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Modification of the existing maximum residue levels for valifenalate in various crops

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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 Hungary to modify the existing maximum residue levels (MRLs) for the active substance valifenalate in various crops. The data submitted in support of the request were found to be sufficient to derive MRL proposals for lettuces, tomatoes, aubergines, onions, shallots and garlic. Adequate analytical methods for enforcement are available to control the residues of valifenalate on the commodities under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the long-term intake of residues resulting from the use of valifenalate according to the reported agricultural practices is unlikely to present a risk to consumer health. The short-term intake was not carried out since no acute reference dose (ARfD) is established for valifenalate. The reliable end points, appropriate for use in regulatory risk assessment are presented.

Keywords: valifenalate, lettuces, onions, tomatoes, pesticide, MRL, consumer risk assessment

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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 Hungary (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance valifenalate in lettuces and salad plants, spinaches and similar, watercresses, herbs and edible flowers, tomatoes and aubergines, onions, shallots and garlic. 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) on 25 January 2018. On 6 April 2018, following a request for further clarifications by EFSA, the EMS submitted a revised Evaluation Report, which replaced the previously submitted evaluation report, restricting the intended uses to lettuce, tomatoes, aubergines, onions, shallots and garlic. To accommodate for these intended uses of valifenalate, the EMS proposed to raise the existing MRLs from the limit of quantification (LOQ) 0.01 mg/kg to 8 mg/kg for lettuces; to raise the existing MRLs from the LOQ of 0.01 mg/kg to 0.5 mg/kg for onions, shallots and garlic; and finally to raise the existing MRLs from the LOQ of 0.01 mg/kg to 0.8 mg/kg for tomatoes and aubergines.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under previous MRL assessments and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of valifenalate following foliar spray application was investigated in crops belonging to the groups of fruit crops, root crops and leafy crops.

Based on the metabolic pattern depicted in the different crop categories, the residue definition for plant products was proposed as valifenalate for enforcement and risk assessment. EFSA concluded that for the crops assessed in this application, metabolism of valifenalate in primary crops has been sufficiently addressed and that the previously derived residue definitions are applicable.

Sufficiently validated analytical methods based on high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) 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 the LOQ of 0.01 mg/kg in the crops assessed.

The available residue trials are sufficient to derive MRL proposals of 8.0 mg/kg for lettuces, of 0.8 mg/kg for tomatoes and aubergines and of 0.5 mg/kg for onions, garlic and shallots.

Specific studies investigating the nature and magnitude of valifenalate residues in processed commodities are not required, as the total theoretical maximum daily intake (TMDI) is below the trigger value of 10% of the acceptable daily intake (ADI) for the crops under consideration.

The nature and magnitude of valifenalate residues in rotational crops were not investigated and is not required since soil degradation studies demonstrated a low persistence of valifenalate and its major metabolites IR-5839 and PCBA (4-chlorobenzoic acid) in soil (DT_{90} < 100 days).

Residues of valifenalate in commodities of animal origin were not assessed since the crops under consideration in this MRL application are normally not fed to livestock.

The toxicological profile of valifenalate was assessed in the framework of the European Union (EU) pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.07 mg/kg body weight (bw) per day. An acute reference was deemed unnecessary.

Consumer intake assessment was performed with revision 2 of the EFSA PRIMo. The existing MRLs as established in Regulation (EC) No 396/2005 and the supervised trials median residue (STMR) values as derived for the intended uses on lettuces, tomatoes, aubergines and onions, shallots and garlic were used as input values in the chronic exposure assessment. The acute intake assessment was not carried out since no acute reference dose (ARfD) is established for valifenalate. No chronic consumer intake concern was identified for any of the European diets as the calculated dietary intake accounted for a maximum of 9.7% of the ADI for the WHO Cluster diet B and the contribution of residues expected in the crops under consideration according to the intended uses to the overall long-term exposure is up to 6% of the ADI for lettuces. Consequently, EFSA concludes that the intended uses of valifenalate on lettuces, tomatoes, aubergines and onions, shallots and garlic are acceptable as they will not result in consumer health concerns.

