Report No. 20011174/E1-FPVI
5	2	10	21	28.1	14.3	19.1	DAR; Report No. 20031178/F1-FPVI
6	2.01	12.06	23.4	31.4	13.2	17.7	DAR; Report No. 20011174/E1-FPVI
6	2.02	12.12	26.8	35.9	15.0	20.1	DAR; Report No. 20011174/E1-FPVI
	10.55	10.55	35.2	47.2	22.7	30.4	DAR; Report No. FCS01
5	2.03	10.15	36	48.2	24.1	32.3	DAR; Report No. 20031178/F1-FPVI
	10.154	10.154	37	49.6	24.8	33.2	DAR; Report No. FCS01
SEU							
5	2.02	10.1	4	5.4	2.7	3.6	DAR; Report No. 20031178/F2-FPVI
6	2	12	4.4	5.9	2.5	3.3	DAR; Report no. 20011174/E1-FPVI
5	1.97	9.85	9.9	13.3	6.8	9.2	DAR; Report No. 20031178/F2-FPVI
5	2	10	12	16.1	8.2	10.9	DAR; Report No. 20031178/F1-FPVI
5	1.98	9.9	14	18.8	9.6	12.9	DAR; Report No. 20031178/F1-FPVI

No of applications	Application rate [kg Potassium Phosphonates/ha]	Total application rate [kg Potassium Phosphonates/ha]	Residue level Phosphonic acid [mg/kg]	Residue level fosetyl [mg/kg] (x 1.34)	Residue level Phosphonic acid [mg/kg] normal- ised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phos- phonate/ha) = 6.795 kg Potas- sium phospho- nate/ha	Residue level fosetyl [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potas- sium Phosphonate/ha) = 6.795 kg Potassium phosphonate/ha	Reference
6	2.07	12.42	22.5	30.2	12.3	16.5	DAR; Report No. 20011174/E1-FPVI
6	2.05	12.3	23.5	31.5	13.0	17.4	DAR; Report No. 20011174/E1-FPVI
6	2	12	25.5	34.2	14.4	19.3	DAR; Report No. 20011174/E1-FPVI
5	3.02	15.1	3.5	4.7	1.6	2.1	DAR; Report No. 3310609
6	2	12	4.4	5.9	2.5	3.3	DAR; Report no. 20011174/E1-FPVI
5	3.02	15.1	4.9	6.6	2.2	3.0	DAR; Report No. 3310609
5	3.02	15.1	5.1	6.8	2.3	3.1	DAR; Report No. 3310609
5	3.02	15.1	6.4	8.6	2.9	3.9	DAR; Report No. 3310609
5	2	10	18	24.1	12.2	16.4	DAR; Report No. 20031178/F1-FPVI
5	1.98	9.9	20	26.8	13.7	18.4	DAR; Report No. 20031178/F1-FPVI
6	2.07	12.42	22.5	30.2	12.3	16.5	Report no. 20011174/E1-FPVI
6	2.05	12.3	23.5	31.5	13.0	17.4	Report no. 20011174/E1-FPVI
6	2	12	25.9	34.7	14.7	19.7	Report no. 20011174/E1-FPVI

The residue data are related to the EFSA Conclusion (EFSA Journal 2012;10(12):2963).

New residue data, which are summarised in Appendix 2 and which have not been yet evaluated

No of applications	Application rate [kg Potassium Phosphonates/ha]	Application rate [kg Phosphonic acid/ha]	Total application rate [kg Potassium Phosphonate/ha]	Residue level Phosphonic acid [mg/kg]	Residue level fosetyl [mg/kg] (x 1.34)	Residue level Phosphonic acid [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphonate/ha) = 6.795 kg Potassium phosphonate/ha	Residue level fosetyl [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphonate/ha) = 6.795 kg Potassium phosphonate/ha	Reference
NEU								
3	2.333+2.344+2.259	-	6.936	1.439	1.9	1.4	1.9	SCC-G107TO108-22
3	2.266+2.288+2.314	-	6.868	3.606	4.8	3.6	4.8	SCC-G107TO108-22
3	2.323+2.323+2.341	-	6.987	70.039	93.9	68.1	91.3	SCC-G410TO417-21
3	2.442+2.383+2.418	-	7.243	41.619	55.8	39.0	52.3	SCC-G410TO417-21
3	2.191+2.172+2.337	-	6.7	69.545	93.2	70.5	94.5	SCC-G410TO417-21
3	-	1.5049+1.6211+1.4999	6.985*	16.5	22.1	16.1	21.5	GLP-Study 20-30
3	-	1.4014+1.3635+1.3675	6.240*	18.9	25.3	20.6	27.6	GLP-Study 20-30
3	-	1.5756+1.5554+1.3973	6.838*	85.5	114.6	85.0	113.9	GLP-Study 20-30
SEU								
3	2.301+2.287+2.287	-	6.875	5.818	7.8	5.8	7.7	SCC-G410TO417-21
3	2.284+2.265+2.284	-	6.833	29.112	39.0	29.0	38.8	SCC-G410TO417-21

3	2.303+2.322+2.247	-	6.872	25.403	34.0	25.1	33.7	SCC-G410TO417-21
3	2.441+2.391+2.341	-	7.173	35.345	47.4	33.5	44.9	SCC-G410TO417-21
No of applications	Application rate [kg Potassium Phosphonates/ha]	Application rate [kg Phosphonic acid/ha]	Total application rate [kg Potassium Phosphate/ha]	Residue level Phosphonic acid [mg/kg]	Residue level fosetyl [mg/kg] (x 1.34)	Residue level Phosphonic acid [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphate/ha) = 6.795 kg Potassium phosphonate/ha	Residue level fosetyl [mg/kg] normalised to total rate: 3 x 1.5 kg Phosphonic acid/ha (= 3 x 2.265 kg Potassium Phosphate/ha) = 6.795 kg Potassium phosphonate/ha	Reference
3	2.292+2.284+2.368	-	6.944	16.374	21.9	16.0	21.5	SCC-G410TO417-21
3	-	1.4948+1.4847+1.4847	6.741*	4.67	6.3	4.7	6.3	GLP-Study 20-30
3	-	1.5675+1.4938+1.4887	6.871*	30.5	40.9	30.2	40.4	GLP-Study 20-30
3	-	1.5605+1.4847+1.4847	6.840*	12.7	17.0	12.6	16.9	GLP-Study 20-30

*Total rate of potassium phosphonate was calculated by summing up the individual rates of Phosphonic acid and multiplication with 1.51 (Phosphonic acid => Potassium phosphonate (500 g/L => 755 g/L))

7.3.3.2 Conclusion on the magnitude of residues in plants

The GAP for the use of GWN-10616 on grapes, potatoes and pome fruits is the same for the Central European Zone and the Southern European Zone. The residue data sets performed for Northern and Southern Europe are statistically similar and were therefore merged for MRL setting and risk assessment. This is in accordance to SANTE/2019/12752.

Grapes (NEU, SEU, GAP: 3 x 1500 g Phosphonic/ha, PHI 28 days)

According to SANTE/2019/12752, residue data on wine grapes can be extrapolated to table grapes and *vice versa*.

As the intended GAP on grapes is in line with the GAP considered for MRL setting, the available residue data on grapes (NEU: 16 trials; SEU: 26 trials) sufficiently support the intended use of GWN-10616 on grapes (table and wine grapes) in the Central European Zone.

In the Reg. (EU) 2022/1324, for wine grapes an MRL of 200 mg/kg and for table grapes an MRL of 100 mg/kg were set related to the existing residue definition for enforcement: Fosetyl-AI (sum of fosetyl, Phosphonic acid and their salts, expressed as fosetyl). Based on the available residue data (old and new data), performed in Southern and Northern Europe, the calculated MRL for wine grapes will not be exceeded, the calculated MRL for table grapes will be exceeded.

However, due to the highest residue level of 85 mg/kg for Phosphonic acid, it is assumed that the existing MRLs are still appropriate and an MRL application for the use of GWN-10616 on grapes is not needed. The use on grapes (table and wine grapes) is considered acceptable.

Pome fruits (NEU, SEU, GAP: 2 x 1500 g Phosphonic acid/ha, BBCH 51-69)

According to SANTE/2019/12752, residue data on apples and pears (minimum 4 apple trials) can be extrapolated to the whole group “pome fruits”.

As the intended GAP on apples and pears is in line with the GAP considered for MRL setting, the available residue data on apples (NEU: 7 trials on apples; 2 trials on pears; SEU: 8 trials on apples; 2 trials on pears) sufficiently support the intended use of GWN-10616 on pome fruits in the Central European Zone.

The data submitted show that no exceedance of the MRL will occur.

The use on pome fruits is considered acceptable.

Potatoes (NEU, SEU, GAP: 3 x 1250 g Phosphonic/ha, PHI 7 days)

As the intended GAP on potatoes is in line with the GAP considered for MRL setting, the available residue data on potatoes (NEU: 8 trials; SEU: 8 trials) sufficiently support the intended use of GWN-10616 on potatoes in the Central European Zone.

The data submitted show that no exceedance of the MRL will occur.

Honey

LoA for honey residue data is available.

~~This is good for the applicant. However, to evaluate any data zRMS needs data. Any LoA itself cannot be a base for an assessment. zRMS kindly recommends to complete the missing data as soon as possible.~~

~~Definitely instead of the LoA the applicant have to provide the relevant data.~~

The honey residue study (report no. 143SRFR21C01) has been summarised in A 2.3.6.1.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

Potassium phosphonates are authorised for the use on several crops that might be fed to livestock. The median and maximum dietary burdens are therefore calculated for different groups of livestock using the agreed European methodology. The input values for all relevant commodities have been selected considering the registered uses evaluated under Article 12 of the Regulation (EC) No 396/2005 (see EFSA, 2021). From the intended uses only apples (wet pomace) and potatoes (culls, process waste and dried pulp) might be fed to livestock.

The intended uses on apples and potatoes are covered by the above mentioned input data and the dietary burden calculation has therefore not been adjusted to the input parameters of the intended uses.

Table 7.3-7: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Residue definition 1: Phosphonic acid and its salts, expressed as Phosphonic acid				
1. Forages				
Cabbage, heads leaves	0.2	STMR x CF (Fosetyl), EFSA 2021	1.3	HR x CF (Fosetyl), EFSA 2021
Kale leaves (forage)	4.9	STMR (potassium phosphonates), EFSA 2021	9.9	HR (potassium phosphonates), EFSA 2021
Triticale straw	19.8	STMR (potassium phosphonates), EFSA 2021	81.4	HR (potassium phosphonates), EFSA 2021
Wheat straw	19.8	STMR (potassium phosphonates), EFSA 2021	81.4	HR (potassium phosphonates), EFSA 2021
2. Roots and tubers				
Carrot culls	0.07	Mean (monitoring data), EFSA, 2021	2.03	HR (monitoring data), EFSA 2021
Cassava/topioca roots	0.01	Mean (monitoring data, tentative), EFSA, 2021	0.01	HR (monitoring data, tentative), EFSA 2021
Potato tuber/culls	26.9	STMR (potassium phosphonates), EFSA, 2021	88.6	HR (potassium phosphonates), EFSA, 2021
	Intended use: 13.5	Intended use: STMR: 13.5	Intended use: 65.0	Intended use: HR: 65.0
Swede roots	0.03	Mean (monitoring data, tentative), EFSA, 2021	0.06	HR (monitoring data, tentative), EFSA, 2021

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Turnip roots	0.01	Mean (monitoring data, tentative), EFSA, 2021	0.01	HR (monitoring data, tentative), EFSA, 2021
3. Cereal grains / Crop seeds				
Barley grain	0.04	Mean (monitoring data, tentative), EFSA 2021	0.04	Mean (monitoring data, tentative), EFSA 2021
Bean seed (dry)	0.34	Mean (monitoring data), EFSA 2021	0.34	Mean (monitoring data), EFSA 2021
Corn, field (Maize) grain	0.01	Mean (monitoring data, tentative), EFSA 2021	0.01	Mean (monitoring data, tentative), EFSA 2021
Corn, pop grain	0.01	Mean (monitoring data, tentative), EFSA 2021	0.01	Mean (monitoring data, tentative), EFSA 2021
Cotton undelinted seed	0.09	Mean (monitoring data extrapolated from sunflower seeds, tentative), EFSA 2021	0.09	Mean (monitoring data, extrapolated from sunflower seeds tentative), EFSA 2021
Cowpea seed	0.34	Mean (monitoring data, extrapolated from beans (dry), tentative), EFSA 2021	0.34	Mean (monitoring data, extrapolated from beans (dry), tentative), EFSA 2021
Lupin seed	0.34	Mean (monitoring data, extrapolated from beans (dry), tentative), EFSA 2021	0.34	Mean (monitoring data, extrapolated from beans (dry), tentative), EFSA 2021
Millet rain	0.02	Mean (monitoring data, tentative), EFSA 2021	0.02	Mean (monitoring data, tentative), EFSA 2021
Oat grain	0.06	Mean (monitoring data, tentative), EFSA 2021	0.06	Mean (monitoring data, tentative), EFSA 2021
Pea (Field pea) seed (dry)	0.59	Mean (monitoring data, tentative), EFSA 2021	0.59	Mean (monitoring data, tentative), EFSA 2021
Rye grain	0.08	Mean (monitoring data), EFSA 2021	0.08	Mean (monitoring data), EFSA 2021
Sorghum grain	0.01	Mean (monitoring data, extrapolated from maize, tentative), EFSA 2021	0.01	Mean (monitoring data, extrapolated from maize, tentative), EFSA 2021
Soybean seed	0.12	Mean (monitoring data, tentative), EFSA 2021	0.12	Mean (monitoring data, tentative), EFSA 2021
Triticale grain	23.1	STMR (potassium phosphonates), EFSA 2021	23.1	STMR (potassium phosphonates), EFSA 2021
Wheat grain	23.1	STMR (potassium phosphonates), EFSA 2021	23.1	STMR (potassium phosphonates), EFSA 2021
4. By-products				

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Apple pomace, wet	21.5 Intended use: 3.98	STMR (potassium phosphonates, tentative) x PF (1.1, potassium phosphonates), EFSA 2021 Intended use: (STMR: 4.525) x (PF: 0.88)	21.5 Intended use: 3.98	STMR (potassium phosphonates, tentative) x PF (1.1, potassium phosphonates), EFSA 2021 Intended use: (STMR: 4.525) x (PF: 0.88)
Beet, sugar dried pulp	1.26	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (18), EFSA 2021	1.26	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (18), EFSA 2021
Beet, sugar ensiled pulp	0.21	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (3), EFSA 2021	0.21	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (3), EFSA 2021
Beet, sugar molasses	1.96	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (28), EFSA 2021	1.96	Mean (monitoring data, extrapolated from carrots, tentative) x default PF (28), EFSA 2021
Brewer's grain dried	0.12	Mean (monitoring data, tentative) x default PF (3.3), EFSA 2021	0.12	Mean (monitoring data, tentative) x default PF (3.3), EFSA 2021
Canola (Rape seed) meal	0.08	Mean (monitoring data, tentative) x default PF (2), EFSA 2021	0.08	Mean (monitoring data, tentative) x default PF (2), EFSA 2021
Grapefruits and oranges, dried pulp	74.76	STMR (potassium phosphonates, tentative) x PF (3.2 potassium phosphonates, tentative), EFSA 2021	74.76	STMR (potassium phosphonates, tentative) x PF (3.2 potassium phosphonates, tentative), EFSA 2021
Lemons, limes, and mandarins, dried pulp	74.76	STMR (potassium phosphonates) x PF (3.2 potassium phosphonates, tentative), EFSA 2021	74.76	STMR (potassium phosphonates) x PF (3.2 potassium phosphonates, tentative), EFSA 2021
Coconut meal	0.09	Mean (monitoring data, tentative) x default PF (1.5), EFSA 2021	0.09	Mean (monitoring data, tentative) x default PF (1.5), EFSA 2021
Corn, field milled by-products	0.01	Mean (monitoring data, tentative) x default PF (1), EFSA 2021	0.01	Mean (monitoring data, tentative) x default PF (1), EFSA 2021
Corn, field hominy meal	0.05	Mean (monitoring data, tentative) x default PF (6), EFSA 2021	0.05	Mean (monitoring data, tentative) x default PF (6), EFSA 2021
Corn, field gluten feed	0.02	Mean (monitoring data, tentative) x default PF (2.5), EFSA 2021	0.02	Mean (monitoring data, tentative) x default PF (2.5), EFSA 2021
Corn, field gluten, meal	0.01	Mean (monitoring data, tentative) x default PF (1),	0.01	Mean (monitoring data, tentative) x default PF (1),

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
		EFSA 2021		EFSA 2021
Cotton meal	0.11	Mean (monitoring data, extrapolated from sunflower seeds, tentative) x default PF (1.3), EFSA 2021	0.11	STMR (potassium phosphonates) x default PF (3.3), EFSA 2021
Distiller's grain dried	76.3	STMR (potassium phosphonates) x default PF (3.3), EFSA 2021	76.3	STMR (potassium phosphonates) x default PF (3.3), EFSA 2021
Flaxseed/Linseed meal	0.44	Mean (monitoring data, tentative) x default PF (2), EFSA 2021	0.44	Mean (monitoring data, tentative) x default PF (2), EFSA 2021
Lupin seed meal	0.38	Mean (monitoring data, extrapolated from beans (dry), tentative) x default PF (1.1), EFSA 2021	0.38	Mean (monitoring data, extrapolated from beans (dry), tentative) x default PF (1.1), EFSA 2021
Peanut meal	2.22	Mean (monitoring data, tentative) x default PF (2), EFSA 2021	2.22	Mean (monitoring data, tentative) x default PF (2), EFSA 2021
Potato process waste	57.8	STMR (potassium phosphonates) x PF (2.2, potassium phosphonates, tentative), EFSA 2021	57.8	STMR (potassium phosphonates) x PF (2.2, potassium phosphonates, tentative), EFSA 2021
	Intended use: 12.7	Intended use: (STMR: 13.5) x (PF: 0.97)	Intended use: 12.7	Intended use: (STMR: 13.5) x (PF: 0.97)
Potato dried pulp	129	STMR (potassium phosphonates) x PF (4.8, potassium phosphonates, tentative), EFSA 2021	129	STMR (potassium phosphonates) x PF (4.8, potassium phosphonates, tentative), EFSA 2021
	Intended use: 18.0	Intended use: (STMR: 13.5) x (PF: 1.3)	Intended use: 18.0	Intended use: (STMR: 13.5) x (PF: 1.3)
Rape meal	0.08	Mean (monitoring data, tentative) x default PF (2), EFSA 2021	0.08	Mean (monitoring data, tentative) x default PF (2), EFSA 2021
Rice bran/pollard	2.18	Mean (monitoring data) x default PF (10), EFSA 2021	2.18	Mean (monitoring data) x default PF (10), EFSA 2021
Safflower meal	0.17	Mean (monitoring data, extrapolated from sunflower seeds, tentative) x default PF (2), EFSA 2021	0.17	Mean (monitoring data, extrapolated from sunflower seeds, tentative) x default PF (2), EFSA 2021
Soybean meal	0.16	Mean (monitoring data, tentative) x default PF (1.3), EFSA 2021	0.16	Mean (monitoring data, tentative) x default PF (1.3), EFSA 2021

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Soybean hulls	1.61	Mean (monitoring data, tentative) x default PF (13), EFSA 2021	1.61	Mean (monitoring data, tentative) x default PF (13), EFSA 2021
Sunflower meal	0.17	Mean (monitoring data, tentative) x default PF (2), EFSA 2021	0.17	Mean (monitoring data, tentative) x default PF (2), EFSA 2021
Wheat gluten meal	4.63	STMR (potassium phosphonates) x PF (0.2, potassium phosphonates, tentative), EFSA 2021	4.63	STMR (potassium phosphonates) x PF (0.2, potassium phosphonates, tentative), EFSA 2021
Wheat milled by-products	25.4	STMR (potassium phosphonates) x PF (1.1, potassium phosphonates, tentative), EFSA 2021	25.4	STMR (potassium phosphonates) x PF (1.1, potassium phosphonates, tentative), EFSA 2021

EFSA, 2021: EFSA Journal 2021;19(8):6782, 203 pp (Art. 12)

PF: Processing Factor; for potato processing waste a processing factor of 0.97 and for dried pulp of 1.3 was considered, based on the following processing studies: report no. IF22-06194195 (Doc. No. 638-019, KCA 6.3.3/02, A 2.3.5.2.5) and GLP-21-14 (Doc. No. 633-09001, KCA 6.3.3/01, A 2.3.5.2.4)).

Table 7.3-8: Results of the dietary burden calculation

Relevant groups (subgroups)	Dietary burden expressed in				Most critical subgroup ^(a)	Most critical commodity ^(b)	Trigger exceeded (Y/N)	Comments
	mg/kg bw per day		mg/kg DM					
	Median	Maximum	Median	Maximum				
Cattle (all)	7.564	11.584	242.27	346.78	Dairy cattle	Potato process waste	Y	–
Cattle (dairy only)	7.564	11.584	196.67	301.18	Dairy cattle	Potato process waste	Y	–
Sheep (all)	8.031	11.781	240.93	353.43	Ram/Ewe	Potato process waste	Y	–
Sheep (ewe only)	8.031	11.781	240.93	353.43	Ram/Ewe	Potato process waste	Y	–
Swine (all)	3.972	7.759	172.11	329.69	Swine (finishing)	Potato culls	Y	–
Poultry (all)	4.305	7.849	60.99	109.89	Turkey	Potato culls	Y	–
Poultry (layer only)	3.748	6.326	54.78	92.45	Poultry layer	Potato culls	Y	–

bw: body weight; DM: dry matter.

(a): When one group of livestock includes several subgroups (e.g. poultry 'all' including broiler, layer and turkey), the result of the most critical subgroup is identified from the maximum dietary burdens expressed as 'mg/kg bw per day'.

(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as 'mg/kg bw per day'.

As indicated above the calculated livestock dietary burden (see also Appendix 4) under Article 12 of the Regulation (EC) No 396/2005 (see EFSA, 2021) has not been modified considering individual residue data for the intended uses on grapes, pome fruits and potatoes.

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

Livestock feeding studies on poultry and dairy cows were used to derive MRL and risk assessment values in milk, eggs and tissues (EFSA, 2021a). *“In the framework of the peer review for the renewal of the approval of fosetyl, poultry and ruminants feeding studies were provided (EFSA, 2018e, France 2018a). The laying hens were dosed for 28 consecutive days with Phosphonic acid at dosing levels of 0.95, 3.703 and 11.387 mg/kg bw per day. Residues of fosetyl-Al and Phosphonic acid were found to be below the LOQ of the method for both compounds (0.5 mg/kg) in eggs, muscle, liver and fat at all dose levels. Lactating cows were also dosed for 28 consecutive days with Phosphonic acid at dosing levels of 0.327, 0.982 and 3.273 mg/kg bw per day. This cow feeding study cannot be considered as acceptable to determine the magnitude of Phosphonic acid in milk and tissues as it is significantly underdosed compared to the calculated dietary burden.*

An additional feeding study performed on dairy cows was evaluated in the framework of an MRL application for potassium phosphonates (France, 2018b; EFSA, 2019a). In this study, cows were dosed for 28 consecutive days with potassium phosphonates at levels corresponding to 11, 22 and 66 mg Phosphonic acid equivalents/kg bw per day. Residues of Phosphonic acid were quantified in milk, fat, liver and kidney at all dosing levels. In muscle the residues were below the LOQ (0.5 mg/kg) at the lowest dosing level only.” Since extrapolation from ruminants to pigs is acceptable, results of the livestock feeding study on ruminants were relied upon to derive the MRL and risk assessment values in pigs.

No new data were submitted in the framework of this application.

Conclusion on feeding studies

Considering all registered uses, based on the estimated dietary burden and the results of livestock feeding studies, the animal MRLs derived during the joint review of maximum residue levels (MRLs) for fosetyl, disodium phosphonate and potassium phosphonates according to Art. 12 and Art. 43 of Regulation (EC) No 396/2005 will not be exceeded.

Access to the livestock feeding study is available.

Accepted

7.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

Data/information on processing studies were reviewed during the approval of Potassium phosphonates and were considered acceptable.

Additional studies have been performed and are reported below and summarised in A 2.2.5.2.1 till A 2.2.5.2.5.

7.3.5.1 Available data for all crops under consideration

New processing studies have been submitted by the applicant in the framework of this application. These studies are summarised in the table below. The detailed results are presented in Appendix 2.

Table 7.3-9: Overview of the available processing studies

Processed commodity	Number of trials	Mean/ median PF *	Median CF **	Comments	Reference
EU data					
Enforcement residue definition: Phosphonic acid and its salts expressed as Phosphonic acid.					
Grapes					
Grapes, wine	2	1.3 [red wine: 1.2; white wine: 1.3]	1	-	EFSA, 2012
New data					
Enforcement residue definition: Phosphonic acid and its salts expressed as Phosphonic acid.					
Grapes					
Grapes, must	2	1.06 [red wine: 1.24; white wine: 0.88]	1	-	Report No. FCS01, LoA for the residue study is available. A Tier 2 summary is provided in A 2.3.1.1.1.4.
Grapes, wet pomace	2	1.5 [red wine: 1.02; white wine: 1.98]	1	-	Report No. FCS01, LoA for the residue study is available. A Tier 2 summary is provided in A 2.3.1.1.1.4.
Grapes, wine (stored)	2	1.32 [red wine: 1.36; white wine: 1.28]	1	-	Report No. FCS01, LoA for the residue study is available. A Tier 2 summary is provided in A 2.3.1.1.1.4.
Grapes, wine (young)	2	1.27 [red wine: 1.43; white	1	-	Report No. FCS01, LoA for the residue study is available.

Processed commodity	Number of trials	Mean/ median PF *	Median CF **	Comments	Reference
		wine: 1.11]			A Tier 2 summary is provided in A 2.3.1.1.1.4.
Grapes, wine (bottled) [#]	2	0.81 [red wine: 1.1; white wine: 0.52]	1	-	GLP-STUDY-20-30, Doc. No. 638-015, KCA 6.3.1/01, A 2.2.5.2.2
Pome fruits					
Apple, juice	3	0.89	1	-	SCC-G-401TO409-21-P, Doc. No. 638-001, KCA 6.5.3/13
Apple, wet pomace	3	0.88	1	-	SCC-G-401TO409-21-P, Doc. No. 638-001, KCA 6.5.3/13
Apple, compote	3	0.83	1	-	SCC-G-401TO409-21-P, Doc. No. 638-001, KCA 6.5.3/13
Apple, canned	3	0.56	1	-	SCC-G-401TO409-21-P, Doc. No. 638-001, KCA 6.5.3/13
Apple, dried	3	4.01	1	-	SCC-G-401TO409-21-P, Doc. No. 638-001, KCA 6.5.3/13
Potatoes					
Potatoes, peeled	3	0.74	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02, A 2.3.5.2.5
Potatoes, wet peel	3	0.75	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02, A 2.3.5.2.5
Potatoes, microwaved	3	1.8	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potatoes, baked	3	1.1	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potatoes, fried	3	2.8	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02
Crisps	3	1.5	1	-	IF22-06194195, Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
French fries	3	1.8	1	-	IF22-06194195, Doc. No. 638-019,

Processed commodity	Number of trials	Mean/ median PF *	Median CF **	Comments	Reference
					KCA 6.3.3/02 A 2.3.5.2.5
Potato, flakes	3	0.80	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potato process waste	4	0.97	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5 GLP-21-14 Doc. No. 633-09001 KCA 6.3.3/01 A 2.3.5.2.4
Potato, ensiled	3	1.3	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potato, starch	3	0.11	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potato protein	3	0.17	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potato, dried pulp	4	1.3	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5 GLP-21-14 Doc. No. 633-09001 KCA 6.3.3/01 A 2.3.5.2.4
Potato, boiled	3	1.2	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5
Potato, canned	3	0.57	1	-	IF22-06194195 , Doc. No. 638-019, KCA 6.3.3/02 A 2.3.5.2.5

* The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.

** The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

7.3.5.2 Conclusion on processing studies

According to Commission Regulations (EU) No 283/2013 and 284/2013, processing studies are required, if residues ≥ 0.1 mg/kg occur. In case of residues < 0.1 mg/kg, processing studies are still required, if the

contribution of the crop under consideration to the dietary risk assessment is $\geq 10\%$ ADI.

Processing studies on grapes have been already evaluated in 2012 showing processing factors > 1 for grape must, grape juice and grape wine (young and stored), as well as for apple dried. Processing factors < 1 have been derived for apple wet pomace, compote and canned apples.

Processing studies on potatoes have been conducted, showing a concentration of Phosphonic acid in potato culls, microwaved potatoes, baked potatoes, fried potatoes, crisps, ensiled potatoes, starch, protein, dried pulp and boiled potatoes.

Based on the available processing data for Phosphonic acid the following overall processing factors could be derived:

Processed commodity	Number of studies	Single/mean/median PF
Grapes		
Grapes, must	2	1.06
Grapes, wet pomace	2	1.5
Grapes, wine (stored + bottled)	8	1.24
Grapes, wine (young)	2	1.27
Apples		
Apple, juice	3	0.89
Apple, wet pomace	3	0.88
Apple, compote	3	0.83
Apple, canned	3	0.56
Apple, dried	3	4.01
Potatoes		
Potatoes, peeled	3	0.74
Potatoes, wet peel	3	0.75
Potatoes, microwaved	3	1.8
Potatoes, baked	3	1.1
Potatoes, fried	3	2.8
Crisps	3	1.5
French fries	3	1.8
Potato, flakes	3	0.80
Potato process waste	4	0.97
Potato, ensiled	3	1.3
Potato, starch	3	0.11
Potato protein	3	0.17
Potato, dried pulp	4	1.3
Potato, boiled	3	1.2
Potato, canned	3	0.57

7.3.6 Magnitude of residues in representative succeeding crops

From the intended uses, only potatoes can be grown in rotation.
Considering available data dealing with nature of residues (see 7.2.2.2), no study dealing with magnitude of residues in succeeding crops is needed.

7.3.6.1 Field rotational crop studies (KCA 6.6.2)

Conclusion on rotational crops studies

In the joint review of MRLs for fosetyl, disodium phosphonate and potassium phosphonate according to Articles 12 and 43 of Reg. (EC) No. 396/2005 (EFSA Journal 2021; 19(8):6782) it is stated that the MRLs are expected to cover the possible uptake of Phosphonic acid in succeeding crops resulting from the use of fosetyl, potassium phosphonate and disodium phosphonates in compliance with the authorised GAPs and from the use of other products of agricultural relevance. As the GAP of the intended use in potatoes is covered by the already registered potato uses, no further data are needed..
No new data submitted in the framework of this application.

7.3.7 Other / special studies (KCA6.10, 6.10.1)

From the intended uses, pome fruits and grapes are melliferous and based on the GAP, the application during flowering cannot be excluded. Access for honey residue data is available.

Based on the input data for risk assessment shown below (table 7,3-10) zRMs draws the applicant's attention to STMR value for honey which is included in the mentioned table. This is 10.37 mg/kg (EFSA 2022) consistently with the residue definition "phosphonic acid". The current fosetyl-AI MRL in honey is 0,5 mg/kg. Moreover within the submitted dRR no other phosphonic acid residue data in honey. Therefore zRMS kindly recommends to make the missing data available within the present B7 as soon as possible to avoid future problems with the approval.

7.3.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

No ARfD was set during the peer review of potassium phosphonates. As ARfD was not deemed necessary, acute risk assessment is not relevant.

As the ADI for PRIMo calculation applied by the applicant was outdated, the PRIMo was recalculated according to correct ADI and new residue definition applying the consistent with it input data of the applicant presented below. The gaps were completed for calculation with the new MRLs consistent with the new residue definition..

7.3.8.1 Input values for the consumer risk assessment

Table 7.3-10: Input values for the consumer risk assessment

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Risk assessment residue definition 1: Phosphonic acid and its salts, expressed as Phosphonic acid		
Grapefruits	17.11	STMR-RAC x PeF (0.73) ^(a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
		(EFSA 2021b)
Oranges	17.11	STMR-RAC x PeF (0.73) ^(a) (EFSA 2021b)
Lemons	23.87	STMR-RAC x PeF (0.73) ^(a) (EFSA 2021a)
Limes	23.87	STMR-RAC x PeF (0.73) ^(a) (EFSA 2021a)
Mandarins	23.87	STMR-RAC x PeF (0.73) ^(a) (EFSA 2021a)
Other citrus fruits	17.11	STMR-RAC x PeF (0.73) ^(a) (EFSA 2021b)
Almonds	359	STMR (EFSA 2021a)
Chestnuts	359	STMR (EFSA 2021a)
Hazelnuts/cobnuts	359	STMR (EFSA 2021a)
Pistachios	359	STMR (EFSA 2021a)
Walnuts	359	STMR (EFSA 2021a)
Brazil nuts	64.5	STMR (EFSA 2021a)
Cashew nuts	64.5	STMR (EFSA 2021a)
Macadamias	64.5	STMR (EFSA 2021a)
Pecans	64.5	STMR (EFSA 2021a)
Pine nut kernels	64.5	STMR (EFSA 2021a)
Coconuts	54.0	STMR (EFSA 2021a)
Apples	2.85	STMR (Table 7.3-6)
Pears	2.85	STMR (Table 7.3-6)
Quinces;	20	STMR (Table 7.3-6)
Medlars,	20	STMR (Table 7.3-6)
Loquats/Japanese medlars	20	STMR (Table 7.3-6)
Cherries	2.50	STMR (EFSA 2022b)
Plums	1.77	STMR (EFSA 2022b)
Grapes (table)	13	STMR (Table 7.3-6)
Grapes (wine)	13	STMR (Table 7.3-6)
Strawberries	20.5	STMR (EFSA 2021a)
Blackberries	58.2	STMR (EFSA 2021a)
Dewberries	23.9	STMR (EFSA 2021a)
Raspberries (red and yellow)	58.2	STMR (EFSA 2021a)
Blueberries	42.3	STMR (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Cranberries	0.04	Mean – monitoring data (EFSA 2021a)
Currants (black, red and white)	42.3	STMR (EFSA 2021a)
Gooseberries (green, red and yellow)	42.3	STMR (EFSA 2021a)
Rose hips	1.5	EU MRL (EFSA 2021a)
Mulberries (black and white)	1.5	EU MRL (EFSA 2021a)
Azaroles/Mediterranean medlars	15.0	STMR (EFSA 2021a)
Elderberries	18.4	STMR (EFSA 2021a)
Dates	0.04	Mean – monitoring data (EFSA 2021a)
Figs	0.03	Mean – monitoring data (EFSA 2021a)
Table olives	23.0	STMR (EFSA 2021a)
Kumquats	0.24	Mean – monitoring data (EFSA 2021a)
Carambolas	0.09	Mean – monitoring data (EFSA 2021a)
Kaki/Japanese persimmons	15.0	STMR (EFSA 2021a)
Jambuls/jambolans	1.5	EU MRL (EFSA 2021a)
Litchis/Lychees	0.05	Mean – monitoring data (EFSA 2021a)
Passionfruits/maracujas	1.07	Mean – monitoring data (EFSA 2021a)
Prickly pears/cactus fruits	0.02	Mean – monitoring data (EFSA 2021a)
Star apples/cainitos	0.02	Mean – monitoring data (EFSA 2021a)
American persimmon/Virginia kaki	1.5	EU MRL (EFSA 2021a)
Avocados	16.4	STMR x PF (1.1) EFSA (2021a)
Bananas	0.05	Mean – monitoring data (EFSA 2021a)
Mangoes	0.15	Mean – monitoring data (EFSA 2021a)
Papayas	0.24	Mean – monitoring data (EFSA 2021a)
Granate apples/pomegranates	24.8	STMR (EFSA 2021a)
Cherimoyas	0.03	Mean – monitoring data (EFSA 2021a)
Guavas	1.5	EU MRL (EFSA 2021a)
Pinapples	4.33	STMR x PF (0.83) EFSA (2021a)
Breadfruits	1.5	EU MRL (EFSA 2021a)
Durians	1.5	EU MRL (EFSA 2021a)
Soursops/guanabanas	1.5	EU MRL (EFSA 2021a)
Potatoes	13.5	STMR (Table 7.3-6)
Cassava roots/manioc	0.01	Mean – monitoring data (EFSA 2021a)
Sweet potatoes	0.13	Mean – monitoring data (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Yams	0.01	Mean – monitoring data (EFSA 2021a)
Arrowroots	0.13	Mean – monitoring data (EFSA 2021a)
Beetroots	0.08	Mean – monitoring data (EFSA 2021a)
Carrots	0.07	Mean – monitoring data (EFSA 2021a)
Horseradishes	41.2	STMR (EFSA 2021a)
Jerusalem artichokes	0.02	Mean – monitoring data (EFSA 2021a)
Parsnips	0.24	Mean – monitoring data (EFSA 2021a)
Parsley roots/Hamburg roots parsley	0.21	Mean – monitoring data (EFSA 2021a)
Radishes	13.2	STMR (EFSA 2021a)
Salsifies	0.02	Mean – monitoring data (EFSA 2021a)
Swedes/rutabagas	0.03	Mean – monitoring data (EFSA 2021a)
Turnips	0.01	Mean – monitoring data (EFSA 2021a)
Garlic	4.40	STMR (EFSA 2021a)
Shallots	4.40	STMR (EFSA 2021a)
Spring onions/green onions and Welsh onions	1.45	STMR (EFSA 2023)
Sweet peppers/bell peppers	5.11	STMR (EFSA 2021a)
Aubergines/eggplants	12.7	STMR (EFSA 2021a)
Okra/lady's fingers	0.11	Mean – monitoring data (EFSA 2021a)
Sweet corn	0.05	Mean – monitoring data (EFSA 2021a)
Broccoli	11.4	STMR (EFSA 2021a)
Cauliflowers	11.4	STMR (EFSA 2021a)
Chinese cabbages/pe-tsai	4.90	STMR (EFSA 2021a)
Kales	4.90	STMR (EFSA 2021a)
Lamb's lettuces/corn salads	32.8	STMR (EFSA 2021a)
Lettuces	41.0	STMR (EFSA 2021a)
Escaroles/broad-leaved endives	32.8	STMR (EFSA 2021a)
Roman rocket/rucola	32.8	STMR (EFSA 2021a)
Spinaches	47.0	STMR (EFSA 2021a)
Purslanes	32.8	STMR (EFSA 2021a)
Chards/beet leaves	15.00	STMR (EFSA 2022b)
Grape leaves and similar species	0.10	Mean – monitoring data (EFSA 2021a)
Watercress	0.02	Mean – monitoring data (EFSA 2021a)
Fresh herbs	98.3	STMR (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Beans (with pods)	0.14	Mean – monitoring data (EFSA 2021a)
Beans (without pods)	0.01	Mean – monitoring data (EFSA 2021a)
Peas (with pods)	0.31	Mean – monitoring data (EFSA 2021a)
Peas (without pods)	0.01	Mean – monitoring data (EFSA 2021a)
Lentils (fresh)	0.31	Mean – monitoring data (EFSA 2021a)
Asparagus	0.14	Mean – monitoring data (EFSA 2021a)
Cardoons	0.02	Mean – monitoring data (EFSA 2021a)
Celeries	0.02	Mean – monitoring data (EFSA 2021a)
Leeks	1.45	STMR (EFSA 2023)
Rhubarbs	0.04	Mean – monitoring data (EFSA 2021a)
Bamboo shoots	1.5	EU MRL (EFSA 2021a)
Palm hearts	1.5	EU MRL (EFSA 2021a)
Cultivated fungi	0.06	Mean – monitoring data (EFSA 2021a)
Wild fungi	0.06	Mean – monitoring data (EFSA 2021a)
Mosses and lichens	1.5	EU MRL (EFSA 2021a)
Algae and prokaryotes organisms	1.5	EU MRL (EFSA 2021a)
Beans	0.34	Mean – monitoring data (EFSA 2021a)
Lentils	0.11	Mean – monitoring data (EFSA 2021a)
Peas	0.59	Mean – monitoring data (EFSA 2021a)
Lupins/lupini beans	0.34	Mean – monitoring data (EFSA 2021a)
Linseeds	0.22	Mean – monitoring data (EFSA 2021a)
Peanuts/groundnuts	1.11	Mean – monitoring data (EFSA 2021a)
Poppy seeds	0.09	Mean – monitoring data (EFSA 2021a)
Sesame seeds	0.15	Mean – monitoring data (EFSA 2021a)
Sunflower seeds	0.09	Mean – monitoring data (EFSA 2021a)
Rapeseeds/canola seeds	0.04	Mean – monitoring data (EFSA 2021a)
Soya beans	0.12	Mean – monitoring data (EFSA 2021a)
Mustard seeds	0.09	Mean – monitoring data (EFSA 2021a)
Cotton seeds	0.09	Mean – monitoring data (EFSA 2021a)
Pumpkin seeds	0.10	Mean – monitoring data (EFSA 2021a)
Safflower seeds	0.09	Mean – monitoring data (EFSA 2021a)
Borage seeds	0.09	Mean – monitoring data (EFSA 2021a)
Gold of pleasure seeds	0.09	Mean – monitoring data (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Hemp seeds	0.09	Mean – monitoring data (EFSA 2021a)
Castor beans	0.09	Mean – monitoring data (EFSA 2021a)
Olives for oil production	23.0	STMR (EFSA 2021a)
Oil palm kernels	1.5	EU MRL (EFSA 2021a)
Oil palm fruits	1.5	EU MRL (EFSA 2021a)
Kapok	1.5	EU MRL (EFSA 2021a)
Barley	0.04	Mean – monitoring data (EFSA 2021a)
Buckwheat and other pseudocereals	0.16	Mean – monitoring data (EFSA 2021a)
Maize/corn	0.01	Mean – monitoring data (EFSA 2021a)
Common millet/proso millet	0.02	Mean – monitoring data (EFSA 2021a)
Oat	0.06	Mean – monitoring data (EFSA 2021a)
Rice	0.22	Mean – monitoring data (EFSA 2021a)
Rye	0.08	Mean – monitoring data (EFSA 2021a)
Sorghum	0.01	Mean – monitoring data (EFSA 2021a)
Wheat grains	23.1	STMR (EFSA 2021b)
Tea (dried leaves of Camellia sinensis)	0.11	Mean – monitoring data (EFSA 2021a)
Coffee beans	0.26	Mean – monitoring data (EFSA 2021a)
Herbal infusions (dried, flowers)	0.28	Mean – monitoring data (EFSA 2021a)
Strawberry leaves	380	STMR (EFSA 2022b)
Rooibos	380	STMR (EFSA 2022b)
Mate/matè	380	STMR (EFSA 2022b)
Other herbal infusions (dried leaves)	380	STMR (EFSA 2022b)
Herbal infusions (dried, roots)	400	EU MRL (EFSA 2021a)
Cocoa beans	1.5	EU MRL (EFSA 2021a)
Carobs/Saint John's bread	1.5	EU MRL (EFSA 2021a)
Hops	350	STMR (EFSA 2021a)
Spices (bark)	300	EU MRL (EFSA 2021a)
Spices (roots and rhizome)	0.14	Mean – monitoring data (EFSA 2021b)
Spices (buds)	300	EU MRL (EFSA 2021a)
Spices (flower stigma)	300	EU MRL (EFSA 2021a)
Spices (aril)	300	EU MRL (EFSA 2021a)
Sugar beet roots	0.07	Mean – monitoring data (EFSA 2021a)
Sugar canes	1.5	EU MRL (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Honey and other apicultural products	7.72	STMR (see Appendix 3)
Risk assessment residue definition 2: sum of fosetyl, Phosphonic acid and their salts, expressed as Phosphonic acid		
Apricots	9.55	STMR x CF (EFSA 2021a)
Peaches	9.55	STMR x CF (EFSA 2021a)
Kiwi fruits (green, red, yellow)	23.5	STMR x CF (EFSA 2021a)
Celeriacs/turnip rooted celeries	0.15	STMR x CF (EFSA 2021a)
Onions	11.0	STMR x CF (EFSA 2021a)
Tomatoes	14.4	STMR x CF (EFSA 2021a)
Cucurbits with edible peel	26.0	STMR x CF (EFSA 2021a)
Cucurbits with inedible peel	16.7	STMR x CF (EFSA 2021a)
Brussels sprouts	0.20	STMR x CF x PF (0.93) (EFSA 2021a)
Head cabbages	0.20	STMR x CF (EFSA 2021a)
Kohlrabies	0.68	STMR x CF (EFSA 2021a)
Cresses and other sprouts and shoots	19.0	STMR x CF (EFSA 2021a)
Leaf cresses	19.0	STMR x CF (EFSA 2021a)
Red mustards	19.0	STMR x CF (EFSA 2021a)
Baby leaf crops (including brassica species)	19.0	STMR x CF (EFSA 2021a)
Chards/beet leaves	5.30	STMR x CF (EFSA 2021a)
Witloofs/Belgian endives	40.5	STMR x CF (EFSA 2021a)
Florence fennels	0.23	STMR x CF (EFSA 2021a)
Globe artichokes	15.0	STMR x CF (EFSA 2021a)
Seed spices	74.0	STMR x CF (EFSA 2021a)
Fruit spices	74.0	STMR x CF (EFSA 2021a)
Chicory roots	14.5	STMR x CF (EFSA 2021a)
Risk assessment residue definition 3: Phosphonic acid		
Swine meat	0.50	STMR x CF (EFSA 2021a)
Swine fat	0.50	STMR x CF (EFSA 2021a)
Swine liver	0.50	STMR x CF (EFSA 2021a)
Swine kidney	1.38	STMR x CF (EFSA 2021a)
Bovine and equine meat	0.50	STMR x CF (EFSA 2021a)
Bovine and equine fat	0.61	STMR x CF (EFSA 2021a)
Bovine and equine liver	0.50	STMR x CF (EFSA 2021a)

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Bovine and equine kidney	2.64	STMR x CF (EFSA 2021a)
Sheep and goat meat	0.50	STMR x CF (EFSA 2021a)
Sheep and goat fat	0.65	STMR x CF (EFSA 2021a)
Sheep and goat liver	0.50	STMR x CF (EFSA 2021a)
Sheep and goat kidney	2.81	STMR x CF (EFSA 2021a)
Poultry meat	0.50	STMR x CF (EFSA 2021a)
Poultry fat	0.50	STMR x CF (EFSA 2021a)
Poultry liver	0.50	STMR x CF (EFSA 2021a)
Cattle and horse milk	0.15	STMR x CF (EFSA 2021a)
Sheep and goat milk	0.27	STMR x CF (EFSA 2021a)
Birds eggs	0.50	STMR x CF (EFSA 2021a)
Honey	10.37	STMR (EFSA 2022b)

(a): Peeling factor (Pe) derived for citrus fruits (EFSA, 2021c).

EFSA 2021a: Reasoned opinion on the joint review of maximum residue levels (MRLs) for fosetyl, disodium phosphonate and potassium phosphonates according to Articles 12 and 43 of Regulation (EC) No 396/2005. EFSA Journal 2021;19(8):6782, 203 pp. <https://doi.org/10.2903/j.efsa.2021.6782>

EFSA 2021b: Reasoned Opinion on the modification of the existing MRLs for potassium phosphonates in lemons, limes and mandarins and in herbal infusions from leaves and herbs. EFSA Journal 2021;19(6):6673, 41 pp. <https://doi.org/10.2903/j.efsa.2021.6673>

EFSA 2022b: Modification of the existing maximum residue levels for fosetyl/Phosphonic acid in apricots, cherries and plums resulting from the use of potassium phosphonates. EFSA Journal 2022;20(1):7106, 27 pp. <https://doi.org/10.2903/j.efsa.2022.7106>

EFSA 2023: Modification of the existing maximum residue levels in leeks and spring onions/green onions/Welsh onions resulting from the use of potassium phosphonates. EFSA Journal 2023;21(5):8033, 29 pp. <https://doi.org/10.2903/j.efsa.2023.8033>

The new MRLs (currently not in force yet, for the completion of input data for TMDI recalculation)

Pesticide residue(s) and maximum residue levels (mg/kg)

Code	Products to which MRLs apply	Phosphonic acid and its salts expressed as phosphonic acid(R) Commission Regulation (EU) 2024/2619 not yet applicable	Fosetyl-Al (sum of fosetyl, phosphonic acid and their salts, expressed as fosetyl) Reg. (EU) 2022/1324 applicable
0100000	FRUITS, FRESH or FROZEN; TREE NUTS		
0110010	Grapefruits	100	75
0110020	Oranges	100	75
0110030	Lemons	100	150
0110040	Limes	100	150
0110050	Mandarins	100	150
0110990	Others (2)	100	75
0120010	Almonds	1000	1500
0120020	Brazil nuts	400	500
0120030	Cashew nuts	400	500
0120040	Chestnuts	1000	1500
0120050	Coconuts	400	500
0120060	Hazelnuts/cobnuts	1000	1500
0120070	Macadamias	400	500
0120080	Pecans	400	500
0120090	Pine nut kernels	400	500
0120100	Pistachios	1000	1500
0120110	Walnuts	1000	1500
0120990	Others (2)	400	500
0130010	Apples	70	150
0130020	Pears	70	150
0130030	Quinces	70	150
0130040	Medlars	70	150
0130050	Loquats/Japanese medlars	70	150
0130990	Others (2)	70	150
0140010	Apricots	60	2*

0140020	Cherries (sweet)	8	2*
0140030	Peaches	60	50
0140040	Plums	8	2*
0140990	Others (2)	8	2*
0151010	Table grapes	100	100
0151020	Wine grapes	150	200
0153010	Blackberries	200	300
0153020	Dewberries	80	2*
0153030	Raspberries (red and yellow)	200	300
0153990	Others (2)	80	2*
0154010	Blueberries	150	200
0154020	Cranberries	1.5*	2*
0154030	Currants (black, red and white)	150	200
0154040	Gooseberries (green, red and yellow)	150	200
0154050	Rose hips	1.5*	2*
0154060	Mulberries (black and white)	1.5*	2*
0154070	Azaroles/Mediterranean medlars	50	50
0154080	Elderberries	60	80
0154990	Others (2)	1.5*	2*
0161010	Dates	1.5*	2*
0161020	Figs	1.5*	2*
0161030	Table olives	80	100
0161040	Kumquats	3	2*
0161050	Carambolas	1.5*	2*
0161060	Kaki/Japanese persimmons	50	50
0161070	Jambuls/jambolans	1.5*	2*
0161990	Others (2)	1.5*	2*
0162010	Kiwi fruits (green, red, yellow)	150	200
0162020	Litchis/lychees	1.5*	2*
0162030	Passionfruits/maracujas	20	2*
0162040	Prickly pears/cactus fruits	1.5*	2*
0162050	Star apples/cainitos	1.5*	2*
0162060	American persimmons/Virginia kaki	1.5*	2*
0162990	Others (2)	1.5*	2*
0163010	Avocados	50	70
0163020	Bananas	1.5*	2*
0163030	Mangoes	1.5*	2*
0163040	Papayas	3	2*
0163050	Granate apples/pomegranates	70	90
0163060	Cherimoyas	1.5*	2*
0163070	Guavas	1.5*	2*
0163080	Pineapples	20	50
0163090	Breadfruits	1.5*	2*
0163100	Durians	1.5*	2*
0163110	Soursops/guanabanas	1.5*	2*
0163990	Others (2)	1.5*	2*

0200000	VEGETABLES, FRESH or FROZEN		
0210000	Root and tuber vegetables		
0211000	(a) potatoes	150	200
0212000	(b) tropical root and tuber vegetables	1.5*	2*
0212010	Cassava roots/manioc	1.5*	2*
0212020	Sweet potatoes	1.5*	2*
0212030	Yams	1.5*	2*
0212040	Arrowroots	1.5*	2*
0212990	Others (2)	1.5*	2*
0213000	(c) other root and tuber vegetables except sugar beets		
0213010	Beetroots	1.5*	2*
0213020	Carrots	1.5*	2*
0213030	Celeriacs/turnip rooted celeries	6	8
0213040	Horseradishes	150	200
0213050	Jerusalem artichokes	1.5*	2*
0213060	Parsnips	6	2*
0213070	Parsley roots/Hamburg roots parsley	4	2*
0213080	Radishes	40	25
0213090	Salsifies	1.5*	2*
0213100	Swedes/rutabagas	1.5*	2*
0213110	Turnips	1.5*	2*
0213990	Others (2)	1.5*	2*
0220000	Bulb vegetables		
0220010	Garlic	20	30
0220020	Onions	40	50
0220030	Shallots	20	30
0220040	Spring onions/green onions and Welsh onions	10	30
0220990	Others (2)	10	2*
0230000	Fruiting vegetables		
0231000	(a) Solanaceae and Malvaceae		
0231010	Tomatoes	70	100
0231020	Sweet peppers/bell peppers	70	130
0231030	Aubergines/eggplants	70	100
0231040	Okra/lady's fingers	1.5*	2*
0231990	Others (2)	70	2*
0232000	(b) cucurbits with edible peel	80	
0232010	Cucumbers	80	80
0232020	Gherkins	80	75
0232030	Courgettes	80	100
0232990	Others (2)	80	75
0233000	(c) cucurbits with inedible peel	60	75
0233010	Melons	60	75
0233020	Pumpkins	60	75
0233030	Watermelons	60	75

0233990	Others (2)	60	75
0234000	(d) sweet corn	1.5*	5
0239000	(e) other fruiting vegetables	1.5*	5
0240000	Brassica vegetables(excluding brassica roots and brassica baby leaf crops)		
0241000	(a) flowering brassica	50	70
0241010	Broccoli	50	70
0241020	Cauliflowers	50	70
0241990	Others (2)	50	70
0242000	(b) head brassica	2	10
0242010	Brussels sprouts	2	10
0242020	Head cabbages	2	10
0242990	Others (2)	2	10
0243000	(c) leafy brassica	20	30
0243010	Chinese cabbages/pe-tsai	20	30
0243020	Kales	20	30
0243990	Others (2)	20	30
0244000	(d) kohlrabies	5	10
0250000	Leaf vegetables, herbs and edible flowers		
0251000	(a) lettuces and salad plants		
0251010	Lamb's lettuces/corn salads	150	75
0251020	Lettuces	200	300
0251030	Escaroles/broad-leaved endives	150	75
0251040	Cresses and other sprouts and shoots	150	75
0251050	Land cresses	150	75
0251060	Roman rocket/rucola	150	75
0251070	Red mustards	150	75
0251080	Baby leaf crops (including brassica species)	150	75
0251990	Others (2)	150	75
0252000	(b) spinaches and similar leaves		
0252010	Spinaches	200	300
0252020	Purslanes	100	2*
0252030	Chards/beet leaves	70	15
0252990	Others (2)	70	2*
0253000	(c) grape leaves and similar species	1.5*	2*
0254000	(d) watercresses	1.5*	2*
0255000	(e) witloofs/Belgian endives	150	75
0256000	(f) herbs and edible flowers	300	400
0256010	Chervil	300	400
0256020	Chives	300	400
0256030	Celery leaves	300	400
0256040	Parsley	300	400
0256050	Sage	300	400

0256060	Rosemary	300	400
0256070	Thyme	300	400
0256080	Basil and edible flowers	300	400
0256090	Laurel/bay leaves	300	400
0256100	Tarragon	300	400
0256990	Others (2)	300	400
0260000	Legume vegetables	1.5*	2*
0260010	Beans (with pods)	1.5*	2*
0260020	Beans (without pods)	1.5*	2*
0260030	Peas (with pods)	1.5*	2*
0260040	Peas (without pods)	1.5*	2*
0260050	Lentils	1.5*	2*
0260990	Others (2)	1.5*	2*
0270000	Stem vegetables		
0270010	Asparagus	1.5*	2*
0270020	Cardoons	1.5*	2*
0270030	Celeries	1.5*	2*
0270040	Florence fennels	1.5	2*
0270050	Globe artichokes	100	50
0270060	Leeks	10	30
0270070	Rhubarbs	1.5*	2*
0270080	Bamboo shoots	1.5*	2*
0270090	Palm hearts	1.5*	2*
0270990	Others (2)	1.5*	2*
0280000	Fungi, mosses and lichens	1.5*	2*
0280010	Cultivated fungi	1.5*	2*
0280020	Wild fungi	1.5*	2*
0280990	Mosses and lichens	1.5*	2*
0290000	Algae and prokaryotes organisms	1.5*	2*
0300000	PULSES		2*
0300010	Beans	3	2*
0300020	Lentils	3	2*
0300030	Peas	4	2*
0300040	Lupins/lupini beans	3	2*
0300990	Others (2)	3	2*
0400000	OILSEEDS AND OIL FRUITS		
0401000	Oilseeds		2*
0401010	Linseeds	1.5*	2*
0401020	Peanuts/groundnuts	3	2*
0401030	Poppy seeds	1.5*	2*
0401040	Sesame seeds	1.5*	2*
0401050	Sunflower seeds	1.5*	2*
0401060	Rapeseeds/canola seeds	1.5*	2*
0401070	Soyabeans	1.5*	2*
0401080	Mustard seeds	1.5*	2*
0401090	Cotton seeds	1.5*	2*

0401100	Pumpkin seeds	1.5*	2*
0401110	Safflower seeds	1.5*	2*
0401120	Borage seeds	1.5*	2*
0401130	Gold of pleasure seeds	1.5*	2*
0401140	Hemp seeds	1.5*	2*
0401150	Castor beans	1.5*	2*
0401990	Others (2)	1.5*	2*
0402000	Oil fruits		
0402010	Olives for oil production	80	100
0402020	Oil palms kernels	1.5*	2*
0402030	Oil palms fruits	1.5*	2*
0402040	Kapok	1.5*	2*
0402990	Others (2)	1.5*	2*
0500000	CEREALS		
0500010	Barley	1.5*	2*
0500020	Buckwheat and other pseudocereals	2	2*
0500030	Maize/corn	1.5*	2*
0500040	Common millet/proso millet	1.5*	2*
0500050	Oat	1.5*	2*
0500060	Rice	3	2*
0500070	Rye	1.5*	2*
0500080	Sorghum	1.5*	2*
0500090	Wheat	80	150
0500990	Others (2)	1.5*	2*
0600000	TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS		
0610000	Teas	20*	5*
0620000	Coffee beans	20*	5*
0630000	Herbal infusions from		
0631000	(a) flowers	20*	500
0631010	Chamomile	20*	500
0631020	Hibiscus/roselle	20*	500
0631030	Rose	20*	500
0631040	Jasmine	20*	500
0631050	Lime/linden	20*	500
0631990	Others (2)	20*	500
0632000	(b) leaves and herbs	1500	2000
0632010	Strawberry	1500	2000
0632020	Rooibos	1500	2000
0632030	Mate/maté	1500	2000
0632990	Others (2)	1500	2000
0633000	(c) roots	20*	500
0633010	Valerian	20*	500
0633020	Ginseng	20*	500
0633990	Others (2)	20*	500
0639000	(d) any other parts of the plant	20*	500

0640000	Cocoa beans	20*	2*
0650000	Carobs/Saint John's breads	20*	2*
0700000	HOPS	1500	2000
0800000	SPICES		
0810000	Seed spices	300	400
0810010	Anise/aniseed	300	400
0810020	Black caraway/black cumin	300	400
0810030	Celery	300	400
0810040	Coriander	300	400
0810050	Cumin	300	400
0810060	Dill	300	400
0810070	Fennel	300	400
0810080	Fenugreek	300	400
0810090	Nutmeg	300	400
0810990	Others (2)	300	400
0820000	Fruit spices	300	400
0820010	Allspice/pimento	300	400
0820020	Sichuan pepper	300	400
0820030	Caraway	300	400
0820040	Cardamom	300	400
0820050	Juniper berry	300	400
0820060	Peppercorn (black, green and white)	300	400
0820070	Vanilla	300	400
0820080	Tamarind	300	400
0820990	Others (2)	300	400
0830000	Bark spices	20*	400
0830010	Cinnamon	20*	400
0830990	Others (2)	20*	400
0840000	Root and rhizome spices		
0840010	Liquorice	20*	400
0840020	Ginger (10)		
0840030	Turmeric/curcuma	20*	400
0840040	Horseradish (11)		
0840990	Others (2)	20*	400
0850000	Bud spices	20*	400
0850010	Cloves	20*	400
0850020	Capers	20*	400
0850990	Others (2)	20*	400
0860000	Flower pistil spices	20*	400
0860010	Saffron	20*	400
0860990	Others (2)	20*	400
0870000	Aril spices	20*	400
0870010	Mace	20*	400
0870990	Others (2)	20*	400
0900000	SUGAR PLANTS		
0900010	Sugar beet roots	1.5*	2*

0900020	Sugar canes	1.5*	2*
0900030	Chicory roots	70	75
0900990	Others (2)	1.5*	2*
1000000	PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS		
1010000	Commodities from		
1011000	(a) swine		
1011010	Muscle	0.5	0.7
1011020	Fat	1.5	1.5
1011030	Liver	0.5	0.8
1011040	Kidney	4	6
1011050	Edible offals (other than liver and kidney)	4	6
1011990	Others (2)	0.5	0.5*
1012000	(b) bovine		
1012010	Muscle	0.6	0.7
1012020	Fat	2	1.5
1012030	Liver	0.9	1.5
1012040	Kidney	7	8
1012050	Edible offals (other than liver and kidney)	7	8
1012990	Others (2)	0.6	0.5*
1013000	(c) sheep		
1013010	Muscle	0.6	0.7
1013020	Fat	2	1.5
1013030	Liver	0.9	1.5
1013040	Kidney	7	8
1013050	Edible offals (other than liver and kidney)	7	8
1013990	Others (2)	0.6	0.5*
1014000	d) goat		
1014010	Muscle	0.6	0.7
1014020	Fat	2	1.5
1014030	Liver	0.9	1.5
1014040	Kidney	7	8
1014050	Edible offals (other than liver and kidney)	7	8
1014990	Others (2)	0.6	0.5*
1015000	(e) equine		
1015010	Muscle	0.6	0.5*
1015020	Fat	2	0.5*
1015030	Liver	0.9	0.5
1015040	Kidney	7	0.5
1015050	Edible offals (other than liver and kidney)	7	0.5
1015990	Others (2)	0.6	0.5*
1016000	(f) poultry	0.5	

1016010	Muscle	0.5	0.7
1016020	Fat	0.5	0.7
1016030	Liver	0.5	0.7
1016040	Kidney	0.5	0.5*
1016050	Edible offals (other than liver and kidney)	0.5	0.7
1016990	Others (2)	0.5	0.5*
1017000	(g) other farmed terrestrial animals		
1017010	Muscle	0.6	0.5*
1017020	Fat	2	0.5*
1017030	Liver	0.9	0.5
1017040	Kidney	7	0.5
1017050	Edible offals (other than liver and kidney)	7	0.5
1017990	Others (2)	0.6	0.5*
1020000	Milk	0.4	0.5
1020010	Cattle	0.4	0.5
1020020	Sheep	0.4	0.5
1020030	Goat	0.4	0.5
1020040	Horse	0.4	0.5
1020990	Others (2)	0.4	0.5
1030000	Birds eggs	0.5	0.7
1030010	Chicken	0.5	0.7
1030020	Duck	0.5	0.7
1030030	Geese	0.5	0.7
1030040	Quail	0.5	0.7
1030990	Others (2)	0.5	0.7
1040000	Honey and other apiculture products (7)	100	0.5*
1050000	Amphibians and Reptiles	0.5*	0.5*
1060000	Terrestrial invertebrate animals	0.5*	0.5*
1070000	Wild terrestrial vertebrate animals	0.5*	0.5*
1100000	PRODUCTS OF ANIMAL ORIGIN - FISH, FISHPRODUCTS AND ANY OTHER MARINE AND FRESHWATER FOOD PRODUCTS (8)		
1200000	PRODUCTS OR PART OF PRODUCTS EXCLUSIVELY USED FOR ANIMAL FEED PRODUCTION (8)		
1300000	PROCESSED FOOD PRODUCTS (9)		

7.3.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in A 2.4.

For the chronic dietary risk assessment (IEDI calculation), the STMRs, EU-MRLs and the mean values based on monitoring data as listed in the joint review of maximum residue levels (MRLs) for fosetyl, disodium phosphonate and potassium phosphonates according to Articles 12 and 43 of Regulation (EC) No 396/2005, as well as the STMR values from the latest evaluations in accordance with Article 6 of Regulation (EC) No 396/2005 (EFSA, 2022; see D.2., “consumer risk assessment”) and the STMR values from the intended uses have been considered.

Table 7.3-11: Consumer risk assessment

Unprocessed commodities	
Phosphonic acid	
TMDI (% ADI) according to EFSA PRIMo rev. 3.1	82%
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	21 % (based on DE child)

Consumer risk assessment estimated by the applicant taking into account the data from Table 7.3-10: Input values for the consumer risk assessment

Unprocessed commodities	
Phosphonic acid	
Scenario 1: ADI: 2.25 mg/kg bw/day	
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	21 % (based on DE child)
Scenario 2: ADI: 1 mg/kg bw/day	
IEDI (% ADI) according to EFSA PRIMo rev. 3.1	47 % (based on DE child)

The proposed uses of Phosphonic acid in the formulation GWN-10616 do not represent unacceptable chronic risks for the consumer.

7.4 Combined exposure and risk assessment

7.4.1 Acute consumer risk assessment from combined exposure

The product is a mixture of two active substances (Zoxamide and Potassium phosphonates), but for none of them an acute reference dose has been allocated. Therefore, a combined acute exposure cannot be considered.

7.4.2 Chronic consumer risk assessment from combined exposure

The uses under consideration provide only a minor contribution to the overall chronic exposure of consumers to pesticide residues. The issue requires a more universal consideration and possibly the generic usage of monitoring data. A harmonised approach is not yet available, and currently no specific consideration is warranted in the scope of this evaluation.

7.5 References

ZOXAMIDE

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EC (European Commission) 2018. Final Renewal report for the active substance Zoxamide. SANTE/10052/2018 Rev 2, dated 23 March 2018.

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EFSA (European Food Safety Authority), 2019a. Reasoned Opinion on the modification of the existing maximum residue level for fosetyl/Phosphonic acid for potatoes and wheat. EFSA Journal 2019;17(5):5703.

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EFSA (European Food Safety Authority) 2021b: Reasoned Opinion on the modification of the existing MRLs for potassium phosphonates in lemons, limes and mandarins and in herbal infusions from leaves and herbs. EFSA Journal 2021;19(6):6673, 41 pp

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EFSA (European Food Safety Authority), 2022a. Reasoned Opinion on the modification of the existing maximum residue levels for fosetyl/ Phosphonic acid in chards/beet leaves and honey resulting from the use of potassium phosphonates. EFSA Journal 2022;20(1):6992.

EFSA (European Food Safety Authority), 2022b. Reasoned Opinion on the modification of the existing

maximum residue levels for fosetyl/Phosphonic acid in apricots, cherries and plums resulting from the use of potassium phosphonates. EFSA Journal 2022;20(1):7106.

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France, 2005a. Draft Assessment Report (DAR) on the active substance potassium phosphite prepared by the rapporteur Member State France in the framework of Directive 91/414/EEC, January 2005.

France, 2005b. Final Addendum to Draft Assessment Report on fosetyl-Al, compiled by EFSA, September 2005.

Germany, 2017. Registration Report for LBG-01F34 /Veriphos (ZV1 027207-00/00, 2017).

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. (Doc. No.) Source (where different from company) GLP or GEP status (where relevant) Published or unpublished	Vertebrate study Y/N	Owner
KCA 6.1/09	Sala, A.	2022	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF GWN-8030 IN GRAPES GLP-STUDY-21-101 (432-006) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/10	Sala, A.	2022	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF RH-141452 (TOTAL FRACTION) IN GRAPES GLP-STUDY-21-102 (432-007) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/11	Longhi, D.	2021	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF GWN-8030 IN APPLES GLP-STUDY-21-53 (432-003) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/12	Longhi, D.	2021	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF RH-141452 (TOTAL FRACTION) IN APPLES GLP-STUDY-21-54 (432-005) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/13	Longhi, D.	2023	STORAGE STABILITY OF PHOSPHONIC ACID IN APPLE AND PROCESSED FRACTIONS LBN-0007-2022 (645-001) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/14	Link, T.	2023	STORAGE STABILITY OF MDI-0074 IN POTATO RAC AND PROCESSED PRODUCTS UNDER DEEP FROZEN CONDITIONS – INTERIM REPORT IF23-06197326 (645-004) SGS Institut Fresenius GmbH, Taunusstein, Germany GLP, unpublished	N	XXXX
KCA 6.1/15	Sala, A.	2022	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN GRAPES GLP-STUDY-21-103 (432-008) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX

KCA 6.1/16	Longhi, D.	2021	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN APPLES RAC AND PROCESSED COMMODITIES GLP-STUDY-21-55 (432-004) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.1/17	Longhi, D.	2022	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN POTATO GLP-STUDY-21-52 (432-015) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.3.1/02	Loriau, P.	2022	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 2 AT HARVEST TRIALS IN NORTHERN EUROPE, & 2 DECLINE TRIALS AND 3 AT HARVEST TRIALS IN SOUTHERN EUROPE IN 2021 SCC-G410TO417-21 (632-40001) Redebel s.a., Saint-Amand, Belgium GLP, unpublished	N	XXXX
KCA 6.3.1/03	Loriau, P.	2023	RESIDUE STUDY - RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 1 HARVEST TRIAL IN NORTHERN EUROPE IN 2022 SCC-G107TO108-22 (632-40002) Redebel s.a., Saint-Amand, Belgium GLP, unpublished	N	XXXX
KCA 6.3.2/01	Longhi, D.	2021	DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019) BPL-STUDY-19-000033 FR19GWN01 (632-20001) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.3.2/02	Longhi, D.	2021	DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019 NORTHERN EUROPE - 4 TRIALS YEAR 2019) BPL-STUDY-19-000034 ATA-19-39250 (632-20002) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.3.2/03	Loriau, P.	2022	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES CULTIVATED IN OPEN FIELD CONDITIONS AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 4 DECLINE TRIALS AND 1 AT HARVEST TRIAL IN NORTHERN EUROPE, AND 4 DECLINE TRIALS IN SOUTHERN EUROPE IN 2021 SCC-G401TO409-21 (632-20005) Redebel s.a., Saint-Amand, Belgium GLP, unpublished	N	XXXX

KCA 6.3.2/04	Loriau, P.	2023	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 2 DECLINE TRIALS IN SOUTHERN EUROPE IN 2022 SCC-G105TO106-22 (632-20006) Redebel s.a., Saint-Amand, Belgium GLP, unpublished	N	XXXX
KCA 6.3.3/01	Longhi, D.	2023	GWN-8030, ITS METABOLITES AND PHOSPHONATES IN POTATOES AFTER THREE APPLICATIONS OF GWN-9790 EU AND GWN-10616 IN THE OPEN FIELD (NORTHERN AND SOUTHERN EU, 8 TRIALS, YEAR 2021) GLP-STUDY-21-14 (633-09001) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	XXXX
KCA 6.3.3/02	Meyer, M.	2023	STUDY ON THE RESIDUE BEHAVIOUR OF GWN-8030 AND MDI-0074 IN POTATO AND ITS PROCESSED PRODUCTS AFTER TREATMENT WITH GWN-10616 UNDER FIELD CONDITIONS IN GERMANY, POLAND, NORTHERN FRANCE, ITALY, SPAIN AND GREECE, 2022 IF22-06194195 (638-019) SGS Institut Fresenius GmbH, Taunusstein, Germany GLP, unpublished	N	XXXX
KCA 6.5.3/13	Loriau, P.	2022	RESIDUES OF PHOSPHONIC ACID IN APPLES CULTIVATED IN OPEN FIELD CONDITIONS AND IN PROCESSED APPLES AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 3 TRIALS CONDUCTED IN EUROPE (BELGIUM, THE NETHERLANDS AND SPAIN) IN 2021 SCC-G401TO409-21-P (638-001) Redebel s.a., Saint-Amand, Belgium GLP, unpublished	N	XXXX
KCA 6.5.3/14	Ipach, R.	2010	STUDY ON THE RESIDUE BEHAVIOUR OF PHOSPHONIC ACID IN GRAPES AND GRAPES PROCESS FRACTIONS AFTER APPLICATION OF LBG-01F34 (MAC 94700 F9 UNDER FIELD CONDITIONS (GERMANY, 2009) FSC01 (638-022) DLR-Rheinpfalz, Neustadt, Germany GLP, unpublished	N	LBG
KCA 6.10.1/01	Couture, E.,	2022	HONEY MRL STUDY WITH PHOPHONIC ACID ON PHACELIA IN 2021 143SRFR21C01 (634-96002) SGS Institut Fresenius GmbH, Taunusstein, Germany GLP, unpublished	N	LBG

na = not applicable / ni = not indicated / nr = not relevant

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

ZOXAMIDE

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	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 6.1/01	Ross, J.R.	1998	Storage stability of RH-117281 Residues in grapes, grape juice, raisins and potatoes under conditions of frozen storage Rohm and Haas, McKenzie Laboratories, Enviro Test Laboratories, Report No. 34-98-161, December 15, 1998, ER R61.1 GLP Not published	N	N		XXXX
KCA 6.1/02	Ross, J.R.	1998	Storage stability of RH-141,455 and RH-141,452 residues in potatoes, potato chips and potato flakes under conditions of frozen storage Rohm and Haas, McKenzie Laboratories, Enviro Test Laboratories, Report No. 34-98-162, December 15, 1998, ER R61.2 GLP Not published	N	N		XXXX
KCA 6.1/03	Reibach, P.H.	2000	Storage stability of RH-117,281 residue in potato samples under conditions of frozen storage: Supplement to TR34-98-161 (ER 61.1) Rohm and Haas, Report No. 34-00-80, ER R77.11 GLP Not published	N	N		XXXX
KCA 6.1/04	Weber, H., Kissmann, H.	2014	Storage stability of residues of Zoxamide, RH-150721, RH-1452 and RH-1455 in grape and processed products and potato Eurofins AgroScience Services Chem GmbH, Report No. S12-03952, February 15, 2016 GLP Not published	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.1/05	Sala, A.	2021	STORAGE STABILITY OF ZOXAMIDE RESIDUES UNDER FROZEN CONDITIONS (-18°C) IN GRAPES, GRAPE JUICE AND WINE BPL-STUDY-18-000038 (645-002) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.1/06	Poráčski, K.	2020	MAGNITUDE OF RESIDUES OF ZOXAMIDE IN PHACELIA (PHACELIA TANACETIFOLIA BENTH.) HONEY AFTER THREE APPLICATIONS OF GWN-9790EU UNDER SEMI-FIELD	N	Y	Data/study report already submitted in Annex renewal,	XXXX

			CONDITIONS IN NORTHERN AND SOUTHERN EUROPE 19 48 BTR 0003 (634-96001) BioChem agrar Labor für biologische und chemische Analytik GmbH, Gerichshain, Germany GLP, unpublished			thus data protection is still applicable.	
KCA 6.1/07	Sala, A.	2020	VALIDATION OF AN ANALYTICAL METHOD TO DETERMINE ZOXAMIDE RESIDUES IN GRAPE, POTATO, TOMATO, CUCUMBER, AND ONION RAW AGRICULTURAL AND PROCESSED COMMODITIES BPL-STUDY-18-000085 (432-009) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.2.1/01	Reibach, P.H., Spencer W.O.	1998	¹⁴ C-RH-117,281: Nature of the residue in fruiting grape plants Rohm and Haas, American Agricultural Services, Inc. (AASI), Report No. 34-98-49, ER R14.5 GLP Not published	N	N		XXXX
KCA 6.2.1/02	Reibach, P.H., Spencer W.O.	1998	¹⁴ C-RH-117,281: Nature of the residue in potato Rohm and Haas, American Agricultural Services, Inc. (AASI), Report No. 34-98-50, September 17, 1998, ER R14.3 GLP Not published	N	N		XXXX
KCA 6.2.1/03	Graves, D.D., Reibach, P.H.	2000	Consideration of the difference in the magnitude of the residues of RH-7281 in grapes from supervised field residue trials compared to the ¹⁴ C grape metabolism Study ER 14.5 Rohm and Haas, Report No. 34-00-83, ER R76.6 GLP Not published	N	N		XXXX
KCA 6.2.1/04	Staffa, C., Möndel, M.	2014	¹⁴ C-phenyl UL Zoxamide: Plant metabolism in grape RLP AgroScience GmbH, Report No. AS209, July 15, 2014 GLP Not published	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.2.1/05	Sharma, A.K.	1999	RH-117,281: Nature of residue in fruiting tomato plants Rohm and Haas, Grayson Research, LLC, Report No. 34-99-159, December 14, 1999 GLP Not published	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.2.1/06	Sharma, A.K.	1999	RH-117,281: Nature of residue in cucurbits (cucumber) Rohm and Haas, Grayson Research, LLC, Report No. 34-99-57, November 30, 1999 GLP Not published	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.2.1/07	Hein, W.	2014	[Phenyl-UL- ¹⁴ C] Zoxamide: Plant metabolism in pea RLP AgroScience GmbH, Report No. AS290, June 12, 2014	N	Y	Data/study report already submitted in Annex renewal,	XXXX

			GLP Not published			thus data protection is still applicable.	
KCA 6.2.1/08	Hein, W.	2014	Extraction efficiency of [phenyl-UL- ¹⁴ C] Zoxamide from plant metabolism samples (pea) RLP AgroScience GmbH, Report No. AS362, June 25, 2014 GLP Not published	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.2.1/09	Wolf, S.	2001	Determination of RH-0721 residues in/on grape (RAC grape) from field trials in Europe (1997/1999) - to support ER 14.5 Rohm and Haas, RCC Ltd., Report No. 799773 March 16, 2001, ER ref. no. R 79.1 GLP Not published	N	N		XXXX
KCA 6.2.3/01	XXXX	1998	Metabolism of 14C-RH-117,281 in lactating goats XXXX, Report No. 34-97-166, September 10, 1998, ER R16.1 XXXX., Report No. RPT00299 GLP Not published	Y	N		XXXX
KCA 6.3.1/01	Longhi, D.	2021	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF WINE GRAPE AND PROCESSED (WINE) IN OPEN FIELD FOLLOWING THREE APPLICATIONS OF THE FORMULATED PRODUCTS GWN-9823, GWN-10616, GWN-10392 (NORTH AND SOUTH EUROPE – 7 trials year 2020) GLP-STUDY-20-30 (638-015) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.1/01	Grist, A.	2018	ZOXAMIDE: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS RB66JN (638-018) Envigo CRS Limited, Alconbury, Cambridgeshire, United Kingdom GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.1/02	Longhi, D.	2019	RH-141452: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS BPL-STUDY-18-000092 (638-008) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.1/03	Longhi, D.	2019	RH-141455: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS BPL-STUDY-19-000009 (638-009) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.1/04	Hueben, M.	2021	HIGH TEMPERATURE HYDROLYSIS - SIMULATED PROCESSING OF 14C- RH-129151 GOW-004/5-42 (638-016) Fraunhofer-Institute for Molecular Biology and Applied Ecology (IME), Schmallenberg, Germany	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still	XXXX

			GLP, unpublished			applicable.	
KCA 6.5.3/01	Longhi, D.	2020	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF TABLE GRAPE AND PROCESSED (RAISIN) IN OPEN FIELD FOLLOWING FIVE AND THREE APPLICATIONS OF THE FORMULATED PRODUCT GWN 9790 EU (SOUTH EUROPE – 1 TRIAL YEAR 2019) BPL-STUDY-19-000058 (638-012) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/02	Maccaferri, L.	2020	MAGNITUDE OF THE RESIDUES OF ZOXAMIDE IN TABLE GRAPE BUNCHES AND IN RAISINS PROCESSED FRACTION, FOLLOWING APPLICATIONS OF ZOXIUM 240 SC. ONE HARVEST TRIAL, SOUTHERN EUROPE – 2018 18097-03R (638-005) Renolab S.r.l., San Giorgio di Piano, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/03	Peterek, S.	2020	MAGNITUDE OF THE RESIDUES OF ZOXAMIDE AND ITS METABOLITES IN GRAPEVINE (RAC BUNCHES) AND PROCESSED FRACTIONS, FOLLOWING APPLICATIONS OF ZOXIUM 240 SC, NORTHERN EUROPE – 2018 AB2-18-35355 (638-007) Staphyt GmbH, Blaufelden, Germany GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/04	Sala, A.	2020	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY WINE GRAPE (BERRIES) AND PROCESSED FRACTIONS (JUICE, WINE) FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (GWN-9790 EU) IN OPEN FIELD CONDITION 2 HARVEST TRIALS, NORTHERN EUROPE, YEAR 2017 BPL-STUDY-19-000041 (638-010) LabAnalysis s.r.l., Casanova Lonati (PV), Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/05	Thomas-Delille, E.	2020	DETERMINATION OF ZOXAMIDE AND ITS METABOLITE RH-150721 RESIDUES IN WINE GRAPE AND PROCESSED FRACTIONS FOLLOWING FIVE FOLIAR APPLICATIONS WITH ZOXIUM 240 SC UNDER FIELD CONDITIONS IN NORTHERN EUROPE IN 2017 B7284 (638-020) Anadiag, Haguenau, France GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/06	Sala, A.	2020	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY WINE GRAPE (BERRIES) AND PROCESSED FRACTIONS (JUICE, WINE) FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (GWN-9790 EU) IN OPEN FIELD CONDITION 2 HARVEST TRIALS, SOUTHERN EUROPE, YEAR 2017 BPL-STUDY-19-000051 (638-011) LabAnalysis s.r.l., Casanova Lonati (PV), Italy	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX

			GLP, unpublished				
KCA 6.5.3/07	Casalinuovo, L.	2020	DETERMINATION OF ZOXAMIDE AND HIS METABOLITE RH-150721 RESIDUES IN RAW AGRICULTURAL COMMODITY RED GRAPES AND PROCESSED FRACTION FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (ZOXAMIDE 240 G/L) (SOUTH EUROPE - 2 TRIALS YEAR 2017) BIU-005-17 (638-021) Research Centre BioSpheres, Lodi, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/08	Maccaferri, L.	2019	DETERMINATION OF THE RESIDUES OF ZOXAMIDE AND / OR PHOSPHOROUS ACID IN TABLE GRAPE RAW AGRICULTURAL COMMODITY FOLLOWING FIVE APPLICATIONS OF GOW F 716, ZOXIUM 240 SC, GOW F 316 IN OPEN FIELD CONDITION (ONE HARVEST TRIAL, ITALY 2017) 17120-01R (638-003) Renolab S.r.l., San Giorgio di Piano, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/09	Maccaferri, L.	2019	DETERMINATION OF THE RESIDUES OF ZOXAMIDE AND / OR PHOSPHOROUS ACID IN RAW AGRICULTURAL COMMODITY OF GRAPEVINE AND PROCESSED COMMODITIES (JUICE, MUST, YOUNG WINE AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF GOW F 716, ZOXIUM 240 SC, GOW F 316 IN OPEN FIELD CONDITION (ONE HARVEST TRIAL, ITALY 2017) 17120-02R (638-004) Renolab S.r.l., San Giorgio di Piano, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/10	Maccaferri, L.	2020	MAGNITUDE OF RESIDUES OF ZOXAMIDE ENANTIOMERS AND METABOLITES IN GRAPES AND PROCESSED COMMODITIES (JUICE, MUST, YOUNG WINE AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF GOW F 716 AND ZOXIUM 240 SC IN OPEN FIELD CONDITION (ITALY 2017) 19200-01R (638-006) Renolab S.r.l., San Giorgio di Piano, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA 6.5.3/11	Romanini, M.	2011	DETERMINATION OF CYMOXANIL AND ZOXAMIDE RESIDUES AT HARVEST IN RAW AND PROCESSED AGRICULTURAL COMMODITY GRAPE (BUNCH, MUST YOUNG AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF HARPON WG (CYMOXANIL 33% + ZOXAMIDE 33% WG) (CYMOXANIL 33 % + ZOXAMIDE 33 % WG) – FOUR TRIALS, ITALY 2010 CREG2117 (638-013) Research Centre "E. Gagliardini", Salerano sul Lambro, Italy GLP, unpublished	N	Y	Data/study report already submitted in Annex renewal, thus data protection is still applicable.	XXXX
KCA	Romanini, M.	2011	DETERMINATION OF CYMOXANIL AND ZOXAMIDE RESIDUES AT HARVEST IN RAW	N	Y	Data/study report already	XXXX

6.5.3/12			AND PROCESSED AGRICULTURAL COMMODITY GRAPE (BUNCH, MUST YOUNG AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF HARPOX WG (CYMOXANIL 33% + ZOXAMIDE 33% WG) – FOUR TRIALS, ITALY 2010 CREG2120 (638-014) Research Centre "E. Gagliardini", Salerano sul Lambro, Italy GLP, unpublished			submitted in Annex renewal, thus data protection is still applicable.	
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POTASSIUM PHOSPONATES

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
KCA 6.1/08	Witte, A.	2003	Determination of the Storage Stability of Phosphorous Acid on Laboratory-Fortified Grapes, 2003 Arbeitsgemeinschaft GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH, Eutinger Str. 24 D-75223 Niefern-Öschelbronn, Germany; Report no. Study code: 20011211/01-RSS GLP Unpublished	N	LBG
KCA 6.1/18	Rosati, D., Venet, C.	2007	Storage stability of residues of fosetyl-Al (AE F053616) and its metabolite (Phosphorous Acid : AE 0540099) in grape, potato, cucumber and cabbage during deep freeze storage for at least 24 months Bayer CropScience S.A., Lyon, France; Report No.: MR-07/364 GLP Unpublished	N	Bayer Crop- Science (out of data protection)
KCA 6.5.3/01	Röser, K.	2003	Determination of Phosphorous Acid in Grapes and Processed Goods After 5 Applications of LBG-01F34, Active Ingredient Potassium Phosphite, at 4 Sites in France, Arbeitsgemeinschaft GAB Biotechnologie GmbH & IFU Umweltanalytik GmbH, Eutinger Str. 24 D-75223 Niefern-Öschelbronn, Germany; Report no: 20031178/F2-FPVI GLP Unpublished	N	LBG

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 ZOXAMIDE

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

A 2.1.1.1.1 Storage stability of residues in plant products

A 2.1.1.1.1.1 Study 1 - Grapes (RAC and processed commodities)

Comments of zRMS: Latvia	<p>The following conclusion (+ deviations) of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX and its affiliates in May 2021:</p> <p>The study is compliant with the requirements of OECD TG 506 and considered acceptable.</p> <p>Residues of zoxamide and metabolites RH-141452 and RH-24549 in grape brunches, grape juice and wine are stable for at least 26 months when stored at -18°C or below. Metabolite RH-141288 is stable for 18 months in grape brunches, for 26 months in grape juice and wine. Metabo-lite RH-150721 is stable at least 24 months in grape brunches, grape juice, and wine. RH-129151 is stable for 3 months in grape brunches, grape juice, and wine.</p>
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This active substance related study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.1/05
Report:	STORAGE STABILITY OF ZOXAMIDE RESIDUES UNDER FROZEN CONDITIONS (-18°C) IN GRAPES, GRAPE JUICE AND WINE, Sala, A., 2021, report No. BPL-STUDY-18-000038, Doc. No. 645-002
Guideline(s):	SANTE/2020/12830, Rev.1 (2021), SANCO/3029/99, rev. 4 (2000), SANCO/825/00 rev.8.1 (2010)
Deviations:	<p>None</p> <p>The recovery results for (R)-RH-150721 (>110%) and (S)-RH-150721 (>110%) were above the acceptability range (70-110%) in the samples 18/38/WI/84R, 18/38/WI/85R and 18/38/WI/90R. The R2 value for the calibration curve of RH-129151 A and RH-129151 B were below the acceptability range (>0.99). However, the analytical results in aforementioned batches were discarded. Two freshly spiked samples for the T0 checkpoint and the retain samples for 3 months checkpoint (18/38WI/91T and 18/38/WI/92T) were analysed.</p> <p>The recovery results for RH-129151 (A) (<70%) and RH-129151 (B) (<70%) was below the acceptability range (70-110%) in the samples 18/38/GJ/49R and 18/38/GJ/50R. However, the analytical results for the aforementioned procedural recoveries, including the samples they covered during the checkpoint (18/38/GJ/46C, 18/38/GJ/47T and 18/38/GJ/48T), were discarded. The</p>

respective retain samples (18/38/GJ/51T and 18/38/GJ/52T) were analysed. The recovery check results for RH-141452 (>110%) and RH-24549 (>110%) were above the acceptability range (70-110%) in the samples 18/38/GB/9R and 18/38/GB/10R. However, the analytical results for the aforementioned procedural recoveries, including the samples they covered during the checkpoint (18/38/GB/6C, 18/38/GB/7T and 18/38/GB/8T), were discarded. The respective retain samples (18/38/GB/11T and 18/38/GB/12T) were analysed. In samples 18/38/23R and 18/38/24R the analytes (R)-RH-150721 and (S)-RH-150721 showed recovery values slightly above (approx. 130%) the acceptance range (70-110%). However, since the values obtained for the treated samples was corrected by the mean value for the procedural recoveries, the overestimation has been corrected. These deviations were regarded to have no impact on the study integrity.

