

REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: SAP50SCF

Product name(s): FOLPEC

Chemical active substance: folpet, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT/

(authorization)

Applicant: Selectis Produtos para a Agricultura, S.A.

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August 2024 (final Core Assessment)

October 2024 (updated final Core Assessment)

Version history

When	What
December 2023	V0 - Initial version submitted by the Selectis Produtos para a Agricultura, S.A. for submission to Poland in the frame of new PPP registration (According Art. 33 of Regulation EC No 1107/2009)
April 2024	V1 – Updated version submitted by the Selectis Produtos para a Agricultura, S.A. answering Poland request in the frame of new PPP registration (According Art. 33 of Regulation EC No 1107/2009).
May 2024	V2 – Updated version submitted by the Selectis Produtos para a Agricultura, S.A. answering Poland comments in the frame of new PPP registration (According Art. 33 of Regulation EC No 1107/2009).
June 2024	Initial zRMS assessment The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey . Not agreed or not relevant information are struck through and shaded for transparency. Following the evaluation and before sending the document for commenting, all coloured highlighting was removed, from the parts updated by the Applicant, for better legibility.
August 2024	Final report (Core Assessment updated following the commenting period) No additional information or assessments after the commenting period.
October 2024	Final Report updated after LoA submission Additional information included by the zRMS in the report are highlighted in yellow . Not agreed or not relevant information are struck through and shaded for transparency.

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

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 SAP50SCF are presented in **Table 7.1.1-1**. They have been selected from the individual GAPs in the CEU for wheat and barley. A list of all intended uses within the CEU is given in Part B, Section 0.

Both proposed uses in wheat and barley correspond to the critical GAP. Proposed uses are the same but in different crops. Therefore, critical uses are those presented under uses number 1 and 2 in the GAP in table 7.1-1.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRL for Folpet of 0.4 mg/kg in wheat and of 2 mg/kg in barley as laid down in Reg. (EU) 396/2005 is not expected.

The chronic and the short-term intakes of folpet residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, Czech Republic agrees with the authorization of the intended uses.

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

Data gaps: None

~~The applicant should submit a letter of access to the metabolism study on poultry.~~

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			PHI (days)	Conclusion
						Type	Conc. of as	method kind	growth stage & season	number min max	interval between applications (min)	g a.s./hL min max	water L/ha min max	g a.s./ha min max		
1	Wheat	CEU (DE, RO, PL, HU, CZ, SK, AT, SI, BE, NL)	SAP50SCF	F	Septoria	SC	500 g/L	Tractor mounted spray	BBCH 30-59	2	14 days	112,5-400	150-400	450-600	42	A
2	Barley	CEU (DE, RO, PL, HU, CZ, SK, AT, SI, BE, NL)	SAP50SCF	F	Helminthosporium	SC	500 g/L	Tractor mounted spray	BBCH 30-59	2	14 days	112,5-400	150-400	450-600	42	A

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** Use also code numbers according to Annex I of Regulation (EU) No 396/2005

*** 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

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 SAP50SCF is composed of folpet.

Table 7.1-2 Toxicological reference values for the dietary risk assessment of folpet

Reference value	Source	Year	Value	Study relied upon	Safety factor
folpet - Parent compound					
ADI	Dir 07/05	2009	0.1 mg/kg bw/days	1 year dog study supported by the 2 year rat study	100
ARfD	Dir 07/05	2009	0.2 mg/kg bw/day	teratogenicity study in rabbits	100

7.1.2.1 Summary for folpet

Table 7.1-3 Summary for folpet

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	Wheat	Yes	Yes (8)	Yes	Yes	Yes	No	No
2	Barley	Yes	Yes (8)	Yes	Yes	Yes		No

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

New information regarding the nature of the residue in plants and animals has not been provided. Available information from the DAR and RAR has been considered enough to support the proposed use in cereals.

New residue studies are provided for wheat and barley according with the proposed use. Residues of folpet and phthalimide are quantified in all samples. Data package provided is considered to be enough to cover the proposed use in cereals.

Nature of the residues in rotational crops does not need to be investigated due to its low persistence in soil (<100 days). Residue data in succeeding crops are not required.

One study already assessed in RAR – that has also been summarized here for the sake of completeness – addresses the nature of residues in processed commodities. Processing studies in wheat are not required since the residues are in all trials below 0.1 mg/kg and its impact in diet is below 10% of ADI and ARfD. Regarding barley, new processing studies have been submitted.

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.

Regarding other studies, residues in honey should not be required until the renewal of the active substance take place. Indeed, AIR peer review under new data requirements is still ongoing at the time of this submission. Therefore, currently the old data requirements still apply and residues in honey do not need to be addressed at this stage.

Consumer risk assessment has been assessed, with no chronic risk as well as no acute risk to be expected. TDMI accounts for 59% of ADI and IESTI ranges from 3% of ARfD in wheat to 6% of ARfD in barley.

7.1.2.3 Summary for SAP50SCF

Table 7.1-4 Information on SAP50SCF (KCA 6.8)

Crop	PHI for SAP50SCF proposed by applicant	PHI/ Withholding period* sufficiently supported for	PHI for SAP50SCF proposed by zRMS	zRMS Comments (if different PHI proposed)
		Folpet		
Wheat	42	Yes	42	-
Barley	42	Yes	42	-

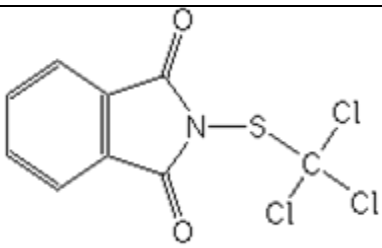
NR: not relevant

* Purpose of withholding period to be specified

7.2 Folpet

General data on folpet are summarized in the table below (last updated 20/09/2022)

Table 7.2-1 General information on folpet

Active substance (ISO Common Name)	Folpet
IUPAC	N-(trichloromethylthio)phthalimide
Chemical structure	
Molecular formula	C ₉ H ₄ Cl ₃ NO ₂ S
Molar mass	296.6 g/mol
Chemical group	Phthalimides fungicides such as captan or captafol
Mode of action (if available)	It inhibits many oxidative enzymes, carboxylases and enzymes involved with phosphate metabolism and citrate synthesis
Systemic	No Yes
Company (ies)	Makhteshim Agan International (MKA)*
Rapporteur Member State (RMS)	Austria (former RMS: Italy)
Approval status	Approved 01/10/2007 (2007/5/EC) ¹
Restriction	Use restricted as fungicide.
Review Report	SANCO/10032/2006 – rev. 5 11/07/2008
Current MRL regulation	Reg. (EU) 2023/1042
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, 2009)
EFSA Journal: conclusion on article 12	Yes (EFSA, 2014)
Current MRL applications on intended uses	No

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

The stability of residues for Folpet was already addressed during the EU Review process. New stability studies have been submitted by the applicant in the framework of this application. Due to some difficulties found during the development of the method of analysis, the stability studies could not be started in its due time and are still ongoing at the time of submission of this dossier. The studies will be provided once finished and results summarized in **Table 7.2-2** below will be updated. Interim reports for 1 year storage in wheat and barley grain and straw are provided; this on year time interval covers the storage that has taken place in residue trials, proving stability of residues up to one year. The study will be continued

¹ OJ L 35, 8.2.2007, p. 11–17

to prove stability for longer intervals, as well as for additional folpet metabolites, not relevant for this dossier. So this interim is equivalent to a final report, as far as the current dossier is considered. The detailed as-sessment of these studies is presented in Appendix 2.

Table 7.2-2 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 (only Folpet)			
Plant products			
Grapes	High acid content	>12 months	Italy, 2005
Grapes juice	High acid content	1 month	Italy, 2005
Cereal (grain and straw)	Dry commodities	>12 months	Italy, 2005
Tomato (whole fruit)	High water content	3 months	Italy, 2005
Tomato (pure and paste)	High acid content	1 month	Italy, 2005
New data (Folpet and phthalimide)			
Plant products			
Wheat (grain)	High starch content	340 days (interim) 18 months (ongoing)	Gordo, J. 2024. Report n° EST06/22.
Barley (grain)	High starch content	340 days (interim) 19 months (ongoing)	Gordo, J. 2024. Report n° EST06/22.
Wheat (straw)	Other commodities	362 days (interim) 18 months (ongoing)	Joos, S. 2024. Report n° S22-07592
Barley (straw)	Other commodities	362 days (interim) 19 months (ongoing)	Joos, S. 2024. Report n° S22-07592
Wheat (whole plant)	High water content	362 days (interim) 20 months (ongoing)	Joos, S. 2024. Report n° S22-07592
Barley (whole plant)	High water content	362 days (interim) 19 months (ongoing)	Joos, S. 2024. Report n° S22-07592
Beer	High water content	6 months	Joos, S. 2024. Report n° S22-07592

Conclusion on stability of residues during storage

The stability of residues for the active substance folpet was already addressed during the EU Review process. It has been proved that folpet is stable on cereal grain and straw for more than one year. In the magnitude studies, wheat and barley grain and straw underwent a maximum storage interval of 340 days and are thus partially covered by the available stability data. Furthermore, new data are provided to cover the stability of both folpet and phthalimide in cereal matrices (whole plant, grain and straw) and processed products (beer). The study was ongoing at the moment of the initial submission and the report covering 12 months interval for cereal matrices and 6 months interval for beer is provided here. No further data is required.

zRMS comments:

Cereal grain is considered as a high starch content commodity, whole plant of cereals is high water content commodity and straw is other commodity according to the OECD 506.

The stability of residues for the active substance folpet were reviewed at the EU level.

According to the EFSA Scientific Report (2009) 297, 54-80 – “Conclusion on the peer review of folpet”:

Storage stability data were presented for grapes, grain and straw, whole tomato, tomato pure and paste, grape juice. Folpet is stable in grapes, grain and straw for periods longer than 1 year.

No data are available for phthalimide.

In summary, according to the unprotected data, the active substance folpet was shown to be stable under frozen storage for 12 months in cereal grains and straw, but storage stability data of phthalimide are not available.

Two new studies on storage stability data of folpet and phthalimide (Gordo, J. 2024, Report n° EST06/22 and Joos, S. 2024, Report n° S22-07592) are provided. The studies are ongoing at the moment of initial zRMS assessment. On May 2024 interim reports have been provided by Applicant. Residues of folpet and phthalimide are stable at –

18°C when stored for up to 11-12 months in high starch content commodities (wheat and barley grain) and in high water content commodities (whole plant of cereals), in other commodities (straw) and for 6 months in beer. Since the maximum storage period of cereals samples in the magnitude studies was 350 days, it appears that the new storage stability data cover this time.

For folpet and phthalimide in beer, the maximum storage intervals from sampling until extraction were 140 days and new storage stability data cover this time.

These data are sufficient to support the residue trials on cereals.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

In some trial studies, timing between sample extraction and analysis overpassed 24 hours. However, in all studies, recovery experiments were performed concurrently with the analysed samples. The recovery rates for the studies presented in this dossier were acceptable, meaning that residues were stable in the sample extracts.

Available data

No further data is required.

Conclusion on stability of residues in sample extracts

Extracts of residue samples of folpet in cereals were shown to be stable for at least 7 days for wheat and 12 days for barley.

zRMS comments:

Procedural recoveries obtained during residue analysis demonstrate the stability of residues of folpet in sample extracts. No additional study is required.

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

Studies on metabolism of folpet in plants were already addressed during the EU Review process and were considered acceptable. Uptake, translocation and metabolism of folpet were evaluated in in DAR on folpet (Italy, 2005), Volume 3, B7. Information on crops tested, application and sampling details are given in **Table 7.2-3** below.

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 [kg a.s./ha]	No	Sampling (DAT)	Remarks	
EU data								
Fruits and fruiting vegetable	Grapes	U-phenyl	Foliar treatment, F	1.5	3	23	-	Italy, 2005
	Avocados		Foliar treatment, F	3.36	3	21, 97	-	
	Tomatoes	Carbonyl	Soil treatment, G	0.1 mg/plants	1	1, 4, 7, 11	-	EFSA, 2009
Root and tuber vegetables	Potatoes	U-phenyl	Foliar treatment	2	5	1 (after 1 st , 2 nd and 3 rd application) 3, 5 D (after last application)	-	Italy, 2005
Cereals	Winter wheat	U-phenyl	Foliar treatment	1.6	2	1, at BBCH 83, at harvest	-	Italy, 2005

Summary of plant metabolism studies reported in the EU

The metabolism of folpet in plants was investigated on winter wheat, grapes and avocados under similar modes of application. The metabolism of folpet was similar in the investigated crops. In addition, studies on tomatoes and potatoes were also submitted giving information on the nature of residues translocated from roots to foliar parts and from leaves to tubers.

In wheat samples taken at normal harvest, the highest residue levels were identified in both grain and straw (23 and 15 mg eq/kg, respectively). Folpet (35.8 % TRR) and its metabolites phthalimide² (31.6 % TRR) and phthalic acid (11.2 % TRR) were the major compounds in grain. The situation was similar in straw. Metabolism studies in grapes and avocados showed that folpet residues easily go through fruit peel. In these crops, parent compound was further degraded, accounting for only 0.5 to 12.8 % of the TRR in mature fruits. The main identified metabolites were phthalic acid (81.9 % TRR in avocado) and its conjugate (41.4 % TRR in grape), both resulting from phthalimide hydrolysis. Phthalimide only accounted for 0.86 to 3.9 % of the TRR in fruits. Other metabolites were found in very small amounts.

Metabolism studies in tomatoes and potatoes gave information on the nature of residues translocated from roots to foliar parts and from leaves to tubers. Residues were rapidly absorbed from the nutrient solution by tomato roots and translocated to tops. However, translocation from foliar parts to roots is limited. In these conditions, phthalic acid and phthalamic acid³ were the most important components of the residues. About 63 to 80 % of the TRR were due to these compounds in tomatoes and potatoes. Very low levels of parent compound (<0.1 % TRR) indicate that folpet does not translocate from fruits to tubers nor from roots to tops. Phthalimide accounted for 0.5 % of the TRR in potato tubers and up to 5.9 % TRR in tomatoes. Unknown metabolites were also present at 2.9 to 14.1 % of the TRR. These were tentatively identified as phthalamic acid derivative.

The metabolism of folpet is similar in the investigated crops. The parent compound is first degraded to phthalimide through release of the trichloromethylthioside chain. The thiophosgene produced through this cleavage is assumed to be rapidly transformed into CO₂ and incorporated in natural plant components, as demonstrated with metabolism studies on captan. Phthalimide is further hydrolysed to phthalamic acid, phthalic acid and related conjugates (EFSA, 2009). Phthalic acid and phthalamic acid are of no particular concern. Furthermore, phthalic acid and phthalamic acid can naturally occur in the environment and they cannot be considered as specific to folpet. Therefore, both phthalic acid and phthalamic acid should not be taken into account in the residue definition.