EFSA proposes to amend the existing MRLs as reported in the summary table below.

Full details of all end points and the consumer risk assessment can be found in Appendices B–D.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Valifenalate				
0231010	Tomatoes	0.1	0.8	The submitted data on tomatoes are sufficient to derive a MRL proposal for the indoor uses. Risk for consumers unlikely
0231030	Aubergines/ eggplants	0.1	0.8	
0251020	Lettuces	0.01*	8.0	The submitted data are sufficient to derive a MRL proposal for the indoor use. Risk for consumers unlikely
0220020	Onions	0.01*	0.5	The submitted data on onions are sufficient to derive a MRL proposal for the NEU outdoor use with an extrapolation to shallots and garlic. Risk for consumers unlikely
0220030	Shallots	0.01*	0.5	
0220010	Garlic	0.01*	0.5	

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.

Table of contents

Abstract 1
Summary 3
Assessment 6
1. Residues in plants 7
1.1. Nature of residues and methods of analysis in plants 7
1.1.1. Nature of residues in primary crops 7
1.1.2. Nature of residues in rotational crops 7
1.1.3. Nature of residues in processed commodities 7
1.1.4. Methods of analysis in plants 7
1.1.5. Stability of residues in plants 7
1.1.6. Proposed residue definitions 7
1.2. Magnitude of residues in plants 8
1.2.1. Magnitude of residues in primary crops 8
1.2.2. Magnitude of residues in rotational crops 9
1.2.3. Magnitude of residues in processed commodities 9
1.2.4. Proposed MRLs 9
2. Residues in livestock 9
2.1. Nature of residues and methods of analysis in livestock 9
2.2. Magnitude of residues in livestock 9
3. Consumer risk assessment 9
4. Conclusion and Recommendations 10
References 10
Abbreviations 10
Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs 12
Appendix B – List of end points 13
Appendix C – Pesticide Residue Intake Model (PRIMo) 17
Appendix D – Input values for the exposure calculations 19
Appendix E – Used compound codes 20

Assessment

The detailed description of the intended uses of valifenalate, which are the basis for the current maximum residue level (MRL) application, is reported in Appendix A.

Valifenalate is the ISO common name for methyl (3*RS*)-3-(4-chlorophenyl)-*N*-[*N*-(isopropoxycarbonyl)-L-valyl]-β-alaninate (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Valifenalate was evaluated in the framework of Directive 91/414/EEC[1] with Hungary designated as rapporteur Member State (RMS) for the representative use as foliar spraying against downy mildew on grapes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2013). Valifenalate has been approved[2] for the use as fungicide on 1 July 2014.

The European Union (EU) MRLs for valifenalate are established in Annex III of Regulation (EC) No 396/2005.[3] The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has not yet been completed. European Food Safety Authority (EFSA) has issued one reasoned opinion on the modification of MRLs for valifenalate in tomatoes and aubergines (EFSA, 2009). The proposals from this reasoned opinion have been considered in recent regulation(s)[4] for EU MRL legislation.

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 Hungary (evaluating Member State, EMS) to modify the existing MRLs for the active substance valifenalate in lettuces and salad plants, spinaches and similar, watercresses, herbs and edible flowers, tomatoes and aubergines, onions, shallots and garlic. 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) on 25 January 2018. In April 2018, the EMS submitted a revised Evaluation Report, restricting the intended uses to lettuces, tomatoes, aubergines, onions, shallots and garlic. To accommodate for the intended uses of valifenalate, the EMS proposed to raise the existing MRLs from the limit of quantification (LOQ) 0.01 mg/kg to 8.0 mg/kg for lettuces; to raise the existing MRLs from the LOQ 0.01 mg/kg to 0.5 mg/kg for onions, shallots and garlic; and finally to raise the existing MRLs from the LOQ 0.01 mg/kg to 0.8 mg/kg for tomatoes and aubergines.