GLP: Yes
Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material	Zoxamide (R+S)	Zoxamide (R+S)
Lot/Batch #:	BCBW0947	BCBZ7753
Purity (%):	99.6	99.6
Stability of test compound/Reference item	October 2020	November 2021
Spiking level (mg/kg):	0.1	0.1
Test material	(R)-RH-150721	(S)-RH-150721
Lot/Batch #:	HHGCP012-00-1	HHGCP013-00-1
Purity:	99.41	99.45
Stability of test compound/Reference item	Feb 2023	Feb 2023
Spiking level (mg/kg):	0.05	0.05
Test material	RH-141452	(R)-RH-141288
Lot/Batch #:	021109	HHGCP010-00-1
Purity:	99.82	98.96
Stability of test compound/Reference item	For duration of the study	For duration of the study
Spiking level (mg/kg):	0.1	0.05
Test material	(S)-RH-141288	(RS)-RH-129151
Lot/Batch #:	HHGCP011-00-1	EPP/JMK 065.11
Purity:	99.01	99.4
Stability of test compound/Reference item	Feb 2023	Feb. 2023
Spiking level (mg/kg):	0.05	0.1
Test material	RH-24549	
Lot/Batch #:	79942-1-10	
Purity:	99.34	
Stability of test compound/Reference item	Feb. 2023	
Spiking level (mg/kg):	0.1	

Test commodity

Crop:	Grapes		
Crop part or processed commodity:	Grape berries	Juice	Wine
Sample size:	12.5 g	12.5 g	12.5 g

Study design

The freezer storage stability of Zoxamide (sum of isomers), (R)-Zoxamide and (S)-Zoxamide and its metabolite RH-141452 in grape bunches as raw agricultural commodity (RAC) and its processed commodities (grape juice and wine) under frozen conditions (at $\leq -18^{\circ}\text{C}$) has been investigated for a period of 26 months. In addition, the storage stability of the metabolites RH-150721 (sum of isomers), (R)-RH-150721 and (S)-RH-150721, RH-141288 (sum of isomers), (R)-RH-141288 and (S)-RH-141288, RH-129151 (sum of isomers), (A)-RH-129151 and (B)-RH-129151 and RH-24549 in grape bunches and processed samples was checked.

Samples were fortified with 0.1 or 0.05 (enantiomers) mg/kg by addition of 125 μL of a spiking solution, a mixture containing all reference items together in acetonitrile. The spiked samples were mixed and immediately stored in the freezer. The stock and standard solutions of Zoxamide and its metabolites in acetonitrile stored in acetonitrile was freshly prepared for each analytical session.

The samples were analysed for recoveries after storage of $\leq -18^{\circ}\text{C}$ initially after fortification (day zero) and at 3, 6, 12, 18 and 26 months of storage. At each sampling point, 1 untreated blank and 2 specimens fortified freshly at (at 0.1 or 0.05 (enantiomers) mg/kg as procedural recoveries were analysed with fortified, stored frozen specimens. In addition, in samples stored frozen for 22 months, Zoxamide, (R)-Zoxamide and (S)-Zoxamide was determined.

Methods:

The method for the determination of Zoxamide and its metabolites was successfully validated in study BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and the limit of detection (LOD) for Zoxamide and its metabolites are presented in Table A 1:

Table A 1 **LOQ and LOD of analytes**

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (enantiomer A)*	0.005	0.0015
RH-129151 (enantiomer B)*	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

*The enantiomers (R)-RH-129151 and (S)-RH-129151 are named as RH-129151 (A) and RH-129151 (B) since it was not clear yet what signal is related at each enantiomer since only the racemate standard was provided.

The maximum extraction to analysis time period of the samples was < 3 days for grapes and the processed commodities.

The procedural recoveries fortified with 0.1 mg/kg or 0.05 mg/kg (enantiomer) run concurrently with the storage samples and were stored and handled the same way as the storage samples. The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07). This time period was

not exceeded in the current study, and thus, confirming the stability of Zoxamide and its metabolites for the longest storage period.

Procedural recoveries were in the range of 70 - 110 %, except for RH-150721 (racemate, R, S) at storage after 12 months with recoveries slightly above the range, confirming the validity of the method on the day of analysis.

Results

Table A 2: Summary of concurrent recoveries from grape bunches

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev **
(R)-Zoxamide					
Grape bunches	0.05	0	12.5 g (2)	103.2, 95.8	99.5
	0.05	3	12.5 g (2)	109.1, 101.8	105.5
	0.05	6	12.5 g (2)	94.3, 95.2	94.8
	0.05	12	12.5 g (2)	103.6, 100.9	102.2
	0.05	18	12.5 g (2)	85.0, 83.1	84.0
	0.05	22	12.5 g (2)	103.4, 99.1	101.3
	0.05	26	12.5 g (2)	97.2, 96.4	96.8
(S)-Zoxamide					
Grape bunches	0.05	0	12.5 g (2)	99.5, 92.8	96.2
	0.05	3	12.5 g (2)	109.1, 100.8	105.0
	0.05	6	12.5 g (2)	98.6, 106.6	102.6
	0.05	12	12.5 g (2)	107.3, 104.4	105.8
	0.05	18	12.5 g (2)	80.3, 78.8	79.6
	0.05	22	12.5 g (2)	103.7, 99.4	101.6
	0.05	26	12.5 g (2)	98.7, 96.2	97.5
Zoxamide (sum)					
Grape bunches	0.1	0	12.5 g (2)	101.4, 94.3	97.8
	0.1	3	12.5 g (2)	109.1, 101.3	105.2
	0.1	6	12.5 g (2)	96.5, 100.9	98.7
	0.1	12	12.5 g (2)	105.5, 102.7	104.1
	0.1	18	12.5 g (2)	82.7, 81.0	81.8
	0.1	22	12.5 g (2)	103.6, 99.3	101.4
	0.1	26	12.5 g (2)	98.0, 96.3	97.1
RH-141452					
Grape bunches	0.1	0	12.5 g (2)	100.5, 92.1	96.3
	0.1	3	12.5 g (2)	100.2, 105.0	102.6
	0.1	6	12.5 g (2)	101.4, 103.6	102.5

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.1	12	12.5 g (2)	103.7, 101.7	102.7
	0.1	18	12.5 g (2)	100.4, 101.1	100.7
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	96.1, 97.3	96.7
(R)-RH-141288					
Grape bunches	0.05	0	12.5 g (2)	99.4, 90.4	94.9
	0.05	3	12.5 g (2)	96.4, 90.7	93.6
	0.05	6	12.5 g (2)	96.6, 99.8	98.2
	0.05	12	12.5 g (2)	109.1, 107.7	108.4
	0.05	18	12.5 g (2)	91.5, 85.3	88.4
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	99.6, 88.1	93.9
(S)-RH-141288					
Grape bunches	0.05	0	12.5 g (2)	99.7, 96.8	98.3
	0.05	3	12.5 g (2)	103.4, 103.2	103.3
	0.05	6	12.5 g (2)	95.7, 100.3	98.0
	0.05	12	12.5 g (2)	106.6, 109.1	107.9
	0.05	18	12.5 g (2)	88.7, 84.3	86.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	91.5, 87.7	89.6
RH-141288 (sum)					
Grape bunches	0.1	0	12.5 g (2)	99.6, 93.6	96.6
	0.1	3	12.5 g (2)	99.9, 97.0	98.4
	0.1	6	12.5 g (2)	96.2, 100.1	98.1
	0.1	12	12.5 g (2)	107.9, 108.4	108.1
	0.1	18	12.5 g (2)	90.1, 84.8	87.5
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	95.6, 87.9	81.7
RH-129151 A					
Grape bunches	0.05	0	12.5 g (2)	81.8, 79.6	80.7
	0.05	3	12.5 g (2)	81.6, 88.4	85.0
	0.05	6	12.5 g (2)	76.6, 79.4	78.0
	0.05	12	12.5 g (2)	94.0, 93.7	93.9
	0.05	18	12.5 g (2)	94.2, 93.2	93.7

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	96.7, 99.6	98.2
RH-129151 B					
Grape bunches	0.05	0	12.5 g (2)	81.9, 78.2	80.0
	0.05	3	12.5 g (2)	79.9, 96.7	88.3
	0.05	6	12.5 g (2)	75.9, 81.2	78.6
	0.05	12	12.5 g (2)	96.7, 98.4	97.6
	0.05	18	12.5 g (2)	94.4, 95.5	95.0
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	97.6, 102.3	100.0
RH-129151 (sum)					
Grape bunches	0.1	0	12.5 g (2)	81.9, 78.9	80.4
	0.1	3	12.5 g (2)	80.8, 92.6	86.7
	0.1	6	12.5 g (2)	76.3, 80.3	78.3
	0.1	12	12.5 g (2)	95.4, 96.1	95.7
	0.1	18	12.5 g (2)	94.3, 94.4	94.3
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	97.2, 101.0	99.1
RH-24549					
Grape bunches	0.1	0	12.5 g (2)	106.8, 99.3	103.1
	0.1	3	12.5 g (2)	98.4, 102.5	100.5
	0.1	6	12.5 g (2)	105.4, 107.4	106.4
	0.1	12	12.5 g (2)	101.2, 102.3	101.7
	0.1	18	12.5 g (2)	95.7, 99.1	97.4
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	97.3, 97.8	97.6
(R)-RH-150721					
Grape bunches	0.05	0	12.5 g (2)	101.6, 106.2	103.9
	0.05	3	12.5 g (2)	109.4, 108.8	109.1
	0.05	6	12.5 g (2)	100.4, 93.6	97.0
	0.05	12	12.5 g (2)	135.9, 135.4	135.7
	0.05	18	12.5 g (2)	100.3, 96.5	98.4
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	106.7, 97.2	102.0

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
(S)-RH-150721					
Grape bunches	0.05	0	12.5 g (2)	109.3, 106.4	107.8
	0.05	3	12.5 g (2)	109.2, 107.7	108.5
	0.05	6	12.5 g (2)	106.1, 109.9	108.0
	0.05	12	12.5 g (2)	132.5, 131.7	132.1
	0.05	18	12.5 g (2)	104.1, 100.9	102.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	108.8, 106.7	107.8
RH-150721 (sum)					
Grape bunches	0.1	0	12.5 g (2)	105.5, 106.3	105.9
	0.1	3	12.5 g (2)	109.3, 108.3	108.8
	0.1	6	12.5 g (2)	103.3, 101.8	102.5
	0.1	12	12.5 g (2)	134.2, 133.6	133.9
	0.1	18	12.5 g (2)	102.2, 98.7	100.5
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	107.8, 102.0	104.9

* Fortification to extraction interval

** Standard deviation not relevant in case of two samples

na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Table A 3: Summary of concurrent recoveries from grapes juice.

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
(R)-Zoxamide					
Grape juice	0.05	0	12.5 g (2)	102.2, 105.3	103.8
	0.05	3	12.5 g (2)	104.7, 109.0	106.9
	0.05	6	12.5 g (2)	101.8, 107.8	104.8
	0.05	12	12.5 g (2)	97.3, 97.5	97.4
	0.05	18	12.5 g (2)	96.9, 94.3	95.6
	0.05	22	12.5 g (2)	92.7, 90.7	91.7
	0.05	26	12.5 g (2)	95.0, 90.4	92.7
(S)-Zoxamide					
Grape juice	0.05	0	12.5 g (2)	104.3, 105.8	105.0
	0.05	3	12.5 g (2)	106.5, 109.5	108.0

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.05	6	12.5 g (2)	106.3, 109.5	107.9
	0.05	12	12.5 g (2)	99.3, 98.4	98.9
	0.05	18	12.5 g (2)	95.7, 95.1	95.4
	0.05	22	12.5 g (2)	92.0, 89.3	90.7
	0.05	26	12.5 g (2)	101.9, 94.5	98.2
Zoxamide (sum)					
Grape juice	0.1	0	12.5 g (2)	103.3, 105.6	104.4
	0.1	3	12.5 g (2)	105.6, 109.3	107.4
	0.1	6	12.5 g (2)	104.1, 108.7	106.4
	0.1	12	12.5 g (2)	98.3, 98.0	98.1
	0.1	18	12.5 g (2)	96.3, 94.7	95.5
	0.1	22	12.5 g (2)	92.4, 90.0	91.2
	0.1	26	12.5 g (2)	98.5, 92.5	95.5
RH-141452					
Grape juice	0.1	0	12.5 g (2)	105.8, 105.9	105.8
	0.1	3	12.5 g (2)	104.7, 106.3	105.5
	0.1	6	12.5 g (2)	106.9, 106.8	106.8
	0.1	12	12.5 g (2)	104.4, 100.3	102.3
	0.1	18	12.5 g (2)	101.9, 104.6	103.2
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	92.8, 95.5	94.2
(R)-RH-141288					
Grape juice	0.05	0	12.5 g (2)	108.5, 109.9	109.2
	0.05	3	12.5 g (2)	107.5, 113.0	110.5
	0.05	6	12.5 g (2)	98.7, 101.3	100.0
	0.05	12	12.5 g (2)	101.9, 99.2	100.6
	0.05	18	12.5 g (2)	94.5, 94.3	94.4
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	93.7, 89.9	91.8
(S)-RH-141288					
Grape juice	0.05	0	12.5 g (2)	104.1, 101.4	102.8
	0.05	3	12.5 g (2)	91.7, 89.7	90.7
	0.05	6	12.5 g (2)	105.4, 107.5	106.4
	0.05	12	12.5 g (2)	100.0, 98.7	99.3

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.05	18	12.5 g (2)	94.4, 94.6	94.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	91.9, 93.5	92.7
RH-141288 (sum)					
Grape juice	0.1	0	12.5 g (2)	106.3, 105.7	106.0
	0.1	3	12.5 g (2)	99.6, 101.4	100.5
	0.1	6	12.5 g (2)	102.1, 104.4	103.2
	0.1	12	12.5 g (2)	101.0, 99.0	100.0
	0.1	18	12.5 g (2)	94.5, 94.5	94.5
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	92.8, 91.7	92.3
RH-129151 A					
Grape juice	0.05	0	12.5 g (2)	85.4, 78.4	81.9
	0.05	3	12.5 g (2)	83.8, 82.8	83.3
	0.05	6	12.5 g (2)	83.4, 84.5	84.0
	0.05	12	12.5 g (2)	97.4, 93.5	95.5
	0.05	18	12.5 g (2)	86.3, 84.5	85.4
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	105.8, 108.2	107.0
RH-129151 B					
Grape juice	0.05	0	12.5 g (2)	84.1, 83.4	83.8
	0.05	3	12.5 g (2)	80.7, 82.1	81.4
	0.05	6	12.5 g (2)	81.4, 82.4	81.9
	0.05	12	12.5 g (2)	97.6, 93.1	95.4
	0.05	18	12.5 g (2)	81.0, 80.0	80.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	97.0, 102.0	99.5
RH-129151 (sum)					
Grape juice	0.1	0	12.5 g (2)	84.8, 80.9	82.8
	0.1	3	12.5 g (2)	82.3, 82.5	82.4
	0.1	6	12.5 g (2)	82.4, 83.5	82.9
	0.1	12	12.5 g (2)	97.5, 93.3	95.4
	0.1	18	12.5 g (2)	83.7, 82.3	83.0
	0.1	22	12.5 g (2)	na	na

Matrix	Spike level (mg/kg)	Storage In- terval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev **
	0.1	26	12.5 g (2)	101.4, 105.1	103.3
RH-24549					
Grape juice	0.1	0	12.5 g (2)	105.4, 102.7	104.0
	0.1	3	12.5 g (2)	105.3, 103.5	104.4
	0.1	6	12.5 g (2)	102.8, 104.9	103.8
	0.1	12	12.5 g (2)	101.7, 97.4	99.6
	0.1	18	12.5 g (2)	105.5, 108.3	106.9
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	94.1, 94.9	94.5
(R)-RH-150721					
Grape juice	0.05	0	12.5 g (2)	108.3, 109.9	109.1
	0.05	3	12.5 g (2)	103.4, 104.8	104.1
	0.05	6	12.5 g (2)	103.1, 102.7	102.9
	0.05	12	12.5 g (2)	105.7, 108.4	107.0
	0.05	18	12.5 g (2)	109.1, 109.2	109.2
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	94.8, 101.5	98.2
(S)-RH-150721					
Grape juice	0.05	0	12.5 g (2)	108.0, 108.6	108.3
	0.05	3	12.5 g (2)	109.2, 109.7	109.4
	0.05	6	12.5 g (2)	98.8, 106.0	102.4
	0.05	12	12.5 g (2)	104.2, 106.8	105.5
	0.05	18	12.5 g (2)	108.8, 108.1	108.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	97.7, 102.5	100.1
RH-150721 (sum)					
Grape juice	0.1	0	12.5 g (2)	108.2, 109.3	108.7
	0.1	3	12.5 g (2)	106.3, 107.3	106.8
	0.1	6	12.5 g (2)	101.0, 104.4	102.7
	0.1	12	12.5 g (2)	105.0, 107.6	106.3
	0.1	18	12.5 g (2)	109.0, 108.7	108.8
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	96.3, 102.0	99.1

* Fortification to extraction interval ** Standard deviation not relevant in case of two samples
na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Table A 4 **Summary of concurrent recoveries from wine.**

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean ± std dev **
(R)-Zoxamide					
Grape wine	0.05	0	12.5 g (2)	88.1, 84.0	86.0
	0.05	3	12.5 g (2)	96.0, 99.3	97.7
	0.05	6	12.5 g (2)	100.8, 95.2	98.0
	0.05	12	12.5 g (2)	104.2, 102.5	103.4
	0.05	18	12.5 g (2)	108.9, 103.3	106.1
	0.05	22	12.5 g (2)	92.8, 89.4	91.1
	0.05	26	12.5 g (2)	96.7, 100.1	98.4
(S)-Zoxamide					
Grape wine	0.05	0	12.5 g (2)	87.7, 84.1	85.8
	0.05	3	12.5 g (2)	96.4, 99.5	98.0
	0.05	6	12.5 g (2)	101.7, 97.0	99.3
	0.05	12	12.5 g (2)	104.0, 101.7	102.8
	0.05	18	12.5 g (2)	106.0, 101.2	103.6
	0.05	22	12.5 g (2)	91.4, 89.4	90.4
	0.05	26	12.5 g (2)	97.1, 93.8	95.5
Zoxamide (sum)					
Grape wine	0.1	0	12.5 g (2)	87.9, 84.1	86.0
	0.1	3	12.5 g (2)	96.2, 99.4	97.8
	0.1	6	12.5 g (2)	101.3, 96.1	98.7
	0.1	12	12.5 g (2)	104.1, 102.1	103.1
	0.1	18	12.5 g (2)	107.5, 102.3	104.9
	0.1	22	12.5 g (2)	92.1, 89.4	90.8
	0.1	26	12.5 g (2)	96.9, 97.0	96.9
RH-141452					
Grape wine	0.1	0	12.5 g (2)	102.8, 103.7	103.2
	0.1	3	12.5 g (2)	100.7, 98.8	99.8
	0.1	6	12.5 g (2)	101.3, 98.7	100.0
	0.1	12	12.5 g (2)	97.5, 98.4	97.9
	0.1	18	12.5 g (2)	95.7, 98.0	96.8
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	95.4, 94.7	95.1
(R)-RH-141288					

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
Grape wine	0.05	0	12.5 g (2)	82.0, 78.4	80.2
	0.05	3	12.5 g (2)	88.4, 92.2	90.3
	0.05	6	12.5 g (2)	98.5, 95.9	97.2
	0.05	12	12.5 g (2)	100.7, 101.7	101.2
	0.05	18	12.5 g (2)	105.6, 99.7	102.7
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	89.9, 92.9	91.4
(S)-RH-141288					
Grape wine	0.05	0	12.5 g (2)	80.3, 77.4	78.8
	0.05	3	12.5 g (2)	86.9, 91.4	89.1
	0.05	6	12.5 g (2)	100.2, 98.1	99.2
	0.05	12	12.5 g (2)	108.4, 108.8	108.6
	0.05	18	12.5 g (2)	103.2, 100.2	101.7
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	99.0, 99.9	99.5
RH-141288 (sum)					
Grape wine	0.1	0	12.5 g (2)	81.2, 77.9	79.5
	0.1	3	12.5 g (2)	87.7, 91.8	89.7
	0.1	6	12.5 g (2)	99.4, 97.0	98.2
	0.1	12	12.5 g (2)	104.6, 105.3	104.9
	0.1	18	12.5 g (2)	104.4, 100.0	102.2
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	94.5, 96.4	95.4
RH-129151 A					
Grape wine	0.05	0	12.5 g (2)	86.1, 95.9	91.0
	0.05	3	12.5 g (2)	83.8, 78.6	81.2
	0.05	6	12.5 g (2)	75.2, 73.1	74.1
	0.05	12	12.5 g (2)	100.6, 101.6	101.1
	0.05	18	12.5 g (2)	90.9, 87.5	89.2
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	88.0, 86.8	87.4
RH-129151 B					
Grape wine	0.05	0	12.5 g (2)	84.3, 82.1	83.2
	0.05	3	12.5 g (2)	78.1, 80.1	79.1

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.05	6	12.5 g (2)	71.6, 72.6	72.1
	0.05	12	12.5 g (2)	102.8, 103.4	103.1
	0.05	18	12.5 g (2)	90.3, 88.3	89.3
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	92.2, 90.9	91.6
RH-129151 (sum)					
Grape wine	0.1	0	12.5 g (2)	85.2, 89.0	87.1
	0.1	3	12.5 g (2)	81.0, 79.4	80.2
	0.1	6	12.5 g (2)	73.4, 72.9	73.1
	0.1	12	12.5 g (2)	101.7, 102.5	102.1
	0.1	18	12.5 g (2)	90.6, 87.9	89.3
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	90.1, 88.9	89.5
RH-24549					
Grape wine	0.1	0	12.5 g (2)	99.1, 98.8	99.0
	0.1	3	12.5 g (2)	97.8, 97.2	97.5
	0.1	6	12.5 g (2)	104.1, 99.4	101.8
	0.1	12	12.5 g (2)	101.1, 99.8	100.4
	0.1	18	12.5 g (2)	101.7, 109.8	105.7
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	98.0, 96.6	97.3
(R)-RH-150721					
Grape wine	0.05	0	12.5 g (2)	98.6, 94.3	96.4
	0.05	3	12.5 g (2)	105.7, 109.1	107.4
	0.05	6	12.5 g (2)	101.6, 103.1	102.3
	0.05	12	12.5 g (2)	108.1, 109.4	108.8
	0.05	18	12.5 g (2)	107.5, 104.5	106.0
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	105.7, 104.7	105.2
(S)-RH-150721					
Grape wine	0.05	0	12.5 g (2)	96.6, 93.3	94.9
	0.05	3	12.5 g (2)	109.4, 109.2	109.3
	0.05	6	12.5 g (2)	106.8, 103.7	105.2
	0.05	12	12.5 g (2)	107.6, 106.8	107.2

Matrix	Spike level (mg/kg)	Storage Interval (months) *	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev **
	0.05	18	12.5 g (2)	104.8, 104.2	104.5
	0.05	22	12.5 g (2)	na	na
	0.05	26	12.5 g (2)	109.8, 108.0	108.9
RH-150721 (sum)					
Grape wine	0.1	0	12.5 g (2)	97.6, 93.8	95.7
	0.1	3	12.5 g (2)	107.6, 109.2	108.4
	0.1	6	12.5 g (2)	104.2, 103.4	103.8
	0.1	12	12.5 g (2)	107.9, 108.1	108.0
	0.1	18	12.5 g (2)	106.2, 104.4	105.3
	0.1	22	12.5 g (2)	na	na
	0.1	26	12.5 g (2)	107.8, 106.4	107.1

* Fortification to extraction interval

** Standard deviation not relevant in case of two samples

na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Table A 5: Stability of residues in grape bunches following storage at $\leq -18^{\circ}\text{C}$.

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
(R)-Zoxamide					
Grape bunches	0.05	0	0.0509, 0.0455	103.2, 92.4	98.3
	0.05	3	0.0544, 0.0539	109.7, 108.9	103.6
	0.05	6	0.0497, 0.0507	100.0, 102.2	106.6
	0.05	12	0.0583, 0.0588	117.6, 118.7	115.7
	0.05	18	0.0554, 0.0515	107.7, 103.5	125.7
	0.05	22	0.0526, 0.0534	105.5, 107.2	104.9
	0.05	26	0.0415, 0.0415	83.4, 83.6	86.3
(S)-Zoxamide					
Grape bunches	0.05	0	0.0490, 0.0449	99.3, 91.2	99.1

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	3	0.0532, 0.0536	108.3, 108.4	103.1
	0.05	6	0.0524, 0.0543	105.5, 109.5	104.8
	0.05	12	0.0608, 0.0615	122.7, 124.1	116.6
	0.05	18	0.0499, 0.0476	100.5, 95.6	123.2
	0.05	22	0.0526, 0.0534	105.4, 107.2	104.6
	0.05	26	0.0396, 0.0418	79.6, 84.1	84.0
Zoxamide (sum)					
Grape bunches	0.1	0	0.0999, 0.0904	101.3, 91.8	98.7
	0.1	3	0.1081, 0.1075	109.0, 108.7	103.4
	0.1	6	0.1021, 0.1049	102.8, 105.9	105.7
	0.1	12	0.1190, 0.1203	120.2, 121.4	116
	0.1	18	0.1033, 0.0992	104.1, 99.6	124.4
	0.1	22	0.1053, 0.1069	105.5, 107.2	104.8
Grape bunches	0.1	26	0.0811, 0.0833	81.5, 83.9	85.2
RH-141452					
Grape bunches	0.1	0	0.0983, 0.0918	99.0, 92.7	119.3
	0.1	3	0.1083, 0.1054	107.5, 104.9	103.5
	0.1	6	0.1046, 0.1062	104.3, 106.1	102.6
	0.1	12	0.1109, 0.1109	110.9, 111.0	108.1
	0.1	18	0.1056, 0.1059	105.4, 105.3	104.7
	0.1	22	na	na	na

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	26	0.1058, 0.1056	96.1, 97.3	100
(R)-RH-141288					
Grape bunches	0.05	0	0.0523, 0.0493	104.4, 98.6	107.0
	0.05	3	0.0555, 0.0538	106.1, 103.1	111.8
	0.05	6	0.0522, 0.0537	99.5, 102.7	103.0
	0.05	12	0.0608, 0.0600	116.4, 114.8	106.6
	0.05	18	0.0591, 0.0567	112.8, 107.9	124.9
	0.05	22	na	na	na
	0.05	26	0.0360, 0.0368	68.7, 70.2	74.0
(S)-RH-141288					
Grape bunches	0.05	0	0.0485, 0.0483	95.3, 95.2	96.8
	0.05	3	0.0499, 0.0509	100.4, 102.7	98.4
	0.05	6	0.0517, 0.0521	103.8, 104.9	106.4
	0.05	12	0.0536, 0.0551	108.0, 111.0	101,5
	0.05	18	0.0541, 0.0501	108.8, 100.4	120.9
	0.05	22	na	na	na
	0.05	26	0.0319, 0.0349	64.1, 70.3	75.0
RH-141288 (sum)					
Grape bunches	0.1	0	0.1007, 0.0976	99.85, 96.9	101.9
	0.1	3	0.1054, 0.1048	103.3, 102.9	104.8
	0.1	6	0.1038, 0.1058	101.7, 103.8	104.7
	0.1	12	0.1144, 0.1151	112.2, 112.9	104.2

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	18	0.1132, 0.1068	110.8, 104.2	122.9
	0.1	22	na	na	na
	0.1	26	0.0679, 0.0718	66.4, 70.3	74.5
RH-129151 (A)					
Grape bunches	0.05	0	0.0498, 0.0388	101.2, 79.1	111.8
	0.05	3	0.0214, 0.0188	42.9, 37.9	47.5
	0.05	6	0.0102, 0.0109	20.5, 21.8	27.1
	0.05	12	0.0068, 0.0073	13.6, 14.7	15.1
	0.05	18	0.0060, 0.0049	12.1, 9.9	11.7
	0.05	22	na	na	na
	0.05	26	0.0029, 0.0027	5.8, 5.5	6.5
RH-129151 (B)					
Grape bunches	0.05	0	0.0403, 0.0391	101.0, 79.5	112.8
	0.05	3	0.0205, 0.0180	41.1, 36.2	43.8
	0.05	6	0.0086, 0.0096	17.3, 19.3	23.3
	0.05	12	0.0064, 0.0070	12.9, 14.1	13.8
	0.05	18	0.0054, 0.0046	10.8, 9.3	10.5
	0.05	22	na	na	na
	0.05	26	0.0028, 0.0027	5.7, 5.4	6.2
RH-129151 (sum)					
Grape bunches	0.1	0	0.0900, 0.0779	101.1, 79.3	112.2
	0.1	3	0.0419, 0.0368	42.0, 37.1	45.6

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	6	0.0189, 0.0205	18.9, 20.6	25.2
	0.1	12	0.0132, 0.0143	13.3, 14.4	14.4
	0.1	18	0.0114, 0.0096	11.5, 9.6	11.1
	0.1	22	na	na	na
	0.1	26	0.0057, 0.0055	5.8, 5.5	6.3
RH-24549					
Grape bunches	0.1	0	0.1097, 0.1008	107.1, 98.6	99.8
	0.1	3	0.1224, 0.1176	113.8, 109.6	111.1
	0.1	6	0.1136, 0.1169	106.1, 109.4	101.2
	0.1	12	0.1067, 0.1079	99.9, 101.1	98.8
	0.1	18	0.1045, 0.1076	97.7, 100.2	101.6
	0.1	22	na	na	na
	0.1	26	0.0890, 0.0894	83.0, 83.4	82.3
(R)-RH-150721					
Grape bunches	0.05	0	0.0449, 0.0459	101.6, 104.1	98.9
	0.05	3	0.0644, 0.0624	134.0, 134.2	122.9
	0.05	6	0.0558, 0.0568	119.7, 122.1	124.6
	0.05	12	0.0554, 0.0545	119.0, 119.4	87.8
	0.05	18	0.0632, 0.0637	135.6, 136.2	138.1
	0.05	22	na	na	na
	0.05	26	0.0409, 0.0413	87.7, 88.5	81.8
(S)-RH-150721					

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
Grape bunches	0.05	0	0.0478, 0.0465	108.8, 106.2	99.7
	0.05	3	0.0686, 0.0649	150.0, 142.2	134.7
	0.05	6	0.0584, 0.0604	127.4, 132.1	120.1
	0.05	12	0.0558, 0.0572	122.1, 125.2	93.6
	0.05	18	0.0717, 0.0730	156.7, 159.0	154.0
	0.05	22	na	na	na
	0.05	26	0.0504, 0.0413	109.9, 114.3	100.9
RH-150721 (sum)					
Grape bunches	0.1	0	0.0927, 0.0924	105.2, 105.2	99.3
	0.1	3	0.1310, 0.1273	142.0, 138.2	128.8
	0.1	6	0.1142, 0.1172	123.6, 127.1	122.2
	0.1	12	0.1111, 0.1127	120.6, 122.3	90.7
	0.1	18	0.1349, 0.1367	146.2, 147.6	146.2
	0.1	22	na	na	na
	0.1	26	0.0504, 0.0524	98.8, 101.4	91.5

* Fortification to extraction interval

** Corrected for concurrent-recoveries

na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Table A 6: Stability of residues in grape juice following storage at <-18°C.

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
(R)-Zoxamide					
Grape juice	0.05	0	0.0498, 0.0515	101.2, 104.2	98.9

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	3	0.0527, 0.0540	106.1, 108.9	100.6
	0.05	6	0.0542, 0.0547	108.9, 109.8	104.4
	0.05	12	0.0549, 0.0559	110.3, 112.6	114.5
	0.05	18	0.0560, 0.0568	112.7, 114.2	118.7
	0.05	22	0.0524, 0.0536	104.8, 107.6	115.8
	0.05	26	0.0486, 0.0448	97.4, 90.0	101.1
(S)-Zoxamide					
Grape juice	0.05	0	0.0496, 0.0517	100.6, 104.7	97.8
	0.05	3	0.0539, 0.0540	108.6, 108.9	100.6
	0.05	6	0.0527, 0.0542	106.0, 108.7	99.5
	0.05	12	0.0558, 0.0560	112.0, 112.8	113.7
	0.05	18	0.0549, 0.0557	110.5, 112.0	116.6
	0.05	22	0.0519, 0.0529	103.9, 106.2	115.9
	0.05	26	0.0460, 0.0457	92.3, 91.8	93.8
Zoxamide (sum)					
Grape juice	0.1	0	0.0994, 0.1031	100.9, 104.5	98.4
	0.1	3	0.1066, 0.1088	107.4, 108.9	100.7
	0.1	6	0.1069, 0.1088	107.5, 109.3	101.9
	0.1	12	0.1107, 0.1120	111.2, 112.7	114.1
	0.1	18	0.1109, 0.1125	111.6, 113.1	117.7

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	22	0.1043, 0.1065	104.4, 106.9	115.8
	0.1	26	0.0946, 0.0905	94.9, 90.9	97.3
RH-141452					
Grape juice	0.1	0	0.1032, 0.1033	104.1, 104.0	98.4
	0.1	3	0.1033, 0.1074	103.1, 107.2	99.6
	0.1	6	0.1062, 0.1061	105.8, 105.6	99.0
	0.1	12	0.1066, 0.0164	106.1, 106.1	103.7
	0.1	18	0.1052, 0.1077	104.9, 107.3	102.8
	0.1	22	na	na	na
	0.1	26	0.0874, 0.0879	86.8, 87.4	92.5
(R)-RH-141288					
Grape juice	0.05	0	0.0527, 0.0542	105.6, 108.2	97.9
	0.05	3	0.0555, 0.0559	111.0, 112.0	100.9
	0.05	6	0.0559, 0.0557	106.6, 105.9	106.3
	0.05	12	0.0532, 0.0513	101.2, 97.9	98.9
	0.05	18	0.0538, 0.0551	104.3, 106.7	111.8
	0.05	22	na	na	na
	0.05	26	0.0452, 0.0422	86.0, 80.3	90.6
(S)-RH-141288					
Grape juice	0.05	0	0.0519, 0.0519	102.4, 101.9	99.4
	0.05	3	0.0468, 0.0457	92.1, 90.1	100.3
	0.05	6	0.0526, 0.0538	105.6, 107.7	100.3

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	12	0.0494, 0.0486	98.9, 97.7	99.0
	0.05	18	0.0495, 0.0498	99.4, 99.9	105.5
	0.05	22	na	na	na
	0.05	26	0.0408, 0.0359	81.7, 72.1	83.0
RH-141288 (sum)					
Grape juice	0.1	0	0.1047, 0.1061	104.0, 105.1	98.6
	0.1	3	0.1022, 0.1017	101.6, 101.1	100.8
	0.1	6	0.1086, 0.1094	106.1, 106.8	103.1
	0.1	12	0.1025, 0.0999	100.1, 97.8	98.9
	0.1	18	0.1033, 0.1049	101.9, 103.3	108.6
	0.1	22	na	na	na
	0.1	26	0.0861, 0.0781	83.9, 76.2	86.7
RH-129151 (A)					
Grape juice	0.05	0	0.0439, 0.0434	89.5, 88.1	108.4
	0.05	3	0.0109, 0.0135	21.9, 27.1	29.4
	0.05	6	0.0037, 0.0060	7.5, 12.0	11.5
	0.05	12	0.0017, 0.0016	3.3, 3.2	3.5
	0.05	18	0.0029, 0.0027	5.8, 5.5	6.6
	0.05	22	na	na	na
	0.05	26	0.0017, 0.0017	3.4, 3.4	3.2
RH-129151 (B)					
Grape juice	0.05	0	0.0406, 0.0417	82.7, 84.7	99.9

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	3	0.0095, 0.0119	19.0, 24.0	26.4
	0.05	6	0.0036, 0.0055	7.2, 10.9	11.1
	0.05	12	0.0022, 0.0021	4.5, 4.2	4.5
	0.05	18	0.0034, 0.0033	6.7, 6.6	8.3
	0.05	22	na	na	na
	0.05	26	0.0011, 0.0011	2.3, 2.3	2.3
RH-129151 (sum)					
Grape juice	0.1	0	0.0846, 0.0851	86.1, 86.4	104.2
	0.1	3	0.0205, 0.0255	20.5, 25.6	27.9
	0.1	6	0.0073, 0.0115	7.4, 11.5	11.3
	0.1	12	0.0039, 0.0037	3.9, 3.7	4.0
	0.1	18	0.0063, 0.0061	6.3, 6.1	7.5
	0.1	22	na	na	na
	0.1	26	0.0028, 0.0028	2.9, 2.9	2.8
RH-24549					
Grape juice	0.1	0	0.1082, 0.1075	105.8, 104.9	101.3
	0.1	3	0.1156, 0.1155	107.9, 107.9	103.4
	0.1	6	0.1067, 0.1080	99.5, 100.6	96.4
	0.1	12	0.1113, 0.1044	103.6, 97.5	101.0
	0.1	18	0.1148, 0.1144	107.2, 106.7	94.4
	0.1	22	na	na	na
	0.1	26	0.967, 0.0958	89.9, 89.2	94.8

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
(R)-RH-150721					
Grape juice	0.05	0	0.0474, 0.0484	107.4, 109.3	99.4
	0.05	3	0.0557, 0.0555	126.3, 125.8	121.1
	0.05	6	0.0586, 0.0606	125.6, 129.5	123.9
	0.05	12	0.0693, 0.0702	148.2, 150.4	139.5
	0.05	18	0.0637, 0.0643	136.5, 137.7	125.5
	0.05	22	na	na	na
	0.05	26	0.0665, 0.0592	141.9, 126.6	136.9
(S)-RH-150721					
Grape juice	0.05	0	0.0468, 0.0474	106.6, 107.9	99.1
	0.05	3	0.0598, 0.0580	130.6, 126.7	117.6
	0.05	6	0.0594, 0.0595	129.6, 129.5	126.6
	0.05	12	0.0765, 0.0781	166.4, 170.4	159.6
	0.05	18	0.0685, 0.0692	149.4, 150.9	138.3
	0.05	22	na	na	na
	0.05	26	0.0749, 0.0687	162.9, 149.6	156.1
RH-150721 (sum)					
Grape juice	0.1	0	0.0942, 0.0958	107.0, 108.6	99.2
	0.1	3	0.1156, 0.1135	128.5, 126.3	119.3
	0.1	6	0.1181, 0.1201	127.6, 129.5	125.2
	0.1	12	0.1458, 0.1483	157.3, 160.4	149.5
	0.1	18	0.1322, 0.1335	143.0, 144.3	132.0

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	22	na	Na	na
	0.1	26	0.1415, 0.1279	152.4, 138.1	146.6

* Fortification to extraction interval

** Corrected for concurrent-recoveries

na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Table A 7: Stability of residues in wine following storage at <-18°C.

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
(R)-Zoxamide					
Wine	0.05	0	0.0391, 0.0403	79.0, 81.4	93.3
	0.05	3	0.0486, 0.0517	99.4, 103.6	103.9
	0.05	6	0.0525, 0.0523	105.4, 105.3	107.6
	0.05	12	0.0604, 0.0600	121.5, 120.8	117.2
	0.05	18	0.0781, 0.0695	155.4, 139.7	139.0
	0.05	22	0.0497, 0.0481	99.9, 96.4	107.7
	0.05	26	0.0441, 0.0466	88.7, 93.9	92.8
(S)-Zoxamide					
Wine	0.05	0	0.0394, 0.0401	79.5, 81.0	93.6
	0.05	3	0.0488, 0.0504	97.9, 100.9	101.4
	0.05	6	0.0527, 0.0523	105.8, 105.2	106.2
	0.05	12	0.0605, 0.0608	121.8, 122.3	118.8
	0.05	18	0.0795, 0.0684	158.2, 137.4	142.7

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	22	0.0496, 0.0481	99.6, 96.4	108.4
	0.05	26	0.0447, 0.0447	89.9, 90.0	94.2
Zoxamide (sum)					
Wine	0.1	0	0.0785, 0.0803	79.3, 81.2	93.3
	0.1	3	0.0974, 0.1021	98.7, 102.3	102.8
	0.1	6	0.1051, 0.1046	105.6, 105.3	106.8
	0.1	12	0.1209, 0.1208	121.7, 121.6	117.9
	0.1	18	0.1576, 0.1379	156.8, 138.6	140.8
	0.1	22	0.0993, 0.0962	99.8, 96.4	108.0
	0.1	26	0.0888, 0.0913	89.3, 92.0	93.5
RH-141452					
Wine	0.1	0	0.1040, 0.1018	104.8, 102.7	100.6
	0.1	3	0.1015, 0.1067	100.9, 106.4	103.9
	0.1	6	0.1022, 0.1015	101.7, 101.2	101.5
	0.1	12	0.1035, 0.1041	103.2, 103.8	105.7
	0.1	18	0.1026, 0.1015	101.1, 101.0	104.4
	0.1	22	na	na	na
	0.1	26	0.0829, 0.0837	82.7, 83.5	87.4
(R)-RH-141288					
Wine	0.05	0	0.0389, 0.0382	77.6, 76.2	95.9
	0.05	3	0.0433, 0.0442	82.4, 83.9	92.1

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	6	0.0529, 0.0522	100.9, 99.5	103.1
	0.05	12	0.0558, 0.0560	106.4, 106.9	105.4
	0.05	18	0.0856, 0.0624	161.5, 118.9	136.5
	0.05	22	na	na	na
	0.05	26	0.0509, 0.0429	97.0, 82.0	97.9
(S)-RH-141288					
Wine	0.05	0	0.0381, 0.0384	74.6, 75.3	95.2
	0.05	3	0.0392, 0.0417	76.9, 81.7	89.0
	0.05	6	0.0500, 0.0498	100.3, 100.0	101.0
	0.05	12	0.0548, 0.0543	110.0, 109.0	100.8
	0.05	18	0.0789, 0.0560	156.7, 112.3	132.3
	0.05	22	na	na	na
	0.05	26	0.0447, 0.0402	89.7, 80.8	85.7
RH-141288 (sum)					
Wine	0.1	0	0.0770, 0.0766	76.1, 75.8	95.5
	0.1	3	0.0826, 0.0859	79.7, 82.8	90.5
	0.1	6	0.1029, 0.1019	100.6, 99.8	102.0
	0.1	12	0.1105, 0.1103	108.2, 108.0	103.1
	0.1	18	0.1642, 0.1185	159.1, 115.6	134.6
	0.1	22	na	na	na
	0.1	26	0.0956, 0.0832	93.4, 81.4	91.6
RH-129151 (A)					

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
Wine	0.05	0	0.0428, 0.0420	86.8, 85.2	94.5
	0.05	3	0.0017, 0.0018	3.4, 3.6	4.3
	0.05	6	0.0009, 0.0009	1.9, 1.9	2.6
	0.05	12	0.0004, 0.0004	0.7, 0.7	0.7
	0.05	18	0.0019, 0.0019	3.9, 3.9	4.4
	0.05	22	na	na	na
	0.05	26	0.0003, 0.0003	0.6, 0.6	0.7
RH-129151 (B)					
Wine	0.05	0	0.0414, 0.0402	83.9, 81.5	99.4
	0.05	3	0.0022, 0.0023	4.4, 4.5	5.7
	0.05	6	0.0011, 0.0010	2.2, 2.1	2.9
	0.05	12	0.0004, 0.0005	0.8, 0.9	0.8
	0.05	18	0.0022, 0.0021	4.3, 4.1	4.7
	0.05	22	na	na	na
	0.05	26	0.0002, 0.0002	0.5, 0.5	0.5
RH-129151 (sum)					
Wine	0.1	0	0.0843, 0.0822	85.4, 83.4	96.9
	0.1	3	0.0039, 0.0041	3.9, 4.1	5.0
	0.1	6	0.0020, 0.0019	2.1, 2.0	2.7
	0.1	12	0.0008, 0.0008	0.8, 0.8	0.8
	0.1	18	0.0041, 0.0040	4.1, 4.0	4.6
	0.1	22	na	na	na

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.1	26	0.0005, 0.0005	0.6, 0.6	0.7
RH-24549					
Wine	0.1	0	0.1005, 0.0996	98.2, 97.3	98.8
	0.1	3	0.1063, 0.1097	99.0, 102.4	103.3
	0.1	6	0.1069, 0.1052	99.6, 98.2	97.2
	0.1	12	0.1099, 0.1093	102.6, 102.0	101.9
	0.1	18	0.1141, 0.1074	105.3, 100.1	97.2
	0.1	22	na	na	na
	0.1	26	0.0944, 0.0936	88.0, 87.4	90.1
(R)-RH-150721					
Wine	0.05	0	0.0412, 0.0415	93.0, 93.7	96.8
	0.05	3	0.0542, 0.0570	115.8, 121.6	110.5
	0.05	6	0.0557, 0.0543	119.2, 116.4	115.2
	0.05	12	0.0665, 0.0689	142.6, 147.6	133.4
	0.05	18	0.1088, 0.0853	230.5, 182.4	194.7
	0.05	22	na	na	na
	0.05	26	0.0562, 0.0461	120.4, 98.8	104.2
(S)-RH-150721					
Wine	0.05	0	0.0412, 0.0422	93.6, 95.8	99.8
	0.05	3	0.0608, 0.0637	132.1, 138.3	123.7
	0.05	6	0.0587, 0.0561	127.8, 122.4	118.9
	0.05	12	0.0729, 0.0749	159.1, 163.5	150.5

Matrix	Spike level (mg/kg)	Storage interval (months)	Individual recovered residues (mg/kg)	Individual recoveries of actual initial, uncorrected (%)	Mean recovery of actual initial, corrected (%)
	0.05	18	0.0987, 0.0808	213.0, 176.0	186.1
	0.05	22	na	na	na
	0.05	26	0.0608, 0.0491	132.5, 107.2	110.1
RH-150721 (sum)					
Wine	0.1	0	0.0825, 0.0837	93.3, 94.8	98.2
	0.1	3	0.1149, 0.1207	124, 130.0	117.2
	0.1	6	0.1144, 0.1104	123.5, 119.4	117.1
	0.1	12	0.1395, 0.1438	150.9, 155.6	141.9
	0.1	18	0.2075, 0.1661	221.8, 179.2	190.4
	0.1	22	na	na	na
	0.1	26	0.1169, 0.0952	126.5, 103.0	107.1

* Fortification to extraction interval

** Corrected for concurrent recoveries

na not applicable; an additional checkpoint was added only for Zoxamide (sum of isomers), (R)-Zoxamide, (S)-Zoxamide

Conclusion

The freezer storage stability (at $\leq -18^{\circ}\text{C}$) of Zoxamide and its metabolites (RH-150721 (R, S and sum), RH-129151 (R, S and sum), RH-24549, RH-141288 (R, S and sum), RH-141455 and RH-141452) in grape fruits/bunches, grape juice and wine was studied in recovery experiments according to OECD 506 (2007). The results demonstrate the stability of the analytes Zoxamide, RH-141452 and RH-24549 in the frozen raw agricultural and processed commodities for at least 26 months. In addition, the metabolite RH-141288 - which can occur in processed commodities - was demonstrated to be stable for ≥ 26 months in grape juice and wine. The freezer storage stability of RH-150721 for ≥ 24 months in grape fruits/bunches, juice and wine has been confirmed. Freezer storage stability for RH-129151 over a period of at least 3 months (shortest period tested in this study) could not be demonstrated.

A 2.1.1.1.2 Storage stability of residues in animal products

A 2.1.1.1.2.1 Study 1 – Honey (report No. 19 48 BTR 0003)

Comments of zRMS: Latvia	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX and its affiliates in May 2021:</p> <p>The study is acceptable.</p> <p>The study was performed according to “Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey” (SANTE/11956/2016 rev. 9).</p> <p>The zoxamide residues in Phacelia honey from the four treated trials were 0.0784 mg/kg, not detectable (< LOD of 0.003 mg/kg), and 2 x <LOQ (< 0.01 mg/kg).</p> <p>Deviations: In trial 19BTR0003_T3 the following specimen could not be generated as intended (no honey available):</p> <p>19BTR0003_06-T-A1 19BTR0003_06-T-A2 19BTR0003_06-T-R1 19BTR0003_06-T-R2 19BTR0003_06-T-PD</p> <p>Trial 3 was therefore repeated</p>
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This active substance related study has already been provided to the RMS Latvia . Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.1/06
Report:	MAGNITUDE OF RESIDUES OF ZOXAMIDE IN PHACELIA (PHACELIA TANACETIFOLIA BENTH.) HONEY AFTER THREE APPLICATIONS OF GWN-9790EU UNDER SEMI-FIELD CONDITIONS IN NORTHERN AND SOUTHERN EUROPE, Poráčki, K., 2020, report No. 19 48 BTR 0003, Doc. No. 634-96001
Guideline(s):	OECD No. 506, Series on Testing and Assessment No. 72 and Series on Pesticides No. 39. ENV/JM/MONO(2007)17, SANCO/10684/2009, SANCO/825/00 rev. 8.1 (2010), SANTE/11813/2017 rev. 0, SANTE/11956/2016 rev. 9
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Zoxamide (R+S)	(R)-Zoxamide	(S)-Zoxamide
Lot/Batch #:	776908	RH-117, 281 Optical Rotation (+) Peak # 2	RH-117, 281 Optical Rotation (+) Peak # 1
Purity:	99.8	97.2	97.5
CAS #:	156052-68-5	-	-
Stability of test compound/	Expiry date:	Expiry date:	Expiry date:

Reference item:	01.08.2021	19.03.2022	19.03.2022
Spiking levels:	0.1	0.05	0.05

Test commodity

Processed commodity:	Honey
Sample size:	3.00 g each

Study design

The freezer storage stability of Zoxamide (sum) and (R)-Zoxamide and (S)-Zoxamide in honey was performed by analysing honey samples fortified with Zoxamide (sum), (R)-Zoxamide and (S)-Zoxamide. The storage stability testing was performed within the honey residue study. In this section only the storage stability testing will be summarised. The residue part will be summarised in A 2.1.7.1.

The samples were analysed for recoveries after storage of ≤ -18 °C initially after fortification (day zero) and after a storage of 85 days. At day 0, 1 control sample (not spiked) and 2 replicate spiked samples (at 0.1 mg/kg racemate) were analysed directly. After a storage of 85 days at a temperature of -18°C , 1 control sample and 2 replicate spiked stored samples were analysed along with fresh prepared samples on the same concentration level (at 0.1 mg/kg racemate).

Methods:

The method was successfully validated in honey in the analytical part of the honey residue study.

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg of Zoxamide (racemate) and 0.005 mg/kg of the single enantiomers. The limit of detection (LOD) was 0.003 mg/kg of Zoxamide (racemate) and 0.0015 mg/kg of the single enantiomers.

The maximum extraction to analysis time period of the samples was 1 day. The procedural recoveries fortified with 0.01 mg/kg and 1.0 mg/kg Zoxamide (racemate) run concurrently with the storage samples and were handled the same way as the storage samples, demonstrating the stability of 85 days in sample extracts for the longest storage period and the accuracy on the day of analysis.

Results

Table A 8: Summary of concurrent recoveries of Zoxamide (racemate) from honey

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev
Zoxamide (racemate)					
Honey	0.01	85 days	3 g (2)	84, 84, 87, 80, 79	83 \pm 4.2
	1.0	85 days	3 g (2)	92.4, 91.2, 92.1, 91.7, 90.8	92 \pm 0.72

Table A 9: Stability of Zoxamide (racemate) residues in honey following storage at -18°C.

Matrix	Spike level (mg/kg)	Storage interval (days)*	Individual recovered residues (mg/kg)**	Individual recoveries (%)
Zoxamide (racemate)				
Honey	0.1	0	0.090, 0.092	nr
	0.1	85	0.092, 0.091	nr

* Fortification to extraction interval

** Corrected for concurrent-recoveries at the fortification level of 0.1 mg/kg

nr not relevant

Conclusion

Based on the presented freezer storage stability data it was demonstrated that Zoxamide is stable at -18°C for at least 85 days (2.8 months) in honey. The storage stability covers the maximum storage period in the honey residue study and no further data are needed.

A 2.1.1.1.3 Storage stability of residues in sample extracts

A 2.1.1.1.3.1 Grapes - Zoxamide

Comments of zRMS:	<p>The validation has been accepted.</p> <p>The objective of this study was the validation of the analytical method to determine Zoxamide in grapes. The analytical determination was carried out using a HPLC-MS/MS method, validated in compliance with SANTE/2020/12830, Rev.1 guideline. External standard calibration was used to quantify Zoxamide in the samples.</p> <p>The extraction efficiency of the analyte in grapes samples was verified according to SANTE 2017/10632 rev. 3 in the GLP study BPL-STUDY-18-000085. Detailed results are pasted below in the grey summary table ‘Zoxamide determination in grapes (HPLC-MS/MS) - validation results summary’ (page 125)</p>
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Reference:	KCA 6.1/09
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF GWN-8030 IN GRAPES, Sala, A., 2022, report No. GLP-STUDY-21-101, Doc. No. 432-006
Guideline(s):	SANTE/2020/12830 rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Zoxamide
Lot/Batch #:	BCCF6644
Purity:	99.5 %
CAS #:	156052-68-5
Stability of test compound/ Reference item:	Feb 2024

Spiking levels:	25.28 µg/L
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Study design

The stability of the Zoxamide in the final sample extract of grape when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) extract was spiked with known amounts of analyte at the concentration of 25.28 µg/L. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of Zoxamide was successfully validated in study GLP-STUDY-21-101 (“Validation of an analytical method for the determination of GWN-8030 in grapes”, Doc. No. 432-006). The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results

The results of the spiking experiments are summarised in Table A 10.

Table A 10 Stability of Zoxamide in grape extract following storage at $5 \pm 3^\circ\text{C}$

Matrix	Analyte	Spiked concentration	T0 – Peak area (primary detection)	After 3 days – Peak area (primary detection)	Stability [%]
Grape extract	Zoxamide	25.28 µg/L	Area analyte: 8685	Area analyte: 8078	93.3

Conclusion

The stability of Zoxamide in the grape extract can be considered proven for 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

Zoxamide determination in grapes (HPLC-MS/MS) - validation results summary

HPLC-MS/MS determination of GWN-8030 - validation results summary																																							
Parameter	Result					SANTE/2020/12830 rev.1																																	
Matrix effect	- 17.25 % / not significant					< ±20%																																	
Calibration (matrix-matched)	Range: 0.506 – 50.55 µg/L in solution Range: 0.002 – 0.2 mg/kg on sample (from 20 % of LOQ to 20xLOQ)					At least from 30% of LOQ to at least 20% above the highest level																																	
	The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.					Residuals randomly distributed																																	
	<table><tr><td>Level</td><td>Concentration (mg/kg)</td><td>Transition</td><td>% Recovery</td><td>% RSD</td></tr><tr><td rowspan="2">LOQ (n = 5)</td><td rowspan="2">0.01</td><td>Primary (336/186.9)</td><td>104.6</td><td>4.1</td></tr><tr><td>Confirmatory (336/159)</td><td>102.0</td><td>5.1</td></tr><tr><td rowspan="2">10xLOQ (n = 5)</td><td rowspan="2">0.1</td><td>Primary (336/186.9)</td><td>98.4</td><td>3.9</td></tr><tr><td>Confirmatory (336/159)</td><td>96.9</td><td>3.7</td></tr><tr><td rowspan="2">Overall (n = 10)</td><td rowspan="2">/</td><td>Primary (336/186.9)</td><td>101.5</td><td>5.0</td></tr><tr><td>Confirmatory (336/159)</td><td>99.5</td><td>5.1</td></tr></table> n = number of replicates					Level	Concentration (mg/kg)	Transition	% Recovery	% RSD	LOQ (n = 5)	0.01	Primary (336/186.9)	104.6	4.1	Confirmatory (336/159)	102.0	5.1	10xLOQ (n = 5)	0.1	Primary (336/186.9)	98.4	3.9	Confirmatory (336/159)	96.9	3.7	Overall (n = 10)	/	Primary (336/186.9)	101.5	5.0	Confirmatory (336/159)	99.5	5.1	<u>LOQ level (0.01 mg/kg)</u> recoveries 70 – 110% RSD ≤20% <u>10xLOQ level (0.1 mg/kg)</u> recoveries 70 – 110% RSD ≤15% (limits more restrictive than the guideline requirements)				
	Level	Concentration (mg/kg)	Transition	% Recovery	% RSD																																		
	LOQ (n = 5)	0.01	Primary (336/186.9)	104.6	4.1																																		
			Confirmatory (336/159)	102.0	5.1																																		
	10xLOQ (n = 5)	0.1	Primary (336/186.9)	98.4	3.9																																		
			Confirmatory (336/159)	96.9	3.7																																		
	Overall (n = 10)	/	Primary (336/186.9)	101.5	5.0																																		
Confirmatory (336/159)			99.5	5.1																																			
Limit of quantification (LOQ)	verified at 0.01 mg/kg recovery and repeatability data in compliance with the guideline					LOQ: lowest validated level with sufficient recovery and precision																																	
Limit of detection (LOD)	verified at 0.002 mg/kg (20% of LOQ) signal/noise ratio higher than 3					LOD < 30% of LOQ																																	
Selectivity and specificity	Verified: no interferences found in untreated samples in amounts higher than 30% of the LOQ (< LOD)					Blank values not higher than 30% of LOQ																																	
Confirmation	Confirmation achieved by simultaneous determination of a confirmatory MS/MS transition. Calibration data, recovery and precision in compliance with the requirements					Confirmation by monitoring at least 1 additional MS/MS transition, providing linearity, recovery, precision, selectivity																																	
Stability of the analyte in the sample extract	93.3 % (primary ion) and 92.8 % (confirmatory ion) after 3 days in the dark at 5 ± 3°C					70-120%																																	
Stability of the analyte in the standard solution	Stock solution (1000 mg/L) is stable for 123 days if stored in the dark at 5 ± 3°C (mean peak area difference of the stored solution and a freshly prepared solution: 0.77%)					Mean peak area difference of the stored solution and a freshly prepared solution: < 10%																																	
Parameter	Result					SANTE 2017/10632 rev. 3																																	
Extraction efficiency	The extraction efficiency of Zoxamide in grape samples using the extraction procedure adopted in this study was successfully demonstrated in the study coded BPL-STUDY-18-000085					Extraction efficiency considered sufficiently proven if the residue extracted with the method under validation and the residue extracted with the method reported in the metabolism study differ no more than 30%																																	

A 2.1.1.1.3.1 Grapes – RH-141452

Comments of zRMS:	<p>The validation has been accepted.</p> <p>The objective of this study was the validation of the analytical method to determine RH-141452 (total fraction) in grape samples. The analytical determination was carried out using a HPLC-MS/MS method, validated in compliance with SANTE/2020/12830, Rev.1 guideline. The method was based on an alkaline hydrolysis and an extraction followed by a HPLC-HRMS/MS. The extraction efficiency of the analyte in high acid content matrices has been verified according to SANTE 2017/10632 rev. 3 in the GLP study BPL-STUDY-18-000085. Results of the validation parameters and the extraction efficiency are summarised as follows:</p>
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HPLC-MS/MS determination of RH-141452 - validation results summary						
Parameter	Result					SANTE/2020/12830 rev.1
Matrix effect	- 23.2 % / significant matrix effect					< ±20%
Calibration (matrix-matched)	Range: 0.536 – 53.60 µg/L in solution Range: 0.002144 – 0.2144 mg/kg on sample (from 20 % of LOQ to 20xLOQ)					At least from 30% of LOQ to at least 20% above the highest level
	The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.					Residuals randomly distributed
Recovery and precision repeatability	Level	Concentration (mg/kg)	Transition	% Recovery	% RSD	LOQ level (0.01 mg/kg) recoveries 70 – 110% RSD ≤20% 10xLOQ level (0.1 mg/kg) recoveries 70 – 110% RSD ≤15% (limits more restrictive than the guideline requirements)
	LOQ (n = 5)	0.01	Primary (218.9621)	84.9	5.5	
			Confirmatory (144.9617)	86.3	9.0	
	10xLOQ (n = 5)	0.1	Primary (218.9621)	92.3	2.4	
			Confirmatory (144.9617)	99.3	3.2	
	Overall (n = 10)	/	Primary (218.9621)	88.6	5.9	
			Confirmatory (144.9617)	92.8	9.5	
n = number of replicates						
Limit of quantification (LOQ)	verified at 0.01 mg/kg recovery and repeatability data in compliance with the guideline					LOQ: lowest validated level with sufficient recovery and precision
Limit of detection (LOD)	verified at 0.002 mg/kg (20% of LOQ) signal/noise ratio higher than 3					LOD < 30% of LOQ
Selectivity and specificity	Verified: no interferences found in untreated samples in amounts higher than 30% of the LOQ (< LOD)					Blank values not higher than 30% of LOQ
Confirmation	Confirmation achieved by simultaneous determination of a confirmatory MS/MS transition. Calibration data, recovery and precision in compliance with the requirements					Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity
Stability of the analyte in the sample extract	100.4 % (primary ion) after 3 days in the dark at 5 ± 3°C					70-120%
Stability of the analyte in the standard solution	+ 6.8% after 130 days in the dark at 5 ± 3°C					Mean peak area difference of the stored solution and a freshly prepared solution: < 10%
Parameter	Result					SANTE 2017/10632 rev. 3
Extraction efficiency	The extraction efficiency of Zoxamide in grape samples using the extraction procedure adopted in this study was successfully demonstrated in the study coded BPL-STUDY-18-000085					Extraction efficiency considered sufficiently proven if the residue extracted with the method under validation and the residue extracted with the method reported in the metabolism study differ no more than 30%

Reference: KCA 6.1/10
Report: VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF RH-141452 (TOTAL FRACTION) IN GRAPES, Sala, A., 2022, report No. GLP-STUDY-21-102, Doc. No. 432-007
Guideline(s): SANTE/2020/12830 rev. 1 (2021)
Deviations: None
GLP: Yes
Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	RH-141452
Lot/Batch #:	55954-24-06
Purity:	99.55 %
CAS #:	89894-53-1

Stability of test compound/ Reference item:	Aug 2029
Spiking levels:	26.80 µg/L

Study design

The stability of the RH-141452 in the final sample extract of grape when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) ex-tract was spiked with known amounts of analyte at the concentration of 26.80 µg/L. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of RH-141452 was successfully validated in study GLP-STUDY-21-102 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in grapes”, Doc. No. 432-007).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results

The results of the spiking experiments are summarised in Table A 11.

Table A 11 Stability of RH-141452 in grape extract following storage at $5 \pm 3^\circ\text{C}$

Matrix	Analyte	Spiked concentration	T0 – Peak area (primary detection)	After 3 days – Peak are (primary detection)	Stability [%]
Grape extract	RH-141452	26.80 µg/L	Area analyte: 867376	Area analyte: 870530	100.4

Conclusion

The stability of RH-141452 in the grape extract is stable for 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

A 2.1.1.1.3.2 Grapes, potato (RAC and processed) – Zoxamide, RH-141452, RH-150721

Comments of zRMS: Latvia	The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 5 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021: The HPLC-MS/MS and HPLC-HRMS/MS method was acceptably validated for the analysis of zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities. All mean accuracy and precision values are met requirements of SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4. guidelines: mean recovery (accuracy) per level in the range 70-110 %, RSD% per level (precision) $\leq 20\%$. The limit of quantification (all analyte/matrix) is 0.01 mg/kg.
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	accuracy and precision data at this level resulted in compliance with guidelines SANCO/825/00 rev.8.1 and SANCO/3029/99 rev.4 complies SANTE/2020/12830, Rev.1. The LOQ for each enantiomer is 0.005 mg/kg. For metabolite RH-129151 (sum of R and S enantiomers) was used for validation due to lack of analyte. The extraction efficiency of the analytical method was acceptably verified according to SANTE 2017/10632 rev. 3.
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.1/07
Report:	VALIDATION OF AN ANALYTICAL METHOD TO DETERMINE ZOX-AMIDE RESIDUES IN GRAPE, POTATO, TOMATO, CUCUMBER, AND ONION RAW AGRICULTURAL AND PROCESSED COMMODITIES, Sala, A., 2020, report No. BPL-STUDY-18-000085, Doc. No. 432-009
Guideline(s):	SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev. 4 (2000)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Zoxamide
Lot/Batch #:	BCBW0947
Purity:	99.6 % Racemic mixture (50:50 R/S enantiomers ratio)
CAS #:	156052-68-5
Stability of test compound/ Reference item:	Oct 2020
Spiking levels:	1 mg/kg
Test material:	(R)-RH-150721
Lot/Batch #:	HHGCP012-00-1
Purity:	99.41% w/w
Stability of test compound/ Reference item:	One year from date of manufacture (re-analysis).
Spiking levels:	1 mg/kg
Test material:	(S)-RH-150721
Lot/Batch #:	HHGCP013-00-1
Purity:	99.45%
Stability of test compound/ Reference item:	One year from date of manufacture (re-analysis).
Spiking levels:	1 mg/kg
Lot/Batch #:	RH-141452
Purity:	021109
Stability of test compound/ Reference item:	Expected 2 years from the certification date.
Spiking levels:	1 mg/kg

Study design

The stability of Zoxamide and its metabolites in the final sample extract of grape (grape, grape juice, wine, raisin) and potato (potato tuber, fried potato, potato flakes), when stored for 3 days under dark and refrigerated conditions at 4 °C has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) ex-tracts of each commodity were fortified with 0.1 mg/kg.

Methods

The method for the determination of Zoxamide and its metabolites was successfully validated in study BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Table A 12: LOQ and LOD of the analytes

Analyte	LOD [mg/kg]	LOQ [mg/kg]
(R)-Zoxamide	0.0015	0.005
(S)-Zoxamide	0.0015	0.005
(R)-RH-150721	0.0015	0.005
(S)-RH-150721	0.0015	0.005
RH-141452	0.003	0.01

Results

The results of the spiking experiments are summarised in Table A 13 and Table A 19.

Table A 13 Recovery results in grape berries at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	36668	35804	+2 %
(S)-Zoxamide		37017	35183	+5 %
(R)-RH-150721		96071	86536	+11 %
(S)-RH-150721		73408	65351	+12 %
RH-141452		4720291	4552744	+ 4 %

Table A 14 Recovery results in grape juice at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	36509	38320	-5 %
(S)-Zoxamide		35479	38050	-7 %
(R)-RH-150721		112470	106314	+6 %
(S)-RH-150721		79191	67306	+18 %
RH-141452		4748546	5103356	-7 %

Table A 15 Recovery results in wine at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	39993	38703	+3 %
(S)-Zoxamide		38793	37083	+5 %
(R)-RH-150721		129662	111231	+17 %
(S)-RH-150721		45947	40706	+13 %
RH-141452		3807390	3513297	+8 %

Table A 16 Recovery results in raisins at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	29310	29031	+1 %
(S)-Zoxamide		25356	25898	-2 %
(R)-RH-150721		18012	16244	+11 %
(S)-RH-150721		14187	13146	+8 %
RH-141452		3701846	3782619	-2 %

Table A 17 Recovery results in potato tubers at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	42346	41228	+3 %
(S)-Zoxamide		38039	36026	+6 %
(R)-RH-150721		70570	68612	+3 %
(S)-RH-150721		38016	33005	+15 %
RH-141452		5538133	5486130	+1 %

Table A 18 Recovery results in potato flakes at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	72118	71142	+1 %
(S)-Zoxamide		70090	70089	0 %
(R)-RH-150721		220753	230163	-4 %
(S)-RH-150721		262715	269992	-3 %
RH-141452		4274147	5126473	-17 %

Table A 19 Recovery results in fried potatoes at 4 °C

Analyte	Fortification level	Analyte peak are		Analyte stability in extract (%)
		Extract stored 3 days at 4 °C	Extract analysed immediately after preparation	
(R)-Zoxamide	0.1	67530	67644	0
(S)-Zoxamide		63616	64392	-1 %
(R)-RH-150721		213040	214765	-1 %
(S)-RH-150721		253982	260703	-3 %
RH-141452		5278327	5168572	+2 %

The stability of additional metabolites have been tested within the method validation in several commodities. But these data will not be presented as the metabolites are not part of the residue definition and the commodities are not relevant for the intended uses.

Conclusion

The stability of Zoxamide and its metabolites in extracts of grapes (grape berries, juice, wine, raisins) and potatoes (tuber, flakes, fried potatoes) is shown for 3 days at 4°C in dark conditions since the recovery of the stored spiked sample below 20 % measured against the freshly prepared one.

A 2.1.1.1.3.3 Apples – Zoxamide

Comments of zRMS:	<p>The validation has been accepted.</p> <p>The objective of this study was the validation of the analytical method to determine Zoxamide in apple. The analytical determination was carried out using a HPLC-MS/MS method, validated in compliance with SANTE/2020/12830, Rev.1 guideline. The method consisted of an extraction of the analyte followed by a HPLC-MS/MS analysis using external standard solutions. The extraction efficiency of the analytical method has been verified according to SANTE 2017/10632 rev. 3. Results of the validation parameters and the extraction efficiency were summarised as follows below (grey table).</p>
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Reference:	KCA 6.1/11
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF GWN-8030 IN APPLES, Longhi, D., 2021, report No. GLP-STUDY-21-53, Doc. No. 432-003
Guideline(s):	SANTE/2020/12830 rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Zoxamide
Lot/Batch #:	BCBZ7753
Purity:	99.6 %
CAS #:	89894-53-1
Stability of test compound/	Nov 2021

Reference item:	
Spiking levels:	24.95 µg/L

Study design

The stability of Zoxamide in the final sample extract of apples when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) extract was spiked with known amounts of analyte at the concentration of 24.95 µg/L. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of Zoxamide was successfully validated in study GLP-STUDY-21-53 (“Validation of an analytical method for the determination of GWN-8030 in apples”, Doc. No. 432-003). The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results

The results of the spiking experiments are summarised in Table A 20.

Table A 20 Stability of Zoxamide in apple extract following storage at $5 \pm 3^\circ\text{C}$

Matrix	Analyte	Spiked concentration	T0 – Peak area (primary detection)	After 3 days – Peak are (primary detection)	Stability [%]
Apple extract	Zoxamide	24.95 µg/L	Area analyte: 18597	Area analyte: 19065	102.5

Conclusion

The stability of Zoxamide in the apple extract is shown for 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

HPLC-MS/MS determination of GWN-8030 - validation results summary						
Parameter	Result					SANTE/2020/12830 rev.1 limit
Matrix effect	- 20.2 % / significant					< ±20%
Calibration (matrix-matched)	Range: 0.4990 – 49.90 µg/L in solution Range: 0.002 – 0.2 mg/kg on sample (from 20 % of LOQ to 100 % above 10xLOQ)					At least from 30% of LOQ to at least 20% above the highest level
	The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.					Residuals randomly distributed
Recovery and precision (repeatability)	Level	Concentration (mg/kg)	Transition	% Recovery	% RSD	<u>LOQ level (0.01 mg/kg)</u> recoveries 70 – 110% RSD ≤20% <u>10xLOQ level (0.1 mg/kg)</u> recoveries 70 – 110% RSD ≤15% (limits more restrictive than the guideline requirements)
	LOQ (n = 5)	0.01	Primary (336/186.9)	106.0	3.5	
			Confirmatory (336/159)	106.1	3.2	
	10xLOQ (n = 5)	0.1	Primary (336/186.9)	96.8	2.9	
			Confirmatory (336/159)	96.3	2.6	
	Overall (n = 10)	/	Primary (336/186.9)	101.4	5.7	
			Confirmatory (336/159)	101.2	5.8	
n = number of replicates						
Limit of quantification (LOQ)	verified at 0.01 mg/kg recovery and repeatability data in compliance with the guideline					LOQ: lowest validated level with sufficient recovery and precision
Limit of detection (LOD)	verified at 0.002 mg/kg (20% of LOQ) signal/noise ratio higher than 3					LOD < 30% of LOQ
Selectivity and specificity	Verified: no interferences found in untreated samples in amounts higher than 30% of the LOQ (< LOD)					Blank values not higher than 30% of LOQ
Confirmation	Confirmation achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements					Confirmation by monitoring at least 1 SRM transition, providing linearity, recovery, precision, selectivity
Stability of the analyte in the sample extract	102.5 % after 3 days in the dark at 5 ± 3°C					70-120%
Stability of the analyte in the standard solution	Stock solution at about 1000 mg/L is stable for 123 days if stored in the dark at 5 ± 3°C (mean peak area difference of the stored solution and a freshly prepared solution: 0.77%)					Mean peak area difference of the stored solution and a freshly prepared solution: < 10%
Parameter	Result					SANTE 2017/10632 rev. 3 limit
Extraction efficiency	The extraction efficiency of Zoxamide from high water commodity matrices using the extraction procedure adopted in this study has already been successfully demonstrated in the mentioned study BPL-STUDY-18-000085					Extraction efficiency considered sufficiently proven if the residue extracted with the method under validation and the residue extracted with the method reported in the metabolism study differ no more than 30%

A 2.1.1.1.3.4 Apples – RH-141452

Comments of zRMS:	<p>The validation has been accepted.</p> <p>The objective of this study was the validation of the analytical method to determine RH-141452 (total fraction) in apple. The analytical determination was carried out using a HPLC-HRMS method, validated in compliance with SANTE/2020/12830, Rev.1 guideline. The method consisted of a base hydrolysis of the sample and an extraction of the analyte from the matrix, followed by a HPLC-HRMS analysis. The extraction efficiency of the analytical method has been verified according to SANTE 2017/10632 rev. 3. Results of the validation parameters and the extraction efficiency were below summarised (grey table).</p>
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Reference:	KCA 6.1/12
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF RH-141452 (TOTAL FRACTION) IN APPLES, Longhi, D., 2021, report No. GLP-STUDY-21-54, Doc. No. 432-005
Guideline(s):	SANTE/2020/12830 rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	RH-141452
Lot/Batch #:	55954-24-06
Purity:	99.55 %
CAS #:	89894-53-1
Stability of test compound/ Reference item:	Aug 2029
Spiking levels:	10.84 µg/L

Study design

The stability of the RH-141452 in the final sample extract of apple when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) extract was spiked with known amounts of analyte at the concentration of 10.84 µg/L. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of RH-141452 was successfully validated in study GLP-STUDY-21-54 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in apples”, Doc. No. 432-005).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results

The results of the spiking experiments are summarised in Table A 21.