The toxicological relevance of phthalimide has been extensively discussed during the peer-review under Council Directive 91/414/EEC and additional toxicological data were assessed following the inclusion of Folpet (Italy, 2008). Based on these studies, it was agreed by experts that phthalimide is less toxic than

² 1H-isindole-1,3(2H)-dione,

³ 2-carbamoylbenzoic acid

folpet. However, a complete toxicological assessment of this metabolite was not available and no toxicological endpoints could be derived. In the absence of such data, the toxicological endpoints of folpet were used for phthalimide.

Summary of new plant metabolism studies

No additional metabolism studies are required for this dossier as the monograph data covers uses on cereals.

Conclusion on metabolism in primary crops

Folpet is extensively degraded in all crops, especially in fruits and potatoes. EFSA (2009) concludes that the residue for enforcement and risk assessment purpose in all plant commodities can be defined as folpet and phthalimide. Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and/or degradation products and the capabilities of enforcement analytical methods, the residue definitions for risk assessment and enforcement as proposed in the framework of the peer review (EFSA, 2009) were: sum of folpet and phthalimide, expressed as folpet.

zRMS comments:

The metabolism of folpet in primary crops following foliar application in crops belonging to the groups of fruit crops (grapes, avocados, tomatoes), root crops (potatoes) and cereals/grass (wheat) has been investigated in the framework of the EU pesticides peer review and the MRL review (EFSA, 2009, 2014).

Folpet was extensively metabolised in all tested crops, especially in fruits and potatoes, to phthalimide, phthalamic acid and phthalic acid (EFSA, 2021).

Residue definitions:

The residue definitions for risk assessment and enforcement as proposed in the framework of the peer review (EFSA, 2009) were sum of folpet and phthalimide, expressed as folpet.

The residue definition for enforcement in plant commodities set in Regulation (EC) No 396/2005 (Reg. (EU) 2023/1042) is identical with the above mentioned residue definition.

For the intended uses on barley and wheat the metabolic behaviour in primary crops is sufficiently addressed. No additional study is required.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

EFSA Journal 2021;19(5):6578

The crops under consideration may be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review, the DT_{90} values for folpet, phthalimide and the soil metabolites phthalic acid and phthalamic acid are expected to range between 1 and 94 days (under laboratory conditions) which are below the trigger value of 100 days.

Additionally, the half-lives of folpet and phthalimide are < 3 days under field conditions (EFSA, 2009, 2014). According to the European guidelines on rotational crops (OECD, 2018), further investigation of residues in rotational crops is not required and relevant residues in rotational crops are not expected.

No new data submitted in the framework of this application.

Conclusion on metabolism in rotational crops

No data on the nature of residues in rotational crops is required for the intended use.

zRMS comments:

Data presented by Applicant in point 7.2.2.2 are sufficient. No additional study is required.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Residue levels of 0.01 mg/kg or higher may occur in barley and wheat grains which may be processed. Therefore, data on the nature of the residue in processed commodities is discussed below.

Available data

One new hydrolysis study available from RAR has been evaluated and accepted by EFSA in the frame of folpet renewal and is presented here. This study is summarized in **Table 7.2-4** below. The detailed results of this study are presented in Appendix 2 for the sake of completeness, as they have been already evaluated at EU level, under the framework of folpet renewal.

Table 7.2-4 Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) [%]	Reference
EU data		
Pasteurisation (20 min, 90°C, pH 4)	Phthalimide (97.8 %) Phthalamic acid (0.4%) Phthalic acid (1.0 %) Unidentified 3 (0.5%)	EFSA, 2023 M Fitzmaurice and E Mackenzie, 2007, report No OZ/07/007*
Baking, boiling, brewing (60 min, 100°C, pH 5)	Phthalimide (56.1 %) Phthalamic acid (2.8%) Phthalic acid (40.7 %)	
Sterilisation (20 min, 120°C, pH 6)	Phthalimide (6.0 %) Phthalamic acid (32.8%) Phthalic acid (44.9 %) 2-Cyanobenzoic acid (11%) Unidentified 1 (4.5%)	

* Selectis Produtos para a Agricultura, S.A. has LoA from ASCENZA AGRO

Conclusion on nature of residues in processed commodities

Based on the available data it can be concluded that folpet is rapidly hydrolyzed into phthalimide, phthalamic acid and phthalic acid under standard hydrolysis conditions.

zRMS comments:

EFSA (2014) concluded that *In the framework of the peer review, only studies conducted at room temperature were available to investigate the effect of processing on the nature of folpet. Although these studies indicate the transformation of folpet into phthalimide and phthalic acid, they were not deemed sufficient to conclude on the nature of the residue in processed commodities (EFSA, 2009). In the framework of an MRL application, studies simulating representative hydrolytic conditions for pasteurisation (20 minutes at 90°C, pH 4), boiling/brewing/baking (60 minutes at 100°C, pH 5) and sterilisation (20 minutes at 120°C, pH 6) were provided and evaluated (EFSA, 2011a). The results of the studies indicated that folpet is completely degraded during processing; phthalimide is formed predominantly under conditions of pasteurisation (92 % TRR) while levels of phthalic acid increase under conditions simulating boiling/brewing/baking (42.2 % TRR) and sterilisation (91.4 % TRR). After processing, the main residues are therefore composed of metabolites already identified in the plant metabolism study where phthalimide was found to be the only metabolite of toxicological relevance (see also section 3.1.1.1). Consequently, as for the primary crops, the relevant residue for enforcement and risk assessment in processed commodities is defined as the sum of folpet and phthalimide, expressed as folpet.*

The hydrolysis studies demonstrate that folpet is completely degraded during processing; phthalimide is formed predominantly under conditions of pasteurisation, while levels of phthalic acid increase under conditions simulating boiling/brewing/baking and sterilisation. Considering that phthalimide was the only compound of toxicological relevance, the relevant residue for enforcement and risk assessment in processed commodities was also defined as the sum of folpet and phthalimide, expressed as folpet.

Residue definition:

The residue definition for processed products as proposed in the framework of the peer review (EFSA, 2009) is sum of folpet and phthalimide, expressed as folpet.

One study on the nature of residues in processed commodities is provided. The results showed that folpet is rapidly hydrolyzed into phthalimide, phthalamic acid and phthalic acid under standard hydrolysis conditions. This study also provided for the renewal process of folpet has been assessed in RAR and accepted by EFSA in folpet peer review (2023).

AIR peer review is still ongoing at the time of this submission. Therefore, currently the old endpoints still apply and the results of M Fitzmaurice and E Mackenzie study (2007, report No OZ/07/007) and the possibly new residue definition for processed commodities do not need to be discussed at this stage.

No additional data are required.

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

Table 7.2-5 Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Fruits and fruiting vegetable (grapes, avocados, tomatoes), root and tuber vegetables (potatoes) and cereals (winter wheat)
Rotational crops covered	Not relevant
Metabolism in rotational crops similar to metabolism in primary crops?	Not relevant
Processed commodities	Folpet is rapidly hydrolyzed into phthalimide, phthalamic acid and phthalic acid under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Sum of folpet and phthalimide expressed as folpet (Reg. (EU) 2018/832 2023/1042)
Plant residue definition for risk assessment	Sum of folpet and phthalimide, expressed as folpet (EFSA, 2009, 2014)
Conversion factor from enforcement to RA	-

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

Available data

Studies on metabolism of folpet in livestock have been evaluated during the EU Review process and were considered acceptable. Metabolism studies in lactating goats have been assessed in the framework of the EU pesticides peer review and the EFSA MRL review (EFSA, 2009, 2014). The studies were performed for the parent only but were considered acceptable since folpet was extensively metabolised during the study to generate thiophosgene and phthalimide. Thiophosgene is further converted to thiazolidine and incorporated into natural products such as amino acids, sugars and fats whereas phthalimide is metabolised to phthalamic acid and phthalic acid. The latter one may dehydrate to phthalic anhydride, but this reaction is expected to be reversible and phthalic acid is likely to be formed again via hydrolysis in aqueous solutions. As a similar metabolic pathway was found in rodents, the findings in ruminants can be extrapolated to pigs (EFSA, 2014). A more recent study in poultry was submitted in the framework of the renewal (Austria, 2018).

Studies are summarised in **Table 7.2-6** below. Further data on the metabolism of folpet in livestock is therefore not required.

Table 7.2-6 Summary of animal metabolism studies

Table 7/2-6 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	Lactating goat	Benzene ring [U-phenyl- ¹⁴ C]folpet	1	14-24 mg/kg diet/day	6	Milk	twice daily	Italy, 2005 (DAR)
						Urine and faeces	daily	
						Tissues	at sacrifice	
		[trichloromethyl- ¹⁴ C]folpet	1	14-24 mg/kg diet/day	6	Milk	twice daily	
						Urine and faeces	daily	
						Tissues	at sacrifice	
Poultry	Laying hens	[U-phenyl- ¹⁴ C] folpet	10 per groups	0.020 mg/kg bw/d (0.31 mg/kg feed) Or 0.63 mg/kg bw/d (10 mg/kg feed)	7	Eggs	Twice daily	Austria 2018 (RAR)
						Excreta	Twice daily	
						Tissues	at sacrifice	
New data								
No new data provided								

Summary of animal metabolism studies reported in the EU

In ruminants, the substance is extensively metabolised and excreted and was not found in any edible tissue. After oral administration for 6 days at dose rate of 14 mg/kg diet, residues in animal tissues were very low and no sign of accumulation is present. Only in liver and kidneys Total Radioactive Residues were above 0.01 mg eq folpet/kg (0.02 and 0.05 mg/kg respectively). The metabolism was found to be similar to that observed in rats with hydrolysis of the nitrogen-sulphur bond leading to thiophosgen and phthalimide which is further metabolised to phthalamic acid and phthalic acid.

In eggs and tissues, the total residues were less than 1% of the total radioactive residue (TRR). Apart from folpet (3.8% and 51% TRR in the low and high dose group respectively) the following metabolites were identified in the excreta for the low and high dose group respectively: phthalimide (4.9% and 5.4% TRR), phthalic acid (22.1% and 12.6% TRR), phthalamic acid (21.3% and 11.4% TRR) and phthalic anhydride (8.2% and 5.2% TRR). These results suggest a similar metabolic pathway between poultry and ruminants. Therefore, the residue definition derived for ruminants and pigs is also applicable for poultry commodities.

Summary of new animal metabolism studies

No new study provided and no further data required.

Conclusion on metabolism in livestock

Based on the studies in ruminants and poultry, the following residue definition was derived for enforcement and risk assessment in animal commodities except honey: phthalimide expressed as folpet. The residue is not fat soluble (EFSA, 2009, 2014, 2021).

Taking into account both the results of the metabolism study and dietary burden results no residue of folpet or phthalimide above the usual LOQ of method of analysis are expected.

zRMS comments:

The nature of folpet residues in commodities of animal origin was investigated in the framework of Directive 91/414/EEC (EFSA, 2009). Reported metabolism studies include two studies in lactating goats using U-¹⁴C-phenyl and ¹⁴C-trichloromethyl labelled folpet.

Residue definitions:

The residue for enforcement and risk assessment in commodities of ruminants and pigs was defined as phthalimide, expressed as folpet (EFSA, 2009).

In the framework of the peer review, the proposed residue was not considered to be fat soluble (EFSA, 2009).

A new metabolism study in poultry was provided and assessed in the framework of renewal of active substance (2018). The results suggest a similar metabolic pathway between poultry and ruminants. The overall picture of the animal metabolism studies, the current animal residue definition for enforcement and risk assessment is confirmed as phthalimide, expressed as folpet.

It should be noted that Selectis is not owner of new metabolism study in poultry and Selectis should submit a new study. However, taking into consideration art. 62 of Reg (EU) 1107/2009 ‘Member States shall not accept duplication of tests’, thus a new study should not be conducted to support the intended uses.

SELECTIS Reply:

ASCENZA are currently under negotiation with Adama Makhteshim Ltd, the data owner, for the co-ownership of the study [REDACTED] (2015) [REDACTED] (KCA 6.2.2/01), according with Article 62 of the Regulation 1107/2009. Article 62 also allows member States to use vertebrate studies for the purpose of the application of a prospective applicant who has not been able to reach agreement on sharing the data with the data owners. Evidence for the ongoing negotiations are shared within this reply.

Additionally, we would like to inform you that we are in a joint task force with Adama Makhteshim Ltd (data owner of the mentioned study), with the common purpose of the renewal of the active substance Folpet under AIR3 (we are both notifier of Folpet).

Therefore, it is expected from the applicant to submit a letter of access to the metabolism study on poultry.

October 2024: The applicant submitted a letter of access for folpet to the metabolism study on poultry.

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

Table 7.2-7 Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	4 days in milk
	3 days in egg white and 7 days in egg yolk
Animal residue definition for monitoring	Phthalimide expressed as folpet (SANTE/10334/2021 Reg. (EU) 2023/1042)
Animal residue definition for risk assessment	Phthalimide expressed as folpet (EFSA 2009, 2014)
Conversion factor	/
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	No

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 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 summarized in the Table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.2-8 Summary of new data supporting the intended uses of SAP50SCF and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels [mg/kg] E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR [mg/kg]	HR [mg/kg]	Unrounded OECD calculator MRL [mg/kg]	Current EU MRL [mg/kg] Reg. (EU) 2023/1042	MRL compliance
Wheat grain	New trials	N-EU	Trials GAP: 2 x 0.60 kg a.s. /ha, up to BBCH61, PHI 34-78 E=RA: 4x<0.03, 0.032, 0.044, 0.060, 0.087					
	Overall supporting data for cGAP	N-EU	E=RA: 4x<0.03, 0.032, 0.044, 0.060, 0.087	0.03	0.09	0.15	0.4	Yes
Wheat straw	New trials	N-EU	Trials GAP: 2 x 0.60 kg a.s. /ha, up to BBCH61, PHI 34-78 E=RA: 1.7, 2 x 1.8, 2 x 3.4, 3.9, 5.0, 7.6					
	Overall supporting data for cGAP	N-EU	E=RA: 1.7, 2 x 1.8, 2 x 3.4, 3.9, 5.0, 7.6	3.40	7.60	-		
Barley grain	New trials	N-EU	Trials GAP: 2 x 0.60 kg a.s. /ha, up to BBCH61, PHI 34-50 E=RA: <0.03, 0.047, 0.050, 0.072, 0.28, 0.29, 0.34, 0.75.					
	Overall supporting data for cGAP	N-EU	E=RA: <0.03, 0.047, 0.050, 0.072, 0.28, 0.29, 0.34, 0.75.	0.18	0.75	1.50	2	Yes
Barley straw	New trials	N-EU	Trials GAP: 2 x 0.60 kg a.s. /ha, up to BBCH61, PHI 34-50 E=RA: 2 x 1.70, 2.10, 2.70, 3.50, 3.90, 4.50, 8.50					

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels [mg/kg] E = according to enforcement residue definition RA = according to risk assessment residue definition	STM [mg/kg]	HR [mg/kg]	Unrounded OECD calculator MRL [mg/kg]	Current EU MRL [mg/kg] Reg. (EU) 2023/1042	MRL compliance
	Overall supporting data for cGAP	N-EU	E=RA: 2 x 1.70, 2.10, 2.70, 3.50, 3.90, 4.50, 8.50	3.10	8.5	-		

N/A: Not applicable

7.2.3.2 Conclusion on the magnitude of residues in plants

Wheat and barley are major crops in CEU countries and though require 8 NEU residue data in each crop, as the product is to be sprayed in the crop after the forming of the edible part. Those data have been provided.