EFSA based its assessment on the evaluation reports submitted by the EMS (Hungary, 2018), the DAR (and its addendum) (Hungary, 2012, 2013) prepared under Council Directive 91/414/EEC, the Commission review report on valifenalate (European Commission, 2013), the conclusion on the peer review of the pesticide risk assessment of the active substance valifenalate (EFSA, 2013) as well as the conclusions from the previous EFSA-reasoned opinion on valifenalate (EFSA, 2009).

For this application, the data requirements established in Regulation (EU) No 544/2011[5] 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, 2017; 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[6].

As the review of the existing MRLs under Article 12 of Regulation 396/2005 is not yet finalised, the conclusions reported in this reasoned opinion should be taken as provisional and might need to be reconsidered in the light of the outcome of the MRL review.

[1] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1–32.

[2] Commission Implementing Regulation (EU) No 144/2014 of 14 February 2014 approving the active substance valifenalate, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. OJ L 45, 15.2.2014, p. 7–11.

[3] 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, 16.03.2005, p. 1–16.

[4] For an overview of all MRL Regulations on this active substance, please consult: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN

[5] 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.

[6] 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.

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

The evaluation reports submitted by the EMS (Hungary, 2018) 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.

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 valifenalate following foliar treatment has been investigated in fruit crops (grapes), root crops (potatoes) and leafy crops (lettuces) in the framework of the EU pesticides peer review and demonstrated that the parent valifenalate was the predominant compound of the total residues in all crop categories. In metabolism studies, the ratio of isomers was shown to be unchanged (EFSA, 2013).

1.1.2. Nature of residues in rotational crops

All crops under consideration may be grown in rotation. Therefore, the possible occurrence of residues in rotational crops resulting from the use on primary crops has to be assessed. The soil degradation studies demonstrated a low persistence of valifenalate and its major metabolites IR-5839 and PCBA (4-chlorobenzoic acid) in soil ($DT_{90} < 100$ days) (EFSA, 2013). Thus, further studies to address the nature and magnitude of the residues of valifenalate in succeeding crops are not required in accordance with the current recommendations.

1.1.3. Nature of residues in processed commodities

Although the level of residues in the crops under consideration is ≥ 0.1 mg/kg, there is no need to investigate the effect of industrial and/or household processing on the nature of the residues as the chronic exposure is low (2.9% acceptable daily intake (ADI) (WHO Cluster diet B)) and the contribution of the crops under consideration that are consumed after processing is not more than 1.0% of the ADI (tomatoes).

1.1.4. Methods of analysis in plants

The analytical methods for the determination of valifenalate residues in plant commodities have been investigated in the framework of the peer review and were shown to be fully validated at the LOQ of 0.01 mg/kg in high water content (potato tubers), high acid content (grapes) matrices and in wine (EFSA, 2013).

1.1.5. Stability of residues in plants

The storage stability of valifenalate in plants stored under frozen conditions was investigated in the framework of a previous MRL assessment and the EU pesticides peer review (EFSA, 2009, 2013). Storage stability data are also available for the metabolite IR-5839. According to these studies, the compounds are stable for up to 24 months in high water content (tomatoes, potatoes), high acid content (grapes) matrices and in wine (EFSA, 2009, 2013).

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in primary crops, a general residue definition for plant products was proposed as valifenalate for enforcement and risk assessment (EFSA, 2013). EFSA concludes that for the crops under consideration in this application, the proposed residue definitions are still applicable.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of valifenalate residues resulting from the reported good agricultural practices (GAPs) on the crops under consideration, EFSA considered all residue trials reported by the RMS in its evaluation reports (Hungary, 2018). All the considered residue trials samples were stored within storage time periods covered by acceptable storage stability data for the parent compound. According to the assessment of the RMS, the analytical methods used were sufficiently validated and fit for purpose.