Table A 21 **Stability of RH-141452 in apple extract following storage at $5 \pm 3^\circ\text{C}$**

Matrix	Analyte	Spiked concentration	T0 – Peak area (primary detection)	After 3 days – Peak are (primary detection)	Stability [%]
Apple extract	RH-141452	10.84 µg/L	Area analyte: 1027323	Area analyte: 1005908	97.9

Conclusion

The stability of RH-141452 in the apple extract is stable for 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

RH-141452 determination in apple (HPLC- HRMS) - validation results summary							
Parameter	Result					SANTE/2020/12830 rev.1 limit	
Matrix effect	- 8.26 % / not significant					< ±20%	
Calibration (matrix-matched)	Range: 1.084 – 75.88 µg/L in solution Range: 0.002 – 0.2 mg/kg on sample (from 20 % of LOQ to 40 % above 10xLOQ)					At least from 30% of LOQ to at least 20% above the highest level	
	The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.					Residuals randomly distributed	
Recovery and precision (repeatability)	Level	Concentration (mg/kg)	Signal	% Recovery	% RSD	<u>LOQ level (0.01 mg/kg)</u> recoveries 70 – 110% RSD ≤20%	
	LOQ (n = 5)	0.01	Primary signal (218.9621) Confirmatory signal (144.9617)	89.6 89.6	3.3 2.0		
	10xLOQ (n = 5)	0.1	Primary signal (218.9621) Confirmatory signal (144.9617)	91.4 88.9	2.7 3.5	<u>10xLOQ level (0.1 mg/kg)</u> recoveries 70 – 110% RSD ≤15% (limits more restrictive than the guideline requirements)	
	Overall (n = 10)	/	Primary signal (218.9621) Confirmatory signal (144.9617)	90.5 89.3	3.0 2.7		
	n = number of replicates						
	Limit of quantification (LOQ)	verified at 0.01 mg/kg recovery and repeatability data in compliance with the guideline					LOQ: lowest validated level with sufficient recovery and precision
	Limit of detection (LOD)	verified at 0.002 mg/kg (20% of LOQ) signal/noise ratio higher than 3					LOD < 30% of LOQ
Selectivity and specificity	Verified: no interferences found in untreated samples in amounts higher than 30% of the LOQ (< LOD)					Blank values not higher than 30% of LOQ	
Confirmation	Confirmation achieved by simultaneous determination of a confirmatory signal. Calibration data, recovery and precision in compliance with the requirements					Confirmation by monitoring at least 1 additional fragment ion, providing linearity, recovery, precision, selectivity	
Stability of the analyte in the sample extract	97.9 % after 3 days in the dark at 5 ± 3°C					70-120%	
Stability of the analyte in the standard solution	+ 6.8% after 130 days in the dark at 5 ± 3°C					< 10%	
Parameter	Result					SANTE 2017/10632 rev. 3 limit	
Extraction efficiency	The extraction efficiency of RH-141452 from high water commodity matrices using the extraction procedure adopted in this study has already been successfully demonstrated in the mentioned study BPL-STUDY-18-000085					Extraction efficiency considered sufficiently proven if the residue extracted with the method under validation and the residue extracted with the method reported in the metabolism study differ no more than 30%	

A 2.1.2 Nature of residues in plants, livestock and processed commodities

A 2.1.2.1 Nature of residue in plants

A 2.1.2.1.1 Nature of residue in primary crops

No new data are submitted in the framework of this application.

A 2.1.2.1.2 Nature of residue in rotational crops

No new data are submitted in the framework of this application.

A 2.1.2.1.1.3 Nature of residues in processed commodities

A 2.1.2.1.1.4 Study 1

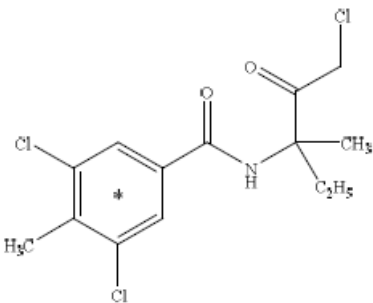
Comments of zRMS: Latvia	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The study is acceptable and demonstrates that zoxamide degrades in all three incubated buffer systems.</p> <p>The study was performed in compliance with the OECD Guideline for the Testing of Chemicals No. 507: Nature of the Pesticide Residues in Pro-cessed Commodities – High Temperature Hydrolysis (October 2007)</p>
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This active substance related study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.5.1/01
Report:	ZOXAMIDE: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS, Grist, A., 2018, report No. RB66JN, Doc. No. 638-018
Guideline(s):	OECD No. 507 (2007)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

Materials and methods

Materials and methods

Radiolabelled test item:	 <p>* [phenyl-U-¹⁴C]-Zoxamide</p>
Specific activity:	1.74 GBq/mmol at 336.6 amu
Lot/batch no.:	QW55QS/OOE01/03
CAS no. (Zoxamide, unlabelled)	156052-68-5
Radiochemical purity:	99.0 %
Expiry date:	12 July 2019

The study was conducted to provide information on the effects of hydrolysis on the Zoxamide metabolite RH-141452. Therefore, it was exposed to conditions representative for pasteurisation, baking/brewing/boiling, and sterilisation.

The water used for buffer solution preparation was obtained from an Elga reverse osmosis system. Buffer at concentrations of 0.01 M were prepared as follows:

- pH 4.0 Potassium hydrogen phthalate (1.02 g) was dissolved in ca 450 mL of water and the solution diluted to a final volume of 500 mL with water.
- pH 5.0 Glacial acetic acid (0.3 mL) was dissolved in ca 450 mL of water, the pH adjusted to 5.0 with 1.0 M sodium hydroxide solution and the solution diluted to a final volume of 500 mL with water.
- pH 6.0 Sodium dihydrogen orthophosphate dihydrate (0.78 g) was dissolved in approximately 450 mL of water, the pH adjusted to 6.0 with 1.0 M sodium hydroxide solution and the solution diluted

to a final volume of 500 mL with water. The buffer solutions were filled in sterilised test vessels (borosilicate glass tubes) under aseptic conditions. A fortification solution of [phenyl- ^{14}C]-Zoxamide in acetonitrile was prepared at a nominal concentration of 50 mg/L. The actual concentration of Zoxamide in the fortification solutions was determined in triplicate just before test item application. For test item application, separate portions (140 mL) of the buffer solutions were treated with each an aliquot (1.4 mL) of the test item stock solution to give nominal concentrations of 0.5 mg/L Zoxamide in the test systems. The proportion of co-solvent was 1 % (v/v). The conditions of incubation were as follows:

pH	Temperature (°C)	Time (minutes)	Process represented
4	90	20	Pasteurisation
5	100	60	Baking, brewing, boiling
6	120*	20	Sterilisation

The application conditions (pH and temperature) were recorded. Immediately after set up of the test systems and at the end of the incubation in the cooled down samples, the radioactivity in the buffer was determined in solution with Ultima Gold (Perkin Elmer) by liquid scintillation counting with automatic quench correction. The portion of unchanged Zoxamide and its radiolabelled degradation products were analysed by reversed phase HPLC with UV and radio-detection concurrently to external standard solutions. Identification was confirmed by HPLC-MS/MS. Samples were stored in the refrigerator and deep frozen ($\leq -15^\circ\text{C}$) until analysis.

Results

Incubation temperatures were within $\pm 5^\circ\text{C}$ of the target value, the pH remained within ± 0.1 units of the target pH. The correct dosing of the test item at study start was confirmed. The recovery of radioactivity from the buffer solutions was in the range 93.1 – 105.9 % of applied radioactivity (AR).

Samples incubated at pH 4 and pH 5 were stored for at max. 33 days (for HPCL analysis) and 183 days (for LC-MS/MS analysis) in the freezer, samples incubated at pH 6 were stored for at max. 33 days (for HPCL analysis) and 134 days (for LC-MS/MS analysis). Overall, there was no significant degradation of the samples after frozen storage. Minor differences in the profiles of the HPLC and LC-MS/MS radio-chromatograms were observed, specifically for RH-129151 in the pH 4 and pH 5 incubated buffers.

Degradation of Zoxamide was detected in all three buffers. In the treated and incubated pH 4 buffer samples Zoxamide was hydrolysed to one major degradation product, RH-150721 (mean of 46.7 % TRR, 0.234 mg/L), and three minor degradation products, RH-24549 (mean of 9.7 % TRR, 0.049 mg/L), RH-129151 (mean of 4.4 % TRR, 0.022 mg/L) and RH-141288 (mean of 1.1 % TRR, 0.006 mg/L).

In the treated and incubated pH 5 buffer samples, Zoxamide was hydrolysed to three major degradation products, RH-150721 (mean of 11.0 % TRR, 0.056 mg/L), RH-24549 (mean of 62.7 % TRR, 0.314 mg/L) and RH-129151 (mean of 13.1 % TRR, 0.066 mg/L), and to one minor metabolite, RH-141288 (mean of 8.1 % TRR, 0.041 mg/L).

In the treated and incubated pH 6 buffer samples, Zoxamide was hydrolysed to RH-150721 (mean of 0.7 % TRR, 0.004 mg/L), RH-141288 (mean of 27.3 % TRR, 0.146 mg/L), RH 24549 (mean of 43.0 % TRR, 0.23 mg/L) and RH 129151 (mean of 20.8 % TRR, 0.111 mg/L).

Table A 22: Identification of compounds from high temperature hydrolysis study

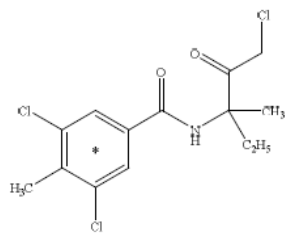
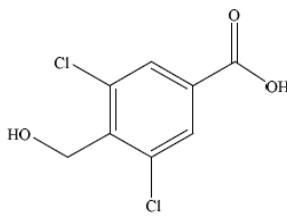
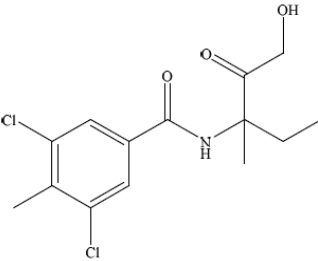
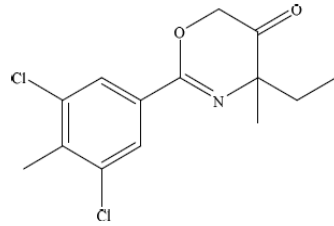
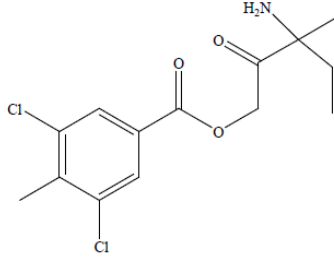
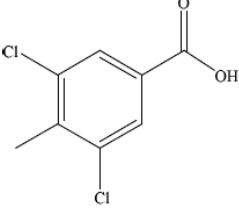
Common name/code ID No.	Chemical name	Chemical structure
Zoxamide	3,5-dichloro-N-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-4-Methylbenzamide	
RH-141452	3,5-dichloro-4-(hydroxymethyl)benzoic acid	
RH-141288	3,5-dichloro-N-(1-hydroxy-3-methyl-2-oxopentan-3-yl)-4-Methylbenzamide	
RH-129151	2-(3,5-dichloro-4-methylphenyl)-4-ethyl-4-methyl-4H-1,3-oxazin-5(6H)-one	
RH-1507212	3-amino-3-methyl-2-oxopentyl-3,5-dichloro-4-methylbenzoate hydrochloride	
RH-24549	3,5-dichloro-4-methylbenzoic acid	

Table A 23: Standard hydrolysis study of Zoxamide

Process represented	T° (°C)	Time (min)	pH	Parent Initial conc. (mg/L)	% of TRR (initial)					
					Zox- amide *	RH- 150721 *	RH- 141288 *	RH- 24549 *	RH- 129151 *	Total
Pasteurization	90	20	4	0.5	35.3	46.7	1.1	9.7	4.4	97.2
Baking, brewing, boiling	100	60	5	0.5	1.2	11.0	8.1	62.7	13.1	96.1
Sterilization	120	20	6	0.5	0.8	0.7	27.3	43.0	20.8	92.6

*mean of two incubations

Zoxamide and metabolites appearing > 10 % are written in bold letters.

Conclusions

[¹⁴C]-Zoxamide was shown to be hydrolytically unstable for all hydrolytic conditions tested in this study: at pH 4 and 90 °C simulating pasteurisation, at pH 5 and 100 °C simulating baking/brewing/boiling and at pH 6 and 120 °C simulating the process of sterilisation.

Zoxamide hydrolysed to form RH-150721 (up to a mean maximum of 46.7 % TRR, 0.234 mg/L), RH 141288 (up to a mean maximum of 27.3 % TRR, 0.146 mg/L), RH-24549 (up to a mean maximum of 62.7 % TRR, 0.314 mg/L), RH 129151 (up to a mean maximum of 20.8 % TRR, 0.111 mg/L) and up to 6 unknown degradation products (< 1.7 % TRR, < 0.009 mg/L).

Based on the results summarised in the table above, the following hydrolytic pathway of Zoxamide under simulated processing is proposed:

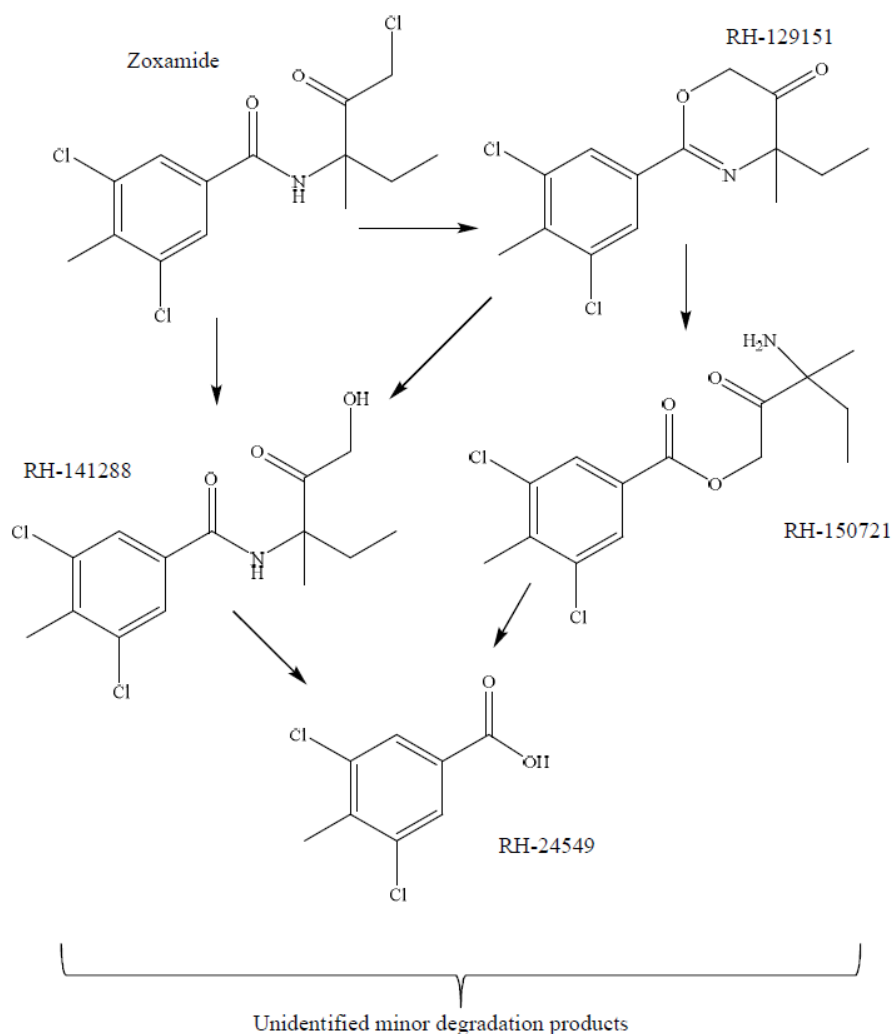


Figure A 1: Proposed pathway of Zoxamide under simulated processing conditions.

A 2.1.2.1.1.5 Study 2

Comments of zRMS: Latvia	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The study is acceptable and demonstrates that RH-141452 is stable and stays unchanged under the conditions simulating pasteurization, baking/brewing/boiling and sterilization.</i></p>
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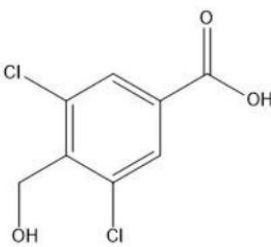
This active substance related study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference: KCA 6.5.1/02
Report: RH-141452: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS, Longhi, D., 2019, report No. BPL-STUDY-18-000092, Doc. No. 638-008

Guideline(s):	OECD No. 111, CIPAC MT 75.3, SANCO/825/00 rev.8.1 (2010), OECD No. 507, ISO 6222:2001
Deviations:	None
GLP:	Yes
Acceptability:	Yes

Materials and methods

Materials and methods

Test material:	RH-141452
	
Purity:	99.82 % (w/w)
Lot/batch no.:	21109
Analysis date:	22 May 2018
Expiry date:	2 years from analysis : 22 May 2020

The study was conducted to provide information on the effects of hydrolysis on the Zoxamide metabolite RH-141452. Therefore, it was exposed to conditions representative for pasteurisation, baking/brewing/boiling, and sterilisation.

The water used for buffer solutions was UPLC grade water. Buffers were prepared as follows:

- pH 4.0: 90 mL of a solution of 0.1 N NaOH (402 mg of NaOH pellets in 100 mL purified water) and 500 mL of a solution of 0.1 M monopotassium citrate (11.521 g of monopotassium citrate in 500 mL purified water) were diluted with purified water to a volume of 1 L.
- pH 5.0: 8 mL of a solution of 0.667 M disodium phosphate (2.377 g of Na₂HPO₄ in 250 mL purified water) and 992 mL of a solution of 0.667 M monopotassium phosphate (18.156 g of KH₂PO₄ in 2 L of purified water) were pulled.
- pH 6.0: 111 mL of a solution of 0.667 M disodium phosphate (2.377 g of Na₂HPO₄ in 250 mL of purified water) and 889 mL of a solution of 0.667 M monopotassium phosphate (18.156 g of KH₂PO₄ in 2 L of purified water) were pulled.

The buffer solutions were filled in sterilised glass vials and tubes under a laminar flow hood. Sterility was reached carrying out sterilisation of buffers, glassware and all the necessary equipment in an autoclave at 121°C for 15 minutes. Sterility was checked on samples prepared ad-hoc before and after the incubation, using a colony counting method.

Fortification solutions in acetonitrile were prepared and applied to the test vessels. The actual concentration of RH-141452 in matrix-matched fortification solutions were determined 5-fold just before test item application. For test item application, portions of the buffer solutions were treated with an aliquot of the test item stock solution to give nominal concentrations of 10 mg/L RH-141452 in the test systems. Triplicate test samples per buffer were prepared and incubated in an oven at 90 °C and 100 °C and in an autoclave at 120 °C. The incubation conditions were as follows:

pH	Temperature (°C)	Time (minutes)	Process represented
4	90	20	Pasteurisation
5	100	60	Baking, brewing, boiling
6	120*	20	Sterilisation

Freshly prepared buffers were analysed concurrently. Blank buffers served as a control.

The application conditions (pH and temperature) were recorded.

The stability of the analyte was checked by HPLC-DAD comparing the response of the analyte before and after the incubation at the different conditions.

Immediately after set up of the test systems and at the end of the incubation in the cooled down samples, aliquots of the buffer samples were directly injected in a HPLC-DAD system. Concentrations of the test item were determined using matrix-matched calibration solutions. The analytical method with an LOQ of 1 mg/L in all buffers was validated according to the SANCO/825/00 rev. 8.1 guideline. The confirmation of the analyte identification was performed using a high-resolution mass spectrometer detector and a DAD detector recording the UV spectra between 200 and 400 nm. Both the MS and the UV spectra of the standard and of the sample before and after each incubation were compared. The same profile confirmed the identification of the analyte detected in the samples.

Results

Sterility checked on samples prepared ad-hoc before and after the incubation showed a number of colony-forming unit less than 1 (CFU < 1) for each analysed sample, demonstrating that the tests were carried out in sterile conditions. Incubation temperatures were within $\pm 5^\circ\text{C}$ of the target value, the pH remained within ± 0.1 units of the target pH. The correct dosing of the test item at study start was confirmed. Blank buffers did not show any analyte or contaminants.

The effects of the different hydrolysis conditions on the analyte RH-141452 were evaluated for buffer concentrations of 10 mg/L RH-141452. In Table A 24, the mean and the relative standard deviations (RSDs) of the buffer samples analysed before and after the incubation are presented:

Table A 24: High temperature hydrolysis of RH-141452 – summary of the results

	Before the incubation		After the incubation		Residual amount (%)* Mean (mg/L)
	Mean (mg/L)	RSD (%)	Mean (mg/L)		
pH 4, 90 °C, 20 min Pasteurisation	9.812	0.890	9.735	0.181	99.22
pH 5, 100°C, 60 min Baking, brewing, boiling	9.686	0.281	9.762	0.987	100.8
pH 6, 120 °C, 20 min Sterilisation	9.692	0.651	9.623	0.196	99.29

*Residual amount: percentage ratio between the mean of the results obtained from the analyses after the incubation and those before. It is a number that indicates the ratio of non-hydrolysed analyte.

As shown in Table A 24, the amount of non-hydrolysed RH-141452 is higher than 99.2 % in all three buffers. No degradation products were found. The identity of the analyte was verified with high-resolution HPLC-MS (HPLC-HRMS), both before and after the incubation.

Conclusions

The Zoxamide metabolite RH-141452 is therefore regarded stable under the conditions simulating

pasteurisation (pH 4, 90°C for 20 minutes), baking/brewing/boiling (pH 5, 100°C for 60 minutes) and sterilisation (pH 6, 120°C for 20 minutes).

A 2.1.2.1.1.6 Study 3

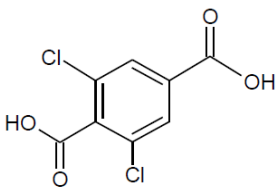
Comments of zRMS: Latvia	The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021: <i>The study is acceptable and demonstrates that RH-141455 is stable and stays unchanged under the conditions simulating pasteurization, baking/brewing/boiling and sterilization.</i>
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This active substance related study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.5.1/03
Report:	RH-141455: HYDROLYSIS UNDER SIMULATED PROCESSING CONDITIONS, Longhi, D., 2019, report No. BPL-STUDY-19-000009, Doc. No. 638-009
Guideline(s):	SANCO/825/00 rev.8.1 (2010), OECD No. 111, OECD No. 507, ISO 6222:2001, CIPAC MT 75.3
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

Materials and methods

Test material:	RH-141455
	
Purity:	94.53 % (w/w)
Lot/batch no.:	14-SBT-100-1
Analysis date:	18 Dec 2018
Expiry date:	2 years from analysis : 18 Dec 2020

The study was conducted to provide information on the effects of hydrolysis on the Zoxamide metabolite RH-141455. Therefore, it was exposed to conditions representative for pasteurisation, baking/brewing/boiling, and sterilisation.

The water used for buffer solutions was UPLC grade water. Buffers were prepared as follows:

- pH 4.0: 90 mL of a solution of 0.1 N NaOH (402 mg of NaOH pellets in 100 mL purified water) and 500 mL of a solution of 0.1 M monopotassium citrate (11.521 g of monopotassium citrate in 500 mL purified water) were diluted with purified water to a volume of 1 L.

- pH 5.0: 8 mL of a solution of 0.667 M disodium phosphate (2.377 g of Na₂HPO₄ in 250 mL purified water) and 992 mL of a solution of 0.667 M monopotassium phosphate (18.156 g of KH₂PO₄ in 2 L of purified water) were pulled.
- pH 6.0: 111 mL of a solution of 0.667 M disodium phosphate (2.377 g of Na₂HPO₄ in 250 mL of purified water) and 889 mL of a solution of 0.667 M monopotassium phosphate (18.156 g of KH₂PO₄ in 2 L of purified water) were pulled.

The buffer solutions were filled in sterilised glass vials and tubes under a laminar flow hood. Sterility was reached carrying out sterilisation of buffers, glassware and all the necessary equipment in an autoclave at 121°C for 15 minutes. Sterility was checked on samples prepared ad-hoc before and after the incubation, using a colony counting method.

Fortification solutions in acetonitrile were prepared and applied to the test vessels. The actual concentration of RH-141455 in fortification solutions were determined 5-fold just before test item application. For test item application, portions of the buffer solutions were treated with an aliquot of the test item stock solution to give nominal concentrations of 10 mg/L RH-141455 in the test systems. Triplicate test samples per buffer were prepared and incubated in an oven at 90 °C and 100 °C and in an autoclave at 120 °C. The incubation conditions were as follows:

pH	Temperature (°C)	Time (minutes)	Process represented
4	90	20	Pasteurisation
5	100	60	Baking, brewing, boiling
6	120*	20	Sterilisation

Freshly prepared buffers were analysed concurrently. Blank buffers served as a control.

The application conditions (pH and temperature) were recorded.

The stability of the analyte was checked by HPLC-DAD comparing the response of the analyte before and after the incubation at the different conditions.

Immediately after set up of the test systems and at the end of the incubation in the cooled down samples, aliquots of the buffer samples were directly injected in a HPLC-DAD system. Concentrations of the test item were determined using external calibration solutions. The analytical method with an LOQ of 1 mg/L in all buffers was validated according to the SANCO/825/00 rev. 8.1 guideline. The confirmation of the analyte identification was performed using a high-resolution mass spectrometer detector and a DAD detector recording the UV spectra between 200 and 400 nm. Both the MS and The UV spectra of the standard and of the sample before and after each incubation were compared. The same profile confirmed the identification of the analyte detected in the samples.

Results

Sterility checked on samples prepared ad-hoc before and after the incubation showed a number of colony-forming unit less than 1 (CFU < 1) for each analysed sample, demonstrating that the tests were carried out in sterile conditions. Incubation temperatures were within $\pm 5^\circ\text{C}$ of the target value, the pH remained within ± 0.1 units of the target pH. The correct dosing of the test item at study start was confirmed. Blank buffers did not show any analyte or contaminants.

The effects of the different hydrolysis conditions on the analyte RH-141455 were evaluated for buffer concentrations of 10 mg/L RH-141455.

In Table A 25, the mean and the relative standard deviations (RSDs) of the buffer samples analysed before and after the incubation are presented:

Table A 25: High temperature hydrolysis of RH-141455 – summary of the results

	Before the incubation		After the incubation		Residual amount (%)* Mean (mg/L)
	Mean (mg/L)	RSD (%)	Mean (mg/L)		
pH 4, 90 °C, 20 min Pasteurisation	9.806	0.046	9.746	1.021	99.39
pH 5, 100°C, 60 min Baking, brewing, boiling	9.944	0.561	9.840	0.528	98.95
pH 6, 120 °C, 20 min Sterilisation	9.791	0.120	9.767	0.186	99.75

*Residual amount: percentage ratio between the mean of the results obtained from the analyses after the incubation and those before. It is a number that indicates the ratio of non-hydrolysed analyte.

As shown in Table A 25, the amount of non-hydrolysed RH-141455 is higher than 99.95 % in all three buffers. No degradation products were found. The identity of the analyte was verified with high-resolution HPLC-MS (HPLC-HRMS), both before and after the incubation.

Conclusions

The Zoxamide metabolite RH-141455 is therefore regarded stable under the conditions simulating pasteurisation (pH 4, 90°C for 20 minutes), baking/brewing/boiling (pH 5, 100°C for 60 minutes) and sterilisation (pH 6, 120°C for 20 minutes).

A 2.1.2.1.1.7 Study 4

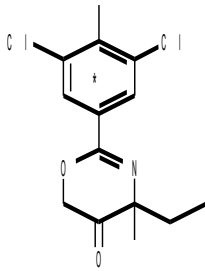
Comments of zRMS: Latvia	The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021: The study is acceptable. The metabolism path of RH-129151 under hydro-lytic conditions is similar to the metabolism of zoxamide. The recoveries of RH-129151 after the incubation period was lowest at pH 4 with a mean value of 3.4% TRR (0.04 mg/L), followed by pH 5 with a mean value of 26.8% TRR (0.27 mg/L), and the highest amount of 53.9% TRR (0.53 mg/L) at pH 6.
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This active substance related study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake. The study is only indicated in the list of data submitted or referred to by the applicant and relied on.

Reference:	KCA 6.5.1/04
Report:	HIGH TEMPERATURE HYDROLYSIS - SIMULATED PROCESSING OF 14C- RH-129151, Hueben, M., 2021, report No. GOW-004/5-42, Doc. No. 638-016
Guideline(s):	OECD No. 507 (2007)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

Materials and methods

Materials and methods

Test material	¹⁴ C-RH-129151
	 <p>* denotes ¹⁴C-label position</p>
Specific activity:	5.90 MBq/mg (48.14 mCi/mmol)
Lot/batch no.:	11561RXB002-4
Radiochemical purity:	98.2 %
Expiry date:	September 2021

The study was conducted to provide information on the effects of hydrolysis on [¹⁴C]-RH-129151 (racemate). Therefore, it was exposed to conditions representative for pasteurisation, baking/brewing/boiling, and sterilisation.

The water used for buffer solution preparation was obtained from a reverse osmosis system. Buffer at concentrations of 0.01 M were prepared from purchased buffer concentrates. At pH 4 and pH 5 the buffers were based on citric acid/hydrochloric acid and the pH 6 buffer was based on citric acid/sodium hydroxide. The buffer solutions were heat sterilised and were filled in sterilised test vessels (quartz glass tubes) under aseptic conditions. An application solution of [phenyl-U-¹⁴C]- RH-129151 in acetonitrile was prepared at a nominal concentration of 1 mg/mL.

The actual concentration of RH-129151 in the application solutions was determined in triplicate by liquid scintillation counting (LSC) before test initiation.

For test item application, every single sample of the buffer solutions was treated with an aliquot (19 µL) of the test item application solution adjusted with 181 µL acetonitrile to give nominal concentrations of 1 mg/L ¹⁴C-labelled RH-129151 in the test systems. Immediately after application the actual concentration of RH-129151 was determined in every sample. The proportion of co-solvent (acetonitrile) in each sample was 1 % (v/v). The conditions of incubation were as follows:

pH	Temperature (°C)	Time (minutes)	Process represented
4	90	20	Pasteurisation
5	100	60	Baking, brewing, boiling
6	120*	20	Sterilisation

The test conditions (temperature) during each incubation procedure were recorded. Immediately after incubation and cooling down process, all samples were stabilised by diluting 1:1 with acetonitrile and additionally, samples at pH 5 and pH 6, were acidified (stabilised) with formic acid to approx. pH 4.

The radioactivity in buffered samples was determined in solution with Ultima Gold (Perkin Elmer) by liquid scintillation counting with automatic quench correction immediately after application and at the end of the incubation.

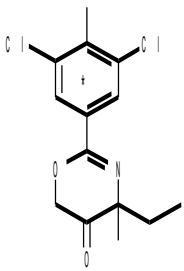
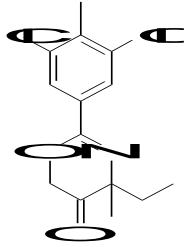
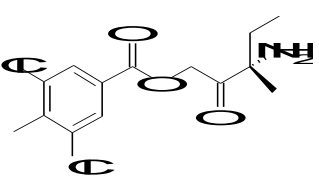
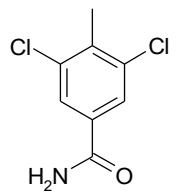
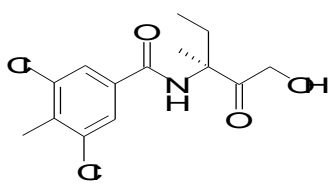
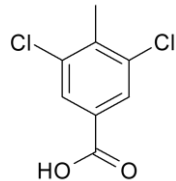
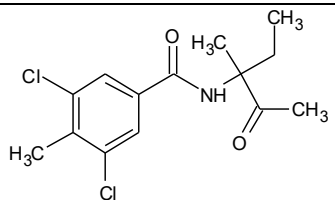
The portions of unchanged RH-129151 and its radiolabelled degradation products were analysed by reversed phase radio- and UV-HPLC. Identification was confirmed by HR-LC-MS/MS. Initial analysis was performed immediately (within 15 minutes) after cooling down process. RH-129151 and the reference substances (except RH-127450) were found to be stable in water: acetonitrile (1:1 v/v) at approx. pH 4, if analysed directly (within 15 minutes). Remaining sample material was stored in the refrigerator and deep

frozen ($\leq -18^{\circ}\text{C}$).

Samples incubated at pH 4, pH 5 and pH 6 were stabilised (with acetonitrile at approx. pH 4) and analysed immediately by radio-HPLC and thereafter stored for 2 months (for HR-LC-MS/MS analysis) in the freezer. Additionally, a storage stability experiment was performed with the parent item RH-129151 and the reference item RH-150721 in buffered water solutions (with pH 4, 5 and 6; max. 3.7 vol.-% acetonitrile in the final solutions) in the dark at room temperature ($20 \pm 2^{\circ}\text{C}$) for about 30 hours.

For identification of the metabolites, the following reference substances were used and the following criteria for identification were obtained:

Table A 26: Pattern identification of RH-129151 and metabolites in aqueous buffer solutions by HR-LC-MS/MS

Common name / code	Chemical structure	Elemental formula	Exact mass [m/z]	Exact mass (positive ion mode) [m/z]	Rt at MS [min]
¹⁴ C-RH-129151 (test item)		C ₁₄ H ₁₅ Cl ₂ NO ₂	301.05123	302.05850	9.42
¹² C-RH-129151		C ₁₄ H ₁₅ Cl ₂ NO ₂	299.04798	300.05526	9.42
¹² C-RH-150721 (isomers)		C ₁₄ H ₁₇ Cl ₂ NO ₃	317.05855	318.06583	5.15
¹² C-RH-139432		C ₈ H ₇ Cl ₂ NO	202.99047	203.99829	5.34
¹² C RH-141288 (isomers)		C ₁₄ H ₁₇ Cl ₂ NO ₃	317.05855	316.05127 (negative)	6.20
¹² C RH-24549		C ₈ H ₆ Cl ₂ O ₂	203.97448	202.96721 (negative)	6.38
¹² C RH-127450		C ₁₄ H ₁₇ Cl ₂ NO ₂	301.06363	300.05636 (negative)	7.25

Note: the structure of ¹²C-S-RH-150721 isomer and ¹²C-S-RH-141288 isomer is exemplary shown.

Results

Incubation temperatures were within $\pm 5^{\circ}\text{C}$ of the target value, the pH remained within ± 0.1 units of the target during the course of the study.

Samples incubated at pH 4, pH 5 and pH 6 were stabilised (with acetonitrile at approx. pH 4) and analysed immediately by radio-HPLC and thereafter stored for 2 months (for HR-LC-MS/MS analysis) in the freezer. Overall, there was no significant degradation of the samples after frozen storage. Only minor differences ($< 5\%$ quantitative) in the radio-chromatograms were recorded directly after incubation and after freezer storage, just before HR-LC-MS/MS confirmatory analysis.

The correct dosing of the test item at study start was confirmed by radio-HPLC. A total balance of radio-activity was established for every sample. The recovery from the buffer solutions was in the range of 90 – 110 % of applied radioactivity (AR) for all individual samples.

Degradation of RH-129151 was observed under all three incubation conditions.

In the treated samples incubated at pH 4, RH-129151 was found at mean amounts of 3.4 % TRR (0.04 mg/L) at the end of incubation period. It was hydrolysed to form two major degradation products: RH-150721, observed at mean amount of 70.8 % TRR (0.04 mg/L) and RH-24549, observed at mean amount of 13.6 % TRR (0.10 mg/L). Additionally, three minor degradation products were found: RH-139432 was detected at mean amount of 4.1 % TRR (0.03 mg/L), further two unidentified degradation products were observed at mean amounts of 3.5 % TRR (0.04 mg/L precursor equivalent concentrations) and 4.6 % TRR (0.05 mg/L precursor equivalent concentrations). According to the guideline, no further identification is to be done, due to minor amounts of unknown degradation products detected at $< 5\%$ TRR. In the treated samples incubated at pH 5, RH-129151 was found at mean amount of 26.8 % TRR (0.27 mg/L) at the end of incubation. Only one degradation product was found by radio-HPLC, which has been identified as RH-24549 and detected at mean amount of 73.2 % TRR (0.50 mg/L).

In the treated samples incubated at pH 6, RH-129151 was found at mean amount of 53.9 % TRR (0.53 mg/L) at the end of incubation. It was hydrolysed to form two major degradation products: RH-141288, observed at mean amount of 26.7 % TRR (0.28 mg/L) and RH-24549, observed at mean amount of 13.8 % TRR (0.09 mg/L). Additionally, one minor degradation product, RH-139432, was detected at mean amount of 5.6 % TRR (0.04 mg/L).

Table A 27: Standard hydrolysis study of [^{14}C]-RH-129151 – summary of the results (% TRR)*

Process represented	T° (°C)	Time (min)	pH	Parent Initial conc. (mg/L)	% of TRR (initial)					
					RH-129151 *	RH-24549 *	RH-150721 *	RH-139432 *	RH-141288 *	Total
Pasteurization	90	20	4	1	3.4	13.6	70.8	4.1	--	91.9
Baking, brewing, boiling	100	60	5	1	26.8	73.2	--	--	--	100
Sterilization	120	20	6	1	53.9	13.8	--	5.6	26.7	100

*mean of two incubations

Zoxamide and metabolites appearing $> 10\%$ are written in bold letters.

Additionally, a storage stability experiment was performed with the parent item RH-129151 and the reference item RH-150721 in buffered water solutions (with pH 4, 5 and 6; max. 3.7 vol.-% acetonitrile in the final solutions) in the dark at room temperature ($20 \pm 2^{\circ}\text{C}$) for about 30 hours. For this experiment, an appropriate volume of the corresponding substance dissolved in acetonitrile was applied, to give a final compound concentration of 20 mg/L, each. As a result, the parent item RH-129151 hydrolysed very fast in all acidic buffered samples to low mean amounts of 4.5 % (pH 4), 5.7 % (pH 5) and 6.1 % (pH 6) of initial substance concentrations. The reference item RH-150721 was relative stable in pH 4 buffer solutions with

a mean amount of 93.8 % and in pH 5 buffer solutions with a mean amount of 83.0 %. At pH 6 this compound hydrolysed to a mean amount of 20.1 % within 30 hours at $20 \pm 2^\circ\text{C}$ in the dark.

The study was conducted to provide information on the effects of hydrolysis on RH-129151 under conditions representative for pasteurisation, baking/brewing/boiling, and sterilisation. The study was performed with radiolabelled test item.

RH-129151 was hydrolysed under the following processing conditions: At pH 4 and 90°C for 20 min (pasteurisation), at pH 5 and 100°C for 60 min (baking, brewing and boiling) and at pH 6 and 120°C for 20 min (sterilisation).

The amount of hydrolysed RH-129151 was depending on the hydrolysis conditions. The recoveries of RH-129151 after the incubation period was lowest at pH 4 with a mean value of 3.4 % TRR (0.04 mg/L), followed by pH 5 with a mean value of 26.8 % TRR (0.27 mg/L), and the highest amount of 53.9 % TRR (0.53 mg/L) at pH 6.

RH-129151 hydrolysed to form RH-150721 (up to a maximum value of 70.8 % TRR at pH4), RH-141288 (up to a maximum value of 26.7 % TRR at pH 6), RH-24549 (up to a maximum value of 73.2 % TRR at pH 5), RH-139432 (up to a maximum value of 5.6 % TRR at pH 6) and two not identified minor degradation products observed only at pH 4 at an amount of 3.5 % TRR and 4.6 % TRR.

Conclusions

[^{14}C]-RH-129151 was hydrolysed under the following processing conditions tested in this study: at pH 4 and 90°C simulating pasteurisation, at pH 5 and 100°C simulating baking/brewing/boiling and at pH 6 and 120°C simulating the process of sterilisation.

The amount of hydrolysed RH-129151 was depending on the hydrolysis conditions. The recoveries of RH-129151 after the incubation period was lowest at pH 4 with a mean value of 3.4 % TRR (0.04 mg/L), followed by pH 5 with a mean of 26. % TRR (0.27 mg/L), and the highest amount of 53.9 % TRR (0.53 mg/L) at pH 6.

RH-129151 hydrolysed to form RH-150721 (up to a maximum value of 70.8 % TRR at pH 4), RH-141288 (up to a maximum value of 26.7 % TRR at pH 6), RH-24549 (up to a maximum value of 73.2 % TRR at pH 5), RH-139432 (up to a maximum value of 5.6 % TRR at pH 6) and two not identified minor degradation products observed only at pH 4 at an amount of 3.5 % TRR and 4.6 % TRR.

Samples incubated at pH 4, pH 5 and pH 6 were analysed immediately by radio-HPLC and were stored for 2 months (for HR-LC-MS/MS analysis) in the freezer. Overall, there was no significant degradation of the samples after frozen storage.

Additionally, the storage stability of the parent RH-129151 and the reference item RH-150721 in buffered solutions at room temperature ($20^\circ\text{C} \pm 2^\circ\text{C}$) in the dark for 30 hours. The parent item RH-129151 hydrolysed very fast in all buffered samples to low amounts of 4.5 % (pH 4), 5.7 % (pH 5) and 6.1 % (pH 6) of initial substance concentration. The reference item RH-150721 was relative stable at pH 4 with 93.8 % and at pH 5 with 83.0 %. At pH 6, this compound hydrolysed to 35.6 %

Based on the results summarised in the table above, the following hydrolytic pathway of RH-129151 under simulated processing is proposed:

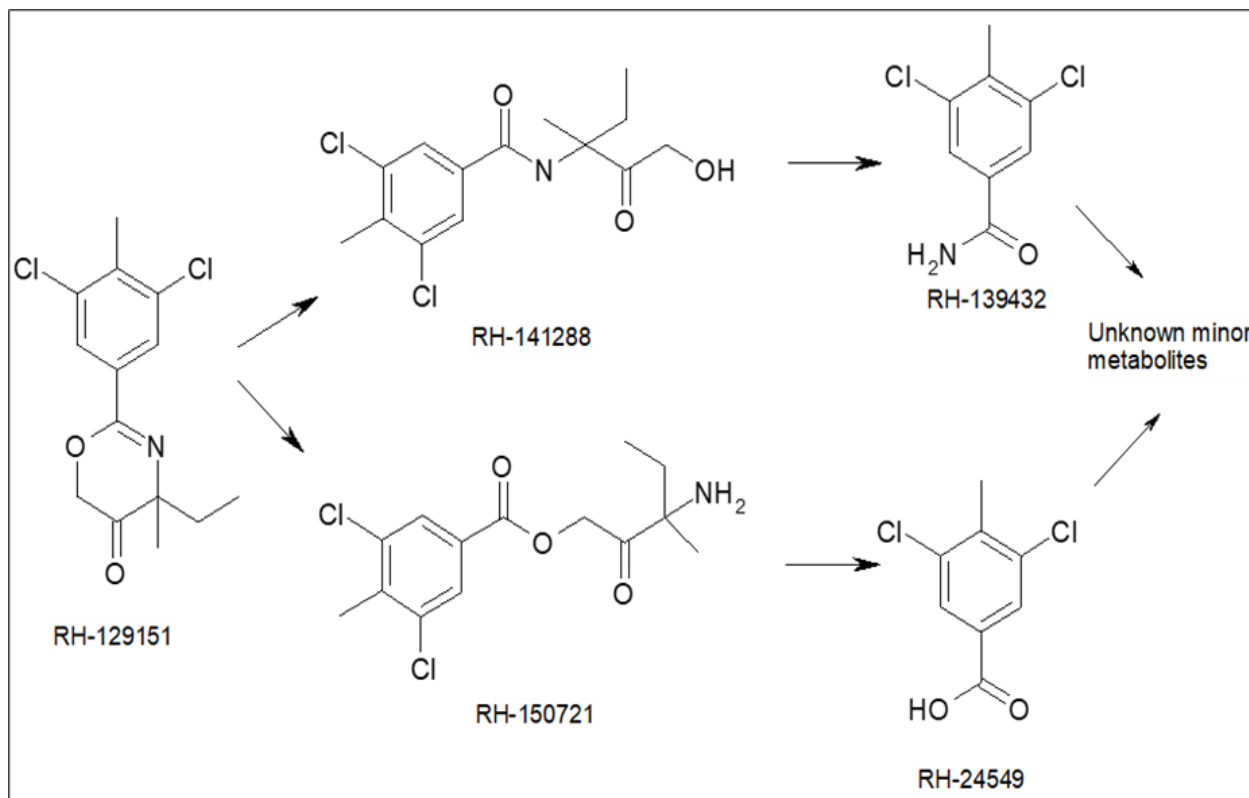


Figure A 2: Proposed pathway of RH-129151 under simulated processing conditions.

A 2.2 Nature of residues in livestock

No new data are submitted in the framework of this application.

A 2.2.1 Magnitude of residues in plants

A 2.2.1.1 Grapes (table and wine)

Table A 28: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application (min)	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2017)	5	180	8	BBCH 15-79	28
cGAP EU (Art. 12)	Pending				
Intended cGAP (# 1)	3	180	8	BBCH 14-79	28

A 2.2.1.1.1 Study 1 (report No. GLP-Study-20-30) – Southern and Northern Europe

Comments of zRMS: Latvia	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The study is acceptable.</p> <p>The concentration of zoxamide and its metabolites were determined in grapes and/or processed specimens. Trials performed under Northern and Southern European conditions. Each trial was carried out performing 3 applications of three different plant protection products at their worst-case application rates. Foliar applications were made with a spray with an interval of 7 days and a last application 28 days before harvest.</p> <p>Max. Storage interval between sampling and analysis: Wine grape: 67-69 days Wine: 14 days</p> <p>The residue found in treated grape bunches were (use pattern 3x180 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.218 to 0.905 mg/kg. - For RH-141452, the residue 28 DALA were 0.01 mg/kg - Total residues were from 0.233 to 0.920 mg/kg <p>The residue found in treated grape bunches were (use pattern 3x150 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.123 to 0.644 mg/kg. - For RH-141452, the residue 28 DALA were 0.0192 mg/kg - Total residues were from 0.123 to 0.673 mg/kg <p>The residue found in processed grapes (wine) were:</p> <ul style="list-style-type: none"> - For zoxamide, the residues were from 0.01 to 0.0181 mg/kg - For RH-141452, the residue were 0.01 mg/kg - Total residues were from 0.025 to 0.033 mg/kg <p>For other metabolites residues were below LOQ.</p> <p>Deviations: Trial: CMN-20-44059 ES06: The application 1 has been done with BBCH 81 instead of BBCH 15-79, as required in the Study Plan. This happens because at the</p>
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	<p>moment of the signature of the SP the field crop was at BBCH 81. Deviation with an impact. However, all the applications doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 ES06: The application 2 has been done 6 days after application 1, instead of 7-8 days - as required in the Study Plan. This was due to logistic adjustments and the field technician didn't realise that -1 day was not allowed. However, this deviation has no impact on the study integrity since it is still in the $\pm 25\%$ range for the application pattern intended with a 7-8 days interval.</p> <p>Trial: CMN-20-44059 FR02: Sampling S2 (1 DALA) and S3 (3 DALA) were not done. This occurred because the field technician didn't take into account the amendment no. 1 to the study plan. Deviation with an impact: the trial CMN-44059 FR02 (DEC-2) has become a decline with 5 points instead of 7 points.</p> <p>Trial: CMN-20-44059 HU04: Samples collected at 0 DALA were delivered at ambient temperature instead of refrigerated condition (with dry ice) to the Field Test Site. This occurred due to an error of the field technician that didn't correctly understand the study plan. An impact on the integrity of the study was not assumed since the maximum period between sampling and freezing in the Test Site Facility was about 6 hours (at ambient temperature).</p> <p>Trial: CMN-20-44059 FR01: Dry ice was not used during the samplings since the field was close to the Test Site Facility. No impact on the integrity of the study assumed since the maximum period between sampling in the field and freezing in the Test Site Facility was only 3 hours for sampling 1, 1 hour 20 minutes for sampling 2, 1 hour 15 minutes for sampling 3, 1 hour 5 minutes for sampling 4, 2 hours 5 minutes for sampling 5, and 1 hour 5 minutes for sampling 6 – each at ambient temperature. The max. storage period for sampling 7 was 2 hours 35 minutes (samples cooled with frozen gel packs).</p> <p>Trial: CMN-20-44059 FR02: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact on the integrity of the study since the maximum period between sampling in the field and freezing in the Test Site Facility was 1 hour for sampling 1, 15 minutes for sampling 4, 20 minutes for sampling 5, 15 minutes for sampling 6, and 16 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR05: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact since the maximum period between sampling in the field and freezing in the Test Site Facility was 3 hours for sampling 1, 2 hours for sampling 4, 2 hours 30 minutes for sampling 5, 2 hours and 35 minutes for sampling 6, and 4 hours and 30 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR01: Chemical products with phosphonate and zoxamide as active ingredients were applied in the field where the trial was set up. No impact on the results for zoxamide and metabolites. Impact for the results for phosphonic acid on grape bunches, for which residues in the untreated control samples were detected, and on wine at 0 and 28 DALA, for which residues in the untreated control sample were detected. This was solved by subtracting the untreated control sample results from the treated ones.</p> <p>Trials CMN-20-44059 FR02, FR05, HU03, HU04, ES07: The applications have not been done between BBCH 15 and BBCH 79 as requested in the Study Plan. This deviation had an impact on the study. However, the application pattern and doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 FR05: The farmer contract was signed on 04/08/2020, one day after the first application (03/08/2020). This deviation was regarded to have no impact on the study.</p> <p>During the processing phase the mustimeter 34MUS16 was used from 28/08/2020 to 03/09/2020 (checking date) without writing the procedural check before its use (the technician did the check but forgot to write it). This deviation was regarded to have no impact on the study.</p>
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	<p><i>On 08/10/2020, during the processing phase, the MLF (malolactic fermentation) was recorded as finished on the data sheets (fermentation and red wine) and k metabisulphite was added on 09/10/2020 (at the end of MLF), but the chromatography paper spots of malic acid were present for U2. Therefore, k metabisulphite seems to be added on the wine U2 before the end of the malolactic fermentation. This deviation was regarded to have no impact on the residues in the wine, but only on its organoleptic properties.</i></p> <p><i>During the analytical phase the recovery check results at LOQ level for the analytes RH-141288 and RH-150721 were outside (> 110%) the permitted range (70-110%) for analytical batch 200902 GLP-STUDY-20-30. This deviation was solved with no impact on the study results since the samples in this sequence were re-extracted and analysed, discarding the previously obtained values.</i></p> <p><i>During the analysis of analytical batch 200904-GLP-STUDY-20-30 the calibration point at level 3 (Uva L3) in the calibration curve had a response higher than expected. It has therefore not been considered to establish the actual calibration line. This deviation was regarded to have no impact on the study results since the calibration range related to the method validation has not altered, and 4 points were regarded enough to derivate a suitable calibration line with $r^2 > 0.99$.</i></p> <p><i>During the analysis of the analytical batch 200924-GLP-STUDY-20-30 (4C N) the calibration check results for (R)-RH-141288 (147.3%), (S)-RH-141288 (266.7%) and (S)-RH-150721 (141.3%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200924-GLP-STUDY-20-30 (4C B) the calibration check results of (R)-RH-150721 (136.9%) and (S)-RH-150721 (132.4%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200929-GLP-STUDY-20-30 the calibration check results of (R)-RH-150721 (126.8%) and (S)-RH-150721 (135.5%) were outside the acceptable range (80% - 120%). However, this deviation was regarded to have no impact on the study integrity. All samples analysed in these batches have concentrations < LOQ for the mentioned analytes, therefore the calibration check value could not affect the reported values anyway. This deviation was solved with no impact on the study.</i></p> <p><i>During the analysis of the analytical batch 201117 GLP-STUDY-20-30 (white wine) a calibration point for the analyte (S)-RH-141288 had a lower response in comparison to the regression line. This value was excluded and a 4-point calibrating line was established. As a consequence, since the recovery check at 10 x LOQ (GLP-SMPL-20-724/NH RC2) was no longer inside the calibration range, it could not be evaluated. However; this deviation was regarded to have no impact on the study results since 4 calibration points were regarded enough for the interpolation and to quantify the analyte content in the samples.</i></p> <p><i>The untreated white wine sample GLP-SMPL-20-724 was found to contain 1.61 mg/kg of phosphonic acid, presumably due to the reasons explained in deviation 8. External standard calibration solutions for white wine were initially established using the extracts of this sample. This resulted in a signal higher than 30% of the LOQ. They were therefore invalidated. The batch was therefore re-elaborated using the calibration curve for red wine that was analysed in the same analytical sequence, recalculating the recovery check values by subtracting the values of the untreated (white wine) sample. This deviation was regarded to have no impact on the study results since the calibration using matrix-matched reference solution in red wine has the same matrix effect on phosphonic acid than white wine (demonstrated by the recovery check and by a standard at level L3 prepared in white wine).</i></p>
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.3.1/01
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF WINE GRAPE AND PROCESSED (WINE) IN OPEN FIELD FOLLOWING THREE APPLICATIONS OF THE FORMULATED PRODUCTS GWN-9823, GWN-10616, GWN-10392 (NORTH AND SOUTH EUROPE – 7 trials year 2020, Longhi, D., 2021, report No. GLP-STUDY-20-30, Doc. No. 638-015
Guideline(s):	SANTE/2020/12830, Rev.1 (2021), SANCO/825/00 rev.8.1 (2010), OECD No. 508, OECD No. 509, SANCO/3029/99 rev. 4 (2000), 7029/VI/95 rev.5 (1997)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN 10616	GWN 10392 / Tempio	GWN 9823 WG / Reboot
Formulation:	Suspension concentrates (SC)	Suspension concentrates (SC)	Water dispersible granules (WG)
CAS#:	Zoxamide: 156052-68-5 Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2	Zoxamide: 156052-68-5 Benalaxyl-M: 98243-83-5	Zoxamide: 156052-68-5 Cymoxanil: 57966-95-7
Lot/Batch #:	2006669001	N062/20	GSOL9018
Content of a.s. (actual):	Zoxamide: 64 g/L Phosphonic acid: 505 g/L	Zoxamide: 232.1 g/L Benalaxyl-m: 158.4 g/L	Non GLP certificate (data taken forward to calculate actual application rates): Zoxamide: 33.1 % w/w Cymoxanil 33.0 % w/w GLP certificate: Zoxamide: 32.6 % w/w or 326.0 g/kg Cymoxanil: 33.8 % w/w or 337.7 g/kg
Manufacturing date:	15 June 2020	-	January 2019
Stability of test compound (expiry date):	2 years from manufacturing:	18.08.2022	January 2021 (non-GLP

			certificate) 15 December 2022 (GLP certificate)
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Study design:

Five decline cure trials and two at harvest trials in grapes have been performed in Southern (Southern France – 1 location, Spain – 2 locations) and Northern Europe (Hungary – 2 locations, Northern France – 2 locations) in 2020.

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated with three different plant protection products:

GWN-10616: a SC formulation containing Zoxamide and potassium phosphonates;

GWN-10392 / Tempio®, a SC formulation containing Zoxamide and benalaxyl-m;

GWN-9823 / Reboot®, a WG formulation containing Zoxamide and cymoxanil)

Three trials were divided in sub-plots, each sub-plot treated with one of the formulations listed above.

The different plant protection products were applied three times by spraying at the following nominal application rates:

GWN-10616: 180 g/ha Zoxamide,

GWN-10392 / Tempio®: 157.5 g/ha of Zoxamide and

GWN-9823 / Reboot®: 148.5 g/ha of Zoxamide

with an interval of 7 days and a PHI of 28 days.

Only the trials treated with GWN-10616 have been considered for MRL setting and risk assessment.

Samples were taken both for residues analysis and for processing. Details for processing are described in A 2.1.5.2.7.

In at-harvest trials, samples of grapes were taken at day of application and 28 days after last application. In the decline curve trials, samples were taken at day of application and 1, 3, 7, 14, 21 and 28 days after last application.

These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.1.1.

Methods:

The method for the determination of Zoxamide and its metabolites was successfully validated in study BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) and the limit of detection (LOD) for Zoxamide and its metabolites are presented in Table A 29.

Table A 29: LOQ and LOD of the analytes

Analyte	LOD [mg/kg]	LOQ [mg/kg]
(R)-Zoxamide	0.0015	0.005
(S)-Zoxamide	0.0015	0.005
Zoxamide (sum)	0.003	0.01
(R)-RH-141288	0.0015	0.005
(S)-RH-141288	0.0015	0.005
RH-141288 (sum)	0.003	0.01
(R)-RH-150721	0.0015	0.005
(S)-RH-150721	0.0015	0.005
RH-150721 (sum)	0.003	0.01

Analyte	LOD [mg/kg]	LOQ [mg/kg]
RH-129151 (enantiomer A)*	0.0015	0.005
RH-129151 (enantiomer B)*	0.0015	0.005
RH-129151 (sum)*	0.003	0.01
RH-141452	0.003	0.01
RH-24549	0.003	0.01

*The enantiomers (R)-RH-129151 and (S)-RH-129151 are named as RH-129151 (A) and RH-129151 (B) since it was not clear yet what signal is related at each enantiomer since only the racemate standard was provided.

The maximum sampling to extraction interval in the NEU and SEU trials for Zoxamide and its metabolites at a temperature of $\leq -18^{\circ}\text{C}$ was max. 59 and 69 days, respectively, for berries. The final extracts in samples of RAC and processed commodities were analysed within 3 days for Zoxamide and its metabolites after storage at 4°C , except for RH-129151, which was analysed within 24 hours.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability of Zoxamide and its metabolites in sample extracts. The recoveries were within the range between 70 – 110 %. The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at LOQ level (0.01 mg/kg) and at 100x LOQ (1 mg/kg) for the non-hydrolysed samples or at LOQ level (0.01 mg/kg) and at 10x LOQ (0.1 mg/kg) for the hydrolysed samples. The recoveries of Zoxamide and its metabolites were always within the range of 70 - 110 % of nominal and thus, confirming the accuracy of the analytical method on the day of analysis.

Results

Table A 30: Summary of the study 1 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)													PHI (days)	Details on trial	
			g a.s./ha	Water (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549			RH-141452
(a)	(b)					(c)																(d)	(e)	
Plot 1 – GWN-10616																								
14CMN-20-44059 FR01 51420 Nogent l'Abbesse Grand Est Northern France (N-EU) 2020	Grape vine/ Chardonnay (VITVI)	1. Year 2004	190.7	496535	38.438.4	1. 13/07/2020	BBCH 79	Wine grape bunches	0.428	0.415	0.843	nd	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	0	
		2. From 23/05/2020 to 01/06/2020	205.4	495495	38.438.4	2. 20/07/2020			0.443	0.444	0.887	nd	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	1	
		3. 24/08/2020	190.1			3. 27/07/2020			0.538	0.539	1.077	nd	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	3	
									0.503	0.497	1.000	nd	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0044)	7	
									0.279	0.275	0.554	nd	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0064)	14	
									0.519	0.637	1.156	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0076)	21	
								0.159	0.172	0.331	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0070)	28		
								Wine	0.0106	0.00755	0.0181	0.00505	0.00664	0.0117	nd	nd	nd	nd	nd	nd	<LOQ (0.0058)	28		

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)													PHI (days)	Details on trial	
			g a.s./ha	Water (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549			RH-141452
(a)	(b)					(c)																	(d)	(e)
CMN-20-44059 HU03 5094 – Tiszajeno Jász-Nagykun-Szolnok Hungary (N-EU) 2020	Grape vine/ Cserszegi Fűszeizes (VITVI)	1. 10/09/1995 2. From 20/06/2020 to 06/07/2020 3. 03/09/2020	199.7 197.1 177.1	624 616 553	32.0 32.0 32.0	1. 23/07/2020 2. 30/07/2020 3. 06/08/2020	BBCH 81	Wine grape bunches	0.456	0.449	0.905	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0067)	28	
CMN-20-44059 HU04 8297 – Tapolca-Diszel Veszprém Hungary (N-EU) 2020	Grape vine/ Welschriesling (VITVI)	1. Year 1995 2. From 11/05/2020 to 26/05/2020 3. 22/09/2020	177.6 172.8 173.3	740 720 722	24.0 24.0 24.0	1. 11/08/2020 2. 18/08/2020 3. 25/08/2020	BBCH 83	Wine grape bunches	0.302	0.302	0.604	nr	nr	nr	nr	nr	nr	nr	nr	nd	nd	nd	0	
									0.349	0.346	0.695	nr	nr	nr	nr	nr	nr	nr	nd	nd	1			
									0.413	0.407	0.820	nr	nr	nr	nr	nr	nr	nr	nd	<LOQ (0.0040)	3			
									0.476	0.487	0.963	nr	nr	nr	nr	nr	nr	nr	nd	<LOQ (0.0042)	7			
									0.347	0.351	0.698	nr	nr	nr	nr	nr	nr	nr	nd	<LOQ (0.0046)	14			
									0.208	0.205	0.413	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0054)	21			
									0.298	0.293	0.591	nr	nr	nr	nr	nr	nr	nr	nr	nd	28			
Plot 2 – GWN-10392																								
			161	395	40.8				0.396	0.406	0.802	nr	nd	nd	nd	nr	nd	nd	nr	nd	nd	nd	0	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)													PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549		
(a)	(b)	(b)				(c)																(d)	(e)
CMN-20-44059 FR02 71350 – Saint Gervais en Vallière Bourgogne France Comté – France (N-EU) 2020	Grape vine/ Pinot noir (VITVI)	1. 01/04/2014	150	368	40.8	27/07/2020	BBCH 83	Wine grape bunches	0.354	0.348	0.702	nd	nd	nd	nd	nd	nr	nr	nr	nd	<LOQ 0.0058)	7	
		2. 03/08/2020				03/08/2020			0.364	0.356	0.720	nd	nd	nd	nd	nr	nr	nr	nd	<LOQ 0.0083)	14		
		3. 10/08/2020				10/08/2020			0.204	0.200	0.404	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ 0.0068)	21		
		0 to 15/06/2020							0.254	0.244	0.498	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ 0.0075)	28		
Plot 3 – GWN-9823																							
CMN-20-44059 HU04 8297 Tapolca-Diszel Veszprém Hungary (N-EU) 2020	Grape vine/ Welschriesling (VITVI)	1. Year 1995	141	756	18.6	11/08/2020	BBCH 83	Wine grape bunches	0.285	0.280	0.565	nr	nr	nr	nr	nr	nd	nd	nd	nd	nd	0	
		2. From 11/05/2020 to 26/05/2020	146	784	18.6	18/08/2020			0.266	0.262	0.529	nr	nr	nr	nr	nr	nd	nd	nd	nd	nd	1	
		3. 22/09/2020	151	808	18.6	25/08/2020			0.482	0.499	0.981	nr	nr	nr	nr	nr	nd	nd	nd	nd	nd	3	
									0.281	0.280	0.561	nr	nr	nr	nr	nr	nd	nd	nd	nd	<LOQ 0.0030)	7	
									0.193	0.196	0.388	nr	nr	nr	nr	nr	nd	nd	nd	nd	nd	14	
									0.167	0.169	0.336	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	21
									0.181	0.177	0.358	nr	nr	nr	nr	nr	nr	nr	nr	nd	28		

nd = not detectable, nr = not relevant

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A2.2.3.1.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

- (c) Year must be indicated
 - (d) Days after last application (Label pre-harvest interval, PHI, underline)
 - (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
- LOQ: 0.01 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549
LOQ: 0.005 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)-RH-141288, (S)-RH-141288
LOD: 0.003 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549
LOD: 0.0015 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)-RH-141288, (S)-RH-141288

Table A 31: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Com-modity/ Variety	Date of 1.Sowing or planting 2.Flow-ering 3. Har-vest	Application rate per treatment			Dates of treat-ment or no. of treat-ments and last date	Growt h stage at last treat-ment or date	Por-tion ana-lysed	Residues (mg/kg)													PHI (days)	De-tail s on tria l
			g a.s./ ha	Wa-ter (L/ha)	g a.s./h L				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-141288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549	RH-141452	
(a)	(b)					(c)																(d)	(e)
Plot 1 – GWN-10616																							
CMN-20-44059 FR05 30 300 Beaucaire Occitane France (S-EU) 2020	Grape vine/ Cabernet Sauvignon (VITVI)	1. Year 1991	189.4	394	48.0	03/08/2020	BBCH 85	Wine grape bunches	0.183	0.180	0.363	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	0
		2. From 20/05/2020 to 10/06/2020	188.2	392	48.0	10/08/2020			0.171	0.171	0.342	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	1
		3. 14/09/2020	188.2			17/08/2020			0.132	0.126	0.258	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	3
									0.082	0.081	0.162	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	8
									0.086	0.083	0.169	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	14
									0.188	0.183	0.371	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0035)	21
									0.117	0.115	0.231	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0034)	28
								Wine	< LOQ (0.00413)	< LOQ (0.0037)	< LOQ (0.0079)	< LOQ (0.0037)	0.0051	< LOQ (0.0088)	nd	nd	nd	nd	nd	nd	nd	<LOQ (0.0043)	28
CMN-20-44059 ES06 21720 Rociana del Condado Andalu-cia Spain (S-EU)	Grape vine/ Zalema (VITVI)	1. Febru-ary 2000	198.7	828	24.0	09/07/2020	BBCH 83	Wine grape bunches	0.215	0.215	0.430	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	0
		2. From 29/04/2020 to 16/05/2020	189.3	786	24.0	15/07/2020			0.381	0.388	0.768	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	1
		3. 19/08/2020	188.7			22/07/2020			0.303	0.300	0.603	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	3
									0.093	0.101	0.195	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	7
									0.064	0.064	0.127	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	14
									0.189	0.184	0.373	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	21
									0.109	0.109	0.218	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0037)	28

Trial No./ Location/ EU zone/ Year	Com- modity/ Variety	Date of 1.Sowing or planting 2.Flow-ering 3. Har-vest	Application rate per treatment			Dates of treat-ment or no. of treat-ments and last date	Growt h stage at last treat-ment or date	Port- ion ana-lysed	Residues (mg/kg)													PHI (days)	De- tail s on tria l	
			g a.s./ ha	Wa- ter (L/h a)	g a.s./h L							Zoxamide -(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-141288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)			RH-129151-(B)
(a)	(b)					(c)																	(d)	(e)
2020																								
CMN-20-44059 ES07	Grape vine/ Palo-mino	1. 30/01/2018 2. From 25/04/2020 to 10/05/2020 3. 27/08/2020	197.8 188.2 188.2	824 784 784	24.0 24.0 24.0	16/07/2020 23/07/2020 30/07/2020	BBCH 83	Wine grape bunches	0.193	0.193	0.387	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0061)	28	
11560 Trebujena Andalu-cia	(VITVI)																							
Spain (S-EU) 2020																								
Plot 2 - GWN-10392																								
CMN-20-44059 ES06	Grape / Zalema	1. Febru-ary 2000 2. From 29/04/2020 to 16/05/2020 3. 19/08/2020	161 157 161	797 778 797	20.2 20.2 20.2	09/07/2020 15/07/2020 22/07/2020	BBCH 83	Wine grape bunches	0.471	0.466	0.937	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0038)	0	
21720 Rociana del Con-dado Andalu-cia	(VITVI)								0.218	0.223	0.441	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	1	
									0.237	0.256	0.493	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	3	
									0.313	0.312	0.625	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	7	
									0.194	0.195	0.389	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	14	
									0.352	0.349	0.701	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	<LOQ (0.0093)	21	
									0.0701	0.0665	0.137	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	28	
CMN-20-44059 ES07	Grape vine/ Palo-mino	1. 30/01/2018 2. From 25/04/2020	170 156 156	844 772 772	20.2 20.2 20.2	16/07/2020 23/07/2020	BBCH 83	Wine grape bunches	0.323	0.320	0.644	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	0.0192	28	
11560																								

Trial No./ Location/ EU zone/ Year	Com- modity/ Variety	Date of 1.Sowing or planting 2.Flow- ering 3. Har- vest	Application rate per treatment			Dates of treat- ment or no. of treat- ments and last date	Growt h stage at last treat- ment or date	Por- tion ana- lysed	Residues (mg/kg)													PHI (days)	De- tail s on tria l
			g a.s./ ha	Wa- ter (L/ha)	g a.s./h L				Zoxamide -(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-141288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549	RH-141452	
(a)	(b)					(c)																(d)	(e)
Trebu- jena Andalu- cia Spain (S-EU) 2020	(VITVI)	20 to 10/05/20 20 3. 27/08/20 20				30/07/20 20																	
Plot 3 - GWN-9823																							
CMN-20- 44059 ES06 21720 Rociana del Con- dado Andalu- cia Spain (S-EU) 2020	Grape vine/ Zalema (VITVI)	1. Febru- ary 2000	150 146	803 797	18.6 18.6	09/07/20 20	BBCH 83	Wine grape bunch es	0.219	0.219	0.438	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	0
		2. From 29/04/20 20	147	789		15/07/20 20			0.109	0.108	0.217	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	1
		3. 19/08/20 20				22/07/20 20			0.312	0.344	0.656	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	3
									0.115	0.115	0.230	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	7
									0.0771	0.0774	0.154	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	14
									0.065	0.0640	0.129	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	21
									0.0605	0.0623	0.123	nr	nr	nr	nr	nr	nr	nr	nr	nr	nr	nd	28

nr = not detectable, nr = not relevant

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.1.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

- (c) Year must be indicated
 - (d) Days after last application (Label pre-harvest interval, PHI, underline)
 - (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
- LOQ: 0.01 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549
LOQ: 0.005 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)-RH-141288, (S)-RH-141288
LOD: 0.003 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549
LOD: 0.0015 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)-RH-141288, (S)-RH-141288

A 2.2.1.1.2 Study 2 (report No. SCC-Study-G410TO417-21) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The southern data are not relevant for the CEU zone.</p> <p>The objective of the field phase was to conduct trials in grapevines cultivated in open field conditions in Northern and Southern Europe and to provide to the analytical test site specimens resulting from 3 foliar applications with 3.0 L/ha of GWN-10616 (i.e. 180 g a.s./ha of Zoxamide) and 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid]).</p> <p>Three trials were conducted in Northern Europe (Belgium, The Netherlands) and five trials were conducted in Southern Europe (Italy, Spain).</p> <p>All maintenance products (plant protection products and fertilizers) were used simultaneously on both plots during the conduct of each trial (from first application to final sampling). Climatic conditions were normal. The first application was done at 7-8 DBA2, the second application was done at 7-9 DBA3 and the third application was done at 26-29 DBH. No additional adjuvants, surfactants or mixing partners were used for the applications.</p> <p>In the DCS trials, samplings were done at 0, 2-3, 6-7, 14-15 and 27-28 DALA. In the HS trials, samplings were done at 0 and 26-29 DALA.</p> <p>The objective of the analytical phase was to determine Zoxamide and Potassium phosphonate [expressed in equivalent Phosphonic acid] residues. Residues of metabolite RH-141452 were also determined as total fraction (a hydrolysis to release matrix-conjugated compounds was necessary). Residues in grapes without stems and caps were analysed.</p> <p>The validated (GLP-STUDY-21-101) method for Zoxamide used LC-MS/MS. The LOQ was 0.01. The linearity was checked by a 5-points calibration curve (single injection) using matrix-matched analytical standard solutions. For the procedural recoveries 4 fortification levels were tested. All samples were analysed within 24 hours from extraction.</p> <p>The analytical method for the determination of RH-141452 was validated in GLP-STUDY-21-102 also used LC-MS/MS. The LOQ was 0.01. All extracts were analysed within 1 day from the sample extraction. The linearity was checked by a 5-points calibration curve using matrix-matched standards. Procedural recoveries were carried out on 2 fortification levels.</p> <p>The analytical method for the determination of phosphonic acid in grape samples was validated in the study GLP-STUDY-21-103 used LC-MS/MS with the LOQ of 0.01. The linearity was checked also by a 5-points matrix-matched calibration, the procedural recoveries were carried out on 3 fortification levels. All samples were analysed within 24 hours from extraction.</p>
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Reference:	KCA 6.3.1/02
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 2 AT HARVEST TRIALS IN NORTHERN EUROPE, & 2 DECLINE TRIALS AND 3 AT HARVEST TRIALS IN SOUTHERN EUROPE IN 2021, Loriau, P., 2022, report No. SCC-G410TO417-21, Doc. No. 632-40001
Guideline(s):	SANTE/2019/12752, SANTE/2020/12830 rev.1 (2021), ENV/JM/MONO(2007)17, ENV/JM/MONO(2011)50/Rev1 (2016), OECD No. 509 (2021)
Deviations:	None
GLP:	Yes

Acceptability: Yes

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Three decline curve trials and 5 at harvest trials in grapes have been performed in Southern (Italy – four locations, Spain – 1 location) and Northern Europe (Belgium – 2 locations, The Netherlands – 1 location) in 2021.

Each trial consisted of two plots: 1 plot (control) was left untreated, and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rates of 180 g a.s./ha with an interval of 7-8 days and a PHI of 28 days.

In at-harvest trials, samples of grapes were taken at day of application and 27/28/29 days after last application. In the decline curve trials, samples were taken at day of application and 2/3, 6/7, 14/15 and 27/28 days after last application.

These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.1.2.

Methods:

The method for the determination of Zoxamide and its metabolite RH-141452 was successfully validated in study GLP-STUDY-21-101 (“Validation of an analytical method for the determination of GWN-8030 in grapes”, Doc. No. 432-006) and GLP-STUDY-21-102 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in grapes”, Doc. No. 432-007). Additional validation data (storage of Standard solutions) were performed in Study GLP-STUDY-21-53 (“Validation of an analytical method for the determination of GWN-8030 in Apples”, Doc. No. 432-003) and GLP-STUDY-21-54 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in Apples”, Doc. No. 432-005).

The method validations are described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) the analytes Zoxamide and its metabolite RH-141452 was 0.01 mg/kg. The limit of detection (LOD) was 0.002 mg/kg for both analytes.

The maximum sampling to extraction interval was 83 days for Zoxamide and RH-141452 in grape berries at a temperature of -18°C for NEU and SEU trials.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours. Thus, a storage stability testing is not needed.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 10x LOQ (0.1 mg/kg), at 100x LOQ (1 mg/kg; Zoxamide only) and 1000x LOQ (10 mg/kg; Zoxamide only). The mean recoveries for Zoxamide and its metabolite RH-141452, except for the fortification level at 100 x LOQ for Zoxamide (114.4 %) were always within the range of 70 - 110 % of nominal showing overall relative standard deviations below 12 % for Zoxamide and below 7 % for RH-141452 and thus, confirming the accuracy of the analytical method on the day of analysis.

Results

Table A 32: Summary of the study 2 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH-141452		
(a)	(a)	(b)				(c)					(d)	(e)
SCC-G410TO417-21 G410-21F 1401 Baulers Belgium (N-EU) 2021	Grapevine/ Muscat bleu (VITVI)	1. 2013 2. from 26/06/2021 to 10/07/2021 3. 24/09/2021	185 185 186	821 821 827	22.5 22.5 22.5	11/08/2021 19/08/2021 27/08/2021	BBCH 85	Grape bunches	1.305 1.099 1.172 0.990 <u>0.616</u>	<LOQ <LOQ 0.01188 0.01643 <u>0.01653</u>	0 3 7 14 28	
SCC-G410TO417-21 G411-21F 7804 Ostiches Belgium (N-EU) 2021	Grapevine/ Auxerrois (VITVI)	1. 2019 2. from 30/06/2021 to 15/07/2021 3. 08/10/2021	194 189 192	862 842 854	22.5 22.4 22.5	24/08/2021 01/09/2021 09/09/2021	BBCH 81	Grape bunches	0.612 <u>0.190</u>	<LOQ <LOQ	0 29	
SCC-G410TO417-21 G412-21F 6562 KC Groesbeek The Netherlands (N-EU) 2021	Grapevine/ Cabernet blanc (VITVI)	1. 2006 2. from 19/06/2021 to 29/06/2021 3. 13/10/2021	174 173 186	677 671 722	25.7 25.8 25.8	30/08/2021 07/09/2021 16/09/2021	BBCH 83	Grape bunches	0.853 <u>0.511</u>	<LOQ <LOQ	0 27	

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.1.2.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

LOD: 0.002 mg/kg for Zoxamide and RH-141452

Table A 33: Summary of the study 2 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
(a)	(b)	(b)				(c)					(d)	(e)
SCC-G410TO417-21 G413-21F 74011 Castellaneta Italy (S-EU) 2021	Grapevine/ Cabernet Sauvignon (VITVI)	1. 2002 2. from 10/06/2021 to 18/06/2021 3. 01/10/2021	174 173 186	677 671 722	25.7 25.8 25.8	18/08/2021 26/08/2021 03/09/2021	BBCH 83	Grape bunches	0.449 0.510 0.351 0.235 <u>0.281</u>	<LOQ <LOQ <LOQ <LOQ <LOQ	0 3 7 14 28	
SCC-G410TO417-21 G414-21F 94010 Calascibetta Italy (S-EU) 2021	Grapevine/ Sangiovese (VITVI)	1. 2005 2. from 10/06/2021 to 26/06/2021 3. 05/10/2021	182 180 182	1008 1000 1008	18.1 18.0 18.1	24/08/2021 31/08/2021 08/09/2021	BBCH 85	Grape bunches	1.052 0.877 1.009 0.622 <u>0.539</u>	<LOQ <LOQ <LOQ <LOQ <LOQ	0 2 6 15 27	
SCC-G410TO417-21 G415-21F 94017 Regalbuto Italy (S-EU) 2021	Grapevine/ Frappato (VITVI)	1. 2016 2. from 22/05/2021 to 12/06/2021 3. 30/09/2021	183 185 179	1017 1025 992	18.0 18.0 18.0	18/08/2021 26/08/2021 03/09/2021	BBCH 87	Grape bunches	0.630 <u>0.573</u>	<LOQ <LOQ	0 27	
SCC-G410TO417-21 G416-21F 95030 Nicolosi Italy (S-EU) 2021	Grapevine/ Nerello Mascalese (VITVI)	1. 2011 2. from 07/05/2021 to 21/05/2021 3. 29/09/2021	194 190 186	1078 1056 1033	18.0 18.0 18.0	16/08/2021 24/08/2021 01/09/2021	BBCH 83-85	Grape bunches	0.833 <u>0.350</u>	<LOQ <LOQ	0 28	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
(a)	(a)	(b)				(c)					(d)	(e)
SCC-G410TO417-21 G417-21F 09463 Haza (Burgos) Spain (S-EU) 2021	Grapevine/ Tempranillo (VITVI)	1. 2005 2. from 15/06/2021 to 20/06/2021 3. 05/10/2021	182 181 188	810 807 836	22.5 22.4 22.5	25/08/2021 02/09/2021 09/09/2021	BBCH 83-85	Grape bunches	0.203 <u>0.174</u>	<LOQ <u><LOQ</u>	0 26	

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.1.2.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

LOD: 0.002 mg/kg for Zoxamide and RH-141452

A 2.2.1.1.3 Study 3 (report No. SCC-Study-G107TO108-22) – Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The objective of the field phase was to conduct 2 trials in grapevine cultivated in open field conditions in Belgium and The Netherlands with 3 foliar applications of 180 g a.s./ha of Zoxamide and 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid]. Climatic conditions were normal. The first application was done at 7-8 DBA2, the second at 8 DBA3 and the third at 26-27 DBH. No additional adjuvants, surfactants or mixing partners were used for the applications. In the DCS trial, samplings of grapes were done at 0, 4, 7, 13 and 27 DALA. In the harvest trial, samplings of grapes were done at 0 and 26 DALA. The analytical phase was done in a same manner like in the previous study. The subjects of the determinations were also Zoxamide, Potassium phosphonate and metabolite RH-141452. LC-MS/MS determination was also applied.</p>
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Reference:	KCA 6.3.1/03
Report:	RESIDUE STUDY - RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 1 HARVEST TRIAL IN NORTHERN EUROPE IN 2022, Loriau, P., 2023, report No. SCC-G107TO108-22, Doc. No. 632-40002
Guideline(s):	ENV/JM/MONO(2007)17, (EU) No. 283/2013, SANTE/2019/12752, SANTE/2020/12830, rev. 1 (2021), OECD No.509 (2021), ENV/JM/MONO(2007)17, OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Potassium phosphonate: 726.6 g/L Phosphonic acid: 481.2 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Two supervised residue trials (1 at harvest trials and 1 decline curve trial) were conducted during 2021 on grapes in Belgium (1 location) and The Netherlands (1 location). Each trial consisted of two plots: 1 plot (control) was left untreated, and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rates of 180 g a.s./ha with an interval of 7-8 days and a PHI of 28 days.

