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Modification of the existing maximum residue levels for folpet in apples and pears

European Food Safety Authority (EFSA),
Alba Brancato, Daniela Brocca, Chloe De Lentdecker, Zoltan Erdos, Lucien Ferreira, Luna Greco, Samira Jarrah, Dimitra Kardassi, Renata Leuschner, Christopher Lythgo, Paula Medina, Ileana Miron, Tunde Molnar, Alexandre Nougadere, Ragnor Pedersen, Hermine Reich, Angela Sacchi, Miguel Santos, Alois Stanek, Juergen Sturma, Jose Tarazona, Anne Theobald, Benedicte Vagenende, Alessia Verani and Laura Villamar-Bouza

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Belchim Crop Protection NV/SA submitted a request to the competent national authority in France to modify the existing maximum residue levels (MRL) for the active substance folpet in apples and pears. The data submitted in support of the request were found to be sufficient to derive MRL proposals for these two crops. Appropriate analytical methods allowing monitoring the proposed MRLs are available. Based on the risk assessment results, EFSA concluded that the short-term and long-term intakes of residues resulting from the intended uses of folpet according to the reported agricultural practice are unlikely to present a risk to consumers' health.

Keywords: folpet, phthalimide, apples, pears, pesticide, MRL, consumer risk assessment

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Correspondence: pesticides.mrl@efsa.europa.eu

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Belchim Crop Protection NV/SA submitted an application to the competent national authority in France (evaluating Member State (EMS)), to modify the existing maximum residue levels (MRL) for the active substance folpet in apples and pears. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA). To accommodate for the intended uses of folpet, the EMS proposed to raise the existing MRLs from the limit of quantification (LOQ) to 0.3 mg/kg.

EFSA based its assessment on the revised evaluation report submitted by the EMS, the draft assessment report (DAR) and its addenda prepared under Directive 91/414/EEC, the Commission review report on folpet, the conclusion on the peer review of the pesticide risk assessment of the active substance folpet as well as the conclusions from previous EFSA reasoned opinions on folpet.

The metabolism of folpet in primary crops was investigated following foliar applications in crops belonging to the groups of fruit crops and cereals and following soil application in root and tuber vegetables. Studies investigating the effect of processing on the nature of folpet (hydrolysis studies) demonstrated that the active substance is not stable. Folpet degraded completely to phthalimide and phthalic acid, observed also in primary plant metabolism. As the proposed uses of folpet are on permanent crops, investigations of residues in rotational crops are not required.

Based on the metabolic pattern identified in metabolism studies, hydrolysis studies and the toxicological significance of metabolites, the residue definitions for enforcement and risk assessment in plants and processed products were proposed as the sum of folpet and phthalimide, expressed as folpet.

EFSA concluded that for the crops assessed in this application, metabolism of folpet in fruits and the possible degradation in processed products have been sufficiently addressed and that the previously derived residue definitions are applicable.

Sufficiently validated analytical methods are available to quantify residues in the crops assessed in this application according to the enforcement residue definition. The methods enable quantification of residues at or above 0.05 mg/kg for folpet and at or above 0.02 mg/kg for phthalimide.

The available residue trials were sufficient to derive a MRL proposal of 0.3 mg/kg for the intended uses on apples and, by extrapolation, on pears. According to the assessment of the EMS, the residue trials were supported by validated analytical methods and acceptable as per storage stability.

Processing factors (PF) for apple processed products were derived from the processing studies submitted and are recommended to be included in Annex VI of Regulation (EC) No 396/2005:

- apple, juice: PF < 0.75
- apple, puree: PF 0.75
- apple, canned: PF < 0.75

Apple by-product wet pomace is used as a feed product in the diet of ruminants. Hence, a potential carry-over into food of animal origin was assessed. The calculated livestock dietary burden exceeded the trigger value of 0.1 mg/kg dry matter (DM) for all relevant species. However, the contribution of folpet residues in apple pomace to the total livestock exposure from existing uses was insignificant. Therefore, a modification of the existing MRLs for commodities of bovine, sheep and goat was not considered necessary.

The toxicological profile of folpet was assessed in the framework of the European Union (EU) pesticides peer review and the data were sufficient to derive an acceptable daily intake (ADI) of 0.1 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.2 mg/kg bw. The toxicological reference values of the parent apply to the metabolite phthalimide for the consumer risk assessment.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). For the long-term exposure, the intended uses under assessment and the authorised uses of folpet previously assessed by EFSA were considered. The short-term risk assessment was performed only with regard to the crops under consideration.