The number of residue trials and extrapolations were evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2017).

The results of the residue trials, the related risk assessment input values (highest residue (HR), supervised trials median residue (STMR)) and the MRL proposals are summarised in Appendix B.1.2.1.

Lettuces

In total, six independent outdoor trials on lettuce are available which are representative for the intended southern Europe (SEU) outdoor GAP; two of the submitted trials were considered as not valid, since the samples were taken at a later preharvest interval (PHI) compared to the intended GAP (21 days instead of 7 days). At least two of the valid trials were performed in open leave lettuce varieties. Considering that lettuce is a major crop, at least eight valid residue trials would be required to derive a MRL proposal. An indicative MRL was calculated based on the incomplete data set (i.e. 0.3 mg/kg).

For the indoor GAP, in total, nine trials on lettuce were provided; however, two trials were considered replicates as these were conducted under the same experimental conditions. Thus, in total, eight independent indoor trials on lettuce are available for the EU indoor GAP. Five of the valid trials were performed in open leave lettuce varieties. The indoor residue data set clearly leads to higher residue levels in lettuces compared to the residue levels from the outdoor trials.

Considering the available data, it seems that the indoor use leads to higher residue levels compared to the SEU outdoor use. Based on the indoor data set, a MRL proposal of 8 mg/kg was derived.

Tomatoes

In total, 10 outdoor trials on tomato reflecting the northern Europe (NEU) GAP were submitted; however, three trials were considered as replicates as they were conducted under the same experimental conditions. Thus, in total, seven independent outdoor trials on tomato are available for the NEU outdoor GAP. Considering that tomato is a major crop, at least eight valid residue trials would be required to derive a MRL proposal. An indicative MRL proposal was calculated for the NEU outdoor GAP (i.e. 0.5 mg/kg).

For the indoor GAP, 12 valid trials on tomato were provided; however, four trials were considered as replicates as conducted under the same experimental conditions. Thus, in total, eight independent indoor trials on tomato are available for the EU indoor GAP.

Considering the available trials, it seems that the indoor use leads to higher residue levels compared to the NEU outdoor use.

Based on the indoor data set, a MRL proposal of 0.8 mg/kg was derived.

Aubergines/eggplants

No specific trials in aubergines were provided. However, considering that for aubergines, the intended GAP is identical with the GAP for tomatoes, the applicant requested to use the residue trials in tomatoes and to derive a MRL proposal by extrapolation in accordance with the EU guidance document (European Commission, 2017). Since aubergines are a minor crop, at least four trials are required. The available studies are sufficient to derive MRL proposals for the intended indoor and the NEU outdoor use (i.e. 0.8 mg/kg and 0.5 mg/kg, respectively).

Thus, for aubergines, a MRL proposal of 0.8 mg/kg was derived which covers the indoor and the NEU outdoor use.

Onions

In total, 12 outdoor trials on onions compliant with the NEU outdoor GAP were submitted; however, four trials were considered as replicates as they were carried out under the same experimental conditions. Thus, in total, eight independent outdoor trials on onions are available for the NEU outdoor GAP which is sufficient to derive a MRL proposal of 0.5 mg/kg for onions.

Shallots, garlic

No specific trials in shallots and garlic were provided. However, considering that the intended GAPs are identical with the GAP for onions, the applicant requested to use the residue trials in onions and to derive a MRL proposal by extrapolation in accordance with the EU guidance document (European Commission, 2017).

Thus, for shallots and garlic, a MRL proposal of 0.5 mg/kg was derived.

1.2.2. Magnitude of residues in rotational crops

Rotational crops field trials addressing the magnitude of residues of valifenalate are not required.

1.2.3. Magnitude of residues in processed commodities

No specific processing studies were submitted; considering the low dietary intake, such studies are not required.