In at harvest trials, samples of grapes were taken at day of application and 27 days after last application. In the decline curve trials, samples were taken at day of application and 4, 7, 13 and 27 days after last application. These supervised residue trials provide data relevant to conditions in the Northern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.1.3.

Methods:

The method for the determination of Zoxamide and its metabolite RH-141452 was successfully validated in study GLP-STUDY-21-101 ("Validation of an analytical method for the determination of GWN-8030 in grapes", Doc. No. 432-006) and GLP-STUDY-21-102 ("Validation of an analytical method for the determination of RH-141452 (total fraction) in grapes", Doc. No. 432-007). Additional validation data (storage of Standard solutions) were performed in Study GLP-STUDY-21-53 ("Validation of an analytical method for the determination of GWN-8030 in Apples", Doc. No. 432-003) and GLP-STUDY-21-54 ("Validation of an analytical method for the determination of RH-141452 (total fraction) in Apples", Doc. No. 432-005).

Both method validations are described in detail in Part B, Section 5 ("*Analytical Methods*").

The limit of quantification (LOQ) the analytes Zoxamide, RH-141452 was 0.01 mg/kg. The limit of detection (LOD) was 0.002 mg/kg for both analytes.

The maximum sampling to extraction interval was 92 days for Zoxamide and 96 days for RH-141452 in grape berries at a temperature of -18°C.

The final extracts in all RAC samples were analysed within 24 hours for Zoxamide and its metabolite RH-141452. Thus, a storage stability testing is not needed.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg) and at 10x LOQ (0.1 mg/kg for RH-141452) and at 200x LOQ (2.0 mg/kg for Zoxamide). The recoveries for Zoxamide and its metabolite RH-141452 were always within the range of 70 - 110 % of nominal with relative standard deviations below 3 % for Zoxamide and below 6 % for RH-141452 and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 34: Summary of the study 3 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
(a)	(b)	(b)				(c)					(d)	(e)
SCC-G107TO108 G107-22F 1401 Baulers Belgium (N-EU) 2022	Grapevine/ Bronner (VITVI)	1. 2013 2. from 10/06/2022 to 15/06/2022 3. 14/09/2022	185 186 180	824 828 798	22.5 22.5 22.6	02/08/2022 10/08/2022 28/08/2022	BBCH 83-85	Grape bunches	0.401 0.575 0.639 0.441 <u>0.340</u>	<LOQ <LOQ <LOQ <LOQ <LOQ	0 4 7 13 27	
SCC-G107TO108 G108-22F 6562 Groesbeek The Netherlands (N-EU) 2022	Grapevine/ Cabernet blanc (VITVI)	1. 2006 2. from 06/06/2021 to 15/06/2021 3. 28/09/2021	180 182 184	700 707 715	25.7 25.7 25.7	18/08/2022 25/08/2022 02/09/2022	BBCH 79-81	Grape bunches	0.411 <u>0.208</u>	<LOQ <LOQ	0 26	

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.1.3.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

LOD: 0.002 mg/kg for Zoxamide and RH-141452

A 2.2.1.2 Pome fruits

Table A 35: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2017)	No representative use within the renewal process.				
cGAP EU (Art. 12)	Pending				
Intended cGAP (# 3)	2	180	6-8	BBCH 51-69	nr

nr: not relevant

A 2.2.1.2.1 Study 1 (report No. BPL-STUDY-19-000033) – Southern Europe

Comments of zRMS:	<p>The study has been accepted. It is not relevant for the current zone.</p> <p>The obtained residue data can be used as supplemental information only.</p> <p>The objective of this study was the determination of phosphonic acid, Zoxamide (as sum of enantiomers), and separately (R)-Zoxamide, (S)-Zoxamide, and metabolites RH-150721 (as sum of enantiomers) and separately (R)-RH-150721, (S)-RH-150721; RH-129151 (as sum of enantiomers) and separately (R)-RH-129151 and (S)-RH-129151; RH-141288 (as sum of enantiomers) and separately (R)-RH-141288 and (S)-RH-141288; moreover RH-24549 and RH-141452 in apple and pear.</p>
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Reference: KCA 6.3.2/01

Report: DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019), Longhi, D., 2021, report No. BPL-STUDY-19-000033; Doc. No. 632-20001

Guideline(s): OECD No. 509 (2009), SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev.4 (2000), SANTE/2020/12830 Rev. 1 (2021)

Deviations: None

GLP: Yes

Acceptability: Yes/supplemental

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	Zoxium 240 SC	GWN-10616
Formulation:	Suspension concentrate	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	SIPAL7001	L1801669001
Content of a.s. (actual):	Zoxamide: 242.9 g/L	Zoxamide: 59.67 g/L Phosphonic acid: 514.5 g/L Potassium phosphonate ^a : 753.5 g/L
Stability of test compound (expiry date):	31/10/2019	03/01/2020

^a Calculated considering the molecular weight of Phosphonic acid and monopotassium phosphonate.

Study design:

Two supervised residue trials (at harvest trials) were conducted during 2019 on pome fruits (1 in apples and 1 in pears) in 2 locations in Italy. Each trial consisted of three subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulations Zoxium 240 SC or GWN-10616 at the nominal application rates of 180 g a.s./ha at BBCH 69.

Only the trials treated with GWN-10616 have been considered for MRL setting and risk assessment.

Samples of apples and pears were taken at BBCH 87 in the at-harvest trials. These supervised residue trials provide data relevant to conditions in the Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.2.1.

Methods:

The method for the determination of Zoxamide and its metabolites was successfully validated in study BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and the limit of detection (LOD) for Zoxamide and its metabolites are presented in Table A 36.

Table A 36: LOQ and LOD of the analytes

Analyte	LOD [mg/kg]	LOQ [mg/kg]
(R)-Zoxamide	0.0015	0.005
(S)-Zoxamide	0.0015	0.005
Zoxamide (sum)	0.003	0.01
(R)-RH-141288	0.0015	0.005
(S)-RH-141288	0.0015	0.005
RH-141288 (sum)	0.003	0.01
(R)-RH-150721	0.0015	0.005
(S)-RH-150721	0.0015	0.005
RH-150721 (sum)	0.003	0.01
RH-129151 (enantiomer A)*	0.0015	0.005
RH-129151 (enantiomer B)*	0.0015	0.005
RH-129151 (sum)	0.003	0.01
RH-141452	0.003	0.01
RH-24549	0.003	0.01

*The enantiomers (R)-RH-129151 and (S)-RH-129151 are named as RH-129151 (A) and RH-129151 (B) since it was not clear yet what signal is related at each enantiomer since only the racemate standard was provided.

The maximum sampling to extraction interval at -18°C was 29 days for Zoxamide and its metabolites in apples and pears. The maximum extraction to quantification interval at 4°C was < 1 day for all metabolites. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.005 or 0.01 mg/kg) and at 10x LOQ (0.05 or 0.1 mg/kg). The recoveries for Zoxamide and its metabolites were always within the range of 70 - 110 %. Thus, the accuracy of the analytical method on the day of analysis was confirmed.

Results:

Table A 37: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commod- ity/ Vari- ety	Date of 1.Sowing or planting 2.Flower- ing 3. Harvest	Application rate per treatment			Dates of treatment or no. of treat- ments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)													PHI (days)	Details on trial
			g a.s./ ha	Wa- ter (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549		
(a)	(b)					(c)																(d)	(e)
FR19GWNP11 MR01 44123 Boara (FE) Italy (S-EU) 2019	Apple/ Imperatore	1. na	188	1035	18.2	12/04/2019 18/05/2019	BBCH 69	Apple	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	145	Zoxium 240 SC
		2. na 3. 10/09/2019	186 178 177	1023 1042 1035	18.2 17.1 17.1				nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	145	GWN- 10616
FR19GWNP21 LG01 44045 XII Mo- relli (FE) Italy (S-EU) 2019	Pear/ Abate Fetel	1. na	189	1037	18.2	02/04/2019 08/04/2019	BBCH 69	Pear	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	147	Zoxium 240 SC
		2. na 3. 02/09/2019	196 175 177	1075 1025 1037	18.2 17.1 17.1				nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	147	GWN- 10616

nd: below the limit of detection (< LOD); na: not applicable

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.2.1

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.003 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOD: 0.0015 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

LOQ: 0.01 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOQ: 0.005 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

A 2.2.1.2.2 Study 2 (report No. BPL-STUDY-19-000034) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The objective of this study was the determination of phosphonic acid, Zoxamide (as sum of enantiomers), and separately (R)-Zoxamide, (S)-Zoxamide, and metabolites RH-150721 (as sum of enantiomers) and separately (R)-RH-150721, (S)-RH-150721; RH-129151 (as sum of enantiomers) and separately RH-129151 (A) and RH-129151 (B) (since only the racemate standard was provided); RH-141288 (as sum of enantiomers) and separately (R)-RH-141288 and (S)-RH-141288; moreover RH-24549 and RH-141452 in apple and pear from 6 harvest trials (3 apple and 3 pear) set in Italy, Northern France, Poland and Hungary. Each of them was carried out with 2 applications on different plots with ZOXIUM 240 SC (GWN 9790 EU; (T1)) and GWN 10616 (T2).</p> <p>Zoxamide moiety determinations were performed by an LC-MS/MS method validated in the study BPL-STUDY-18-000085 in grape, potato, tomato, cucumber, and onion consistently with SANTE/2020/12830 rev.1. The metabolite RH-141452 for determination was hydrolysed to free form from the conjugated one. Phosphonic acid was determined using an LC-MS/MS method validated in the study BPL-STUDY-19-000111.</p> <p>For Zoxamide moiety for all fortification levels the recoveries were within the acceptable range of 70-110% except of Zoxamide (R), Zoxamide (S), RH-141288 (R) and RH-141288 (S) in pear (not hydrolysed), which were higher than 110 % (<i>deviation 1</i>). For RH-141452, hydrolysed, and phosphonic acid for all fortification levels the recoveries were within the acceptable range of 70-110%. The methods meet the requirements of the guideline SANTE/2020/12830, Rev. 1.</p> <p>5 deviations were issued for the field and analytical phase without any impact on the study.</p>
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Reference: KCA 6.3.2/02

Report: DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019 NORTHERN EUROPE - 4 TRIALS YEAR 2019), Longhi, D., 2021, report No. BPL-STUDY-19-000034, Doc. No. 632-20002

Guideline(s): OECD No. 509 (2009), SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev.4 (2000), SANTE/2020/12830 Rev. 1 (2021)

Deviations: 5 minor, the study not affected

GLP: Yes

Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	Zoxium 240 SC	GWN-10616
Formulation:	Suspension concentrate (SC)	Suspension concentrate (SC)
CAS#:	Zoxamide: 156052-68-5	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	SIPAL7001	L1801669001

Content of a.s. (actual):	Zoxamide: 242.9 g/L	Zoxamide: 59.67 g/L Phosphonic acid: 514.5 g/L Potassium phosphonate ^a : 753.5 g/L
Stability of test compound (expiry date):	31/10/2019	03/01/2020

^a Calculated considering the molecular weight of Phosphonic acid and monopotassium phosphonate.

Study design:

Six at harvest trials in grapes have been performed in Southern (Italy – 2 locations) and Northern Europe (Hungary – 1 location, Northern France – 1 location, Poland – 2 locations) in 2019 in pome fruits (3 in apples and 3 in pears).

Each trial consisted of three subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulations Zoxium 240 SC or GWN-10616 at the nominal application rates of 180 g a.s./ha with the last application at BBCH 69.

Only the trials treated with GWN-10616 have been considered for MRL setting and risk assessment.

Samples of apples and pears were taken at BBCH 87 in the at-harvest trials. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.2.2.

Methods:

The method for the determination of Zoxamide and its metabolites was successfully validated in study BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and the limit of detection (LOD) for Zoxamide and its metabolites are presented in Table A 38.

Table A 38: LOQ and LOD of the analytes

Analyte	LOD [mg/kg]	LOQ [mg/kg]
(R)-Zoxamide	0.0015	0.005
(S)-Zoxamide	0.0015	0.005
Zoxamide (sum)	0.003	0.01
(R)-RH-141288	0.0015	0.005
(S)-RH-141288	0.0015	0.005
RH-141288 (sum)	0.003	0.01
(R)-RH-150721	0.0015	0.005
(S)-RH-150721	0.0015	0.005
RH-150721 (sum)	0.003	0.01
RH-129151 (enantiomer A)*	0.0015	0.005
RH-129151 (enantiomer B)*	0.0015	0.005
RH-129151 (sum)*	0.003	0.01
RH-141452	0.003	0.01
RH-24549	0.003	0.01

*The enantiomers (R)-RH-129151 and (S)-RH-129151 are named as RH-129151 (A) and RH-129151 (B) since it was not clear yet what signal is related at each enantiomer since only the racemate standard was provided.

The maximum sampling to extraction interval at -18°C was 29 days for Zoxamide and its metabolites in apples and pears for trials performed in Northern and Southern Europe. The maximum extraction to quantification interval at 4°C was < 1 day for all metabolites. Procedural recoveries were handled and stored

in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %, except for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-141288 and (S)-141288 with recoveries > 110 %. Since the analytes were found in amounts lower than the LOQ, the analytical batch was accepted.

The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.005 or 0.01 mg/kg) and at 10x LOQ (0.05 or 0.1 mg/kg). The recoveries for Zoxamide and its metabolites were always within the range of 70 - 110 % of nominal (except for (R)-Zoxamide, (S)-Zoxamide, (R)-RH-141288 and (S)-141288 with recoveries > 110 % showing overall relative standard deviations of ≤ 20 %). Since the analytes were found in amounts lower than the LOQ, the analytical batch was accepted, and thus, the accuracy of the analytical method on the day of analysis was confirmed.

Results:

Table A 39: Summary of the study 2 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commod- ity/ Vari- ety	Date of 1.Sowing or planting 2.Flower- ing 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)														PHI (days)	Remarks
			g a.s./ ha	Wa- ter (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)- RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)- RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549	RH-141452		
ATA-19-39250 PL03	Pear/ Izolda	1. 21/03/2004	185 194	1016 1010	18.2 19.2	25/04/2019 01/05/2019	BBCH 69	Pear	<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	105	Zoxium 240 SC
62 404 Sa- marzewo, Wiekopolskie	(PYUCO)	2. from 12/04/2019 to 06/05/2019 3. 14/08/2019	173 172	1013 1004	17.1 17.1				nd	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	105
Poland (N-EU) 2019																								
ATA-19-39250 PL04	Pear/ Konfer- encja	1. 10/09/2018	187 185	512 507	36.5 36.5	26/04/2019 02/05/2019	BBCH 69	Pear	nd	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	116	Zoxium240 SC
96 521 Gizyczki, Łódzkie	(PYUCO)	2. from 12/04/2019 to 05/05/2019 3. 26/08/2019	169 170	494 495	34.3 34.3				<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	116
Poland (N-EU) 2019																								
ATA-19-39250 FR 05	Apple/ Fréquin Rouge	1. 01/03/2013	169 178	557 585	30.4 30.4	30/04/2019 06/05/2019	BBCH 68	Apple	<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	158	Zoxium 240 SC
80260 Saint Gratien Hauts de France	(MABSD)	2. from 24/04/2019 to 10/05/2019 3. 11/10/2019																						
Northern France (N-EU) 2019																								

Trial No./ Location/ EU zone/ Year	Commod- ity/ Vari- ety	Date of 1.Sowing or planting 2.Flower- ing 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)													PHI (days)	Remarks	
			g a.s./ ha	Wa- ter (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-41288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)	RH-24549			RH-141452
			167 172	587 603	28.5 28.5				<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	158	GWN-10616
ATA-19-39250 HU06 6795 Bordány Csongrád Country Hungary (N-EU) 2019	Apple/ Idared (MABSD)	1. more than 12 years 2. from 11/04/2019 to 29/04/2019 3. 28/08/2019 3. 10/	193 174	635 765	30.4 22.8	24/04/2019 29/04/2019	BBCH 69	Apple	<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	121	Zoxium 240 SC
			182 182	638 835	31.0 21.8				<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd

nd: below the limit of detection (< LOD)

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.2.2.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOQ: 0.005 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

LOD: 0.003 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOD: 0.0015 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

Table A 40: Summary of the study 2 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commod- ity/ Vari- ety	Date of 1.Sowing or planting 2.Flower- ing 3. Harvest	Application rate per treatment			Dates of treatment or no. of treat- ments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)												PHI (days)	De- tails on trial *	
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide –(R)	Zoxamide-(S)	Zoxamide (sum)	(R)- RH-50721	(S)-RH-150721	RH-150721 (sum)	(R)-RH-141288	(S)-RH-141288	RH-141288 (sum)	RH-129151-(A)	RH-129151-(B)	RH-129151-(sum)			RH-24549
(a)	(b)					(c)																(d)	(e)
ATA-19-39250 IT01 37050 Albaro (VR) Italy (S-EU) 2019	Apple/ Golden de- licious	1. 1977	187	513	36.4	17/04/2019	BBCH 69	Apple	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	140	Zoxium 240 SC
		2. from 27/03/2019 to 10/04/2019 3. 11/09/2019	189 180.2 182.0	516 524 532	36.4 34.4 34.2	24/04/2019			nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	140	GWN-10616
ATA-19-39250 IT02 46032 Castelbel- forte (MN) Italy (S-EU) 2019	Pear/ Abate	1. March 2009	185.1	712	26.0	09/04/2019	BBCH 67	Pear	<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	137	Zoxium 240 SC
		2. from 04/04/2019 to 25/04/2019 3. 30/08/2019	178.3 164.6 175.6	686 673 717	25.9 24.5 24.5	15/04/2019			<LOQ	<LOQ	<LOQ	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	137	GWN-10616

nd: below the limit of detection (< LOD)

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.2.2.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOQ: 0.005 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

LOD: 0.003 mg/kg for Zoxamide (sum), RH-150721 (sum), RH-129151 (sum), RH-141288 (sum), RH-141452, RH-24549

LOD: 0.0015 mg/kg for (R)-Zoxamide, (S)-Zoxamide, (R)- RH-150721, (S)-RH-150721, RH-129151 (A), RH-129151 (B), (R)- RH-141288, (S)-RH-141288

A 2.2.1.2.3 Study 3 (report No. SCC-G401T0409-21) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of the study was to determine residues of GWN-8030 (Zoxamide) and Potassium phosphonate [expressed in equivalent Phosphonic acid]. Residues of metabolite RH-141452 were also determined as total fraction (a hydrolysis step to release potentially matrix-conjugated compounds was necessary). Residues in apple RAC (whole fruits without stem) were analysed.</p> <p>The LC-MS/MS methods applied for the determination were as follows: of Zoxamide in apple AM-GLP-STUDY-21-53, of RH-141452 in apple AM-GLP-STUDY-21-54, and of Phosphonic acid AM-GLP-STUDY-21-55.</p> <p>The LOQs were 0.01 mg/kg. The relevant validation parameters as required.</p> <p>Note: some samples were taken during the field phase for a processing study SCC-G401T0409-21-P conducted in parallel to the residue study SCC-G401T0409-21.</p>
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Reference:	KCA 6.3.2/03
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES CULTIVATED IN OPEN FIELD CONDITIONS AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 4 DECLINE TRIALS AND 1 AT HARVEST TRIAL IN NORTHERN EUROPE, AND 4 DECLINE TRIALS IN SOUTHERN EUROPE IN 2021, Loriau, P., 2022, report No. SCC-G401T0409-21, Doc. No. 632-20005
Guideline(s):	ENV/JM/MONO(2007)17, SANTE/2020/12830 rev.1 (2021), SANTE/2019/12752, ENV/JM/MONO(2011)50/Rev1 (2016), OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Nine supervised residue trials (8 decline curve trials and 1 at harvest trial) in pome fruits have been performed in Southern (Greece, Spain, Italy, Southern France, 1 location each) and Northern Europe (Belgium, Germany, The Netherlands, Poland and Hungary, 1 location each) in 2021. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rate of 180 g Zoxamide/ha with last application at BBCH 69.

Samples of apples were taken at BBCH 75, BBCH 79, BBCH 85 and BBCH 87-89 in the decline curve trials and at BBCH 87 in the at-harvest trials. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.2.3.

Methods:

The method for the determination of Zoxamide was successfully validated in study GPL-STUDY-21-53 (“Validation of an analytical method for the determination of GWN-8030 in apples”, Doc. No. 432-003).

The method for the determination of RH-141452 was successfully validated in study GPL-STUDY-21-54 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in apples”, Doc. No. 432-005).

Both method validations are described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for Zoxamide and its metabolite RH-141452 is 0.01 mg/kg and the limit of detection (LOD) is 0.002 mg/kg.

The maximum sampling to extraction interval at -18°C was for the Northern trials 28 days for Zoxamide and its metabolite RH-141452 and for the Southern trials 30 days. The maximum extraction to quantification interval at 4°C was 3 days for Zoxamide and RH-141452. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The extract stability of Zoxamide and its metabolite RH-141452 in the final extracts kept at $5 \pm 3^\circ\text{C}$ for 3 days was successfully verified in the GLP study no. GPL-STUDY-21-53 and GPL-STUDY-21-54, respectively, in addition (see KCA 6.1/11 and KCA 6.1/12). Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 10x LOQ (0.1 mg/kg). The recoveries for Zoxamide and its metabolite RH-141452 were always within the range of 70 - 110 % of nominal showing overall relative standard deviations < 10 % for Zoxamide and < 13 % for RH-141452 and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 41: Summary of the study 3 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
(a)	(a)	(b)				(c)					(d)	(e)
SC C-G401T0409-21 G401-21F 4280 Merdorp Belgium (N-EU) 2021	Apple/ Jonagold (MABSD)	1. 2013 2. from 26/04/2021 to 10/05/2021 3. 14/09/2021	166 161	552 538	30.1 29.9	03/05/2021 10/05/2021	BBCH 69	Apple	0.0158 <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ	51 95 115 127	Normal commercial harvest
SC C-G401T0409-21 G402-21F 41472 Neuss Germany (N-EU) 2021	Apple/ Delbar (MABSD)	1. 2006 2. from 26/04/2021 to 17/05/2021 3. 15/09/2021	183 181	609 602	30.0 30.1	11/05/2021 17/05/2021	BBCH 69	Apple	<LOQ <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	59 78 94 121	Normal commercial harvest
SC C-G401T0409-21 G403-21F 4011 EX Zoelen The Netherlands (N-EU) 2021	Apple/ Elstar (MABSD)	1. 2005 2. 24/04/2021 to 18/05/2021 3. 20/09/2021	181 182	604 607	30.0 30.0	12/05/2021 18/05/2021	BBCH 69	Apple	<LOQ <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	59 78 97 125	Normal commercial harvest

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days) (d)	Details on trial (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
SC C-G401T0409-21 G404-21F 64-606 Wychowaniec Popowko) Poland (N-EU) 2021	Apple/ Boskop (MABSD)	1. 2019 2. 06/05/2021 to 19/05/2021 3. 30/09/2021	198 178	659 594	30.0 30.0	12/05/2021 19/05/2021	BBCH 69	Apple	<LOQ <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	61 96 124 134	Normal commercial harvest
SC C-G401T0409-21 G405-21F 6795 Bordany Hungary (N-EU) 2021	Apple/ Jonaprince (MABSD)	1. 2008 2. 26/04/2021 to 12/05/2021 3. 13/09/2021	178 190	593 632	30.0 30.1	05/05/2021 10/05/2021	BBCH 69	Apple	0.024	<LOQ	126	Normal commercial harvest

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.2.3.

- (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Zoxamide and RH-141452

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

Table A 42: Summary of the study 3 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days) (d)	Details on trial* (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
SC C-G401T0409-21 G406-21F 62370 Reynies Southern France (S-EU) 2021	Apple/ Golden Pink (MABSD)	1. 2008 2. from 02/04/2021 to 30/04/2021 3. 22/09/2021	179 178	597 593	30.0 30.0	24/04/2021 30/04/2021	BBCH 69	Apple	0.0215 <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	61 88 122 143	Normal commercial harvest
SC C-G401T0409-21 G407-21F 95019 Zafferana Et- nae Italy (S-EU) 2021	Apple/ Red delicious (MABSD)	1. 2002 2. from 26/04/2021 to 13/05/2021 3. 05/10/2021	175 175	680 681	25.7 25.7	06/05/2021 13/05/2021	BBCH 69	Apple	0.0323 0.0193 <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	81 120 138 145	Normal commercial harvest
SC C-G401T0409-21 G408-21F 26540 Alfaro Spain (S-EU) 2021	Apple/ Fuji (MABSD)	1. 2004 2. 30/03/2021 to 13/04/2021 3. 18/10/2021	187 169	726 659	25.8 25.6	07/04/2021 13/04/2021	BBCH 69	Apple	0.0359 <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	51 93 139 188	Normal commercial harvest
SC C-G401T0409-21 G409-21F 58300 Esovalta (Pella)) Greece (S-EU) 2021	Apple/ Granny Smith (MABSD)	1. 2012 2. 05/04/2021 to 20/04/2021 3. 24/09/2021	178 183	693 713	25.7 25.7	14/04/2021 21/04/2021	BBCH 69	Apple	0.0139 <LOQ <LOQ <LOQ	<LOQ <LOQ <LOQ <LOQ	77 111 140 156	Normal commercial harvest

Residue levels of Zoxamide and its metabolites are <LOQ in untreated samples.

* Residue data for Phosphonic acid are presented in A 2.2.3.2.3.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Zoxamide and RH-141452

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

A 2.2.1.2.4 Study 4 (report No. G105TO106-22) – Southern Europe

Comments of zRMS:	The study has been accepted, however the residue data are not relevant for CEU zone; it can be applied as supplementary. In determinations of zoxamide and phosphonic acid all mean recoveries at each fortification level were in the range of 70 – 110 % with relative standard deviations below 20 %.
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Reference:	KCA 6.3.2/04
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 2 DECLINE TRIALS IN SOUTHERN EUROPE IN 2022, Loriau, P., 2023, report No. SCC-G105TO106-22, Doc. No. 632-20006
Guideline(s):	ENV/JM/MONO(2007)17, SANTE/2019/12752, SANTE/2020/12830, rev. 1 (2021), OECD No. 509 (20219)
Deviations:	None
GLP:	Yes
Acceptability:	Yes, as supplementary

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Two supervised residue trials (2 decline curve trials) in pome fruits have been performed in Southern Europe (Greece, Italy, 1 location each) in 2022. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rate of 180 g Zoxamide/ha with last application at BBCH 69.

Samples of apples were taken at BBCH 75/77, BBCH 79, BBCH 85 and BBCH 87-89 in the decline curve trials. These supervised residue trials provide data relevant to conditions in the Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.2.4.

Methods:

The method for the determination of Zoxamide was successfully validated in study GPL-STUDY-21-53 (“Validation of an analytical method for the determination of GWN-8030 in apples”, Doc. No. 432-003).

The method for the determination of RH-141452 was successfully validated in study GPL-STUDY-21-54 (“Validation of an analytical method for the determination of RH-141452 (total fraction) in apples”, Doc. No. 432-005).

Both method validations are described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for Zoxamide and its metabolite RH-141452 is 0.01 mg/kg and the limit of detection (LOD) is 0.002 mg/kg.

The maximum sampling to extraction interval at -18°C was 20 days for Zoxamide and its metabolite RH-141452. The maximum extraction to quantification interval at $5 \pm 3^\circ\text{C}$ was < 1 day for Zoxamide and RH-141452. Thus, no storage stability data are needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The extract stability of Zoxamide and its metabolite RH-141452 in the final extracts kept at $5 \pm 3^\circ\text{C}$ for 3 days was successfully verified in the GLP study no. GPL-STUDY-21-53 and GPL-STUDY-21-54, respectively, in addition (see KCA 6.1/11 and KCA 6.1/12).

Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Results:

Table A 43: Summary of the study 4 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)		PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zoxamide	RH- 141452		
(a)	(a)	(b)				(c)					(d)	(e)
SCC-G105T0106-22 G105-22F 95039 Zafferana Italy (S-EU) 2022	Apple/ Golden Delici- ous (MABSD)	1. 1985 2. from 03/05/2022 to 17/05/2022 3. 30/09/2022	178 181	694 703	25.7 25.7	11/05/2022 17/05/2022	BBCH 69	Apple	0.0141 0.0137 <LOQ <u>0.0183</u>	nd nd nd <u>nd</u>	80 108 129 136	Normal commercial harvest
SCC-G105T0106-22 G106-22F 58002 Neos Agios Athanasios Greece (S-EU) 2022	Apple/ Super chief (MABSD)	1. 2012 2. 01/05/2022 to 10/05/2022 3. 20/09/2022	182 177	708 689	25.7 25.7	04/05/2022 10/05/2022	BBCH 69	Apple	<LOQ nd nd <u>nd</u>	nd nd nd <u>nd</u>	101 115 125 133	Normal commercial harvest

nd: below the limit of detection (< LOD)

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

* Residue data for Phosphonic acid are presented in A 2.2.3.2.4.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Zoxamide and RH-141452

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

A 2.2.1.3 Potatoes

Table A 44: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2017)	5	180	8	BBCH 20-80	28
cGAP EU (Art. 12)	Pending				
Intended cGAP (# 5)	3	150	7	BBCH 89	7

A 2.2.1.3.1 Study 1 (report No. GLP-21-14) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of this study was to determine the residues level of Zoxamide, its metabolites RH-141452 and RH-141455 and Potassium phosphonates (expressed as phosphonic acid and fosetyl equivalents) in potatoes after spray application of one of the following products: GWN-9790 EU (SC containing 240 g/L Zoxamide), GWN-10616 (SC containing 60 g/L Zoxamide and 755 g/L Potassium phosphonates (504 g/L Phosphorous acid)). The study trials were performed on potatoes in 8 different locations in France, Poland, Spain and Italy. The study included also processing samples taken from 3 trials to produce potato culls, potato waste and potato dried pulp sub-samples.</p> <p>The determination of zoxamide in potato tubers was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-50. Zoxamide was determined as racemate (no chiral column) based on BPL-STUDY-18-000085 method. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of total RH-141452 and RH-141455 (sum of the free fractions and the conjugated ones) in potato tuber was performed by LC-MS/MS method with a sample hydrolysis step validated in the concurrent study BPL-STUDY-18-000085. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of phosphonic acid (fosetyl equivalents) in potato tuber and processed commodities (potato culls, potato waste and potato dried pulp) was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-52. The extraction efficiency was not required to verify since this method was based on the extraction procedure which was used and accepted in the Fosetyl RAR.</p> <p>Procedural recovery values were obtained in parallel to the analyte measurements, confirming the robustness and repeatability of the method.</p>
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Reference:	KCA 6.3.3/01
Report:	GWN-8030, ITS METABOLITES AND PHOSPHONATES IN POTATOES AFTER THREE APPLICATIONS OF GWN-9790 EU AND GWN-10616 IN THE OPEN FIELD (NORTHERN AND SOUTHERN EU, 8 TRIALS, YEAR 2021), Longhi, D., 2023, report No. GLP-STUDY-21-14, Doc. No. 633-09001
Guideline(s):	OECD No. 509 (2009), 7029/VI/95 rev. 5 (1997), SANTE/2019/12752 (2019), SANTE/2020/12830 rev. 1 (2021), SANTE 2017/10632 rev. 3 (2017), OECD No. 508
Deviations:	None

GLP: Yes
Acceptability: Yes

Material, study design and methods

Material / test item:

Test material:	Zoxium 240 SC	GWN-10616
Formulation:	Suspension concentrate	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	ZA2701	P2102669001
Content of a.s. (actual):	Zoxamide: 239 g/L	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Manufacturing date:	27/01/2021	01/03/2021
Stability of test compound (expiry date):	At least 2 years from the production date.	At least 2 years from the production date.

Study design:

Four at harvest trials in potatoes have been performed in Southern (Italy – 1 location, Spain – 1 location) and Northern Europe (Northern France – 1 location, Poland – 1 location) in 2021.

Each trial consisted of two plots: 1 plot (control) was left untreated, and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rates of 180 g a.s./ha with an interval of 7 days and a PHI of 7 days. Four additional trials have been treated with three times with at the nominal application rate of 180 g a.s./ha with Zoxium 240 SC. These trials are indicated for completeness sake but are not considered for MRL application and risk assessment.

In at harvest trials, samples of potatoes were taken at 7 days after the last application. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone.

The residue data for Phosphonic acid are presented in A 2.2.3.3.1.

Methods:

The method for the determination of Zoxamide and its metabolites RH-141452 and RH-141455 was successfully validated in study GLP-STUDY-21-50 (“Validation of an analytical method for the determination of GWN-8030 in potato”, Doc. No. 432-016) and BPL-STUDY-18-000085 (“Validation of an analytical method to determine Zoxamide residues in grape, potato, tomato, cucumber, and onion raw agricultural and processed commodities”, Doc. No. 432-009).

The method validations are described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) the analytes Zoxamide and its metabolites RH-141452 and RH-141455 was 0.01 mg/kg in potato tubers. The limit of detection (LOD) was 0.002 mg/kg for Zoxamide and 0.003 mg/kg for RH-141452 and RH-141455.

The maximum sampling to extraction interval was 23 days for Zoxamide and 30 days for RH-141452 and RH-141455 in potato tubers at a temperature of $\leq -18^{\circ}\text{C}$. The final extracts in samples of RAC were analysed within 24 hours. Thus, a storage stability testing is not needed.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg) and at 10x LOQ (0.1 mg/kg). The mean recoveries for Zoxamide and its metabolites RH-141452 and RH-141455 were always within the range of 70 - 110 % of nominal showing overall relative standard deviations of < 15 % and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 45: Summary of the study 1 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days) (d)	Details on trial (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
TGT-21-49177 FR01 08190 - Sault Saint Remy Grand Est Northern France (N-EU) 2021	Potato/ Carolus (SOLTU)	1. 27/04/2021 2. from 18/06/2021 to 24/06/2021 3. 23/08/2021	170 183 184	382 411 413	44.6 44.6 44.6	02/08/2021 09/08/2021 16/08/2021	BBCH 48	Potato tubers	<LOQ	<LOQ	<LOQ	7	Zoxium 240 SC
TGT-21-49177 FR02 62860 - Inchy en Artois Hauts de France Northern France (N-EU) 2021	Potato/ Desire (SOLTU)	1. 30/04/2021 2. from 02/07/2021 to 22/07/2021 3. 25/08/2021	173 179 177	383 397 392	45.1 45.1 45.1	04/08/2021 11/08/2021 18/08/2021	BBCH 46	Potato tubers	<LOQ	<LOQ	<LOQ	7	GWN-10616
TGT-21-49177 PL03 63-220 - Parzew Wielkopolskie Poland (N-EU) 2021	Potato/ Gala (SOLTU)	1. 01/04/2021 2. from 28/06/2021 to 17/07/2021 3. 11/08/2021	183 177 174	307 297 292	59.7 59.7 59.7	21/07/2021 28/07/2021 04/08/2021	BBCH 48	Potato tubers	<LOQ	<LOQ	<LOQ	7	Zoxium 240 SC

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
(a)	(a)	(b)				(c)						(d)	(e)
TGT-21-49177 PL04 14-100 - Kajokow Warmińsko-Mazur- skie Poland (N-EU) 2021	Potato/ Ignacy (SOLTU)	1. 27/04/2021 2. from 28/06/2021 to 02/08/2021 3. 30/08/2021	180 180 182	307 307 310	58.8 58.8 58.8	09/08/2021 16/08/2021 23/08/2021	BBCH 48	Potato tubers	<LOQ	<LOQ	<LOQ	7	GWN-10616

Residue levels of Zoxamide and its metabolites RH-141452 and RH-141455 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.3.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide, RH-141452 and RH-141455

LOD: 0.002 mg/kg for Zoxamide, 0.003 mg/kg for RH-141452 and RH-141455

Table A 46: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
(a)	(a)	(b)				(c)						(d)	(e)
TGT-21-49177 ES05 11540 - Sanlucar de Barrameda Andalucia Spain (S-EU) 2021	Potato/ Spunta (SOLTU)	1. 20/04/2021 2. from 10/06/2021 to 28/06/2021 3. 19/07/2021	179 177 193	500 497 540	35.7 35.7 35.7	28/06/2021 05/07/2021 12/07/2021	BBCH 48	Potato tubers	<LOQ	<LOQ	<LOQ	7	Zoxium 240 SC
TGT-21-49177 ES06 11140 - Conil de la Frontera Andalucia Spain (S-EU) 2021	Potato/ Panamera (SOLTU)	1. 18/03/2021 2. from 15/06/2021 to 27/07/2021 3. 03/08/2021	193 176 174	547 500 493	35.3 35.3 35.3	13/07/2021 20/07/2021 27/07/2021	BBCH 48	Potato tubers	<LOQ	<LOQ	<LOQ	7	GWN-10616
TGT-21-49177 IT07 15053 - Castel- nuovo Scrivia Piemonte Italy (S-EU) 2021	Potato/ Vivaldi (SOLTU)	1. 23/03/2021 2. from 20/05/2021 to 10/06/2021 3. 16/08/2021	183 176 185	408 392 412	44.9 44.9 44.9	26/07/2021 02/08/2021 09/08/2021	BBCH 49	Potato tubers	<LOQ	<LOQ	<LOQ	7	Zoxium 240 SC

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
(a)	(a)	(b)				(c)						(d)	(e)
TGT-21-49177 IT08 46014 - Castel- lucchio Lombardy Italy (S-EU) 2021	Potato/ Hermes (SOLTU)	1. 26/02/2021 2. from 01/06/2021 to 20/06/2021 3. 29/07/2021	172 178 185	489 505 525	35.3 35.3 35.3	08/07/2021 15/07/2021 22/07/2021	BBCH 48/49	Potato tubers	<LOQ	<LOQ	<LOQ	7	GWN-10616

Residue levels of Zoxamide and its metabolites RH-141452 and RH-141455 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.3.1

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Zoxamide, RH-141452 and RH-141455

LOD: 0.002 mg/kg for Zoxamide, 0.003 mg/kg for RH-141452 and RH-141455

A 2.2.1.3.2 Study 2 (report No. IF22-06194195) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The study included 15 supervised residue trials conducted in Germany, Poland, Northern France, Italy, Spain and Greece during the 2022-2023 season. 8 trials were conducted as decline trials, 4 as harvest trials and 3 were conducted as processing trials. The spraying applications were performed at 19-23 DBH, 13-16 DBH and 6-8 DBH with a nominal rate of 2.5 L test item/ha.</p> <p>The purpose of the study in general was to determine the magnitude of the residues of zoxamide and its metabolites (RH-141452, RH-141455), and phosphonic acid in potato tubers after 3 foliar applications of GWN-10616 (60 g/L zoxamide and 755 g/L dipotassium phosphonates i.e. 500 g/L phosphonic acid). In addition, residues of phosphonic acid were also determined in whole potatoes prior to processing.</p> <p>The purpose of the processing phase was the generation of processed products of potato i.e. peeled potatoes, wet peel, microwaved/boiled potatoes, baked potatoes, fried potatoes, crisps, French fries, flakes, process waste, ensiled, starch, potato protein, dried pulp and canned potatoes, and then the determination of the residue levels of phosphonic acid to calculate the processing factors in the context of three foliar applications of GWN-10616.</p> <p>For all determinations 3 separate methods were used, validated in study IF23-06197316. Final determination was achieved by LC-MS/MS.</p> <p>To continuously prove the validity of the analytical method procedural recovery specimens were prepared by fortification of untreated specimen material. Fortification was performed with fortification solution containing Zoxamide, RH-141452, RH-141455 and phosphonic acid. The fortification levels were at LOQ and at least one higher level for each analyte in potato sample. Procedural recoveries were handled and stored in the same way and for the same time period as the analytical samples that have been prepared within the same analytical set.</p> <p>The storage period of deep-frozen samples intended for zoxamide determination ranged between 153 and 357 days, for RH-141452 and RH-141455 ranged between 196 and 401 days and for phosphonic acid between 115 and 321 days. The storage time of the deep-frozen processed fraction specimens ranged between 169 and 287 days.</p> <p>The study report is very detailed and included many amendments. However, they have no impact on the study. The relevant results are given below by the applicant.</p>
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Reference: KCA 6.3.3/02

Report: STUDY ON THE RESIDUE BEHAVIOUR OF GWN-8030 AND MDI-0074 IN POTATO AND ITS PROCESSED PRODUCTS AFTER TREATMENT WITH GWN-10616 UNDER FIELD CONDITIONS IN GERMANY, POLAND, NORTHERN FRANCE, ITALY, SPAIN AND GREECE, 2022, Gabriel, E.J., 2023, report No. IF22-06194195, Doc. No. 638-019

Guideline(s): 7029/VI/95 - rev.5, SANTE/2019/12752, OECD No. 509, OECD Series on Testing and Assessment, Number 96 (2008), OECD No. 508 (2008), ENV/JM/MONO(2007)17, SANTE/2020/12830 Rev. 1

Deviations: Yes, no impact on the study

GLP: Yes

Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Twelve supervised residue trials (8 decline curve trials and 4 at harvest trials) in potatoes have been performed in Southern (Greece, Spain, Italy, 2 locations each) and Northern Europe (Germany, Poland and Northern France, 2 location each) in 2022. In addition, three processing trials in Germany, Northern France and Italy have been conducted. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rate of 150 g Zoxamide/ha and a PHI of 7 days.

Samples of apples were taken at day 0, and 3 and 7 ± 1 days after last application in the decline curve trials and at day 0 and 7 ± 1 days after last application in the at-harvest trials and the processing trials. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Phosphonic acid are presented in A 2.2.3.3.2.

Methods:

The method for the determination of Zoxamide, RH-141452 and RH-141455 was successfully validated in study IF23-06197316 ("Validation of analytical methods for determination of GWN-8030, MDI-0043, MDI-0050 and MDI-0074 in potato matrices", Doc. No. 432-017).

The method validation is described in detail in Part B, Section 5 ("*Analytical Methods*").

The limit of quantification (LOQ) for Zoxamide and its metabolites RH-141452 and RH-141455 is 0.01 mg/kg and the limit of detection (LOD) is 0.002 mg/kg.

The maximum sampling to extraction interval at -18°C was for the Northern trials 351 days for Zoxamide and 395 days for its metabolites RH-141452 and RH-141455 and for the Southern trials 357 days for Zoxamide and 401 days for its metabolites. The maximum extraction to quantification interval at 4°C was 1 days for Zoxamide and for its RH-141452 and RH-141455. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 10x LOQ (0.1 mg/kg). The recoveries for Zoxamide and its metabolites RH-141452 and RH-141455 were always within the range of 70 - 110 % of nominal showing overall relative standard deviations ≤ 3.1 % for Zoxamide and ≤ 2.1 % for RH-141452 and ≤ 7.3 % for RH-141455 and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 47: Summary of the study 2 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days) (d)	Details on trial (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
IF22-06194195 22-00356-01 16835 Wulkow Germany 2022	Potato/ Euroflora	1. 12.04.2022 2. 07.06.- 12.07.2022 3. 19.09.2022	148 145 145	403 393 393	37 37 37	29.08.2022 05.09.2022 12.09.2022	46 47 48	Tuber	< 0.01	< 0.01	< 0.01	0 3 7	
IF22-06194195 22-00356-02 55-210 Krzelków Poland 2022	Potato/ Wineta	1. 26.04.2022 2. 10.06.- 22.06.2022 3. 05.08.2022	148 148 147	302 302 299	49 49 49	15.07.2022 21.07.2022 28.07.2022	48 48 48	Tuber	< 0.01	< 0.01	< 0.01	0 3 8	
IF22-06194195 22-00356-03 51110 Aumécourt- Northern France 2022	Potato/ Elodie	1. 18.05.2022 2. 07.07.- 11.07.2022 3. 16.08.2022	147 144 150	349 343 358	42 42 42	26.07.2022 02.08.2022 09.08.2022	45 47 47	Tuber	< 0.01	< 0.01	< 0.01	0 3 7	
IF22-06194195 22-00356-04 51130 Germinon Northern France 2022	Potato/ Elodie	1. 22.05.2022 2. 15.07.- 20.07.2022 3. 17.08.2022	153 144 152	313 293 311	49 49 49	26.07.2022 01.08.2022 09.08.2022	47 47 49	Tuber	< 0.01	< 0.01	< 0.01	0 3 8	
IF22-06194195 22-00356-09 79353 Bahlingen- Germany 2022	Potato/Ditta	1. 09.04.2022 2. 01.07.- 15.07.2022 3. 01.08.2022	153 151 150	416 412 408	37 37 37	11.07.2022 18.07.2022 25.07.2022	43 – 45 45 – 47 47	Tuber	0.01	< 0.01	< 0.01	0 7	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
(a)	(a)	(b)				(c)						(d)	(e)
IF22-06194195 22-00356-10 88-400 Żnin Poland 2022	Potato/Euro- starch	1. 23.04.2022 2. 15.06.- 03.07.2022 3. 06.09.2022	152 150 151	309 306 308	49 49 49	16.08.2022 23.08.2022 30.08.2022	44 45 48	Tuber	<u>< 0.01</u>	<u>< 0.01</u>	<u>< 0.01</u>	0 7	

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.3.2.

- (a) According to CODEX Classification / Guide
 - (b) Only if relevant
 - (c) Year must be indicated
 - (d) Days after last application (Label pre-harvest interval, PHI, underline)
 - (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
- LOD: 0.002 mg/kg for Zoxamide and RH-141452
LOQ: 0.01 mg/kg for Zoxamide and RH-141452

Table A 48: Summary of the study 2 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days) (d)	Details on trial (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
IF22-06194195 22-00356-05 20049 Caleppio di Settala Italy 2022	Potato/ Kenne- bec	1. 29.03.2022 2. nr 3. 26.07.2022	143 151 144	388 412 392	37 37 37	04.07.2022 12.07.2022 19.07.2022	41 43 – 45 47	Tuber	<u>≤ 0.01</u>	<u>≤ 0.01</u>	<u>≤ 0.01</u>	0 3 7	
IF22-06194195 22-00356-06 41510 Mareina del Alcor Spain 2022	Potato/Spunta	1. 01.10. 2022 2. na 3. 11.01.2023	146 145 144	396 394 392	37 37 37	19.12.2022 27.12.2022 04.01.2023	44 46 47	Tuber	<u>≤ 0.01</u>	<u>≤ 0.01</u>	<u>≤ 0.01</u>	0 3 7	
IF22-06194195 22-00356-07 29749 Almayate Spain 2022	Potato/Rudolph	1. 28.10.2022 2. mid Jan. 2023 till harvest 3. 07.02.2023	148 149 149	404 406 404	37 37 37	18.01.2023 24.01.2023 30.01.2023	43 47 47	Tuber	<u>≤ 0.01</u>	<u>≤ 0.01</u>	<u>≤ 0.01</u>	0 3 8	
IF22-06194195 22-00356-08 57006 Lakkia Greece 2022	Potato/Spunta	1. 17.08.2022 2. 10.10.- 20.10.2022 3. 09.11.2022	152 151 152	413 411 413	37 37 37	17.01.2022 24.10.2022 01.11.2022	39 43 45	Tuber	<u>≤ 0.01</u>	<u>≤ 0.01</u>	<u>≤ 0.01</u>	0 3 8	
IF22-06194195 22-00356-11 20059 Vimercate Italy 2022	Potato/Wizard	1. 08.04.2022 2. 30.05.- 15.06.2022 3. 26.07.2022	154 144 154	420 392 420	37 37 37	07.07.2022 13.07.2022 20.07.2022	41 45 47	Tuber	<u>≤ 0.01</u>	<u>≤ 0.01</u>	<u>≤ 0.01</u>	0 6	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)			PHI (days) (d)	Details on trial (e)
			g a.s./ ha	Water (L/ha)	g a.s./hL				Zox- amide	RH- 141452	RH- 141455		
IF22-06194195 22-00356-12 66033 Perithorio- Greece 2022	Potato/Electra	1. 10.04.2022 2. 05.08.- 15.08.2022 3. 29.08.2022	150 152 150	408 413 409	37 37 37	08.08.2022 16.08.2022 22.08.2022	39 43 46	Tuber	<u>≤ 0.01</u>			0 7	

Residue levels of Zoxamide and its metabolite RH-141452 are <LOQ in untreated samples.

Residue data for Phosphonic acid are presented in A 2.2.3.3.2.

na: not applicable

nr: not recorded

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Zoxamide and RH-141452

LOQ: 0.01 mg/kg for Zoxamide and RH-141452

A 2.2.2 Magnitude of residues in livestock

A 2.2.2.1 Livestock feeding studies

No new data are submitted in the framework of this application.

A 2.2.3 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.2.3.1 Distribution of the residue in peel/pulp

Not required for the intended uses. No new data were submitted in the framework of this application.

A 2.2.3.2 Processing studies on a core set of representative processes

A 2.2.3.2.1 Study 1 (report No. BPL-19-000058) – Grape processing (raisins)

<p>Comments of zRMS: Latvia</p>	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The study is acceptable.</i></p> <p><i>The objective of this study was the determination of the residues of Zoxamide and its metabolites in table grape and processed (raisin), coming from 1 decline trial (DEC) set in open field in Southern Europe (Italy). The trial was carried out performing 5 and 3 applications of the product ZOXIUM 240 SC (representing 180 g/ha zoxamide at each application). The sampling was carried out 0, 7, 14, 21 and 27 DALA.</i></p> <p><i>Max. storage interval between sampling and analysis:</i> <i>table grapes: 26 days</i> <i>raisins: 6-7 days</i></p> <p><i>The residue found in treated grape (berries) were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues 27 DALA were 0.537 and 0.430 mg/kg.</i> - <i>For RH-141452 (total fraction), the residues 27 DALA were 0.0133 mg/kg and below LOQ.</i> - <i>For other metabolites, the residues 27 DALA were below LOQ or not detectable.</i> - <i>Total residues were from 0.445 to 0.557 mg/kg</i> <p><i>The residue found in processed grapes (raisins) were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues 27 DALA were 0.596 mg/kg.</i> - <i>For RH-141288(sum), the residues 27 DALA were 0.0424 mg/kg.</i> - <i>For RH-129151 (sum), the residues 27 DALA were 0.0214 mg/kg.</i> - <i>For RH-141452 (total fraction), the residues 27 DALA were 0.0572 mg/kg.</i> - <i>Total residues were 0.683 mg/kg</i> <p><i>For other metabolites residues were below LOQ.</i></p> <p><i>Deviations:</i></p>
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	<i>The recovery values for the analytes (R)-RH-150721 and (S)-RH-150721 on recovery check samples BPL-SMPL-19-002114/NH RC1 and BPL-SMPL-19-002114/NH RC2 were found to be above the range allowed by the SANCO/3030/99 rev. 4 and SANCO/825/00 rev. 8.1 (70 - 110%). Since the recovery values were above the permitted range, the concentrations of the analytes under examination have been overestimated, what is regarded a worst-case. Since the analytes (R)-RH-150721 and (S)-RH-150721 were still detected at concentrations <LOQ, the overestimation was regarded to have no impact on the integrity of the results.</i>
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/01
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF TABLE GRAPE AND PROCESSED (RAISIN) IN OPEN FIELD FOLLOWING FIVE AND THREE APPLICATIONS OF THE FORMULATED PRODUCT GWN 9790 EU (SOUTH EUROPE – 1 TRIAL YEAR 2019), Longhi, D., 2020, report No. BPL-STUDY-19-000058, Doc. No. 638-012
Guideline(s):	SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev. 4 (2000)
Deviations:	None Yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test item:	GWN 9790 EU / Zoxium 240 SC
Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch #:	SIPAL7001
Content of active substance (actual):	Zoxamide: 242.9 g/L (R/S Zoxamide ratio: 50/50)
Manufacturing date:	31/10/2017
Stability of test compound (expiry date):	2 years from the production date if kept under proper storage conditions: 31/10/2019

Study design:

One decline trial in grapes (consisting of one processing plot and one residue plot) has been performed in Southern Europe (Italy) in 2019. In this section only the processing plot is summarised.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)- RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodity (raisins).

The trial consisted of 3 plots: 1 plot (control) was left untreated, another plot was treated either five (for processing) or three times (for residues) with Zoxium 240 SC at an application rate of 0.75 L/ha (180 g

a.s./ha) with an interval of 8 days and a PHI of 27 days. Samples were taken both for residues analysis and for processing. Samples were taken both for residues analysis and for processing.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions within 1 day after sampling. Processing of the samples (i.e., drying of grape fruits) started on the day of harvest. Specimens for residue analysis were frozen at -18°C within 24 hours after sampling and stored frozen until the analysis.

During processing, samples of raisins were collected. The processed specimens were frozen within 8 hours after sampling and kept frozen until analysis.

Procedure of the grapes processing into raisins is shown in Figure A 3.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009), which has been validated according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4. This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830. The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 49.

Table A 49 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to analysis interval at a temperature of $\leq -18^{\circ}\text{C}$ was 26 days for grape berries, and 6 - 7 days for raisins.

The final extracts in samples of RAC and processed commodities were analysed within 3 days for Zoxamide and its metabolites after storage at 4°C, except for RH-129151, which was analysed within 24 hours. The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

Nevertheless, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The procedural recoveries were in the range of 70 – 110 % for all analytes, except for grapes; 1 x LOQ and 10 x LOQ for (R)-RH-150721 (147.3 and 162.5 %, respectively) and (S)-RH-150721 (133.1 and 140.8 %, respectively), which results in an overestimation of the determined analytes. As the residue levels of both metabolites in grapes are below 0.01 mg/kg, the overestimation was regarded to have no impact on the integrity of the results.

Results:

The results of the processing study on grapes are summarised in Table A 50.

Table A 50: Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Zoxamide (sum)</i>							
Table grapes	0.537	27	Raisins	0.596	1.11	1	
<i>RH-150721 (sum)</i>							
Table grapes	<LOD (=0.003 mg/kg)	27	Raisins	0.424	-	0.753 (see Table A 64)	

* Processing factor

** Conversion factor

Calculated by the applicant

- 4 - Removal of the non-conforming berries as size for the table grape variety, and with injury and/or damage by fungal diseases and/or pests
- 5 - Weighing of the grapes sample just before the beginning of the processing
- 6 - Fractionation of the grapes bunches into small groups of berries
- 7 - Placement of the berries on single layers in a desiccator; the temperature of the flow of hot and dry air has to be within the range of 45-65 °C, depending on the type of grapes
- 8 - Monitoring of the drying phase (daily visual control of the product and possible analysis of the moisture content of the dry berries)
- 8 - Collection of the dry berries (raisin) when the moisture content is <18%
- 10 - Temporary storage of the raisin daily collected in a freezer until the end of the drying process
- 11 - Weighing of the total amount of raisin immediately after the last collection of dry berries
- 12 - Non-GLP analytical control of the finished product - raisin (moisture content)
- 13 - Packaging of the finished product (raisin)

Figure A 3: Procedure of the grapes processing into raisins

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC applied at a rate of 0.180 kg a.s./ha with an interval of 8 days and a PHI of 27 days. In grape bunches RAC prior to processing total residues of Zoxamide at a level of 0.537 mg/kg were found.

The processing factor is 1.11 for raisins from table grapes indicating that Zoxamide concentrate in this commodity slightly.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.2 Study 2 (report No. 18097-03R) – Grape processing (raisins)

<p><i>Comments of zRMS: Latvia</i></p>	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The study is acceptable.</i></p> <p><i>Residue specimens of grape bunches grown under cultural practice typical for grape in open field conditions and processed raisin specimens have been generated to determine the magnitude of residue of zoxamide and its metabolites. A single harvest trial was carried out on table grape raw agricultural commodity in open field conditions in SEU. Five foliar applications were made with a spray interval of 7-8 days. A single sampling was performed at commercial harvest (28 DALA).</i></p> <p><i>Max. Storage interval between sampling and analysis:</i> <i>table grapes: 481 days</i> <i>raisins: 484 days</i></p> <p><i>The residue found in treated grape (berries) were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues 28 DALA were 0.52 mg/kg.</i> - <i>For RH-141452 (total fraction), the residues 28 DALA were 0.011 mg/kg.</i> - <i>For other metabolites, the residues 28 DALA were below LOQ or not detectable.</i> - <i>Total residues were 0.537 mg/kg</i> <p><i>The residue found in processed grapes (raisins) were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues 28 DALA were 0.90 mg/kg.</i> - <i>For RH-141452 (total fraction), the residues 28 DALA were 0.043 mg/kg.</i> - <i>For RH-150721(sum), the residues 28 DALA were 0.056 mg/kg.</i> - <i>For RH-141288 (sum), the residues 28 DALA were 0.013 mg/kg.</i> - <i>Total residues were 0.965 mg/kg</i> <p><i>For other metabolites residues were below LOQ.</i></p> <p><i>Deviations</i></p> <p><i>Due to response instability in analytical sequence with both solvent and matrix standards, the matrix effects were not calculated. This deviation was regarded as not relevant for the integrity of the study since the analysis is performed with matrix matched standards.</i></p> <p><i>For some analyte / matrix combinations the mean recovery was >110 % but <120 %. Since recovery values of 70-120% for the here implied concentration ranges of 0.01-0.1 mg/kg are acceptable according to SANCO/825/00 rev. 8.1 (2010), this deviation from the study plan is regarded as not relevant.</i></p>
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/02
Report:	MAGNITUDE OF THE RESIDUES OF ZOXAMIDE IN TABLE GRAPE BUNCHES AND IN RAISINS PROCESSED FRACTION, FOLLOWING APPLICATIONS OF ZOXIUM 240 SC. ONE HARVEST TRIAL, SOUTHERN EUROPE – 2018, Maccaferri, L., 2020, report No. 18097-03R, Doc. No. 638-005
Guideline(s):	SANCO/825/00 rev. 8.1, SANCO/3029/99 rev. 4., 1607/VI/97 - rev. 2 (1999), 7029/VI/95 - rev. 5 (1997), 7035/VI/95 - rev. 5 (1997), 7525/VI/95 rev 10.2 (2016), OECD No. 508
Deviations:	None ; yes, no impact

GLP: Yes
Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test item:	GWN 9790 EU / Zoxium 240 SC
Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch #:	SIPAL7001
Content of active substance (actual):	Zoxamide: 242.9 g/L (R/S Zoxamide ratio: 50/50)
Manufacturing date:	31/10/2017
Stability of test compound (expiry date):	2 years from the production date: 31/10/2019

Study design:

One at harvest trial in grapes has been performed in the open field in Southern Europe (Italy) in 2018.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)- RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodity (raisins).

The trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated with 5 applications of Zoxium 240 SC at an application rate of 0.75 L/ha (180 g a.s./ha) with an interval of 7-8 days and a PHI of 28 days. Samples were taken both for residues analysis and for processing.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions within 8 hours after sampling. Processing of the samples (i.e. drying of grape fruits) started within 24 hours after harvest. Specimens for residues analysis were frozen at $\leq -18^{\circ}\text{C}$ within 8 hours after sampling in the field and remained deep frozen until extraction and analysis.

During processing, samples of raisins were collected stored frozen (-18°C) until analysis.

Procedure of the grapes processing into raisins is shown in Figure A 4.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009), which has been validated according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4. This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830.

The method has been re-validated within the analytical phase of the study.

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The concentration of Zoxamide (R, S and sum) and its metabolites RH-150721 (R, S and sum), RH-141288 (R, S and sum), RH-129151 (A and B), RH-24549 and RH-141452 were determined in grapes and/or processed specimens.

For metabolite RH-129151 the correlation between the absolute configuration of the enantiomer (R) or (S) and the corresponding chromatographic peaks was not available; therefore, the first eluted peak was assigned as RH-129151 (A) and the second eluted peak as RH-129151 (B).

The metabolite RH-141452, which was known to form conjugates with matrix molecules (e.g. sugars), was released in an additional hydrolysis step to establish total fractions in addition to the free fractions in the matrices.

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 51.

Table A 51 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to analysis interval at a temperature of $\leq -18^{\circ}\text{C}$ was 481 days for grape berries, and 484 days for raisins.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours after preparation. Thus, no storage stability data for the extracts are needed.

Nevertheless, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all analytes, except for free RH-141452 in grapes at 0.01 mg/kg and total RH-141452 in grapes at 0.1 mg/kg with mean recoveries slightly above 110 %, but which are still in accordance to SANTE/2020/12830, confirming the analytical method on the day of analysis.

Results:

The results of the processing study on grapes are summarised in Table A 52.

Table A 52. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Zoxamide (sum)</i>							
Table grapes	0.52	28	Raisins	0.90	1.73	1	
<i>RH-150721 (sum)</i>							
Table grapes	<LOQ (<0.01 mg/kg)	28	Raisins	0.056	-	0.066 (see Table A 64)	

* Processing factor

** Conversion factor

Calculated by the applicant

- 4 - Removal of the non-conforming berries as size for the table grapes variety, and with injury and/or damage from diseases and pests
- 5 - Weighing of the table grapes sample just before the beginning of the processing
- 6 - Fractionation of the grapes bunches into small groups of berries
- 7 - Placement of the berries on single layers in a desiccator; the temperature of the flow of hot and dry air has to be within the range of 45-65 °C, depending on the type of grapes
- 8 - Monitoring of the drying phase (daily visual control of the product and possible analysis of the moisture content of the dried berries)
- 9 - Collection of the dry berries (raisin) when the moisture content is <18%
- 10 – Temporary storage of the raisin daily collected in a freezer until the end of the drying process
- 11 - Weighing of the total amount of raisin immediately after the last collection of dry berries
- 12 - Non-GLP analytical control of the finished product - raisin (moisture content)
- 13 - Packaging of the finished product (raisin)

Figure A 4: Procedure of the grapes processing into raisins

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC applied at a rate of 0.180 kg a.s./ha with an interval of 7-8 days and a PHI of 28 days. In grape bunches RAC prior to processing total residues of Zoxamide at a level of 0.52 mg/kg were found.

The processing factor is 1.73 for raisins from table grapes indicating that Zoxamide concentrate in this commodity.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.3 Study 3 (report No. AB2-18-35355) – Grape processing (juice, must, wine)

<p>Comments of zRMS: Latvia</p>	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The study is acceptable.</i></p> <p><i>The objective of the study was to determine the magnitude of residues of zoxamide and its metabolites in raw agricultural commodity specimens of grapevine (RAC bunches) and processed fractions after five applications of Zoxium 240 SC. Target application rate was 0.75 L/ha (representing 180 g/ha zoxamide at each application) and target application timing was 60 (± 4), 52 (± 4), 44 (± 3), 36 (± 3) and 28 (± 2) days before harvest.</i></p> <p><i>The residue found in treated grapevine bunches were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues were 1.34 mg/kg just after the last application and residues decreased from 1.43 mg/kg to 1.03 mg/kg from 6 to 22 days after last application (DALA). At 28-30 DALA (commercial harvest) residues were at 0.94 mg/kg and 1.22 mg/kg.</i> - <i>For RH-141452 (total), the residues were below LOQ just after the last application and residues ranged from below LOQ to 0.016 mg/kg from 6 to 22 DALA. At 28-30 DALA (commercial harvest) residues were at 0.016 mg/kg and 0.021 mg/kg.</i> - <i>For RH-24549, no residues above LOQ were found for all samplings.</i> - <i>For RH-150721 (sum), the residues were 0.011 mg/kg just after the last application and below LOQ from 6 to 22 DALA. At 28-30 DALA (commercial harvest) residues were at below LOQ and 0.013 mg/kg.</i> - <i>For RH-129151 (sum), no residues above LOQ were found for all samplings in the trial DE01 and DE02.</i> - <i>For RH-141288 (sum), the residues were below LOQ just after the last application and 0.010 mg/kg at 6 DALA. For all other samplings no residues above LOQ were found.</i> - <i>Total residues for grape bunches were from 0.964 to 1.252 mg/kg.</i> <p><i>The residues found in treated processing specimens were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues were at 0.033 mg/kg 0.055 mg/kg in juice (pre-pasteurisation), at 0.47 mg/kg and 1.00 mg/kg in must, at 0.069 mg/kg and 0.18 mg/kg in young wine and at 0.052 mg/kg and 0.14 mg/kg in bottled wine. No residues above LOQ were found in juice (post-pasteurisation).</i> - <i>For RH-141452 (total), the residues were below LOQ and 0.01 mg/kg in must, below LOQ and 0.013 mg/kg in young wine and below LOQ and 0.013 mg/kg in bottled wine. No residues above LOQ were found in juice (pre- and post-pasteurisation).</i> - <i>For RH-24549, no residues above LOQ were found in any processed fraction.</i> - <i>For RH-150721 (sum), the residues were at 0.022 mg/kg 0.03 mg/kg in juice (post-pasteurisation), at 0.013 mg/kg and 0.031 mg/kg in young wine and at 0.025 mg/kg and 0.058 mg/kg in bottled wine. No residues above LOQ were found in juice (pre-pasteurisation) and must.</i> - <i>For RH-129151 (sum) and RH-141288 (sum), no residues above LOQ were found in any processed fraction.</i> - <i>Total residues for juice were 0.025 mg/kg</i> - <i>Total residues for must were from 0.485 to 1.020 mg/kg</i> - <i>Total residues for young wine were from 0.090 to 0.195 mg/kg</i>
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	<p>- Total residues for old wine were from 0.065 to 0.165 mg/kg</p> <p>Deviations</p> <p><i>Due to response instability in analytical sequence with both solvent and matrix standards, the matrix effects were not calculated. This deviation from the study plan is regarded to be not relevant for the integrity of the study since the analysis of residues has been performed by matrix matched standards.</i></p> <p><i>Mean recoveries below 70 % were found for RH-129151 A and RH-129151 B in young wine at 0.05 mg/L, while the corresponding mean recoveries at LOQ were in the range 70 - 110 %. However, as the residues of these analytes in young wine samples were found below the LOQ, the results were not corrected by taking into account a recovery factor.</i></p> <p><i>For analytes/matrices combination with mean recoveries > 110 %, the high recovery is probably due to the interconversion among the analytes, present at the same time and in the same concentration in the recovery extracts, while in the corresponding “real” samples this condition does not occur. The recovery factor was not applied to the residues results in order to remain the worst-case.</i></p>
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/03
Report:	MAGNITUDE OF THE RESIDUES OF ZOXAMIDE AND ITS METABOLITES IN GRAPEVINE (RAC BUNCHES) AND PROCESSED FRACTIONS, FOLLOWING APPLICATIONS OF ZOXIUM 240 SC, NORTHERN EUROPE – 2018, Peterek, S., 2020, report No. AB2-18-35355, Doc. No. 638-007
Guideline(s):	SANCO 7035/VI/95 rev.5 (1997), SANCO 7029/VI/95 rev.5 (1997), OECD TG 509 (2009), OECD TG 508 (2008), SANCO/3029/99, rev. 4 (2000), SANCO/825/00 rev.8.1 (2010)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test item:	GWN 9790 EU / Zoxium 240 SC
Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch No.	SIPAL7001
Content of active substance (actual):	Zoxamide: 239.47 g/L (R/S Zoxamide ratio: 50/50)
Date of the Certificate of Analysis (CoA)	05/06/2018
Stability of test compound (expiry date):	2 years after the CoA emission: 05/06/2020

Study design:

One harvest and one decline trial in grapes have been performed in Northern Europe (Germany) in 2018.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)-RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodities (filtered fresh and pasteurised juice and must, young and bottled red and white wine).

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated five times with each 0.75 L/ha GWN 9790 EU (180 g Zoxamide/ha) with an interval of 7-9 days and a PHI of 28 days and 30 days. The test item has been applied with airblast sprayers to reflect common agricultural practice. Samples were taken both for residues analysis and for processing.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions within 1 day after sampling. All other specimens for residue analysis were frozen down within 4 hours after sampling and kept frozen at $\leq -18^{\circ}\text{C}$ until analysis.

During processing, limpid juice samples (specimens collected before and after the pasteurization of filtered juice) and samples from red wine and white wine making (specimens collected after grapes crushing (must), wine filtration (young wine) and an ageing period of 2-3 months (bottled wine)) were collected. The processed specimens were frozen down and kept frozen until analysis.

Procedures about processing are presented in Figures A 5 to A 7.

Methods:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009). This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830. The method has been (re-)validated according to guidelines SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4 within the analytical phase of the study.

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The concentration of Zoxamide (R, S and sum) and its metabolites RH-150721 (R, S and sum), RH-141288 (R, S and sum), RH-129151 (A and B), RH-24549 and RH-141452 were determined in grapes and/or processed specimens.

For metabolite RH-129151 the correlation between the absolute configuration of the enantiomer (R) or (S) and the corresponding chromatographic peaks was not available; therefore, the first eluted peak was assigned as RH-129151 (A) and the second eluted peak as RH-129151 (B).

The metabolite RH-141452, which was known to form conjugates with matrix molecules (e.g. sugars), was released in an additional hydrolysis step to establish total fractions in addition to the free fractions in the matrices.

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 53:

Table A 53 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to extraction interval was 458 – 495 days.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours after preparation. Thus, no storage stability data for the extracts are needed. Nevertheless, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all analytes, except for the following analytes and matrices with mean recoveries slightly above 110 %, but which are still in accordance to SANTE/2020/12830, confirming the analytical method on the day of analysis.

- (S)-Zoxamide, (R)-RH 141288 and (S)-RH-141288 at 0.005 mg/kg in bottled wine
- (A) RH-129151 and (B) RH-129151 at 0.005 mg/kg in juice post-pasteurisation and bottled wine
- RH-24549 at 0.01 mg/L in juice post-pasteurisation, young wine and bottled wine; at 0.1 mg/kg in must, juice post-pasteurisation and bottled wine
- Free RH-141452 at 0.01 mg/kg in juice post-pasteurisation, bottled wine
- Free RH-141452 at 0.1 mg/kg in grapes, juice post-pasteurisation, bottled wine
- Total RH-141452: at 0.01 mg/kg in juice post-pasteurisation, in must and in young wine; at 0.1 mg/kg in grape, in juice post-pasteurisation and in young wine

For the following analytes and matrices the mean recovery was slightly below 70 %:

- (A) RH-129151 (64.7 %) and (B) RH-129151 (63.5 %) at 0.05 mg/kg in young wine

Results:

The results of the processing study on grapes are summarised in Table A 54.

Table A 54. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Resi- due (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/ Reference</i>
<i>Zoxamide (sum)</i>							
Wine grapes (red wine)	0.94	28	Limpid juice (pre-pasteurisation)	0.030	0.032	1	
			Limpid juice (post-pasteurisation)	<0.01	<0.01	1	
			Must	1.00	1.06	1	
			Young wine	0.07	0.074	1	
			Bottled wine	0.045	0.048	1	
<i>RH-150721 (sum)</i>							
Wine grapes (red wine)	<LOQ (=0.01 mg/kg)	28	Limpid juice (pre-pasteurisation)	<LOD*	-	0.33	For the calculation of the conversion factors: see Table A 64
			Limpid juice (post-pasteurisation)	0.02	-	2	
			Must	<LOQ	-	0.01	
			Young wine	0.013	-	0.35	
			Bottled wine	0.026	-	0.56	
<i>Zoxamide (sum)</i>							
Wine grapes (white wine)	1.22	30	Limpid juice (pre-pasteurisation)	0.051	0.042	1	
			Limpid juice (post-pasteurisation)	<0.01	<0.01	1	
			Must	0.47	0.385	1	
			Young wine	0.18	0.148	1	
			Bottled wine	0.15	0.123	1	
<i>RH-150721 (sum)</i>							
Wine grapes (red wine)	0.013	30	Limpid juice (pre-pasteurisation)	<0.01	-	0.196	For the calculation of the conversion factors: see Table A 64.
			Limpid juice (post-pasteurisation)	0.029	-	2.9	
			Must	<0.01	-	0.021	
			Young wine	0.033	-	0.18	
			Bottled wine	0.062	-	0.41	

* Processing factor; ** Conversion factor

Calculated by the applicant

- 4A - Weighing of the grapes sample immediately before the beginning of the processing
- 5A - Crushing-pressing of the grapes to obtain the raw must
- 6A - Non-GLP analytical assessment for the raw must (routine chemical analysis)
- 7A - Addition to the raw must of the following oenological products: preservative - sulphur dioxide, 100-120 mg/L; pectolytic enzyme, 1-5 g/100kg
- 8A - Settling of the raw must under conditions of low temperature (2-6°C) for minimum 24 hours (temperature monitoring)
- 9A - Racking of the must at the end of the settling process and visual control of its turbidity
- 10A - Possible further addition to the limpid must of the following oenological products: vegetable gelatine 10-30 g/100 kg; bentonite, 20-50 g/100kg
- 11A - Racking of the settled must at the end of the second settling process
- 12A - Filtration of the must by means of cellulose fibre layers and/or capsules of different materials and with different porosity of the membranes (up to 1.2 µm) in order to obtain a limpid/shiny product
- 13A - Packaging of limpid juice in suitable glass bottles
- 14A - Pasteurization of the packaged juice at 80-90°C for at least 30 min., monitoring the temperature of the product
- 15A - Cooling-down of the pasteurized juice (<40°C), monitoring the temperature of the product

Figure A 5: Procedure of the grapes processing into Limpid juice

- 4B - Weighing of the grapes sample just before the beginning of the processing
- 5B - Removal of the stalks and crushing of the grape
- 6B - Non-GLP analytical assessment for the raw must (routine chemical analysis)
- 7B - Addition to the raw must of following oenological products: preservative - sulphur dioxide 50-70 mg/L; yeasts nutrient - ammonium phosphate up to 180 mg/L of nitrogen (if necessary); selected yeasts for the must fermentation - suitable trade strain, 20-30 g/100Kg
- 8B - Placement of the sample in a thermo-conditioned room (15-20 °C) for the fermentation / peels maceration phases (temperature monitoring)
- 9B - Daily control of the fermentation process by means of a specific instrument: recording of sugar content ("Babo) and temperature (°C)
- 10B - Maceration of the peels in the must during the fermentation phase
- 11B - Separation of the solid part (macerated peels) from the liquid part (fermenting must) at 8-9° of alcohol - drawing-off phase (end of the peels maceration phase)
- 12B - Racking of the raw wine at the end of the fermentation process
- 13B - Non-GLP analytical assessment for the raw wine (routine chemical analysis)
- 14B - Addition to the raw wine of following oenological products: preservative - sulphur dioxide, up to 90-100 mg/L; clarifying agents - gelatine 5-10 g/100Kg and/or bentonite 30-40 g/100Kg
- 15B - Storage of the raw wine sample at -5°C for the tartaric stabilization - duration of the phase minimum 3 weeks (temperature monitoring)
- 16B - Racking of the stabilized wine at the end of the phase described above
- 17B - Non-GLP analytical assessment for the stabilized wine (routine chemical analysis)
- 18B - Addition of sulphur dioxide to the stabilized wine (maximum limit of 150 mg/L)
- 19B - Filtration of the wine by means of capsules of different materials and with different porosity of the membranes (up to 0.65 µm) to obtain a limpid/shiny product

Figure A 6: Procedure of the red wine-making

- 4C - Weighing of the grapes sample just before the beginning of the processing
- 5C - Crushing-pressing of the grapes to obtain the raw must
- 6C - Non-GLP analytical assessment for the raw must (routine chemical analysis)
- 7C - Addition to the raw must of following oenological products: preservative - sulphur dioxide, 50-60 mg/L; clarifying agents - potassium caseinate 5-10 g/100Kg and/or bentonite 20-30 g/100Kg; yeasts nutrient - ammonium phosphate, up to 180 mg/L of nitrogen (if necessary); selected yeasts for the must fermentation - suitable trade strain, 20-30 g/100Kg
- 8C - Placement of the must sample in a thermo-conditioned room (15-20°C) for the fermentation phase (temperature monitoring)
- 9C - Daily control of the fermentation process by means of a specific instrument (non-GLP assessment): recording of sugar content ("Babo) and temperature (°C)
- 10C - Racking of the raw wine at the end of the fermentation process
- 11C - Non-GLP analytical assessment for the raw wine (routine chemical analysis)
- 12C - Addition to the raw wine of following oenological products: preservative - sulphur dioxide, up to 90-100 mg/L; clarifying agents - potassium caseinate 5-20 g/100Kg and/or bentonite 20-30 g/100Kg
- 13C - Storage of the raw wine at -5°C for the tartaric stabilization - duration of the phase minimum 3 weeks (temperature monitoring)
- 14C - Racking of the stabilized wine at the end of the phase described above
- 15C - Non-GLP analytical assessment for the stabilized wine (routine chemical analysis)
- 16C - Addition of sulphur dioxide to the stabilized wine (maximum limit of 150 mg/L)
- 17C - Filtration of the wine by means of capsules of different materials and with different porosity of the membranes

Figure A 7: Procedure of the white wine making

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC applied at a rate of 0.180 kg a.s./ha with an interval of 7-9 days and a PHI of 28 days. In grape bunches RAC prior to processing total residues of Zoxamide ranged from 0.94 to 1.22 mg/kg.

The processing factor is 1.06 for must from red wine grapes indicates that Zoxamide concentrates in this processed commodity. The processing factors are 0.032, <0.01, 1.06, 0.074 and 0.048 for fresh juice (pre-pasteurisation), fresh juice (post-pasteurisation), must, young wine and bottled wine, respectively, from red wine grapes and 0.042, <0.01, 0.385, 0.148 and 0.123 for fresh juice (pre-pasteurisation), fresh juice (post-pasteurisation), must, young wine and bottled wine from white wine, respectively, which indicates that residues do not concentrate in these commodities.

