Review of the existing maximum residue levels for valifenalate according to Article 12 of Regulation (EC) No 396/2005

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide valifenalate. To assess the occurrence of valifenalate residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Commission Regulation (EU) No 188/2011, as well as European authorisations reported by Member States and the UK (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and one MRL proposal derived by EFSA still requires further consideration by risk managers.

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Keywords: valifenalate, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, fungicide

Requestor: European Commission

Question number: EFSA-Q-2014-00207

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Declarations of interest: The declarations of interest of all scientific experts active in EFSA’s work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch.

Acknowledgement: EFSA wishes to thank the rapporteur Member State Hungary for the preparatory work and Stathis Anagnos, Laszlo Bura and Silvia Ruocco for the support provided to this scientific output.

Suggested citation: 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, Ragnor Pedersen, Reich H, Miguel Santos, Scarlato AP, Theobald A, Vagenende B and Verani A, 2021. Reasoned Opinion on the review of the existing maximum residue levels for valifenalate according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2021;19(5):6591, 34 pp. https://doi.org/10.2903/j.efsa.2021.6591

ISSN: 1831-4732

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The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.
Summary

Valifenalate was approved on 1 July 2014 by means of Commission Implementing Regulation (EU) No 144/2014 in the framework of Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011.

As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 20 March 2020, EFSA initiated the collection of data for this active substance. In a first step, Member States and the UK were invited to submit by 20 April 2020 their national Good Agricultural Practices (GAPs) in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State, Hungary, to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States and the UK were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 3 July 2020. On the basis of all the data submitted by Member States and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked the RMS to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report, together with Pesticide Residues Intake Model (PRIMo) calculations and an updated GAP overview file were provided by the RMS to EFSA on 21 September 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report.

Based on the information provided by the RMS, Member States and the EURLs, and taking into account the conclusions derived by EFSA in the framework of Commission Regulation (EU) No 188/2011, EFSA prepared in January 2021 a draft reasoned opinion, which was circulated to Member States and EURLs for consultation via a written procedure. Comments received by 19 February 2021 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of valifenalate in plants was investigated in primary crops and according to the results of the metabolism studies, the residue definition for enforcement and risk assessment can be proposed as valifenalate. Although a metabolism study is available for rotational crops, a specific residue definition for these crops is not deemed necessary considering the very low persistence of valifenalate in the soil. No residue definition is deemed necessary neither for processed commodities.

Fully validated analytical methods are available for the enforcement of the proposed residue definition in high water content, high acid content, high oil content and dry commodities at the limit of quantification (LOQ) of 0.01 mg/kg. According to the EURLs the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation, except for tomato where a tentative MRL was derived.

Valifenalate is authorised for use on crops that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg dry matter, further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Nevertheless, the metabolism of valifenalate residues in livestock was investigated in lactating goats at dose rate covering the maximum dietary burdens calculated in this review. According to the results of this study, a residue definition for enforcement and risk assessment is proposed as valifenalate and valifenalate acid (IR5839). If new uses were to be granted in the future triggering the need to set MRLs in livestock commodities, additional toxicological data on valifenalate acid would be required to confirm this residue definition. An analytical method for the enforcement of the proposed residue definition is not available. However, according to the EURLs, the LOQs of 0.01 mg/kg for valifenalate and 0.02 mg/kg for IR5839 are achievable by using the QuEChERS method in routine analyses in milk and liver and should be achievable also in other matrix groups (e.g. kidney, muscle, fat). The analytical standard of valifenalate acid (IR5839) is not commercially available.

Chronic consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure represented...
0.7% of the acceptable daily intake (ADI) (’PT General’ diet). Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance. This indicative exposure calculation did not indicate a risk to consumer’s health.
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**Background**

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the Regulation’) establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for that active substance.

Valifenalate was approved on 1 July 2014 by means of Commission Implementing Regulation (EU) No 144/2014\(^3\) in the framework of Regulation (EC) No 1107/2009\(^4\) as amended by Commission Implementing Regulations (EU) No 540/2011\(^5\) and 541/2011\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, in the framework of Commission Regulation (EU) No 188/2011\(^7\) valifenalate was evaluated by Hungary, designated as rapporteur Member State (RMS). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA scientific output (EFSA, 2013).

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU), and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Regulation (EC) No 1107/2009 is therefore insufficient for the assessment of all existing MRLs for a given active substance.

To gain an overview of the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residues Overview File (PROFile). The PROFile is an inventory of all pesticide residues data relevant to the risk assessment and MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities;
- the analytical methods for enforcement of the proposed MRLs.

As the basis for the MRL review, on 20 March 2020, EFSA initiated the collection of data for this active substance. In a first step, Member States and the UK\(^8\) were invited to submit by 20 April 2020 their Good Agricultural Practices (GAPs) that are authorised nationally, in a standardised way, in the format of specific GAP forms. In the framework of this consultation 18 Member States and the UK provided feedback on their national authorisations of valifenalate. Based on the GAP data submitted, the designated RMS, Hungary, was asked to identify the critical GAPs to be further considered in the

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\(^1\) Regulation (EC) No 396/2005 of the European 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. Repealed by Regulation (EC) No 1107/2009.