According to the available data, the intended uses on wheat and barley are considered acceptable. The data show that no exceedance of the MRL will occur.

The uses are considered acceptable.

zRMS comments:

The proposed uses for SAP50SCF are wheat and barley.

Wheat and barley are the major crops in northern Europe. A minimum of eight trials representative of the proposed growing area are required (SANTE/2019/12752).

16 independent trials were conducted in Northern Europe according to the OECD Test No. 509 to gain the residue level of folpet and its two metabolites phthalimide and phthalic acid in wheat (8 trials) and barley (8 trials) specimens (whole plant, grain and straw) following two foliar applications of SAP50SCF, containing folpet as active ingredient (500 g a.s./L, equivalent to 600 g a.s./ha).

Trials GAP for wheat: 2 x 0.60 kg a.s. /ha with 12-21 days between application, up to BBCH 61, PHI 34-78.

Trials GAP for barley: 2 x 0.60 kg a.s. /ha with 12-21 days between application, up to BBCH 61, PHI 34-50.

The presented residue trials cover the intended uses.

The residues of folpet (sum of folpet and phthalimide expressed as folpet) in the wheat grain samples were $4 \times < 0.03$, 0.032, 0.044, 0.060, 0.087 mg/kg.

The residues of folpet (sum of folpet and phthalimide expressed as folpet) in the barley grain samples were < 0.03 , 0.047, 0.050, 0.072, 0.28, 0.29, 0.34, 0.75 mg/kg.

The value of EU MRL for folpet on wheat and barley equals 0.4 mg/kg and 2 mg/kg, respectively (Reg. (EU) 2023/1042). The residues arising from the proposed uses will not exceed the MRLs established for cereals.

The current EU MRLs for folpet are sufficient to support the proposed uses.

Additional studies are not required to support the proposed uses of SAP50SCF.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

The dietary burden calculation has been performed following the assessment recently performed by EFSA (EFSA, 2021). The input values used have been included below in the 2017 Animal Model, the most critical value between EFSA data and new data evaluated in this dossier has been selected.

Input values used are included in table 7.2-9 and results of the dietary burden calculation are shown in table 7.2-10.

Table 7.2-9 Input values for the dietary burden calculation (considering the uses evaluated by EFSA (2021) and 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: Sum of folpet and phthalimide, expressed as folpet				
Barley straw	3.10	STMR	8.50	HR
Oat straw	3.10	STMR	8.50	HR
Rye straw	3.40	STMR	9.10	HR (EFSA, 2014)
Triticale straw	3.40	STMR	9.10	HR (EFSA, 2014)
Wheat straw	3.40	STMR	9.10	HR (EFSA, 2014)
Potato culls	0.10	STMR (EFSA, 2014)	0.10	HR (EFSA, 2014)
Barley grain	0.18	STMR	-	-
Oat grain	0.18	STMR	-	-
Rye grain	0.12	STMR (EFSA, 2014)	-	-
Triticale grain	0.12	STMR (EFSA, 2014)	-	-
Wheat grain	0.12	STMR (EFSA, 2014)	-	-
Apple, wet pomace	0.3	STMR (EFSA, 2017)xPF(5) ^(a)	-	-
Brewers' grain	0.003	STMRxPF (0.016)	-	-
Distiller's grain	0.40	STMR (EFSA, 2014)xPF(3.3) ^(a)	-	-
Potato, process waste	2.00	STMR (EFSA, 2014)xPF(20) ^(a)	-	-
Potato, dried pulp	3.80	STMR (EFSA, 2014)XPF(38) ^(a)	-	-
Wheat gluten meal	0.22	STMRxPF(1.8) ^(a)	-	-
Wheat, milled by-products	0.84	STMRxPF(7.0) ^(a)	-	-

STMR: supervised trials median residue; HR: highest residue; PF: processing factor.

(a): In the absence of processing factors supported by data for distiller's grain, potato process waste, potato dried pulp, wheat gluten meal and wheat milled by-products, default processing factors (in bracket) were respectively included in the calculation to consider the potential concentration of residues in these commodities.

Table 7.2-10 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: Sum of folpet and phthalimide, expressed as folpet					
Cattle (all diets)	0,239	0,309	Potato, process waste	9,68	Y
Cattle (dairy only)	0,239	0,309	Potato, process waste	8,04	Y
Sheep (all diets)	0,292	0,413	Potato, process waste	12,40	Y
Sheep (ewe only)	0,292	0,413	Potato, process waste	12,40	Y
Swine (all diets)	0,084	0,084	Potato, process waste	3,64	Y
Poultry (all diets)	0,083	0,128	Wheat, straw	1,86	Y
Poultry (layer only)	0,083	0,128	Wheat, straw	1,86	Y

* These categories correspond to those (formerly) assessed at EU level.

zRMS comments:

Wheat and barley are used for livestock feed purposes.

The previous dietary burden calculation (EFSA, 2021) to estimate whether the intended use of folpet would have an impact on the residues expected in food of animal origin has been updated.

The calculated dietary burdens for all groups of livestock were found to exceed the trigger value of 0.004 mg/kg bw/day. Further investigation of folpet residues is therefore required in all commodities of animal origin.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

The calculated dietary burdens for poultry and ruminants exceed the trigger value of 0.10 mg/kg bw/day. Thus, the results of the metabolism studies were used for further considerations.

According to poultry metabolism study, no residues above the LOQ are expected in any tissues or in eggs. Indeed, at the dose of 10 mg/kg feed for folpet tested in the metabolism study in poultry, being the closest one to the maximum dietary burden for poultry, the estimated total residues are far below the LOQ (0.01 mg/kg). Therefore no feeding studies in poultry are required.

According to the metabolism study in ruminants no residues above LOQ are expected in tissues or milk. The rate tested in the metabolism study in lactating ruminants covers the dietary intake for dairy and meat ruminants calculated above. Following an administration of 24 mg trichloromethyl-¹⁴C-folpet/ kg diet (equivalent to 0.367 mg/kg bw/day) residues of 0.181 mg folpet eq./kg (milk, plateau concentration), 0.25 mg folpet eq./kg (liver) and 0.16 mg folpet eq./kg (kidney) were found. Following an administration of 13.6 mg benzene-¹⁴C-folpet/ kg diet (equivalent to 0.344 mg/kg bw/day) residues of 0.006 mg folpet eq./kg (milk, plateau concentration), 0.022 mg folpet eq./kg (liver) and 0.055 mg folpet eq./kg (kidney) were found. Based on dietary burden results, residue levels are not expected to occur in ruminant matrices at levels above the LOQ of 0.05 mg/kg. Therefore no feeding studies in lactating ruminants are required.

This same conclusion has been reached by EFSA on the frame of Folpet conclusion of peer review (2023): *“The dietary burden calculation, indicates already an exceedance of the dietary burden trigger value for both, ruminants and poultry. Based on the results of the metabolism studies and the preliminary dietary burden calculation, residues are not expected in poultry and ruminant commodities.”*

MRL calculations	Ruminant				Pig/Swine		Poultry		Fish	
Highest expected intake (mg/kg bw/d) (mg/kg DM for fish)	Beef cattle	0.164	Ram/Ewe	0.444	Breeding	0.009	Broiler	0.019	Carp	0.208
	Dairy cattle	0.261	Lamb	0.566	Finishing	0.011	Layer	0.097	Trout	0.118
							Turkey	0.016	Fish intake >0.1 mg/kg DM	
Intake >0.004 mg/kg bw	Yes		Yes		Yes		Yes		Yes	
Feeding study submitted	No		No		No		No		No	
	Feeding study covered by available metabolism studies. No residues above 0.01 mg/kg in milk and any edible tissue are expected. No feeding studies required.						Feeding study covered by available metabolism studies. No residues above 0.01 mg/kg in milk and any edible tissue are expected. No feeding studies required.		The uptake of folpet and phthalimide residues by fish is considered to be negligible due to the low bioconcentration and bioaccumulation potential of folpet and its metabolites and the fast depuration of folpet residues by fish. No study required	
Representative feeding level (mg/kg bw/d, mg/kg DM for fish) and N rates	Level	Beef: N Dairy: N	Level	Lamb: N Ewe: N	Level	N rate Breed/Finish	Level	B or T: N Layer: N	Level	N rate Carp/Trout
	Estimated HR ^(a) at 1N	MRL proposals	Estimated HR ^(a) at 1N	MRL proposals	Estimated HR ^(a) at 1N	MRL proposals	Estimated HR ^(a) at 1N	MRL proposals	Estimated HR ^(a) at 1N	MRL proposals
Muscle										
Fat										
Meat ^(b)										
Liver										
Kidney										
Milk ^(a)										
Eggs										
Method of calculation ^(c)										

(a): Estimated HR calculated at 1N level (estimated mean level for milk).

STMR calculations	Ruminant				Pig/Swine		Poultry		Fish	
Median expected intake (mg/kg bw/d) (mg/kg DM for fish)	Beef cattle	0.023	Ram/Ewe	0.051	Breeding	0.009	Broiler	0.019	Carp	
	Dairy cattle	0.035	Lamb	0.065	Finishing	0.011	Layer	0.033	Trout	
							Turkey	0.016		
Representative feeding level (mg/kg bw/d, mg/kg DM for fish) and N rates	Level	Beef: N Dairy: N	Level	Lamb: N Ewe: N	Level	N rate Breed/Finish	Level	B or T: N Layer: N	Level	N rate Carp/Trout
	Mean level in feeding level	Estimated STMR ^(b) at 1N	Mean level in feeding level	Estimated STMR ^(b) at 1N	Mean level in feeding level	Estimated STMR ^(b) at 1N	Mean level in feeding level	Estimated STMR ^(b) at 1N	Mean level in feeding level	Estimated STMR ^(b) at 1N
Muscle										
Fat										
Meat ^(a)										
Liver										
Kidney										
Milk										
Eggs										
Method of calculation ^(c)										

(a): STMR in meat calculated for mammalian on the basis of 20% fat + 80% muscle and 10% fat + 90% muscle for poultry

(b): When the mean level is set at the LOQ, the STMR is set at the LOQ.

(c): The OECD guidance document on residues in livestock (series on pesticide 73) recommends three different approaches to derive MRLs for animal products; by applying a transfer factor (Tf), by interpolation (It) or by linear regression (Ln). Fill in method(s) considered to derive the MRL proposals.

Conclusion on feeding studies

No feeding studies are required. The requested uses do not modify the theoretical maximum daily intake for animals, there is no risk for animal MRL to be exceeded.

zRMS comments:

It should be noted that Selectis is not owner of new metabolism study in poultry and no data are available to demonstrate that values of MRL in poultry commodities would not be exceeded.

A new metabolism study in poultry was provided and assessed in the framework of renewal of active substance (2018) (see zRMS comments in point 7.2.2.5). Ascenza are currently under negotiation with Adama Makhteshim Ltd, the data owner.

Pending the submission of the letter of access to the study it can be concluded that 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.

October 2024: The applicant submitted a letter of access for folpet to the metabolism study on poultry. The above conclusions are still valid.

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

New studies were also submitted by the applicant.

7.2.5.1 Available data for all crops under consideration

A total of 6 residue trials (3 in wheat and 3 in barley) for processing were initially set during 2021 to determine the processing factors for both folpet and phthalimide. However, from these 6 trials only samples from 2 trials on barley could be processed and analysed. The samples of the rest of the trials were lost since samples were thawed during the processing phase.

Actually, for wheat, as the residue are all below 0.1 mg/kg and the ADI and ARfD are below 10%, processing studies are not required to support wheat in the present dossier. In consequence, no additional processing trials have been undertaken.

For barley, new processing studies have been submitted by the applicant in the framework of this application. As the processing factor (PF) in the two processing barley studies does not differ more than 50%, according to OECD guideline OECD 508 “*Magnitude of the Pesticide Residues in Processed Commodities*”, no additional trials on barley processing are required. These studies are summarized in **Table 7.2-11** below. The detailed results are presented in Appendix 2.

Table 7.2-11 Overview of the available processing studies

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
New data					
Sum of folpet and phthalimide, expressed as folpet					
Barley, brewing malt	2	0.028	-	-	KCA 6.5.3/01
Barley, malt sprout	2	0.125	-	-	
Barley, dried brewer's grain	2	0.016	-	-	
Barley, brewing yeast	2	<0.03	-	-	
Barley, beer	2	<0.03	-	-	

* 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.

7.2.5.2 Conclusion on processing studies

Processing studies are available for the following intended crop: ~~wheat and~~ barley. For wheat, no processing studies are required in the present dossier, due to residue levels and impact on diet. For barley, robust processing factors were obtained for processing to beer as given in **Table 7.2-11** above, with PF differing less than 50% in the 2 studies performed. No more data is required.

zRMS comments:

Processing studies are normally necessary if the residue level > 0.1 mg/kg in RAC or if the total theoretical maximum daily intake (TMDI) is higher than 10% of the ADI. For wheat HR value equals 0.087 mg/kg, so processing studies for wheat are not needed.

New two studies on processing barley have been provided. As the processing factor (PF) in the two processing barley studies does not differ more than 50%, according to the OECD guideline OECD 508 “*Magnitude of the Pesticide Residues in Processed Commodities*”, no additional trials on barley processing are required. The studies are considered acceptable. More details are in Appendix 2.

No additional data required.

7.2.6 Magnitude of residues in representative succeeding crops

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The crops under consideration may be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review, the DT₉₀ values for folpet, phthalimide and the soil metabolites phthalic acid and phthalamide are expected to range between 1 and 94 days (under laboratory conditions) which are below the trigger value of 100 days.

Additionally, the half-lives of folpet and phthalimide are < 3 days under field conditions (EFSA, 2009, 2014). According to the European guidelines on rotational crops (European Commission, 1997c), further investigation of residues in rotational crops is not required and relevant residues in rotational crops are not expected.

No new data submitted in the framework of this application.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

No data submitted and no further data required.

zRMS comments:

Data presented by Applicant in point 7.2.6 are sufficient.
No additional study is required.

7.2.7 Other / special studies (KCA 6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of SAP50SCF. Therefore, other special studies are not needed.

Specifically, residues in honey should not be required until the renewal of the active substance take place. Indeed, AIR peer review under new data requirements is still ongoing at the time of this submission. Therefore, currently the old data requirements still apply and residues in honey do not need to be addressed at this stage.

zRMS comments:

According to SANTE/11956/2016 rev. 9, 14 September 2018 wheat and barley are not considered melliferous crops. Therefore, residues in honey are not expected from the use of SAP50SCF under consideration. No additional data are required.