The study is compliant to OECD No. 508, valid, scientifically acceptable, and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.4 Study 4 (report No. BPL-19-000041)/ Study 5 (report No. . B7284) – Grape processing (juice, wine)

<p>Comments of zRMS: Latvia</p>	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The studies are acceptable (Partially)</p> <p>The aim of these studies was to evaluate the magnitude of zoxamide and its metabolites in grapes (RAC bunches) and processed samples (grape juice and wine) after five foliar applications of the formulated product Zoxium 240 SC (240 g/L), at the rate of 0.75 L/ha (representing 180 g/ha zoxamide at each application). The applications were made at 7-8 days interval and the last application was performed 26 days before harvest for the trial B7284 CZ1 and 20 days before harvest for the trial B7284 BW1. Trials were conducted under field conditions at 2 sites in Northern Europe.</p> <p>Max. Storage interval between sampling and analysis: for grapes (berries): 605-643 days for juice: 604-632 days for young wine: 550-591 days for stored wine: 368-406 days</p> <p>The residue values in grape berries from trial no. B7284 BW1, are only available for a PHI of 20 days (this is outside the $\pm 25\%$ range), have not been taken into account for the consumer risk assessment.</p> <p>The residue found in treated grape (berries) were:</p> <ul style="list-style-type: none"> - For zoxamide (sum), the residues 20 DALA were between 0.805 mg/kg and 1.400 mg/kg and 26 DALA between 1.353 mg/kg and 1.620 mg/kg. - For RH-129151 (sum), the residues were from 0.0124 mg/kg to 0.0195 mg/kg 20 DALA, and from 0.0166 to 0.0192 mg/kg 26 DALA. - For RH-150721 (sum), RH-141288 (sum), RH-24549 and RH-141452, the residues were below LOQ or not detectable. - Total residues were 1.525 mg/kg. <p>The residues found in treated processing specimens were:</p> <ul style="list-style-type: none"> - For zoxamide (sum), the residues were at 0.0108 mg/kg (20 DALA) and 0.0284 mg/kg (26 DALA) in juice, at 0.0173 mg/kg (20 DALA) and 0.0508 mg/kg (26 DALA) in young wine, below LOQ (20 DALA) and 0.0503 mg/kg (26 DALA) in bottled wine. - For RH-150721 (sum), the residues were at 0.0106 mg/kg (20 DALA) and 0.0471 mg/kg (26 DALA) in juice, at 0.0135 mg/kg (20 DALA) and 0.0235 mg/kg (26 DALA) in young wine, at 0.0130 mg/kg (20 DALA) and 0.0448 mg/kg (26 DALA) in bottled wine. - Total residues for juice were 0.043 mg/kg - Total residues for young wine were 0.066 mg/kg - Total residues for old wine were 0.065 mg/kg <p>For RH-141288 (sum), RH-129151 (sum), RH-24549 and RH-141452, the residues were below LOQ or not detectable.</p> <p>Deviations: Deviation on trial B7284 BW1: Due to the mechanically harvest of the vineyard by</p>
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	<p><i>the farmer, the field principal investigator anticipated the sampling at harvest and performed is 20 days after last application instead of 28 (± 2) days after last application, as required by the study plan.</i></p> <p><i>Deviation on trial B7284 BW1: At sampling the minimum weight of 60 kg required for the specimens B7284 BW1/UH/P and B7284 BW1/TH/P was not reached; it was only 58.438 kg and 58.091 kg, respectively. This deviation has no impact on the integrity of the data since the weights were sufficient to perform the processing phase.</i></p> <p><i>Deviation on trial B7284 CZ1: The samples for processing were shipped under ambient conditions instead of under refrigerated conditions as required by the study plan due to organisational reason. However, the sanitary status of the specimens was good at receipt.</i></p> <p><i>The processing phase of trial B7284 BW1 was started 14 days after receipt of the samples instead of the next day after receipt at the samples, as required by the study plan. However, according to the analytical results, this deviation was regarded acceptable.</i></p>
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These studies have already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/04
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY WINE GRAPE (BERRIES) AND PROCESSED FRACTIONS (JUICE, WINE) FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (GWN-9790 EU) IN OPEN FIELD CONDITION 2 HARVEST TRIALS, NORTHERN EUROPE, YEAR 2017, Sala, A., 2020, report No. BPL-STUDY-19-000041, Doc. No. 638-010
Guideline(s):	SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev. 4 (2000)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes Partially

And

Reference:	KCA 6.5.3/05
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITE RH-150721 RESIDUES IN WINE GRAPE AND PROCESSED FRACTIONS FOLLOWING FIVE FOLIAR APPLICATIONS WITH ZOXIUM 240 SC UNDER FIELD CONDITIONS IN NORTHERN EUROPE IN 2017, Thomas-Delille, E., 2020, report No. B7284, Doc. No. 638-020
Guideline(s):	7029/VI/95 - rev.5, SANTE/2019/12752, OECD No. 509, OECD Series on Testing and Assessment, Number 96 (2008), OECD No. 508 (2008), ENV/JM/MONO(2007)17, SANTE/2020/12830 Rev. 1
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes Partially

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test item:	GWN 9790 EU / Zoxium 240 SC
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Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch #:	SB 2401
Content of active substance (actual):	Zoxamide 232 g/L (R/S Zoxamide ratio: 50/50)
Stability of test compound (expiry date):	April 2018

Study design:

Two at harvest trials in grapes have been performed in Northern Europe (Germany and Czech Republic) in 2017.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)- RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in processed commodities (juice, young and bottled red and white wine).

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated five times with each 0.75 L/ha GWN 9790 EU (180 g Zoxamide/ha) with an interval of 7-8 days and a PHI of 26 days and 20 days. Samples were taken both for residues analysis and for processing.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions within 1 day after sampling. All other specimens for residue analysis were frozen down within 4 hours after sampling and kept frozen at $\leq -18^{\circ}\text{C}$ until analysis.

During processing, juice samples (specimens collected after the pasteurization of clear juice) and samples wine after clarification (young wine) and an ageing period of 6 months (stored wine)) were collected. The processed specimens were frozen down and kept frozen until analysis.

Processing flowcharts are presented in Figures A 8 to A 10.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009). This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830.

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The concentration of Zoxamide (R, S and sum) and its metabolites RH-150721 (R, S and sum), RH-141288 (R, S and sum), RH-129151 (A and B), RH-24549 and RH-141452 were determined in grapes and/or processed specimens.

For metabolite RH-129151 the correlation between the absolute configuration of the enantiomer (R) or (S) and the corresponding chromatographic peaks was not available; therefore, the first eluted peak was assigned as RH-129151 (A) and the second eluted peak as RH-129151 (B).

The metabolite RH-141452, which was known to form conjugates with matrix molecules (e.g. sugars), was released in an additional hydrolysis step to establish total fractions in addition to the free fractions in the matrices.

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 55.

Table A 55 **LOQ and LOD of analytes**

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to extraction interval was 605 – 643 days for grape berries, 604 – 632 days for juice, 550-591 days for young wine and 368 – 406 days for stored wine.

The final extracts in samples of RAC and processed commodities were analysed within 3 days for Zoxamide and its metabolites after a storage at a temperature at 4°C and within 24 hours for RH-129151. The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

In addition, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all analytes, spiked at LOQ and 10x LOQ, covering the highest residue level, confirming the analytical method on the day of analysis.

Results:

The results of the processing study on grapes are summarised in Table A 56.

Table A 56. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed com- modity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/ Reference</i>
<i>Zoxamide (sum)</i>							
Wine grapes (red wine)	1.507 [#] 1.585 ^{##}	26	Juice (post-pasteuri- sation)	0.0284	0.019 [#] 0.018 ^{##}	1	
			Young wine	0.0508	0.034 [#] 0.032 ^{##}	1	
			Bottled wine	0.0503	0.033 [#] 0.032 ^{##}	1	
<i>RH-150721 (sum)</i>							
Wine grapes (red wine)	<LOQ (=0.01 mg/kg)	26	Juice (post-pasteuri- sation)	0.0471	-	1.754	For the calcu- lation of the conversion
			Young wine	0.0235	-	0.490	

Table A 56. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed com- modity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/ Reference</i>
<i>Zoxamide (sum)</i>							
			Bottled wine	0.0448	-	0.942	factors: see Table A 64
Wine grapes (white wine)	1.046 [#] 0.869 ^{##}	20	Juice (post-pasteuri- sation)	0.0108	0.010 [#] 0.012 ^{##}	1	
			Young wine	0.0173	0.016 [#] 0.020 ^{##}	1	
			Bottled wine	<0.01	<0.01 [#] <0.01 ^{##}	1	
<i>RH-150721 (sum)</i>							
Wine grapes (white wine)	<LOQ (=0.01 mg/kg)	20	Juice (post-pasteuri- sation)	0.0106	-	1.037	For the calcu- lation of the conversion factors: see Table A 64
			Young wine	0.0135	-	0.827	
			Bottled wine	0.0130	-	1.38	

* Processing factor

** Conversion factor

Mean of 3 analytical determinations were calculated: 2 grape samples analysed just before processing phase start and 1 grape sample from the field was analysed.

Mean of 2 grape samples analysed just before processing phase start was calculated.

Calculated by the applicant

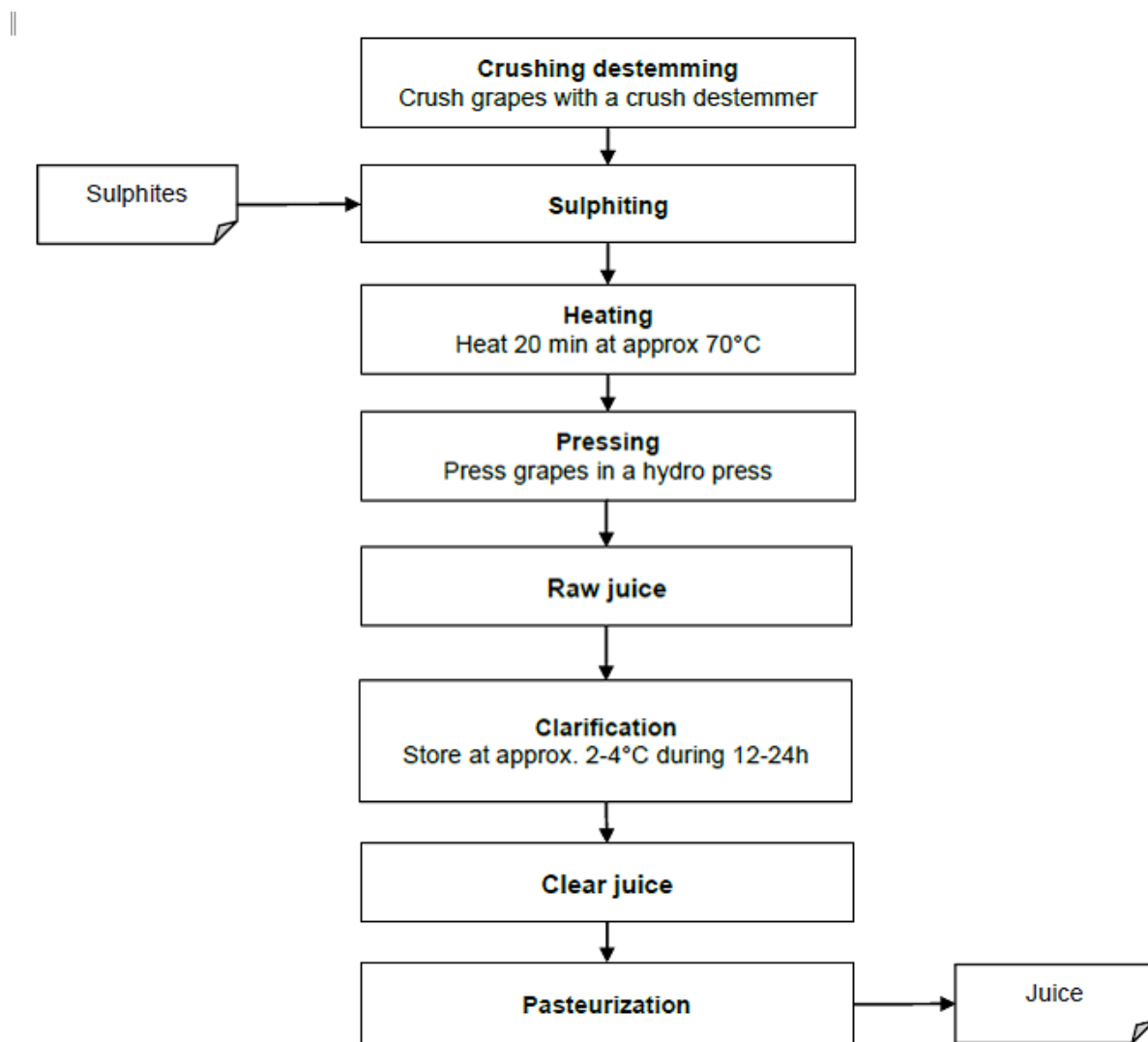


Figure A 8: Processing flowchart for white grape juice

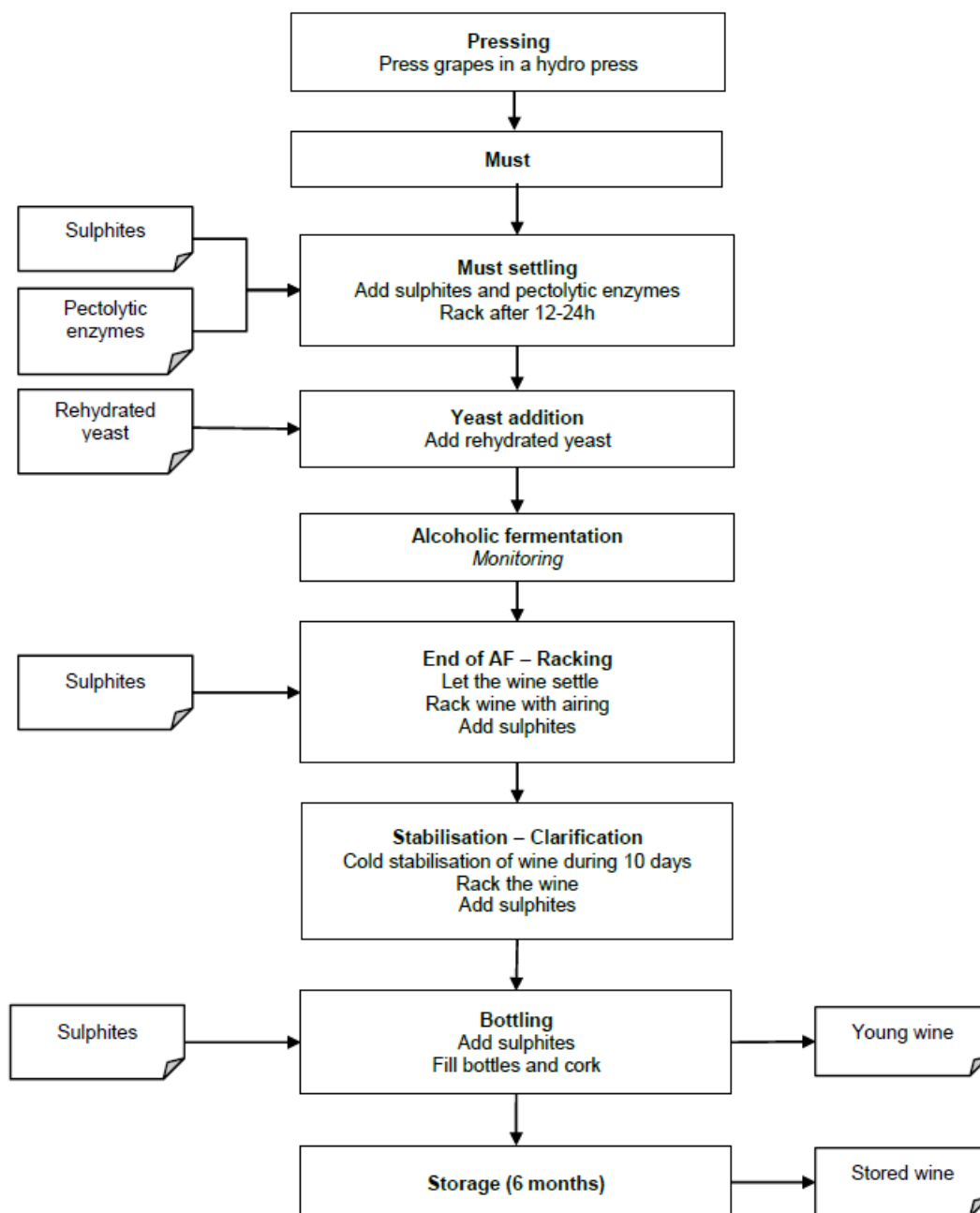


Figure A 9: Processing flowchart for white wine

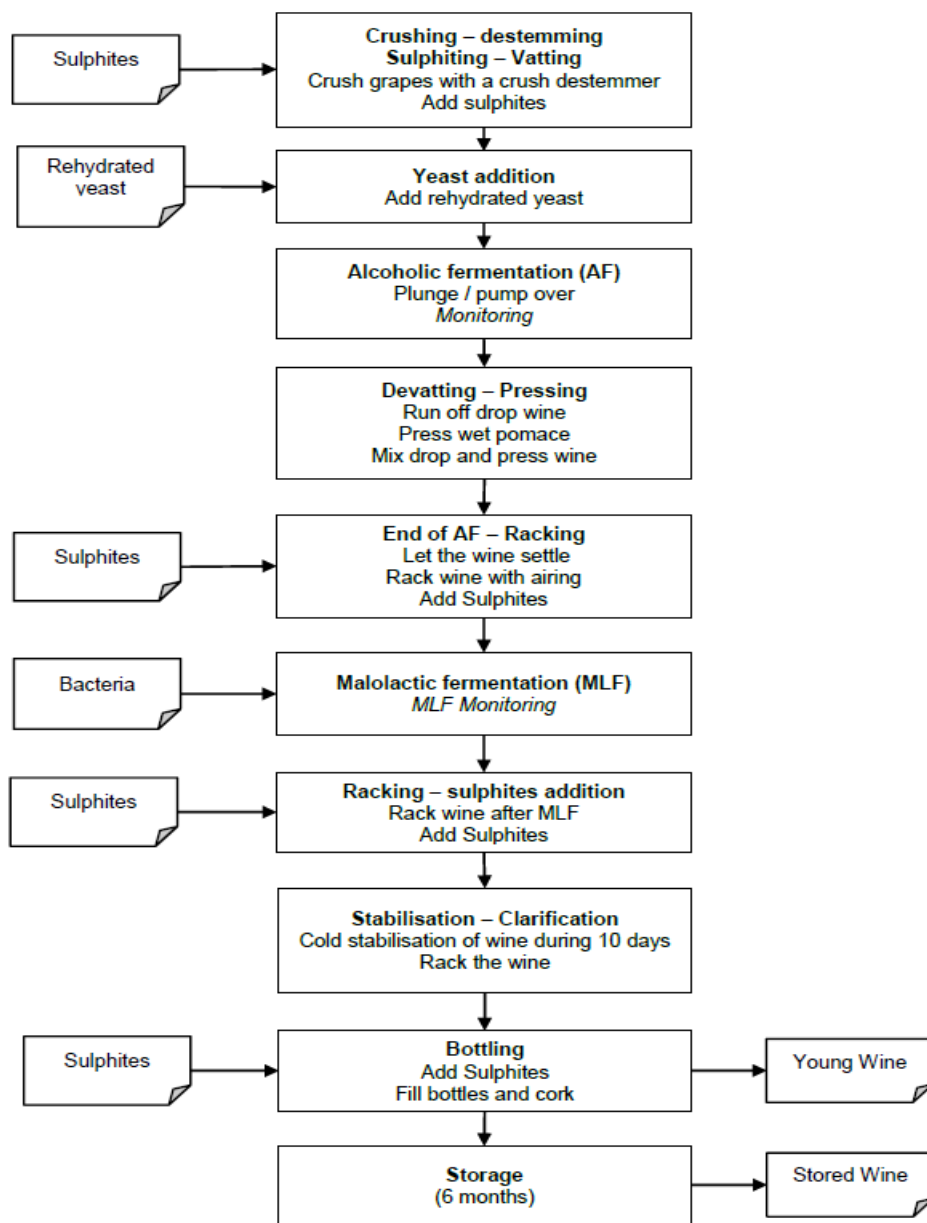


Figure A 10: Processing flowchart for red wine

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC applied at a nominal rate of 0.180 kg a.s./ha with an interval of 7-8 days and a PHI of 26 days and 20 days. In grape bunches RAC prior to processing total residues of Zoxamide ranged from 0.869/1.05 to 1.585/1.507 mg/kg.

The processing factors are 0.019/0.018, 0.034/0.032, 0.033/0.032 for juice (post-pasteurisation), young and bottled wine, respectively, from red wine grapes and 0.010/0.012, 0.016/0.020 and <0.01/<0.01 for juice (post-pasteurisation), young wine and bottled, respectively, from white wine grapes, indicating that residues do not concentrate in these commodities.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.5 Study 6 (report No. BPL-STUDY-19-000051)/ Study 7 (report No. BIU-005-17) – Grape processing (juice, wine)

<p>Comments of zRMS: Latvia</p>	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX and its affiliates in May 2021:</i></p> <p><i>The studies are acceptable.</i></p> <p><i>The aim of these studies was to evaluate the magnitude of zoxamide and its metabolites in grapes (RAC bunches) and processed samples (grape juice and wine) after five foliar applications of the formulated product Zoxium 240 SC (240 g/L), at the rate of 0.75 L/ha (representing 180 g/ha zoxamide at each application). Trials were conducted under field conditions at 2 sites in Southern Europe.</i></p> <p><i>Max. Storage interval between sampling and analysis:</i> <i>for grapes (barriers): 617-634 days</i> <i>for juice: 614-629 days</i> <i>for young wine: 480-482 days</i> <i>for bottled wine: 343-345 days</i></p> <p><i>The residue found in treated grape (berries) were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues 27 DALA were 1.406 mg/kg and 28 DALA 0.452 mg/kg.</i> - <i>For RH-141452 (total fraction), the residues 28 DALA were 0.0188 mg/kg.</i> - <i>For RH-150721 (sum), RH-141288 (sum), RH-129151 (sum) and RH-24549, the residues were below LOQ or not detectable.</i> <p><i>The residues found in treated processing specimens were:</i></p> <ul style="list-style-type: none"> - <i>For zoxamide (sum), the residues were at 0.116 mg/kg (27 DALA) and 0.183 mg/kg (28 DALA) in juice, below LOQ in young wine, and not detected in bottled wine.</i> - <i>For RH-150721 (sum), the residues were at 0.0577 mg/kg (27 DALA) and 0.0384 mg/kg (28 DALA) in young wine, at 0.0535 mg/kg (27 DALA) and 0.0309 mg/kg (28 DALA) in bottled wine.</i> - <i>For RH-24549, the residues were at 0.0204 mg/kg (27 DALA) and 0.0140 mg/kg (28 DALA) in bottled wine.</i> <p><i>For RH-141452, the residues were at 0.0121 mg/kg (28 DALA) in young wine and 0.0127 mg/kg (28 DALA) in bottled wine.</i></p> <p><i>Deviations</i></p> <p><i>Due to the dry season the bunches did not reach the quantity assumed by the study plan. As a result, from trial I/ZO17/GR01 only 26.5 and 24 kg were collected from the control and the treated plot, respectively, and from trial I/ZO17/GR02 only 20 and 22 kg from the control and the treated plot, respectively. However, these amounts were regarded sufficient for the intended processing phase and thus the study plan deviation regarded to not impact the integrity of the study.</i></p> <p><i>Due to the limited bunch weights the juice samples received from trial I/ZO17/GR02 were also reduced, but still sufficient for the following residue analysis. This deviation was therefore regarded to not impact the integrity of the study.</i></p> <p><i>The following recovery checks were slightly higher than the intended accuracy validation range (70-110%):</i></p>
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	<p>19/51/GJ/RC3/NH/2: 118.9% for analyte (S)-Zoxamide 19/51/GJ/RC1/NH: 118.8% for analyte (S)-RH-141288 19/51/GJ/RC2/NH: 113.6% for analyte (S)-RH-141288 19/51/WI/RC1/NH: 121.7% for analyte (R)-RH-150721 19/51/WI/RC2/NH: 118.5% for analyte (R)-RH-150721 19/51/WI/RC1/NH: 114.8% for analyte (S)-RH-150721 19/51/WI/RC2/NH: 124.4% for analyte (S)-RH-150721 However, these deviations were regarded to have no impact on the integrity of the study results since the recoveries reported above are slightly higher than maximum allowed (70-110%) – and therefore represent worst-case values.</p>
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These studies have already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/06
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY WINE GRAPE (BERRIES) AND PROCESSED FRACTIONS (JUICE, WINE) FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (GWN-9790 EU) IN OPEN FIELD CONDITION 2 HARVEST TRIALS, SOUTHERN EUROPE, YEAR 2017, Sala, A., 2020, report No. BPL-STUDY-19-000051, Doc. No. 638-011
Guideline(s):	SANCO/3029/99 rev. 4 (2000), SANCO/825/00 rev.8.1 (2010)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

And

Reference:	KCA 6.5.3/07
Report:	DETERMINATION OF ZOXAMIDE AND HIS METABOLITE RH-150721 RESIDUES IN RAW AGRICULTURAL COMMODITY RED GRAPES AND PROCESSED FRACTION FOLLOWING FIVE APPLICATIONS OF ZOXIUM 240 SC (ZOXAMIDE 240 G/L) (SOUTH EUROPE - 2 TRIALS YEAR 2017), Casalnuovo, L., 2020, report No. BIU-005-17, Doc. No. 638-021
Guideline(s):	SANCO/825/00 rev. 8.1 (2010), SANCO/3029/99, rev. 4 (2000), OECD No. 508 (2008), OECD No. 509 (2009)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test item:	GWN 9790 EU / Zoxium 240 SC
Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch No.	SB 2401
Content of active substance (actual):	Zoxamide: 232 g/L (R/S Zoxamide ratio: 50/50)

Stability of test compound (expiry date):	April 2018
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Study design:

Two at harvest trials in grapes have been performed in Southern Europe (Italy) in 2017.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)-RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodities (juice, young and bottled red wine).

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated five times with Zoxium 240 SC at an application rate of 0.75 L/ha (180 g Zoxamide/ha) with an interval of 7-9 days and a PHI of 27 and 28 days. The test item has been applied with a knapsack sprayer to reflect common agricultural practice. Samples were taken both for residues analysis and for processing.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions within 1 day after sampling. The processing started at the day of arrival.

All other specimens for residue analysis were frozen within 5 hours and 10 minutes after sampling. They were stored at $\leq -18^{\circ}\text{C}$ until analysis.

During processing, samples of juice (specimens collected before the pasteurization of clear juice) and samples wine after filtration (young wine) and an ageing period of 4-5 months (stored wine)) were collected. The processed specimens were frozen down and kept frozen until analysis.

Processing flow chart is presented in Figure A 11.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009). This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830.

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The concentration of Zoxamide (R, S and sum) and its metabolites RH-150721 (R, S and sum), RH-141288 (R, S and sum), RH-129151 (A and B), RH-24549 and RH-141452 were determined in grapes and/or processed specimens.

For metabolite RH-129151 the correlation between the absolute configuration of the enantiomer (R) or (S) and the corresponding chromatographic peaks was not available; therefore, the first eluted peak was assigned as RH-129151 (A) and the second eluted peak as RH-129151 (B).

The metabolite RH-141452, which was known to form conjugates with matrix molecules (e.g., sugars), was released in an additional hydrolysis step to establish total fractions in addition to the free fractions in the matrices.

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 57.

Table A 57 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003

Analyte	LOQ [mg/kg]	LOD [mg/kg]
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to extraction interval was 630-634 days for grape berries, 627-629 days for juice, 480-482 days for young wine and 343-345 days for stored wine.

The final extracts in samples of RAC and processed commodities were analysed within 3 days for Zoxamide and its metabolites after a storage at a temperature at 4°C and within 24 hours for RH-129151. The stability of the analytes Zoxamide, RH-150721 and RH-141452 in the final extracts kept at 4°C for 3 days was successfully verified in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

In addition, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The procedural recoveries were in the range of 70 – 110 % for all analytes, except for the following analytes and matrices with mean recoveries slightly above 110 %, confirming the analytical method on the day of analysis:

(S)-Zoxamide at 0.5 mg/kg in grape juice

(S)-RH-141288 at 0.005 mg/kg in grape juice and at 0.05 mg/kg in grape juice

(R)-RH-150721 at 0.005 mg/kg in wine and at 0.05 mg/kg in wine

(S)-RH-150721 at 0.005 mg/kg in wine and at 0.05 mg/kg in wine

Results:

The results of the processing study on grapes are summarised in Table A 58.

Processing factors were calculated for Zoxamide, according to the proposed residue definition for grapes.

Table A 58. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

RAC	Residues in RAC (mg/kg)	PHI (days)	Processed commodity	Residue (mg/kg)	PF*/#	CF**/#	Comments/Reference
Zoxamide (sum)							
Wine grapes (red wine)	1.406	27	Juice (post-pasteurisation)	0.116	0.083	1	
			Young wine	< 0.01	< 0.01	1	
			Bottled wine	< 0.01	< 0.01	1	
RH-150721 (sum)							
Wine grapes (red wine)	< LOQ (=0.01 mg/kg)	27	Juice (post-pasteurisation)	<LOD	-	0.086	For the calculation of the conversion factors: see Table A 64
			Young wine	0.0577	-	6.1	
			Bottled wine	0.0535	-	5.66	
Zoxamide (sum)							

Table A 58. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Zoxamide (sum)</i>							
Wine grapes (red wine)	0.452	28	Juice (post-pasteurisation)	0.183	0.405	1	
			Young wine	< 0.01	<0.02	1	
			Bottled wine	< 0.01	<0.02	1	
<i>RH-150721 (sum)</i>							
Wine grapes (red wine)	< LOQ (=0.01 mg/kg)	28	Juice (post-pasteurisation)	<LOD	-	0.055	For the calculation of the conversion factors: see Table A 64
			Young wine	0.0384	-	4.06	
			Bottled wine	0.0309	-	3.27	

* Processing factor

** Conversion factor

Calculated by the applicant

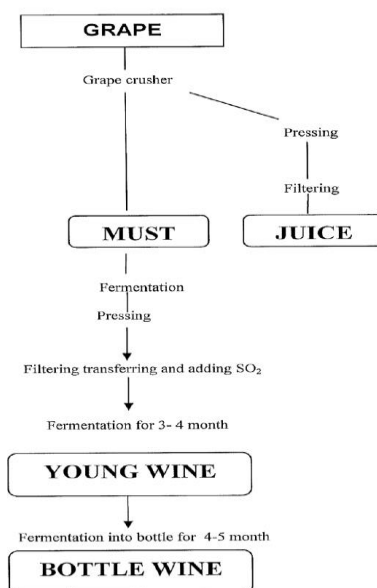


Figure A 11: Processing flowchart for juice and wine

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC applied at a rate of 0.180 kg a.s./ha with an interval of 7-9 days and a PHI of 27 and 28 days. In grape bunches RAC prior to processing total residues of Zoxamide ranged from 0.452 to 1.406 mg/kg.

The processing factors are 0.08 and 0.4 for grape juice from wine grapes indicating that Zoxamide do not concentrate in this commodity. In young and bottled wine, residues below LOQ were found for Zoxamide. Thus, a concentration of Zoxamide in these commodities can be excluded. Processing factors were <0.01 and <0.02 for young wine and bottled wine.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.6 Study 8 (report No. 17120-01R)/Study 9 (report No. 17120-01R)/Study 10 (report No. 19200-01R) – Grape processing (juice, must, wine)

Comments of zRMS: Latvia	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The residue values for grape berries and processed commodities from these trials have not been taken into account for the consumer risk assessment due to the fact that they are not covered by the available freezer storage stability data.</i></p> <p><i>Content of active substance were 60 g/L zoxamide:</i></p> <ul style="list-style-type: none"> - Total residues found in young wine were 0,027 mg/kg - Total residues found in old wine were 0,024 mg/kg <p><i>Content of active substance were 240 g/L zoxamide:</i></p> <ul style="list-style-type: none"> - Total residues found in young wine were 0,071 mg/kg - Total residues found in old wine were 0,060 mg/kg <p>Deviations:</p> <p><i>Due to response instability in analytical sequence with both solvent and matrix standards, the matrix effects were not calculated. This deviation was regarded as not relevant for the integrity of the study since the analysis is performed with matrix matched standards.</i></p> <p><i>For some analyte / matrix combinations the mean recovery was >110 % but ≤120 %. Since recovery values of 70-120% for the here implied concentration ranges of 0.01-0.1 mg/kg and below (0.005-0.05 mg/kg) are acceptable according to SANCO/825/00 rev. 8.1 (2010), this deviation from the study plan is regarded as not relevant.</i></p> <p><i>For the following analyte / matrix combination the mean recovery was < 70 %: (A) RH-129151 and (B) RH-129151 at 0.05 mg/L in young wine. However, the overall mean recovery for young wine (at different fortification levels) was 72.7 ±15.9 %.</i></p>
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These active substance related studies have already been provided to the RMS. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/8
Report:	DETERMINATION OF THE RESIDUES OF ZOXAMIDE AND / OR PHOSPHOROUS ACID IN TABLE GRAPE RAW AGRICULTURAL COMMODITY FOLLOWING FIVE APPLICATIONS OF GOW F 716, ZOXIUM 240 SC, GOW F 316 IN OPEN FIELD CONDITION (ONE HARVEST TRIAL, ITALY 2017), Maccaferri, L., 2019, report No. 17120-01R, Doc. No. 638-003
Guideline(s):	7525/VI/95 - rev. 10.1 (2015), 7029/VI/95 - rev. 5 (1997), 1607/VI/97 - rev. 2, (1999), SANCO/3029/99 rev. 4
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

And

Reference:	KCA 6.5.3/9
Report:	DETERMINATION OF THE RESIDUES OF ZOXAMIDE AND / OR PHOSPHOROUS ACID IN RAW AGRICULTURAL COMMODITY OF GRAPEVINE AND PROCESSED COMMODITIES (JUICE, MUST, YOUNG WINE AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF GOW F 716, ZOXIUM 240 SC, GOW F 316 IN OPEN FIELD CONDITION (ONE HARVEST TRIAL, ITALY 2017), Maccaferri, L., 2019, report No. 17120-02R, Doc. No. 638-004
Guideline(s):	SANCO/3029/99 rev. 4, 1607/VI/97 - rev. 2, (1999), 7029/VI/95 - rev. 5 (1997), 7035/VI/95 - rev. 5 (1997), PP 1/268(1), CEB method n. 143 (2011), 7525/VI/95 rev 10.1 (2015)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

And

Reference:	KCA 6.5.3/10
Report:	MAGNITUDE OF RESIDUES OF ZOXAMIDE ENANTIOMERS AND METABOLITES IN GRAPES AND PROCESSED COMMODITIES (JUICE, MUST, YOUNG WINE AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF GOW F 716 AND ZOXIUM 240 SC IN OPEN FIELD CONDITION (ITALY 2017), Maccaferri, L., 2020, report No. 19200-01R, Doc. No. 638-006
Guideline(s):	SANCO/3029/99, rev. 4 (2000), SANCO/825/00 rev.8.1 (2010)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test item	GWN 9790 EU / Zoxium 240 SC	GOW F 716
Formulation:		
CAS # (active substance):	Zoxamide:156052-68-5	Zoxamide: 156052-68-5 Dipotassium phosphonate (K ₂ HPO ₃): 13492-26-7 Monopotassium phosphonate (KH ₂ PO ₃): 13977-65-6
Lot/Batch No.	SB 2401	P1612669001
Content of active substance (actual):	Zoxamide: 232 g/L (R/S Zoxamide ratio: 50/50)	Zoxamide: 65.5 g/L (R/S Zoxamide ratio: 50/50) Phosphonic acid: 498 g/L Potassium phosphonate: 752 g/L
Stability of test compound (expiry date):	April 2018	December 2018

Study design:

One at harvest trial in grapes has been performed in Southern Europe (Italy) in 2019. In this section only the processing plots are summarised. The residue plots are summarised in A XXX.

The trial consisted of 3 plots: 1 plot (control) was left untreated, 2 plots for residues and 2 plots for processing were treated five times with Zoxium 240 SC (containing nominally 240 g/L Zoxamide) or GOW F 716 (containing nominally 60 g/L Zoxamide) at a rate 180 g a.s./ha with an interval of 8 ± 1 days and a PHI of 27 days. Samples were taken both for residues analysis and for processing.

One plot was also treated with GOW F 316 (containing nominally Dipotassium phosphonate and Monopotassium phosphonate at a nominal content of 504 g/L Phosphonic acid will not be summarised within this dRR.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)-RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodities (limpid juice, must, young wine and bottled wine).

The raw agricultural commodities (grape bunches) for processing were shipped under cold conditions (5 °C) to the processing site. They were delivered at the processing site in good conditions. Processing of the samples started within 24 hours after sampling. Specimens for residue analysis were frozen at -18°C within 3 hours (report 17120-02R) and 24 hours (report 17120-01R) after sampling and stored frozen until the analysis.

During processing, samples of limpid juice, must, young wine and bottled wine were collected. The processed specimens were frozen at -18°C after sampling and kept frozen until analysis.

Procedure of the grapes processing into limpid juice, must, young wine and bottled wine are shown in Figure A 12 to A 13.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009, which has been validated according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4. This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830.

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 59.

Table A 59 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to analysis interval at a temperature of $\leq -18^{\circ}\text{C}$ was 846 days for fruits and grape juice, 853 days for must, 743 days for young wine and 660 days for bottled wine.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours for Zoxamide and its metabolites. The final extracts in samples of RAC and processed commodities were analysed within 24 hours after preparation. Thus, no storage stability data for the extracts are needed. Nevertheless, procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all analytes, except for the following, but which are still in accordance to SANTE/2020/12830, confirming the analytical method on the day of analysis.

- (S)-Zoxamide, (R)-RH 141288 and (S)-RH-141288 at 0.005 mg/kg in bottled wine
- (A) RH-129151 and (B) RH-129151 at 0.005 mg/kg in limpid juice and bottled wine
- RH-24549 at 0.01 mg/L in limpid juice, young wine and bottled wine; at 0.1 mg/kg in must, limpid juice and bottled wine
- Free RH-141452 at 0.01 mg/kg in limpid juice, bottled wine
- Free RH-141452 at 0.1 mg/kg in limpid juice, bottled wine
- Total RH-141452 at 0.01 mg/kg in limpid juice, must and in young wine; at 0.1 mg/kg in grape, in limpid juice and young wine

For the following analytes and matrices the mean recovery was slightly below 70 %:

- (A) RH-129151 (64.7 %) and (B) RH-129151 (63.5 %) at 0.05 mg/kg in young wine

Results:

The results of the processing study on grapes are summarised in Table A 60.

Table A 60. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed com- modity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/ Reference</i>
<i>Zoxamide (sum)</i>							
Wine grapes (white wine)/ Zoxium 240 SC	0.260	27	Limpid juice	<0.01	<0.04	1	
			Must	0.22	0.846	1	
			Young wine	0.051	0.196	1	
			Bottled wine	0.043	0.165	1	
<i>RH-150721 (sum)</i>							
Wine grapes (white wine)/ Zoxium 240 SC	<LOQ (=0.01 mg/kg)	27	Limpid juice	0.010	-	1.06	For the calcu- lation of the conversion factors: see Table A 64
			Must	<LOD	-	0.045	
			Young wine	0.015	-	0.312	
			Bottled wine	0.021	-	0.512	
<i>Zoxamide (sum)</i>							
Wine grapes	0.22	27	Limpid juice	0.014	0.063	1	
			Must	0.24	1.09	1	
			Young wine	<0.01	<0.05	1	

Table A 60. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Zoxamide (sum)</i>							
(white wine)/ GOW F 716			Bottled wine	<0.01	<0.05	1	
<i>RH-150721 (sum)</i>							
Wine grapes (white wine)/ GOW F 716	<LOQ (=0.01 mg/kg)	27	Limpid juice	<LOQ	-	0.714	For the calculation of the conversion factors: see Table A 64
			Must	<LOD	-	0.042	
			Young wine	0.018	-	3.27	
			Bottled wine	0.027	-	6.09	

* Processing factor
** Conversion factor
Calculated by the applicant

4A - Weighing of the grapes sample immediately before the beginning of the processing
5A - Crushing-pressing of the grapes to obtain the raw must
6A – Non-GLP analytical assessment of the raw must
7A - Addition to the raw must of the following oenological products: preservative - sulphur dioxide, 100-120 mg/L; pectolytic enzyme, 2-5 g/100 kg
8A - Settling of the raw must under conditions of low temperature (2-5°C) for minimum 24 hours (temperature monitoring)
9A - Racking of the must at the end of settling process and visual control of its turbidity
10A – Possible further addition to the limpid must of the following oenological products: vegetable gelatine 10-30 g/100 kg; bentonite, 20-50 g/100 kg
11A - Racking of the settled must at the end of the second settling process
12A - Filtration of must by means of cartridges with different porosity (up to 1.2 µm) in order to obtain a limpid product
13A - Packaging of limpid juice into glass bottles
14A - Pasteurization of the packaged juice at 80-90°C for at least 30 min., monitoring the temperature of the product
15A - Cooling-down of the pasteurized juice (<40°C), monitoring the temperature of product

Figure A 12: Procedure of the grapes processing into limpid juice

- 4B - Weighing of grapes sample just before the beginning of the processing
- 5B - Crushing-pressing of the grapes to obtain the must
- 6B - Non-GLP analytical assessment of the must
- 7B - Addition to the raw must of following oenological products: preservative - sulphur dioxide, 50-60 mg/L; clarifying agents – potassium caseinate 5-10 g/100 Kg and/or bentonite 20-30 g/100 Kg; yeasts nutrient – ammonium sulphate, up to 180 mg/L of nitrogen (if necessary); selected yeasts for must fermentation – suitable trade strain, 20-30 g/100 Kg
- 8B - Placement of the must sample in a thermo-conditioned room (15-20°C) for the fermentation phase (temperature monitoring)
- 9B - Daily control of the fermentation process by means of a specific instrument (non-GLP assessment): recording of sugar content (°Babo) and temperature (°C)
- 10B - Racking of the raw wine at the end of fermentation process
- 11B - Non-GLP analytical assessment of the raw wine
- 12B - Addition to the raw wine of following oenological products: preservative - sulphur dioxide, up to 90-100 mg/L; clarifying agents – potassium caseinate 5-20 g/100 Kg and/or bentonite 20-30 g/100 Kg
- 13B - Storage of the raw wine at -5° C for the tartaric stabilization – duration of the phase minimum 3 weeks (temperature monitoring)
- 14B - Racking of the stabilized wine at the end of the phase described above
- 15B - Non-GLP analytical assessment of the stabilized wine
- 16B - Addition of sulphur dioxide to the stabilized wine (maximum limit of 150 mg/L)
- 17B - Filtration of the wine by means of cartridges with different porosity (up to 0.65 µm) to obtain a limpid/shiny product

Figure A 13: Procedure of the grapes processing into white wine making

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with GWN 9790 EU / Zoxium 240 SC and GOW F 716 applied at a rate of 0.180 kg a.s./ha with an interval of 8 ± 1 days and a PHI of 27 days. In grape bunches RAC prior to processing total residues of Zoxamide at a level of 0.24 mg/kg (GWN 9790 EU / Zoxium 240 SC) and 0.22 mg/kg (GOW F 716) were found.

The processing factors are $<0.04/0.063$ for limpid juice, $0.846/1.09$ for must, $0.196/<0.05$ for young wine and $0.165/<0.05$ for bottled wine from table grapes indicating that Zoxamide do not concentrate in these commodities.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.7 Study 11 (report No. GLP-STUDY-20-30) – Grape processing (wine)

<p>Comments of zRMS: Latvia</p>	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The study is acceptable.</p> <p>The concentration of zoxamide and its metabolites were determined in grapes and/or processed specimens. Trials performed under Northern and Southern European conditions. Each trial was carried out performing 3 applications of three different plant protection products at their worst-case application rates. Foliar applications were made with a spray with an interval of 7 days and a last application 28 days before harvest.</p> <p>Max. Storage interval between sampling and analysis: Wine grape: 67-69 days Wine: 14 days</p> <p>The residue found in treated grape bunches were (use pattern 3x180 g ai/ha):</p>
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	<ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.218 to 0.905 mg/kg. - For RH-141452, the residue 28 DALA were 0.01 mg/kg - Total residues were from 0.233 to 0.920 mg/kg <p>The residue found in treated grape bunches were (use pattern 3x150 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.123 to 0.644 mg/kg. - For RH-141452, the residue 28 DALA were 0.0192 mg/kg - Total residues were from 0.123 to 0.673 mg/kg <p>The residue found in processed grapes (wine) were:</p> <ul style="list-style-type: none"> - For zoxamide, the residues were from 0.01 to 0.0181 mg/kg - For RH-141452, the residue were 0.01 mg/kg - Total residues were from 0.025 to 0.033 mg/kg <p>For other metabolites residues were below LOQ.</p> <p>Deviations:</p> <p>Trial: CMN-20-44059 ES06: The application 1 has been done with BBCH 81 instead of BBCH 15-79, as required in the Study Plan. This happens because at the moment of the signature of the SP the field crop was at BBCH 81. Deviation with an impact. However, all the applications doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 ES06: The application 2 has been done 6 days after application 1, instead of 7-8 days - as required in the Study Plan. This was due to logistic adjustments and the field technician didn't realise that -1 day was not allowed. However, this deviation has no impact on the study integrity since it is still in the $\pm 25\%$ range for the application pattern intended with a 7-8 days interval.</p> <p>Trial: CMN-20-44059 FR02: Sampling S2 (1 DALA) and S3 (3 DALA) were not done. This occurred because the field technician didn't take into account the amendment no. 1 to the study plan. Deviation with an impact: the trial CMN-44059 FR02 (DEC-2) has become a decline with 5 points instead of 7 points.</p> <p>Trial: CMN-20-44059 HU04: Samples collected at 0 DALA were delivered at ambient temperature instead of refrigerated condition (with dry ice) to the Field Test Site. This occurred due to an error of the field technician that didn't correctly understand the study plan. An impact on the integrity of the study was not assumed since the maximum period between sampling and freezing in the Test Site Facility was about 6 hours (at ambient temperature).</p> <p>Trial: CMN-20-44059 FR01: Dry ice was not used during the samplings since the field was close to the Test Site Facility. No impact on the integrity of the study assumed since the maximum period between sampling in the field and freezing in the Test Site Facility was only 3 hours for sampling 1, 1 hour 20 minutes for sampling 2, 1 hour 15 minutes for sampling 3, 1 hour 5 minutes for sampling 4, 2 hours 5 minutes for sampling 5, and 1 hour 5 minutes for sampling 6 – each at ambient temperature. The max. storage period for sampling 7 was 2 hours 35 minutes (samples cooled with frozen gel packs).</p> <p>Trial: CMN-20-44059 FR02: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact on the integrity of the study since the maximum period between sampling in the field and freezing in the Test Site Facility was 1 hour for sampling 1, 15 minutes for sampling 4, 20 minutes for sampling 5, 15 minutes for sampling 6, and 16 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR05: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact since the maximum period between sampling in the field and freezing in the Test Site Facility was 3 hours for sampling 1, 2 hours for sampling 4, 2 hours 30 minutes for sampling 5, 2 hours and 35 minutes for sampling 6, and 4 hours and 30 minutes for sampling 7 – samples always cooled with frozen gel packs.</p>
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	<p>Trial: CMN-20-44059 FR01: Chemical products with phosphonate and zoxamide as active ingredients were applied in the field where the trial was set up. No impact on the results for zoxamide and metabolites. Impact for the results for phosphonic acid on grape bunches, for which residues in the untreated control samples were detected, and on wine at 0 and 28 DALA, for which residues in the untreated control sample were detected. This was solved by subtracting the untreated control sample results from the treated ones.</p> <p>Trials CMN-20-44059 FR02, FR05, HU03, HU04, ES07: The applications have not been done between BBCH 15 and BBCH 79 as requested in the Study Plan. This deviation had an impact on the study. However, the application pattern and doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 FR05: The farmer contract was signed on 04/08/2020, one day after the first application (03/08/2020). This deviation was regarded to have no impact on the study.</p> <p>During the processing phase the mustimeter 34MUS16 was used from 28/08/2020 to 03/09/2020 (checking date) without writing the procedural check before its use (the technician did the check but forgot to write it). This deviation was regarded to have no impact on the study.</p> <p>On 08/10/2020, during the processing phase, the MLF (malolactic fermentation) was recorded as finished on the data sheets (fermentation and red wine) and k metabisulphite was added on 09/10/2020 (at the end of MLF), but the chromatography paper spots of malic acid were present for U2. Therefore, k metabisulphite seems to be added on the wine U2 before the end of the malolactic fermentation. This deviation was regarded to have no impact on the residues in the wine, but only on its organoleptic properties.</p> <p>During the analytical phase the recovery check results at LOQ level for the analytes RH-141288 and RH-150721 were outside ($> 110\%$) the permitted range (70-110%) for analytical batch 200902 GLP-STUDY-20-30. This deviation was solved with no impact on the study results since the samples in this sequence were re-extracted and analysed, discarding the previously obtained values.</p> <p>During the analysis of analytical batch 200904-GLP-STUDY-20-30 the calibration point at level 3 (Uva L3) in the calibration curve had a response higher than expected. It has therefore not been considered to establish the actual calibration line. This deviation was regarded to have no impact on the study results since the calibration range related to the method validation has not altered, and 4 points were regarded enough to derivate a suitable calibration line with $r^2 > 0.99$.</p> <p>During the analysis of the analytical batch 200924-GLP-STUDY-20-30 (4C N) the calibration check results for (R)-RH-141288 (147.3%), (S)-RH-141288 (266.7%) and (S)-RH-150721 (141.3%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200924-GLP-STUDY-20-30 (4C B) the calibration check results of (R)-RH-150721 (136.9%) and (S)-RH-150721 (132.4%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200929-GLP-STUDY-20-30 the calibration check results of (R)-RH-150721 (126.8%) and (S)-RH-150721 (135.5%) were outside the acceptable range (80% - 120%). However, this deviation was regarded to have no impact on the study integrity. All samples analysed in these batches have concentrations $< \text{LOQ}$ for the mentioned analytes, therefore the calibration check value could not affect the reported values anyway. This deviation was solved with no impact on the study.</p> <p>During the analysis of the analytical batch 201117 GLP-STUDY-20-30 (white wine) a calibration point for the analyte (S)-RH-141288 had a lower response in comparison to the regression line. This value was excluded and a 4-point calibrating line was established. As a consequence, since the recovery check at $10 \times \text{LOQ}$ (GLP-SMPL-20-724/NH RC2) was no longer inside the calibration range, it could not be evaluated. However; this deviation was regarded to have no impact on the</p>
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	<p>study results since 4 calibration points were regarded enough for the interpolation and to quantify the analyte content in the samples.</p> <p>The untreated white wine sample GLP-SMPL-20-724 was found to contain 1.61 mg/kg of phosphonic acid, presumably due to the reasons explained in deviation 8. External standard calibration solutions for white wine were initially established using the extracts of this sample. This resulted in a signal higher than 30% of the LOQ. They were therefore invalidated. The batch was therefore re-elaborated using the calibration curve for red wine that was analysed in the same analytical sequence, recalculating the recovery check values by subtracting the values of the untreated (white wine) sample. This deviation was regarded to have no impact on the study results since the calibration using matrix-matched reference solution in red wine has the same matrix effect on phosphonic acid than white wine (demonstrated by the recovery check and by a standard at level L3 prepared in white wine).</p>
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This study has already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	See KCA 6.3.1/01
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF WINE GRAPE AND PROCESSED (WINE) IN OPEN FIELD FOLLOWING THREE APPLICATIONS OF THE FORMULATED PRODUCTS GWN-9823, GWN-10616, GWN-10392 (NORTH AND SOUTH EUROPE – 7 trials year 2020, Longhi, D., 2021, report No. GLP-STUDY-20-30, Doc. No. 638-015
Guideline(s):	SANTE/2020/12830, Rev.1 (2021), SANCO/825/00 rev.8.1 (2010), OECD No. 508, OECD No. 509, SANCO/3029/99 rev. 4 (2000), 7029/VI/95 rev.5 (1997)
Deviations:	None ; no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN 10616	GWN 10392 /Tempio	GWN 9823 WG / Reboot
Formulation:	Suspension concentrates (SC)	Suspension concentrates (SC)	Water dispersible granules (WG)
CAS # (active substance):	Zoxamide: 156052-68-5 Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2	Zoxamide: 156052-68-5 Benalaxyl-M: 98243-83-5	Zoxamide: 156052-68-5 Cymoxanil: 57966-95-7
Lot/Batch #:	2006669001	N062/20	GSOL9018
Content of active substance (actual):	Zoxamide: 64 g/L Phosphonic acid: 505 g/L Potassium phosphonate: 762.6 g/L	Zoxamide: 232.1 g/L Benalaxyl-m: 158.4 g/L	Non GLP certificate (data taken forward to calculate actual application rates): Zoxamide: 33.1 % w/w Cymoxanil 33.0 % w/w GLP certificate: Zoxamide: 32.6 % w/w or 326.0 g/kg Cymoxanil: 33.8 % w/w or 337.7 g/kg
Manufacturing date:	15 June 2020	-	January 2019
Stability of test compound (expiry date):	2 years from manufacturing:	18.08.2022	January 2021 (non-GLP certificate) 15 December 2022 (GLP certificate)

Study design:

Five decline cure trials and two at harvest trials (5 residue and 2 processing trials) in grapes has been performed in Southern (Southern France, Spain) and Northern Europe (Hungary, Northern France) in 2020.

Each trial was carried out performing 3 applications of three different plant protection products (GWN-10616, a SC formulation containing Zoxamide and potassium phosphonates; GWN-10392 / Tempio®, a SC formulation containing Zoxamide and benalaxyl-m; GWN-9823 / Reboot®, a WG formulation containing Zoxamide and cymoxanil) at their worst-case application rates (180 g/ha Zoxamide and 1500 g/ha of potassium phosphonates, 157.5 g/ha of Zoxamide and 105 g/ha of benalaxyl-m, and 148.5 g/ha of Zoxamide and 148.5 g/ha of cymoxanil, respectively) with an interval of 7 days and a PHI of 28 days. The test items were applied with airblast sprayers to reflect common agricultural practice. Untreated control plots were included in each trial.

In this section only the processing trials, which were treated with GWN-10616 are summarised. The residue trials are summarised in A 2.1.3.1.1.

The magnitude of residues of Zoxamide (sum R and S isomers) and its metabolites RH-141452 (free and total), RH-150721 (as sum of R and S isomers), (R)-RH-150721, (S)-RH-150721, RH-129151 (as sum of R and S isomers), (R)-RH-129151, (S)-RH-129151, RH-24549, RH-141288 (as sum of R and S isomers), (R)-RH-141288 and (S)-RH-141288 have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodity (bottled red and white wine).

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions. Processing of the samples started on the day of delivery, within 24 hours after sampling. Specimens for residue analysis were frozen at -18°C within 6 hours after sampling and stored frozen until the analysis.

During processing, samples of bottled red and white wine were collected. The processed specimens were frozen at -18°C after sampling and kept frozen until analysis.

Procedure flowcharts of the grapes processing into young wine are shown in Figure A 14 and A 15.

Method:

The method validation was performed within the study report BPL-STUDY-18-000085 (Doc. No. 432-009), which has been validated according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4. This method can be considered also to be validated in compliance to the requirements of SANTE/2020/12830. The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) and limit of detection (LOD) for the analytes Zoxamide and its metabolites RH-141452, RH-150721, RH-24549, RH-129151 and RH-141288 are presented in Table A 61.

Table A 61 LOQ and LOD of analytes

Analyte	LOQ [mg/kg]	LOD [mg/kg]
Zoxamide (sum)	0.01	0.003
(R)-Zoxamide	0.005	0.0015
(S)-Zoxamide	0.005	0.0015
RH-141452 (free)	0.01	0.003
RH-141452 (total)	0.01	0.003
RH-150721 (sum)	0.01	0.003
(R)-RH-150721	0.005	0.0015
(S)-RH-150721	0.005	0.0015
RH-129151 (sum)	0.01	0.003
RH-129151 (A)	0.005	0.0015
RH-129151 (B)	0.005	0.0015
RH-141288 (sum)	0.01	0.003
(R)-RH-141288	0.005	0.0015
(S)-RH-141288	0.005	0.0015
RH-24549	0.01	0.003

The maximum sampling to extraction interval for Zoxamide and its metabolites at a temperature of $\leq -18^{\circ}\text{C}$ was max. 69 days for fruits and max. 14 days for bottled wine. The final extracts in samples of RAC and processed commodities were analysed within 3 days for Zoxamide and its metabolites after storage at 4°C , except for RH-129151, which was analysed within 24 hours. The stability of the analytes in the final extracts kept at 4°C for 3 days was successfully verified for all metabolites relevant for residue definition the in the GLP study no. BPL-STUDY-18-000085 (please refer to KCA 6.1/07).

Procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all analytes.

Results:

The results of the processing study on grapes are summarised in Table A 62.

Table A 62. Residue data from grape processing study with Zoxamide (sum) and RH-150721 (sum)

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Zoxamide (sum)</i>							
Wine grapes (white wine)/ GWN-10616	0.331	28	Bottled wine	0.0181	0.05	1	
<i>RH-150721 (sum)</i>							
Wine grapes (white wine)/ GWN-10616	<LOD (=0.003 mg/kg)	28	Bottled wine	0.0117	-	0.685	For the calculation of the conversion factors: see Table A 64
<i>Zoxamide (sum)</i>							
Wine grapes (red wine)/ GWN-10616	0.231	28	Bottled wine	< 0.01	<0.04	1	
<i>RH-150721 (sum)</i>							
Wine grapes (red wine)/ GWN-10616	< LOD (=0.003 mg/kg)	28	Bottled wine	< LOQ (=0.01 mg/kg)	-	0.046	For the calculation of the conversion factors: see Table A 64

* Processing factor

** Conversion factor

Calculated by the applicant

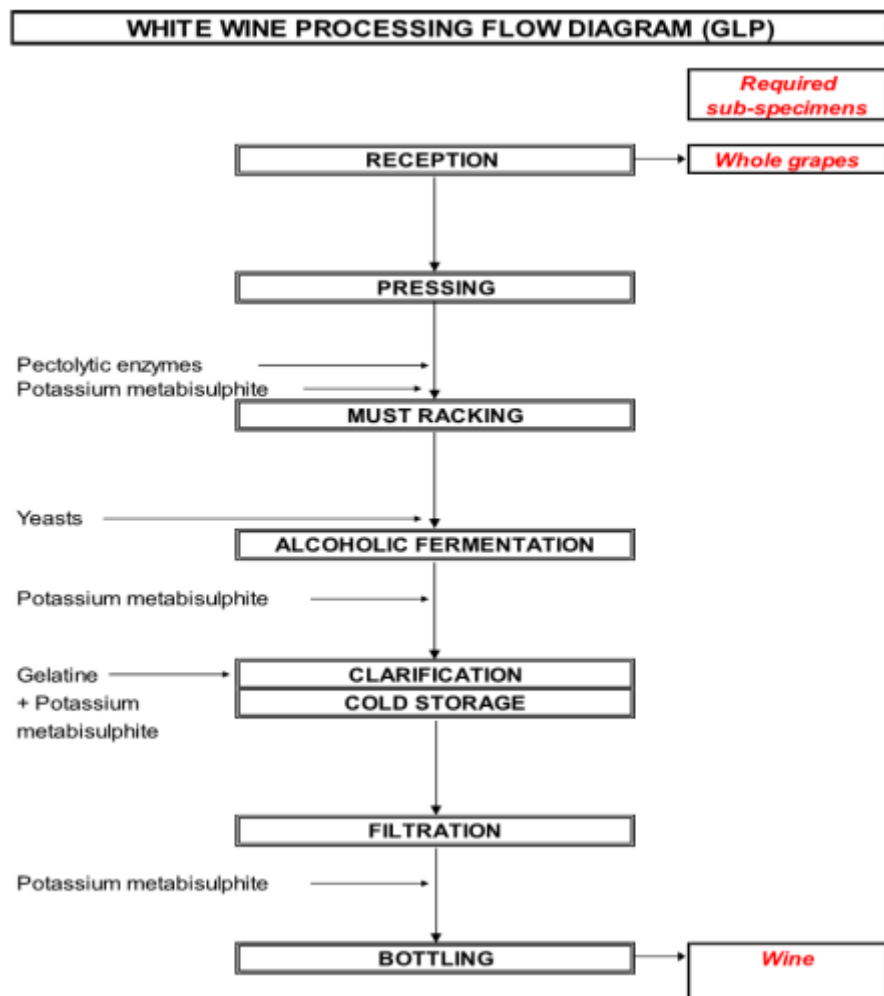


Figure A 14: Procedure of the grapes processing into white wine making

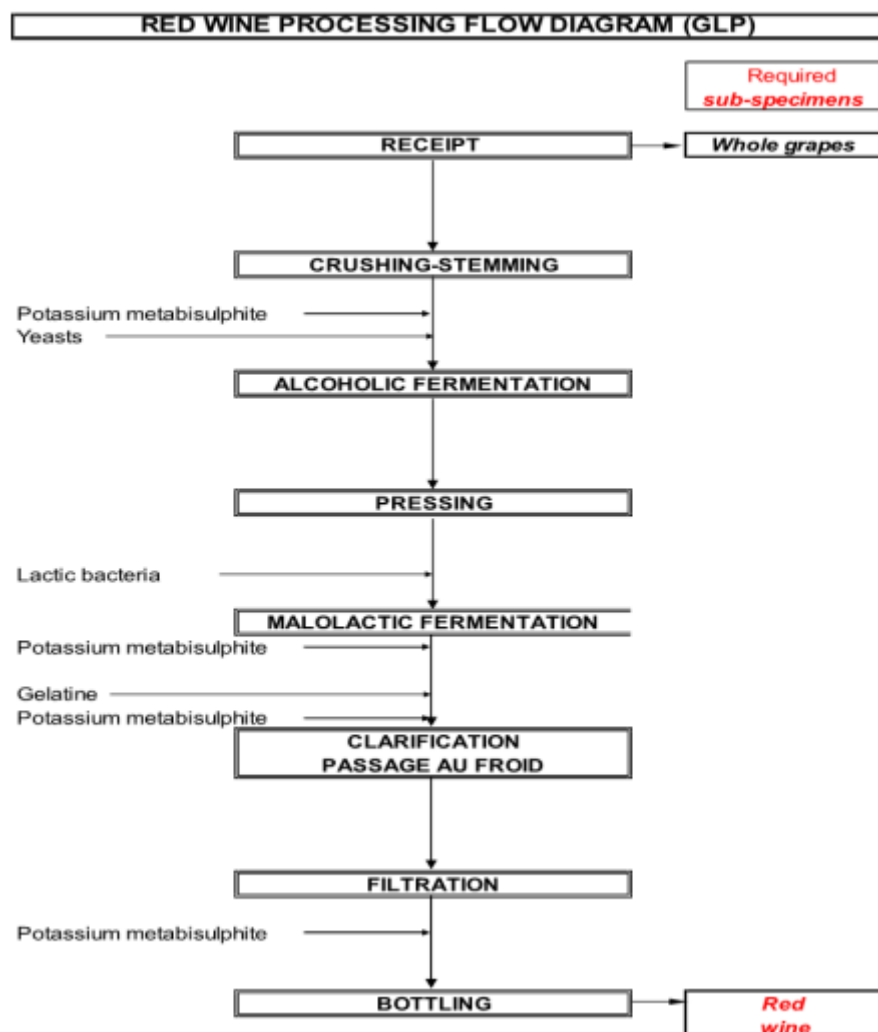


Figure A 15: Procedure of the grapes processing into red wine making

Conclusion

Residues in grapes and grapes processed commodities were determined after 3 applications with GWN 10616 applied at a rate of 0.180 kg a.s./ha with an interval of 7 days and a PHI of 28 days. In grape bunches RAC prior to processing total residues of Zoxamide at a level of 0.231 and 233 mg/kg were found.

In one trial a processing factor of 0.05 for white wine from wine grapes indicating that Zoxamide does not concentrate in this commodity. In the second trial no processing factor could be derived as no residues of Zoxamide could be found in red wine.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.2.3.2.8 Study 12 (report No. CREG2117)/Study 13 (report No. CREG2120) – Grape processing (must, wine)

<p>Comments of zRMS: Latvia</p>	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p><i>The study is acceptable.</i></p> <p><i>The concentration of zoxamide and its metabolites were determined in grapes and/or processed specimens (must, young and old wine). Trials performed under Northern and Southern European conditions. Each trial was carried out performing 5 applications 0.15 kg as/ha plant protection product. Foliar applications were made with a spray with an interval of 6-7 days and a last application 28 days before harvest. All specimens for residue analysis were stored and shipped under deep frozen conditions until sample extraction and analysis. Samples for processing were stored under refrigerated conditions (at around 5 ° C) until processing.</i></p> <p><i>Max. Storage interval between sampling and analysis:</i> <i>N-EU zone: 128 days</i> <i>S-EU zone: 159 days</i></p> <p><i>The highest residues for zoxamide observed were:</i></p> <ul style="list-style-type: none"> <i>- 0.8598 mg/kg in bunches</i> <i>- 0.0346 mg/kg in must</i> <i>- 0.0228 mg/kg in young wine</i> <i>- 0.0186 mg/kg in bottled wine</i> <p><i>For other metabolites residues were below LOQ.</i></p>
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These studies have already been provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	KCA 6.5.3/11
Report:	DETERMINATION OF CYMOXANIL AND ZOXAMIDE RESIDUES AT HARVEST IN RAW AND PROCESSED AGRICULTURAL COMMODITY GRAPE (BUNCH, MUST YOUNG AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF HARPOX WG (CYMOXANIL 33 % + ZOXAMIDE 33 % WG) (CYMOXANIL 33 % + ZOXAMIDE 33 % WG) – FOUR TRIALS, ITALY 2010, Romanini, M., 2011, report No. CREG2117, Doc. No. 638-013
Guideline(s):	SANCO/825/00 rev.7 (2004), SANCO/3029/99 rev. 4 (2000)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

And

Reference:	KCA 6.5.3/12
Report:	DETERMINATION OF CYMOXANIL AND ZOXAMIDE RESIDUES AT HARVEST IN RAW AND PROCESSED AGRICULTURAL COMMODITY GRAPE (BUNCH, MUST YOUNG AND BOTTLED WINE) FOLLOWING FIVE APPLICATIONS OF HARPOX WG (CYMOXANIL 33 % + ZOXAMIDE 33 % WG) – FOUR TRIALS, ITALY 2010, Romanini, M., 2011, report No. CREG2120, Doc. No. 638-014

Guideline(s): SANCO/825/00 rev.7 (2004), SANCO/3029/99 rev. 4 (2000)

Deviations: ~~None~~

Deviation for trial 80100 AN1 (FJCZ1 O/GR02) - shipment of specimens for processing: The transport duration of grapes processing specimens (between the expedition made just after the sampling and the receipt at the processing facility) was 10 days, whereas the study plan required that they should be delivered as quickly as possible. The specimens were firstly delivered to a wrong address (error of the transport company), then transferred to the processing facility. However, this deviation was regarded to have no impact on the study since the specimens were shipped deep frozen.

Deviation for trial 60100 AN2 (F/CZ1 O/GR03): The trial was performed on white grapes instead of red grapes, as requested in the study plan. Deviation for trial 80100 AN1 (F/CZ101GR02): No retain specimens were sampled for the specimens for processing. These deviations were regarded to not change the integrity of the study.

GLP: Yes

Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	Harpon WG
Formulation:	Water dispersible granules (WG)
CAS # (active substance):	Zoxamide:156052-68-5 Cymoxanil: 57966-95-7
Lot/Batch #:	XE28160A11
Content of active substance (actual):	33 % Cymoxanil + 33 % Zoxamide (nominal) 32.7 % Cymoxanil + 33.5 % Zoxamide (analysed)
Stability of test compound (expiry date):	June 2011

Study design:

Four at harvest trials (3 residue trials and 1 processing trial) in grapes has been performed in Southern Europe (Italy) and four at harvest trials (3 residue trials and 1 processing trial) in Northern Europe (Northern France and Czech Republic) in 2010. In this section only the processing trials are summarised.

Each processing trial consisted of 2 plots: 1 plot (control) was left untreated, 1 plot for processing was treated five times with Harpon WG (containing nominally Cymoxanil 33 % + Zoxamide 33 % WG) at a rate 150 g a.s./ha with an interval of 6-7 days and a PHI of 28 days. Samples were taken both for residues analysis and for processing.

The magnitude of residues of Zoxamide have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodity (must, young and bottled wine).

The raw agricultural commodities (grape bunches) for processing were shipped under cool conditions (5 °C) to the processing site. They were delivered at the processing site in good conditions. Processing of the samples started on the day of delivery. within 24 hours after sampling. Specimens for residue analysis were frozen at -20°C and stored frozen until the analysis.

During processing, samples of must, young and bottled red wine were collected. The processed specimens were frozen at -20°C after sampling and kept frozen until analysis.

Flowcharts of the grapes processing into wine are shown in Figure A 16.

Method:

The method validation was performed within the studies Romanini, M., 2011, report No. BPL-CREG2117 and Romanini, M., 2011, report No. CREG2120, which has been validated according to SANCO/825/00 rev. 8.1 and SANCO/3029/99 rev. 4.

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Zoxamide was determined with an analytical method that consisted of a solvent extraction by Ultra-turrax (bunch samples) or by shaking (processed samples). The extract containing the active ingredient was cleaned up by liquid-liquid partition and by SPE chromatography, then analysed by gas chromatography equipped with an ECD. The methods have been validated according to SANCO/825/00 rev. 7 and SANCO/3029/99 rev. 4.

The limit of quantification (LOQ) was 0.01 mg/kg for Zoxamide in all matrices, the limit of detection (LOD) was 0.0051 mg/kg.

The maximum sampling to analysis interval for Zoxamide at a temperature of $\leq -18^{\circ}\text{C}$ was 159 days.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours after extraction. Thus, no storage stability data for the extracts are needed.

Procedural recoveries were handled and stored in the same way and for the same time period as the analytical specimens that have been prepared within the same analytical set. The mean procedural recoveries were in the range of 70 – 110 % for all matrices.

Results:

The results of the processing study on grapes are summarised in Table A 63.

Table A 63. Residue data from grape processing study with Zoxamide (sum)

RAC	Residues in RAC (mg/kg)	PHI (days)	Processed commodity	Residue (mg/kg)	PF*/#	CF**/#	Comments/Reference
Wine grapes (red wine)	0.275	28	Must	0.0166	0.060	1	
			Young wine	0.0191	0.069	1	
			Bottled wine	0.0186	0.068	1	
Wine grapes (white wine)/	0.298	28	Must	0.0346	0.116	1	
			Young wine	0.0228	0.077	1	
			Bottled wine	<0.01	<0.03	1	

* Processing factor

** Conversion factor

Calculated by the applicant

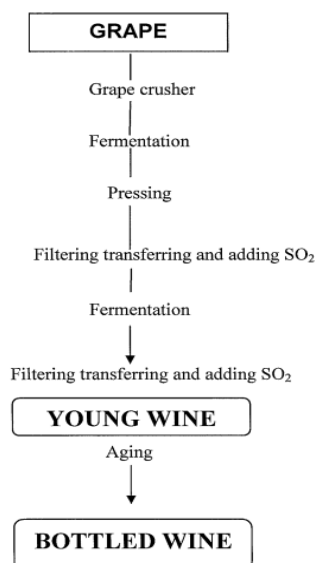


Figure A 16: Flowchart of the grapes processing into must, young and bottled wine

Conclusion

Residues in grapes and grapes processed commodities were determined after 5 applications with Harpon WG (containing nominally Cymoxanil 33 % + Zoxamide 33 % WG) at a rate 150 g a.s./ha with an interval of 6-8 days and a PHI of 28 days. In grape bunches RAC residues of Zoxamide at a level of 0.275 mg/kg (red wine grapes) and 0.298 mg/kg (white wine grapes) were found.

The processing factors are 0.60, 0.069 and 0.068 for must, young and bottled wine, respectively from red wine grapes and 0.116, 0.077 and <0.03 for must, young and bottled wine, respectively from white wine grapes, indicating that Zoxamide does not concentrate in these commodities.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grapes processed commodities.

Summary of processing factors

Out of the new presented supervised residue trials provided with this submission, processing factors (and the related median values) have been calculated. In case of residue levels below LOQ in processed commodities, for the calculation of the processing factors a residue level of 0.01 mg/kg was considered.

Table A 64. Summary of processing factors for Zoxamide

Commodity	Processing factor	Reference / study no.	Mean /Median ^{#/+}
Grapes			
Raisins	1.11	BPL-STUDY-19-000058	
	1.73	18097-03R	
			1.42 (n=2)
Juice before pasteurisation	0.032	AB2-18-35355	
	0.042	AB2-18-35355	
			0.037 (n=2)
Juice after pasteurisation	<0.01	AB2-18-35355	
	<0.01	AB2-18-35355	
	0.019 ^{##} /0.018 ^{###}	BPL-STUDY-19-000041	
	0.010 ^{##} /0.012 ^{###}	BPL-STUDY-19-000041	
	0.083	BPL-STUDY-19-000051	
	0.405	BPL-STUDY-19-000051	
	0.063	19200-01R	

Commodity	Processing factor	Reference / study no.	Mean /Median ^{#/+}
Must	<0.04	19200-01R	
			0.030 ^{##} /0.029 ^{###} (n=8)
	1.06	AB2-18-35355	
	0.385	AB2-18-35355	
	1.09	19200-01R	
	0.846	19200-01R	
	0.060	CREG2117/CREG2120	
	0.116	CREG2117/CREG2120	
			0.616 (n=6)
Young wine	0.074	AB2-18-35355	
	0.148	AB2-18-35355	
	0.034 ^{##} /0.032 ^{###}	BPL-STUDY-19-000041	
	0.016 ^{##} /0.020 ^{###}	BPL-STUDY-19-000041	
	<0.01	BPL-STUDY-19-000051	
	<0.02	BPL-STUDY-19-000051	
	<0.05	19200-01R	
	0.196	19200-01R	
	0.069	CREG2117/CREG2120	
	0.077	CREG2117/CREG2120	
			0.060 (n=10)
Bottled wine	0.048	AB2-18-35355	
	0.123	AB2-18-35355	
	0.033 ^{##} /0.032 ^{###}	BPL-STUDY-19-000041	
	<0.01 [#] / [#] <0.01 ^{##}	BPL-STUDY-19-000041	
	<0.01	BPL-STUDY-19-000051	
	<0.02	BPL-STUDY-19-000051	
	<0.05	19200-01R	
	0.165	19200-01R	
	0.050	GLP-STUDY-20-30	
	<0.040	GLP-STUDY-20-30	
	0.068	CREG2117/CREG2120	
	<0.03	CREG2117/CREG2120	
			0.044 (n=12)

- [#] The mean value of the two Pf is calculated to give the processing factor. In case of three or more processing tests, the processing factor is the median of the single factors from each test
The resulting processing factor is indicated with a “<”. For the calculation of the mean/median processing factor, a residue factor of <0.01 is considered as 0.01.
- ^{##} mean of 3 analytical determinations were calculated: 2 grape samples analysed just before processing phase start and 1 grape sample from the field was analysed.
- ^{###} mean of 2 grape samples analysed just before processing phase start was calculated.
- ⁺ Calculated by the applicant

Summary of processing data for RH-150721 and Zoxamide

The residue data for RH-150721 in processed commodities have already been submitted to RMS Latvia. An overview of the available data is presented in Table A 64.

Table A 64. Summary of residue data for wine grapes

Crop	Region	GAP	Formulation	PHI	Commodity analysed	Residues Zoxamide [mg/kg]	Residues RH-150721 (sum) [mg/kg]	Residues RH-150721 (sum) [mg/kg], expressed as Zoxamide equivalents, multiplication of RH-150721 residue levels with 1.058 [#]	Conversion factor [#]	Reference
Wine grapes	N-EU	5x 180 g a.s./ha, 7-8 days interval	Zoxium 240 SC	28	Juice	0.030*/< LOQ**	<LOD*/0.02**	0.011*/0.021**	0.35*/2.1**	Peterek 2020 AB2-18-35355 *pre-pasteurisation/ ** post-pasteurisation
					Must	1.00	< LOQ (0.004)	0.011	0.01	
					Wine, young	0.07	0.013	0.014	0.20	
					Wine, bottled	0.045	0.026	0.028	0.61	
				30	Juice	0.051*/<LOQ**	<LOD*/0.027**	0.011*/0.029**	0.207*/2.86**	
					Must	0.47	<LOQ (0.003)	0.011	0.02	
					Wine, young	0.18	0.031	0.033	0.18	
					Wine, bottled	0.15	0.059	0.062	0.42	
Wine grapes	N-EU	5x 180 g a.s./ha, 7-8 days interval	Zoxium 240 SC	20	Juice	0.0108	0.0106	0.011	1.038	Sala 2020 BPL-STUDY-19-000041 & Thomas-Delille 2020 B7284
					Wine, young	0.0173	0.0135	0.014	0.826	
					Wine, bottled	<LOQ	0.0130	0.014	1.375	
				26	Juice	0.0284	0.0471	0.050	1.755	
					Wine, young	0.0508	0.0235	0.025	0.489	
					Wine bottled	0.0503	0.0448	0.047	0.942	
Wine grapes	N-EU	3x 180 g a.s./ha, 7-	GWN-10616	28	Wine bottled	0.0181	0.0117	0.012	0.684	Longhi 2021

Crop	Region	GAP	Formulation	PHI	Commodity analysed	Residues Zoxamide [mg/kg]	Residues RH-150721 (sum) [mg/kg]	Residues RH-150721 (sum) [mg/kg], expressed as Zoxamide equivalents, multiplication of RH-150721 residue levels with 1.058 [#]	Conversion factor [#]	Reference
		8 days interval								GLP-STUDY-20-30
Table grapes	S-EU	5x 180 g a.s./ha, 7-8 days interval	Zoxium 240 SC	27	Raisins	0.596	0.424	0.449	0.753	Longhi, 2020, BPL-STUDY-19-000058
Table grapes	S-EU	5x 180 g a.s./ha, 7-8 days interval	Zoxium 240 SC	28	Raisins	0.900	0.056	0.059	0.066	Maccaferri, 2020, 18097-03R
Wine grapes	S-EU	5x 180 g a.s./ha, 7-8 days interval	Zoxium 240 SC	27	Juice	0.116	<LOD	0.011	0.091	Sala 2020 BPL-STUDY-19-000051 & Casalino 2020 BIU-005-17
					Wine, young	< LOQ	0.0577	0.0610	6.105	
				28	Wine bottled	<LOD	0.0535	0.0566	5.660	
					Juice	0.183	<LOD	0.011	0.058	
					Wine, young	<LOQ	0.0384	0.0406	4.063	
					Wine, bottled	<LOD	0.0309	0.0327	3.269	
Wine grapes	S-EU	5x 180 g a.s./ha, 7-8 days interval	GOW-F716 Zoxium 240 SC	27	Juice	0.014	<LOQ	0.011	0.756	Maccaferri 2020 19200-01R
					Must	0.240	<LOD	0.011	0.044	
					Wine, young	0.0058	0.018	0.019	3.27	
					Wine, bottled	0.0047	0.027	0.029	6.078	
				27	Juice	<LOD	0.010	0.011	1.058	
					Must	0.22	<LOD	0.011	0.048	

Crop	Region	GAP	Formulation	PHI	Commodity analysed	Residues Zoxamide [mg/kg]	Residues RH-150721 (sum) [mg/kg]	Residues RH-150721 (sum) [mg/kg], expressed as Zoxamide equivalents, multiplication of RH-150721 residue levels with 1.058 [#]	Conversion factor [#]	Reference
					Wine, young Wine, bottled	0.051 0.043	0.015 0.021	0.016 0.022	0.311 0.517	
Wine grapes	S-EU	3x 180 g a.s./ha, 7-8 days interval	GWN-10616	28	Wine, bottled	0.231	<LOQ	0.011	0.046	Longhi 2021 GLP-STUDY-20-30
					Juice, pre- and post-pasteurisation				0.90	
					Raisins				0.41	
					Wine, young and bottled				0.76	

In case of residue levels <LOQ, the residue level at LOQ (=0.01 mg/kg) was considered.

Molecular weight: Zoxamide: 336.6 g/mol; RH-150721: 318.20 g/mol; Zoxamide = RH-150721: x 1.058)

Conversion factor: residue level of RH-150721 (expressed as Zoxamide) divided by residue level of Zoxamide; mean (in case of 2 individual values) or median (in case of >2 individual values) conversion factor was calculated

Wine from study Longhi 2021 (GLP-STUDY-20-30) are indicated as young wine.

[#] Calculated by the applicant

A 2.2.4 Magnitude of residues in representative succeeding crops

No new data are submitted in the framework of this application.

A 2.2.5 Other/Special Studies

A 2.2.5.1 Study 1 – Residue study in honey (report No. 19 48 BTR 0003)

Comments of zRMS: Latvia	<p><i>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</i></p> <p>The study is acceptable.</p> <p>The study was performed according to “Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey” (SANTE/11956/2016 rev. 9).</p> <p>The zoxamide residues in Phacelia honey from the four treated trials were 0.0784 mg/kg, not detectable (< LOD of 0.003 mg/kg), and 2 x <LOQ (< 0.01 mg/kg).</p> <p>Deviations: In trial 19BTR0003_T3 the following specimen could not be generated as intended (no honey available):</p> <p>19BTR0003_06-T-A1 19BTR0003_06-T-A2 19BTR0003_06-T-R1 19BTR0003_06-T-R2 19BTR0003_06-T-PD</p> <p>Trial 3 was therefore repeated</p>
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This study has been already provided to the RMS Latvia. Thus, the summary of the study is only presented for completeness sake.

Reference:	See KCA 6.1/06
Report:	MAGNITUDE OF RESIDUES OF ZOXAMIDE IN PHACELIA (PHACELIA TANACETIFOLIA BENTH.) HONEY AFTER THREE APPLICATIONS OF GWN-9790EU UNDER SEMI-FIELD CONDITIONS IN NORTHERN AND SOUTHERN EUROPE, Poráčki, K., 2020, report No. 19 48 BTR 0003, Doc. No. 634-96001
Guideline(s):	OECD No. 506, Series on Testing and Assessment No. 72 and Series on Pesticides No. 39. ENV/JM/MONO(2007)17, SANCO/10684/2009, SANCO/825/00 rev. 8.1 (2010), SANTE/11813/2017 rev. 0, SANTE/11956/2016 rev. 9
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods:

Material / test item:

Test material:	Zoxium 240 SC / GWN-9790EU
Formulation:	Suspension concentrate (SC)
CAS # (active substance):	156052-68-5
Lot/Batch #:	18011201-72-52

Content of active substance (actual):	240g/L Zoxamide (nominal), 21.49 % w/w (analysed) (R/S Zoxamide ratio: 50/50)
Stability of test compound (expiry date):	13/01/2023

Test system

Species:	Honey bees
Crop:	<i>Phacelia tanacetifolia</i> BENTH.
Trial size (treated area):	216 m ² (192.5 m ² effective crop size).