\(^3\) 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.

\(^4\) 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.

\(^5\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

\(^6\) Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.

\(^7\) Commission Regulation (EU) No 188/2011 of 25 February 2011 laying down detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market 2 years after the date of notification of that Directive. OJ L 53, 26.2.2011, p. 51–55.

\(^8\) The United Kingdom withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and with the established transition period, the EU requirements on data reporting also apply to the United Kingdom data collected until 31 December 2020.
assessment, in the format of a specific GAP overview file. Subsequently, in a second step, Member States and the UK were requested to provide residue data supporting the critical GAPs by 3 July 2020.

On the basis of all the data submitted by Member States and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked RMS, Hungary, to complete the PROFile and to prepare a supporting evaluation report. The PROFile and the supporting evaluation report, together with the Pesticide Residues Intake Model (PRIMo) calculations and an updated GAP overview file, were submitted to EFSA on 21 September 2020. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report.

Considering all the available information, EFSA prepared in January 2021 a draft reasoned opinion, which was circulated to Member States and EURLs for commenting via a written procedure. All comments received by 19 February 2021 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Hungary, 2020), taking into account also the information provided by Member States during the collection of data, and the EURLs report on analytical methods (EURLs, 2020) are considered as main supporting documents to this reasoned opinion and, thus, made publicly available.

In addition, further supporting documents to this reasoned opinion are the completeness check report (EFSA, 2021a) and the Member States consultation report (EFSA, 2021b). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Furthermore, the exposure calculations for all crops reported in the framework of this review performed using the EFSA Pesticide Residues Intake Model (PRIMo) and the PROFile as well as the GAP overview file listing all authorised uses are key supporting documents and made publicly available as background documents to this reasoned opinion. A screenshot of the report sheet of the PRIMo is presented in Appendix C.

Terms of Reference

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

The active substance and its use pattern

Valifenalate is the ISO common name for Methyl (3RS)-3-(4-chlorophenyl)-N-[N-(isopropoxycarbonyl)-L-valyl]-b-alaninate (IUPAC). Technical valifenalate is an equimolar mixture of the diastereomers (S,R) and (S,S). The chemical structure of the active substance and its main metabolites are reported in Appendix F.

The EU MRLs for valifenalate are established in Annex IIIA of Regulation (EC) No 396/2005. Codex maximum residue limits (CXLs) for this active substance are not yet available. An overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

Table 1: Overview of the MRL changes since the entry into force of Regulation (EC) No 396/2005

| Procedure                  | Legal implementation | Remarks                                                                                                                                 |
|----------------------------|----------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| MRL application            | Regulation (EU) 2019/50(a) | Various crops (EFSA, 2018b)                                                                                                                                                                      |
| MRL application            | Regulation (EU) No 750/2010(b) | Tomatoes and aubergines (EFSA, 2009)                                                                                                                                                             |
| Implementation of CAC     | Not yet legally implemented | The use of valifenalate was assessed by the JMPR (FAO, 2020); however, the proposed maximum residue levels not yet adopted by the Codex Alimentarius Commission (CAC). |

(a): Commission Regulation (EU) 2019/50 of 11 January 2019 amending Annexes II, III, IV and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for chlorantraniliprole, clomazone, cyclaniliprole, fenazaquin, fenpicoxamid, fluocoxastrobin, lambda-cyhalothrin, mepiquat, onion oil, thioldoprid and valifenalate in or on certain products. OJ L 10, 14.1.2019, p. 8–59.

(b): Commission Regulation (EU) No 750/2010 of 7 July 2010 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 certain pesticides in or on certain products. OJ L 220, 21.8.2010, p. 1–56.
For the purpose of this MRL review, all the uses of valifenalate currently authorised within the EU as submitted by the Member States and the UK during the GAP collection have been reported by the RMS in the GAP overview file. The critical GAPs identified in the GAP overview file were then summarised in the PROFile and considered in the assessment. The details of the authorised critical GAPs for valifenalate are given in Appendix A. The RMS did not report any uses authorised in third countries that might have a significant impact on international trade.

Assessment

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the evaluation report accompanying the PROFile (Hungary, 2020);
- the draft assessment report (DAR) and its addenda prepared under Council Directive 91/414/EEC (Hungary, 2012, 2013);
- the conclusion on the peer review of the pesticide risk assessment of the active substance valifenalate (EFSA, 2013);
- the review report on valifenalate (European Commission, 2014);
- the previous reasoned opinions on valifenalate (EFSA, 2009, 2018b).

The assessment is performed in accordance with the legal provisions of the uniform principles for evaluation and authorisation of plant protection products as set out in Commission Regulation (EU) No 546/20119 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1997a–g, 2000, 2010a,b, 2017; OECD, 2008, 2011, 2013).