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 Point 7.1.2).

7.2.8.1 Input values for the consumer risk assessment

The consumer risk assessment has been done using MRLs as currently in force in Regulation (EU) No ~~2922/93~~ 2023/1042. The Excel sheet EFSA PRIMo rev 3.1 has been used to do the calculations.

Table 7.2-12 Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value [mg/kg]	Comment	Input value [mg/kg]	Comment
Sum of folpet and phthalimide expressed as folpet				
All commodities	MRL	Regulation (EU) No 2023/1042	MRL	Regulation (EU) No 2023/1042

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.2-13 Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	59% (based on PT General)
IEDI (% ADI) according to EFSA PRIMo	Not required.
IESTI (% ARfD) according to EFSA PRIMo*	Highest IESTI Unprocessed: Barley: 6% Highest IESTI Processed: Barley / cooked 4%
NTMDI (% ADI) **	Not required
NEDI (% ADI)**	Not required
NESTI (% ARfD) **	Not required

* include raw and processed commodities if both values are required for PRIMo.

** if national model is available

The proposed uses of folpet the formulation SAP50SCF do not represent unacceptable acute and chronic risks for the consumer.

zRMS comments:

A consumer risk assessment was performed with revision 3.1 of EFSA Pesticide Residues Intake Model (PRIMo Rev. 3.1). The Reg. (EU) 2023/1042 for folpet is now in force.

The highest Theoretical Maximum Daily Intake (TMDI) is 59% of the ADI for the PT General. The highest contribution (50% of the ADI) is from wine grapes.

The highest International Estimated Short-Term Intake (IESTI) is at 6% and 5% of the ARfD for the consumption of barley by children and by adults respectively and for processed commodities at 4% of the ARfD from the consumption of barley/cooked for children and 0.9% of the ARfD from the consumption of wheat/bread/pizza for adults.

The proposed uses of folpet in the product SAP50SCF do not represent unacceptable acute and chronic risks for the consumer.

7.5 References

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EFSA (European Food Safety Authority), 2012b. Reasoned opinion on the modification of the existing MRL(s) for folpet in wine grapes. 12 June 2012. EFSA Journal 2012;10(6):2769.

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EFSA (European Food Safety Authority), Anastassiadou M, Bellisai G, Bernasconi G, Brancato A, Carrasco Cabrera L, Ferreira L, Greco L, Jarrah S, Kazocina A, Leuschner R, Magrans JO, Miron I, Nave S, Pedersen R, Reich H, Santos M, Scarlato AP, Theobald A, Vagenende B and Verani A, 2021. Reasoned Opinion on the modification of the existing maximum residue levels for folpet in barley, oat, rye and wheat. EFSA Journal 2021; 19(5):6578, 31 pp. <https://doi.org/10.2903/j.efsa.2021.6578>

EFSA (European Food Safety Authority), 2023. Peer review of the pesticide risk assessment of the active substance folpet. EFSA Journal 2023;21(8):8139. <https://doi.org/10.2903/j.efsa.2023.8139>

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Italy, 2008. Addendum to the draft assessment report on the active substance folpet prepared by the rapporteur Member State Italy in the framework of Council Directive 91/414/EEC, March 2008. Available online: www.efsa.europa.eu

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OECD, 2018. Guidance document on residues in rotational crops. Series on pesticides No 97 and Series on testing and assessment No 278.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7.2.1/01	J. Gordo	2024	Stability Study of Folpet and Metabolites in Cereals Stored Under Deep Freezing Conditions Laboratorio Residuos de Pesticidas Ascenza Agro SA. Report n° EST06/22 (study ongoing). Interim report for 12 months storage time. GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.1/02	S. Jooss	2024	Storage Stability of Folpet and its Metabolites in Various Matrices under Deep Frozen Conditions Eurofins Agroscience Services. Report N°: S22-07592 (study ongoing). Interim report for 12 months storage time. GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.3/01 (field phase)	A.S. Lesbazeilles Beauvalon	2022	Magnitude of the residue of folpet in representative winter wheat Raw Agricultural Commodities after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern Europe- 2021 SGS Report n° 21-00160 GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.3/02 (analytical phase)	S. Jooss	2022	Study on the residue behaviour of folpet and its metabolites in wither wheat after two applications of SAP50SCF (Folpet 500 g/l, SC) in Northern Europe – 2021. Eurofins Agroscience Services Report No: S22-03719 GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.3/03 (field phase)	A.S. Lesbazeilles Beauvalon	2022	Magnitude of the residue of folpet in representative barley Raw Agricultural Commodities after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern Europe SGS Report n° 21-00139 GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.3/04 (analytical phase)	S. Jooss	2022	Study on the residue behaviour of folpet and tis metabolites in barley after two applications of SAP50SCF (Folpet 500 g/l, SC) in Northern Europe – 2021 Eurofins Agroscience Services Report No: S22-01157 GLP Unpublished	N	ASCENZA AGRO
KCP 7.2.5/01 (processing phase)	C. Milhan	2022	Magnitude of the residue of folpet in processed fractions of barley after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern and Southern Europe Staphyt Report n° CMN-21-48321 GLP Unpublished	N	ASCENZA AGRO

KCP 7.2.5/02 (analytical phase)	S. Jooss	2022	Study on the residue behaviour of folpet and its metabolites in processed fractions of barley after one application of SAP50SCF (Folpet 500 g/l) in Northern Europe – 2021 Eurofins Agrosience Services Report No: S22-04739 GLP Unpublished	N	ASCENZA AGRO
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List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.1	Fuchsbichler, G	1995	Folpet, investigation of the storage stability in white and red grapes. Report n° HVA 12/94 Company file: R-8096 ADAMA Makhteshim Ltd., V20481, R-34718 GLP, unpublished	N	Makhteshim
KCA 6.1	Byast, M.G.	1997	Determination of freezer storage stability for folpet in wheat, grain and straw over a period of 12 months in compliance with good laboratory practice. Oxford Analytical Ltd., Report No.: OA00382. Company file: R-9156 GLP, Unpublished	N	Makhteshim
KCA 6.1	Singer, G.M.	-	Summary of storage stability studies of folpet on various raw agricultural commodities. American Agricultural Services, Inc., company file: R-9142 Not GLP, unpublished	N	Makhteshim
KCA 6.2.1	Crowe, A.	1995	Folpet: distribution and metabolism in winter wheat. Pharmaco LSR Ltd., Report No. 95/MAK204/0049 (company file: R-7823) GLP, unpublished	N	Makhteshim
KCA 6.2.1	O'Connor, J. Mester, T.C	1994	Folpet: nature of residue on grapes. Pharmaco LSR Ltd., Report No 93/WLS019/0962 GLP, unpublished Field report: Nature of the residue study LX1145-05[(14C)-folpet] on grapes in California. Landis International, Inc. report Protocol No.14503B004. (company file: R-6403a). GLP, Unpublished.	N	Makhteshim
KCA 6.2.1	Toia, R.F Collins, E.H	1994	Nature of residue (14C)-folpet (LX1145-05) in avocados applied under field conditions. PREL West Inc., Report No.417W-2. (Company file: R-7302) GLP, Unpublished	N	Makhteshim
KCA 6.2.1	Cheng, H.M.	1980	[Carbonyl-14C] folpet metabolism in tomato plants. Chevron Chemical Company, Report No.721.14 (Company file: R-7036) Not GLP, Unpublished	N	Makhteshim
KCA 6.2.1	Crowe, A.	1999	Folpet: metabolism in potatoes. Huntigdon Life Sciences Ltd., Report No. MAK506/992098 (Company file: R-10347). GLP, Unpublished	N	Makhteshim
KCA 6.2.2	██████	1997a	14C-folpet metabolism in the lactating goat (part A). 14C trichloromethyl folpet: material balance of dosed radioactivity. ██████ GLP, unpublished	Y	Makhteshim
KCA 6.2.2	██████	2015	Metabolism and disposition of [14C]Folpet in the Laying Hen ██████ GLP, unpublished	Y	ADM

KCA 6.3.1	Turner, M.G. Byast, M.G.	1996a	<p>Determination of folpet residues in winter wheat (field phase). Oxford Plant Sciences, Report No. OPS/00519/MAK</p> <p>Determination of folpet residues in winter wheat, grain and straw treated with Folpan 80 WDG. Oxford Analytical Ltd., Report No. OA00346/R52862.</p> <p>Determination of folpet residues in decline samples of winter wheat treated with Folpan 80 WDG. Oxford Analytical Ltd., Report No OA00345/R52862. Company file R8580</p> <p>GLP, unpublished</p>	N	Makhteshim
KCA 6.3.1	Turner, M.G., Byast, M.G.	1996b	<p>Determination of propiconazole, fenpropimorph, prochloraz and folpet residues in winter wheat and winter barley (field phase). Oxford Plant Sciences, Report No. OPS/00514/MAK.</p> <p>Determination of folpet in harvest samples of winter wheat, grain and straw treated with Folpan 80 WDG. Oxford Analytical Ltd., Report No. OA00341/R52855.</p> <p>Determination of folpet in decline samples of winter wheat treated with Folpan 80 WDG. Oxford Analytical Ltd., Report No. OA00344/R52855. Company file: R-8559 GLP, Unpublished</p>	N	Makhteshim
KCA6.3.1	Mellet, M.	1993	<p>Determination des résidus de folpel dans des échantillons de céréales après application du produit Folpan SC. Anadiag S.A. unpublished report No RF2095 GLP, unpublished</p>	N	Makhteshim
KCA6.3.1	Mellet, M	1994	<p>Determination des résidus de folpel et de phthalimide dans des échantillons de céréales après application des produits Folpan SC et Folpan WDG. Anadiag S.A. unpublished report No RF4019 GLP, unpublished</p>	N	Makhteshim
KCA6.3.1	Wasser, C.	1996	<p>Folpan SC. Magnitude of the residues in wheat. Anadiag S.A. unpublished report No. R5072 (Company file: R-8676a) GLP, unpublished</p>	N	Makhteshim
KCA6.3.1	Mende, P., Hautavoine, V.	1996b	<p>Residue analysis of folpet and prochloraz in wheat and barley treated with Bumper F from residue trials in France. Report n° 96025/F1-RFWC</p> <p>Residue study – field phase. Gaining of samples for the determination of residues of propiconazole and folpet after treatment with Bumper F in cereals under field conditions in France. Biotek Agriculture, Report BKA/618/96/RES Company file : R-9376</p> <p>GLP, unpublished</p>	N	Makhteshim
KCA 6.3.1	Perney, A.	2002	<p>Determination of folpet and phthalimide residues in winter wheat following treatments with the preparation Folpan 80 WDG under field conditions in France in 2001 Anadiag Reports RA1044 (company file R-13050) GLP, unpublished</p>	N	Makhteshim

KCA 6.5.1	M Fitzmaurice and E Mackenzie,	2007	[14C]-Folpet: Investigation of the Nature of the Potential Residue in the Products of Industrial Processing or Household Preparation Report n° OZ/07/007 GLP Unpublished	N	ASCENZA AGRO LoA
KCA 6.5.3	Perny, A	2002b	Determination of folpet and phthalimide residues in processed fractions (grain, flour, total bran, regrinding and bread) after treatment of winter wheat with the preparation Fopan 80 WDG under field conditions in France in 2001. Anadiag S.A., Report No RA1044 PRO (company file R-13053) GLP, Unpublished	N	Makhteshim

List of data relied on and not submitted by the applicant but necessary for evaluation

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
-	-	-	-	-	-

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Folpet

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

Comments of zRMS:	<p>The study is ongoing. The current interim report reflects the results for folpet and phthalimide obtained after 340 days of storage.</p> <p>The results of Gordo study demonstrate the stability of residues of folpet and phthalimide upon deep frozen storage at – 18 °C for up to 340 days months in wheat and barley grain.</p> <p>The performance of the analytical method was demonstrated by recovery tests injected concurrently with the samples. The results achieved fulfill with the criteria set on SANTE/2020/12830.</p> <p>The results of the interim report are acceptable.</p>
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Reference: KCP 7.2.1/01

Report Stability Study of Folpet and Metabolites in Cereals Stored Under Deep Freezing Conditions. Gordo, J. 2024. Laboratorio Resíduos de Pesticidas Ascenza Agro SA. Report nº EST06/22 (study ongoing) Interim report at 12 months.

Guideline(s): Yes.
 - OECD Series on Principles of GLP and Compliance Monitoring: Number 1, OECD Principles on Good Laboratory Practice (as revised in 1997) (ENV/MC/CHEM(98)17).
 - Decreto-Lei nº 99/2000 of 30 May 2000 (Portuguese decree on OECD Principles of GLP).

Deviations: TBC

GLP: Yes

Acceptability: Yes

Materials and methods

The objective of the current study is to evaluate the stability of:
 Folpet, Phthalimide and Phthalic acid residues in grains of wheat and barley under freezing storage conditions (≤ -18 °C) over a period of 18 months for wheat and 19 months for barley;
 This study will be conducted by spiking untreated samples at least ten times the limit of quantification of the method.

The analytical work will be performed using method that was validated under Laboratório de Resíduos de Pesticidas GLP study nº VAL22/21.

Internal samples will be available in order to perform the study. The absence of Folpet and metabolites residues will be checked prior to the quantification of the spiked samples.

Samples will be extracted following analytical method that was validated at Laboratório de Resíduos de Pesticidas under GLP study Nº VAL22/21 which follows the QuEChERS method.

The quantification will be done by a liquid chromatography coupled to tandem mass spectrometry.

The stability study will be as described below:

- Several aliquots from previous processed and homogenous samples will be stored in frozen conditions;
- Analytical portions will be stored at ≤ -18 °C until analysis;
- Samples will be spiked at ten times the limit of quantification of the analytical method;
- Three replicates of supplemented samples will be analysed at the same day of the fortification procedure (zero time), together with a control sample and a recovery test;
- Analytical portions supplemented will be analysed according to the storage described in the table below, at freezing conditions;
- Supplemented samples will be analysed in triplicate;
- In each instrumental analysis day, at least one spike will be done to run together with supplemented samples and one control sample;
- If necessary, dilutions will be done in order to quantify in the validated calibration range;
- Additional samples will be prepared in order to repeat or extend the storage timing if needed.

The storage stability of samples will be evaluated over the period described in the table below.

The analytical work could be distributed in several ways. The table below describes the experimental work design that will be followed.

Specimen	Series	Day of Supplementation and Storage	Planned Storage Period (months)
Wheat grain	S ₀	0	0
	S ₃₆₅	0	365
	S ₄₈₉	0	489
	S ₅₅₁	0	551
Barley grain	S ₀	0	0
	S ₃₆₅	0	365
	S ₅₂₀	0	520
	S ₅₈₂	0	582

In each analytical series a tolerance of 5 days will be allowed. As long as it leads to storage periods longer than the target time in each analytical series, bigger tolerances will be allowed without need of a formal deviation.