Study design:

During the growing season in 2020 four separate field trials were conducted at various places in Southern Spain and Eastern Germany. Trials 19BTR0003_T1 and 19BTR0003_T2 (subsequently named T1 and T2) were performed in the area of Eastern Germany (Leipzig and Lossatal; Saxony; Germany), respectively. Trials 19BTR0003_T3 and 19BTR0003_T4 (subsequently named T3 and T4) were performed in the area of Southern Spain (Utrera & Adriano; Andalusia; Spain). The tunnel residue trials consist of two side-by-side plots:

One control tunnel remained untreated, one tunnel was treated. Each tunnel covered an area of 216 m² (192.5 m² effective crop size).

GWN-9790EU was applied three times at a rate equivalent to 180 g a.s./ha of Zoxamide (0.75 L product/ha; based on nominal content). The initial spray volume amounted 400 L/ha and the three applications were carried during the flowering of Phacelia at crop growth stages BBCH 61-65 (at the last application). A water supply for the bees was placed into each tunnel. During application, these water suppliers were covered with a plastic foil to prevent contamination.

Two assessments of the colony condition were performed per plot, once before the last application and once directly before sampling. For each trial, the colony condition of the hives was assessed before the last application and shortly before the removing of the honey combs by checking for the obvious presence of diseases, the brood and food status (area containing eggs, larvae, pupae and nectar as well as pollen). Furthermore, the development of the colonies was assessed by estimating the number of worker bees within a hive.

The bee hives were set up in the tunnels after the last application and remained in the tunnels until the honey showed a water content < 20 %. The water content was determined with a refractometer. Approximately 9 to 14 days after the placement of the colonies, honey combs were removed from the bee hives and gathered in the laboratory using a honey extractor. After examining the water content with a refractometer, the honey samples were sealed in separate labelled containers and stored at ≤ -18°C until analysis. Each sample contained about 100 g of Phacelia honey.

These supervised residue trials provide data relevant to conditions in the Northern and the Southern Europe.

Methods:

The method for the determination of Zoxamide was successfully validated in the analytical phase of the honey residue study.

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) for Zoxamide (racemate) is 0.01 mg/kg and the limit of detection (LOD) 0.003 mg/kg. The limit of quantification (LOQ) for Zoxamide ((R) -, and (S)-enantiomer) is 0.005 mg/kg and the limit of detection (LOD) 0.0015 mg/kg.

The maximum sampling to extraction interval was 83 days in honey, covered by the storage stability data in honey summarised in A 2.1.1.1.2.1.

The maximum extraction to analysis interval was 6 days. The mean procedural recoveries were in the range of 70 – 110 % for all analytes. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg for Zoxamide,

racemate), at 100x LOQ (1 mg/kg for Zoxamide, racemate). The recoveries for Zoxamide were always within the range of 70 - 110 % of nominal showing relative standard deviations of ≤ 20 % and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

The residue levels in honey in four independent trials, performed under Southern European (Spain) and Northern European (Germany) growing conditions during the 2020 growing season were determined after application of GWN-9790EU (a 240 g/L Zoxamide SC formulation) at a worst-case use pattern of 3 x 180 g a.s./ha with a minimum interval of 7(+1) days under semi-field conditions (in field tunnels). Applications took place over the full flowering phase of the crop.

The tunnel study design ensured that the bee colonies only had access to the GWN-9790EU treated crop. Pollen analysis confirmed that the bees gathered nectar mainly from the treated Phacelia.

The residue data on honey are summarised in the following table:

Table A 65: Residue levels of Zoxamide in honey

EU zone / country	Trial No.	Treatment group	Residues of Zoxamide (mg/kg)
Northern EU Germany 04319 Leipzig	T1	Control	< LOD
		Test item	0.0784
Northern EU Germany 04808 Lossatal	T2	Control	< LOD
		Test item	< LOQ
Southern EU Spain 41710 Utrera	T3	Control	< LOD
		Test item	< LOQ
Southern EU Spain 41728 Adriano (Dos Hermanas)	T4	Control	< LOD
		Test item	< LOD

LOQ: 0.010 mg/kg of Zoxamide (sum)

LOD: 0.003 mg/kg of Zoxamide (sum)

Conclusion

Based on the available residue data, it was shown that residues up to 0.0784 mg/kg can be found in honey samples, when Zoxamide is applied at a rate of 3 x 180 g a.s./ha with a minimum interval of 7(+1) days. The data submitted show that an exceedance of the MRL will occur. However, as in 3 of 4 trials the residue level is <0.01 mg/kg and only 1 trial is slightly exceeded, it is assumed that the existing MRL is still appropriate and an MRL application for the use of GWN-10616 on honey is not needed.

A 2.3 PHOSPHONIC ACID

A 2.3.1 Stability of residues

A 2.3.1.1 Stability of residues during storage of samples

A 2.3.1.1.1 Storage stability of residues in plant products

A 2.3.1.1.1.2 Study 1 (report No. LBN-0007-2022) – Apple (RAC and processed commodities)

Comments of zRMS:

The study has been accepted.

The objective of this study was the evaluation of the storage stability at -18°C in dark condition of phosphonic acid in apple (RAC, high water), apple juice, apple compote (sauce/puree), canned apples, dried apples and apple wet pomace. The storage stability was evaluated over a period of 6 months. The determinations were carried out involving the analytical LC-MS/MS method in the presence of an isotope-labelled internal standard (ILIS), developed and validated in the study GLP-STUDY-21-55. In the below table MRM transitions can be seen.

Analyte	Retention time (approx, min)	Detection ¹	Precursor ion (m/z)	Product ion (m/z)
Phosphonic acid	4 - 5	Primary	81	79.0
		Confirmatory		63.0
¹⁸ O ₃ -Phosphonic acid (ILIS)	4 - 5	/	87	85

¹ Quantification was performed using the primary detection

The obtained results show that the analyte phosphonic acid is stable for 6 months at -18°C in the dark in apple RAC and processed commodities (apple juice, apple sauce/puree, canned apple, dried apple and apple wet pomace) as the decline is < 30 %.

Reference:	KCA 6.1/13
Report:	STORAGE STABILITY OF PHOSPHONIC ACID IN APPLE AND PROCESSED FRACTIONS, Longhi, D., 2023, report No. LBN-0007-2022, Doc. No. 645-001
Guideline(s):	OECD No. 506 (2007), ENV/JM/MONO (2007)17, SANTE/2020/12830 Rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Phosphonic acid
Lot/Batch #:	1200710
Purity:	96.1 % (g/g)
CAS #:	13598-36-2
Stability of test compound/ Reference item:	Expiry date: 08/12/2024
Spiking levels:	1 mg/kg: apple fruit (RAC), apple juice, apple sauce/puree, canned apple 5 mg/kg: dried apple and apple wet pomace

Test commodity

Crop:	Apples					
Crop part or processed commodity:	Apple, fruits (RAC)	Apple, juice	Apple, wet pomace	Apple compote	Apples, canned	Apples, dried
Sample size:	10 g	10 g	4 g	10 g	10 g	4 g

Study design

The freezer storage stability of Phosphonic acid in apples (fruits and processed commodities: apple juice; apple, wet pomace; apple, compote; apple, canned; apple, dried) was performed by analysing apple samples fortified with Phosphonic acid at 100x LOQ (1 mg/kg for apple fruit (RAC), apple juice, apple sauce/puree, canned apple and 5 mg/kg for dried apple and apple wet pomace) at day 0.

The samples were analysed for recoveries after storage of ≤ -18 °C initially after fortification (day zero) and at 6 months for apple, fruit (RAC), apple juice, apple (wet pomace), apple compote, canned apples, dried apples. At each sampling point, 1 untreated blank and 2 specimens fortified freshly at 1 mg/kg (100x LOQ) with Phosphonic acid as procedural recoveries were analysed with 3 fortified, stored frozen specimens. At day 0, for method validation 5 specimens were fortified at 1 mg/kg (100x LOQ) together with 2 specimens fortified at 1 mg/kg (100x LOQ) for storage testing with Phosphonic acid in apple samples. The specimens were extracted and analysed together with the blank controls corresponding to 0 months storage (initial fortification).

Methods:

The method was successfully validated in study GLP-STUDY-21-55 (Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities”, Doc. No. 432-004). The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg for apple fruit, apple compote, canned apple, apple juice and 0.05 mg/kg for dried apples and apple, wet pomace.

The maximum extraction to analysis time period stored at 5 ± 3 °C of the samples was < 1 day. The procedural recoveries fortified with 1 mg/kg for apple fruit (RAC), apple juice, apple sauce/puree, canned apple and 5 mg/kg for dried apple and apple wet pomace run concurrently with the storage samples and were stored and handled the same way as the storage samples., demonstrating the stability of Phosphonic acid in sample extracts for the longest storage period and the accuracy on the day of analysis.

Results:

Table A 66: Summary of concurrent recoveries of Phosphonic acid from apple matrices.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev
Phosphonic acid					
Apple fruit	1	0	10 g (5)	102.5, 103.2, 102.8, 104.4, 101.6	102.9 \pm 1.0
Apple fruit	1	183	10 g (2)	98.9, 98.7	98.8
Apple juice	1	0	10 g (5)	98.4, 100.7, 99.8, 100.2, 101.0	100 \pm 1.0
Apple juice	1	182	10 g (2)	93.7, 95.3	94.5
Apple, wet pomace	5	0	4 g (5)	105.3, 99.5, 105.2, 107.4, 98.8	103.2 \pm 3.7
Apple, wet pomace	5	179	4 g (2)	103.5, 106.3	104.9
Apple compote	1	0	10 g (5)	103.6, 105.7, 104.1, 102.9, 104.9	104.2 \pm 1.1
Apple compote	1	182	10 g (2)	102.8, 103.4	103.1
Apple, canned	1	0	10 g (5)	101.5, 104.8, 104.3, 103.4, 104.1	103.6 \pm 1.2
Apple, canned	1	181	10 g (2)	97.0, 96.2	96.6
Apple dried	1	0	4 g (5)	99.9, 98.2, 100.7, 99.0, 100.5	99.7 \pm 1.1
Apple dried	1	179	4 g (2)	106.9, 104.7	105.8

Table A 67: Stability of Phosphonic acid residues in apple matrices following storage at -18 °C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Phosphonic acid				
Apple fruit	1	0	1.004, 1.054	100.8, 103.1
Apple fruit	1	183	0.983, 1.021, 1.017	95.4, 101.0, 100.1
Apple juice	1	0	0.984, 0.991	97.7, 99.1
Apple juice	1	182	0.956, 0.985, 0.963	96.6, 99.8, 96.4
Apple, wet pomace	5	0	5.243, 5.444	102.4, 106.9
Apple, wet pomace	5	179	4.908, 5.078, 4.859	97.0, 99.4, 97.2
Apple compote	1	0	1.054, 1.103	102.2, 108.4
Apple compote	1	182	1.024, 1.043, 1.035	104.2, 102.8, 102.9
Apple, canned	1	0	1.023, 1.051	100.6, 101.8
Apple, canned	1	181	0.987, 0.943, 1.008	97.0, 95.7, 98.8
Apple dried	5	0	5.240, 5.215	100.4, 100.4
Apple dried	5	179	4.904, 5.620	96.0, 109.9, 109.7

Conclusion

Based on the presented freezer storage stability data it was demonstrated that Phosphonic acid is stable at -18°C for around 180 days (6 months) in months in apple, fruit (RAC), apple juice, apple (wet pomace), apple compote, canned apples, dried apples. The storage stability covers the maximum storage period in the apple processing residue study and no further data are needed.

A 2.3.1.1.1.3 Study 2 (report No. IF23-06197326) – Potatoes (RAC and processed commodities)

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of this study was to determine the storage stability of phosphonic acid in potato RAC and processed products (potato tuber, peel (wet), protein, fried potato, crisps, flakes and starch) under storage conditions of $\leq -18^{\circ}\text{C}$ in the dark after 0, 90, 180 and 360 days. This interim report covers the samplings at 0 and 88 days. Triplicate samples of the matrices were analysed for phosphonic acid at zero-time and after 90 days of frozen storage at nominal temperature of $\leq -18^{\circ}\text{C}$. The samples were analysed using procedures described in the method validated in study IF23-06197316.</p> <p>There was no significant decrease in the observed residue level of phosphonic acid in any of the matrices studied after deep frozen storage ($\leq -18^{\circ}\text{C}$) for up to 88 days. Residues of phosphonic acid were confirmed to be stable in matrices studied when stored deep frozen at $\leq -18^{\circ}\text{C}$ for at least 88 days.</p>
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Reference:	KCA 6.1/14
Report:	STORAGE STABILITY OF MDI-0074 IN POTATO RAC AND PROCESSED PRODUCTS UNDER DEEP FROZEN CONDITIONS – INTERIM REPORT, Link, T., 2023, report No. IF23-06197326, Doc. No. 645-004
Guideline(s):	OECD No. 506 (2007), SANTE/2020/12830, Rev.2 (2023), ENV/JM/MONO(2007)17
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Test material/Reference item

Test material:	Phosphonic acid
Lot/Batch #:	1200710
Purity:	96.1 % (g/g)
CAS #:	13598-36-2
Stability of test compound/ Reference item:	Expiry date: 08/12/2024
Spiking levels:	0.20 mg/kg: potato tuber, potato wet peel, potato protein, fried potato, starch 0.50 mg/kg: Crisps 0.60 mg/kg: Flakes

Test commodity

Crop:	Potatoes						
Crop part or processed commodity:	Potato tuber (RAC)	Potato, wet peel	Potato, protein	Fried potato	Starch	Crisps	Flakes
Sample size:	2 g	2 g	1 g	2 g	1 g	2 g	2 g

Study design

The freezer storage stability of Phosphonic acid in potatoes (tuber and processed commodities: potato wet peel, potato protein, fried potato, starch, crisps, flakes) was performed by analysing potato samples fortified with Phosphonic acid at 10x LOQ (0.20 mg/kg for potato tuber (RAC), peel (wet), protein, fried potato and starch, 0.5 mg/kg for crisps and 0.6 mg/kg for flakes at day 0.

The samples were analysed for recoveries after storage of ≤ -18 °C initially after fortification (day zero) and at 3 months (88 days) for potatoes tuber and processed commodities: potato wet peel, potato protein, fried potato, starch, crisps, flakes. The interim report covers the samplings at 0 and 88 days. Additional sampling points will be taken after storage of 180 and 360 days. At day zero, freshly fortified samples were analysed in triplicate with one control sample. After storage for 90, 180 and 360 days (nominal), 1 untreated blank and 2 specimens fortified freshly at 10x LOQ (0.20 mg/kg for potato tuber (RAC), peel (wet), protein, fried potato and starch, 0.5 mg/kg for crisps and 0.6 mg/kg for flakes) with Phosphonic acid as procedural recoveries were analysed with 3 fortified, stored frozen specimens.

Methods:

The method was successfully validated in study IF23-06197316 (“Validation of analytical methods for the determination of GWN-8030, MDI-0043, MDI-0050 and MDI-0074 in potato matrices”, Doc. No. 432-017).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was (0.02 mg/kg for potato tuber (RAC), peel (wet), protein, fried potato and starch, 0.05 mg/kg for crisps and 0.06 mg/kg for flakes.

The maximum extraction to analysis time period stored at 5 ± 3 °C of the samples was < 1 day for potato tuber, wet peel, fried potato, potato crisps, 1 day for protein, and starch and 4 days for flakes. The procedural recoveries fortified with 0.20 mg/kg for potato tuber (RAC), peel (wet), protein, fried potato and starch, 0.5 mg/kg for crisps and 0.6 mg/kg for flakes run concurrently with the storage samples and were stored and handled the same way as the storage samples, demonstrating the stability of Phosphonic acid in sample extracts for the longest storage period and the accuracy on the day of analysis.

Results:

Table A 68: Summary of concurrent recoveries of Phosphonic acid from potato matrices.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev
Phosphonic acid					
Potato tuber	0.20	0	3	101, 105, 106	104 \pm 2.4
Potato tuber	0.20	88	2	95, 97	96
Potato, wet peel	0.20	0	3	107, 107, 105	106 \pm 1.2
Potato, wet peel	0.20	88	2	98, 100	99
Potato protein	0.20	0	3	108, 95, 101	101 \pm 6.5
Potato protein	0.20	88	2	96, 96	96
Fried potato	0.20	0	3	101, 104, 105	103 \pm 2.4

Matrix	Spike level (mg/kg)	Storage Inter- val (days)	Sample size (n)	Individual pro- cedural recov- eries (%)	Mean ± std dev
Fried potato	0.20	88	2	95, 96	95
Crisps	0.20	0	3	101, 102, 104	102 ± 1.5
Crisps	0.20	88	2	101, 98	99
Flakes	0.20	0	3	104, 107, 105	105 ± 1.5
Flakes	0.20	88	2	99, 91	95
Starch	0.20	0	3	100, 103, 105	103 ± 2.5
Starch	0.20	88	2	91, 93	92

Table A 69: Stability of Phosphonic acid residues in potato matrices following storage at -18 °C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%)
Phosphonic acid				
Potato tuber	0.20	0	0.20, 0.21, 0.21	101, 105, 106
Potato tuber	0.20	88	0.20, 0.19, 0.20	99, 97, 98
Potato, wet peel	0.20	0	0.21, 0.21, 0.21	107, 107, 105
Potato, wet peel	0.20	88	0.19, 0.20, 0.21	97, 99, 103
Potato protein	0.20	0	0.22, 0.19, 0.20	108, 95.1, 101
Potato protein	0.20	88	0.17, 0.17, 0.16	83, 87, 81
Fried potato	0.20	0	0.20, 0.21, 0.21	101, 104, 106
Fried potato	0.20	88	0.20, 0.20, 0.20	98, 100, 98
Crisps	0.20	0	0.50, 0.51, 0.52	101, 102, 104
Crisps	0.20	88	0.52, 0.53, 0.52	104, 105, 105
Flakes	0.20	0	0.63, 0.64, 0.63	104, 107, 105
Flakes	0.20	88	0.49, 0.47, 0.51	82, 78, 85
Starch	0.20	0	0.20, 0.21, 0.21	100, 103, 105
Starch	0.20	88	0.19, 0.20, 0.19	96, 100, 96

Conclusion

Based on the presented freezer storage stability data it was demonstrated that Phosphonic acid is stable at -18°C for at least 88 days (3 months) in months in potatoes, tuber (RAC), potato wet peel, potato protein, fried potato, starch, crisps, flakes. The study is still ongoing. However, it is expected that Phosphonic acid will be stable under frozen conditions for at least 360 days, covering the longest storage period.

A 2.3.1.1.1.4 Study 3 – Grapes (processed commodities)

Comments of zRMS:	Any LoA cannot be a presentation subject here. Appendix 2 is intended for the data presentation and evaluation.
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LoA to storage stability data on grape processed commodities is available. ~~Definitely instead of the LoA the applicant have to provide the relevant data.~~

In the freezer storage stability study in grapes (Witte, A., 2003), which was already evaluated by EFSA in 2012, it was shown that Phosphonic acid is stable for 12 months, covering also the max. frozen storage period (12 months) of the processed commodities in the processing studies (Röser, K., 2004; report no. 20031178/F2-FPVI and Ipach, R., 2010; report no. FCS01, KCA 6.3.5/15) (see also Germany 2017: Registration Report Veriphos; ZV 027207-00/00).

A 2.3.1.1.2 Storage stability of residues in animal products

A 2.3.1.1.2.1 Study 1 – Honey

Comments of zRMS:	Any LoA cannot be a presentation subject here. Appendix 2 is intended for the data presentation and evaluation.
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LoA to storage stability data on honey is available. ~~Definitely instead of the LoA the applicant have to provide the relevant data.~~

Storage stability data in honey have been generated within the honey residue study (report no. 143SRFR21C01), which is summarised in A 2.3.6.1.

The maximum storage interval of honey specimens from harvest until analysis was 113 days. Frozen storage stability (< -18°C) of residues of Phosphonic acid was demonstrated within the study for this period of time.

A 2.3.1.1.3 Storage stability of residues in sample extracts

A 2.3.1.1.3.1 Grapes

Comments of zRMS:	<p>The study has been accepted.</p> <p>The aspect of the purpose of the study was the determination of the stability of phosphonic acid in the sample extracts. This study was the validation study of the LC-MS/MS method using the isotope-labelled internal standard (ILIS) to determine phosphonic acid in grape samples. The applicant below shows the stability results. The validation results are as follows:</p>					
	Parameter	Result				
	Matrix effect	- 4.9% / not significant				
	Calibration (matrix-matched)	Range: 1.018 -101.8 µg/L in solution Range: 0.002036 - 0.2036 mg/kg on sample (from 20% of LOQ to 10xLOQ)				
		The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.				
	Recovery and precision (repeatability)	Level	Concentration	Transition	% Recovery	% RSD
		LOQ (n = 5)	0.01 mg/kg	Primary (81/79)	101.4	10.9
				Confirmatory (81/63)	103.5	5.7
		10xLOQ (n = 5)	0.1 mg/kg	Primary (81/79)	103.9	2.8
				Confirmatory (81/63)	102.8	2.3
		Overall (n = 10)	/	Primary (81/79)	102.7	7.53
		n = number of replicates				
	Limit of quantification (LOQ)	verified at 0.01 mg/kg				
	Limit of detection (LOD)	verified at 0.002 mg/kg (20% of LOQ)				
	Selectivity and specificity	Verified: no interferences found untreated samples in amounts higher than the 30% of the LOQ (< LOD)				
	Confirmation	Confirmation achieved by simultaneous determination of a confirmatory MS/MS transition. Calibration data, recovery and precision in compliance with the requirements				
	Stability of the analyte in the sample extract	102.4% after 3 days in the dark at 5 ± 3°C				

Reference:	KCA 6.1/15
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN GRAPES, Sala, A., 2022, report No. GLP-STUDY-21-103, Doc. No. 432-008
Guideline(s):	SANTE/2020/12830 rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Phosphonic acid
Lot/Batch #:	1070272
Purity:	97.4 %
CAS #:	13598-36-2
Stability of test compound/	20 May 2023

Reference item:	
Spiking levels:	50.9 µg/L

Study design

The stability of Phosphonic acid in the final sample extract of grape when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) ex-tract was spiked with known amounts of analyte at the concentration of 25.28 µg/L. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses (ratio between the areas of analyte and ILIS signals) were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-103 (“Validation of an analytical method for the determination of Phosphonic acid in grapes”, Doc. No. 432-008).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results:

The results of the spiking experiments are summarised in Table A 70.

Table A 70 **Stability of Phosphonic acid in grape extract following storage at $5 \pm 3^\circ\text{C}$**

Matrix	Analyte	Spiked Concentration (µg/L)	T0 – Peak area (primary detection)	After 3 days – Peak are (primary detec-tion)	Stability [%]
Grape extract	Phosphonic acid	50.9	Area analyte: 52761 Ares ILIS: 32785 Area ratio: 1.6093	Area analyte: 50381 Area ILIS: 30560 Area ratio: 1.6486	102.4

Conclusion

The stability of Phosphonic acid in the grape extract can be considered proven for 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

A 2.3.1.1.3.2 Apples

Comments of zRMS:	<p>The study has been accepted.</p> <p>The aspect of the purpose of the study was the determination of the stability of phosphonic acid in the sample extracts. This study was the validation study of the analytical method to determine phosphonic acid in apple RAC (high water matrix) and processed commodities (apple juice, apple pomace, apple sauce/puree, canned apples and dried apples (dry / high sugar content). The analytical determination was carried out applying a LC-MS/MS method using an isotope-labelled internal standard (ILIS). The analytical method was based on the multi-residual EURL-SRM method (QuPPe PO Method). The validation results were as required. The stability results are described below by the applicant.</p>
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Reference:	KCA 6.1/16
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN APPLES RAC AND PROCESSED COMMODITIES, Longhi, D., 2021, report No. GLP-STUDY-21-55, Doc. No. 432-004
Guideline(s):	SANTE/2020/12830 rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Test material/Reference item

Test material:	Phosphonic acid	
Lot/Batch #:	1070272	
Purity:	97.4 %	
CAS #:	13598-36-2	
Stability of test compound/ Reference item:	20 May 2023	
Spiking levels:	Apple	48.0 µg/L
	Dried apple, apple wet pomace	100.9 µg/L
	Apple sauce/puree, canned apple, apple juice	50.45 µg/L

Study design

The stability of Phosphonic acid in the final sample extract of apple (RAC and processed commodities) when stored for 4 days (RAC) and 3 days (processed commodities) under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) extract was spiked with known amounts of analyte at the concentration of 48 µg/L for apple, 100.9 mg/L for dried apple and apple wet pomace and 50.45 µg/L for apple sauce/puree, canned apple, apple juice. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses (ratio between the areas of analyte and ILIS signals) were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-55 (“Validation of an analytical method for the determination of Phosphonic acid in apples”, Doc. No. 432-004).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results:

The results of the spiking experiments are summarised in Table A 71.

Table A 71 Stability of phosphonic in apple extract following storage at 5 ± 3 °C

Matrix extract	Analyte	Storage period (days)	Phosphonic acid (µg/L)	ILIS conc. (µg/L)	T0 – Peak area (primary detection)	After 3 days – Peak area (primary detection)	Stability %
Apple	Phosphonic acid	4	48.0	10	Analyte area: 37871 ILIS area: 5348 Area ratio: 7.081	Analyte area: 31217 ILIS area: 4447 Area ratio: 7.020	99.1
Dried apple		3	100.9	50	Analyte area: 43607 ILIS area: 17987 Area ratio: 2.424	Analyte area: 41607 ILIS area: 15013 Area ratio: 2.771	114.3
Apple wet pomace		3	100.9	50	Analyte area: 44941 ILIS area: 18887 Area ratio: 2.381	Analyte area: 43379 ILIS area: 16036 Area ratio: 2.705	113.6
Apple sauce/puree		3	50.45	10	Analyte area: 26546 ILIS area: 4062 Area ratio: 6.535	Analyte area: 28165 ILIS area: 4097 Area ratio: 6.875	105.2
Canned apple		3	50.45	10	Analyte area: 16596 ILIS area: 2555 Area ratio: 6.495	Analyte area: 21194 ILIS area: 2952 Area ratio: 7.180	110.5
Apple juice		3	50.45	10	Analyte area: 21282 ILIS area: 3003 Area ratio: 7.087	Analyte area: 17157 ILIS area: 2281 Area ratio: 7.522	106.1

Conclusion

The stability of Phosphonic acid in the apple extract of apples (RAC) is shown for 3 days and of processed commodities (dried apple, apple wet pomace, apple sauce/puree, canned apple and apple juice) at $5 \pm 3^\circ\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

A 2.3.1.1.3.3 Potatoes

Comments of zRMS:	The study has been accepted.														
	The aspect of the purpose of the study was the determination of the stability of phosphonic acid in the sample extracts. This study was the validation study of the LC-MS/MS method to determine phosphonic acid in potato tuber and processed samples (potato waste and potato dried pulp). The method was based on the EURL-SRM QuPPe-PO-Method. The determination with LC-MS/MS was performed in the presence of an internal standard (¹⁸ O ₃ -Phosphonic acid).														
	The stability found was described below by the applicant. The summary of the validation results is as follows:														
	Parameter	Result													
	Matrix effect	<table><tr><th>Matrix</th><th>Matrix effect</th></tr><tr><td>Potato tuber</td><td>- 38% (significant)</td></tr><tr><td>Potato waste</td><td>- 37% (significant)</td></tr><tr><td>Potato dried pulp</td><td>- 33% (significant)</td></tr></table>		Matrix	Matrix effect	Potato tuber	- 38% (significant)	Potato waste	- 37% (significant)	Potato dried pulp	- 33% (significant)				
Matrix	Matrix effect														
Potato tuber	- 38% (significant)														
Potato waste	- 37% (significant)														
Potato dried pulp	- 33% (significant)														
Calibration (matrix-matched)	<table><tr><th>Matrix</th><th>Range (µg/L)</th><th>Range (mg/kg)</th></tr><tr><td>Potato tuber</td><td>1.00 – 100 (20% LOQ – 100% above 10xLOQ)</td><td>0.002 – 0.2</td></tr><tr><td>Potato waste</td><td>0.5 – 50 (20% LOQ – 100% above 10xLOQ)</td><td>0.002 – 0.2</td></tr><tr><td>Potato dried pulp</td><td>0.5 – 50 (20% LOQ – 100% above 10xLOQ)</td><td>0.002 – 0.2</td></tr></table>			Matrix	Range (µg/L)	Range (mg/kg)	Potato tuber	1.00 – 100 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2	Potato waste	0.5 – 50 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2	Potato dried pulp	0.5 – 50 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2
	Matrix	Range (µg/L)	Range (mg/kg)												
	Potato tuber	1.00 – 100 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2												
	Potato waste	0.5 – 50 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2												
	Potato dried pulp	0.5 – 50 (20% LOQ – 100% above 10xLOQ)	0.002 – 0.2												
The regression residuals plots show that residuals are randomly distributed, hence demonstrating the linear calibration.															

Recovery and precision (repeatability)	Potato tuber				
	Level	Concentration	Transition	% Recovery	% RSD
	LOQ (n = 5)	0.01 mg/kg	Primary (81/79)	79.5	15.0
			Confirmatory (81/63)	91.3	3.4
	10xLOQ (n = 5)	0.1 mg/kg	Primary (81/79)	79.6	3.9
			Confirmatory (81/63)	78.7	4.2
	Overall (n = 10)	/	Primary (81/79)	79.6	10.3
			Confirmatory (81/63)	85.0	8.6
	Potato wastes				
	Level	Concentration	Transition	% Recovery	% RSD
	LOQ (n = 5)	0.01 mg/kg	Primary (81/79)	99.2	1.6
			Confirmatory (81/63)	102	1.0
	10xLOQ (n = 5)	0.1 mg/kg	Primary (81/79)	98.5	0.72
			Confirmatory (81/63)	100	1.6
	Overall (n = 10)	/	Primary (81/79)	98.9	1.2
			Confirmatory (81/63)	101	1.7
	Potato dried pulp				
	Level	Concentration	Transition	% Recovery	% RSD
	LOQ (n = 5)	0.01 mg/kg	Primary (81/79)	98.2	3.5
			Confirmatory (81/63)	95.7	4.3
	10xLOQ (n = 5)	0.1 mg/kg	Primary (81/79)	102	1.7
			Confirmatory (81/63)	100	0.85
	Overall (n = 10)	/	Primary (81/79)	99.9	3.1
			Confirmatory (81/63)	98.0	3.8
	n = number of replicates				
Limit of quantification (LOQ)	verified at 0.01 mg/kg recovery and repeatability data in compliance with the guideline				
Limit of detection (LOD)	Verified for each matrix at 0.002 mg/kg (20% of LOQ) signal/noise ratio higher than 3				
Selectivity and specificity	Verified for each matrix: no interferences found untreated samples in amounts higher than the 30% of the LOQ (< LOD)				
Confirmation	Confirmation achieved by simultaneous determination of a confirmatory SRM transition. Calibration data, recovery and precision in compliance with the requirements				
Stability of the analyte in the samples extract	Verified for 3 days at 5 ± 3°C in the dark (potato tuber: 100.1%, potato waste: 101.6%, potato dried pulp: 106.6%)				
Stability of the analyte in the standard solution	Verified for 74 days at 5 ± 3°C in the dark (stock solution in water): the difference from the stored and a fresh solution was 0.8%				

Reference:	KCA 6.1/17
Report:	VALIDATION OF AN ANALYTICAL METHOD FOR THE DETERMINATION OF PHOSPHONIC ACID IN POTATO, Longhi, D., 2022, report No. GLP-STUDY-21-52, Doc. No. 432-015
Guideline(s):	SANTE/2020/12830, rev.1 (2021), SANTE 2017/10632 rev. 3 (2017)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Test material/Reference item

Test material:	Phosphonic acid
Lot/Batch #:	1070272
Purity:	97.4 %
CAS #:	13598-36-2

Stability of test compound/ Reference item:	20 May 2023	
Spiking levels:	Potato tuber	49.75 µg/L
	Potato waste, Potato dried pulp	24.88 µg/L

The stability of Phosphonic acid in the final sample extract of potato (RAC and processed commodities) when stored for 3 days under dark and refrigerated conditions at $5 \pm 3^\circ\text{C}$ has been studied by recovery experiments.

Stored samples were analysed concurrently with freshly spiked samples. For spiking, final (blank) extract was spiked with known amounts of analyte at the concentration of 49.75 µg/L for potato tuber and 24.88 µg/L for potato waste and potato dried pulp. The stability in the extract was tested for a period of 3 days at $5 \pm 3^\circ\text{C}$ in dark conditions: after this period, the stored sample was analysed concurrently with a freshly prepared matrix-matched standard solution at the same concentration, used as reference for time 0. The measured instrumental responses (ratio between the areas of analyte and ILIS signals) were compared and the stability was expressed as the percentage ratio between the responses of the spiked extract analysed after 3 days and the freshly spiked one.

Methods

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-52 (“Validation of an analytical method for the determination of Phosphonic acid in potato”, Doc. No. 432-015).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) was 0.002 mg/kg.

Results:

The results of the spiking experiments are summarised in Table A 72.

Table A 72 **Stability of Phosphonic acid in potato extract following storage at $5 \pm 3^\circ\text{C}$**

Matrix	Analyte	Spiked Concentration (µg/L)	T0 – Peak area (primary detection)	After 3 days – Peak area (primary detection)	Stability [%]
Potato tuber	Phosphonic acid	49.75	Area analyte: 2678345 Area ILIS: 538737 Area ratio: 4.972	Area analyte: 2259879 Area ILIS: 454025 Area ratio: 4.977	100.1
Potato waste		24.88	Area analyte: 1913220 Area ILIS: 603965 Area ratio: 3.168	Area analyte: 1742674 Area ILIS: 541379 Area ratio: 3.219	101.6

Matrix	Analyte	Spiked Concentration (µg/L)	T0 – Peak area (primary detection)	After 3 days – Peak are (primary detection)	Stability [%]
Potato dried pulp		24.88	Area analyte: 1752217 Ares ILIS: 517484 Area ratio: 3.386	Area analyte: 1660162 Ares ILIS: 460073 Area ratio: 3.608	106.6

Conclusion

The stability of Phosphonic acid in the potato extract (RACA dn processed commodities (potato waste and potato dried pulp) is shown for 3 days at $5 \pm 3^{\circ}\text{C}$ in dark conditions since the recovery of the stored spiked sample is within the range of 70-120% measured against the freshly prepared one, as required by the SANTE/2020/12830 rev.1 guideline.

A 2.3.2 Nature of residues in plants, livestock and processed commodities

A 2.3.2.1 Nature of residue in plants

A 2.3.2.2 Nature of residue in primary crops

No new data were submitted in the framework of this application.

A 2.3.2.3 Nature of residue in rotational crops

No new data were submitted in the framework of this application.

A 2.3.2.4 Nature of residues in processed commodities

No new data were submitted in the framework of this application.

A 2.3.2.5 Nature of residues in livestock

No new data were submitted in the framework of this application.

A 2.3.3 Magnitude of residues in plants

A 2.3.3.1 Grapevines

Table A 73: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2012) (Potassium phosphonate)	6	2904 (Potassium phosphonate)	9 ± 1 days	--	60
cGAP EU (Art. 12)	4	2244 (Potassium phosphonate)	12	BBCH 15-83	42
Intended cGAP (# 1)	3	2265 (Potassium phosphonate) 1500 (Phosphonic acid)	8	BBCH 79	28

A 2.3.3.1.1 Study 1 (report No. GLP-Study-20-30) – Southern and Northern Europe

Comments of zRMS: Latvia	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The study is acceptable.</p> <p>The concentration of zoxamide and its metabolites were determined in grapes and/or processed specimens. Trials performed under Northern and Southern European conditions. Each trial was carried out performing 3 applications of three different plant protection products at their worst-case application rates. Foliar applications were made with a spray with an interval of 7 days and a last application 28 days before harvest.</p> <p>Max. Storage interval between sampling and analysis: Wine grape: 67-69 days Wine: 14 days</p> <p>The residue found in treated grape bunches were (use pattern 3x180 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.218 to 0.905 mg/kg. - For RH-141452, the residue 28 DALA were 0.01 mg/kg - Total residues were from 0.233 to 0.920 mg/kg <p>The residue found in treated grape bunches were (use pattern 3x150 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.123 to 0.644 mg/kg. - For RH-141452, the residue 28 DALA were 0.0192 mg/kg - Total residues were from 0.123 to 0.673 mg/kg <p>The residue found in processed grapes (wine) were:</p> <ul style="list-style-type: none"> - For zoxamide, the residues were from 0.01 to 0.0181 mg/kg
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	<ul style="list-style-type: none"> - For RH-141452, the residue were 0.01 mg/kg - Total residues were from 0.025 to 0.033 mg/kg <p>For other metabolites residues were below LOQ.</p> <p>Deviations:</p> <p>Trial: CMN-20-44059 ES06: The application 1 has been done with BBCH 81 instead of BBCH 15-79, as required in the Study Plan. This happens because at the moment of the signature of the SP the field crop was at BBCH 81. Deviation with an impact. However, all the applications doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 ES06: The application 2 has been done 6 days after application 1, instead of 7-8 days - as required in the Study Plan. This was due to logistic adjustments and the field technician didn't realise that -1 day was not allowed. However, this deviation has no impact on the study integrity since it is still in the $\pm 25\%$ range for the application pattern intended with a 7-8 days interval.</p> <p>Trial: CMN-20-44059 FR02: Sampling S2 (1 DALA) and S3 (3 DALA) were not done. This occurred because the field technician didn't take into account the amendment no. 1 to the study plan. Deviation with an impact: the trial CMN-44059 FR02 (DEC-2) has become a decline with 5 points instead of 7 points.</p> <p>Trial: CMN-20-44059 HU04: Samples collected at 0 DALA were delivered at ambient temperature instead of refrigerated condition (with dry ice) to the Field Test Site. This occurred due to an error of the field technician that didn't correctly understand the study plan. An impact on the integrity of the study was not assumed since the maximum period between sampling and freezing in the Test Site Facility was about 6 hours (at ambient temperature).</p> <p>Trial: CMN-20-44059 FR01: Dry ice was not used during the samplings since the field was close to the Test Site Facility. No impact on the integrity of the study assumed since the maximum period between sampling in the field and freezing in the Test Site Facility was only 3 hours for sampling 1, 1 hour 20 minutes for sampling 2, 1 hour 15 minutes for sampling 3, 1 hour 5 minutes for sampling 4, 2 hours 5 minutes for sampling 5, and 1 hour 5 minutes for sampling 6 – each at ambient temperature. The max. storage period for sampling 7 was 2 hours 35 minutes (samples cooled with frozen gel packs).</p> <p>Trial: CMN-20-44059 FR02: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact on the integrity of the study since the maximum period between sampling in the field and freezing in the Test Site Facility was 1 hour for sampling 1, 15 minutes for sampling 4, 20 minutes for sampling 5, 15 minutes for sampling 6, and 16 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR05: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact since the maximum period between sampling in the field and freezing in the Test Site Facility was 3 hours for sampling 1, 2 hours for sampling 4, 2 hours 30 minutes for sampling 5, 2 hours and 35 minutes for sampling 6, and 4 hours and 30 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR01: Chemical products with phosphonate and zoxamide as active ingredients were applied in the field where the trial was set up. No impact on the results for zoxamide and metabolites. Impact for the results for phosphonic acid on grape bunches, for which residues in the untreated control samples were detected, and on wine at 0 and 28 DALA, for which residues in the untreated control sample were detected. This was solved by subtracting the untreated control sample results from the treated ones.</p> <p>Trials CMN-20-44059 FR02, FR05, HU03, HU04, ES07: The applications have not been done between BBCH 15 and BBCH 79 as requested in the Study Plan. This deviation had an impact on the study. However, the application pattern and doses as well as the PHI were respected.</p>
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	<p>Trial: CMN-20-44059 FR05: The farmer contract was signed on 04/08/2020, one day after the first application (03/08/2020). This deviation was regarded to have no impact on the study.</p> <p>During the processing phase the mustimeter 34MUS16 was used from 28/08/2020 to 03/09/2020 (checking date) without writing the procedural check before its use (the technician did the check but forgot to write it). This deviation was regarded to have no impact on the study.</p> <p>On 08/10/2020, during the processing phase, the MLF (malolactic fermentation) was recorded as finished on the data sheets (fermentation and red wine) and k metabisulphite was added on 09/10/2020 (at the end of MLF), but the chromatography paper spots of malic acid were present for U2. Therefore, k metabisulphite seems to be added on the wine U2 before the end of the malolactic fermentation. This deviation was regarded to have no impact on the residues in the wine, but only on its organoleptic properties.</p> <p>During the analytical phase the recovery check results at LOQ level for the analytes RH-141288 and RH-150721 were outside ($> 110\%$) the permitted range (70-110%) for analytical batch 200902 GLP-STUDY-20-30. This deviation was solved with no impact on the study results since the samples in this sequence were re-extracted and analysed, discarding the previously obtained values.</p> <p>During the analysis of analytical batch 200904-GLP-STUDY-20-30 the calibration point at level 3 (Uva L3) in the calibration curve had a response higher than expected. It has therefore not been considered to establish the actual calibration line. This deviation was regarded to have no impact on the study results since the calibration range related to the method validation has not altered, and 4 points were regarded enough to derivate a suitable calibration line with $r^2 > 0.99$.</p> <p>During the analysis of the analytical batch 200924-GLP-STUDY-20-30 (4C N) the calibration check results for (R)-RH-141288 (147.3%), (S)-RH-141288 (266.7%) and (S)-RH-150721 (141.3%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200924-GLP-STUDY-20-30 (4C B) the calibration check results of (R)-RH-150721 (136.9%) and (S)-RH-150721 (132.4%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200929-GLP-STUDY-20-30 the calibration check results of (R)-RH-150721 (126.8%) and (S)-RH-150721 (135.5%) were outside the acceptable range (80% - 120%). However, this deviation was regarded to have no impact on the study integrity. All samples analysed in these batches have concentrations $< \text{LOQ}$ for the mentioned analytes, therefore the calibration check value could not affect the reported values anyway. This deviation was solved with no impact on the study.</p> <p>During the analysis of the analytical batch 201117 GLP-STUDY-20-30 (white wine) a calibration point for the analyte (S)-RH-141288 had a lower response in comparison to the regression line. This value was excluded and a 4-point calibrating line was established. As a consequence, since the recovery check at $10 \times \text{LOQ}$ (GLP-SMPL-20-724/NH RC2) was no longer inside the calibration range, it could not be evaluated. However; this deviation was regarded to have no impact on the study results since 4 calibration points were regarded enough for the interpolation and to quantify the analyte content in the samples.</p> <p>The untreated white wine sample GLP-SMPL-20-724 was found to contain 1.61 mg/kg of phosphonic acid, presumably due to the reasons explained in deviation 8. External standard calibration solutions for white wine were initially established using the extracts of this sample. This resulted in a signal higher than 30% of the LOQ. They were therefore invalidated. The batch was therefore re-elaborated using the calibration curve for red wine that was analysed in the same analytical sequence, recalculating the recovery check values by subtracting the values of the untreated (white wine) sample. This deviation was regarded to have no impact on the study results since the calibration using matrix-matched reference solution in red wine</p>
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	has the same matrix effect on phosphonic acid than white wine (demonstrated by the recovery check and by a standard at level L3 prepared in white wine).
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Reference:	See KCA 6.3.1/01
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF WINE GRAPE AND PROCESSED (WINE) IN OPEN FIELD FOLLOWING THREE APPLICATIONS OF THE FORMULATED PRODUCTS GWN-9823, GWN-10616, GWN-10392 (NORTH AND SOUTH EUROPE – 7 trials year 2020, Longhi, D., 2021, report No. GLP-STUDY-20-30, Doc. No. 638-015
Guideline(s):	SANTE/2020/12830, Rev.1 (2021), SANCO/825/00 rev.8.1 (2010), OECD No. 508, OECD No. 509, SANCO/3029/99 rev. 4 (2000), 7029/VI/95 rev.5 (1997)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN 10616
Formulation:	Suspension concentrates (SC)
CAS#:	Zoxamide: 156052-68-5 Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2
Lot/Batch #:	2006669001
Content of a.s. (actual):	Zoxamide: 64 g/L Phosphonic acid: 505 g/L
Manufacturing date:	15 June 2020
Stability of test compound (expiry date):	2 years from manufacturing:

Study design:

Four decline cure trials and two at harvest trials in grapes have been performed in Southern (Southern France, Spain) and Northern Europe (Hungary, Northern France) in 2020.

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated three times by spraying the SC formulation at the nominal application rate of 1500 g/ha of Phosphonic acid with an interval of 7 days and a PHI of 28 days.

Samples were taken both for residues analysis and for processing. Details for processing are described in A 2.2.5.2.5.

In at-harvest trials, samples of grapes were taken at day of application and 28 days after last application. In the decline curve trials, samples were taken at day of application and 1, 3, 7, 14, 21 and 28 days after last application.

These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.1.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-20-38 (“Analytical method validation to quantify Phosphonic acid residues in grape bunches (acidic matrix)”, Doc. No. 432-010).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for the analyte Phosphonic acid was 1 mg/kg. The limit of detection (LOD) was 0.30 mg/kg.

The maximum sampling to extraction interval for Phosphonic acid at a temperature of $\leq -18^{\circ}\text{C}$ was max. 67 days for berries for NEU and SEU trials. The final extracts in samples of RAC and processed commodities were analysed within 3 days for Phosphonic acid after storage at 4°C .

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability of 3 days in sample extracts. The recoveries were within the range between 70 – 110 %. In addition, the stability of the analytes in the final extracts kept at 4°C for 3 days was successfully verified for Phosphonic acid in the GLP study no. GLP-STUDY-20-38. Thus, the sample extracts were stable for the storage periods between extraction and analysis in this study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed LOQ level (1 mg/kg) and at 10x LOQ (10 mg/kg). The recoveries for Phosphonic acid in berries were always within the range of 70 - 110 % of nominal and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 74: Summary of the study 1 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days) (d)	Details on trial (e)
			g a.s./ ha Phosphonic acid	Water (L/ha)	g a.s./hL Phosphonic acid				Phosphonic acid		
CMN-20-44059 FR01 51420 Nogent l'Abbesse Grand Est Northern France (N-EU) 2020	Grape vine / Char- donnay (VITVI)	1. Year 2004 2. From 23/05/2020 to 01/06/2020 3. 24/08/2020	1504.9 1621.1 1499.9	496 535 495	303 303 303	1. 13/07/2020 2. 20/07/2020 3. 27/07/2020	BBCH 79	Wine grape bunches	15.8 15.1 20.9 17.3 16.2 16.2 <u>16.5</u>	0 1 3 7 14 21 28	Untreated: 5.34 Untreated: 3.75
CMN-20-44059 HU03 5094 – Tiszajeno Jász- Nagykun-Szolnok Hungary (N-EU) 2020	Grape vine / Cser- szegi Fűszeizes (VITVI)	1. 10/09/1995 2. From 20/06/2020 to 06/07/2020 3. 03/09/2020	1575.6 1555.4 1397.3	624 616 553	252.5 252.5 252.5	1. 23/07/2020 2. 30/07/2020 3. 06/08/2020	BBCH 81	Wine grape bunches	<u>85.5</u>	28	Untreated: <LOD
CMN-20-44059 HU04 8297 – Tapolca-Diszel Veszprém Hungary (N-EU) 2020	Grape vine/ Welschriesling (VITVI)	1. Year 1995 2. From 11/05/2020 to 26/05/2020 3. 22/09/2020	1401.4 1363.5 1367.5	740 720 722	189.4 189.4 189.4	1. 11/08/2020 2. 18/08/2020 3. 25/08/2020	BBCH 83	Wine grape bunches	25.7 15.3 26.1 12.9 29.0 16.3 <u>18.9</u>	0 1 3 7 14 21 28	Untreated: <LOD Untreated: <LOD

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline) LOQ: 1 mg/kg for Phosphonic acid

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.30 mg/kg for Phosphonic acid

Table A 75: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(b)	(b)	Phosphonic acid		Phosphonic acid	(c)				(d)	(e)
CMN-20-44059 FR05 30 300 Beaucaire Occitanie France (S-EU) 2020	Grape vine/ Cabernet Sauvignon (VITVI)	1. Year 1991 2. From 20/05/2020 to 10/06/2020 3. 14/09/2020	1495 1485 1485	394 392 392	379 379 379	03/08/2020 10/08/2020 17/08/2020	BBCH 85	Wine grape bunches	4.65 4.72 4.43 3.87 4.34 6.95 <u>4.67</u>	0 1 3 8 14 21 28	Untreated: <LOD Untreated: <LOD
CMN-20-44059 ES06 21720 Rociana del Con- dado Andalucia Spain (S-EU) 2020	Grape vine/ Zalema (VITVI)	1. February 2000 2. From 29/04/2020 to 16/05/2020 3. 19/08/2020	1568 1494 1489	828 789 786	189.4 189.4 189.4	09/07/2020 15/07/2020 22/07/2020	BBCH 83	Wine grape bunches	11.8 12.6 16.0 13.2 16.0 15.4 <u>30.5</u>	0 1 3 7 14 21 28	Untreated: <LOD Untreated: <LOD
CMN-20-44059 ES07 11560 Trebujena Andalucia Spain (S-EU) 2020	Grape vine/ Palomino (VITVI)	1. 30/01/2018 2. From 25/04/2020 to 10/05/2020 3. 27/08/2020	1561 1485 1485	824 784 784	189.4 189.4 189.4	16/07/2020 23/07/2020 30/07/2020	BBCH 83	Wine grape bunches	<u>12.7</u>	28	Untreated: <LOD

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 1 mg/kg for Phosphonic acid; LOD: 0.30 mg/kg for Phosphonic acid

A 2.3.3.1.2 Study 2 (report No. SCC-Study-G410TO417-21) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted. (The southern data are not relevant for the CEU zone).</p> <p>The objective of the field phase was to conduct trials in grapevines cultivated in open field conditions in Northern and Southern Europe and to provide to the analytical test site specimens resulting from 3 foliar applications with 3.0 L/ha of GWN-10616 (i.e. 180 g a.s./ha of Zoxamide) and 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid]).</p> <p>Three trials were conducted in Northern Europe (Belgium, The Netherlands) and five trials were conducted in Southern Europe (Italy, Spain).</p> <p>All maintenance products (plant protection products and fertilizers) were used simultaneously on both plots during the conduct of each trial (from first application to final sampling). Climatic conditions were normal. The first application was done at 7-8 DBA2, the second application was done at 7-9 DBA3 and the third application was done at 26-29 DBH. No additional adjuvants, surfactants or mixing partners were used for the applications.</p> <p>In the DCS trials, samplings were done at 0, 2-3, 6-7, 14-15 and 27-28 DALA. In the HS trials, samplings were done at 0 and 26-29 DALA.</p> <p>The objective of the analytical phase was to determine Zoxamide and Potassium phosphonate [expressed in equivalent Phosphonic acid] residues. Residues of metabolite RH-141452 were also determined as total fraction (a hydrolysis to release matrix-conjugated compounds was necessary). Residues in grapes without stems and caps were analysed.</p> <p>The validated (GLP-STUDY-21-101) method for Zoxamide used LC-MS/MS. The LOQ was 0.01. The linearity was checked by a 5-points calibration curve (single injection) using matrix-matched analytical standard solutions. For the procedural recoveries 4 fortification levels were tested. All samples were analysed within 24 hours from extraction.</p> <p>The analytical method for the determination of RH-141452 was validated in GLP-STUDY-21-102 also used LC-MS/MS. The LOQ was 0.01. All extracts were analysed within 1 day from the sample extraction. The linearity was checked by a 5-points calibration curve using matrix-matched standards. Procedural recoveries were carried out on 2 fortification levels.</p> <p>The analytical method for the determination of phosphonic acid in grape samples was validated in the study GLP-STUDY-21-103 used LC-MS/MS with the LOQ of 0.01. The linearity was checked also by a 5-points matrix-matched calibration, the procedural recoveries were carried out on 3 fortification levels. All samples were analysed within 24 hours from extraction.</p>
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Reference:	See KCA 6.3.1/02
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 2 AT HARVEST TRIALS IN NORTHERN EUROPE, & 2 DECLINE TRIALS AND 3 AT HARVEST TRIALS IN SOUTHERN EUROPE IN 2021, Loriau, P., 2022, report No. SCC-G410TO417-21, Doc. No. 632-40001
Guideline(s):	SANTE/2019/12752, SANTE/2020/12830 rev.1 (2021), ENV/JM/MONO(2007)17, ENV/JM/MONO(2011)50/Rev1 (2016), OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Three supervised residue trials (two at harvest trials and 1 decline curve trial) were conducted during 2021 on grapes in Northern (Belgium - 2 locations, The Netherlands - 1 location) and Southern Europe (Italy – 4 locations, Spain – 1 location). Each trial consisted of two plots: 1 plot (control) was left untreated and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rates of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid] with an interval of 7-8 days and a PHI of 28 days.

In at-harvest trials, samples of grapes were taken at day of application and 27/28/29 days after last application. In the decline curve trials, samples were taken at day of application and 2/3, 6/7, 14/15 and 27/28 days after last application.

These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.2.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-103 (“Validation of an analytical method for the determination of Phosphonic acid in grapes”, Doc. No. 432-008). Additional validation parameters were performed in study GLP-STUDY-21-55 (“Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities”, Doc. No. 432-004).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for the analyte Phosphonic acid was 0.01 mg/kg. The limit of detection (LOD) was 0.002 mg/kg.

The maximum sampling to extraction interval was 84 days for Phosphonic acid in grape berries at a temperature of -18°C for NEU and SEU trials.

The final extracts in samples of RAC and processed commodities were analysed within 24 hours. Thus, a storage stability testing is not needed.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 10x LOQ (0.1 mg/kg) and at 10000x LOQ (100 mg/kg). The mean recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing relative standard deviations of below 11.5 % and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 76: Summary of the study 2 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha Potassium Phospho- nate	Water (l/ha)	g a.s./hl Potassium Phospho- nate				Phosphonic acid		
(a)	(b)					(c)				(d)	(e)
SCC-G410TO417-21 G410-21F 1401 Baulers Belgium (N-EU) 2021	Grapevine/ Muscat bleu (VITVI)	1. 2013 2. from 26/06/2021 to 10/07/2021 3. 24/09/2021	2323 2323 2341	821 821 827	283 283 283	11/08/2021 19/08/2021 27/08/2021	BBCH 85	Grape bunches	37.277 41.572 57.790 61.022 <u>70.039</u>	0 3 7 14 28	Untreated: 0.173 mg/kg Untreated: 0.102 mg/kg Untreated: 0.185 mg/kg Untreated: 0.092 mg/kg Untreated: 0.209 mg/kg
SCC-G410TO417-21 G411-21F 7804 Ostiches Belgium (N-EU) 2021	Grapevine/ Auxerrois (VITVI)	1. 2019 2. from 30/06/2021 to 15/07/2021 3. 08/10/2021	2442 2383 2418	862 842 854	283 283 283	24/08/2021 01/09/2021 09/09/2021	BBCH 81	Grape bunches	30.068 <u>41.619</u>	0 29	Untreated: <LOQ Untreated: <LOQ
SCC-G410TO417-21 G412-21F 6562 KC Groesbeek The Netherlands (N-EU) 2021	Grapevine/ Cabernet blanc (VITVI)	1. 2006 2. from 19/06/2021 to 29/06/2021 3. 13/10/2021	2191 2172 2337	677 671 722	324 324 324	30/08/2021 07/09/2021 16/09/2021	BBCH 83	Grape bunches	33.205 <u>69.545</u>	0 27	Untreated: 0.028 mg/kg Untreated: 0.033 mg/kg

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.2.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

Table A 77: Summary of the study 2 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha Potassium phospho- nate	Water (l/ha)	g a.s./hl Potassium phospho- nate				Phosphonic acid		
(a)	(b)					(c)				(d)	(e)
SCC-G410TO417-21 G413-21F 74011 Castellaneta Italy (S-EU) 2021	Grapevine/ Cabernet Sauvignon (VITVI)	1. 2002 2. from 10/06/2021 to 18/06/2021 3. 01/10/2021	2301 2287 2287	812 807 807	283 283 283	18/08/2021 26/08/2021 03/09/2021	BBCH 87	Grape Bunches	5.525 5.682 5.994 5.386 <u>5.818</u>	0 3 7 14 28	Untreated: 0.306 mg/kg Untreated: 0.339 mg/kg Untreated: 0.255 mg/kg Untreated: 0.299 mg/kg Untreated: 0.335 mg/kg
SCC-G410TO417-21 G414-21F 94010 Calascibetta Italy (S-EU) 2021	Grapevine/ Sangiovese (VITVI)	1. 2005 2. from 10/06/2021 to 26/06/2021 3. 05/10/2021	2284 2265 2284	1008 1000 1008	227 227 227	24/08/2021 31/08/2021 08/09/2021	BBCH 85	Grape Bunches	14.694 17.308 28.177 20.977 <u>29.112</u>	0 2 61 5 27	Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ
SCC-G410TO417-21 G415-21F 94017 Regalbuto Italy (S-EU) 2021	Grapevine/ Frappato (VITVI)	1. 2016 2. from 22/05/2021 to 12/06/2021 3. 30/09/2021	2303 2322 2247	1017 1025 992	226 227 227	18/08/2021 26/08/2021 03/09/2021	BBCH 87	Grape Bunches	13.045 <u>25.403</u>	0 27	Untreated: <LOQ Untreated: <LOQ
SCC-G410TO417-21 G416-21F 95030 Nicolosi Italy (S-EU) 2021	Grapevine/ Nerello Mascalse (VITVI)	1. 2011 2. from 07/05/2021 to 21/05/2021 3. 29/09/2021	2441 2391 2341	1078 1056 1033	226 226 227	16/08/2021 24/08/2021 01/09/2021	BBCH 83-85	Grape Bunches	20.420 <u>35.345</u>	0 28	Untreated: 0.01398 mg/kg Untreated: 0.01740 mg/kg

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha Potassium phospho- nate	Water (l/ha)	g a.s./hl Potassium phospho- nate				Phosphonic acid		
(a)	(a)	(b)				(c)				(d)	(e)
SCC-G410TO417-21 G417-21F 09463 Haza (Burgos) Spain (S-EU) 2021	Grapevine/ Tempranillo (VITVI)	1. 2005 2. from 15/06/2021 to 20/06/2021 3. 05/10/2021	2292 2284 2368	810 807 836	283 283 283	25/08/2021 02/09/2021 09/09/2021	BBCH 83-85	Grape Bunches	5.623 <u>16.374</u>	0 26	Untreated: <LOQ Untreated: <LOQ

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.2.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

A 2.3.3.1.3 Study 3 (report No. SCC-Study-G107TO108-22) – Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The objective of the field phase was to conduct 2 trials in grapevine cultivated in open field conditions in Belgium and The Netherlands with 3 foliar applications of 180 g a.s./ha of Zoxamide and 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid]. Climatic conditions were normal. The first application was done at 7-8 DBA2, the second at 8 DBA3 and the third at 26-27 DBH. No additional adjuvants, surfactants or mixing partners were used for the applications. In the DCS trial, samplings of grapes were done at 0, 4, 7, 13 and 27 DALA. In the harvest trial, samplings of grapes were done at 0 and 26 DALA. The analytical phase was done in a same manner like in the previous study. The subjects of the determinations were also Zoxamide, Potassium phosphonate and metabolite RH-141452. LC-MS/MS determination was also applied.</p>
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Reference:	See KCA 6.3.1/03
Report:	RESIDUE STUDY - RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN GRAPEVINE AFTER THREE FOLIAR APPLICATIONS OF GWN-10616 IN 1 DECLINE TRIAL AND 1 HARVEST TRIAL IN NORTHERN EUROPE IN 2022, Loriau, P., 2023, report No. SCC-G107TO108-22, Doc. No. 632-40002
Guideline(s):	ENV/JM/MONO(2007)17, (EU) No. 283/2013, SANTE/2019/12752, SANTE/2020/12830, rev. 1 (2021), OECD No.509 (2021), ENV/JM/MONO(2007)17, OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Two supervised residue trials (1 at harvest trials and 1 decline curve trial) were conducted during 2021 on grapes in Belgium (1 location) and The Netherlands (1 location). Each trial consisted of two plots: 1 plot (control) was left untreated and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rates of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid] with an interval of 7-8 days and a PHI of 28 days.

In at harvest trials, samples were taken at day of application and 27 days after last application. In the decline curve trials, samples were taken at day of application and 4, 7, 13 and 27 days after last application. These supervised residue trials provide data relevant to conditions in the Northern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.3.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-103 (“Validation of an analytical method for the determination of Phosphonic acid in grapes”, Doc. No. 432-008). Additional validation parameters were performed in study GLP-STUDY-21-55 (“Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities”, Doc. No. 432-004).

Both method validations are described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) the analyte Phosphonic acid was 0.01 mg/kg. The limit of detection (LOD) was 0.002 mg/kg.

The maximum sampling to extraction interval was 96 days for Phosphonic acid in grape berries at a temperature of -18°C.

The final extracts in all RAC samples were analysed within 24 hours. Thus, a storage stability testing is not needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 10x LOQ (0.1 mg/kg) and at 500x LOQ (5.0 mg/kg). The mean recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal with relative standard deviations below 10 % and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 78: Summary of the study 3 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or plant- ing 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha Potassium phospho- nate	Water (L/ha)	g a.s./hL Potassium phospho- nate				Phosphonic acid		
(a)	(b)					(c)				(d)	(e)
SCC-G107TO108 G107-22F 1401 Baulers Belgium (N-EU) 2022	Grapevine/ Bronner (VITVI)	1. 2013 2. from 10/06/2022 to 15/06/2022 3. 14/09/2022	2333 2344 2259	824 828 798	283 283 283	02/08/2022 10/08/2022 28/08/2022	BBCH 83-85	Grape bunches	0.785 1.320 1.598 1.823 <u>1.439</u>	0 4 7 13 27	Residue levels of Phos- phonic acid are <LOQ in untreated samples.
SCC-G107TO108 G108-22F 6562 Groesbeek The Netherlands (N-EU) 2022	Grapevine/ Cabernet blanc (VITVI)	1. 2006 2. from 06/06/2021 to 15/06/2021 3. 28/09/2021	2266 2288 2314	700 707 715	323 323 323	18/08/2022 25/08/2022 02/09/2022	BBCH 79-81	Grape bunches	2.750 <u>3.606</u>	0 26	Residue levels of Phos- phonic acid are <LOQ in untreated samples.

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.1.3.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

A 2.3.3.2 Pome fruits

Table A 79: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2012) (Potassium phosphonate)	No representative use within the 91/414 procedure.				
cGAP EU (Art. 12)	1-6	1980 (Potassium phosphoante)	7	BBCH 9-81	28
Intended cGAP (# 3)	2	2265 (Potassium phosphonate) 1500 (Phosphonic acid)	6-8	BBCH 51-69	nr

A 2.3.3.2.1 Study 1 (report No. BPL-STUDY-19-000033) – Southern Europe

Comments of zRMS:	<p>The study has been accepted. It is not relevant for the current zone.</p> <p>The obtained residue data can be used as supplemental information only.</p> <p>The objective of this study was the determination of phosphonic acid, Zoxamide (as sum of enantiomers), and separately (R)-Zoxamide, (S)-Zoxamide, and metabolites RH-150721 (as sum of enantiomers) and separately (R)-RH-150721, (S)-RH-150721; RH-129151 (as sum of enantiomers) and separately (R)-RH-129151 and (S)-RH-129151; RH-141288 (as sum of enantiomers) and separately (R)-RH-141288 and (S)-RH-141288; moreover RH-24549 and RH-141452 in apple and pear.</p>
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Reference:	See KCA 6.3.2/01
Report:	DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019), Longhi, D., 2021, report No. BPL-STUDY-19-000033; Doc. No. 632-20001
Guideline(s):	OECD No. 509 (2009), SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev.4 (2000), SANTE/2020/12830 Rev. 1 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes/supplemental

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	L1801669001
Content of a.s. (actual):	Zoxamide: 59.67 g/L Phosphonic acid: 514.5 g/L Potassium phosphonate ^a : 753.5 g/L
Stability of test compound (expiry date):	03/01/2020

^a Calculated considering the molecular weight of Phosphonic acid and monopotassium phosphonate.

Study design:

Two supervised residue trials (at harvest trials) were conducted during 2019 on pome fruits (1 in apples and 1 in pears) in 2 locations in Italy. Each trial consisted of three subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rates of 1512 g/ha of Phosphonic acid at BBCH 69.

Samples of apples and pears were taken at BBCH 87 in the at-harvest trials. These supervised residue trials provide data relevant to conditions in the Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.1.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study BPL-STUDY-19-000111 (“Validation of an analytical method for the determination of Phosphonic acid in high water content agricultural commodities (apple)”, Doc. No. 432-014).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) was 1 mg/kg and the limit of detection (LOD) 0.3 mg/kg for Phosphonic acid.

The maximum sampling to extraction interval at -18°C was 25 days for Phosphonic acid in apples and pears. The maximum extraction to quantification interval at 4°C was < 1 day. Thus, no storage stability data are needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (1 mg/kg) and at 10x LOQ (10 mg/kg). The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 80: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Remarks
			g a.s./ ha Phosphonic acid	Water (l/ha)	g a.s./hl Phosphonic acid				Phosphonic acid		
FR19GWNP11 MR01 44123 Boara (FE) Italy (S-EU) 2019	Apple/ Imperatore	1. nr 2. nr 3. 10/09/2019	1540 1530	1042 1035	148 148	12/04/2019 18/05/2019	BBCH 69	Apple	<u>2.85</u>	145	Untreated: < LOQ.
FR19GWNP21 LG01 44045 XII Morelli (FE) Italy (S-EU) 2019	Pear/ Abate Fetel	1. nr 2. nr 3. 02/09/2019 3. 10/	1520 1530	1025 1037	148 148	02/04/2019 08/04/2019	BBCH 69	Pear	<u>5.18</u>	147	Untreated: < LOQ

nr: not recorded

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.1.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.3 mg/kg for Phosphonic acid

LOQ: 1 mg/kg for Phosphonic acid

A 2.3.3.2.2 Study 2 (report No. BPL-STUDY-19-000034) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The objective of this study was the determination of phosphonic acid, Zoxamide (as sum of enantiomers), and separately (R)-Zoxamide, (S)-Zoxamide, and metabolites RH-150721 (as sum of enantiomers) and separately (R)-RH-150721, (S)-RH-150721; RH-129151 (as sum of enantiomers) and separately RH-129151 (A) and RH-129151 (B) (since only the racemate standard was provided); RH-141288 (as sum of enantiomers) and separately (R)-RH-141288 and (S)-RH-141288; moreover RH-24549 and RH-141452 in apple and pear from 6 harvest trials (3 apple and 3 pear) set in Italy, Northern France, Poland and Hungary. Each of them was carried out with 2 applications on different plots with ZOXIUM 240 SC (GWN 9790 EU; (T1)) and GWN 10616 (T2).</p> <p>Zoxamide moiety determinations were performed by an LC-MS/MS method validated in the study BPL-STUDY-18-000085 in grape, potato, tomato, cucumber, and onion consistently with SANTE/2020/12830 rev.1. The metabolite RH-141452 for determination was hydrolysed to free form from the conjugated one. Phosphonic acid was determined using an LC-MS/MS method validated in the study BPL-STUDY-19-000111.</p> <p>For Zoxamide moiety for all fortification levels the recoveries were within the acceptable range of 70-110% except of Zoxamide (R), Zoxamide (S), RH-141288 (R) and RH-141288 (S) in pear (not hydrolysed), which were higher than 110 % (<i>deviation 1</i>). For RH-141452, hydrolysed, and phosphonic acid for all fortification levels the recoveries were within the acceptable range of 70-110%. The methods meet the requirements of the guideline SANTE/2020/12830, Rev. 1.</p> <p>5 deviations were issued for the field and analytical phase without any impact on the study.</p>
Reference:	See KCA 6.3.2/02
Report:	DETERMINATION OF ZOXAMIDE OR ZOXAMIDE + PHOSPHOROUS ACID FOLLOWING MULTIPLE APPLICATIONS OF GWN 9790 EU AND GWN 10616 IN APPLE AND PEAR RAW AGRICULTURAL COMMODITIES (SOUTHERN EUROPE - 2 TRIALS YEAR 2019 NORTHERN EUROPE - 4 TRIALS YEAR 2019), Longhi, D., 2021, report No. BPL-STUDY-19-000034, Doc. No. 632-20002
Guideline(s):	OECD No. 509 (2009), SANCO/825/00 rev.8.1 (2010), SANCO/3029/99 rev.4 (2000), SANTE/2020/12830 Rev. 1 (2021)
Deviations:	5 minor, the study not affected
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	L1801669001
Content of a.s. (actual):	Zoxamide: 59.67 g/L Phosphonic acid: 514.5 g/L Potassium phosphonate ^a : 753.5 g/L
Stability of test compound (expiry date):	03/01/2020

^a Calculated considering the molecular weight of Phosphonic acid and monopotassium phosphonate.

Study design:

Six at harvest trials in grapes have been performed in Southern (Italy – 2 locations) and Northern Europe (Hungary – 1 location, Northern France – 1 location, Poland – 2 locations) in 2019 in pome fruits (3 in apples and 3 in pears).

Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rate of 1512 g Phosphonic acid/ha at BBCH 69.

Samples of apples and pears were taken at harvest at BBCH 87. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.2.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study BPL-STUDY-19-000111 (“Validation of an analytical method for the determination of Phosphonic acid in high water content agricultural commodities (apple)”, Doc. No. 432-014).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) was 1 mg/kg and the limit of detection (LOD) 0.3 mg/kg for Phosphonic acid.

The maximum sampling to extraction interval at -18°C was 30 days for Phosphonic acid in apples and pears for NEU and SEU trials. The maximum extraction to quantification interval at 4°C was < 1 day for all metabolites. Thus, no storage stability data are needed.

However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries of Phosphonic acid were always within the range of 70 - 110 %. Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (1 mg/kg) and at 10x LOQ (10 mg/kg). The recoveries of Phosphonic acid were always within the range of 70 - 110 % of nominal showing an overall relative standard deviation (RSD) of ≤ 20 % and thus, the accuracy of the analytical method on the day of analysis was confirmed.

Results:

Table A 81: Summary of the study 2 trials- Northern Europe

Trial No./ Location/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Remarks
			g a.s./ ha Phosphonic acid	Water (L/ha)	g a.s./hL Phosphonic acid				Phosphonic acid		
ATA-19-39250 PL03 62 404 Samarzewo, Wiekopolskie Poland (N-EU) 2019	Pear/ Izolda (PYUCO)	1. 21/03/2004 2. from 12/04/2019 to 06/05/2019 3. 14/08/2019	1495 1482	1013 1004	148 148	25/04/2019 01/05/2019	BBCH 69	Pear	<u>1.85</u>	105	Residue levels of Phos- phonic acid in all un- treated samples were <LOQ.
ATA-19-39250 PL04 96 521 Gizyczki, Łódzkie Poland (N-EU) 2019	Pear/ Konferencja (PYUCO)	1. 10/09/2018 2. from 12/04/2019 to 05/05/2019 3. 26/08/2019	1460 1462	494 495	296 295	26/04/2019 02/05/2019	BBCH 69	Pear	<u>11.6</u>	116	Residue levels of Phos- phonic acid in all un- treated samples were <LOQ.
ATA-19-39250 FR 05 80260 Saint Gratien Hauts de France Northern France (N-EU) 2019	Apple/ Fréquin Rouge (MABSD)	1. 01/03/2013 2. from 24/04/2019 to 10/05/2019 3. 11/10/2019	1443 1483	587 603	246 246	30/04/2019 06/05/2019	BBCH 68	Apple	<u>1.78</u>	158	Residue levels of Phos- phonic acid in all un- treated samples were <LOQ.
ATA-19-39250 HU06 6795 Bordány Csongrád Country Hungary (N-EU) 2019	Apple/ Idared (MABSD)	1. more than 12 years 2. from 11/04/2019 to 29/04/2019 3. 28/08/2019	1570 1571	638 835	267 188	24/04/2019 29/04/2019	BBCH 69	Apple	<u>2.63</u>	121	Residue levels of Phos- phonic acid in all un- treated samples were <LOQ.

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.2.

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated

- (d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
LOD: 0.3 mg/kg for Phosphonic acid; LOQ: 1 mg/kg for Phosphonic acid

Table A 82: Summary of the study 2 trials - Southern Europe

Trial No./ Location/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Remarks
			g a.s./ ha Phosphonic acid	Water (l/ha)	g a.s./hl Phosphonic acid				Phosphonic acid		
ATA-19-39250 IT01 37050 Albaro (VR) Italy (S-EU) 2019	Apple/ Golden delicious	1. 1977 2. from 27/03/2019 to 10/04/2019 3. 11/09/2019	1554 1570	524 532	148 148	17/04/2019 24/04/2019	BBCH 69	Apple	<u>3.32</u>	140	Untreated: <LOD
ATA-19-39250 IT02 46032 Castelbelforte (MN) Italy (S-EU) 2019	Pear/ Abate	1. March 2009 2. from 04/04/2019 to 25/04/2019 3. 30/08/2019	1419 1514	673 717	211 211	09/04/2019 15/04/2019	BBCH 67	Pear	<u>4.33</u>	137	Untreated: <LOD

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.2.

- (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
LOD: 0.3 mg/kg for Phosphonic acid;
LOQ: 1 mg/kg for Phosphonic acid

A 2.3.3.2.3 Study 3 (report No. SCC-G401T0409-21) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of the study was to determine residues of GWN-8030 (Zoxamide) and Potassium phosphonate [expressed in equivalent Phosphonic acid]. Residues of metabolite RH-141452 were also determined as total fraction (a hydrolysis step to release potentially matrix-conjugated compounds was necessary). Residues in apple RAC (whole fruits without stem) were analysed.</p> <p>The LC-MS/MS methods applied for the determination were as follows: of Zoxamide in apple AM-GLP-STUDY-21-53, of RH-141452 in apple AM-GLP-STUDY-21-54, and of Phosphonic acid AM-GLP-STUDY-21-55.</p> <p>The LOQs were 0.01 mg/kg. The relevant validation parameters as required.</p> <p>Note: some samples were taken during the field phase for a processing study SCC-G401T0409-21-P conducted in parallel to the residue study SCC-G401T0409-21.</p>
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Reference:	See KCA 6.3.2/03
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES CULTIVATED IN OPEN FIELD CONDITIONS AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 4 DECLINE TRIALS AND 1 AT HARVEST TRIAL IN NORTHERN EUROPE, AND 4 DECLINE TRIALS IN SOUTHERN EUROPE IN 2021, Loriau, P., 2022, report No. SCC-G401T0409-21, Doc. No. 632-20005
Guideline(s):	ENV/JM/MONO(2007)17, SANTE/2020/12830 rev.1 (2021), SANTE/2019/12752, ENV/JM/MONO(2011)50/Rev1 (2016), OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Nine supervised residue trials (8 decline curve trials and 1 at harvest trial) in pome fruits have been performed in Southern (Greece, Spain, Italy, Southern France, 1 location each) and Northern Europe (Belgium, Germany, The Netherlands, Poland and Hungary, 1 location each) in 2021. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rate of 2.265 kg Potassium Phosphonate [corresponding to 1.500 kg Phosphonic acid] at BBCH 69.

Samples of apples were taken at BBCH 75, BBCH 79, BBCH 85 and BBCH 87-89 in the decline curve trials and at BBCH 87 in the at harvest trials. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.3.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study GPL-STUDY-21-55 (“Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities”, Doc. No. 432-004)

The method validations are described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) was 0.01 mg/kg and the limit of detection (LOD) 0.002 mg/kg for Phosphonic acid.

The maximum sampling to extraction interval at -18°C was 29 days for Phosphonic acid in apples for NEU and SEU trials. The maximum extraction to quantification interval at 4°C was 4 days for Phosphonic acid. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The extract stability of Phosphonic acid in the final extract kept at $5 \pm 3^\circ\text{C}$ for 4 days was successfully verified in the GLP study no. GPL-STUDY-21-55, in addition.

Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 1000x LOQ (10 mg/kg) and at 2500xLOQ (25 mg/kg). The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing an overall relative standard deviations (RSD) of < 9 % and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 83: Summary of the study 3 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(b)		Potassium phosphonate		Potassium phosphonate	(c)				(d)	(e)
SC C-G401T0409-21 G401-21F 4280 Merdorp Belgium (N-EU) 2021	Apple/ Jonagold (MABSD)	1. 2013 2. from 26/04/2021 to 10/05/2021 3. 14/09/2021	2083 2031	552 538	377.4 377.5	03/05/2021 10/05/2021	BBCH 69	Apple	0.769 1.41 1.52 <u>1.45</u>	51 95 115 127	Untreated: 0.594 mg/kg Untreated: 0.0752 mg/kg Untreated: 0.115 mg/kg Untreated: 0.0927 mg/kg
SC C-G401T0409-21 G402-21F 41472 Neuss Germany (N-EU) 2021	Apple/ Delbar (MABSD)	1. 2006 2. from 26/04/2021 to 17/05/2021 3. 15/09/2021	2298 2273	609 602	377.3 377.6	11/05/2021 17/05/2021	BBCH 69	Apple	0.911 2.06 1.97 <u>2.38</u>	59 78 94 121	Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ
SC C-G401T0409-21 G403-21F 4011 EX Zoelen The Netherlands (N-EU) 2021	Apple/ Elstar (MABSD)	1. 2005 2. 24/04/2021 to 18/05/2021 3. 20/09/2021	2280 2291	604 607	377.5 377.4	12/05/2021 18/05/2021	BBCH 69	Apple	2.17 2.11 1.86 <u>1.22</u>	59 78 97 125	Untreated: <LOQ Untreated: 0.0185 mg/kg Untreated: 0.0144 mg/kg Untreated: 0.0141 mg/kg

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(a)	(b)	Potassium phosphonate		Potassium phosphonate	(c)				(d)	(e)
SC C-G401T0409-21 G404-21F 64-606 Wychowaniec Popowko) Poland (N-EU) 2021	Apple/ Boskop (MABSD)	1. 2019 2. 06/05/2021 to 19/05/2021 3. 30/09/2021	2487 2241	659 594	377.4 377.3	12/05/2021 19/05/2021	BBCH 69	Apple	0.938 3.31 3.85 <u>0.687</u>	61 96 124 134	Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ.
SC C-G401T0409-21 G405-21F 6795 Bordany Hungary (N-EU) 2021	Apple/ Jonaprince (MABSD)	1. 2008 2. 26/04/2021 to 12/05/2021 3. 13/09/2021	2237 2384	593 632	377.2 377.2	05/05/2021 10/05/2021	BBCH 69	Apple	<u>6.40</u>	126	Untreated: 0.0134 mg/kg

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.3.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Phosphonic acid

LOQ: 0.01 mg/kg for Phosphonic acid

Table A 84: Summary of the study 3 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
	(a)	(b)	Potassium phosphonate		Potassium phosphonate	(c)				(d)	(e)
SC C-G401T0409-21 G406-21F 62370 Reynies Southern France (S-EU) 2021	Apple/ Golden Pink (MABSD)	1. 2008 2. from 02/04/2021 to 30/04/2021 3. 22/09/2021	2255 2237	597 593	378 377	24/04/2021 30/04/2021	BBCH 69	Apple	2.06 6.52 6.28 6.86	61 88 122 143	Untreated: 0.393 Untreated: 2.86 Untreated: 2.53 Untreated: 3.37 * Application of Fosetyl in 2019, 2020, of Potas- sium phosphonate in 2019 and of fertilizer based and Phosphorous in 2021. <u>Not considered for MRL setting and risk assessment.</u>
SC C-G401T0409-21 G407-21F 95019 Zafferana Et- nae Italy (S-EU) 2021	Apple/ Red delicious (MABSD)	1. 2002 2. from 26/04/2021 to 13/05/2021 3. 05/10/2021	2199 2204	680 681	323 324	06/05/2021 13/05/2021	BBCH 69	Apple	10.2 10.4 8.56 <u>7.93</u>	81 120 138 145	Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ Untreated: <LOQ

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(a)	(b)	Potassium phosphonate		Potassium phosphonate	(c)				(d)	(e)
SC C-G401T0409-21 G408-21F 26540 Alfaro Spain (S-EU) 2021	Apple/ Fuji (MABSD)	1. 2004 2. 30/03/2021 to 13/04/2021 3. 18/10/2021	2348 2129	726 659	323 323	07/04/2021 13/04/2021	BBCH 69	Apple	5.33 0.53 2.15 <u>1.02</u>	51 93 139 188	Untreated: 0.0595 Untreated: <LOQ Untreated: 0.0361 Untreated: 0.0190
SC C-G401T0409-21 G409-21F 58300 Esovalta (Pella)) Greece (S-EU) 2021	Apple/ Granny Smith (MABSD)	1. 2012 2. 05/04/2021 to 20/04/2021 3. 24/09/2021	2243 2307	693 713	324 324	14/04/2021 21/04/2021	BBCH 69	Apple	0.864 3.83 4.94 5.38	77 111 140 156	Untreated: 0.0934 Untreated: 3.63 Untreated: 4.55 Untreated: 4.33 Application of Fosetyl in 2019 <u>Not considered for MRL setting and risk assessment.</u>

Residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.3.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Phosphonic acid

LOQ: 0.01 mg/kg for Phosphonic acid

A 2.3.3.2.4 Study 4 (report No. G105TO106-22) – Southern Europe

Comments of zRMS:	The study has been accepted, however the residue data are not relevant for CEU zone; it can be supplementary. In determinations of zoxamide and phosphonic acid all mean recoveries at each fortification level were in the range of 70 – 110 % with relative standard deviations below 20 %.
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Reference:	See KCA 6.3.2/04
Report:	RESIDUES OF GWN-8030 AND PHOSPHONIC ACID IN APPLES AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 2 DECLINE TRIALS IN SOUTHERN EUROPE IN 2022, Loriau, P., 2023, report No. SCC-G105TO106-22, Doc. No. 632-20006
Guideline(s):	ENV/JM/MONO(2007)17, SANTE/2019/12752, SANTE/2020/12830, rev. 1 (2021), OECD No. 509 (20219
Deviations:	None
GLP:	Yes
Acceptability:	Yes, supplemental

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Two supervised residue trials (2 decline curve trials) in pome fruits have been performed in Southern Europe (Greece, Italy, 1 location each) in 2022. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated twice by spraying the SC formulation GWN-10616 at the nominal application rate of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1500 g a.s./ha of Phosphonic acid]). with last application at BBCH 69.