EFSA concluded that the proposed uses of folpet on apples and pears will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a risk to consumers' health. EFSA proposes to amend the existing MRLs as reported in the summary table below.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Folpet (sum of folpet and phthalimide, expressed as folpet)[(R)]				
0130010	Apples	0.03*	0.3	NEU/SEU uses supported. Unlikely to pose a consumers' health risk
0130020	Pears	0.03*	0.3	NEU/SEU uses supported by extrapolation from data on apples. Unlikely to pose a consumers' health risk

NEU: northern Europe; SEU: southern Europe; MRL: maximum residue level.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(R): The residue definition differs for the following combinations pesticide-code number: code 1000000 except 1040000: Phthalimide, expressed as folpet.

It is noted that the need for a confirmatory method and independent laboratory validation (ILV) for the determination of phthalimide in high water content commodities was identified in the framework of the MRL review under Article 12 of Regulation (EC) No 396/2005. This data gap has been addressed with this application.

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Background

Regulation (EC) No 396/2005[1] (hereinafter referred to as 'the MRL regulation') establishes the rules governing the setting of pesticide maximum residue levels (MRLs) at European Union (EU) level. Article 6 of the MRL regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC[2], repealed by Regulation (EC) No 1107/2009[3], shall submit an application to a Member State to modify a MRL in accordance with the provisions of Article 7 of the MRL regulation.

The applicant Belchim Crop Protection NV/SA[4] submitted an application to the competent national authority in France, hereafter referred to as the evaluating Member State (EMS), to modify the existing MRLs for the active substance folpet in apples and pears. This application was notified to the European Commission and the European Food Safety Authority (EFSA) and was subsequently evaluated by the EMS in accordance with Article 8 of the MRL regulation.

The EMS summarised the data provided by the applicant in an evaluation report which was submitted to the European Commission and forwarded to EFSA on 15 December 2016. The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2016-00851 and the following subject:

Folpet: MRLs in apples and pears

France proposed to raise the existing MRLs of folpet in apples and pears from the limit of quantification (LOQ) to 0.3 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps or points which needed further clarification, which were requested from the EMS. On June 2017, the EMS submitted the reply in a revised evaluation report (France, 2017), which replaced the previously submitted evaluation report.

Terms of Reference

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall assess the application and the evaluation report and give a reasoned opinion on the risks to the consumer and where relevant to animals associated with the setting of the requested MRLs. The opinion shall include:

- an assessment of whether the analytical method for routine monitoring proposed in the application is appropriate for the intended control purposes;
- the anticipated LOQ for the pesticide/product combination;
- an assessment of the risks of the acceptable daily intake (ADI) and acute reference dose (ARfD) being exceeded as a result of the modification of the MRL;
- the contribution to the intake due to the residues in the product for which the MRLs was requested;
- any other element relevant to the risk assessment.

In accordance with Article 11 of the MRL regulation, EFSA shall give its reasoned opinion as soon as possible and at the latest within 3 months from the date of receipt of the application.

The evaluation report submitted by the EMS (France, 2017) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion. Furthermore, a screenshot of the report sheet of the PRIMo is presented in Appendix C.

The active substance and its use pattern

The detailed description of the intended uses of folpet, which are the basis for the current MRL application, is reported in Appendix A.

[1] Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

[2] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

[4] Belchim Crop Protection NV/SA, Technologielaan, B-1840, Londerzeel, Belgium.

Folpet is the ISO common name for *N*-(trichloromethylthio) phthalimide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Folpet was evaluated in the framework of Directive 91/414/EEC with Italy designated as rapporteur Member State (RMS) for the representative uses as foliar applications to winter wheat, tomatoes and wine grapes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2009). The process of renewal of the first approval has not yet been initiated.

Folpet was approved[5] for the use as fungicide only on 1 October 2007.

The EU MRLs for folpet are established in Annexes II of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2014) and the proposed modifications have been implemented in the MRL legislation.[6]

Assessment

EFSA has based its assessment on the revised evaluation report submitted by the EMS (France, 2017), the DAR and its addenda prepared under Directive 91/414/EEC (Italy, 2004, 2005, 2008), the European Commission review report on folpet (European Commission, 2008), the conclusion on the peer review of the pesticide risk assessment of the active substance folpet (EFSA, 2009) as well as the conclusions from previous EFSA reasoned opinions on folpet (EFSA, 2011, 2014).