1.2.4. Proposed MRLs

The available residue trials are sufficient to derive a MRL proposal for lettuces, tomatoes (with an extrapolation to aubergines) and for onions (with an extrapolation to garlic and shallots).

2. Residues in livestock

2.1. Nature of residues and methods of analysis in livestock

The crops under consideration are not feed items according to the relevant guidance document (OECD, 2013). Therefore, the nature of valifenalate residues in livestock was not investigated and analytical enforcement methods for the determination of valifenalate residues in products of animal origin are not required.

2.2. Magnitude of residues in livestock

The crops under consideration are not feed items according to the EU Guidance document, and therefore, the magnitude of valifenalate residues in livestock was not investigated.

3. Consumer risk assessment

The toxicological profile of valifenalate was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.07 mg/kg body weight (bw) per day whilst an acute reference dose (ARfD) was deemed unnecessary (EFSA, 2013).

The consumer risk assessment was performed with revision 2 of the EFSA PRIMo (Pesticide Residue Intake Model; EFSA, 2007). For the crops under assessment, the STMR values derived from the supervised residue trials were used as input values for calculating the chronic exposure; for the remaining crops/commodities, the existing EU MRLs were used as input values for the exposure calculation. The acute intake assessment was not carried out since no ARfD has been established for valifenalate. The complete list of input values is presented in Appendix D.1.

The summary of consumer intake calculations is available in Appendix C.

No chronic consumer intake concerns were identified for any of the European diets. Total calculated intake values accounted for a maximum of 2.9% of the ADI for WHO Cluster diet B. The contribution of residues expected in the crops under consideration according to the intended uses to the overall long-term exposure is up to 1% of the ADI for tomatoes (see Appendix C). EFSA concludes that the long-term intake of residues of valifenalate resulting from the existing and the intended uses is unlikely to present a risk to consumer health.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive a MRL proposal for lettuces, tomatoes, aubergines, onions, shallots and garlic.

The crops under consideration are not feed items according to the EU Guidance document, and therefore, the nature and magnitude of valifenalate residues in livestock was not investigated.

The MRL recommendations are summarised in Appendix B.3.

EFSA concluded that the proposed use of valifenalate on the above-mentioned crops will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake

ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
DAR	draft assessment report
DAT	days after treatment
DT_{90}	period required for 90% dissipation (define method of estimation)
EMS	evaluating Member State
GAP	Good Agricultural Practice
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
HR	highest residue
IEDI	international estimated daily intake
ILV	independent laboratory validation
IUPAC	International Union of Pure and Applied Chemistry
LOQ	limit of quantification
MRL	maximum residue level
NEU	northern Europe
PBI	plant back interval
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
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
WG	water-dispersible granule
WHO	World Health Organization

Appendix A – Summary of intended GAP 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	Rate	Unit		
Lettuces (0251020)	SEU	F	*Bremia lactucae*	WG	60 g/kg	Foliar spray	14–47	3	7 days	15–75	200–1000	150	g as/ha	7	
Lettuces (0251020)	EU	G	*Bremia lactucae*	WG	60 g/kg	Foliar spray	14–47	3	7 days	15–75	200–1000	150	g as/ha	7	
Tomatoes (0231010) Aubergines/ eggplants (0231030)	NEU	F	*Phytophthora infestans*	WG	60 g/kg	Foliar spray	17–79	3	7 days	25–100	150–600	150	g as/ha	3	
Tomatoes (0231010) Aubergines/ eggplants (0231030)	EU	G	*Phytophthora infestans*	WG	60 g/kg	Foliar spray	17–79	3	7 days	25–100	150–600	150	g as/ha	3	
Onions (0220020) Garlic (0220010) Shallots (0220030)	NEU	F	*Peronospora destructor*	WG	60 g/kg	Foliar spray	20–40	3	7 days	15–75	200–1000	150	g as/ha	3	