Samples of apples were taken at BBCH 75/77, BBCH 79, BBCH 85 and BBCH 87-89 in the decline curve trials. These supervised residue trials provide data relevant to conditions in the Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.2.4.

Methods:

The method for the determination of Zoxamide was successfully validated in study GPL-STUDY-21-55 (“Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities”, Doc. No. 432-004). An extension of the calibration range and the verification of the recoveries at higher levels was validated in the concurrent study LBN-0007-2022, Doc. No. 645-001, KCA 6.1/13)

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) is 0.01 mg/kg and the limit of detection (LOD) is 0.002 mg/kg for Phosphonic acid.

The maximum sampling to extraction interval at -18°C was 55 days for Phosphonic acid. The maximum extraction to quantification interval at $5 \pm 3^\circ\text{C}$ was < 1 day for Phosphonic acid. Thus, no storage stability data in extracts are needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The extract stability of Phosphonic acid in the final extracts kept at $5 \pm 3^\circ\text{C}$ was successfully verified in the GLP study no. GPL-STUDY-21-55 for 4 days, in addition.

Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg), at 200x LOQ (2 mg/kg), 500x LOQ (5 mg/kg), 800x LOQ (8 mg/kg) and at 1000xLOQ (10 mg/kg). The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing relative standard deviations of $\leq 20\%$ and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 85: Summary of the study 4 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(b)		Potassium phosphonate		Potassium phosphonate	(c)				(d)	(e)
SCC-G105T0106-22 G105-22F 95039 Zafferana Italy (S-EU) 2022	Apple/ Golden Delici- ous (MABSD)	1. 1985 2. from 03/05/2022 to 17/05/2022 3. 30/09/2022	2245 2275	694 703	323.5 323.6	11/05/2022 17/05/2022	BBCH 69	Apple	8.36 4.70 2.90 <u>5.92</u>	80 108 129 136	Untreated: <LOD Untreated: <LOD Untreated: <LOD Untreated: <LOD
SCC-G105T0106-22 G106-22F 58002 Neos Agios Athanasios Greece (S-EU) 2022	Apple/ Super chief (MABSD)	1. 2012 2. 01/05/2022 to 10/05/2022 3. 20/09/2022	2292 2229	708 689	323.7 323.4	04/05/2022 10/05/2022	BBCH 69	Apple	4.36 3.97 4.69 <u>4.72</u>	101 115 125 133	Untreated: 0.117 Untreated: 0.102 Untreated: 0.0593 Untreated: 0.0797

* Residue data for Zoxamide and its metabolite Rh-141452 are presented in A 2.1.3.2.4.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOD: 0.002 mg/kg for Phosphonic acid

LOQ: 0.01 mg/kg for Phosphonic acid

A 2.3.3.3 Potatoes

Table A 86: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (EFSA, 2012) (Potassium phosphonate)	No representative use within the 91/414 procedure.				
cGAP EU (Art. 12)	3	3020 (Potassium phosphonate)	7	10 to	7
Intended cGAP (# 5)	3	1887.5 (Potassium phosphonate) 1250 Phosphonic acid	7	BBCH 21-89	7

A 2.3.3.3.1 Study 1 (report No. GLP-21-14) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of this study was to determine the residues level of Zoxamide, its metabolites RH-141452 and RH-141455 and Potassium phosphonates (expressed as phosphonic acid and fosetyl equivalents) in potatoes after spray application of one of the following products: GWN-9790 EU (SC containing 240 g/L Zoxamide), GWN-10616 (SC containing 60 g/L Zoxamide and 755 g/L Potassium phosphonates (504 g/L Phosphorous acid)). The study trials were performed on potatoes in 8 different locations in France, Poland, Spain and Italy. The study included also processing samples taken from 3 trials to produce potato culls, potato waste and potato dried pulp sub-samples.</p> <p>The determination of zoxamide in potato tubers was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-50. Zoxamide was determined as racemate (no chiral column) based on BPL-STUDY-18-000085 method. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of total RH-141452 and RH-141455 (sum of the free fractions and the conjugated ones) in potato tuber was performed by LC-MS/MS method with a sample hydrolysis step validated in the concurrent study BPL-STUDY-18-000085. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of phosphonic acid (fosetyl equivalents) in potato tuber and processed commodities (potato culls, potato waste and potato dried pulp) was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-52. The extraction efficiency was not required to verify since this method was based on the extraction procedure which was used and accepted in the Fosetyl RAR.</p> <p>Procedural recovery values were obtained in parallel to the analyte measurements, confirming the robustness and repeatability of the method.</p>
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Reference: See KCA 6.3.3/01
Report: GWN-8030, ITS METABOLITES AND PHOSPHONATES IN POTATOES

Guideline(s):	AFTER THREE APPLICATIONS OF GWN-9790 EU AND GWN-10616 IN THE OPEN FIELD (NORTHERN AND SOUTHERN EU, 8 TRIALS, YEAR 2021), Longhi, D., 2023, report No. GLP-STUDY-21-14, Doc. No. 633-09001 OECD No. 509 (2009), 7029/VI/95 rev. 5 (1997), SANTE/2019/12752 (2019), SANTE/2020/12830 rev. 1 (2021), SANTE 2017/10632 rev. 3 (2017), OECD No. 508
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Material, study design and methods

Material / test item:

Test material:	Zoxium 240 SC	GWN-10616
Formulation:	Suspension concentrate	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	ZA2701	P2102669001
Content of a.s. (actual):	Zoxamide: 239 g/L g/L	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Manufacturing date:	27/01/2021	01/03/2021
Stability of test compound (expiry date):	At least 2 years from the production date.	At least 2 years from the production date.

Study design:

Four at harvest trials in potatoes have been performed in Southern (Italy – 1 location, Spain – 1 location) and Northern Europe (Northern France – 1 location, Poland – 1 location) in 2021.

Each trial consisted of two plots: 1 plot (control) was left untreated, and one was treated three times by spraying the SC formulation GWN-10616 with 3 L/ha at the nominal application rates of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1512 g a.s./ha of Phosphonic acid]) with an interval of 7 days and a PHI of 7 days.

In 1 trial (FR02), samples were taken both for residues analysis and for processing. Details for processing are described in A 2.2.5.2.4.

In at harvest trials, samples of potatoes were taken at 7 days after the last application. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.2.3.3.1.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-52 (“Validation of an analytical method for the determination of Phosphonic acid in potato”, Doc. No. 432-015).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) of the analyte Phosphonic acid was 0.01 mg/kg in potato tubers. The limit of detection (LOD) was 0.002 mg/kg.

The maximum sampling to extraction interval was 56 days for Phosphonic acid in potato tubers at a temperature of $\leq -18^{\circ}\text{C}$. The final extracts in samples of RAC were analysed within 24 hours. Thus, a storage stability testing is not needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The mean recoveries were within 60 - 120 % and an RSD of 1 % at LOQ level (=0.01 mg/kg) and within 70 - 110 % and an RSD of 1 % at 10000 x LOQ level (=100 mg/kg).

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg) and at 10000x LOQ (100 mg/kg). The mean recoveries for Phosphonic acid were within 60 - 120 % and an RSD of 1 % at LOQ level (=0.01 mg/kg) and within 70 - 110 % and an RSD of 1 % at 10000 x LOQ level (=100 mg/kg) and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 87: Summary of the study 1 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
	(a)	(b)	Phosphonic acid		Phosphonic acid	(c)				(d)	(e)
TGT-21-49177 FR02 62860 - Inchy en Ar- tois Hauts de France Northern France (N-EU) 2021	Potato/ Desire (SOLTU)	1. 30/04/2021 2. from 02/07/2021 to 22/07/2021 3. 25/08/2021	1415.2 1464.8 1446.0	383 397 392	369.2 369.2 369.2	04/08/2021 11/08/2021 18/08/2021	BBCH 46	Potato tubers	<u>53.9</u>	7	Untreated: <LOQ
TGT-21-49177 PL04 14-100 - Kajokowo Warmińsko-Mazur- skie Poland (N-EU) 2021	Potato/ Ignacy (SOLTU)	1. 27/04/2021 2. from 28/06/2021 to 02/08/2021 3. 30/08/2021	1475.8 1475.8 1491.7	307 307 310	481.2 481.2 481.2	09/08/2021 16/08/2021 23/08/2021	BBCH 48	Potato tubers	<u>20.7</u>	7	Untreated: <LOQ

Residue data for Zoxamide and its metabolites are presented in A 2.2.3.3.1.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Phosphonic acid

LOD: 0.002 mg/kg for Phosphonic acid

Table A 88: Summary of the study 1 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial*
			g a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
(a)	(a)	(b)				(c)				(d)	(e)
TGT-21-49177 ES06 11140 - Conil de la Frontera Andalucia Spain (S-EU) 2021	Potato/ Panamera (SOLTU)	1. 18/03/2021 2. from 15/06/2021 to 27/07/2021 3. 03/08/2021	1578.3 1443.6 1424.8	547 500 493	288.7 288.7 288.8	13/07/2021 20/07/2021 27/07/2021	BBCH 48	Potato tubers	<u>7.14</u>	7	Untreated: <LOQ
TGT-21-49177 IT08 46014 - Castel- lucchio Lombardy Italy (S-EU) 2021	Potato/ Hermes (SOLTU)	1. 26/02/2021 2. from 01/06/2021 to 20/06/2021 3. 29/07/2021	1410.9 1459.0 1516.7	489 505 525	288.7 288.7 288.7	08/07/2021 15/07/2021 22/07/2021	BBCH 48/49	Potato tubers	<u>11.6</u>	7	Untreated: 0.01

Residue data for Zoxamide and its metabolites are presented in A 2.2.3.3.1.

- (a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
LOQ: 0.01 mg/kg for Phosphonic acid
LOD: 0.002 mg/kg for Phosphonic acid

A 2.3.3.3.2 Study 2 (report No. IF22-06194195) – Southern and Northern Europe

Comments of zRMS:	<p>The study has been accepted.</p> <p>The study included 15 supervised residue trials conducted in Germany, Poland, Northern France, Italy, Spain and Greece during the 2022-2023 season. 8 trials were conducted as decline trials, 4 as harvest trials and 3 were conducted as processing trials. The spraying applications were performed at 19-23 DBH, 13-16 DBH and 6-8 DBH with a nominal rate of 2.5 L test item/ha.</p> <p>The purpose of the study in general was to determine the magnitude of the residues of zoxamide and its metabolites (RH-141452, RH-141455), and phosphonic acid in potato tubers after 3 foliar applications of GWN-10616 (60 g/L zoxamide and 755 g/L dipotassium phosphonates i.e. 500 g/L phosphonic acid). In addition, residues of phosphonic acid were also determined in whole potatoes prior to processing.</p> <p>The purpose of the processing phase was the generation of processed products of potato i.e. peeled potatoes, wet peel, microwaved/boiled potatoes, baked potatoes, fried potatoes, crisps, French fries, flakes, process waste, ensiled, starch, potato protein, dried pulp and canned potatoes, and then the determination of the residue levels of phosphonic acid to calculate the processing factors in the context of three foliar applications of GWN-10616.</p> <p>For all determinations 3 separate methods were used, validated in study IF23-06197316. Final determination was achieved by LC-MS/MS.</p> <p>To continuously prove the validity of the analytical method procedural recovery specimens were prepared by fortification of untreated specimen material. Fortification was performed with fortification solution containing Zoxamide, RH-141452, RH-141455 and phosphonic acid. The fortification levels were at LOQ and at least one higher level for each analyte in potato sample. Procedural recoveries were handled and stored in the same way and for the same time period as the analytical samples that have been prepared within the same analytical set.</p> <p>The storage period of deep-frozen samples intended for zoxamide determination ranged between 153 and 357 days, for RH-141452 and RH-141455 ranged between 196 and 401 days and for phosphonic acid between 115 and 321 days. The storage time of the deep-frozen processed fraction specimens ranged between 169 and 287 days.</p> <p>The study report is very detailed and included many amendments. However, they have no impact on the study. The relevant results are given below by the applicant.</p>
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Reference: See KCA 6.3.3/02

Report: STUDY ON THE RESIDUE BEHAVIOUR OF GWN-8030 AND MDI-0074 IN POTATO AND ITS PROCESSED PRODUCTS AFTER TREATMENT WITH GWN-10616 UNDER FIELD CONDITIONS IN GERMANY, POLAND, NORTHERN FRANCE, ITALY, SPAIN AND GREECE, 2022, Gabriel, E.J., 2023, report No. IF22-06194195, Doc. No. 638-019

Guideline(s): 7029/VI/95 - rev.5, SANTE/2019/12752, OECD No. 509, OECD Series on Testing and Assessment, Number 96 (2008), OECD No. 508 (2008), ENV/JM/MONO(2007)17, SANTE/2020/12830 Rev. 1

Deviations: Yes, no impact on the study

GLP: Yes

Acceptability: Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate (SC)
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Twelve supervised residue trials (8 decline curve trials and 4 at harvest trials) in potatoes have been performed in Southern (Greece, Spain, Italy, 2 locations each) and Northern Europe (Germany, Poland and Northern France, 2 location each) in 2022. In addition, three processing trials in Germany, Northern France and Italy hve been conducted. Each trial consisted of two subplots: 1 plot (control) was left untreated and one was treated three times by spraying the SC formulation GWN-10616 at the nominal application rate of 1887.5 g/ha Potassium phosphonates [equivalent to 1.250 kg /ha for Phosphonic acid] and a PHI of 7 days. Samples of apples were taken at day 0, and 3 and 7 ± 1 days after last application in the decline curve trials and at day 0 and 7 ± 1 days after last application in the at-harvest trials and the processing trials. These supervised residue trials provide data relevant to conditions in the Northern and Southern European Zone. The residue data for Zoxamide and its metabolites are presented in A 2.1.3.3.2.

Methods:

The method for the determination of Phosphonic acid was successfully validated in study IF23-06197316 (“Validation of analytical methods for determination of GWN-8030, MDI-0043, MDI-0050 and MDI-0074 in potato matrices”, Doc. No. 432-017).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for Phosphonic acid is 0.02 mg/kg and the limit of detection (LOD) is 0.006 mg/kg.

The maximum sampling to extraction interval at -18°C was for the Northern trials 315 days for Phosphonic acid and for the Southern trials 321 days. The maximum extraction to quantification interval at 4°C was 4 days for Phosphonic acid. Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples. Extracts contain isotopically labelled internal standards (IL-IS) for quantification, thus, testing of final volume extract stability was not required since the IL-IS compensate for losses during extract storage according to SANTE/2020/12830 rev. 1.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.02 mg/kg), at 10x LOQ (0.2 mg/kg) and 6050 x LOQ (121 mg/kg). The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing overall relative standard deviations ≤ 10.8 % for Phosphonic acid and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

Table A 89: Summary of the study 2 trials – Northern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days) (d)	Details on trial (e)
			kg a.s./ ha Potassium phosphonate	Water (L/ha)	g a.s./hL Potassium phospho- nate				Phosphonic acid		
IF22-06194195 22-00356-01 16835 Wulkow Germany 2022	Potato/ Euroflora	1. 12.04.2022 2. 07.06.- 12.07.2022 3. 15.09.- 30.9.2022	1.83 1.79 1.79	403 393 393	454 454 454	29.08.2022 05.09.2022 12.09.2022	46 47 48	Tuber	5.2 7.7 <u>7.3</u>	0 3 7	
IF22-06194195 22-00356-02 55-210 Krzelków Poland 2022	Potato/ Wineta	1. 26.04.2022 2. 10.06.- 22.06.2022 3. 01.09.2022	1.83 1.83 1.81	302 302 299	605 605 605	15.07.2022 21.07.2022 28.07.2022	48 48 48	Tuber	15 12 <u>14</u>	0 3 8	
IF22-06194195 22-00356-03 51110 Aumécourt- Northern France 2022	Potato/ Elodie	1. 18.05.2022 2. 07.07.- 11.07.2022 3. 10.08.- 20.08.2022	1.81 1.78 1.86	349 343 358	519 519 519	26.07.2022 02.08.2022 09.08.2022	45 47 47	Tuber	3.3 3.7 <u>7.3</u>	0 3 7	
IF22-06194195 22-00356-04 51130 Germinon Northern France 2022	Potato/ Elodie	1. 22.05.2022 2. 15.07.- 20.07.2022 3. 17.08.2022	1.89 1.78 1.88	313 293 311	606 606 605	26.07.2022 01.08.2022 09.08.2022	47 47 49	Tuber	19 27 <u>26</u>	0 3 8	
IF22-06194195 22-00356-09 79353 Bahlingen- Germany 2022	Potato/Ditta	1. 09.04.2022 2. 01.07.- 15.07.2022 3. 01.08.- 20.08.2022	1.89 1.87 1.87	416 412 408	454 454 454	11.07.2022 18.07.2022 25.07.2022	43 – 45 45 – 47 47	Tuber	7.3 <u>12</u>	0 7	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treat- ment or no. of treatments and last date	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (L/ha)	g a.s./hL				Phosphonic acid		
	(a)	(b)	Potassium phosphonate		Potassium phospho- nate	(c)				(d)	(e)
IF22-06194195 22-00356-10 88-400 Żnin Poland 2022	Potato/Euro- starch	1. 23.04.2022 2. 15.06.- 03.07.2022 3. 06.09.2022	1.87 1.85 1.87	309 306 308	605 605 605	16.08.2022 23.08.2022 30.08.2022	44 45 48	Tuber	20 <u>26</u>	0 7	

Residue data for Zoxamide and its metabolites are presented in A 2.2.3.3.2.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Phosphonic acid

LOD: 0.002 mg/kg for Phosphonic acid

Table A 90: Summary of the study 2 trials – Southern Europe

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days) (d)	Details on trial (e)
			kg a.s./ ha Potassium phosphonate	Water (L/ha)	g a.s./hL Potassium phospho- nate				Phosphonic acid		
IF22-06194195 22-00356-05 20049 Caleppio di Settala Italy 2022	Potato/ Kenne- bec	1. 29.03.2022 2. nr 3. 26.07.2022	1.76 1.87 1.78	388 412 392	454 454 454	04.07.2022 12.07.2022 19.07.2022	41 43 – 45 47	Tuber	1.6 3.3 <u>2.8</u>	0 3 7	
IF22-06194195 22-00356-06 41510 Marcina del Alcor Spain 2022	Potato/Spunta	1. 01.10. 2022 2. na 3. 10.01.- 20.01.2023	1.80 1.79 1.78	396 394 392	454 454 454	19.12.2022 27.12.2022 04.01.2023	44 46 47	Tuber	20 23 <u>28</u>	0 3 7	
IF22-06194195 22-00356-07 29749 Almayate Spain 2022	Potato/Rudolph	1. 28.10.2022 2. mid Jan. 2023 till harvest 3. 07.02. – 10.02.2023	1.84 1.84 1.84	404 406 404	454 454 454	18.01.2023 24.01.2023 30.01.2023	43 47 47	Tuber	29 74 <u>65</u>	0 3 8	
IF22-06194195 22-00356-08 57006 Lakkia Greece 2022	Potato/Spunta	1. 17.08.2022 2. 10.10.- 20.10.2022 3. 09.11.2022	1.87 1.87 1.87	413 411 413	454 454 454	17.01.2022 24.10.2022 01.11.2022	39 43 45	Tuber	35 34 <u>37</u>	0 3 8	
IF22-06194195 22-00356-11 20059 Vimercate Italy 2022	Potato/Wizard	1. 08.04.2022 2. 30.05.- 15.06.2022 3. 26.07.2022	1.91 1.78 1.91	420 392 420	454 454 454	07.07.2022 13.07.2022 20.07.2022	41 45 47	Tuber	3.3 <u>4.2</u>	0 6	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety (a)	Date of 1.Sowing or planting 2.Flowering 3. Harvest (b)	Application rate per treatment			Dates of treat- ment or no. of treatments and last date (c)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)	PHI (days) (d)	Details on trial (e)
			kg a.s./ ha Potassium phosphonate	Water (L/ha)	g a.s./hL Potassium phospho- nate				Phosphonic acid		
IF22-06194195 22-00356-12 66033 Perithorio- Greece 2022	Potato/Electra	1. 10.04.2022 2. 05.08.- 15.08.2022 3. 29.08.2022	1.85 1.87 1.86	408 413 409	454 454 454	08.08.2022 16.08.2022 22.08.2022	39 43 46	Tuber	3.6 <u>13</u>	0 7	

Residue data for Zoxamide and its metabolites are presented in A 2.2.3.3.2.

(a) According to CODEX Classification / Guide

(b) Only if relevant

(c) Year must be indicated

(d) Days after last application (Label pre-harvest interval, PHI, underline)

(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included

LOQ: 0.01 mg/kg for Phosphonic acid

LOD: 0.002 mg/kg for Phosphonic acid

A 2.3.4 Magnitude of residues in livestock

A 2.3.4.1 Livestock feeding studies

No new data were submitted in the framework of this application.

A 2.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.3.5.1 Distribution of the residue in peel/pulp

Not required for the intended uses. No new data were submitted in the framework of this application.

A 2.3.5.2 Processing studies on a core set of representative processes

A 2.3.5.2.1 Study 1 (report No. FCS01) – Grape processing

Comments of zRMS:	Any LoA cannot be a presentation subject here. Appendix 2 is intended for the data presentation and evaluation. The study has already been evaluated by the RMS Germany within the Registration Report for Veriphos (ZV1 027207-00/00, 2017) and considered acceptable.
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LoA to the residue/processing data is available. ~~Definitely instead of the LoA the applicant have to provide the relevant data.~~

Reference:	KCA 6.5.3/14
Report:	STUDY ON THE RESIDUE BEHAVIOUR OF PHOSPHONIC ACID IN GRAPES AND GRAPES PROCESS FRACTIONS AFTER APPLICATION OF LBG-01F34 (MAC 94700 F9 UNDER FIELD CONDITIONS (GERMANY, 2009), Ipach, R., 2010, report No. FCS01, Doc. No. 638-022
Guideline(s):	BBA Guidelines Part IV 3-3.4 and VI, 23-2.3.4, IVA-Guideline "Residue Analysis", SANCO/825/00- rev. 7 (2004); SANCO/3029/99- rev. 4 (2000);
Deviations:	None
GLP:	Yes
Acceptability:	Yes

Material, study design and methods

Material / test item:

Test material:	LBG-01F34
Formulation:	Soluble concentrate (SL)
CAS#:	Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2
Lot/Batch #:	90364943
Content of a.s. (actual):	Phosphonic acid: 499 g/L

Study design:

Processing trials with grapes (1 trial red wine, 1 trial white wine) were conducted with grapes derived from 2 German field trials treated with LBG-01F34 in 2009. LBG-01F34 was applied five times to grapevines with a nominal application rate of approx. 3000 g Potassium phosphonates/ha, corresponding to 2000 g Phosphonic acid equivalents/ha with a water amount of approximately 1600 L/ha. The application interval was 14±1 days. Grapes used for processing were harvested 14 days after the last application.

Samples were processed to red wine or white wine and stems, fresh pomace, must and wine were analysed for residues of Phosphonic acid by LC-MS/MS after extraction of the specimens using methanol/ultrapure water with further homogenisation, centrifugation and decantation. The LOQ of the analytical method was 0.5 mg/kg for grapes and grape processed specimens.

All processing phase described was done according to technological procedures in a laboratory scale for vinification comparable to the processes used for commercial productions of these goods. Since processing to red and white wine is different a description of the steps involved in each is given below:

White wine making

The grapes (harvest Sept 14, 2010, 14 DALA) were crushed, and pressed on the same day. For residue analysis at least 1 kg pomace samples were taken immediately after pressing and frozen in bags of polyethylene at -18°C or colder. The must was sulphured with 50 mg SO₂/L and was left overnight for deposit of the must. Then must was separated and samples for determination of must weight and must acid were taken. For residue analysis 1 L must samples were taken and frozen in glass bottles at -18°C or colder.

Red wine making

The grapes (harvest Sept 21, 2010, 14 DALA) were stemmed and crushed on the same day. One kg stems samples were taken immediately after pressing and frozen in bags of polyethylene at -18°C or colder. The total amount of the crush was sulphured with 50 mg SO₂/L and heated up to approx. 70°C. After heating, the crush was pressed according to good wine making practice. For residue analysis at least 1 kg pomace samples were taken and frozen in bags of polyethylene at -18°C or colder. The must was left overnight to separate. Then must was separated and samples for determination of must weight and must acid were taken. For residue analysis 1 L must samples were taken and frozen in glass bottles at -18°C or colder.

Generation of wine specimen

The separated must was filled immediately into two 25 L glass balloons and mixed with yeast. After fermentation, the young wine was mixed with 100 mg SO₂/L. After the clarification of the young wine, the yeast was separated (wine, 1st separation). The wines of each repetition were mixed with 2 g Bentonit /L wine, and filled into one balloon up to the bung (wine refilling). After another separation and ripening of the wine, a further separation was made (wine, 2nd separation) and the wine was filtered using EK filter units. Immediately after the filtration from each treatment, the wine bottles were filled. The bottles were stored in the cellar at room temperature until shipment for analysis.

Methods:

The principle of the SGS internal analytical method (IF 09/01419442) includes extraction of the specimens with solvent methanol/ultrapure water with further homogenization, centrifugation and decantation. All specimens were analysed for residues of phosphorous acid by LC-MS/MS.

For validation of the analytical method, 17 control specimens were fortified at levels of 0.5/5/25/50/75/100 mg/kg yielding the mean recovery rate of 95 % (84.8 – 101.6 %), with a mean SD of 10.6.

The limit of quantification (LOQ) was 0.5 mg/kg and the limit of detection (LOD) was < 0.05 mg/kg.

The maximal storage period for the RAC and processed commodities was 12 months.

Results:

The results of the processing study on grapes are summarised in the following table.

Table A 100 Residue data from grape processing study with Phosphonic acid

RAC	Residues in RAC (mg/kg)	PHI (days)	Processed commodity	Residue (mg/kg)	PF*/#	CF**	Comments/Reference
Phosphonic acid							
Wine grapes (white wine)/ LBG01F34	37.0	14	Wet pomace	73.3	1.98	1	
			Must	32.6	0.88	1	
			Wine (after filling)	40.9	1.11	1	
			Wine (6 months storage)	47.5	1.28	1	
Wine grapes (red wine)/ LBG01F34	35.3	14	Wet pomace	36.0	1.02	1	
			Must	43.9	1.24	1	
			Wine (after filling)	50.5	1.43	1	
			Wine (6 months storage)	48.0	1.36	1	

* Processing factor

** Conversion factor

Conclusion

Residues in grapes and grape processed commodities were determined after five applications with LBG-01F34 applied at a nominal application rate of 2000 g/ha of Phosphonic acid with an interval of 14 ± 1 days and a PHI of 14 days.

The treated fresh pomace for white wine presented almost twice the residue level as the treated fresh pomace for red wine. A slight difference in the residue level of must for red wine and red wine after filling was observed with respect to the must for white wine and white wine after filling. No significant differences were observed on wine after 6 months storage between red and white wine.

A 2.3.5.2.2 Study 2 (report No. GLP-STUDY-20-30) – Grape processing

<p>Comments of zRMS: Latvia</p>	<p>The following conclusion of zRMS Latvia was taken from Circa and originated from part B section 7 core assessment for products GF-1045, GF-1057, GWN-9790EU, GWN-9823, GWN-9963, GOW F911 WG, GOW F113 finalised in September 2023 as updated set of zoxamide data after AIR submitted by XXXX. and its affiliates in May 2021:</p> <p>The study is acceptable.</p> <p>The concentration of zoxamide and its metabolites were determined in grapes and/or processed specimens. Trials performed under Northern and Southern European conditions. Each trial was carried out performing 3 applications of three different plant protection products at their worst-case application rates. Foliar applications were made with a spray with an interval of 7 days and a last application 28 days before harvest.</p> <p>Max. Storage interval between sampling and analysis: Wine grape: 67-69 days Wine: 14 days</p> <p>The residue found in treated grape bunches were (use pattern 3x180 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.218 to 0.905 mg/kg. - For RH-141452, the residue 28 DALA were 0.01 mg/kg - Total residues were from 0.233 to 0.920 mg/kg <p>The residue found in treated grape bunches were (use pattern 3x150 g ai/ha):</p> <ul style="list-style-type: none"> - For zoxamide, the residues 28 DALA were from 0.123 to 0.644 mg/kg. - For RH-141452, the residue 28 DALA were 0.0192 mg/kg - Total residues were from 0.123 to 0.673 mg/kg <p>The residue found in processed grapes (wine) were:</p> <ul style="list-style-type: none"> - For zoxamide, the residues were from 0.01 to 0.0181 mg/kg - For RH-141452, the residue were 0.01 mg/kg - Total residues were from 0.025 to 0.033 mg/kg <p>For other metabolites residues were below LOQ.</p> <p>Deviations:</p> <p>Trial: CMN-20-44059 ES06: The application 1 has been done with BBCH 81 instead of BBCH 15-79, as required in the Study Plan. This happens because at the moment of the signature of the SP the field crop was at BBCH 81. Deviation with an impact. However, all the applications doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 ES06: The application 2 has been done 6 days after application 1, instead of 7-8 days - as required in the Study Plan. This was due to logistic adjustments and the field technician didn't realise that -1 day was not allowed. However, this deviation has no impact on the study integrity since it is still in the ±25% range for the application pattern intended with a 7-8 days interval.</p> <p>Trial: CMN-20-44059 FR02: Sampling S2 (1 DALA) and S3 (3 DALA) were not done. This occurred because the field technician didn't take into account the amendment no. 1 to the study plan. Deviation with an impact: the trial CMN-44059 FR02 (DEC-2) has become a decline with 5 points instead of 7 points.</p> <p>Trial: CMN-20-44059 HU04: Samples collected at 0 DALA were delivered at ambient temperature instead of refrigerated condition (with dry ice) to the Field Test Site. This occurred due to an error of the field technician that didn't correctly understand the study plan. An impact on the integrity of the study was not assumed</p>
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	<p>since the maximum period between sampling and freezing in the Test Site Facility was about 6 hours (at ambient temperature).</p> <p>Trial: CMN-20-44059 FR01: Dry ice was not used during the samplings since the field was close to the Test Site Facility. No impact on the integrity of the study assumed since the maximum period between sampling in the field and freezing in the Test Site Facility was only 3 hours for sampling 1, 1 hour 20 minutes for sampling 2, 1 hour 15 minutes for sampling 3, 1 hour 5 minutes for sampling 4, 2 hours 5 minutes for sampling 5, and 1 hour 5 minutes for sampling 6 – each at ambient temperature. The max. storage period for sampling 7 was 2 hours 35 minutes (samples cooled with frozen gel packs).</p> <p>Trial: CMN-20-44059 FR02: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact on the integrity of the study since the maximum period between sampling in the field and freezing in the Test Site Facility was 1 hour for sampling 1, 15 minutes for sampling 4, 20 minutes for sampling 5, 15 minutes for sampling 6, and 16 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR05: Dry ice was not used during the samplings because the field was close to the Test Site Facility. No impact since the maximum period between sampling in the field and freezing in the Test Site Facility was 3 hours for sampling 1, 2 hours for sampling 4, 2 hours 30 minutes for sampling 5, 2 hours and 35 minutes for sampling 6, and 4 hours and 30 minutes for sampling 7 – samples always cooled with frozen gel packs.</p> <p>Trial: CMN-20-44059 FR01: Chemical products with phosphonate and zoxamide as active ingredients were applied in the field where the trial was set up. No impact on the results for zoxamide and metabolites. Impact for the results for phosphonic acid on grape bunches, for which residues in the untreated control samples were detected, and on wine at 0 and 28 DALA, for which residues in the untreated control sample were detected. This was solved by subtracting the untreated control sample results from the treated ones.</p> <p>Trials CMN-20-44059 FR02, FR05, HU03, HU04, ES07: The applications have not been done between BBCH 15 and BBCH 79 as requested in the Study Plan. This deviation had an impact on the study. However, the application pattern and doses as well as the PHI were respected.</p> <p>Trial: CMN-20-44059 FR05: The farmer contract was signed on 04/08/2020, one day after the first application (03/08/2020). This deviation was regarded to have no impact on the study.</p> <p>During the processing phase the mustimeter 34MUS16 was used from 28/08/2020 to 03/09/2020 (checking date) without writing the procedural check before its use (the technician did the check but forgot to write it). This deviation was regarded to have no impact on the study.</p> <p>On 08/10/2020, during the processing phase, the MLF (malolactic fermentation) was recorded as finished on the data sheets (fermentation and red wine) and k metabisulphite was added on 09/10/2020 (at the end of MLF), but the chromatography paper spots of malic acid were present for U2. Therefore, k metabisulphite seems to be added on the wine U2 before the end of the malolactic fermentation. This deviation was regarded to have no impact on the residues in the wine, but only on its organoleptic properties.</p> <p>During the analytical phase the recovery check results at LOQ level for the analytes RH-141288 and RH-150721 were outside (> 110%) the permitted range (70-110%) for analytical batch 200902 GLP-STUDY-20-30. This deviation was solved with no impact on the study results since the samples in this sequence were re-extracted and analysed, discarding the previously obtained values.</p> <p>During the analysis of analytical batch 200904-GLP-STUDY-20-30 the calibration point at level 3 (Uva L3) in the calibration curve had a response higher than expected. It has therefore not been considered to establish the actual calibration line.</p>
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	<p><i>This deviation was regarded to have no impact on the study results since the calibration range related to the method validation has not altered, and 4 points were regarded enough to derivate a suitable calibration line with $r^2 > 0.99$.</i></p> <p><i>During the analysis of the analytical batch 200924-GLP-STUDY-20-30 (4C N) the calibration check results for (R)-RH-141288 (147.3%), (S)-RH-141288 (266.7%) and (S)-RH-150721 (141.3%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200924-GLP-STUDY-20-30 (4C B) the calibration check results of (R)-RH-150721 (136.9%) and (S)-RH-150721 (132.4%) were outside of the acceptable range (80% - 120%) defined in the study plan. For the analytical batch 200929-GLP-STUDY-20-30 the calibration check results of (R)-RH-150721 (126.8%) and (S)-RH-150721 (135.5%) were outside the acceptable range (80% - 120%). However, this deviation was regarded to have no impact on the study integrity. All samples analysed in these batches have concentrations < LOQ for the mentioned analytes, therefore the calibration check value could not affect the reported values anyway. This deviation was solved with no impact on the study.</i></p> <p><i>During the analysis of the analytical batch 201117 GLP-STUDY-20-30 (white wine) a calibration point for the analyte (S)-RH-141288 had a lower response in comparison to the regression line. This value was excluded and a 4-point calibrating line was established. As a consequence, since the recovery check at 10 x LOQ (GLP-SMPL-20-724/NH RC2) was no longer inside the calibration range, it could not be evaluated. However; this deviation was regarded to have no impact on the study results since 4 calibration points were regarded enough for the interpolation and to quantify the analyte content in the samples.</i></p> <p><i>The untreated white wine sample GLP-SMPL-20-724 was found to contain 1.61 mg/kg of phosphonic acid, presumably due to the reasons explained in deviation 8. External standard calibration solutions for white wine were initially established using the extracts of this sample. This resulted in a signal higher than 30% of the LOQ. They were therefore invalidated. The batch was therefore re-elaborated using the calibration curve for red wine that was analysed in the same analytical sequence, recalculating the recovery check values by subtracting the values of the untreated (white wine) sample. This deviation was regarded to have no impact on the study results since the calibration using matrix-matched reference solution in red wine has the same matrix effect on phosphonic acid than white wine (demonstrated by the recovery check and by a standard at level L3 prepared in white wine).</i></p>
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Reference:	See KCA 6.3.1/01
Report:	DETERMINATION OF ZOXAMIDE AND ITS METABOLITES IN RAW AGRICULTURAL COMMODITY OF WINE GRAPE AND PROCESSED (WINE) IN OPEN FIELD FOLLOWING THREE APPLICATIONS OF THE FORMULATED PRODUCTS GWN-9823, GWN-10616, GWN-10392 (NORTH AND SOUTH EUROPE – 7 trials year 2020, Longhi, D., 2021, report No. GLP-STUDY-20-30, Doc. No. 638-015
Guideline(s):	SANTE/2020/12830, Rev.1 (2021), SANCO/825/00 rev.8.1 (2010), OECD No. 508, OECD No. 509, SANCO/3029/99 rev. 4 (2000), 7029/VI/95 rev.5 (1997)
Deviations:	None ; yes, no impact
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	GWN 10616
Formulation:	Suspension concentrates (SC)
CAS#:	Zoxamide: 156052-68-5 Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2
Lot/Batch #:	2006669001
Content of a.s. (actual):	Zoxamide: 64 g/L Phosphonic acid: 505 g/L
Manufacturing date:	15 June 2020
Stability of test compound (expiry date):	2 years from manufacturing:

Study design:

Four decline cure trials and two at harvest trials in grapes have been performed in Southern (Southern France, Spain) and Northern Europe (Hungary, Northern France) in 2020.

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated three times by spraying the SC formulation at the nominal application rate of 1500 g/ha of Phosphonic acid with an interval of 7 days and a PHI of 28 days.

Samples were taken both for residues analysis and for processing. In at-harvest trials, samples of grapes were taken at day of application and 28 days after last application. In the decline curve trials, samples were taken at day of application and 1, 3, 7, 14, 21 and 28 days after last application.

In this section only the processing trials, which were treated with GWN-10616 are summarised. The residue trials are summarised in A 2.2.3.1.1.

The magnitude of residues of Phosphonic acid have been analysed in raw agricultural commodity specimens of grapes (bunches) and processed commodity (bottled red and white wine).

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions. Processing of the samples started on the day of delivery. within 24 hours after sampling. Specimens for residue analysis were frozen at -18°C within 6 hours after sampling and stored frozen until the analysis.

During processing, samples of bottled red and white wine were collected. The processed specimens were frozen at -18°C after sampling and kept frozen until analysis.

Procedure flowcharts of the grapes processing into young wine are shown in Figure A 17 and A 18.

Method:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-20-38 (“Analytical method validation to quantify Phosphonic acid residues in grape bunches (acidic matrix)”, Doc. No. 432-010).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) for the analyte Phosphonic acid was 1 mg/kg. The limit of detection (LOD) was 0.30 mg/kg.

The maximum sampling to extraction interval for Phosphonic acid at a temperature of $\leq -18^{\circ}\text{C}$ was max. 15 days for wine for NEU and SEU trials. The final extracts in samples of RAC and processed commodities were analysed within 3 days for Phosphonic acid after storage at 4°C.

Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability of 3 days in sample extracts. The recoveries were within the range between 70 – 110 %. In addition, the stability of the analytes in the final extracts kept at 4°C for 3

days was successfully verified for Phosphonic acid in the GLP study no. GLP-STUDY-20-38. Thus, the sample extracts were stable for the storage periods between extraction and analysis in this study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed LOQ level (1 mg/kg) and at 10x LOQ (10 mg/kg). The recoveries for Phosphonic acid in berries were always within the range of 70 - 110 % of nominal and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

The results of the processing study on grapes are summarised in Table A 91.

Table A 91. Residue data from grape processing study with Phosphonic acid

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Phosphonic acid</i>							
Wine grapes (white wine)/ GWN-10616	16.5	28	Bottled wine	8.61	0.52	1	
Wine grapes (red wine)/ GWN-10616	4.67	28	Bottled wine	5.14	1.1	1	

* Processing factor

** Conversion factor

Calculated by the applicant

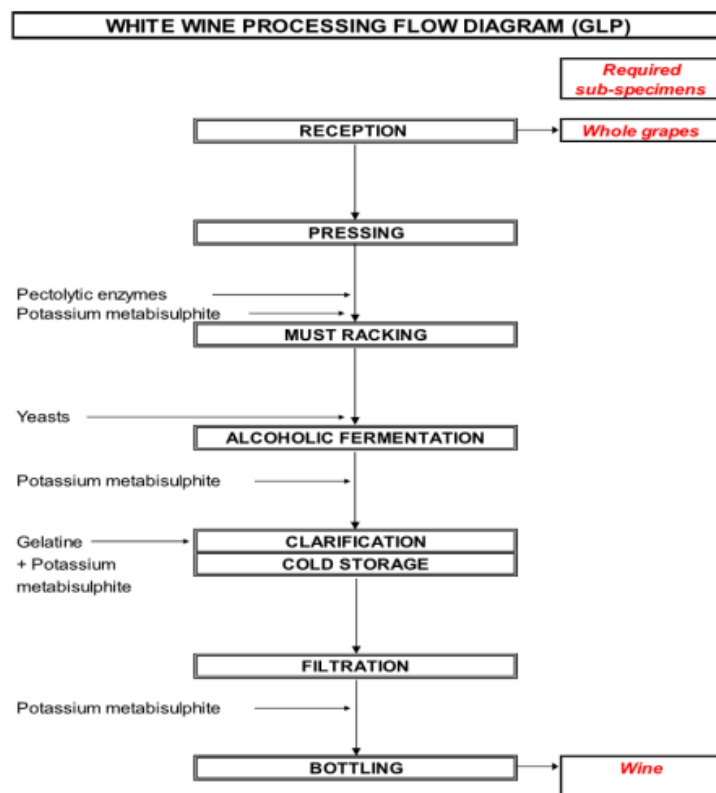


Figure A 17: Procedure of the grapes processing into white wine making

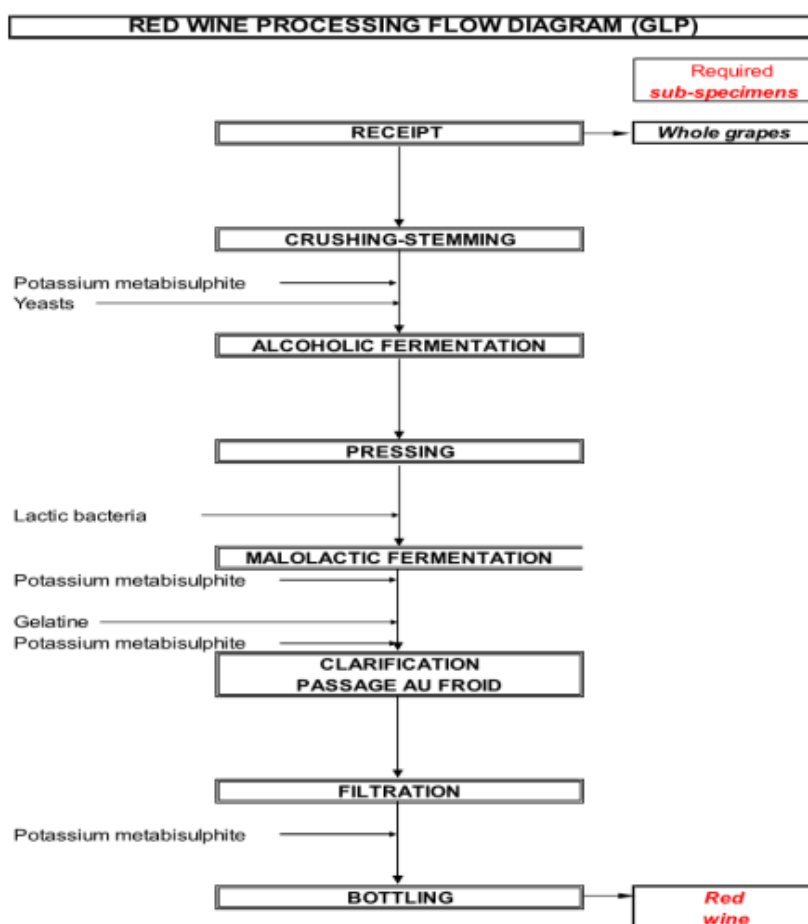


Figure A 18: Procedure of the grapes processing into red wine making

Conclusion

Residues in grapes and grapes processed commodities were determined after 3 applications with GWN 10616 applied at a nominal application rate of 1500 g/ha of Phosphonic acid with an interval of 7 days and a PHI of 28 days. In grape bunches RAC prior to processing total residues of Phosphonic acid at a level of 16.5 and 4.67 mg/kg were found.

For white wine a processing factor of 0.52 could be derived indicating that Phosphonic acid does not concentrate in this commodity. For red wine a processing factor of 1.1 could be derived.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in grape processed commodities.

A 2.3.5.2.3 Study 3 (report No. SCC-STUDY-G401TO409-21-P) – Apple processing

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of the study was to determine residues of GWN-8030 (Zoxamide) and Potassium phosphonate [expressed in equivalent Phosphonic acid]. Residues of metabolite RH-141452 were also determined as total fraction (a hydrolysis step to release potentially matrix-conjugated compounds was necessary). Residues in apple RAC (whole fruits without stem) were analysed.</p> <p>The LC-MS/MS methods applied for the determination were as follows: of Zoxamide in apple AM-GLP-STUDY-21-53, of RH-141452 in apple AM-GLP-STUDY-21-54, and of Phosphonic acid AM-GLP-STUDY-21-55.</p> <p>The LOQs were 0.01 mg/kg. The relevant validation parameters as required.</p>
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Reference:	KCA 6.5.3/13
Report:	RESIDUES OF PHOSPHONIC ACID IN APPLES CULTIVATED IN OPEN FIELD CONDITIONS AND IN PROCESSED APPLES AFTER TWO FOLIAR APPLICATIONS OF GWN-10616 IN 3 TRIALS CONDUCTED IN EUROPE (BELGIUM, THE NETHERLANDS AND SPAIN) IN 2021, Loriau, P., 2022, report No. SCC-G401TO409-21-P, Doc. No. 638-001
Guideline(s):	SANTE/2019/12752, SANTE/2020/12830 rev.1 (2021), ENV/JM/MONO(2007)17, ENV/JM/MONO(2011)50/Rev1 (2016), ENV/JM/MONO(2008)23, OECD No. 508 (2008), OECD No. 509 (2021)
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Materials and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide:156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Two processing trials in apples have been performed in Northern Europe (Germany) and one in Southern Europe (Spain). All processing trials were conducted in 2021.

The processing study SCC-G401TO409-21-P was conducted in parallel with the residue study SCC-G401TO409-21, which is summarised in A 2.2.3.2.3.

The magnitude of residues of Phosphonic acid have been analysed in raw agricultural commodity specimens of apples and processed commodities (apple juice, apple wet pomace, apple compote, canned apples and dried apples).

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated twice by spraying with each 3 L/ha GWN-10616 (i.e. 2265 g a.s. of Potassium phosphonate [corresponding to 1500 g a.s./h of Phosphonic acid] with an interval of 6-7 days. The last application was done at BBCH 69.

The samples for processing were taken at BBCH 87-89.

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site within 6 hours after sampling. All other specimens for residue analysis were frozen down within 5 hours after sampling and kept frozen at $\leq -18^{\circ}\text{C}$ until analysis.

During processing, samples of apple juice, apple wet pomace, apple compote, canned apples and dried apples were collected. The processed specimens were frozen down and kept frozen until analysis.

Procedures about processing are presented in Figures A 19 to A 21.

Methods:

The method validation was performed within the GLP-study GLP-STUDY-21-55 ("Validation of an analytical method for the determination of Phosphonic acid in apples RAC and processed commodities", Longhi, D., 2021).

The method validation is described in detail in Part B, Section 5 ("*Analytical Methods*").

The limit of quantification (LOQ) for Phosphonic acid was 0.01 mg/kg for apple RAC, apple, compote, canned apple and apple juice and 0.05 mg/kg for dried apple and apple wet pomace. The limit of detection (LOD) for Phosphonic acid was 0.002 mg/kg for apple RAC, apple compote, canned apple and apple juice and 0.013 mg/kg for dried apple and apple wet pomace.

The maximum sampling to extraction interval at -18°C was 141 days for Phosphonic acid in apples (RAC and processed commodities). The maximum extraction to quantification interval at $5 \pm 3^{\circ}\text{C}$ was 3 days for Phosphonic acid in apples (RAC and processed commodities). Procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

The extract stability of Phosphonic acid in the final extract kept at $5 \pm 3^{\circ}\text{C}$ for 4 days was successfully verified in the GLP study no. GPL-STUDY-21-55, in addition.

Thus, the sample extracts were stable for the storage periods between extraction and analysis in this residue study.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg, apple RAC, apple compote, canned apple, apple juice, 0.05 mg/kg for dried apple and apple wet pomace), at 10x LOQ (0.1 mg/kg, apple RAC, apple compote, canned apple, apple juice, 0.5 mg/kg for dried apple and apple wet pomace), at 200xLOQ (10 mg/kg for dried apple and apple wet pomace) and at 1000x LOQ (10 mg/kg for apple RAC, apple compote, canned apple, apple juice). The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing a relative standard deviations (RSD) of $\leq 20\%$ and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

The results of the processing study on apples are summarised in Table A 92.

Table A 92: Residue data from apple processing study with Phosphonic acid

<i>RAC</i>	<i>Residues in RAC (un-washed sample, mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*</i>	<i>CF**</i>	<i>Comments/Reference</i>
G401-21F-P							
Apple	0.786, 1.12 Mean: 0.953	127	Apple juice	0.901	0.94	1	
		127	Apple wet pomace	1.60	1.68	1	
		127	Apple compote	0.824	0.86	1	
		127	Canned apples	0.532	0.56	1	
		127	Dried apples	5.31	5.57	1	
G403-21F-P							
Apple	1.46, 1.40 Mean: 1.43	125	Apple juice	1.24	0.87	1	
		125	Apple wet pomace	1.26	0.88	1	
		125	Apple compote	1.04	0.73	1	
		125	Canned apples	0.744	0.52	1	
		125	Dried apples	5.73	4.01	1	
G408-21F-P							
Apple	1.92, 1.44	188	Apple juice	1.49	0.89	1	
		188	Apple wet pomace	1.28	0.76	1	
		188	Apple compote	1.40	0.83	1	
		188	Canned apples	0.948	0.56	1	
		188	Dried apples	5.20	3.10	1	

* Processing factor

** Conversion factor

LOQ: 0.01 mg/kg for apple RAC, apple, compote, canned apple and apple juice and

LOQ: 0.05 mg/kg for dried apple and apple pomace.

LOD: 0.002 mg/kg for apple RAC, apple compote, canned apple and apple juice and

LOD: 0.013 mg/kg for dried apple and apple pomace.

Table A 93: Median result of Processing Factor (PF) calculation

Fraction	Individual Processing factors (PF)	Calculated Processing factor (PF) (median)
Apple juice	0.87, 0.89, 0.94	0.89
Apple wet pomace	0.76, 0.88, 1.68	0.88
Apple compote	0.73, 0.83, 0.86	0.83
Canned apples	0.52, 0.56, 0.56	0.56
Dried apples	3.10, 4.01, 5.57	4.01

Processing steps

Px1 & Px2 - Apples not processed (Event SP1A & SP1B)

Without any rinsing, apples were manually sorted. Only healthy fruits were sampled. Stems were removed and discarded.

Minimum 1 kg of apples was sampled for specimens SP1A & SP1B

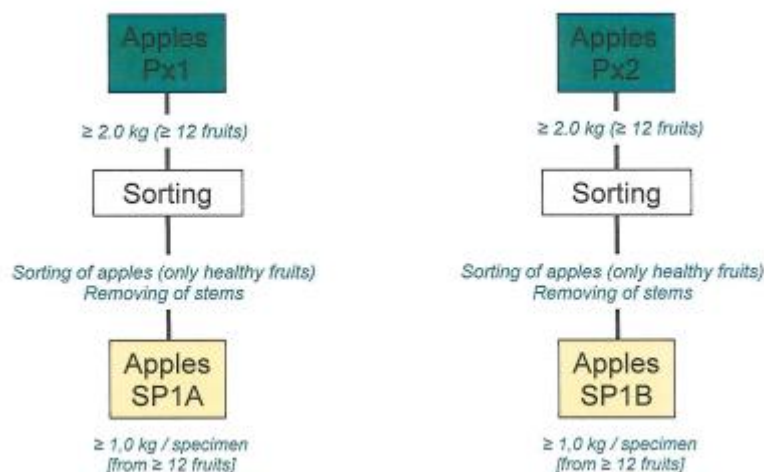


Figure A 19: Apples not processed

Px3 - Apple juice and Apple wet pomace (Event SP1C & SP1D)

Apples were rinsed in tap water for 1 to 2 minutes following a ratio of 1:1 (water:apple). Apples were manually sorted. Only healthy fruits were used for processing. Stems were removed and discarded. Without any peeling, the cores of the apples were removed and discarded. Then, apples were chopped into smaller pieces with a knife in order to introduce them in the juice extractor. During extraction, apple juice was separated from apple pomace (pulp). Due to the extraction, scum appeared on the top of the juice. It was removed before pH checking and pasteurisation. After juice extraction, the pH of the juice was measured. As the pH was between 3.0 and 4.0, no adjustment with citric acid was needed. Before packaging, apple juice was pasteurised by bringing at 82-90°C for 1 to 2 minutes. Juice was kept at ambient temperature for cooling down. Minimum 0.5 kg of wet pomace was sampled for specimens SP1D. Minimum 1 kg of juice was sampled for specimens SP1C.

Px3 - Apple compote (Event SP1E)

Apples were rinsed in tap water for 1 to 2 minutes following a ratio of 1:1 (water:apple). Apples were manually sorted. Only healthy fruits were used for processing. Stems were removed and discarded. Without any peeling, cores of apples were removed and discarded. Then, apples were chopped into smaller pieces with a knife. Apples were cooked with water and sugar in boiling water (95-100°C) for 5 to 10 minutes. The ratio water:apples:sugar was 0.1:1:0.1. After cooking, compote was mixed for homogenisation. As the pH was between 3.0 and 4.5, no adjustment with citric acid was needed. Minimum 0.5 kg of compote was sampled for specimens SP1E.

Px3 - Canned apples (Event SP1F)

Apples were rinsed in tap water for 1 to 2 minutes following a ratio of 1:1 (water:apple). Apples were manually sorted. Only healthy fruits were used for processing. Stems were removed and discarded. Apple cores were removed and discarded. Then, apples were peeled. Apples were chopped into smaller pieces (~1.5 cm x 1.5 cm) with a knife. Apples were blanched in boiling water (95-100°C) for 1 to 2 minutes with a ratio water:apples of 0.1:1. After blanching, a syrup was separately prepared with the water used for blanching. The ratio water:apples:sugar for syrup was 0.25:1:0.15. Apples and syrup were then mixed. As the pH was between 3.0 and 4.5, no adjustment with citric acid was needed. Canned apples were pasteurised by bringing at 82-90°C for 1 to 2 minutes. Canned apples are kept at ambient temperature for cooling down.

Minimum 0.5 kg of canned apples was sampled for specimens SP1F. Ratio syrup:apple in specimen (0.4:1.0) was respected.

Px3 - Dried apples (Event SP1G)

Apples were rinsed in tap water for 1 to 2 minutes following a ratio of 1:1 (water:apple). Apples were manually sorted. Only healthy fruits were used for processing. Stems were removed and discarded. Without any peeling, cores of apples were removed and discarded. Then, with a slicer, apples were sliced in rings of around 0.3 to 0.5 cm. The slices were placed in an air dryer in order to reach a weight reduction $\geq 80\%$. Dried apples are kept at ambient temperature for cooling down. Minimum 0.15 kg of dried apples was sampled for specimens SP1G.

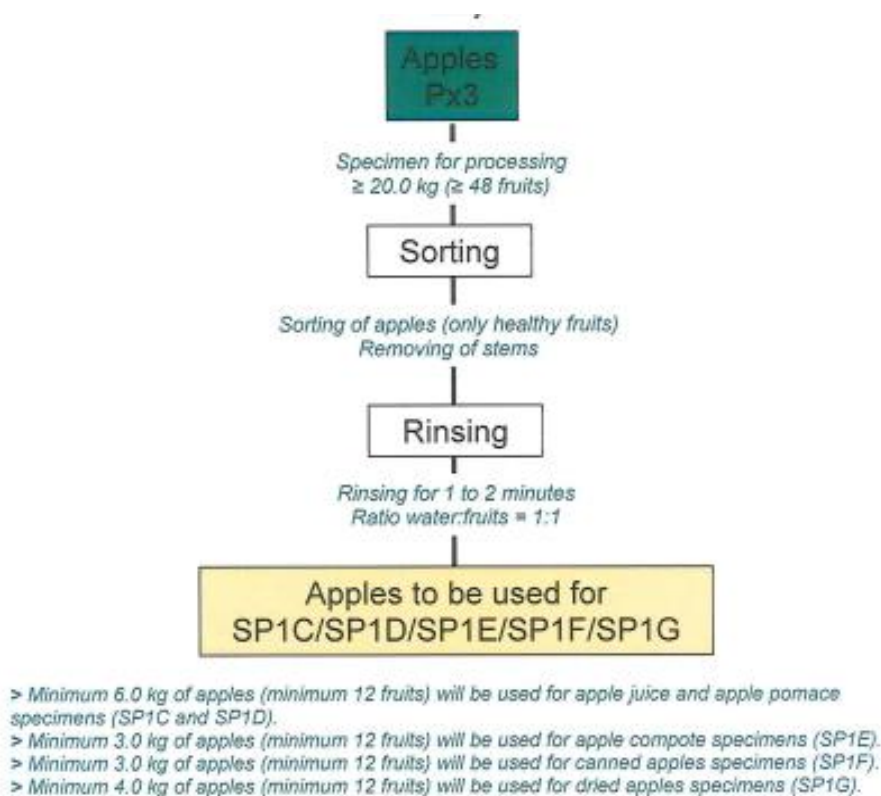


Figure A 20: Apples prepared for processing

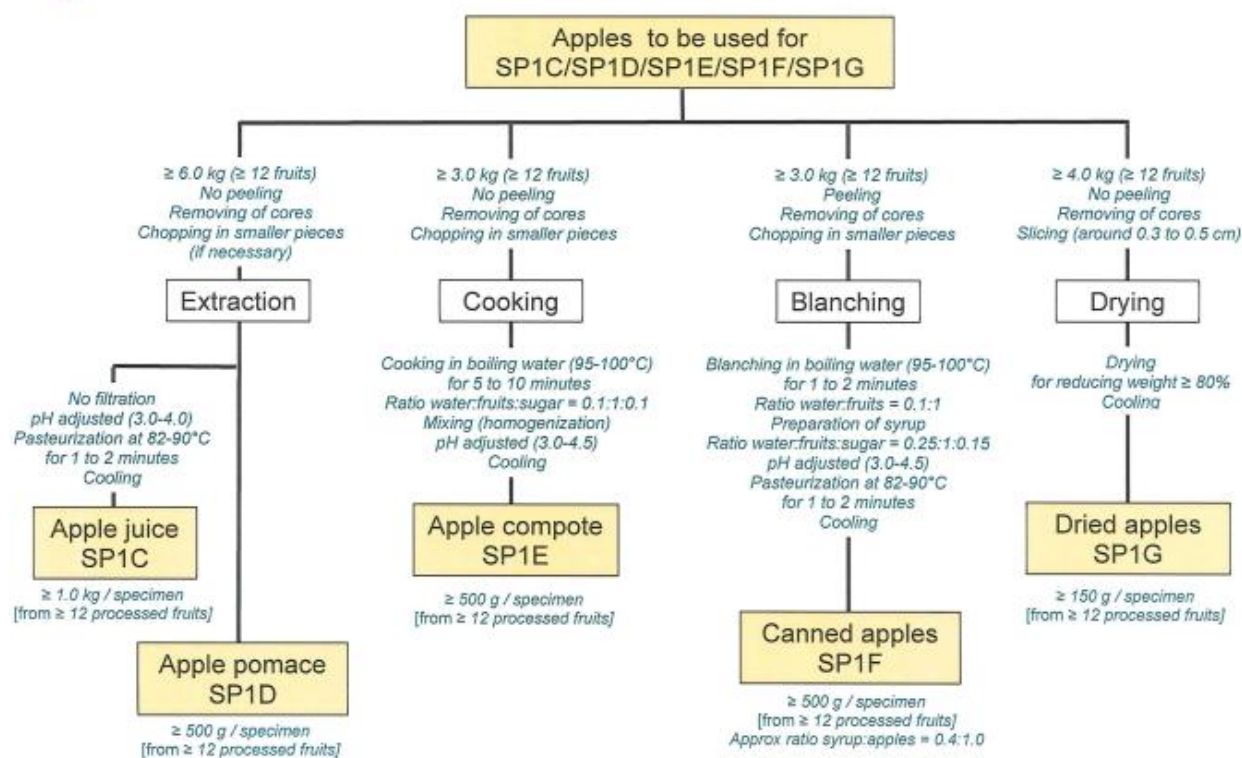


Figure A 21: Apples processing

Conclusion

Residues in apples RAC and apple processed commodities were determined after spraying with GWN-10616 twice with each 3 L/ha (i.e. 2265 g a.s. of Potassium phosphonate [corresponding to 1500 g a.s./h of Phosphonic acid] with an interval of 6-7 days. The last application was done at BBCH 69. In apple fruits RAC prior to processing a mean residue level of Phosphonic acid of 0.953, 1.43 and 1.68 mg/kg were found in three trials.

The median processing factor is 0.89 for apple juice, 0.88 for apple wet pomace, 0.83 for apple compote, 0.56 for canned apples and 4.01 for dried apples. The processing study indicates that Phosphonic acid does not concentrate in the processed commodities (apple juice, apple wet pomace, apple compote and canned apples). However, it was shown that Phosphonic acid concentrate in dried apples.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in apple processed commodities.

A 2.3.5.2.4 Study 5 (report No. GLP-STUDY-21-14) – Potato processing

Comments of zRMS:	<p>The study has been accepted.</p> <p>The purpose of this study was to determine the residues level of Zoxamide, its metabolites RH-141452 and RH-141455 and Potassium phosphonates (expressed as phosphonic acid and fosetyl equivalents) in potatoes after spray application of one of the following products: GWN-9790 EU (SC containing 240 g/L Zoxamide), GWN-10616 (SC containing 60 g/L Zoxamide and 755 g/L Potassium phosphonates (504 g/L Phosphorous acid)). The study trials were performed on potatoes in 8 different locations in France, Poland, Spain and Italy. The study included also processing samples taken from 3 trials to produce potato culls, potato waste and potato dried pulp sub-samples.</p> <p>The determination of zoxamide in potato tubers was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-50. Zoxamide was determined as racemate (no chiral column) based on BPL-STUDY-18-000085 method. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of total RH-141452 and RH-141455 (sum of the free fractions and the conjugated ones) in potato tuber was performed by LC-MS/MS method with a sample hydrolysis step validated in the concurrent study BPL-STUDY-18-000085. The extraction efficiency of the analytical method was also verified within this study.</p> <p>The determination of phosphonic acid (fosetyl equivalents) in potato tuber and processed commodities (potato culls, potato waste and potato dried pulp) was performed by LC-MS/MS method validated in the concurrent study GLP-STUDY-21-52. The extraction efficiency was not required to verify since this method was based on the extraction procedure which was used and accepted in the Fosetyl RAR.</p> <p>Procedural recovery values were obtained in parallel to the analyte measurements, confirming the robustness and repeatability of the method.</p>
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Reference:	See KCA 6.3.3/01
Report:	GWN-8030, ITS METABOLITES AND PHOSPHONATES IN POTATOES AFTER THREE APPLICATIONS OF GWN-9790 EU AND GWN-10616 IN THE OPEN FIELD (NORTHERN AND SOUTHERN EU, 8 TRIALS, YEAR 2021), Longhi, D., 2023, report No. GLP-STUDY-21-14, Doc. No. 633-09001
Guideline(s):	OECD No. 509 (2009), 7029/VI/95 rev. 5 (1997), SANTE/2019/12752 (2019), SANTE/2020/12830 rev. 1 (2021), SANTE 2017/10632 rev. 3 (2017), OECD No. 508
Deviations:	None
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

Material, study design and methods

Material / test item:

Test material:	Zoxium 240 SC	GWN-10616
Formulation:	Suspension concentrate	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	ZA2701	P2102669001
Content of a.s. (actual):	Zoxamide: 239 g/L g/L	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Manufacturing date:	27/01/2021	01/03/2021
Stability of test compound (expiry date):	At least 2 years from the production date.	At least 2 years from the production date.

Study design:

Four at harvest trials in potatoes have been performed in Southern (Italy – 1 location, Spain – 1 location) and Northern Europe (Northern France – 1 location, Poland – 1 location) in 2021.

Each trial consisted of two plots: 1 plot (control) was left untreated, and one was treated three times by spraying the SC formulation GWN-10616 with 3 L/ha at the nominal application rates of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1512 g a.s./ha of Phosphonic acid]) with an interval of 7 days and a PHI of 7 days.

In 1 trial (FR02), samples were taken both for residues analysis and for processing. In at harvest trials, samples of potatoes were taken at 7 days after the last application.

In this section only the processing trial is summarised. Residue trials for Phosphonic acid are described in A 2.2.3.3.1.

The magnitude of residues of Phosphonic acid have been analysed in raw agricultural commodity specimens of potatoes (tuber) and processed commodities (potato waste, dried pulp).

The raw agricultural commodities (grape bunches) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site in good conditions. Processing of the samples started on the day of delivery. within 24 hours after sampling. Specimens for residue analysis were frozen at -18°C.

During processing, samples of potato culls, potato waste and potato dried pulp were collected. The processed specimens were frozen at -18°C after sampling and kept frozen until analysis.

Procedure flowcharts of the potato processing into dried pulp are shown in Figure A 22.

Method:

The method for the determination of Phosphonic acid was successfully validated in study GLP-STUDY-21-52 (“Validation of an analytical method for the determination of Phosphonic acid in potato”, Doc. No. 432-015).

The method validation is described in detail in Part B, Section 5 (“Analytical Methods”).

The limit of quantification (LOQ) of the analyte Phosphonic acid was 0.01 mg/kg in potato tuber, cull, waste, and dried pulp. The limit of detection (LOD) was 0.002 mg/kg.

The maximum sampling to extraction interval was 56 days for Phosphonic acid in potato tubers, 51 days in potato waste, 49 days in dried pulp and 55 days in potato cull at a temperature of $\leq -18^{\circ}\text{C}$. The final extracts in samples of RAC were analysed within 24 hours. Thus, a storage stability testing in extracts is not needed. However, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.01 mg/kg) and at 10x LOQ (0.1 mg/kg) for potato waste, potato dried pulp, 400 x LOQ level (=4 mg/kg for potato waste), at 10000 x LOQ level (=100 mg/kg for potato tuber and potato culls and at 60000 x LOQ level (=600 mg/kg for potato dried pulp).

The mean recoveries were within 60 - 120 % and an RSD of < 30 % at LOQ level (=0.01 mg/kg) for potato tuber, potato waste, potato dried pulp and potato culls, within 70 - 120 % and an RSD of < 30 % at 10 x LOQ level (=0.1 mg/kg) for potato waste, potato dried pulp, within 70 – 110 % and an RSD of 10 % at 400 x LOQ level (=4 mg/kg for potato waste), at 10000 x LOQ level (=100 mg/kg for potato tuber and potato culls and at 60000 x LOQ level (=600 mg/kg for potato dried pulp).

Results:

The results of the processing study on potatoes are summarised in Table A 94.

Table A 94. Residue data from potato processing study with Phosphonic acid

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*/#</i>	<i>CF**/#</i>	<i>Comments/Reference</i>
<i>Phosphonic acid</i>							
Potato	49.0	7	Potato waste	3.71	0.08	1	
			Dried pulp	127	2.59	1	

* Processing factor

** Conversion factor

Calculated by the applicant

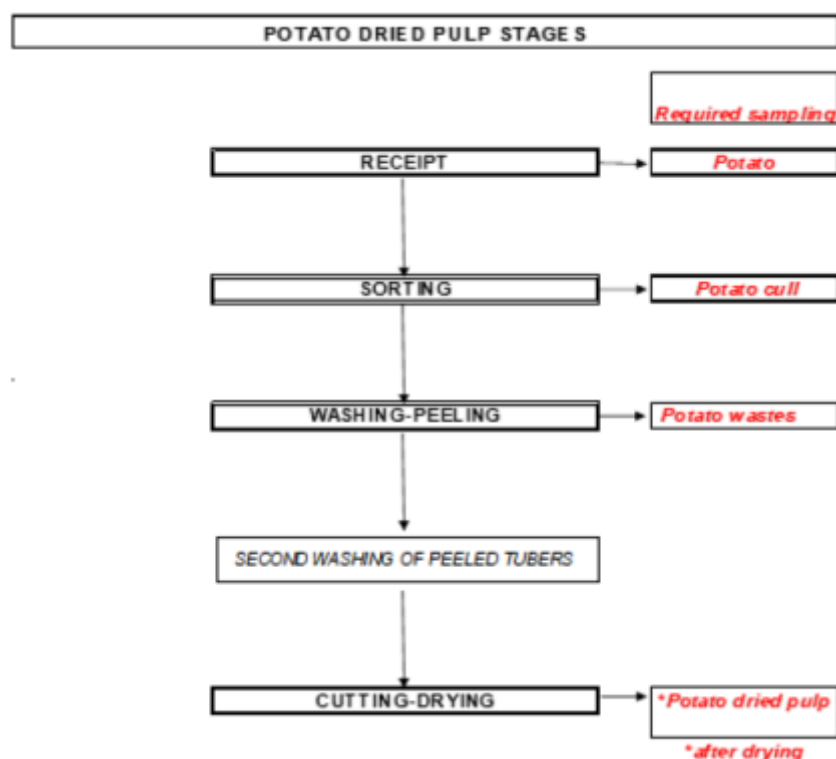


Figure A 22: Procedure of the potato processing into dried pulp

Conclusion

Residues in potatoes and potatoes processed commodities were determined after 3 applications with GWN 10616 applied at a nominal application rate of 2265 g a.s./ha of Potassium phosphonate [corresponding to 1512 g a.s./ha of Phosphonic acid]) with an interval of 7 days and a PHI of 7 days.

In potato tubers RAC prior to processing total residues of Phosphonic acid at a level of 49 mg/kg were found.

For potato waste a processing factor of 0.08 was derived indicating that Phosphonic acid does not concentrate in this commodity. For potato dried pulp a processing factor of 2.59, could be derived.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in potato processed commodities.

A 2.3.5.2.5 Study 6 (report No. IF22-06194195) – Potato processing

Comments of zRMS:	<p>The study has been accepted.</p> <p>The study included 15 supervised residue trials conducted in Germany, Poland, Northern France, Italy, Spain and Greece during the 2022-2023 season. 8 trials were conducted as decline trials, 4 as harvest trials and 3 were conducted as processing trials. The spraying applications were performed at 19-23 DBH, 13-16 DBH and 6-8 DBH with a nominal rate of 2.5 L test item/ha.</p> <p>The purpose of the study in general was to determine the magnitude of the residues of zoxamide and its metabolites (RH-141452, RH-141455), and phosphonic acid in potato tubers after 3 foliar applications of GWN-10616 (60 g/L zoxamide and 755 g/L dipotassium phosphonates i.e. 500 g/L phosphonic acid). In addition, residues of phosphonic acid were also determined in whole potatoes prior to processing.</p> <p>The purpose of the processing phase was the generation of processed products of potato i.e. peeled potatoes, wet peel, microwaved/boiled potatoes, baked potatoes, fried potatoes, crisps, French fries, flakes, process waste, ensiled, starch, potato protein, dried pulp and canned potatoes, and then the determination of the residue levels of phosphonic acid to calculate the processing factors in the context of three foliar applications of GWN-10616.</p> <p>For all determinations 3 separate methods were used, validated in study IF23-06197316. Final determination was achieved by LC-MS/MS.</p> <p>To continuously prove the validity of the analytical method procedural recovery specimens were prepared by fortification of untreated specimen material. Fortification was performed with fortification solution containing Zoxamide, RH-141452, RH-141455 and phosphonic acid. The fortification levels were at LOQ and at least one higher level for each analyte in potato sample. Procedural recoveries were handled and stored in the same way and for the same time period as the analytical samples that have been prepared within the same analytical set.</p> <p>The storage period of deep-frozen samples intended for zoxamide determination ranged between 153 and 357 days, for RH-141452 and RH-141455 ranged between 196 and 401 days and for phosphonic acid between 115 and 321 days. The storage time of the deep-frozen processed fraction specimens ranged between 169 and 287 days.</p> <p>The study report is very detailed and included many amendments. However, they have no impact on the study. The relevant results are given below by the applicant.</p>
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Reference:
Report:

See KCA 6.3.3/02
STUDY ON THE RESIDUE BEHAVIOUR OF GWN-8030 AND MDI-0074 IN POTATO AND ITS PROCESSED PRODUCTS AFTER TREATMENT WITH GWN-10616 UNDER FIELD CONDITIONS IN GERMANY, POLAND, NORTHERN FRANCE, ITALY, SPAIN AND GREECE, 2022, Gabriel, E.J., 2023, report No. IF22-06194195, Doc. No. 638-019

Guideline(s):	7029/VI/95 - rev.5, SANTE/2019/12752, OECD No. 509, OECD Series on Testing and Assessment, Number 96 (2008), OECD No. 508 (2008), ENV/JM/MONO(2007)17, SANTE/2020/12830 Rev. 1
Deviations:	Yes, no impact on the study
GLP:	Yes
Acceptability:	Yes

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

Materials and methods

Material / test item:

Test material:	GWN-10616
Formulation:	Suspension concentrate
CAS#:	Zoxamide: 156052-68-5 Phosphonic acid: 13598-36-2
Lot/Batch #:	P2102669001
Content of a.s. (actual):	Zoxamide: 58.8 g/L Phosphonic acid: 481.2 g/L Potassium phosphonate: 726.6 g/L
Stability of test compound (expiry date):	01/03/2023

Study design:

Three processing trials in potatoes have been performed in Northern Europe (Germany and Northern France) and one in Southern Europe (Italy). All processing trials were conducted in 2022/2023.

The residue trials were conducted in parallel, which are summarised in A 2.2.3.3.2.

The magnitude of residues of Phosphonic acid have been analysed in raw agricultural commodity specimens of potatoes and processed commodities (peeled potatoes, wet peel, microwaved potatoes, boiled potatoes, baked potatoes, fried potatoes, crisps, French fries, flakes, process waste, ensiled, starch, potato protein, dried pulp and canned potatoes).

Each trial consisted of 2 plots: 1 plot (control) was left untreated, another plot was treated three times by spraying with each 2.5 L/ha GWN-10616 (i.e. 1887.5 g a.s. of Potassium phosphonates [corresponding to 1250 g a.s./h of Phosphonic acid]) with an interval of 6-7 days and a PHI of 7 days at harvest.

The raw agricultural commodities (potato tubers) for processing were shipped under ambient conditions to the processing site. They were delivered at the processing site within 6 hours after sampling. The specimens for residue analysis were frozen down within 6 hours after sampling and kept frozen at $\leq -18^{\circ}\text{C}$ until analysis.

During processing, samples of whole potatoes (prior to processing), peeled potatoes, wet peel, microwaved potatoes, boiled potatoes, baked potatoes, fried potatoes, crisps, French fries, flakes, process waste, ensiled, starch, potato protein, dried pulp and canned potatoes were collected. The processed specimens were stored frozen at $\leq -18^{\circ}\text{C}$ until analysis.

Procedures about processing are presented in Figures A 23 to A 33.

Methods:

The method validation was performed within the GLP-study IF23-06197316 (“Validation of analytical methods for determination of GWN-8030, MDI-0043, MDI-0050 and MDI-0074 in potato matrices”, Link, T., 2023).

The method validation is described in detail in Part B, Section 5 (“*Analytical Methods*”).

The limit of quantification (LOQ) for Phosphonic acid was 0.02 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved potatoes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp, 0.04 mg/kg for process waste, 0.05 mg/kg for crisps and canned potatoes and 0.06 mg/kg for flakes. The limit of detection (LOD) for Phosphonic acid

was 0.006 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved potatoes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp, 0.012 mg/kg for process waste, 0.015 mg/kg for crisps and canned potatoes and 0.018 mg/kg for flakes.

The maximum sampling to extraction interval at -18°C was up to 288 days for Phosphonic acid in potatoes (whole potatoes, prior to processing and processed commodities). The maximum extraction to quantification interval at $5 \pm 3^\circ\text{C}$ was 4 days for Phosphonic acid in apples (RAC and processed commodities). Extracts contain isotopically labelled internal standards (IL-IS) for quantification, testing of final volume extract stability is not required since the IL-IS compensate for losses during extract storage according to SANTE/2020/12830 rev. 1. Nevertheless, procedural recoveries were handled and stored in the same way and for the same time periods as the analytical samples thereby proving stability in sample extracts. The recoveries were within the range between 70 – 110 %.

Recovery experiments were carried out within the analytical series in order to demonstrate the validity of the analytical method. Procedural recoveries were performed at 1x LOQ (0.02 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved potatoes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp, process waste; 0.04 mg/kg for process waste, 0.05 mg/kg for crisps and canned potatoes and 0.06 mg/kg for flakes), at 10x LOQ (0.2 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved potatoes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp, process waste; 0.4 mg/kg for process waste, 0.5 mg/kg for crisps and canned potatoes and 0.6 mg/kg for flakes), at 1020/1717x LOQ (51 mg/kg for crisps/ 103 mg/kg for flakes), at 2550/2580/2600 x LOQ (51 mg/kg for microwaved potatoes, wet peel/ canned potatoes/ process waste, fried potatoes and starch) and 5050/5100/5200x LOQ (whole potatoes (prior to processing), potato protein/ peeled potatoes, French fries, ensiled potatoes, dried pulp, ensiled potatoes, baked potatoes/boiled potatoes and potato protein).

The recoveries for Phosphonic acid were always within the range of 70 - 110 % of nominal showing a relative standard deviations (RSD) of $\leq 20\%$ and thus, confirming the accuracy of the analytical method on the day of analysis.

Results:

The results of the processing study on potatoes are summarised in Table A 95.