Results and discussions:

Table A 1: Summary of concurrent recoveries of folpet and phtalamide from wheat and barley grain

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)
Folpet				
Wheat grain	0.1	0	1	78.4

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)
	0.1	340	1	74.7
Barley grain	0.1	0	1	122.9
	0.1	340	1	84.3
Phtalamide				
Wheat grain	0.1	0	1	108.7
	0.1	340	1	88.8
Barley grain	0.1	0	1	125.8
	0.1	340	1	109.5

Table A 2: Stability of folpet and phtalamide residues in wheat and barley grain following storage at -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual (mean) recovered residues (mg/kg)	Individual recoveries (%)
Folpet				
Wheat grain	0.100	0	0.120 0.110 0.100 (0.110)	109.2
	0.100	340	0.120 0.110 0.110 (0.110)	111.8
Barley grain	0.100	0	0.074 0.093 0.096 (0.088)	87.8
	0.100	340	0.110 0.100 0.110 (0.110)	106.5
Phtalamide				
Wheat grain	0.100	0	0.088 0.100 0.099 (0.096)	95.5
	0.100	340	0.100 0.110 0.110 (0.110)	107.4
Barley grain	0.100	0	0.087 0.110 0.120 (0.110)	105.6
	0.100	340	0.100 0.100 0.098 (0.100)	100.4

Conclusion

The stability results after storage at or below -18 °C, for 340 days, is demonstrated for folpet and phthalimide in wheat grain and barley grain.

A 2.1.1.1.1.2 Study 2

Comments of zRMS:	<p>The study is ongoing. This is interim report at 12 months.</p> <p>The results of Jooss study demonstrate the stability of residues of folpet and phthalimide upon deep frozen storage at – 18 °C for up to 12 months in wheat (whole plant), barley (whole plant), wheat (straw), barley (straw) and up to 6 months for beer.</p> <p>For all matrices the applicability/suitability of the methods was successfully demonstrated according to SANTE/2020/12830, rev. 2.</p> <p>The results of the interim report are acceptable.</p>
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Reference:	KCP 7.2.1/02
Report	Storage Stability of Folpet and its Metabolites in Various Matrices under Deep Frozen Conditions. Jooss, S. 2024. Eurofins Agrosience Services. Report N°: S22-07592 (study ongoing). Interim report at 12 months.
Guideline(s):	<p>Yes.</p> <p>Guideline 7032/VI/95 rev.5 (Appendix H) of the Commission of the European Communities</p> <p>OECD Test Guideline No 506.</p>
Deviations:	TBC
GLP:	Yes
Acceptability:	Yes

Materials and methods

The objective of the study is to obtain data about the storage stability of folpet and its metabolites PI, PA and PLA in/on representative cereal matrices and beer at ≤ 18 °C (target) in the dark over a storage period of up to 20 months in accordance with guideline 7032/VI/95 rev.5 (Appendix H) of the Commission of the European Communities and OECD Test Guideline No 506.

Matrix Types, Origin, Preparation and Storage:

- Wheat & Barley whole plant (high water) and Wheat & Barley straw (dry): The sample material will be thoroughly homogenised in a knife mill or a cutter and if necessary with dry ice.
- Beer (high water): Beer will be thawed and homogenized by shaking or stirring before taking aliquots for analysis.

Untreated sample material will be supplied by the Test Facility. Sample material origin will be recorded in the raw data and may be included in the final report. Weighed untreated control samples for preparation of concurrent recoveries will be stored at ≤ -20 °C (target) until fortification and extraction.

Test Method:

Method Reference: S22-01156

Validation Status: Fully validated

Limit of Quantification (LOQ): As validated within S22-01156

Limit of Detection (LOD): Lowest calibration standard (≤ 30 % of the LOQ)

Test Program:

- **Fortification:** An appropriate amount of homogenised sample material is weighed into an appropriate extraction or storage vessel and fortified at the corresponding 10x LOQ level with the test / reference items.

For all samples that are intended to be used for assessment of storage stability (storage samples) the analytes will be fortified separately. All freshly prepared fortification samples for demonstrating the analytical performance of the method (recovery samples) may be prepared by fortifying all analytes jointly.

The spiking procedure should be undertaken in the same way as the spiking of the samples in the validation of the analytical methods.

After fortification, the storage vessels will be sealed with screw caps and placed into the deep freezer.

For day 0 testing a set of three (3) storage samples will be prepared. For each of the other storage intervals (12, 16/17, 18/19 or 20 months for wheat and barley and 6 months for beer) a set of at least two (2) storage samples for analysis is prepared per analyte.

In addition, a number of four (4) complete interval sets for wheat and barley and two (2) complete interval sets for beer will be prepared per analyte and matrix at the beginning of the experimental phase for possible extension of the storage interval or as backup for a failure.

The backup samples may be used in case the analysis of the original storage samples failed and a repetition is required. The backup samples may also be used to cover additional testing intervals.

- **Sample Storage and Analysis:** The samples have to be kept in the dark at a storage temperature of $\leq 20^{\circ}\text{C}$ (target). The temperature has to be recorded during the entire storage period.

On day 0, three (3) of the storage samples per analyte and matrix will be analysed together with one (1) control sample, while the rest of fortified samples are put into the freezer.

Furthermore, and in order to demonstrate suitability/applicability three (3) recovery samples at the LOQ are analysed at day 0 for each matrix and analyte.

For each further testing interval (12, 16/17, 18/19 or 20 months for wheat and barley and 6 months for beer) two (2) storage samples per analyte and matrix will be analysed together with one (1) control sample and two (2) procedural recoveries at the level of 10x LOQ.

Results and discussions:

Table A 3: Summary of concurrent recoveries of folpet and phtalamide from wheat whole plant and straw, barley whole plant and straw and beer.

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev
Folpet					
Wheat whole plant	0.01	0	3	90.8 96.4 90.8	92.7 \pm 3.5
	0.10	362	2	90.8 98.4	94.6
Wheat straw	0.01	0	3	88.4 97.6 93.6	95.6 \pm 4.8
	0.10	362	2	95.8 104.0	99.8
Barley whole plant	0.01	0	3	69.2 69.2 72.8	71.0 \pm 3.6
	0.10	362	2	84.0 89.6	86.8

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%)	Mean \pm std dev
Barley straw	0.01	0	3	84.8 83.6 77.6	80.6 \pm 5.3
	0.10	362	2	81.2 86.8	84.0
Beer	0.01	0	3	83.4 80.5 101.0	90.8 \pm 16.0
	0.10	120	2	94.0 94.2	94.1
	0.10	181	2	90.3 97.4	93.9
Phtalamide					
Wheat whole plant	0.01	0	3	109.0 112.0 102.0	108.0 \pm 4.7
	0.10	361	2	94.3 90.3	92.3
Wheat straw	0.05	0	3	110.0 112.0 106.0	109.0 \pm 4.2
	0.50	361	2	101.0 97.6	99.2
Barley whole plant	0.01	0	3	84.4 89.2 89.2	87.6 \pm 3.2
	0.10	361	2	92.4 97.2	95.0
Barley straw	0.05	0	3	111.0 115.0 106.0	111.0 \pm 5.6
	0.50	361	2	98.5 105.0	102.0
Beer	0.01	0	3	117.0 119.0 118.0	118.0 \pm 0.8
	0.10	119	2	83.1 87.2	85.3
	0.10	180	2	97.7 103.0	100.0

Table A 4: Stability of folpet and phtalamide residues in wheat whole plant and straw, barley whole plant and straw and beer following storage at or below -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Mean recovery * (%)
Folpet				
Wheat whole plant	0.10	0	0.104 0.094 0.096	98.0
	0.10	362	82.8	80.0

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Mean recovery * (%)
			77.2	
Wheat straw	0.10	0	0.127 0.130 0.132	117.0
	0.10	362	0.089 0.084	72.6
Barley whole plant	0.10	0	0.088 0.085 0.082	85.1
	0.10	362	0.081 0.088	84.4
Barley straw	0.20**	0	0.200 0.192 0.174	94.3
	0.10	362	0.104 0.101	103.0
Beer	0.10	0	0.114 0.109 0.108	110.0
	0.10	120	0.085 0.093	88.9
	0.10	181	0.077 0.084	80.5
Phthalamide				
Wheat whole plant	0.10	0	0.126 0.129 0.125	116.0
	0.10	361	0.102 0.102	92.5
Wheat straw	0.5	0	0.424 0.476 0.428	88.5
	0.5	361	0.424 0.378	80.2
Barley whole plant	0.10	0	0.114 0.114 0.116	111.0
	0.10	361	0.090 0.092	91.2
Barley straw	0.5	0	0.516 0.460 0.444	94.7
	0.5	361	0.484 0.464	91.7
Beer	0.10	0	0.084 0.084 0.082	83.4
	0.10	119	0.082 0.080	80.8
	0.10	180	0.079 0.078	78.7

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Mean recovery * (%)
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*corrected for for blank residues >30% of LOQ

** spiking error

Conclusion

For folpet and phthalimide in all matrices the average amount of analyte recovered relative to the nominal fortification level was $\geq 70\%$ at any testing interval investigated.

The study is deemed sufficient for assessing the stability of folpet and phthalimide in homogenates of wheat (whole plant), barley (whole plant), wheat (straw), barley (straw) and beer upon storage at $\leq -18^\circ\text{C}$, for 6 months for beer and 12 months for all other matrices respectively.

A 2.1.1.1.2 Storage stability of residues in animal products

No further study submitted and no data required.

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 further study submitted and no data required.

A 2.1.2.1.3 Nature of residues in processed commodities

Comments of zRMS:	The study has been already evaluated at EU level, under the framework of folpet renewal. Based on the available data it can be concluded that folpet is rapidly hydrolyzed into phthalimide, phthalamic acid and phthalic acid under standard hydrolysis conditions.
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Reference:	KCP 7.2.2/01
Report	[¹⁴ C]-Folpet: Investigation of the Nature of the Potential Residue in the Products of Industrial Processing or Household Preparation, M Fitzmaurice and E Mackenzie, 2007, report No OZ/07/007
Guideline(s):	European Council Directive 91/414/EEC as amended by Commission Directive 96/68/EC Section 6.5, Subsection 6.5.1. Guideline 7035/VI/95 Revision 5, Appendix E
Deviations:	No
GLP:	Yes
Acceptability:	Yes

MATERIALS AND METHODS

A hydrolysis study was performed in order to investigate the fate of folpet ingredient under 3 typical conditions of processing simulating representative hydrolytic conditions for pasteurisation (20 minutes at 90°C , pH 4), boiling/brewing/baking (60 minutes at 100°C , pH 5) and sterilisation (20 minutes at 120°C , pH 6, see **Table A 2.1.2.1.3-2**). Buffer solutions containing the radiolabelled folpet at an initial concentration of 0.5 mg/L were incubated in closed high pressure stainless steel vessels placed in an autoclave at the desired temperature. Test solutions were analysed before and after incubation under the above described conditions. Samples were cooled in running water after incubation. Transformation products were identified by co-chromatography by HPLC with certified standards and confirmed by LC-MS/MS.

All samples generated during the study were profiled initially by HPLC on the day of their generation. Processed samples were profiled within 4 hours of their generation. Samples were subsequently stored at $< -15^\circ\text{C}$ in the dark.

RESULTS AND DISCUSSION

Analysis of the buffer solutions hydrolysed under pasteurisation conditions indicated that folpet was degraded to phthalimide, which was the major component present. Folpet was detected at 94.3% of applied radioactivity (0.492 mg/L) before processing, in addition to 5.8% phthalimide (0.015 mg/L). Folpet was not detected after pasteurisation. After processing, phthalimide was detected at 98% of applied radioactivity (0.252 mg/L). Phthalamic acid and phthalic acid were also detected in lower amounts, 0.4 % and 1.0% of applied radioactivity (0.001 and 0.003 mg/L). Folpet and 2-cyanobenzoic acid were not detected (<0.001 mg/L) after processing.

Analysis of the buffer solutions hydrolysed under baking, brewing and boiling conditions indicated that phthalimide and phthalic acid were the major components present. Folpet was detected at 90.6% of applied radioactivity (0.443 mg/L) before processing. Phthalimide and a small amount of an unidentified component (RRT 0.69) were also found at levels of 8.5% and 0.9% of applied radioactivity (0.021 and 0.005 mg/L) before processing. After processing, residues of folpet were not detected. Phthalimide was detected at 56.1% of applied radioactivity (0.136 mg/L) and phthalic acid at 40.7% of applied radioactivity (0.112 mg/L). Phthalamic acid was also detected at 2.8% of applied radioactivity (0.008 mg/L).

Analysis of the buffer solutions hydrolysed under sterilisation conditions indicated that phthalic acid and phthalamic acid were the major components present. Folpet was detected at 97.1% of applied radioactivity (0.489 mg/L) before processing. Small amounts of phthalimide and an unidentified component (RRT 0.90) were also found at levels of 2.2% and 0.7% of applied radioactivity (0.006 and 0.003 mg/L) before processing.

Folpet was not detected after sterilisation. Phthalimide levels were slightly higher at 6.0% of applied radioactivity (0.015 mg/L) but the major degradates were phthalamic and phthalic acid at 32.8% and 44.9% of applied radioactivity (0.091 and 0.126 mg/L). 2-cyanobenzoic acid was also detected at 11.0% of applied radioactivity (0.027 mg/L). A second unidentified component (RRT 0.43) was found at levels of 4.5% of applied radioactivity (0.023 mg/L) after processing.

Table A-1 Identification of compounds from high temperature hydrolysis study

Common name/code ID No.	Chemical structure
Folpet	
Phthalimide	
Phthalamic acid	
Phthalic acid	

Table A-2 Standard hydrolysis study of folpet

Component	Test Conditions					
	Pasteurization		Boiling/brewing/baking		Sterilisation	
	Before Processing	After Processing	Before Processing	After Processing	Before Processing	After Processing
Folpet	94.3	-	90.6	-	97.1	-
Phthalimide	5.8	97.8	8.5	56.1	2.2	6.0
Phthalamic acid	-	0.4	-	2.8	-	32.8
Phthalic acid	-	1.0	-	40.7	-	44.9
2-Cyanobenzoic acid	-	-	-	-	-	11.0
Unidentified 1	-	-	-	-	-	4.5
Unidentified 2	-	-	0.9	-	-	-
Unidentified 3	-	0.5	-	-	-	-
Unidentified 4	-	-	-	-	0.7	-

CONCLUSIONS

The results of this study indicate that residues of folpet are likely to be degraded to form phthalimide, phthalamic acid, phthalic acid and 2-cyanobenzoic acid during processing.

A 2.1.2.2 Nature of residues in livestock

No further study submitted and no data required.