For this application, the data requirements established in Regulation (EU) No 544/2011[7] and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a–g, 2000, 2010a,b, 2016; OECD, 2011, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011.[8]

A selected list of end points of the studies assessed by EFSA in the framework of the MRL review, including the end points of studies submitted in support of the current MRL application, are presented in Appendix B.

1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of folpet in primary crops belonging to the group of fruit crops, root crops and cereals/grass 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.

For the intended uses on apples and pears, the metabolic behaviour in primary crops is sufficiently addressed.

1.1.2. Nature of residues in rotational crops

As the proposed uses of folpet are on permanent crops, investigations of residues in rotational crops are not required.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of folpet residues was assessed in previous EFSA reasoned opinions (EFSA, 2011, 2014). Folpet was shown to degrade completely under the representative processing conditions into phthalimide and phthalic acid.

[5] Commission Directive 2007/5/EC of 7 February 2007 amending Council Directive 91/414/EEC to include captan, folpet, formetanate and methiocarb as active substances. OJ L 35, 8.2.2007, p. 11–17.

[6] Commission Regulation (EU) 2016/156 of 18 January 2016 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for boscalid, clothianidin, thiamethoxam, folpet and tolclofos-methyl in or on certain products. OJ L 31, 6.2.2016, p. 1–44.

[7] Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.

[8] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.

1.1.4. Methods of analysis in plants

The MRL review concluded that folpet and phthalimide can be enforced in the group of high water content commodities, to which apples and pears belong, at the LOQ of 0.05 mg/kg per each analyte, but a confirmatory method and an independent laboratory validation (ILV) were not available and were requested for the determination of phthalimide residues (EFSA, 2014). This data gap has been addressed in the framework of this application.

The applicant submitted additional analytical methods for the determination of folpet and phthalimide residues in high water content commodities (tomatoes) (France, 2017). A gas chromatography with mass spectrometry (GC–MS) method with a LOQ of 0.02 mg/kg was assessed and found to be acceptable for the determination of phthalimide but was not sufficiently specific for folpet residues. Confirmation of residues of folpet and phthalimide in tomato extracts by high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) was provided. The primary method was validated per each analyte, but confirmation was conducted at the lower fortification level only (LOQ of 0.01 mg/kg). The deviation can be considered acceptable as the ILV was performed with the same analytical method at both fortification levels (1X and 10X LOQ).

1.1.5. Stability of residues in plants

The storage stability of folpet and phthalimide in high water content commodities (tomatoes) was assessed in the MRL review (EFSA, 2014). New freezer storage stability data in apple raw fruits and processed products were provided in the framework of the current MRL application. Both compounds showed to be stable for the 12-month period investigated in the study (France, 2017).

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in primary crops and in processed commodities, the following residue definitions were proposed for plant and processed products:

- residue definition for risk assessment: sum of folpet and phthalimide, expressed as folpet;
- residue definition for enforcement: sum of folpet and phthalimide, expressed as folpet.

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical with the above-mentioned residue definition.

For the intended uses on apple and pears, these residue definitions are appropriate and applicable.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the MRL application, the applicant submitted the results of supervised residue trials on apples. The trials were conducted in northern (8 trials) and southern (8 trials) Europe over two seasons according to the intended Good Agricultural Practices (GAPs). The proposed extrapolation of results from apples to pears is acceptable (European Commission, 2016).

The samples were analysed for the parent compound and the metabolite phthalimide, which is included in the residue definition for enforcement and risk assessment. According to the assessment of the EMS, the residue trials were supported by validated analytical methods and acceptable as per storage stability.

1.2.2. Magnitude of residues in rotational crops

Apples and pears are permanent crops, and therefore, the possible transfer of residues of folpet, phthalimide and any relevant soil metabolite to crops that are grown in crop rotation does not need to be investigated.