NEU: northern European Union; SEU: southern European Union; MS; Member State; 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**	**Crop(s)**	**Application(s)**	**Sampling (DAT)**	**Comment/ Source**
	Fruit crops	Grapes (bunches)	Foliar (4 × 150 mg/L) and (4 × 750 mg/L)	74	EFSA (2013)
	Root crops	Potatoes (tubers)	Foliar (3 × 150 g/ha)	21	
	Leafy crops	Lettuces	Foliar (3 × 150 g/ha)	7	
		Grapes (leaves)	Foliar (1 × 0.375 mg/ plant)	0, 1, 3, 8, 14, 23, 30	
Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/ Source**
	Root/tuber crops	Not submitted, not required (DT_{90} < 100 days for valifenalate and major soil metabolites)			
	Leafy crops				
	Cereal (small grain)				
	other				
Processed commodities (hydrolysis study)	**Conditions**		**Stable?**		**Comment/ Source**
	Pasteurisation (20 min, 90°C, pH 4)		Not submitted, not triggered		
	Baking, brewing and boiling (60 min, 100°C, pH 5)				
	Sterilisation (20 min, 120°C, pH 6)				
	Other processing conditions				

DAT: day after treatment; PBI: plant back interval.

Can a general residue definition be proposed for primary crops?	Yes	
Rotational crop and primary crop metabolism similar?	Not triggered	
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not triggered	
Plant residue definition for monitoring (RD-Mo)	Valifenalate (All categories of crops)	
Plant residue definition for risk assessment (RD-RA)	Valifenalate (All categories of crops)	
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	Matrices with high water content and high acid content: HPLC–MS/MS, LOQ 0.01 mg/kg Confirmatory method and ILV available. (EFSA, 2013)	

B.1.1.2. Stability of residues in plants

Plant products (available studies)	**Category**	**Commodity**	**T (°C)**	**Stability period**		**Compounds covered**	**Comment/ Source**
				Value	**Unit**		
	High water content	Tomato	−20	24	months	Parent	EFSA (2009)
		Potato	−20	24	months	Parent	EFSA (2013)
	High acid content	Grape (bunches)	−20	24	months	Parent	EFSA (2013)
	Processed products	Wine	−20	24	months	Parent	EFSA (2013)

B.1.2. Magnitude of residues in plants

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

Commodity	Region/ Indoor[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/Source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)
Lettuces	SEU	< 0.01, 0.016, 0.064, 0.084*, 0.108*, 0.111	Trials are compliant with the GAP. Number of trials not sufficient for deriving a MRL proposal (eight trials would be required). An indicative MRL proposal was calculated	0.3 (indicative calculation)	0.11	0.07
Lettuces	Indoor	0.245, 0.463*, 0.555*, 0.661*, 1.230, 1.320*, 1.790(1)*, 5.138	Sufficient number of GAP compliant trials to derive MRL proposal	8.0	5.14	0.95
Tomatoes Aubergines	NEU	< 0.01(2), 0.01(2), 0.021, 0.045(2), 0.051, 0.088, 0.27	GAP compliant trials performed in tomatoes. For tomatoes, one additional trial would be required. Number of trials is sufficient for extrapolation to aubergines (minor crop). For tomatoes, the calculated MRL is just indicative; for aubergines, the number of trials is sufficient to derive a MRL proposal compliant with the data requirements	0.5 (indicative calculation)	0.27	0.05
Tomatoes Aubergines	Indoor	0.12(2), 0.13, 0.16, 0.2, 0.26(2), 0.33, 0.35(2), 0.38	Sufficient number of GAP compliant trials in tomatoes. Extrapolation to aubergines possible	0.8	0.38	0.23
Onions Garlic Shallot	NEU	0.012(2), 0.018, 0.04(2), 0.07(2), 0.087, 0.122(2), 0.18, 0.26	Sufficient number of trials compliant with the GAP. Extrapolation to shallots and garlic possible	0.5	0.26	0.08

*: Trials were performed with open-leaf varieties.
(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): Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue according to the residue definition for monitoring.
(1): The highest residue value is considered for replicate field trials values considering different experimental conditions.
(2): The mean residue value is considered for replicate field trials values considering the same experimental conditions.