A 2.1.3 Magnitude of residues in plants

A 2.1.3.1 Wheat

Table A-3 Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI [days]
cGAP EU (DAR, Italy, 2005)	2	750 g a.s./ha	7-28 days	Up to z65	42
cGAP EU (Art. 12, EFSA, 2014)	2	750 g a.s./ha	14 days	BBCH 31-59	42
cGAP EU (EFSA, 2021)	2	750 g a.s./ha	14 days	BBCH 31-59	42
Intended cGAP (1)	2	600 g a.s./ha	14 days	BBCH 30-59	42

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0

A 2.1.3.1.1 Study 1

Comments of zRMS:	<p>Eight field trials (4 DCS and 4 HS) were conducted in Northern Europe according to the OECD Test No. 509 to gain the residue level of folpet and its two metabolites phthalimide and phthalic acid in wheat specimens (whole plant, grain and straw) following two foliar applications of SAP50SCF, containing folpet as active ingredient (500 g a.s./L).</p> <p>Analytical phase was performed in independent studies (phase study code is: S22-03719). The study is considered acceptable.</p>
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Reference: KCP 7.2.3/01

Report Magnitude of the residue of folpet in representative winter wheat Raw Agricultural Commodities after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern Europe- 2021, A.S. Lesbazeilles Beauvalon, 2021, report n° 21-00160 (field phase)

Guideline(s): Regulation (EC) N°1107/2009 of 21 October 2009 (Repealing the Council Directive 91/414/EEC) concerning the placing of plant protection products on the market

Commission Regulation (EU) No 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009

General recommendations for the design, preparation and realization of residue trials, 7029/VI/95-rev 5, 22.07.97 and amendments

OECD (2009), Test No. 509: Crop Field Trial, OECD Guidelines for the Testing of Chemicals, Section 5, OECD Publishing.

EU pesticide residue legislation: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 - SANCO/3029/99 rev.4, 11 July 2000

EU pesticide residue legislation: Guidance document on pesticide analytical methods for risk assessment and post-approval control and monitoring purposes – SANTE/2020/12830 rev.1, 24 February 2021

Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17

Deviations: No deviation with impact on quality and integrity of the study.

GLP: Yes

Acceptability: Yes

A study on the magnitude of the residue of folpet and its metabolites in representative winter wheat Raw Agricultural Commodity (RAC) was conducted in Northern Europe, following two foliar application(s) of SAP50SCF, containing folpet as active ingredient (500 g a.s./L).

Eight wheat trials, 4 DCS and 4 HS, were set up in Northern Europe (Northern France, Germany, Hungary and Poland). Each trial consisted of one untreated plot U and one treated plot.

Two foliar applications of SAP50SCF were performed on the treated plot T1 at the target dose rate of 1.2 L/ha formulated product (FP) (equivalent to 600 g a.s./ha). The target spray of water volume was in the range 150 to 400 L/ha, according to Good Agricultural Practices.

The deviations calculated on the amount of formulated product per hectare were all between $\pm 5\%$.

Foliar applications were performed following the actual schedule specified in study plan: SAP50SCF was applied 13-21 DBA2 and at BBCH 61 on plot T1.

In the decline trials (DCS), RAC specimens (whole plants, grain and straw) for analyses were collected at 0 DBLA and at BBCH 89 (commercial harvest) in the control plot and at 0 DALA, 13-15, 27-29 and 34-78 DALA, commercial harvest, (BBCH 89) in the treated plot T1.

In the harvest trials (HS), RAC specimens (grain and straw) for analyses were collected at BBCH 89 (commercial harvest) in the control plot and treated plot (44-56 DALA).

All RAC specimens from plot U and T1, were deep frozen on the day of collection and stored at the target temperature below -18°C . All specimens remained deep frozen during storage at field test sites and homogenization test site, during shipment and storage at the analytical laboratory. RAC specimens were maintained frozen after collection through the shipment for homogenization.

A 2.1.3.1.2 Study 2

Comments of zRMS:	<p>Method validation was not performed within this study because the analytical methods were previously validated in accordance to SANTE/2020/12830, rev.1 for the determination of folpet, phthalimide and phthalic acid in wheat (green material), wheat (grain) and wheat (straw) (as representatives of dry matrices and matrices with high water content) with an LOQ of 0.01 mg/kg for folpet in all matrices and phthalimide in (wheat green material) and wheat (grain) as well as 0.05 mg/kg for phthalic acid in all matrices and phthalimide in wheat (straw) in GLP study S22-01156.</p> <p>With regard to selectivity, accuracy and precision, the analytical methods were applied successfully for each analytical set when analysing the samples of the study. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830.</p> <p>Sufficient stability data are available to support the residue data presented in this study.</p> <p>Trials GAP for wheat: 2 x 0.60 kg a.s. /ha with 12-21 days between application, up to BBCH 61, PHI 34-78.</p> <p>The following residues were detected in the wheat grain samples: E=RA (Sum of folpet and phthalimide expressed as folpet): 4x<0.03, 0.032, 0.044, 0.060, 0.087 mg/kg.</p> <p>The study is considered acceptable.</p>
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Reference:	KCP 7.2.3/02
Report:	Study on the Residue behaviour of folpet and its metabolites in winter wheat after two applications of SAP50SCF (Folpet 500 g/l SC) in Northern Europe – 2021. Sandro Jooss, 2022. Report No: S22-03719 (analytical phase)
Guideline(s):	Commission Regulation (EU) No 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009 SANTE/2020/12830, Rev1 Guidance document on pesticide analytical methods for risk assessment and post-approval control and monitoring purposes. 24/02/2021 OECD Series on Testing and Assessment, Number 72. OECD ENV/JM/MONO(2007)17
Deviations:	No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Yes

The objective of the study was to analyse residues of folpet as well as its two metabolites phthalimide and phthalic acid in wheat specimens with limits of quantification (LOQ) of 0.01 mg/kg for folpet in all matrices and for phthalimide in wheat (whole plant) and wheat (grain) as well as 0.05 mg/kg for phthalimide in wheat (straw) and phthalic acid in all matrices.

Analytical methods:

Extraction of Folpet from Wheat: In brief, samples of wheat (whole plant), wheat (grain) and wheat (straw) were extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed by dispersive SPE with PSA and magnesium sulfate). Quantification was performed by use of LC MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Extraction of Phthalimide from Wheat: In brief, samples of wheat (whole plant), wheat (grain) and wheat (straw) were extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard (addition of internal standard must be adjusted to the necessary dilution) was added to the raw extract before clean-up. Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed concentration and dilution in water containing 0.1% of acetic acid. Quantification was performed by use of LC MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix, except cereal straw, with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ). For cereal straw, the LOQ was 0.05 mg/kg and the LOD was 0.015 mg/kg.

Extraction of Phthalic Acid from Wheat: In brief, samples of wheat (whole plant), wheat (grain) and wheat (straw) were extracted with acetonitrile containing 1% of formic acid and if necessary, after addition of water. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of magnesium sulfate and sodium chloride). Quantification was performed by use of LC MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.05 mg/kg for each matrix with a limit of detection (LOD) set at 0.015 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Method validation and concurrent recoveries: The analytical methods were previously validated at Eurofins Agrosience Services EAG Laboratories GmbH according to SANTE/2020/12830, rev. 1 for wheat (green material), wheat (grain) and wheat (straw) as representatives for dry matrices and matrices with high water content, respectively. Five (5) fortifications of untreated control samples at the level of LOQ and five (5) fortifications at the level of 10x LOQ were performed per analyte/matrix combination. For each analytical set of sample analysis, the method's applicability in terms of accuracy and repeatability was assessed by concurrent recoveries.

For folpet and phthalimide, blank values of control sample materials used for recovery determinations did not exceed a level that would correspond to 30% of the LOQ.

For phthalic acid, blank values of reagents and those control sample materials used for recovery determinations in most cases exceeded a level that would correspond to 30% of the LOQ. Therefore, recoveries for phthalic acid were corrected for both, residues >30% of LOQ detected in control samples and residues >30% of LOQ detected in reagent blanks.

Fortifications for the individual analyte/matrix combinations were performed at levels of 0.01 mg/kg, 0.05 mg/kg, 0.1 mg/kg, 0.5 mg/kg, 2.0 mg/kg, 4.0 mg/kg, 5.0 mg/kg and/or 14 mg/kg and therefore encompassed the range of target analyte concentrations found in the samples of the study.

The accuracy and precision of the method was considered to be acceptable since the mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1 and OECD ENV/JM/MONO(2007)17.

Residue results are summarized in Table A-4 below:

Table A-4 Summary of the studies 1 & 2 trials

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 analyzed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Folpet	Phthalimide	Sum of folpet and phthalimide expressed as folpet		
(a)	(b)					(c)						(d)	(e)
21-00160-01 Poland (Warmińsko- Mazurskie) Janowiec Kościelny 13-111	Winter wheat MONDIA	1. 20/09/20y 2. 23/06 to 06/07/21 3. 27/07/21	548.1 554.40	295.0 298.5	185,8 185,7	08/06/21 23/06/21	55 61	Whole plant Whole plant Whole plant Grain Straw	11 6,4 1,3 0,015 1,6	3,9 2,2 0,58 0,023 1,1	19 11 2,5 <u>0,06</u> 3,9	0 13 27 34 34	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 315 days W.plant: 344 days Straw: 330 days
21-00160-02 Poland (Kujawsko- Pomorskie) Cerekwica 88-400	Winter wheat BATAJA	1. 23/09/20 2. 15/06 to 25/06/21 3. 30/07/21	583.68 728.16	304.0 289.3	192,0 251,7	02/06/21 16/06/21	49 61	Grain Straw	0,004 1,1	0,008 1,1	<u>0,019</u> 3,4	44 44	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 312 days Straw: 320 days
21-00160-03 Hungary (Heves) Maklár H-3397	Winter wheat GENIUS	1. 13/10/20 2. 28/05 to 10/06/21 3. 20/07 to 23/07/21	582.72 569.76	310.0 296.7	188,0 192,0	11/05/21 28/05/21	41 61	Grain Straw	< 0.01 0,80	<0,01 0,45	<u><0,03</u> 1,7	56 56	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 319 days Straw: 327 days

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 analyzed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Folpet	Phthalimide	Sum of folpet and phthalimide expressed as folpet		
(a)	(b)					(c)						(d)	(e)
21-00160-04 Hungary (Szabolcs- Szatmár-Bereg) Nyírttelek H-4461	Winter wheat GK CSILLAG	1. 12/11/20 2. 28/05 to 10/06/21 3. 12/07 to 17/07/21	569.76 550.56	296.7 286.7	192,0 192,0	15/05/21 28/05/21	39 61	Whole plant Whole plant Whole plant Grain Straw	8,9 3,9 2,8 <0,01 3,3	3,6 1,5 0,52 0,011 0,84	16 7,0 3,8 <u>0.032</u> 5,0	0 13 27 78 78	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 326 days W.plant: 370 days Straw: 341 days
21-00160-05 Germany (Schleswig- Holstein) Wallsbüll 24980	Winter wheat TALENT	1. 28/10/20 2. 15/06 to 17/06/21 3. 05/08/21	595.20 576.00	206.7 200.0	288,0 288,0	01/06/21 15/06/21	43 61	Grain Straw	<0.01 4,4	<0.01 1,6	<u><0.03</u> 7,6	51 51	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 306 days Straw: 321 days

21-00160-06 Germany (Brandenburg) Kerzlin 16845	Winter wheat AKTIVUS	1. 01/10/20 2. 07/06 to 10/06/21 3. 19/07 to 25/07/21	576.00 576.00	300.0 300.0	192,0 192,0	17/05/21 07/06/21	39 61	Grain Straw	< 0.01 0,76	<0.01 0,51	<u><0.03</u> 1,8	44 44	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 321 days Straw: 329 days
21-00160-07 Northern France (Haut de France) Mont Notre Dame 02220	Winter wheat CHEVIGNON	1. 16/10/20 2. 15/06 to 19/06/21 3. 20/07 to 30/07/21	564.48 568.32	245.0 246.7	230,4 230,4	02/06/21 14/06/21	59 61	Whole plant Whole plant Whole plant Grain Straw	8,7 2,2 1,7 0,032 1,6	2,7 0,63 0,26 0,027 0,91	14 3,5 2,3 <u>0,087</u> 3,4	0 15 29 36 36	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 322 days W.plant: 353 days Straw: 337 days
21-00160-08 Northern France (Grand-Est) Bourgogne 51110	Winter wheat NEMO	1. 06/11/20 2. 09/06 to 15/06/21 3. 28/07/21	576.00 579.84	250.0 251.7	230,4 230,4	27/05/21 09/06/21	47 61	Whole plant Whole plant Whole plant Grain Straw	9,4 3,4 2,0 <0.01 0,96	1,9 0,73 0,34 0,017 0,44	13 4,8 2,7 <u>0,044</u> 1,8	0 15 28 49 49	Analytical method: S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 314 days W.plant: 358 days Straw: 322 days

A 2.1.3.2 Barley

Table A-5 Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI [days]
cGAP EU (EFSA, 2021)	2	750 g a.s./ha	7-10 days	BBCH 30-59	42
Intended cGAP (1)	2	600 g a.s./ha	14 days	BBCH 30-59	42

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0

A 2.1.3.2.1 Study 1

Comments of zRMS:	<p>Eight field trials (4 DCS and 4 HS) were conducted in Northern Europe according to the OECD Test No. 509 to gain the residue level of folpet and its two metabolites phthalimide and phthalic acid in barley specimens (whole plant, grain and straw) following two foliar applications of SAP50SCF, containing folpet as active ingredient (500 g a.s./L).</p> <p>Analytical phase was performed in independent studies (phase study code is: S22-01157).</p> <p>The study is considered acceptable.</p>
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Reference: KCP 7.2.3/03

Report Magnitude of the residue of folpet in representative barley Raw Agricultural Commodities after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern Europe- 2021, A.S. Lesbazeilles Beauvalon, 2021, report n° 21-00139 (field phase)

Guideline(s): Regulation (EC) N°1107/2009 of 21 October 2009 (Repealing the Council Directive 91/414/EEC) concerning the placing of plant protection products on the market
Commission Regulation (EU) No 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009
General recommendations for the design, preparation and realization of residue trials, 7029/VI/95-rev 5, 22.07.97 and amendments
OECD (2009), Test No. 509: Crop Field Trial, OECD Guidelines for the Testing of Chemicals, Section 5, OECD Publishing.
EU pesticide residue legislation: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 - SANCO/3029/99 rev.4, 11 July 2000
EU pesticide residue legislation: Guidance document on pesticide analytical methods for risk assessment and post-approval control and monitoring purposes – SANTE/2020/12830 rev.1, 24 February 2021
Guidance Document on Pesticide Residue Analytical Methods ENV/JM/MONO(2007)17

Deviations: No deviation with impact on quality and integrity of the study.