1.2.3. Magnitude of residues in processed commodities

Three follow-up processing studies investigating the magnitude of residues in processed apple products were assessed in this MRL application. The samples for processing were taken from the supervised residue trials and analysed for folpet and phthalimide residues. The results showed a reduction of residues in juice, puree and canned apples (residues $\leq$ LOQ of 0.02 mg/kg for folpet and for phthalimide) and a concentration in wet pomace. A balance study was not provided. Nevertheless, further investigations are not required as they are not expected to affect the outcome of the risk assessment.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for the intended northern Europe (NEU) and southern Europe (SEU) uses on apples and pears based on the more critical residue situation in SEU (see Appendix B.1.2.1). In Section 3, EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumers' health risk.

2. Residues in livestock

Apple by-product wet pomace may be used for feed purpose in the diet of ruminants. Hence, it was necessary to estimate whether the intended use of folpet on apples would have an impact on the residues expected in food of animal origin.

EFSA calculated the livestock dietary burden according to the feeding tables listed in the OECD guidance (OECD, 2013) using the supervised trials median residue (STMR)/highest residue (HR) retrieved from the MRL review and updated the intake with the STMR derived for apple multiplied by the processing factor (PF) to estimate the residue in wet pomace. In the absence of specific PFs, default PFs were used for cereal and potato by-products.

The recalculated livestock dietary burden still exceeded the trigger value of 0.1 mg/kg dry matter (DM) for all relevant species. Nevertheless, residues in apple wet pomace are not expected to contribute significantly to the current dietary burden in cattle and sheep, which is mainly driven by potato process waste (see Appendix B.2). Therefore, there is no need to modify the existing MRLs in tissues and milk from bovine, sheep and goats set at the LOQ of 0.05 mg/kg.

The input values for the exposure calculations for livestock are presented in Appendix D.1. The results of the dietary burden calculation are presented in Section B.2.

3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different subgroups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016).

The toxicological reference values for folpet used in the risk assessment (i.e. ADI and ARfD values) were derived in the framework of the EU pesticides peer review (European Commission, 2008). The toxicological end points of the parent apply to phthalimide (EFSA, 2009).

3.1. Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed for the commodities assessed in this application using the HR derived from supervised field trials which can be found in Appendix D.2.

The short-term exposure did not exceed the ARfD for any of the two crops assessed in this application (see Appendix B.3).

3.2. Long-term (chronic) dietary risk assessment

In the framework of the MRL review, a comprehensive long-term exposure assessment was performed taking into account the existing uses at EU level (EFSA, 2014). EFSA updated the calculation with the STMR values derived for apples and pears from the residue trials submitted in support of this MRL application. The input values used in the exposure calculations are summarised in Appendix D.2.

The estimated long-term dietary intake was in the range of 1–22.4% of the ADI. The contribution of residues expected in the commodities assessed in this application to the overall long-term exposure is presented in more detail in Appendix B.3.

EFSA concluded that the long-term intake of residues of folpet resulting from the existing and the intended uses is unlikely to present a risk to consumers' health.

Conclusions and recommendations

The data submitted in support of this MRL application were found to be sufficient to derive a MRL proposal of 0.3 mg/kg for apples and pears.

Adequate analytical methods for enforcement are available to control the residues of folpet in high water content matrices according to the residue definition for enforcement.

Based on the risk assessment results, EFSA concluded that the short-term and long-term intakes of residues resulting from the uses of folpet according to the reported agricultural practices are unlikely to present a risk to consumers' health.

The MRL recommendations are summarised in Appendix B.4.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement to risk assessment residue definition
DALA	days after last application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
dw	dry weight
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GC-MS	gas chromatography with mass spectrometry
HPLC–MS/MS	high performance liquid chromatography with tandem mass spectrometry
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
LOQ	limit of quantification
MRL	maximum residue level
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant-back interval
PF	processing factor
PHI	preharvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
RA	risk assessment
RD	residue definition
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SEU	southern Europe
SMILES	simplified molecular-input line-entry system
STMR	supervised trials median residue
WG	water-dispersible granule

Appendix A – Summary of intended GAPs triggering the amendment of existing EU MRLs

Crop and/or situation	NEU, SEU, MS or country	F G or I[a]	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment			PHI (days)[d]	Remarks
				Type[b]	Conc. a.s.	Method kind	Range of growth stages & season[c]	Number min–max	Interval between application (min)	g a.s./hL min–max	Water L/ha min–max	g a.s./ha min–max		
Apple, Pear	NEU	F	Fungi	WG	800 g/kg	Foliar spray	When first symptoms occur	7	7	150	1,000	1,500	120	Fourth application at BBCH 69-73
Apple, Pear	SEU	F	Fungi	WG	800 g/kg	Foliar spray	When first symptoms occur	7	7	150	1,000	1,500	95	Fourth application at BBCH 69-73

GAP: Good Agricultural Practice; NEU: northern European; SEU: southern European; MS: Member State; a.s.: active substance; WG: water-dispersible granule.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI: minimum preharvest interval.

Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

Primary crops (available studies)	**Crop groups**	**Crops**	**Applications**	**Sampling**
	Fruit crops	Grapes	Foliar, 3 × 1.5 kg/ha, interval 30 days	23 DALA
		Avocados	Foliar, 3 × 3.36 kg/ha, interval 21 days	21, 97 DALA
		Tomatoes	Soil, 1 × 0.1 mg/roots	1, 4, 7, 11 DAT
	Root crops	Potatoes	Foliar, 5 × 2 kg/ha, interval not reported	2–4 h DAT_1, 2–4 h DAT_2, 2–4 h DAT_3, 4, 7 DALA
	Cereals/grass	Wheat	Foliar, 2 × 1.6 kg/ha, interval 24 days	1 DAT_1, 1, 43, 81 DALA
	Active radiolabelled substance: Phenyl-UL-^{14}C (foliar); Carbonyl-^{14}C (soil) folpet. Reference: Italy, 2004; EFSA, 2014			
Rotational crops (available studies)	**Crop groups**	**Crops**	**Applications**	**PBI**
	Not triggered. Reference: EFSA, 2014			
Processed commodities (hydrolysis study)	**Conditions**	**Investigated?**		
	Pasteurisation (20 min, 90°C, pH 4)	Yes		
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes		
	Sterilisation (20 min, 120°C, pH 6)	Yes		
	Active radiolabelled substance: U-phenyl -^{14}C-folpet Comments: Folpet completely degraded predominantly to phthalimide, (pasteurisation: 92% AR; baking, brewing/boiling: 58% AR) with levels of phthalic acid increasing with temperature and pH (baking, brewing/boiling: 42.2% AR; sterilisation 81% AR) Reference: Austria, 2010; EFSA, 2011			

DALA: days after last application; DAT: days after treatment; PBI: plant-back interval; AR: applied radioactivity.

Can a general residue definition be proposed for primary crops?	Yes
Rotational crop and primary crop metabolism similar?	Not applicable (permanent crops)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring (RD-Mo)	Folpet (sum of folpet and phthalimide, expressed as folpet)
Plant residue definition for risk assessment (RD-RA)	Folpet (sum of folpet and phthalimide, expressed as folpet)
Conversion factor (monitoring to risk assessment)	N/A
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	Matrices with high water content: Folpet: GC–MS, LOQ 0.05 mg/kg. Confirmatory method and ILV available (EFSA, 2014)
	Phthalimide: GC–MS, LOQ 0.05 mg/kg (EFSA, 2014); GC-MS, LOQ 0.02 mg/kg. Confirmatory method and ILV available (France, 2017).

B.1.1.2. Stability of residues in plants

Plant products (available studies)	**Category**	**Commodity**	**T (°C)**	**Stability (Months)**
	Folpet			
	High water content	Tomatoes	−18	18
		Apples	−18	12
	Phthalimide			
	High water content	Tomatoes	−18	13
		Apples	−18	12
	Comment: Folpet and phthalimide stable over 12 months in apple juice, pomace, puree and canned apples Reference: EFSA, 2014; France, 2017			

B.1.2. Magnitude of residues in plants

B.1.2.1. Summary of residues data from the supervised residue trials

Crop (supervised trials)	Region/ Indoor[a]	Residue levels observed in the supervised residue trials[b] (mg/kg)	Comments (OECD calculations)	MRL proposals (mg/kg)	HR_{Mo}[c] (mg/kg)	$STMR_{Mo}$[d] (mg/kg)	CF[e]
Apples	NEU	3 × < 0.06; 2 × 0.06; 0.09; 0.10; 0.12	GAP compliant (± 25% rule). Extrapolation to pears	0.2	0.12	0.06	–
Apples	SEU	5 × < 0.06; 0.06; 0.08; 0.19	GAP compliant (± 25% rule). Extrapolation to pears	**0.3**	**0.19**	**0.06**	–