B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	Not triggered	
Residues in rotational and succeeding crops expected based on field rotational crop study?	Not triggered	

B.1.2.3. Processing factors

Not submitted and not required.

B.2. Consumer risk assessment

No ARfD has been considered necessary.

ADI	0.07 mg/kg bw per day (EFSA, 2013)
Highest IEDI, according to EFSA PRIMo	2.9% ADI (WHO Cluster diet B) Contribution of crops assessed: Lettuces: 0.7% of ADI Tomatoes: 1% of ADI Aubergines: 0.1% of ADI Onions: 0.09% of ADI Shallots: 0.009% of ADI Garlic: 0.007% of ADI
Assumptions made for the calculations	The calculation is based on the median residue level derived for lettuces, tomatoes, aubergines, onions, shallots and garlics from the trials assessed in this application For the remaining commodities the MRLs established in Regulation (EC) No 750/2010 were used as input values

B.3. Recommended MRLs

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: valifenalate				
0231010	Tomatoes	0.1	0.8	The submitted data on tomatoes are sufficient to derive a MRL proposal for the indoor uses. Risk for consumers unlikely
0231030	Aubergines/ eggplants	0.1	0.8	
0251020	Lettuces	0.01*	8.0	The submitted data are sufficient to derive a MRL proposal for the indoor use. Risk for consumers unlikely
0220020	Onions	0.01*	0.5	The submitted data on onions are sufficient to derive a MRL proposal for the NEU outdoor use with an extrapolation to shallots and garlic. Risk for consumers unlikely
0220030	Shallots	0.01*	0.5	
0220010	Garlic	0.01*	0.5	

*: 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.

Appendix C – Pesticide Residue Intake Model (PRIMo)

Valifenalate			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0.01	Proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw per day):	**0.07**	ARfD (mg/kg bw):	**n.n.**
Source of ADI:	**EFSA**	Source of ARfD:	**EFSA**
Year of evaluation:	**2013**	Year of evaluation:	**2013**

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL).
The pTMRLs have been submitted to EFSA in September 2006.