GLP: Yes

Acceptability: Yes

A study on the magnitude of the residue of folpet and its metabolites in representative barley Raw Agricultural Commodity (RAC) was conducted in Northern Europe, following one or two foliar application(s) of FOLPET 500 g/L (SAP50SCF) containing folpet as active ingredient (500 g a.s./L). Eight barley trials, 4 DCS and 4 HS, were set up in Northern Europe (Northern France, Germany, Hungary and Poland). Each trial consisted of one untreated plot U and one treated plot T1 or two treated plots T1/T2 (T2 processing plot) in trials -01 (Poland) and -02 (Northern France),

Two foliar applications of SAP50SCF were performed on the treated plot T1 at the target dose rate of 1.2 L/ha formulated product (FP) (equivalent to 600 g a.s./ha). The target spray of water volume was in the range 150 to 400 litres per hectare, according to Good Agricultural Practices.

The deviations calculated on the amount of formulated product per hectare were all between $\pm 5\%$.

Foliar applications were performed following the actual schedule specified in study plan: SAP50SCF was applied 12-15 days before application 2 and at BBCH 61 on plot T1.

In the decline trials (DCS), RAC specimens (whole plants, grain and straw) for analyses were collected at 0 DBLA and at BBCH 89 (commercial harvest) in the control plot and at 0 DALA, 14-15, 27-33 and 40-48 DALA for commercial harvest (BBCH 89) in the treated plots.

In the harvest trials (DCS), RAC specimens (grain and straw) for analyses were collected at BBCH 89 (commercial harvest) in the control plot and treated plot (34-50 DALA).

All RAC specimens from plot U and T1, were deep frozen on the day of collection and stored at the target temperature below -18°C . All specimens remained deep frozen during storage at the test sites, during shipment and storage at the analytical laboratory. RAC specimens were maintained frozen after collection through the shipment for homogenization.

For processing trials, one foliar application was performed on the treated plot T2 at the target dose rate of 6.0 L/ha formulated product (FP) (equivalent to 3000 g a.s./ha). The target spray of water volume was in the range 150 to 400 litres per hectare, according to Good Agricultural Practices. The deviations calculated on the amount of formulated product per hectare were all between $\pm 5\%$. One foliar application was performed at BBCH 61 on the treated plot T2 and samplings were done in plots U/T2, with grain, at BBCH 89, commercial harvest, at 40-41 DALA. Specimens from plot T2, with an additional specimen of grain from plot U, were kept at ambient temperature before shipment at ambient temperature to the processing facility. Temperature was recorded with a data logger.

For the sake of clarity, the residue data on the processing field phases will be included and summarized in the point A.2.1.5.” Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)”.

A 2.1.3.2.2 Study 2

Comments of zRMS:	<p>Method validation was not performed within this study because the analytical methods were previously validated in accordance to SANTE/2020/12830, rev.1 for the determination of folpet, phthalimide and phthalic acid in wheat (green material), wheat (grain) and wheat (straw) (as representatives of dry matrices and matrices with high water content) with an LOQ of 0.01 mg/kg for folpet in all matrices and phthalimide in (wheat green material) and wheat (grain) as well as 0.05 mg/kg for phthalic acid in all matrices and phthalimide in wheat (straw) in GLP study S22-01156.</p> <p>With regard to selectivity, accuracy and precision, the analytical methods were applied successfully for each analytical set when analysing the samples of the study. The mean recoveries at each fortification level comply with the standard acceptance criteria of the guidance document SANTE/2020/12830.</p> <p>Sufficient stability data are available to support the residue data presented in this study.</p> <p>Trials GAP for barley: 2 x 0.60 kg a.s. /ha with 12-21 days between application, up to BBCH 61, PHI 34-50.</p> <p>The following residues were detected in the barley grain samples: E=RA (Sum of folpet and phthalimide expressed as folpet): <0.03, 0.047, 0.050, 0.072, 0.28, 0.29, 0.34, 0.75 mg/kg.</p> <p>The study is considered acceptable.</p>
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Reference:

KCP 7.2.3/04

Report:

Study on the residue behaviour of folpet and its metabolites in barley after two applications of SAP50SCF (Folpet 500 g/l, SC) in Northern Europe – 2021. S. Jooss, 2022. Report No: S22-01157 (analytical phase)

Guideline(s):	Commission Regulation (EU) No 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009 SANTE/2020/12830, Rev1 Guidance document on pesticide analytical methods for risk assessment and post-approval control and monitoring purposes. 24/02/2021 OECD Series on Testing and Assessment, Number 72. OECD ENV/JM/MONO(2007)17
Deviations:	No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Yes

MATERIALS AND METHODS

The objective of the study was to analyse residues of folpet as well as its two metabolites phthalimide and phthalic acid in barley specimens with limits of quantification (LOQ) of 0.01 mg/kg for folpet in all matrices and for phthalimide in barley (whole plant) and barley (grain) as well as 0.05 mg/kg for phthalimide in barley (straw) and phthalic acid in all matrices.

Analytical Methods

Extraction of Folpet from Barley: In brief, samples of barley (whole plant), barley (grain) and barley (straw) were extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed by dispersive SPE with PSA and magnesium sulfate). Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Extraction of Phthalimide from Barley: In brief, samples of barley (whole plant), barley (grain) and barley (straw) were extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard (addition of internal standard must be adjusted to the necessary dilution) was added to the raw extract before clean-up. Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed by concentration and dilution in water containing 0.1% of acetic acid. Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix, except cereal straw, with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ). For cereal straw, the LOQ was 0.05 mg/kg and the LOD was 0.015 mg/kg.

Extraction of Phthalic Acid from Barley: In brief, for phthalic acid, samples of barley (whole plant), barley (grain) and barley (straw) were extracted with acetonitrile containing 1% of formic acid after addition of water. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of magnesium sulfate and sodium chloride). Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.05 mg/kg for each matrix with a limit of detection (LOD) set at 0.015 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Method Validation and Concurrent Recoveries: The analytical methods were previously validated at Eurofins Agrosience Services EAG Laboratories GmbH according to SANTE/2020/12830, rev. 1 for

wheat (green material), wheat (grain) and wheat (straw) as representatives for dry matrices and matrices with high water content, respectively. Five (5) fortifications of untreated control samples at the level of LOQ and five (5) fortifications at the level of 10x LOQ were performed per analyte/matrix combination. For each analytical set of sample analysis, the method's applicability in terms of accuracy and repeatability was assessed by concurrent recoveries. At least three (3) fortifications of untreated control samples at the level of LOQ and three (3) fortifications at the level of 10x LOQ were performed for each analyte/matrix combination.

For folpet and phthalimide, blank values of control sample materials used for recovery determinations in several cases exceeded a level that would correspond to 30 % of the LOQ. Recoveries were corrected in this case.

For phthalic acid, blank values of reagents and those control sample materials used for recovery determinations in all cases exceeded a level that would correspond to 30 % of the LOQ. Therefore, recoveries for phthalic acid were corrected for both, residues >30% of LOQ detected in control samples and residues >30% of LOQ detected in reagent blanks.

Fortifications for the individual analyte/matrix combinations were performed at levels of 0.01 mg/kg, 0.05 mg/kg, 0.1 mg/kg, 0.5 mg/kg, 0.6 mg/kg, 2.0 mg/kg, 5.0 mg/kg and/or 14 mg/kg and therefore encompassed the range of target analyte concentrations found in the samples of the study.

The accuracy and precision of the methods was considered to be acceptable since the mean recoveries at each fortification level for each analyte/matrix combination comply with the standard acceptance criteria of the guidance document SANTE/2020/12830, rev. 1 and OECD ENV/JM/MONO(2007)17.

Residue results are summarized in Table A-6 below:

Table A-6 Summary of the studies 1 & 2 trials

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 analyzed	Residues (mg/kg)			PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hl				Folpet	Phthalimide	Sum of folpet and phthalimide expressed as folpet		
(a)	(a)	(b)				(c)						(d)	(e)
21-00139-01 Poland(Pomorskie) Angowice 89-620	Spring barley PROPINO	1. 05/04/21 2. 21/06 to 30/06/21 3. 01/08/21	757.64	203.7	371,9	07/06/21 21/06/21	43 61	Whole plant	13	3,0	19	0	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 306 days W.plant: 345 days Straw: 316 days
			748.34	201.2	371,9			Whole plant	1,7	1,5	4,8	15	
								Whole plant	1,1	0,53	2,2	30	
								Grain	0,18	0,053	<u>0,28</u>	41	
								Straw	1,3	1,3	3,9	41	
21-00139-02 Northern France (Grand-Est) Avancon 08300	Spring barley RGT PLANET	1. 02/03/21 2. 16/06 to 20/06/21 3. 24/07 to 25/07/21	757.64	280.0	270,6	02/06/21 14/06/21	51 61	Whole plant	8,500	3,472	15,500	0	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 314 days W.plant: 374 days Straw: 324 days
			771.28	285.0	270,6			Whole plant	1,7	0,27	2,2	15	
								Whole plant	0,37	0,098	0,57	33	
								Grain	0,023	0,024	<u>0,072</u>	40	
								Straw	1,5	0,60	2,7	40	

21-00139-03 Hungary (Heves) Maklár H-3397	Winter barley SU ELLEN	1. 05/10/20 2. 17/05 to 22/05/21 3. 26/06 to 28/06/21	719.20 760.74	290.0 306.7	248,0 248,0	03/05/21 17/05/21	41 61	Grain Straw	0,018 2,7	0,016 0,42	<u>0,050</u> 3,5	42 42	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 340 days Straw: 350 days
21-00139-04 Germany (Schleswig Holstein) Wallsbüll 24980	Winter barley KWS	1. 10/10/20 2. 15/06 to 17/06/21 3. 19/07/21	768.80 775.00	206.7 208.3	371,9 372,1	31/05/21 15/06/21		Grain Straw	0,48 5,6	0,13 1,5	<u>0,75</u> 8,5	34 34	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 319 dasy Straw: 329 days
21-00139-05 Poland (Kujawsko- Pomorskie) Szelejewo 88-410	Winter barley KOSMOS	1. 15/09/20 2. 08/06 to 20/06/21 3. 15/07/21	753.30 729.74	303.7 294.3	248,0 248,0	27/05/21 10/06/21	58 61	Grain Straw	< 0.01 0,86	< 0.02 0,64	<u><0.03</u> 2,1	35 35	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 323 days Straw:333 days

21-00139-06 Northern France (Grand-Est) Bourgogne 51110	Spring barley PLANET	1. 28/02/21 2. 09/06 to 15/06/21 3. 28/07/21	713.62 758.88	240.0 255.0	297,3 297,6	28/05/21 10/06/21	43 61	Whole plant Whole plant Whole plant Grain Straw	11 3,6 2,3 0,013 0,86	4,1 0,47 0,36 0,017 0,40	20 4,6 3,0 <u>0,047</u> 1,7	0 14 27 48 48	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 310 days W.plant: 356 days Straw: 320 days
21-00139-07 Germany (Brandenburg) Teschendorf 16775	Winter barley KWS FARO	1. 12/10/20 2. 30/05 to 01/06/21 3. 12/07 to 16/07/21	773.76 753.92	260.0 253.3	297,6 297,6	10/05/21 31/05/21	39 61	Grain Straw	0,20 0,87	0,07 0,41	<u>0,34</u> 1,7	50 50	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 325 days Straw:335 days
21-00139-08 Hungary (Borsod- Abaúj-Zemplén) Monok H-3905	Winter barley ANTONELLA	1. 05/10/20 2. 18/05 to 23/05/21 3. 02/07 to 03/07/21	714.86 719.20	288.3 290.0	248,0 248,0	06/05/21 19/05/21	41 61	Whole plant Whole plant Whole plant Grain Straw	4,5 3,7 2,6 0,19 1,9	3,0 0,96 0,33 0,051 1,3	11 5,6 3,3 <u>0,29</u> 4,5	0 15 28 44 44	S22-01156 LOQ: 0.01 mg/kg folpet (grain and straw), phthalimide (grain) 0.05 mg/kg phthalimide (straw) <u>Maximum storage:</u> Grain: 336 days W.plant: 378 days Straw: 346 days

- (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 2.1.4 Magnitude of residues in livestock

No further study submitted and no data required.

A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.1.5.1 Distribution of the residue in peel/pulp

Not relevant.

A 2.1.5.2 Processing studies on a core set of representative processes

A 2.1.5.2.1 Study 1

Comments of zRMS:	The study was evaluated by zRMS-Greece in RR of SAP50SCF (December 2023). The study is considered acceptable.
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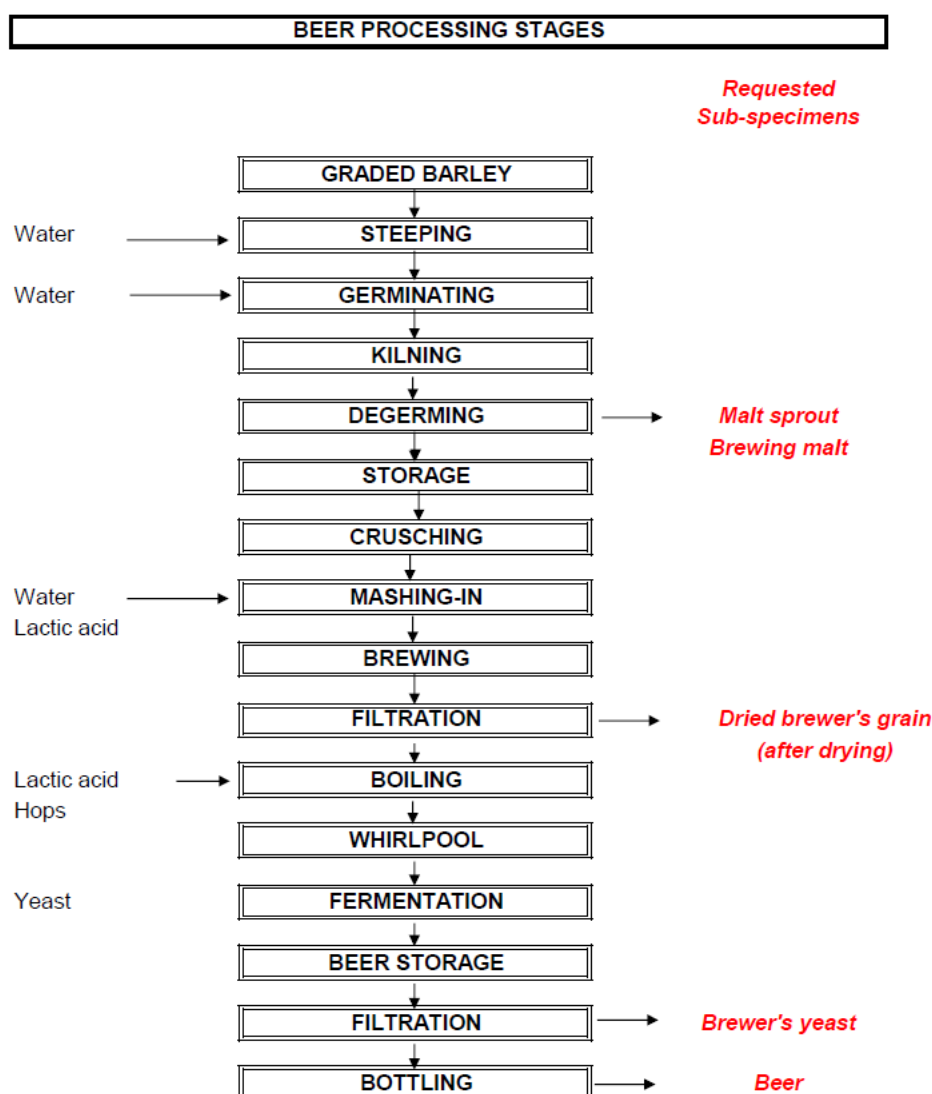
Reference:	KCP 7.2.5/01
Report	Magnitude of the residue of folpet in processed fractions of barley after two applications of SAP50SCF (Folpet 500 g/L, SC) in Northern and Southern Europe - 2021, C. MILHAN, 2021, CMN-21-48321 (processing phase)
Guideline(s):	Processing studies (SANCO 7035/VI/95 rev.5, 22 July 1997). OECD Guideline for the Testing of Chemicals: Nature of the Pesticide Residues in Processed Commodities - High Temperature Hydrolysis (TG 507 published on 16 October 2007). OECD Guideline for the Testing of Chemicals: Magnitude of pesticide residues in Processed Commodities (TG 508 published on 3 October 2008).
Deviations:	No impact.
GLP:	Yes
Acceptability:	Yes

MATERIALS AND METHODS

A follow up study was performed on the processing of barley grains to malt sprout, brewing mal, dried brewer's grain, brewer's yeast and beer. In three trials in Poland (21-00139-01; KCP 6.3.1/04), Northern (21-00139-02; KCP 6.3.1/04) and Southern France (21-00157-03; KCP 6.3.1/03), barley crops were sprayed with folpet (500 g/L) with one application of 3000 g a.s./ha (under trials 21-00139-01, 21-00139-02 and 21-00157-03). However, samples from the trial 21-00157-03 were lost because sub-specimens were thawed during storage.