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level.
(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials.
(b): Mo: residue level according to the monitoring residue definition.
RA: residue level according to the residue definition for risk assessment. A conversion factor of 2 was used to express the concentrations of phthalimide as folpet equivalents (MW folpet/MW phthalimide = 296.546/147.133).
(c): Highest residue according to the residue definition for monitoring.
(d): Supervised trials median residue according to the residue definition for monitoring.
(e): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

B.1.2.2. Residues in succeeding crops

Confined rotational crop study (quantitative aspect)	N/A (permanent crops)
Field rotational crop study	N/A (permanent crops)

B.1.2.3. Processing factors

Processed commodity	Number of valid studies	Processing Factor (PF)		CF_P[(a)]
		Individual values	Median PF	
Apple, juice	3	< 0.43; < 0.75; < 1.00	< 0.75	–
Apple, puree	3	< 0.43; 0.75; < 1.00	0.75	–
Apple, canned	3	< 0.43; < 0.75; < 1.00	< 0.75	–
Apple, wet pomace	3	0.57; 1.83; 4.50	1.83	–

(a): Conversion factor for risk assessment in the processed commodity is the same as derived from the raw commodities.

B.2. Residues in livestock

Relevant groups	Dietary burden expressed in				Most critical subgroup[(a)]	Most critical commodity[(a)]	Trigger exceeded (Y/N)
	mg/kg bw per day		mg/kg DM				
	Median	Maximum	Median	Maximum			
Cattle (all)	0.206	0.288	7.00	9.14	Dairy cattle	Potato process waste	Y
Cattle (dairy only)	0.206	0.288	5.35	7.49	Dairy cattle	Potato process waste	Y
Sheep (all)	0.237	0.377	7.11	11.32	Ram/Ewe	Potato process waste	y
Sheep (ewe only)	0.237	0.377	7.11	11.32	Ram/Ewe	Potato process waste	Y
Swine (all)	0.084	0.084	3.62	3.62	Swine (breeding)	Potato process waste	Y
Poultry (all)	0.071	0.124	1.01	1.82	Poultry layer	Wheat straw	Y
Poultry (layer only)	0.060	0.124	0.87	1.82	Poultry layer	Wheat straw	Y

bw: body weight; DM: dry matter.
(a): Calculated for the maximum dietary burden.

B.2.1. Nature of residues and methods of analysis in livestock

Not relevant (a modification of existing MRLs in products of animal origin is not necessary).

B.2.2. Magnitude of residues in livestock

Not relevant.

B.3. Consumer risk assessment

ARfD	0.2 mg/kg bw (European Commission, 2008)
Highest IESTI, according to EFSA PRIMo	Apples: 9.3% of ARfD Pears: 8.7% of ARfD
Assumptions made for the calculations	The calculation is based on the highest residue levels in raw agricultural commodities that would be expected according to the intended uses.

ADI	0.1 mg/kg bw per day (European Commission, 2008)
Highest IEDI, according to EFSA PRIMo	22.4% ADI (French all population) Contribution of crops assessed: Apples: 0.72% of ADI Pears: 0.04% of ADI
Assumptions made for the calculations	The calculation is based on the median residue levels in raw agricultural commodities that would be expected according to the intended and authorised uses. The contributions of commodities where no use was reported or appropriately supported in the framework of the MRL review were not included in the calculation.

B.4. Recommended MRLs

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Folpet (sum of folpet and phthalimide, expressed as folpet)[(R)]				
0130010	Apples	0.03*	0.3	NEU/SEU uses supported. Unlikely to pose a consumers' health risk
0130020	Pears	0.03*	0.3	NEU/SEU uses supported by extrapolation from data on apples. Unlikely to pose a consumers' health risk

NEU: northern Europe; SEU: southern Europe; MRL: maximum residue level.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(R): The residue definition differs for the following combinations pesticide-code number: code 1000000 except 1040000: Phthalimide, expressed as folpet.

Appendix C – Pesticide Residue Intake Model (PRIMo)

Folpet			
Status of the active substance:	**Approved**	Code no.	
LOQ (mg/kg bw):		Proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw per day):	**0.1**	ARfD (mg/kg bw):	**0.2**
Source of ADI:	**COM**	Source of ARfD:	**COM**
Year of evaluation:	**2008**	Year of evaluation:	**2008**

MRLs according to Reg. (EU) No 2016/156 plus MRL proposal apples and pears.