Table A 95: Residue data from potato processing study with Phosphonic acid

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*</i>	<i>CF**</i>	<i>Comments/ Reference</i>
22-00356-13 (EU-22-1638-01)							
Potatoes	13.0, 8.9 Mean: 11	7	Peeled potatoes	8.7	0.79	1	
		7	Wet peel	13	1.2	1	
		7	Microwaved potatoes	20	1.8	1	
		7	Boiled potatoes	13	1.2	1	
		7	Baked potatoes	17	1.5	1	
		7	Fried potatoes	33	3.0	1	
		7	Crisps	17	1.5	1	
		7	French fries	19	1.7	1	
		7	Flakes	6	0.55	1	
		7	Process waste	14	1.27	1	

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*</i>	<i>CF**</i>	<i>Comments/ Reference</i>
		7	Ensiled potatoes	23	2.1	1	
		7	Starch	2.5	0.23	1	
		7	Potato protein	4.0	0.36	1	
		7	Dried pulp	18	1.6	1	
		7	Canned potatoes	6.3	0.57	1	
22-00356-14 (EU-22-1638-02)							
Potatoes	8.1, 6.9 Mean: 7.5	7	Peeled potatoes	3.7	0.49	1	
		7	Wet peel	5.6	0.75	1	
		7	Microwaved potatoes	9.2	1.2	1	
		7	Boiled potatoes	9.1	1.2	1	
		7	Baked potatoes	7.9	1.1	1	
		7	Fried potatoes	13	1.7	1	
		7	Crisps	11	1.5	1	
		7	French fries	15	2.0	1	
		7	Flakes	6	0.80	1	
		7	Process waste	8.5	1.1	1	
		7	Ensiled potatoes	5.5	0.73	1	
		7	Starch	0.84	0.11	1	
		7	Potato protein	1.2	0.16	1	
		7	Dried pulp	7.8	1.0	1	
		7	Canned potatoes	3	0.40	1	
22-00356-15 (EU-22-1638-03)							
Potatoes	6.6, 3.3 Mean: 5.0	7	Peeled potatoes	3.7	0.74	1	
		7	Wet peel	2.7	0.54	1	
		7	Microwaved potatoes	9	1.8	1	
		7	Boiled potatoes	2.9	0.58	1	
		7	Baked potatoes	5.1	1.0	1	
		7	Fried potatoes	14	2.8	1	
		7	Crisps	7.9	1.6	1	
		7	French fries	9.1	1.8	1	

<i>RAC</i>	<i>Residues in RAC (mg/kg)</i>	<i>PHI (days)</i>	<i>Processed commodity</i>	<i>Residue (mg/kg)</i>	<i>PF*</i>	<i>CF**</i>	<i>Comments/Reference</i>
		7	Flakes	19	3.8	1	
		7	Process waste	4.2	0.84	1	
		7	Ensiled potatoes	6.5	1.3	1	
		7	Starch	0.50	0.10	1	
		7	Potato protein	0.87	0.17	1	
		7	Dried pulp	1.1	0.22	1	
		7	Canned potatoes	3.2	0.64	1	

* Processing factor

** Conversion factor

LOQ: 0.02 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved pota-toes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp

LOQ: 0.04 mg/kg for process waste

LOQ: 0.05 mg/kg from crisps

LOQ: 0.06 mg/kg for flakes

LOD: 0.006 mg/kg for whole potatoes (prior to processing), peeled potatoes, wet peel, starch, microwaved pota-toes, boiled potatoes, baked potatoes, potato protein, fried potatoes, French fries, ensiled potatoes, dried pulp

LOD: 0.012 mg/kg for process waste

LOD: 0.015 mg/kg from crisps

LOD: 0.018 mg/kg for flakes

Table A 96: Median result of Processing Factor (PF) calculation

Fraction	Individual Processing factors (PF)	Calculated Processing factor (PF) (median)
Peeled potatoes	0.79, 0.49, 0.74	0.74
Wet peel	1.2, 0.75, 0.54	0.75
Microwaved potatoes	1.8, 1.2, 1.8	1.8
Boiled potatoes	1.2, 1.2, 0.58	1.2
Baked potatoes	1.5, 1.1, 1.0	1.1
Fried potatoes	3.0, 1.7, 2.8	2.8
Crisps	1.5, 1.5, 1.6	1.5
French fries	1.7, 2.0, 1.8	1.8
Flakes	0.55, 0.80, 3.8	0.80
Process waste	1.27, 1.1, 0.84	1.1
Ensiled potatoes	2.1, 0.73, 1.3	1.3
Starch	0.23, 0.11, 0.10	0.11
Potato protein	0.36, 0.16, 0.17	0.17
Dried pulp	1.6, 1.0, 0.22	1.0
Canned potatoes	0.57, 0.40, 0.64	0.57

Processing steps

Peeling:

Whole potatoes were washed in water with about 1 L of water per 1 kg of specimen and strained.

After washing, the potatoes were peeled with a peeler /knife.

Just after peeling, sub-specimens of peeled potatoes and sub-specimens of wet peel were randomly sampled.

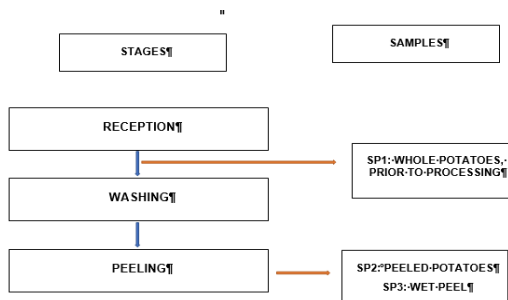


Figure A 23: Peeling

Boiled potatoes

After washing and peeling, the potatoes were chopped into smaller pieces and cooked in boiling brine at around 100°C for 15 min. The ratio water:tubers:salt was approximately 1 kg:1 kg:0.01 kg (+/- 0.01 kg). The water covered the tubers.

Boiled potatoes were collected randomly, sampled, packed, and weighed.

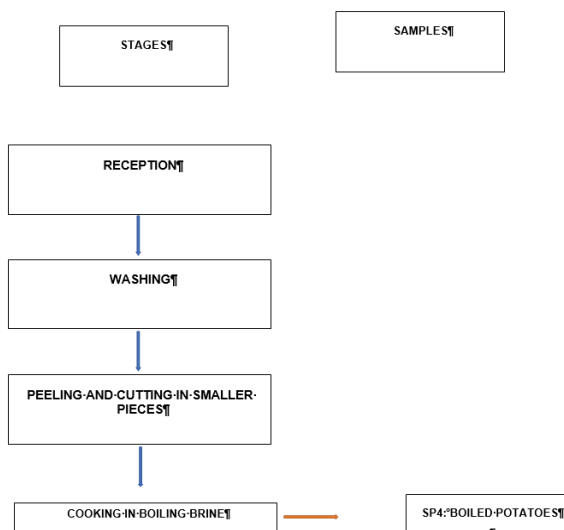


Figure A 24: Processing step: Boiled potatoes

Microwaved potatoes

After washing, the unpeeled potatoes cooked in a microwave at 850 Watts for around 25 min. During cooking, tubers were covered, and a small quantity of water was put in the dish. The ratio water: tubers was approximately 0.1 kg :1 kg (+/- 0.01 kg).

Microwaved potatoes were collected randomly, sampled, packed, and weighed.

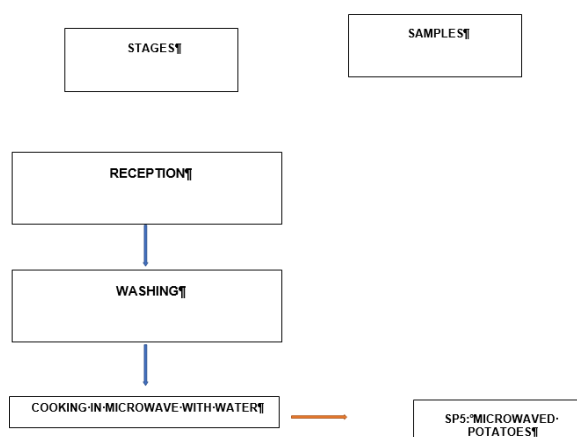


Figure A 25: Processing step: Microwaved potatoes

Baked potatoes

After washing, the unpeeled potatoes were chopped into smaller pieces (about 3 to 5 cm) using a knife. Tubers were baked in an oven at a temperature of around 160 - 200°C for 42 min to 59 min. The potatoes were baked. During baking, tubers were not covered.

Baked potatoes were collected randomly, sampled, packed, and weighed.

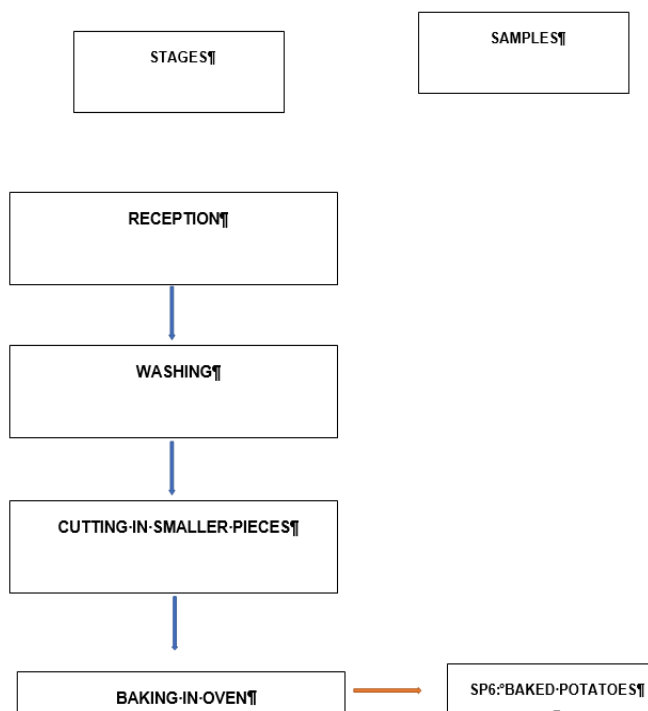


Figure A 26: Processing step: Baked potatoes

Fried potatoes

After washing, the potatoes were chopped into quarters or eighths and put in a fryer containing oil at temperature of around 160-180°C for 15 min to 18 min. Potatoes were dried on a paper tissue for at least 10 minutes.

Salt was then added to the potatoes and mixed. The ratio salt: tubers was approx. 1 kg :0.002 kg (+/- 0.001 kg).

Then the potato pieces were put on a baking sheet.

Potatoes were cooked in an oven at a maximum temperature of 197-208°C for 15 min to 18 min.

Fried potatoes were collected randomly, sampled, packed, and weighed.

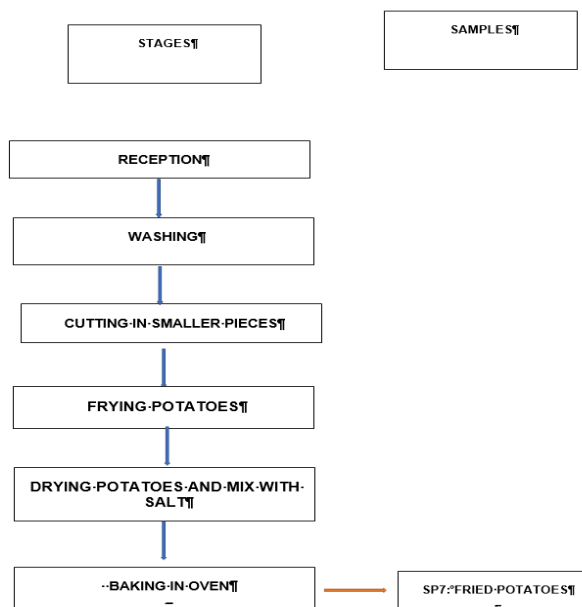


Figure A 27: Processing step: Fried potatoes

Crisps

After peeling, tubers were sliced in crisps of maximum 3 mm using a mandolin. Damaged, stained or badly cut peeled potatoes constitute waste. The waste was weighed and was put aside to carry out the sampling of process waste.

Crisps were cooked in boiling water (66-85 °C) for 2 min to 3 min. Crisps were drained and dried on a paper tissue.

Crisps were put in a fryer containing oil at a temperature of around 160-179°C for approximately 3 min.

Crisps were dried on a paper tissue and salted. The ratio crisp:salt was approx.100 g:1 g (+/- 1 g).

Crisps were collected randomly, sampled, packed, and weighed.

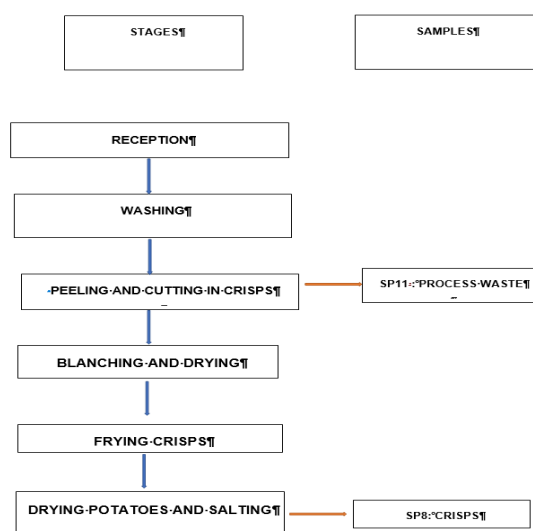


Figure A 28: Processing step: Crisps

French fries

Washed and peeled tubers were cut in fries with 1 cm thick using a knife or any specific equipment. Damaged, stained or badly cut peeled potatoes and unmarketable fries constitute waste. The waste was weighed and was put aside to carry out the sampling of process waste.

Fries were cooked in boiling water (75-100°C) for 1 to 3 min. Fries were drained and dried on a paper tissue.

Fries were put in a fryer containing oil at a temperature of 134-180°C for 5 min to 8 minutes for the first frying. At least 10 minutes after the first frying, fries were fried a second time. Fries were dried on a paper tissue. French fries were collected randomly, sampled, packed, and weighed.

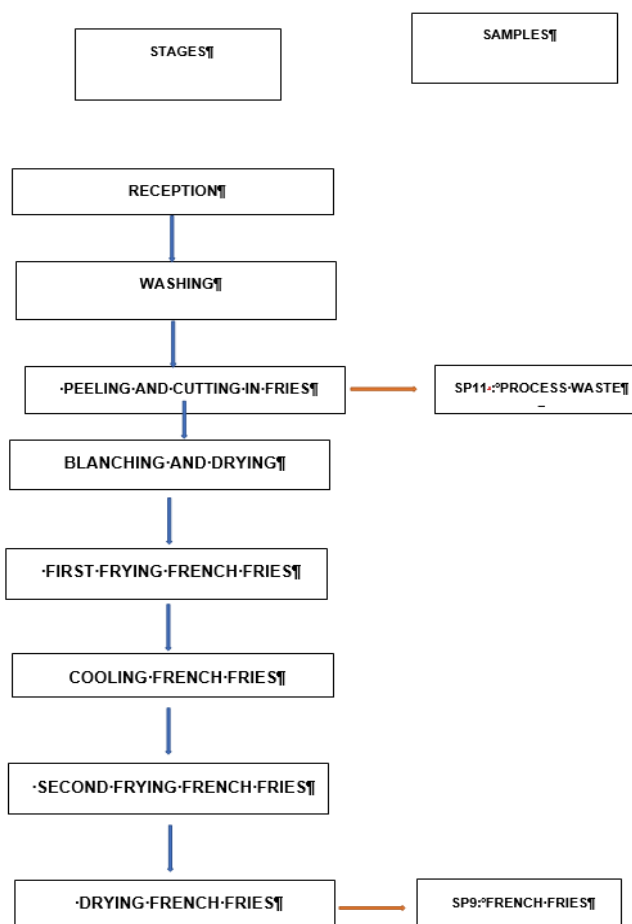


Figure A 29: Processing step: French fries

Flakes

Washed and peeled tubers were sliced. Damaged, stained or badly cut peeled potatoes constitute waste. The waste was weighed and was put aside to carry out the sampling of process waste.

Peeled potatoes were blanched at a temperature of around 70-90° C for 15 min to 19 min and were cooled down in water for 15 min.

The potatoes were cooked at a temperature of around 95-105°C for 15 min to 19 min and then mixed to obtain mashed potatoes.

The puree was dried at a temperature of around 120°C for 72 to 120 min. The dried puree was crushed to obtain the flakes.

Flakes were collected randomly, sampled, packed, and weighed.

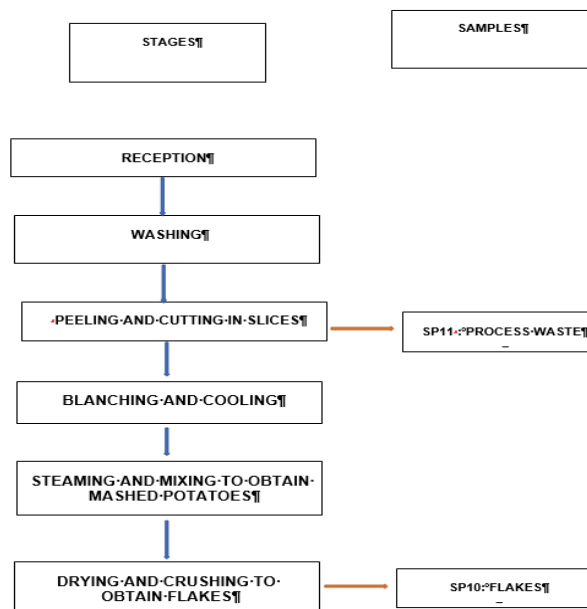


Figure A 30: Processing step: Flakes

Process waste

Damaged, stained or badly cut peeled potatoes were recovered from the crisps, French fries and flakes process.

Process waste was collected randomly, sampled, packed, and weighed.

Ensiled

After washing, the potatoes were crushed, piled up and covered with a lid loaded with sand or other materials.

The temperature was measured once a week. The pH was measured at the beginning of the ensiled. After two months, the pH was measured, and the ensiled potatoes were collected.

Ensiled was collected randomly, sampled, packed, and weighed.

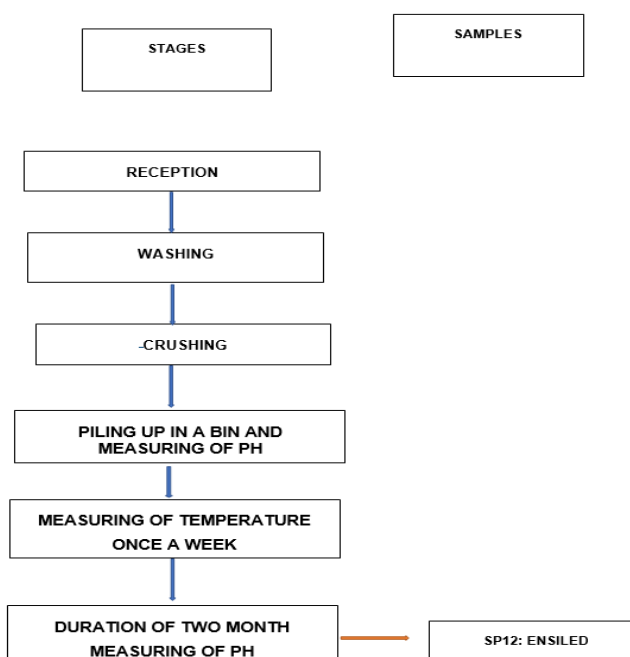


Figure A 31: Processing step: Ensiled potatoes

Starch

Washed and peeled tubers were grated. In the soaking phase: the potatoes were put into a saucepan and covered with water (about 1 L of water per 1 kg of specimen). In the following spin phase, the potatoes were drained with a sieve (covered with a filter paper). All these steps (soak and spin) were repeated four times until the liquid coming out of it was almost completely transparent.

The extracted liquid was kept, and the pulp of potatoes was put aside to carry out the dried pulp process.

The extracted liquid was let sit for 20 to 25 min. The starch has settled to the bottom of the pan. The excess liquid was removed and set aside to carry out the protein process.

The same amount of lukewarm water was added to the starch and let sit for 20 to 25 min. The water was removed and set aside to carry out the protein process.

The wet starch was put in a dehydrator and dried at a temperature of around 50 to 60 °C for 12* hours (720 min) until it was dry and hard.

Starch was collected randomly, sampled, packed, and weighed.

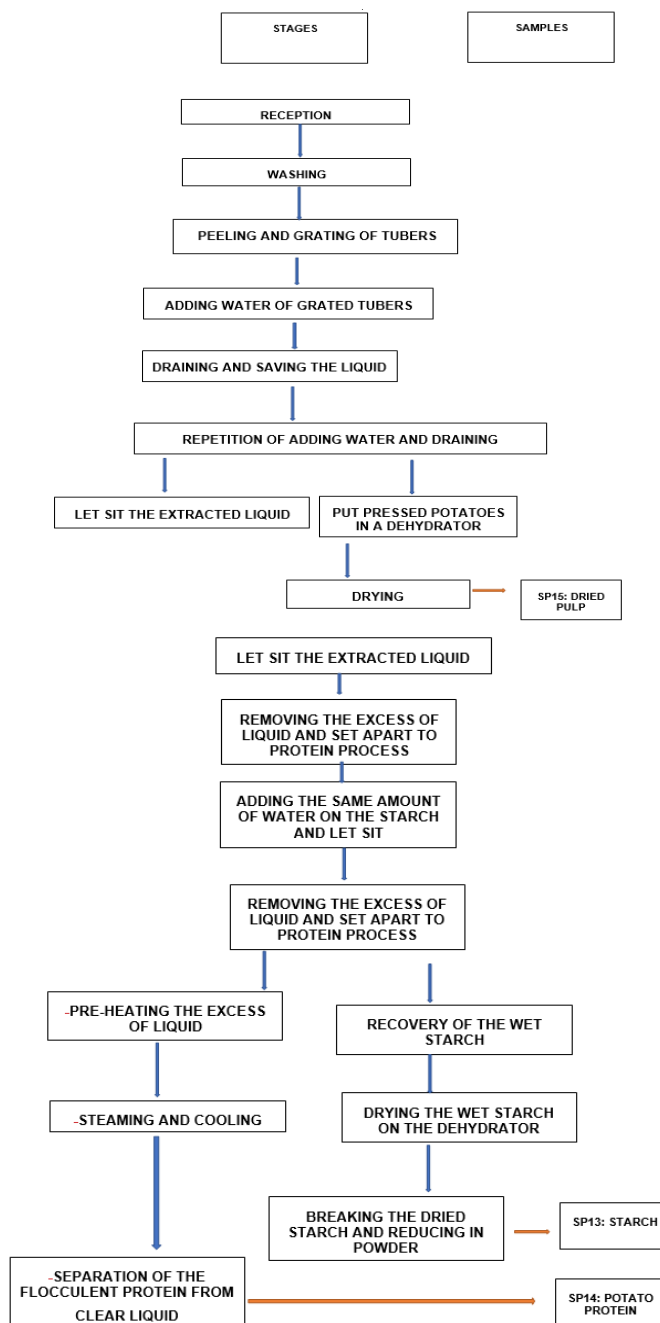


Figure A 32:

Processing step: Starch, potato protein, and dried pulp

Potato protein

The excess of liquid of the starch process was pre-heated to 45 - 55°C and then cooked at a temperature between 83 and 100°C for around 4 to 12 min. Then it was cooled to obtain potato protein suspension.

The flocculent protein was separated from clear liquid.

Potato protein was collected randomly, sampled, packed, and weighed.

Dried pulp

The pulp of potatoes of starch process was put in a dehydrator and dried at a temperature of 50 to 68°C. The drying cycle was 8 hours to 12 hours to dry the pulp until the moisture was visually reached.

Dried pulp was collected randomly, sampled, packed and weighed.

Canned potatoes

Washed potatoes were peeled and cut into cubes (about 1 to 2 cm³) using a knife. Tubers were cooked in boiling brine (95-104°C) for around 5 min. The ratio water:tubers:salt was approximately 1 kg:1 kg:0.03 kg (+/- 0.01 kg). The water covered the tubers.

A conditioning brine is prepared with water and salt with ratio water:salt 1 kg: 0.03 kg.

Then glass jars were filled with a minimum of two third (2/3) of blanched potatoes and of one third (1/3) of brine.

The canned potatoes were then sterilized at 116-121°C for 10 to 13 min. The canned potatoes were cooled down before sampling.

Canned potatoes were collected randomly, sampled, packed, and weighed.

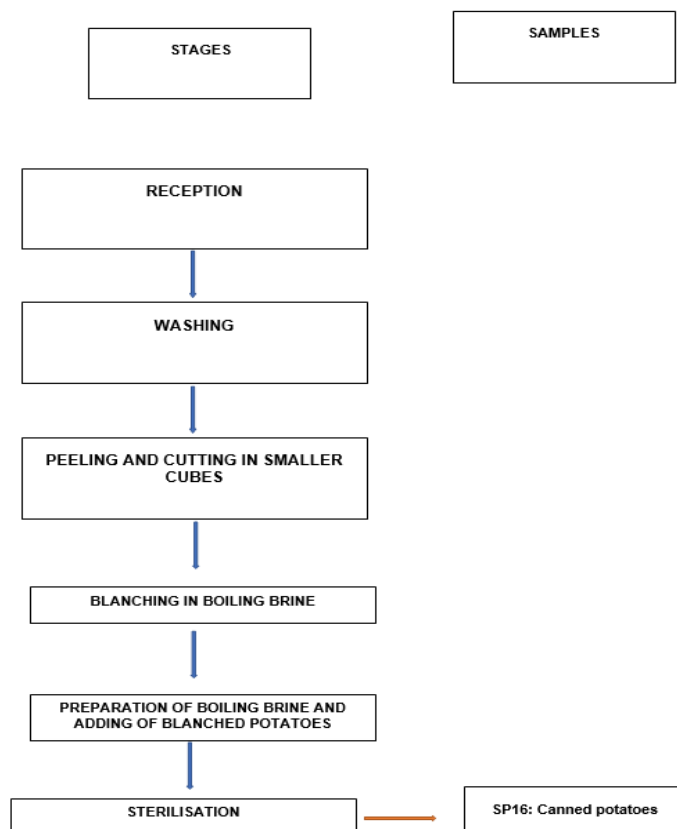


Figure A 33: Processing step: Canned potatoes

Conclusion

Residues in potato RAC and potato processed commodities were determined after spraying with GWN-10616 three times with each 2.5 L/ha GWN-10616 (i.e. 1887.5 g a.s. of Potassium phosphonate [corresponding to 1250 g a.s./h of Phosphonic acid] with an interval of 6-7 days and a PHI of 7 days at harvest. In whole potatoes prior to processing a mean residue level of Phosphonic acid of 11, 7.5 and 5 mg/kg were

found in three trials.

The median processing factor is 0.74 in peeled potatoes, 0.75 in wet peel, 1.2 in boiled potatoes, 1.8 in microwaved potatoes, 1.1 in baked potatoes, 2.8 in fried potatoes, 1.5 in crisps, 1.8 in French fries, 0.80 in flakes, 1.1 in process waste, 1.3 in ensiled potatoes, 0.11 in starch, 0.17 in potato protein, 1.0 in dried pulp and 0.57 in canned potatoes. The processing study indicates that Phosphonic acid does not concentrate in the processed commodities: peeled potatoes, wet peel, flakes, starch, protein, dried pulp and canned potatoes. However, it was shown that Phosphonic acid concentrate in boiled potatoes, microwaved potatoes, baked potatoes, fried potatoes, crisps, French fries, process waste and ensiled potatoes.

The study is compliant to OECD No. 508, valid, scientifically acceptable and appropriate for the assessment of the magnitude of residues in apple processed commodities.

Summary of processing factors

Based on the processing trials provided with this submission, processing factors (and die related median values) have been calculated. In case of residue levels below LOQ in processed commodities, for the calculation of the processing factors a residue level of 0.01 mg/kg was considered.

Table A 97 Summary of processing factors for Phosphonic acid

Commodity	Processing factor	Reference / study no.	Single/Median
Potatoes			
Potatoes, peeled	0.79, 0.49, 0.74	IF22-06194195	0.74 (n=3)
Potatoes, wet peel	1.2, 0.75, 0.54	IF22-06194195	0.75 (n=3)
Potatoes, microwaved	1.8, 1.2, 1.8	IF22-06194195	1.8 (n=3)
Potatoes, baked	1.5, 1.1, 1.0	IF22-06194195	1.1 (n=3)
Potatoes, fried	3.0, 1.7, 2.8	IF22-06194195	2.8 (n=3)
Crisps	1.5, 1.5, 1.6	IF22-06194195	1.5 (n=3)
French fries	1.7, 2.0, 1.8	IF22-06194195	1.8 (n=3)
Potato, flakes	0.55, 0.80, 3.8	IF22-06194195	0.80 (n=3)
Potato process waste	0.08 [#]	GLP-STUDY-21-14	0.97 (n=4) [#]
	1.27, 1.1, 0.84	IF22-06194195	
Potato, ensiled	2.1, 0.73, 1.3	IF22-06194195	1.3 (n=3)
Potato, starch	0.23, 0.11, 0.10	IF22-06194195	0.11 (n=3)
Potato protein	0.36, 0.16, 0.17	IF22-06194195	0.17 (n=3)
Potato, dried pulp	2.59 [#]	GLP-STUDY-21-14	1.3 (n=4) [#]
	1.6, 1.0, 0.22	IF22-06194195	
Potato, boiled	1.2, 1.2, 0.58	IF22-06194195	1.2 (n=3)
Potato, canned	0.57, 0.40, 0.64	IF22-06194195	0.57 (n=3)

[#] Calculated by the applicant

Magnitude of residues in representative succeeding crops

No new data were submitted in the framework of this application.

A 2.3.6 Other/Special Studies

A 2.3.6.1 Study 1 – Residue study in honey

Comments of zRMS:	Any LoA cannot be a presentation subject here. Appendix 2 is intended for the data presentation and evaluation.
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LoA to the honey residue data is available.

Comments of zRMS:	The study has been accepted.
	Important note to the entity granting the LoA: All data marked in yellow below in the study description were independently provided by the applicant. The evaluator

	himself only assessed the provided study and wrote an overall conclusion in the gray box, without disclosing any data: [REDACTED] The objectives of 4 tunnel trials were to determine the magnitude of residues of phosphonic acid in honey and flowers following exposure of honeybees to treated Phacelia tanacetifolia plants with the validated LC-MS/MS method. Two specific transitions for each analyte were monitored. The LOQ was 0.05 mg/kg. All validation parameters were within the required range. [REDACTED]
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The study is summarised in the following:

Reference:	KCA 6.10.1/01
Report:	HONEY MRL STUDY WITH PHOPHONIC ACID ON PHACELIA IN 2021, Couture, E., 2022, report No. 143SRFR21C01, Doc. No. 634-96002
Guideline(s):	SANTE/11956/2016 rev. 9, OECD No. 509, OECD No. 506, ENV/JM/MONO(2007)17
Deviations:	Yes, 4 with none or minor impact on the study
GLP:	Yes
Acceptability:	Yes

Executive summary

The objective of the study was to determine the magnitude of residues of Phosphonic acid in flowers and in honey following exposure of honeybees to treated Phacelia tanacetifolia plants – EPPO code: PHCTA, after one application with LBG-01F34, a soluble concentrate (SL) formulation containing Potassium Phosphonates as active substance, under semi-field conditions at a nominal rate of 20 L f.p./ha at BBCH 61-65. This study included four supervised trials conducted in Northern Europe (France and Poland) and Southern Europe (France and Spain) during the 2021 season. The aim of those trials was to obtain honey from each of the employed colonies, which is exclusively produced from the nectar of Phacelia plants, confined under gauze tunnels. Also, Phacelia flower samples were collected just after application.

The trials consisted of two plots: a treated plot and an untreated control plot.

Beehives were introduced into the tunnel at the evening before or at the morning of application. Samples of flowers were collected on the day of application, when the spray had dried, but before the release of the bees.

Honey specimens were taken 7-25 days after application (BBCH 67-69) to get mature honey (water content < 20%). Honey specimens were collected from combs, which were installed empty shortly before the exposure phase, or parts of combs that were empty at the start of the trial.

Flower and honey specimens were analysed for residues of Phosphonic acid.

Residue levels in control samples ranged from < 0.05 to 0.09 mg/kg in honey and from < 0.05 to 1.33 mg/kg in flowers. Residue levels above the LOQ could be due to sampling of contaminated honey in the hive (collected by the bees before the experimental phase) or contaminations of test sites before the field phase. In treated specimens of phacelia honey, the residues of Phosphonic acid ranged from 1.89 mg/kg to 15.19 mg/kg mg/kg.

Phosphonic acid residues in treated samples of flowers were found at levels between 535.03 and 2644.26 mg/kg.

Material, study design and methods

Material / test item:

Test material:	LBG-01F34
Formulation:	Soluble concentrate (SL)
CAS#:	Potassium phosphonates, expressed as Phosphonic acid: 13598-36-2
Lot/Batch #:	2103649024
Content of a.s. (actual):	Phosphonic acid: 507 g/L

Study design:

Four field trials were conducted in Northern Europe (Northern France and Poland) and Southern Europe (Southern France and Spain) in order to determine the magnitude of residues of Phosphonic acid in Phacelia (Phacelia tanacetifolia) honey after one application of LBG-01F34 under semi-field conditions (tunnel trial).

The trials consisted of two plots, one untreated and one treated plot. The test item LBG-01F34 was applied as foliar application at growth stage BBCH 61-65. The application rate was 20 L f.p./ha which corresponds to 15.1 kg Potassium Phosphonates/ha or 10.14 kg Phosphonic acid equiv./ha (2.25N). The water volume used was 200-400 L/ha.

The tunnel plots comprised 200 to 270 m² with a tunnel height of > 2.5 to 3.0 m and were surrounded by a gauze mesh with < 3 mm mesh width. A water supply for the bees was placed in each tunnel. There was a minimum distance of ≥ 1 m between treated and untreated plots.

Samples of flowers were collected on the day of application, when the spray had dried, but before the release of the bees. All floral parts were collected (sepal, petal, stamen, carpel, flower stalk), without the stem. Samples were stored deep-frozen within 2h after sampling.

Honey specimens (shipment samples for analysis and retain samples) were taken 7-25 days after application (BBCH 67-69) at maturity of honey (water content < 20%). Samples were stored deep-frozen (≤ -18°C) within 4.7 h. Samples were kept deep-frozen (≤ 18°C) throughout shipment and until analysis.

Methods:

Honey and flower specimens were analysed for residues of Phosphonic acid using BASF method 886594: Phosphonic acid residues were extracted with methanol/water (50/50, v/v). An aliquot of the extract was diluted with 0.5% of formic acid in water prior to final determination by HPLC-MS/MS.

The method was validated within the study at two fortification levels at the limit of quantification (0.05 mg/kg) and 10 × LOQ (0.5 mg/kg) in honey and flower matrices in compliance with SANTE/2020/12830, Rev.1 guideline. The limit of detection (LOD) was 0.014 mg/kg for each matrix.

Storage stability:

The maximum storage interval of honey specimens from harvest until analysis was 113 days. Frozen storage stability (< -18°C) of residues of Phosphonic acid was demonstrated within the study for this period of time. The time between extraction and measurement of samples was 1 day. Stability of Phosphonic acid in honey and flower extracts at 4°C was demonstrated for 13 days.

Results:

For three trials, residue levels of Phosphonic acid in control samples of honey and/or flower were equal to or slightly higher than the LOQ (0.05 mg/kg). These results could be due to accidental contaminations of test sites before the field phase or sampling of contaminated honey in the hive (collected by the bees before the experimental phase).

However, these slight contaminations are negligible compared to the high levels of residues found in the

treated samples.

Phosphonic acid residues in treated samples of flowers were found at levels between 535.03 and 2644.26 mg/kg.

Phosphonic acid residues in treated samples of honey taken at maturity 7 - 25 DAA were found at levels between 1.89 and 15.19 mg/kg.

Table A 98 Residue levels of Phosphonic acid in Phacelia honey

Trial	Plot No.	Sampling timing	Residue level Phosphonic acid [mg/kg]
SRFR21-001-143FC01	Control (C101)	Maturity	0.09
SRFR21-001-143FC01	Treated (T102)	Maturity	15.19
SRFR21-002-143FC01	Control (C101)	Maturity	0.05
SRFR21-002-143FC01	Treated (T102)	Maturity	8.80
SRPL21-003-143FC01	Control (C101)	Maturity	< 0.05
SRFR21-003-143FC01	Treated (T102)	Maturity	6.63
SRES21-339-143FC	Control (C101)	Maturity	0.06
SRES21-339-143FC	Treated (T102)	Maturity	1.89

Table A 99 Residue levels of Phosphonic acid in Phacelia flowers

Trial	Plot No.	DAA	Residue level Phosphonic acid [mg/kg]
SRFR21-001-143FC01	Control (C101)	0	1.33
SRFR21-001-143FC01	Treated (T102)	0	2644.26
SRFR21-002-143FC01	Control (C101)	0	0.15
SRFR21-002-143FC01	Treated (T102)	0	1187.42
SRPL21-003-143FC01	Control (C101)	0	< 0.05
SRFR21-003-143FC01	Treated (T102)	0	535.03
SRES21-339-143FC	Control (C101)	0	< 0.05
SRES21-339-143FC	Treated (T102)	0	569.99

DAA: Days after application

CONCLUSION


Regarding the residue levels in honey:

Residue levels of Phosphonic acid in control samples ranged from < 0.05 to 0.09 mg/kg.

In treated specimens of honey, taken at maturity, the residues levels of Phosphonic acid ranged from 1.89 to 15.19 mg/kg (2.25N).

A 2.4
A 2.5
Zoxamide

Pesticide Residue Intake Model (PRIMo)
IEDI calculations



European Food Safety Authority
EFSA PRIMo revision 3.1; 2021/01/06

Zoxamide

LOQs (mg/kg) range from: 0.01 to: 0.05

Toxicological reference values

ADI (mg/kg bw/day): 0.5 ARD (mg/kg bw): not necessary

Source of ADI: EFSA Source of ARD: EFSA

Year of evaluation: 2017 Year of evaluation: 2017

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:


Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

Calculated exposure (% of ADI)		Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	MRSLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)	
TMDI/NEDI/IEDI calculation (based on average food consumption)	0.2%	PT general	1.12	0.2%	Wine grapes	0.0%	Potatoes	0.0%	Table grapes	0.0%	0.2%
	0.2%	NL toddler	0.94	0.1%	Table grapes	0.0%	Apples	0.0%	Pears	0.0%	0.2%
	0.2%	FR adult	0.90	0.2%	Wine grapes	0.0%	Table grapes	0.0%	Apples	0.0%	0.2%
	0.2%	DE child	0.81	0.1%	Table grapes	0.0%	Apples	0.0%	Potatoes	0.0%	0.2%
	0.2%	RO general	0.77	0.1%	Wine grapes	0.0%	Potatoes	0.0%	Table grapes	0.0%	0.2%
	0.1%	GEMS/Food G07	0.74	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	GEMS/Food G11	0.62	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	IE adult	0.60	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	GEMS/Food G08	0.59	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	NL child	0.58	0.1%	Table grapes	0.0%	Apples	0.0%	Potatoes	0.0%	0.1%
	0.1%	GEMS/Food G15	0.57	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	DE women 14-50 yr	0.48	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Apples	0.0%	0.1%
	0.1%	DE general	0.46	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Apples	0.0%	0.1%
	0.1%	GEMS/Food G06	0.46	0.1%	Table grapes	0.0%	Potatoes	0.0%	Wine grapes	0.0%	0.1%
	0.1%	DK adult	0.45	0.1%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	UK adult	0.44	0.1%	Wine grapes	0.0%	Potatoes	0.0%	Table grapes	0.0%	0.1%
	0.1%	NL general	0.38	0.0%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	UK vegetarian	0.36	0.1%	Wine grapes	0.0%	Potatoes	0.0%	Table grapes	0.0%	0.1%
	0.1%	GEMS/Food G10	0.33	0.0%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.1%
	0.1%	FR child 3-15 yr	0.32	0.0%	Wine grapes	0.0%	Table grapes	0.0%	Apples	0.0%	0.1%
	0.0%	PL general	0.23	0.0%	Table grapes	0.0%	Potatoes	0.0%	Apples	0.0%	0.0%
	0.0%	UK toddler	0.21	0.0%	Table grapes	0.0%	Potatoes	0.0%	Apples	0.0%	0.0%
	0.0%	ES adult	0.20	0.0%	Wine grapes	0.0%	Potatoes	0.0%	Table grapes	0.0%	0.0%
	0.0%	FI 3 yr	0.20	0.0%	Potatoes	0.0%	Table grapes	0.0%	Apples	0.0%	0.0%
	0.0%	FR toddler 2-3 yr	0.19	0.0%	Wine grapes	0.0%	Apples	0.0%	Potatoes	0.0%	0.0%
	0.0%	FI adult	0.17	0.0%	Wine grapes	0.0%	Table grapes	0.0%	Potatoes	0.0%	0.0%
	0.0%	DK child	0.17	0.0%	Table grapes	0.0%	Potatoes	0.0%	Apples	0.0%	0.0%
	0.0%	FI 6 yr	0.16	0.0%	Potatoes	0.0%	Table grapes	0.0%	Apples	0.0%	0.0%
	0.0%	UK infant	0.12	0.0%	Potatoes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	SE general	0.11	0.0%	Potatoes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	LT adult	0.11	0.0%	Potatoes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR infant	0.09	0.0%	Potatoes	0.0%	Apples	0.0%	Wine grapes	0.0%	0.0%
0.0%	ES child	0.08	0.0%	Potatoes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%	
0.0%	IT toddler	0.08	0.0%	Table grapes	0.0%	Potatoes	0.0%	Apples	0.0%	0.0%	
0.0%	IT adult	0.08	0.0%	Table grapes	0.0%	Apples	0.0%	Potatoes	0.0%	0.0%	
0.0%	IE child	0.04	0.0%	Table grapes	0.0%	Potatoes	0.0%	Apples	0.0%	0.0%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Zoxamide is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMo when the UK was a member of the European Union.

Phosphonic acid: TMDI recalculated by zRMS



European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

Phosphonic acid

LOQs (mg/kg) range from: _____ to: _____

Toxicological reference values

ADI (mg/kg bw/day): 1 ARfD (mg/kg bw): not necessary

Source of ADI: Pt. A 19.02 Source of ARfD: EFSA

Year of evaluation: 2023 Year of evaluation: 2013

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

		No of diets exceeding the ADI : ---						Exposure resulting from			
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI(NED)/IEDI calculation (based on average food consumption)	82%	GEMS/Food G08	817,76	25%	Tomatoes	17%	Wheat	7%	Watermelons		
	73%	NL toddler	728,05	13%	Kiwi fruits (green, red, yellow)	9%	Wheat	7%	Tomatoes		
	70%	DE child	702,69	10%	Wheat	7%	Tomatoes	7%	Oranges		
	48%	GEMS/Food G08	482,82	9%	Wheat	8%	Tomatoes	5%	Potatoes		
	48%	NL child	477,92	9%	Wheat	5%	Potatoes	4%	Tomatoes		
	48%	GEMS/Food G10	475,52	10%	Tomatoes	9%	Wheat	4%	Potatoes		
	46%	FR child 3 15 yr	464,07	11%	Wheat	6%	Tomatoes	6%	Oranges		
	46%	RO general	461,22	14%	Tomatoes	12%	Wheat	5%	Potatoes		
	46%	IE adult	459,50	5%	Wheat	5%	Melons	4%	Kiwi fruits (green, red, yellow)		
	44%	GEMS/Food G15	438,95	10%	Wheat	8%	Tomatoes	5%	Potatoes		
	44%	GEMS/Food G07	436,67	10%	Wheat	8%	Tomatoes	5%	Potatoes		
	42%	GEMS/Food G11	424,11	8%	Wheat	6%	Tomatoes	5%	Potatoes		
	42%	IT toddler	418,04	15%	Wheat	10%	Tomatoes	2%	Peaches		
	40%	DK child	398,69	13%	Cucumbers	10%	Wheat	4%	Tomatoes		
	39%	SE general	385,35	7%	Wheat	6%	Potatoes	5%	Tomatoes		
	37%	ES child	368,73	10%	Wheat	7%	Tomatoes	4%	Oranges		
	35%	IT adult	350,37	10%	Wheat	8%	Tomatoes	2%	Other lettuce and other salad plants		
	34%	PT general	340,54	9%	Wheat	7%	Potatoes	6%	Tomatoes		
	32%	FR toddler 2 3 yr	324,23	7%	Wheat	3%	Tomatoes	3%	Kiwi fruits (green, red, yellow)		
	32%	FI 3 yr	322,42	8%	Cucumbers	6%	Potatoes	4%	Tomatoes		
	30%	UK toddler	301,80	9%	Wheat	5%	Potatoes	4%	Tomatoes		
	30%	DE women 14-50 yr	299,16	5%	Tomatoes	5%	Wheat	3%	Oranges		
	29%	ES adult	286,16	5%	Tomatoes	5%	Wheat	2%	Oranges		
	27%	DE general	270,16	5%	Tomatoes	4%	Wheat	3%	Oranges		
	26%	NL general	264,43	4%	Wheat	3%	Potatoes	3%	Tomatoes		
	25%	FR adult	254,98	5%	Wheat	3%	Tomatoes	3%	Wine grapes		
	25%	FI 6 yr	251,01	6%	Cucumbers	5%	Potatoes	3%	Tomatoes		
	22%	UK infant	217,56	6%	Wheat	4%	Potatoes	3%	Tomatoes		
	20%	UK vegetarian	203,58	5%	Wheat	4%	Tomatoes	2%	Potatoes		
	17%	PL general	171,39	6%	Tomatoes	5%	Potatoes	1%	Onions		
	16%	DK adult	164,88	4%	Tomatoes	3%	Wheat	2%	Cucumbers		
	16%	LT adult	164,47	4%	Tomatoes	4%	Potatoes	3%	Cucumbers		
	16%	FR infant	164,12	4%	Courgettes	3%	Potatoes	2%	Wheat		
	16%	UK adult	158,20	4%	Wheat	3%	Tomatoes	2%	Potatoes		
	14%	FI adult	142,29	4%	Tomatoes	3%	Cucumbers	2%	Potatoes		
6%	IE child	57,52	3%	Wheat	0,8%	Potatoes	0,4%	Tomatoes			

Conclusion:
The estimated long-term dietary intake (TMDI/NED/IEDI) was below the ADI.
The long-term intake of residues of Phosphonic acid is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMo when the UK was a member of the European Union.

The applicant IEDI estimation




EFSA PRIMo revision 3.1; 2021/01/06

Phosphonic acid (resulting from use of fosetyl potassium and disodium phosphonates)			
LOQs (mg/kg) range from:		0.1	to: 0.10
Toxicological reference values			
ADI (mg/kg bw/day):		1	ARfD (mg/kg bw): not necessary
Source of ADI:		EFSA 2018	Source of ARfD: EFSA
Year of evaluation:		2018	Year of evaluation: 2018

Input values	
Details - chronic risk assessment	Supplementary results - chronic risk assessment
Details - acute risk	Details - acute risk

Comments: Assuming MRLs will be amended as proposed in the RO on the joint review of MRLs for fosetyl, disodium phosphonates and potassium phosphonates according to Article 12 and 43 of Regulation (EC) No 396/2005 and the RO on the modification of the MRLs in chards/beet leaves and honey (not yet discussed)

Normal mode												
Chronic risk assessment: JMPR methodology (IEDI/TMDI)												
				No of diets exceeding the ADI : ---								Exposure resulting from
	Calculated exposure		Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	MRLs set at the LOQ (in % of ADI)	commodities not under assessmen (in % of ADI)	
	(% of ADI)	MS Diet										
TMDI/NEDI/IEDI calculation (based on average food consumption)	47%	DE child	465.65	10%	Wheat	7%	Oranges	4%	Apples			9%
	46%	NL toddler	463.77	9%	Wheat	6%	Potatoes	4%	Oranges			12%
	44%	GEMS/Food G06	443.10	17%	Wheat	5%	Tomatoes	3%	Potatoes			4%
	36%	NL child	356.72	10%	Wheat	5%	Potatoes	3%	Coconuts			8%
	33%	GEMS/Food G08	329.27	9%	Wheat	5%	Potatoes	2%	Olives for oil production			7%
	32%	GEMS/Food G11	319.02	8%	Wheat	5%	Potatoes	2%	Capers			8%
	31%	FR child 3 15 yr	313.61	11%	Wheat	6%	Oranges	2%	Potatoes			4%
	31%	GEMS/Food G07	311.58	10%	Wheat	5%	Potatoes	2%	Oranges			8%
	30%	IE adult	302.77	5%	Wheat	3%	Potatoes	2%	Oranges			5%
	30%	GEMS/Food G10	300.83	9%	Wheat	4%	Potatoes	2%	Tomatoes			5%
	29%	GEMS/Food G15	287.38	11%	Wheat	5%	Potatoes	2%	Tomatoes			7%
	28%	RO general	281.08	12%	Wheat	5%	Potatoes	3%	Tomatoes			8%
	26%	ES child	262.90	10%	Wheat	4%	Oranges	2%	Potatoes			3%
	25%	PT general	254.77	9%	Wheat	7%	Potatoes	3%	Wine grapes			11%
	25%	IT toddler	252.86	15%	Wheat	2%	Tomatoes	1%	Potatoes			2%
	25%	SE general	246.33	7%	Wheat	6%	Potatoes	2%	Lettuces			6%
	24%	UK toddler	237.49	9%	Wheat	5%	Potatoes	3%	Oranges			6%
	23%	DK child	234.94	10%	Wheat	4%	Cucumbers	3%	Potatoes			4%
	22%	FR toddler 2 3 yr	222.81	7%	Wheat	3%	Potatoes	2%	Oranges			4%
	21%	DE women 14-50 yr	205.13	5%	Wheat	3%	Oranges	1%	Potatoes			4%
	19%	NL general	193.25	4%	Wheat	3%	Potatoes	2%	Oranges			5%
	19%	FI 3 yr	190.46	6%	Potatoes	3%	Wheat	3%	Cucumbers			7%
	19%	IT adult	188.28	10%	Wheat	2%	Tomatoes	2%	Lettuces			1%
	19%	ES adult	186.53	5%	Wheat	2%	Oranges	2%	Lettuces			2%
	19%	DE general	185.39	4%	Wheat	3%	Oranges	2%	Potatoes			4%
	17%	UK infant	165.56	6%	Wheat	4%	Potatoes	2%	Oranges			5%
	16%	FR adult	156.57	5%	Wheat	3%	Wine grapes	1%	Oranges			4%
	15%	FI 6 yr	152.67	5%	Potatoes	2%	Wheat	2%	Cucumbers			6%
	14%	UK vegetarian	142.37	5%	Wheat	2%	Potatoes	1%	Oranges			3%
	12%	UK adult	116.72	4%	Wheat	2%	Potatoes	1%	Wine grapes			3%
	11%	FR infant	108.51	3%	Potatoes	2%	Wheat	1%	Spinaches			3%
	10%	LT adult	104.31	4%	Potatoes	2%	Wheat	1%	Cucumbers			5%
	10%	DK adult	99.40	3%	Wheat	2%	Potatoes	1%	Wine grapes			4%
	10%	PL general	98.50	5%	Potatoes	1%	Tomatoes	1%	Walnuts			6%
	8%	FI adult	81.85	2%	Potatoes	1.0%	Cucumbers	0.8%	Tomatoes			2%
	5%	IE child	46.91	3%	Wheat	0.8%	Potatoes	0.1%	Oranges			1.0%
Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Phosphonic acid (resulting from use of fosetyl potassium and disodium phosphonates) is unlikely to present a public health concern. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.												



European Food Safety Authority
EFSA PRIMo revision 3.1: 2021/01/06

Phosphonic acid (resulting from use of fosetyl potassium and disodium phosphonates)

LOQs (mg/kg) range from: 0.1 to: 0.10

Toxicological reference values

ADI (mg/kg bw/day): 2.25 ARID (mg/kg bw): not necessary

Source of ADI: EFSA Source of ARID: EFSA

Year of evaluation: 2017 Year of evaluation: 2017

Input values

Details - chronic risk assessment

Summary of results - chronic risk assessment

Details - acute risk assessment

Details - acute risk

Comments: Assuming MRLs will be amended as proposed in the RO on the basis of the MRLs for fosetyl, disodium phosphonates and potassium phosphonates according to Article 12 and 43 of Regulation (EC) No 396/2005 and on the modification of the MRLs in chards/beet leaves and honey (not yet discussed)

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---										Exposure resulting from	
Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	MRLs set at the LOQ (in % of ADI)		
									MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)	
TMDI/NEDI/IEDI calculation (based on average food consumption)	21%	DE child	465.92	4%	Wheat	2%	Apples			4%	
	21%	NL toddler	463.89	4%	Wheat	2%	Oranges			5%	
	20%	GEMS/Food G06	443.10	7%	Wheat	1%	Potatoes			2%	
	16%	NL child	356.79	4%	Wheat	1%	Coconuts			4%	
	15%	GEMS/Food G08	329.27	4%	Wheat	0.8%	Olives for oil production			3%	
	14%	GEMS/Food G11	319.02	4%	Wheat	0.8%	Capers			3%	
	14%	FR child 3 15 yr	313.68	5%	Wheat	0.9%	Potatoes			2%	
	14%	GEMS/Food G07	311.58	4%	Wheat	1%	Oranges			3%	
	13%	IE adult	302.77	2%	Wheat	0.8%	Oranges			2%	
	13%	GEMS/Food G10	300.83	4%	Wheat	0.9%	Tomatoes			2%	
	13%	GEMS/Food G15	287.38	5%	Wheat	0.8%	Tomatoes			3%	
	12%	RO general	281.13	5%	Wheat	1%	Tomatoes			4%	
	12%	ES child	262.95	5%	Wheat	1%	Potatoes			1%	
	11%	PT general	254.77	4%	Wheat	3%	Wine grapes			5%	
	11%	IT toddler	252.86	7%	Wheat	0.9%	Potatoes			0.8%	
	11%	SE general	246.42	3%	Wheat	3%	Potatoes			3%	
	11%	UK toddler	237.57	4%	Wheat	2%	Potatoes			2%	
	10%	DK child	234.94	4%	Wheat	2%	Cucumbers			2%	
	10%	FR toddler 2 3 yr	222.92	7%	Wheat	1%	Potatoes			2%	
	9%	DE women 14-50 yr	205.2	2%	Wheat	1%	Oranges			2%	
	9%	NL general	198.2	2%	Wheat	1%	Potatoes			2%	
	8%	FI 3 yr	188.2	3%	Potatoes	1%	Wheat			3%	
	8%	IT adult	188.28	4%	Wheat	0.7%	Tomatoes			0.6%	
	8%	ES adult	186.58	2%	Wheat	1.0%	Oranges			1.0%	
	8%	DE general	185.50	2%	Wheat	1%	Oranges			2%	
	7%	UK infant	165.69	3%	Wheat	2%	Potatoes			1%	
	7%	FR adult	156.62	2%	Wheat	1%	Wine grapes			0.4%	
	7%	FI 6 yr	152.69	2%	Potatoes	1%	Wheat			0.8%	
	6%	UK child	142.37	2%	Wheat	0.8%	Potatoes			0.7%	
	5%	UK adult	116.76	2%	Wheat	0.8%	Potatoes			0.6%	
	5%	UK infant	108.53	1%	Potatoes	0.8%	Wheat			0.6%	
	5%	LT adult	104.31	2%	Potatoes	1%	Wheat			0.5%	
	5%	DK adult	99.40	1%	Wheat	0.8%	Potatoes			0.6%	
	5%	PL general	98.50	2%	Potatoes	0.6%	Tomatoes			0.5%	
	4%	FI adult	81.85	0.7%	Potatoes	0.4%	Cucumbers			0.4%	
	2%	IE child	46.92	1%	Wheat	0.4%	Potatoes			0.1%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Phosphonic acid (resulting from use of fosetyl potassium and disodium phosphonates) is unlikely to present a public health concern.
DISCLAIMER: Dietary data from the UK were included in PRIMo when the UK was a member of the European Union.

Zoxamide

Not required, as an ARfD is not allocated.

Phosphonic acid

Not required, as an ARfD is not allocated.

Zoxamide

Not required, as an ARfD is not allocated.

RH-150721

Phosphonic acid
Not required, as an ARfD is not allocated.

Appendix 3 Additional information provided by the applicant

Mann-Whitney – U-test (α : 0.05)

Zoxamide

Grapes

RD: Zoxamide

Data set	Zoxamide NEU	Zoxamide SEU	Rank Set 1	Rank Set 2
1	0.19	0.17	2	1
2	0.21	0.22	3	4
3	0.33	0.23	7	5
4	0.34	0.28	8	6
5	0.51	0.35	11	9
6	0.59	0.39	14	10
7	0.62	0.54	15	12
8	0.91	0.57	16	13
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean	0.46	0.34
STMR	0.43	0.32
Number of values:	8	8
Sum Rank:	76	60
U ₁ and U ₂ values:	24	40
Critical value:	13	($\alpha=0.05$)
n _a =	8	n _b = 8
Result:	Populations similar	

RD: Zoxamide + RH-141452, calculated as Zoxamide

Data set	Z + Meta* NEU	P + Meta* SEU	Rank Set 1	Rank Set 2
1	0.20	0.18	2	1
2	0.22	0.23	3	4
3	0.31	0.24	7	5
4	0.35	0.29	8	6
5	0.52	0.36	11	9
6	0.60	0.40	14	10
7	0.63	0.55	15	12
8	0.92	0.58	16	13
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean	0.47	0.35
STMR	0.44	0.33
Number of values:	8	8
Sum Rank:	76	60
U ₁ and U ₂ values:	24	40
Critical value:	13	($\alpha=0.05$)
n _a =	8	n _b = 8
Result:	Populations similar	

*Z + Meta: Zoxamide + RH-141452, calculated as Zoxamide

Pome fruits

RD: Zoxamide

RD: Zoxamide + RH-141452, calculated as Zoxamide

Data set	Zoxamide NEU	Zoxamide SEU	Rank Set 1	Rank Set 2
1	0.01	0.01	9	9
2	0.01	0.01	9	9
3	0.01	0.01	9	9
4	0.01	0.01	9	9
5	0.01	0.01	9	9
6	0.01	0.01	9	9
7	0.01	0.01	9	9
8	0.01	0.01	9	9
9	0.02	0.01	19	9
10		0.02		18
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean	0.01	0.01
STMR	0.01	0.01
Number of values:	9	10
Sum Rank:	91	99
U₁ and U₂ values:	44	46
Critical value:	20	($\alpha=0.05$)
$n_a = 9$		$n_b = 10$
Result:	Populations similar	

Data set	Z + Meta* NEU	P + Meta* SEU	Rank Set 1	Rank Set 2
1	0.02	0.02	9	9
2	0.02	0.02	9	9
3	0.02	0.02	9	9
4	0.02	0.02	9	9
5	0.02	0.02	9	9
6	0.02	0.02	9	9
7	0.02	0.02	9	9
8	0.02	0.02	9	9
9	0.03	0.02	19	9
10		0.03		18
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean	0.02	0.02
STMR	0.02	0.02
Number of values:	9	10
Sum Rank:	91	99
U₁ and U₂ values:	44	46
Critical value:	20	($\alpha=0.05$)
$n_a = 9$		$n_b = 10$
Result:	Populations similar	

*Z + Meta: Zoxamide + RH-141452, calculated as Zoxamide

Phosphonic acid

Pome fruits

Data set	Phos. acid NEU	Phos. acid SEU	Rank Set 1	Rank Set 2
1	1.85	2.85	6	9
2	11.60	5.18	17	13
3	1.78	3.32	5	10
4	2.63	4.33	8	11
5	1.45	7.93	4	16
6	2.38	1.02	7	2
7	1.22	5.92	3	14
8	0.69	4.72	1	12
9	6.40		15	
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean 3.33 4.41

STMR 1.85 4.53

Number of values: 9 8

Sum Rank: 66 87

U₁ and U₂ values: 51 21

Critical value: 15 ($\alpha = 0.05$)

$n_a = 8$

$n_b = 9$

Result: **Populations similar**

Potatoes

Data set	Phos. Acid NEU	Phos. Acid SEU	Rank Set 1	Rank Set 2
1	20.70	7.14	11	4
2	53.90	11.60	15	7
3	7.30	2.80	5.5	1
4	14.00	28.00	10	14
5	7.30	65.00	5.5	16
6	26.00	3.70	12.5	2
7	12.00	4.20	8	3
8	26.00	13.00	12.5	9
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean 20.90 16.93

STMR 17.35 9.37

Number of values: 8 8

Sum Rank: 80 56

U₁ and U₂ values: 20 44

Critical value: 13 ($\alpha = 0.05$)

$n_a = 8$

$n_b = 8$

Result: **Populations similar**

Fosetyl

Pome fruits

Data set	Fosetyl NEU	Fosetyl SEU	Rank Set 1	Rank Set 2
1	2.48	3.82	6	9
2	15.54	6.94	17	13
3	2.39	4.45	5	10
4	3.52	5.80	8	11
5	1.94	10.63	4	16
6	3.19	1.37	7	2
7	1.63	7.93	3	14
8	0.92	6.32	1	12
9	8.58		15	
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean 4.47 5.91

STMR 2.48 6.06

Number of values: 9 8

Sum Rank: 66 87

U₁ and U₂ values: 51 21

Critical value: 15 ($\alpha = 0.05$)

$n_a = 8$

$n_b = 9$

Result: Populations similar

Potatoes

Data set	Fosetyl NEU	Fosetyl SEU	Rank Set 1	Rank Set 2
1	72.20	9.60	15	3
2	27.70	15.50	10	6
3	9.80	3.80	4.5	1
4	18.80	37.50	9	13
5	9.80	87.10	4.5	16
6	34.80	49.60	11.5	14
7	16.10	5.60	7	2
8	34.80	17.40	11.5	8
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				
19				
20				
21				
22				
23				
24				
25				

Mean 28.00 28.26

STMR 23.25 16.45

Number of values: 8 8

Sum Rank: 73 63

U₁ and U₂ values: 27 37

Critical value: 13 ($\alpha = 0.05$)

n_a = 8

n_b = 8

Result: **Populations similar**

MRL Calculation - grapes, pome fruits, potatoes, honey

Zoxamide

Grapes – for MRL calculation

Compound	Zoxamide
Crop	Grapes
Region / Country	NEU+SEU
GAP	3x 180 g a.s./ha
Total number of data (n)	16
Percentage of censored data	0%
Number of non-censored data	16
Lowest residue	0.174
Highest residue	0.905
Median residue	0.345
Mean	0.403
Standard deviation (SD)	0.203
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	0.905
- Mean + 4 SD	1.215
- CF x 3 Mean	1.208
Unrounded MRL	<u>1.215</u>
Rounded MRL	<u>1.5</u>

Residues (mg/kg)	
0.340	
0.208	
0.616	
0.190	
0.511	
0.331	
0.591	
0.905	
0.281	
0.539	
0.573	
0.350	
0.174	
0.231	
0.218	
0.387	

Grapes – for STMR calculation for risk assessment

Compound	Zoxamide + RH-141452
Crop	Grapes
Region / Country	NEU+SEU
GAP	3x 180 g a.s./ha
Total number of data (n)	16
Percentage of censored data	0%
Number of non-censored data	16
Lowest residue	0.184
Highest residue	0.915
Median residue	0.355
Mean	0.413
Standard deviation (SD)	0.203
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	0.915
- Mean + 4 SD	1.225
- CF x 3 Mean	1.239
Unrounded MRL	<u>1.239</u>
Rounded MRL	<u>1.5</u>

Residues (mg/kg)	
0.350	
0.218	
0.627	
0.200	
0.521	
0.341	
0.601	
0.915	
0.291	
0.549	
0.583	
0.360	
0.184	
0.241	
0.228	
0.397	

Pome fruits –for MRL calculation

Compound	Zoxamide
Crop	Pome fruits
Region / Country	NEU + SEU
GAP	2x 180 g a.s./ha
Total number of data (n)	19
Percentage of censored data	89%
Number of non-censored data	2
Lowest residue	0.010
Highest residue	0.024
Median residue	0.010
Mean	0.011
Standard deviation (SD)	0.004
Correction factor for censoring (CF)	0.404
<u>Proposed MRL estimate</u>	
- Highest residue	0.024
- Mean + 4 SD	0.026
- CF x 3 Mean	0.014
Unrounded MRL	0.026
Rounded MRL	0.03
High uncertainty of MRL estimate due to high level of censoring.	
Residues (mg/kg)	
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.024	
0.010	*
0.010	*
0.010	*
0.010	*
0.010	*
0.018	
0.010	*
0.010	*
0.010	*

Pome fruits – for STMR calculation for risk assessment

Compound	Zoxamide + RH-141452
Crop	Pome fruits
Region / Country	NEU + SEU
GAP	2x 180 g a.s./ha
Total number of data (n)	19
Percentage of censored data	89%
Number of non-censored data	2
Lowest residue	0.020
Highest residue	0.034
Median residue	0.020
Mean	0.021
Standard deviation (SD)	0.004
Correction factor for censoring (CF)	0.404
<u>Proposed MRL estimate</u>	
- Highest residue	0.034
- Mean + 4 SD	0.036
- CF x 3 Mean	0.026
Unrounded MRL	0.036
Rounded MRL	0.04
High uncertainty of MRL estimate due to high level of censoring.	
Residues (mg/kg)	
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.034	
0.020	*
0.020	*
0.020	*
0.020	*
0.020	*
0.028	
0.020	*
0.020	*
0.020	*

Honey

Compound	Zoxamide
Crop	Honey
Region / Country	NEU + SEU
GAP	3 x 180 g a.s./ha
Total number of data (n)	4
Percentage of censored data	75%
Number of non-censored data	1
Lowest residue	0.010
Highest residue	0.078
Median residue	0.010
Mean	0.027
Standard deviation (SD)	0.034
Correction factor for censoring (CF)	0.500
<u>Proposed MRL estimate</u>	
- Highest residue	0.078
- Mean + 4 SD	0.163
- CF x 3 Mean	0.041
Unrounded MRL	0.163
Rounded MRL	0.2

High uncertainty of
MRL estimate due to
small dataset and
high level of
censoring.

Residues (mg/kg)	
0.010	*
0.010	*
0.010	*
0.078	

Phosphonic acid

Grapes

Compound	Phosphonic acid
Crop	Grapes
Region / Country	NEU + SEU
GAP	3 x 1500 g a.s./ha
Total number of data (n)	42
Percentage of censored data	0%
Number of non-censored data	42
Lowest residue	1.400
Highest residue	85.000
Median residue	13.000
Mean	17.686
Standard deviation (SD)	18.523
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	85.000
- Mean + 4 SD	91.779
- CF x 3 Mean	53.057
Unrounded MRL	91.779
Rounded MRL	100

Residues (mg/kg)	
11.400	
9.200	
14.300	
13.200	
15.000	
22.700	
24.100	
24.800	
1.400	
3.600	
68.100	
39.000	
70.500	
16.100	
20.600	
85.000	
2.700	
2.500	
6.800	
8.200	
9.600	
12.300	
13.000	
14.400	
1.600	
2.500	
2.200	
2.300	
2.900	
12.200	
13.700	
12.300	
13.000	
14.700	
5.800	
29.000	
25.100	
33.500	
16.000	
4.700	
30.200	
12.600	

Pome fruits

Compound	Phosphonic acid
Crop	Pome fruits
Region / Country	NEU + SEU
GAP	2 x 1500 g a.s./ha
Total number of data (n)	17
Percentage of censored data	0%
Number of non-censored data	17
Lowest residue	0.687
Highest residue	11.600
Median residue	2.850
Mean	3.839
Standard deviation (SD)	2.896
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	11.600
- Mean + 4 SD	15.422
- CF x 3 Mean	11.518
Unrounded MRL	15.422
Rounded MRL	15
Residues (mg/kg)	
1.850	
11.600	
1.780	
2.630	
1.450	
2.380	
1.220	
0.687	
6.400	
2.850	
5.180	
3.320	
4.330	
7.930	
1.020	
5.920	
4.720	

Potatoes

Compound	Phosphonic acid
Crop	Potatoes
Region / Country	SEU + NEU
GAP	3 x 1250 g a.s./ha
Total number of data (n)	16
Percentage of censored data	0%
Number of non-censored data	16
Lowest residue	2.800
Highest residue	65.000
Median residue	13.500
Mean	20.996
Standard deviation (SD)	17.957
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	65.000
- Mean + 4 SD	92.824
- CF x 3 Mean	62.989
Unrounded MRL	92.824
Rounded MRL	100
Residues (mg/kg)	
20.700	
53.900	
7.300	
14.000	
7.300	
26.000	
12.000	
26.000	
7.140	
11.600	
2.800	
28.000	
65.000	
37.000	
4.200	
13.000	

Honey

Compound	Phosphonic acid
Crop	Honey
Region / Country	NEU/SEU
GAP	1 x 10140 g a.s. /ha
Total number of data (n)	4
Percentage of censored data	0%
Number of non-censored data	4
Lowest residue	1.890
Highest residue	15.190
Median residue	7.715
Mean	8.128
Standard deviation (SD)	5.522
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	15.190
- Mean + 4 SD	30.216
- CF x 3 Mean	24.383
Unrounded MRL	30.216
Rounded MRL	30
High uncertainty of MRL estimate due to small dataset.	
Residues (mg/kg)	
15.190	
8.800	
6.630	
1.890	

Fosetyl

Grapes

Compound	Fosetyl
Crop	Grapes
Region / Country	NEU + SEU
GAP	3 x 1500 g Phosphonic acid/ha
Total number of data (n)	42
Percentage of censored data	0%
Number of non-censored data	42
Lowest residue	1.900
Highest residue	113.900
Median residue	17.400
Mean	23.698
Standard deviation (SD)	24.828
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	113.900
- Mean + 4 SD	123.009
- CF x 3 Mean	71.093
Unrounded MRL	123.009
Rounded MRL	150

Residues (mg/kg)	
15.300	
12.300	
19.100	
17.700	
20.100	
30.400	
32.300	
33.200	
1.900	
4.800	
91.300	
52.300	
94.500	
21.500	
27.600	
113.900	
3.600	
3.300	
9.200	
10.900	
12.900	
16.500	
17.400	
19.300	
2.100	
3.300	
3.000	
3.100	
3.900	
16.400	
18.400	
16.500	
17.400	
19.700	
7.700	
38.800	
33.700	
44.900	
21.500	
6.300	
40.400	
16.900	

Pome fruits

Compound	Fosetyl
Crop	Apples
Region / Country	NEU + SEU
GAP	2 x 1500 g Phosphonic acid/ha
Total number of data (n)	17
Percentage of censored data	0%
Number of non-censored data	17
Lowest residue	0.920
Highest residue	15.540
Median residue	3.820
Mean	5.144
Standard deviation (SD)	3.880
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	15.540
- Mean + 4 SD	20.663
- CF x 3 Mean	15.432
Unrounded MRL	<u>20.663</u>
Rounded MRL	<u>20</u>

Residues (mg/kg)	
2.480	
15.540	
2.390	
3.520	
1.940	
3.190	
1.630	
0.920	
8.580	
3.820	
6.940	
4.450	
5.800	
10.630	
1.370	
7.930	
6.320	

Potatoes

Compound	Fosetyl
Crop	Potatoes
Region / Country	SEU + NEU
GAP	3 x 1250 g a.s./ha
Total number of data (n)	16
Percentage of censored data	0%
Number of non-censored data	16
Lowest residue	3.800
Highest residue	87.100
Median residue	18.100
Mean	28.131
Standard deviation (SD)	24.054
Correction factor for censoring (CF)	1.000
<u>Proposed MRL estimate</u>	
- Highest residue	87.100
- Mean + 4 SD	124.347
- CF x 3 Mean	84.394
Unrounded MRL	<u>124.347</u>
Rounded MRL	150
Residues (mg/kg)	
72.200	
27.700	
9.800	
18.800	
9.800	
34.800	
16.100	
34.800	
9.600	
15.500	
3.800	
37.500	
87.100	
49.600	
5.600	
17.400	

Honey

Compound	Fosetyl
Crop	Honey
Region / Country	NEU/SEU
GAP	1 x 10140 g a.s. /ha
Total number of data (n)	4
Percentage of censored data	0%
Number of non-censored data	4
Lowest residue	2.533
Highest residue	20.355
Median residue	10.338
Mean	10.891
Standard deviation (SD)	7.400
Correction factor for censoring (CF)	1.000
Proposed MRL estimate	
- Highest residue	20.355
- Mean + 4 SD	40.489
- CF x 3 Mean	32.673
Unrounded MRL	40.489
Rounded MRL	40
High uncertainty of MRL estimate due to small dataset.	
Residues (mg/kg)	
	20.355
	11.792
	8.884
	2.533

Outcome of the animal dietary burden calculation:

Zoxamide

Ruminants, swine and poultry:

Animal burden calculation										Zoxamide + RH-141452, expressed as Zoxamide										
According to: "OECD Guidance Document, Series on testing and assessment No 64 and Series on pesticides No 32" and "OECD Guidance Document on Residues in livestock, Series on Pesticides No 73"																				
Maximum Intake (mg/kg bw/d)	Cattle										Sheep									
	Beef					Dairy					Ram/Ewe					Lamb				
	500 kg 12 kg					650 kg 25 kg					75 kg 2.5 kg					40 kg 1.7 kg				
	0.002					0.003					0.003					0.002				
	mg/kg bw/d %					mg/kg bw/d %					mg/kg bw/d %					mg/kg bw/d %				
Contributor 1	Potato	process waste	40	Potato	process waste	30	Potato	process waste	40	Potato	process waste	40	Potato	process waste	20					
Contributor 2	Potato	culls	30	Potato	culls	30	Potato	culls	30	Potato	culls	30	Potato	culls	20					
Contributor 3																				
Contributor 4																				
Median intake	0.0023					0.0031					0.0032					0.0023				
mg/kg bw/d					mg/kg bw/d					mg/kg bw/d					mg/kg bw/d					

Maximum Intake (mg/kg bw/d)	Swine										Intakes >0.004 mg/kg bw/d are highlighted									
	Breeding					Finishing														
	260 kg 6 kg					100 kg 3 kg														
	0.002					0.002														
	mg/kg bw/d %					mg/kg bw/d %														
Contributor 1	Potato	process waste	20	Potato	culls	50														
Contributor 2	Potato	culls	50	Potato	dried pulp	20														
Contributor 3																				
Contributor 4																				
Median intake	0.002					0.002														
mg/kg bw/d					mg/kg bw/d															

Maximum Intake (mg/kg bw/d)	Poultry										Intakes >0.1 mg/kg DM in red characters														
	Broiler					Layer															Turkey				
	1.7 kg 0.12 kg					1.9 kg 0.13 kg															7 kg 0.5 kg				
	0.001					0.001															0.001				
	mg/kg bw/d %					mg/kg bw/d %															mg/kg bw/d %				
Contributor 1	Potato	culls	10	Potato	culls	10	Potato	culls	20																
Contributor 2	Potato	dried pulp	20	Potato	dried pulp	15																			
Contributor 3																									
Contributor 4																									
Median intake	0.001					0.001					0.001														
mg/kg bw					mg/kg bw					mg/kg bw															

Intakes expressed on the dry mater basis (mg/kg DM)						
mg/kg DM	Cattle		Sheep		Swine	
	Beef	Dairy	Ram/Ewe	Lamb	Breeding	Finishing
Maximum	0.10	0.08	0.10	0.05	0.08	0.05
Median	0.10	0.08	0.10	0.05	0.08	0.05
	Poultry			Intake >0.1 mg/kg DM in red characters		
	Broiler	Layer	Turkey			
Maximum	0.01	0.01	0.02			
Median	0.01	0.01	0.02			

Fish:

Dietary Burden Calculation concerning Zoxamide
DietaryBurdenCalculator 3.0.2
Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Common carp

INPUT

IFN code of components in the diet:

Potato (protein) ---

Target content for Common carp

Crude fat 10.00%

Crude protein 35.00%

Maximum principal content of components in the diet:

Potato (protein) 3.00%

Fish meal(PC) 100.00%

Starch(CC) 100.00%

Oil(F) 100.00%

Percent dry matter of components:

Potato (protein) 89.4%

Zoxamide residues in the components:

Potato (protein) 0.020 mg/kg (STMR-P)

Zoxamide residues in the components (dry matter):

Potato (protein) 0.022 mg/kg (STMR-P)

RESULTS

=====

Maximum dietary burden based on Zoxamide is 0.001 mg/kg (dry matter).

The respective composition of the feed is:

Potato (protein) 3.00%

Fish meal(PC) 43.33%

Starch(CC) 45.96%

Oil(F) 7.70%

The dietary load of Zoxamide caused by the individual components is:

Potato (protein) 100.00%

Fish meal(PC) 0.00%

Starch(CC) 0.00%

Oil(F) 0.00%

Rainbow trout

INPUT

IFN code of components in the diet:

Potato (protein) ---

Target content for Rainbow trout

Crude fat 15.00%

Crude protein 42.00%

Maximum principal content of components in the diet:

Potato (protein) 2.00%

Fish meal(PC) 100.00%

Starch(CC) 100.00%

Oil(F) 100.00%

Percent dry matter of components:

Potato (protein) 89.4%

Zoxamide residues in the components:

Potato (protein) 0.020 mg/kg (STMR-P)

Zoxamide residues in the components (dry matter):

Potato (protein) 0.022 mg/kg (STMR-P)

RESULTS

Maximum dietary burden based on Zoxamide is 0.000 mg/kg (dry matter).

The respective composition of the feed is:

Potato (protein) 2.00%

Fish meal(PC) 53.78%

Starch(CC) 32.00%

Oil(F) 12.22%

The dietary load of Zoxamide caused by the individual components is:

Potato (protein) 100.00%

Fish meal(PC) 0.00%

Starch(CC) 0.00%

Oil(F) 0.00%

Atlantic salmon

INPUT

IFN code of components in the diet:

Potato (protein) ---

Target content for Atlantic salmon

Crude fat 33.00%

Crude protein 36.00%

Maximum principal content of components in the diet:

Potato (protein) 0.00%

Fish meal(PC) 100.00%

Starch(CC) 100.00%

Oil(F) 100.00%

Percent dry matter of components:

Potato (protein) 89.4%

Zoxamide residues in the components:

Potato (protein) 0.020 mg/kg (STMR-P)

Zoxamide residues in the components (dry matter):

Potato (protein) 0.022 mg/kg (STMR-P)

RESULTS

Maximum dietary burden based on Zoxamide is 0.000 mg/kg (dry matter).

The respective composition of the feed is:

Potato (protein) 0.00%

Fish meal(PC) 47.97%

Starch(CC) 21.45%

Oil(F) 30.58%

The dietary load of Zoxamide caused by the individual components is:

Potato (protein) NaN%

Fish meal(PC) NaN%

Starch(CC) NaN%

Oil(F) NaN%

Phosphonic acid (Not adjusted to new data for intended uses.)

Ruminants, swine and poultry:

Animal burden calculation						Phosphonic acid						
According to: "OECD Guidance Document, Series on testing and assessment No 64 and Series on pesticides No 32" and "OECD Guidance Document on Residues in livestock, Series on Pesticides No 73"												
Maximum Intake (mg/kg bw/d)	Cattle						Sheep					
	Beef			Dairy			Ram/Ewe			Lamb		
	500 kg 12 kg			650 kg 25 kg			75 kg 2.5 kg			40 kg 1.7 kg		
	8.323	mg/kg bw/d	%	11.584	mg/kg bw/d	%	11.781	mg/kg bw/d	%	9.655	mg/kg bw/d	%
Contributor 1	Potato	process waste	40	Potato	process waste	30	Potato	process waste	40	Potato	process waste	20
Contributor 2	Potato	culls	30	Potato	culls	30	Potato	culls	30	Potato	culls	20
Contributor 3	Wheat	straw	20	Wheat	straw	20	Wheat	straw	30	Wheat	straw	40
Contributor 4	Triticale	grain	10	Triticale	grain	20			0	Triticale	grain	20
Median intake	5.8144	mg/kg bw/d		7.5642	mg/kg bw/d		8.0310	mg/kg bw/d		5.9026	mg/kg bw/d	

Intakes >0.004 mg/kg bw/d are highlighted

Maximum Intake (mg/kg bw/d)	Swine					
	Breeding			Finishing		
	260 kg 6 kg			100 kg 3 kg		
	7.608	mg/kg bw/d	%	7.759	mg/kg bw/d	%
Contributor 1	Potato	process waste	20	Potato	culls	50
Contributor 2	Potato	culls	50	Potato	dried pulp	20
Contributor 3	Kale	leaves	10	Triticale	grain	30
Contributor 4	Triticale	grain	20			
Median intake	3.972	mg/kg bw/d		3.132	mg/kg bw/d	

Maximum Intake (mg/kg bw/d)	Poultry								
	Broiler		Layer		Turkey				
	1.7 kg 0.12 kg		1.9 kg 0.13 kg		7 kg 0.5 kg				
	6.483	mg/kg bw/d	%	6.326	mg/kg bw/d	%	7.849	mg/kg bw/d	%
Contributor 1	Potato	culls	10	Potato	culls	10	Potato	culls	20
Contributor 2	Potato	dried pulp	20	Potato	dried pulp	15	Distiller's grain	dried	10
Contributor 3	Wheat	grain	70	Wheat	straw	10	Wheat	grain	50
Contributor 4				Wheat	grain	65			
Median intake	4.305	mg/kg bw		3.748	mg/kg bw		3.442	mg/kg bw	

Intakes expressed on the dry mater basis (mg/kg DM)						
mg/kg DM	Cattle		Sheep		Swine	
	Beef	Dairy	Ram/Ewe	Lamb	Breeding	Finishing
Maximum	346.78	301.18	353.4	227.18	329.69	258.64
Median	242.27	196.67	240.93	138.88	172.11	104.39
	Poultry			Intake >0.1 mg/kg DM in red characters		
	Broiler	Layer	Turkey			
Maximum	91.84	92.45	109.89			
Median	60.99	54.78	48.19			