Samples were processed to malt sprout, brewing mal, dried brewer's grain, brewer's yeast and beer shown in **Figure A 2.1.5.2.1-1**. The processing phase was done according to technological procedures in a laboratory scale. All processes were comparable to the processes used for commercial or household productions of the goods produced within this study.

Figure A 2.1.5.2.1-1 Processing flowchart for barley brewing process



CONCLUSION

The following fractions were sampled: grain, homogenized barley grains, brewing malt, homogenized brewing malt, malt sprout, homogenized malt sprout, dried brewers grains, Homogenized dried brewers grain, brewer's yeast and beer. Those samples were analysed for residues in study S22-04739.

A 2.1.5.2.2 Study 2

Comments of zRMS:	The study was evaluated by zRMS-Greece in RR of SAP50SCF (December 2023). The study is considered acceptable.
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Reference:

KCP 7.2.5/02

Report

Study on the residue behaviour of folpet and its metabolites in processed fractions of barley after one application of SAP50SCF (Folpet 500 g/l) in Northern Europe – 2021. S. Jooss, 2022. Report No: S22-04739

Guideline(s):

Commission Regulation (EU) No 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009
SANTE/2020/12830, Rev1 Guidance document on pesticide analytical methods for risk assessment and post-approval control and monitoring purposes. 24/02/2021

OECD Series on Testing and Assessment, Number 72. OECD
ENV/JM/MONO(2007)17

Deviations: No deviation with impact on quality and integrity of the study.
GLP: Yes
Acceptability: Yes

MATERIALS AND METHODS

All samples were received at the test facility in frozen condition. After their arrival at the test facility the samples were stored at $\leq -18^{\circ}\text{C}$ with no exceedance until homogenisation. Samples of barley grain, brewing malt, malt sprouts and dried brewers grain were received homogenized. Samples of brewer's yeast and beer were used without homogenization.

The water content of the matrices was determined using a Sartorius MA150 moisture analyser and representative specimens as follows:

Matrix (specimen)	Water Content (Weight %)	Matrix	Water Content (Weight %)
Barley Grain (CMN-21-48321-001H)	11.46	Dried Brewers Grain (CMN-21-48321-017H)	1.50*
Brewing Malt (CMN-21-48321-005H)	2.37*	Brewer's Yeast (CMN-21-48321-01H)	92.30*
Malt Sprouts (CMN-21-48321-009H)	2.93*	Beer	92**

*mean of three determinations. **water content taken from a food database

Extraction of Folpet from Processed Fractions of Barley: Samples of barley grain, brewing malt, malt sprouts, dried brewers grain, brewer's yeast and beer extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed by dispersive SPE with PSA and magnesium sulfate). Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Extraction of Phthalimide from Processed Fractions of Barley: For phthalimide, samples of barley grain, brewing malt, malt sprouts, dried brewers grain, brewer's yeast and beer were extracted with acetonitrile containing 1% of formic acid and water was added. Isotopically labelled internal standard (addition of internal standard must be adjusted to the necessary dilution) was added to the raw extract before clean-up. Clean-up was carried out by partition into acetonitrile (addition of citrate salts, magnesium sulfate and sodium chloride) followed concentration and dilution in water containing 0.1% of acetic acid. Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.01 mg/kg for each matrix, except cereal straw, with a limit of detection (LOD) set at 0.003 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ). For cereal straw, the LOQ was 0.05 mg/kg and the LOD was 0.015 mg/kg.

Extraction of Phthalic Acid from Processed Fractions of Barley: Samples of barley grain, brewing malt, malt sprouts, dried brewers grain, brewer's yeast and beer were extracted with acetonitrile containing 1% of formic acid and if necessary, after addition of water. Isotopically labelled internal standard was added to the raw extract before clean-up. Addition of internal standard amount must be adjusted depending on the residue level obtained within the samples if residues are higher.

Clean-up was carried out by partition into acetonitrile (addition of magnesium sulfate and sodium chloride). Quantification was performed by use of LC-MS/MS with an isotopically labelled internal standard.

The limit of quantification (LOQ) of the analytical method was 0.05 mg/kg for each matrix with a limit of detection (LOD) set at 0.015 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Extraction of Phthalamic Acid from Processed Fractions of Barley: Samples of barley grain, brewing malt, malt sprouts, dried brewers grain, brewer's yeast and beer were extracted with (water containing 0.1% of ammonium carbonate)/methanol (4/1, v/v). Clean-up was carried out by centrifugation and filtration using a syringe filter. Quantification was performed by use of LC-MS/MS with matrix-matched standards.

The limit of quantification (LOQ) of the analytical method was 0.05 mg/kg for each matrix with a limit of detection (LOD) set at 0.015 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

RESULTS AND DISCUSSIONS

Processing factors were calculated by dividing the residue found in the respective sample by the initial residue in the raw agricultural commodity. A summary of the residues found in the processed samples is given in **Table A-7**.

Table A -7 Residue data from barley grain processing study with folpet

RAC	Residues in RAC (unwashed sample, mg/kg)	PHI [days]	Processed commodity	Residue [mg/kg]	PF*	Comments/ Reference
Barley grain	1,8	41	Brewing malt	0,057	0,032	21-00139-01
Barley grain	1,8	40	Brewing malt	0,043	0,024	21-00139-02
Barley grain	1,8	41	Malt sprout	0,29	0,161	21-00139-01
Barley grain	1,8	40	Malt sprout	0,16	0,089	21-00139-02
Barley grain	1,8	41	Dried brewer's grain	0,039	0,022	21-00139-01
Barley grain	1,8	40	Dried brewer's grain	0,037	0,021	21-00139-02
Barley grain	1,8	41	Brewing yeast	<0.03	<0.02	21-00139-01
Barley grain	1,8	40	Brewing yeast	<0.03	<0.02	21-00139-02
Barley grain	1,8	41	Beer	<0.03	<0.02	21-00139-01
Barley grain	1,8	40	Beer	<0.03	<0.02	21-00139-02

* processing factor

CONCLUSION

Residues of active substance were found not to concentrate in consumable fractions after processing. Processing factors for all fractions varying between 0.02 and 0.161.

A 2.1.6 Magnitude of residues in representative succeeding crops


No study submitted and no further data required.

A 2.1.7 Other/Special Studies

No study submitted and no further data required.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations

 European Food Safety Authority EFSA PRIMo revision 3.1; 2019/03/19		Folpet				Input values					
		LOQs (mg/kg) range from:		0,03	to:		0,15				
		Toxicological reference values									
		ADI (mg/kg bw/day):		0,1		ARID (mg/kg bw):		0,2			
		Source of ADI:				Source of ARID:					
Year of evaluation:				Year of evaluation:							
Comments:											
Normal mode											
Chronic risk assessment: JMPR methodology (IEDI/TMDI)											
		No of diets exceeding the ADI : ---								Exposure resulting from	
TMDI(NED)/IEDI calculation (based on average food consumption)	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)
	59%	PT general	58,92	50%	Wine grapes	4%	Tomatoes	2%	Table grapes	0,6%	2%
	52%	FR adult	51,99	46%	Wine grapes	2%	Tomatoes	0,9%	Wheat	0,6%	0,9%
	48%	RO general	48,43	34%	Wine grapes	10%	Tomatoes	2%	Wheat	1%	2%
	42%	GEMS/Food G07	42,35	30%	Wine grapes	5%	Tomatoes	2%	Table grapes	1%	3%
	35%	GEMS/Food G08	34,64	21%	Wine grapes	6%	Tomatoes	2%	Table grapes	1%	3%
	34%	GEMS/Food G15	34,35	20%	Wine grapes	6%	Tomatoes	2%	Table grapes	1%	3%
	33%	GEMS/Food G11	33,14	20%	Wine grapes	5%	Tomatoes	3%	Table grapes	2%	3%
	33%	IE adult	32,56	25%	Wine grapes	2%	Tomatoes	2%	Table grapes	1%	0,9%
	31%	GEMS/Food G06	31,11	18%	Tomatoes	6%	Table grapes	3%	Wheat	1%	3%
	29%	DE general	28,68	17%	Wine grapes	3%	Tomatoes	3%	HOPS (dried)	1%	2%
	28%	UK adult	28,38	22%	Wine grapes	3%	HOPS (dried)	2%	Tomatoes	0,4%	0,7%
	28%	NL toddler	27,82	9%	Table grapes	5%	Tomatoes	3%	Apples	5%	2%
	27%	DE women 14-50 yr	27,20	17%	Wine grapes	4%	Tomatoes	2%	Table grapes	1%	1%
	25%	DK adult	24,65	19%	Wine grapes	3%	Tomatoes	1%	Table grapes	0,5%	0,4%
	24%	DE child	23,99	8%	Table grapes	5%	Tomatoes	4%	Apples	2%	2%
	23%	UK vegetarian	23,06	16%	Wine grapes	3%	Tomatoes	1%	HOPS (dried)	0,5%	0,9%
	23%	GEMS/Food G10	22,91	8%	Wine grapes	7%	Tomatoes	2%	Table grapes	1%	3%
	19%	FR child 3 15 yr	19,47	7%	Wine grapes	4%	Tomatoes	2%	Table grapes	2%	2%
	19%	NL general	18,82	12%	Wine grapes	2%	Tomatoes	2%	Table grapes	1%	1%
	17%	NL child	17,01	6%	Table grapes	3%	Tomatoes	2%	Apples	2%	2%
	16%	ES adult	15,87	8%	Wine grapes	4%	Tomatoes	1,0%	Barley	0,7%	2%
	13%	FR toddler 2 3 yr	12,52	5%	Wine grapes	2%	Tomatoes	1%	Milk: Cattle	2%	1%
	12%	IT toddler	11,75	7%	Tomatoes	3%	Wheat	0,6%	Table grapes	0,3%	3%
	12%	FI adult	11,68	6%	Wine grapes	3%	Tomatoes	0,7%	Strawberries	0,7%	0,2%
	11%	DK child	10,91	3%	Tomatoes	2%	Wheat	2%	Rye	1%	2%
	10%	UK toddler	10,13	3%	Tomatoes	2%	Wheat	1%	Table grapes	2%	2%
	9%	ES child	9,36	5%	Tomatoes	2%	Wheat	0,6%	Milk: Cattle	1%	2%
	9%	IT adult	9,13	6%	Tomatoes	2%	Wheat	0,8%	Table grapes	0,2%	2%
	9%	FI 3 yr	8,87	3%	Tomatoes	2%	Strawberries	1%	Table grapes	0,6%	0,6%
	8%	UK infant	8,24	2%	Milk: Cattle	2%	Tomatoes	1%	Strawberries	3%	1%
	8%	SE general	7,91	4%	Tomatoes	1%	Wheat	0,8%	Strawberries	1%	1%
	7%	PL general	7,42	4%	Tomatoes	2%	Table grapes	0,6%	Apples	0,3%	
	7%	FI 6 yr	6,69	2%	Tomatoes	1%	Strawberries	1%	Table grapes	0,5%	0,5%
	6%	LT adult	5,59	3%	Tomatoes	0,6%	Apples	0,4%	Wheat	0,6%	0,5%
	4%	FR infant	4,18	0,9%	Strawberries	0,8%	Milk: Cattle	0,8%	Wine grapes	1%	0,3%
	2%	IE child	1,63	0,5%	Wheat	0,3%	Table grapes	0,3%	Tomatoes	0,3%	0,5%
Conclusion: The estimated long-term dietary intake (TMDI/NED/IEDI) was below the ADI. The long-term intake of residues of Folpet is unlikely to present a public health concern.											

A 3.2 IEDI calculations

Not required.

A 3.3 IESTI calculations - Raw commodities

Unprocessed commodities	Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI):				Results for adults No. of commodities for which ARfD/ADI is exceeded (IESTI):			
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	IESTI				IESTI			
	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	6%	Barley	2 / 2	11	5%	Barley	2 / 2	9,7
	3%	Wheat	0,4 / 0,4	5,8	2%	Wheat	0,4 / 0,4	3,4
Expand/collapse list								
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)								

A 3.4 IESTI calculations - Processed commodities

Processed commodities	Results for children				Results for adults			
	No of processed commodities for which ARfD/ADI is exceeded (IESTI):				No of processed commodities for which ARfD/ADI is exceeded (IESTI):			
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	IESTI				IESTI			
	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	4%	Barley / cooked	2 / 2	7,3	0,9%	Wheat / bread/pizza	0,4 / 0,4	1,8
	2%	Wheat / milling (flour)	0,4 / 0,4	4,8	0,8%	Wheat / pasta	0,4 / 0,4	1,5
	2%	Barley / milling (flour)	2 / 2	3,6	0,7%	Wheat / bread (wholemeal)	0,4 / 0,4	1,4
	1%	Wheat / milling (wholemeal)-I	0,4 / 0,4	2,2	0,2%	Barley / beer	2 / 0,01	0,43