Chronic risk assessment – refined calculations

	TMDI (range) in % of ADI minimum – maximum
	1 22
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	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	pTMRLs at LOQ (in % of ADI)
22.4	FR all population	21.1	Wine grapes	0.4	Wheat	0.3	Tomatoes	
15.3	PT General population	13.1	Wine grapes	0.6	Tomatoes	0.5	Potatoes	
14.3	WHO Cluster diet B	9.4	Wine grapes	2.2	Tomatoes	1.0	Wheat	
10.9	WHO cluster diet E	8.5	Wine grapes	0.5	Wheat	0.4	HOPS (dried),	
8.6	IE adult	6.6	Wine grapes	0.3	Strawberries	0.3	Table grapes	
8.3	DK adult	7.3	Wine grapes	0.3	Tomatoes	0.2	Wheat	
7.0	UK Adult	5.7	Wine grapes	0.5	HOPS (dried),	0.3	Tomatoes	
5.6	UK vegetarian	4.3	Wine grapes	0.4	Tomatoes	0.2	HOPS (dried),	
5.4	NL child	1.5	Milk and milk products: Cattle	0.9	Table grapes	0.6	Potatoes	
5.2	WHO Cluster diet F	3.1	Wine grapes	0.5	Tomatoes	0.4	Wheat	
5.2	NL general	3.3	Wine grapes	0.3	Milk and milk products: Cattle	0.3	Tomatoes	
5.2	DE child	1.5	Table grapes	0.7	Apples	0.7	Milk and milk products: Cattle	
4.6	WHO cluster diet D	1.9	Wine grapes	0.8	Wheat	0.7	Tomatoes	
3.8	ES adult	2.2	Wine grapes	0.5	Tomatoes	0.3	Wheat	
3.8	WHO regional European diet	1.2	Wine grapes	0.8	Tomatoes	0.4	Potatoes	
2.9	FR infant	1.3	Milk and milk products: Cattle	0.6	Strawberries	0.4	Potatoes	
2.8	FR toddler	0.8	Strawberries	0.5	Tomatoes	0.5	Potatoes	
2.7	ES child	0.7	Tomatoes	0.6	Milk and milk products: Cattle	0.5	Wheat	
2.3	SE general population 90th percentile	0.6	Milk and milk products: Cattle	0.5	Tomatoes	0.4	Potatoes	
2.3	FI adult	1.6	Wine grapes	0.3	Tomatoes	0.1	Potatoes	
2.2	IT kids/toddler	1.0	Tomatoes	0.8	Wheat	0.2	Strawberries	
2.1	UK Toddler	0.5	Wheat	0.4	Tomatoes	0.3	Potatoes	
1.8	DK child	0.7	Wheat	0.4	Tomatoes	0.2	Potatoes	
1.7	IT adult	0.8	Tomatoes	0.5	Wheat	0.2	Table grapes	
1.5	PL general population	0.6	Tomatoes	0.4	Table grapes	0.3	Potatoes	
1.4	UK Infant	0.3	Potatoes	0.3	Wheat	0.3	Strawberries	
1.4	LT adult	0.4	Tomatoes	0.3	Potatoes	0.2	Milk and milk products: Cattle	

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Folpet is unlikely to present a public health concern.

Acute risk assessment/children – refined calculations	Acute risk assessment/adults/general population – refined calculations

The acute risk assessment is based on the ARfD.

For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002); for lettuce, a variability factor of 5 was used.

In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variabilty factor of 3.

Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100% of the ARfD.

Unprocessed commodities

No of commodities for which ARfD/ADI is exceeded (IESTI 1): ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 1):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---		
IESTI 1	*)	**)	**IESTI 2**	*)	**)	**IESTI 1**	*)	**)	**IESTI 2**	*)	**)
Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
9.3	Apples	0.19 / -	6.9	Apples	0.19 / -	2.1	Apples	0.19 / -	1.8	Apples	0.19 / -
8.7	Pears	0.19 / -	6.2	Pears	0.19 / -	2.0	Pears	0.19 / -	1.6	Pears	0.19 / -
No of critical MRLs (IESTI 1)			---			**No of critical MRLs (IESTI 2)**			---		

Processed commodities

No of commodities for which ARfD/ADI is exceeded: ---				**No of commodities for which ARfD/ADI is exceeded:** ---			
		***)				***)	
Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	
0.4	Pear juice	0.045 / -		0.1	Apple juice	0.045 / -	

*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

**) pTMRL: provisional temporary MRL.

***) pTMRL: provisional temporary MRL for unprocessed commodity.

Conclusion:

For Folpet, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

For processed commodities, no exceedance of the ARfD/ADI was identified.

Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

Feed commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Folpet (sum of folpet and phthalimide, expressed as folpet)				
Barley straw	0.41	STMR (EFSA, 2014)	6.90	HR (EFSA, 2014)
Wheat straw	0.76	STMR (EFSA, 2014)	9.10	HR (EFSA, 2014)
Potato culls	0.10	LOQ (EFSA, 2014)	–	–
Barley grain	0.11	STMR (EFSA, 2014)	–	–
Wheat grain	0.12	STMR (EFSA, 2014)	–	–
Apple, wet pomace	0.11	STMR × PF (1.83)[a]	–	–
Brewers' grain	0.36	STMR (EFSA, 2014) × PF (3.3)[b]	–	–
Distiller's grain	0.40	STMR (EFSA, 2014) × PF (3.3)[b]	–	–
Potato, process waste	2.00	STMR (EFSA, 2014) × PF (20)[b]	–	–
Potato, dried pulp	3.80	STMR (EFSA, 2014) × PF (38)[b]	–	–
Wheat, gluten meal	0.22	STMR (EFSA, 2014) × PF (1.8)[b]	–	–
Wheat, milled by-products	0.84	STMR (EFSA, 2014) × PF (7.0)[b]	–	–

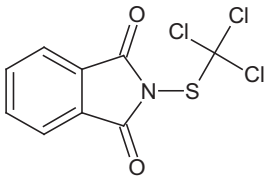
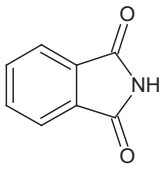
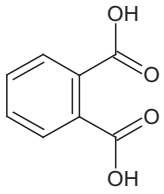
STMR: supervised trials median residue; LOQ: limit of quantification; HR: highest residue; PF: processing factor.
(a): For apple wet pomace, EMS used the highest (4.50) processing factor.
(b): For cereal and potato by-products, default processing factors were included in the calculation to consider the potential concentration of residues in these feed items.

D.2. Consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Apples	0.06	STMR	0.19	HR
Pears	0.06	STMR	0.19	HR
Table grapes	1.18	STMR (EFSA, 2014)		
Wine grapes	5.27	STMR (EFSA, 2014)		
Strawberries	1.30	STMR (EFSA, 2014)		
Table olives	0.15	LOQ (EFSA, 2014)		
Potatoes	0.10	LOQ (EFSA, 2014)		
Radishes	0.04	LOQ (EFSA, 2014)		
Salsifies	0.04	LOQ (EFSA, 2014)		
Tomatoes	0.70	STMR (EFSA, 2014)		
Melons	0.03	STMR (EFSA, 2014)		
Olives for oil production	0.15	LOQ (EFSA, 2014)		
Barley grain	0.11	STMR (EFSA, 2014)		
Wheat grain	0.12	STMR (EFSA, 2014)		
Hops	82.00	STMR (EFSA, 2014)		
Tissues from terrestrial animals[a]	0.05	LOQ (EFSA, 2014)		
Milk[a]	0.05	LOQ (EFSA, 2014)		
Birds eggs[a]	0.05	LOQ (EFSA, 2014)		

STMR: supervised trials median residue; LOQ: limit of quantification.
(a): The risk assessment residue definition in animal matrices is phthalimide, expressed as folpet.

Appendix E – Used compound codes

Code/trivial name	Chemical name/SMILES notation[a]	Structural formula[a]
Folpet	*N*-(trichloromethylthio)phthalimide ClC(Cl)(Cl)SN2C(=O)c1ccccc1C2=O	
Phthalimide	Phthalimide or 1*H*-isoindole-1,3(2*H*)-dione O=C1NC(=O)c2ccccc12	
Phthalic acid	phthalic acid or benzene-1,2-dicarboxylic acid OC(=O)c1ccccc1C(=O)O	

(a): ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs 2015 Release.