Chronic risk assessment – refined calculations

TMDI (range) in % of ADI minimum – maximum	
1	3
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)
2.9	WHO Cluster diet B	1.0	Tomatoes	0.5	Wine grapes	0.5	Lettuce	0.6
1.7	FR all population	1.1	Wine grapes	0.1	Tomatoes	0.1	Lettuce	0.2
1.5	NL child	0.4	Milk and cream,	0.2	Table grapes	0.2	Tomatoes	0.9
1.5	DE child	0.4	Table grapes	0.3	Tomatoes	0.2	Milk and cream	0.7
1.4	ES child	0.6	Lettuce	0.3	Tomatoes	0.2	Milk and cream	0.5
1.4	ES adult	0.7	Lettuce	0.3	Tomatoes	0.1	Wine grapes	0.3
1.4	WHO regional European diet	0.5	Lettuce	0.4	Tomatoes	0.1	Milk and cream	0.3
1.4	PT General population	0.7	Wine grapes	0.3	Tomatoes	0.1	Table grapes	0.2
1.3	IE adult	0.4	Wine grapes	0.1	Tomatoes	0.1	Lettuce	0.5
1.3	FR toddler	0.6	Milk and cream	0.3	Tomatoes	0.1	Potatoes	0.9
1.2	WHO cluster diet E	0.5	Wine grapes	0.2	Tomatoes	0.1	Lettuce	0.4
1.2	UK Toddler	0.3	Sugar beet (root)	0.3	Milk and cream	0.2	Tomatoes	0.9
1.2	WHO Cluster diet F	0.4	Lettuce	0.2	Tomatoes	0.2	Wine grapes	0.3
1.1	IT kids/toddler	0.5	Tomatoes	0.4	Lettuce	0.1	Wheat	0.2
1.1	IT adult	0.5	Lettuce	0.4	Tomatoes	0.1	Wheat	0.1
1.1	UK Infant	0.6	Milk and cream	0.1	Sugar beet (root)	0.1	Tomatoes	1.0
1.0	DK child	0.2	Lettuce	0.2	Milk and cream	0.2	Tomatoes	0.6
0.9	WHO cluster diet D	0.3	Tomatoes	0.1	Wine grapes	0.1	Wheat	0.4
0.9	UK vegetarian	0.2	Wine grapes	0.2	Tomatoes	0.2	Lettuce	0.2
0.9	NL general	0.2	Wine grapes	0.2	Lettuce	0.1	Tomatoes	0.3
0.9	UK Adult	0.3	Wine grapes	0.2	Lettuce	0.1	Tomatoes	0.2
0.8	DK adult	0.4	Wine grapes	0.1	Tomatoes	0.1	Milk and cream	0.2
0.8	SE general population 90th percentile	0.3	Tomatoes	0.2	Milk and cream	0.1	Potatoes	0.4
0.7	FR infant	0.4	Milk and cream	0.1	Potatoes	0.0	Tomatoes	0.6
0.6	PL general population	0.3	Tomatoes	0.1	Table grapes	0.0	Potatoes	0.1
0.5	FI adult	0.1	Tomatoes	0.1	Lettuce	0.1	Wine grapes	0.2
0.5	LT adult	0.2	Tomatoes	0.1	Lettuce	0.1	Milk and cream	0.2

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

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

Acute risk assessment not necessary

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: ---			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)
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)			

*) 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:

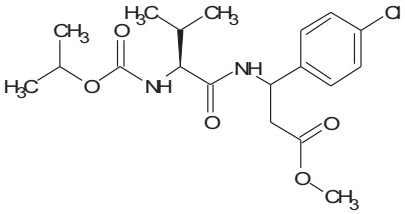
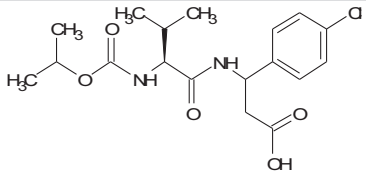
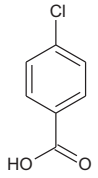
Acute risk assessment not necessary

Appendix D – Input values for the exposure calculations

D.1. Consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Lettuces	0.95	STMR	–	Not relevant since no ARfD has been established for valifenalate
Tomatoes	0.23	STMR	–	
Aubergines	0.23	STMR	–	
Onions	0.08	STMR	–	
Shallots	0.08	STMR	–	
Garlic	0.08	STMR	–	
Other plant and animal commodities	EU MRLs	MRLs listed for the food/feed commodities under Regulation (EC) No 750/2010	–	

Appendix E – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Valifenalate	methyl (3*RS*)-3-(4-chlorophenyl)-*N*-[*N*-(isopropoxycarbonyl)-L-valyl]-β-alaninate Clc1ccc(cc1)C(NC(=O)[C@@H](NC(=O)OC(C)C)C(C)C)CC(=O)OC DBXFMOWZRXXBRN-LWKPJOBUSA-N	
IR-5839	(3*RS*)-3-(4-chlorophenyl)-*N*-[*N*-(isopropoxycarbonyl)-L-valyl]-β-alanine Clc1ccc(cc1)C(NC(=O)[C@@H](NC(=O)OC(C)C)C(C)C)CC(=O)O QRSGZUTWBYAKHI-WMCAAGNKSA-N	
PCBA	4-chlorobenzoic acid OC(=O)c1ccc(Cl)cc1 XRHGYUZYPHTUJZ-UHFFFAOYSA-N	

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 06 September 2017).
(c): ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).