More detailed information on the available data and on the conclusions derived by EFSA can be retrieved from the list of end points reported 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 valifenalate was investigated after foliar treatment in fruits, leafy vegetables and roots and assessed in the framework of the peer review (EFSA, 2013; Hungary, 2013). In all studies, valifenalate was radiolabelled in the chlorophenyl ring of the molecule.

Preliminary studies were performed on young leaves (grapes, tomato, potato) to get information on valifenalate uptake and on metabolites to be identified. After one foliar application of 150 mg a.s./L on vine leaves, 250 mg a.s./L on potato leaves and on tomato leaves, degradation, penetration and translocation of valifenalate was studied in treated leaves and in new leaves grown after treatment. The conclusions reached were comparable. Valifenalate was shown to penetrate slowly and rapidly translocate from the sprayed leaves to the new ones grown after treatment. The majority of residues were found on leaves surface, and the main compound identified was unchanged valifenalate, representing 93–100% of the total radioactive residues (TRR), while other metabolites identified (including valifenalate acid) were not significant. In all three studies, analyses showed that the ratio of S,R/S,S diastereomers did not change.

In grapes, two experiments were made, with four foliar applications of 150 mg a.s./L and four applications at an exaggerate rate of 750 mg a.s./L (dose levels covering the application rate of the GAPs under consideration). The main compound identified was unchanged valifenalate, accounting for 66% TRR (0.13 mg eq/kg) that was present mainly on the grapes surface. Valifenalate acid (IR5839) was present at 13% TRR (0.025 mg eq/kg).

After three foliar applications of 150 g a.s./ha on potato, total radioactivity in tubers amounted for only 0.013 mg/kg. The major metabolites identified in potato tubers were valifenalate acid (IR5839) (15% TRR; 0.002 mg eq/kg), valifenalate acid glucosyl ester (16% TRR; 0.002 mg eq/kg) and β-4-chlorophenylalanine (32% TRR; 0.004 mg eq/kg), while parent valifenalate represented less than 2%.

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9 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.
TRR (< 0.0003 mg eq/kg). Nevertheless, considering the low residue levels it was concluded that no residues are expected in potato tuber.

After three foliar applications of 150 g a.s./ha in lettuce, parent valifenalate was found to be major on the surface and on plant extracts, representing 96% TRR (3.44 mg eq/kg) while other metabolites were identified but not in significant proportions (< 3% TRR).

All studies showed that valifenalate is not extensively metabolised. In general, the parent compound remains unchanged and minor non-significant metabolites are formed. It was also concluded that the ratio of the isomers was unchanged (EFSA, 2013).

The metabolic pathway of valifenalate was similar in fruits, leafy vegetables and roots, considering the metabolites identified in each crop. It involves an O-demethylation resulting in the production of valifenalate acid (IR5839) and conjugation of primary metabolites. EFSA concludes that the metabolism of valifenalate is sufficiently addressed.

1.1.2. Nature of residues in rotational crops

Valifenalate is authorised on crops that may be grown in rotation; however, the laboratory DT90 reported in the soil degradation studies for valifenalate and its main soil metabolites evaluated in the framework of the peer review were far below 100 days. It was concluded that valifenalate and its soil metabolites showed very low to low persistence in soil (EFSA, 2013). Therefore, studies investigating the nature of valifenalate on rotational crops are not required.

Nevertheless, one confined rotational crop study was available and is reported here for completeness. This study was assessed in the framework of a previous MRL application (EFSA, 2009) only. It was not assessed under the peer review for the approval (EFSA, 2013) since the representative use evaluated was on grapes and a study on residues in succeeding crops was thus not required in this framework.

Radiolabelled valifenalate on the chlorophenyl ring was applied at a rate of 1.44 kg a.s./ha onto bare soil. Crops were planted at nominal plant back intervals (PBI) of 30, 120 and 365 days after treatment (DAT). Crops planted at each interval consisted of leafy vegetable (lettuce), roots (carrots) and cereals (wheat). At maturity, the TRR was always below 0.03 mg/kg in edible parts of the crops (carrot roots, lettuce and grain) and decreased over time. In other raw commodities (carrot leaves, forage and straw), TRR ranged between 0.008 and 0.098 mg/kg. The main compound in all cases was parent valifenalate and several metabolites (identical to the ones in primary crops) were identified in trace amounts. It was concluded that the metabolism of valifenalate in rotational crops proceeds in a similar pathway as in primary crops (EFSA, 2009).

1.1.3. Nature of residues in processed commodities

There were no studies investigating the nature of residues of valifenalate in processed commodities available for this review. In some commodities, residues were above 0.1 mg/kg; however, the total exposure to valifenalate residues is not exceeding 1% of the acceptable daily intake (ADI). Therefore, the investigation of the nature of residues in processed commodities is not required.

1.1.4. Methods of analysis in plants

During the peer review, three hyphenated analytical methods based on high-performance liquid chromatography (HPLC) coupled to MS/MS detection were validated in various crops with a limit of quantification (LOQ) of 0.01 mg/kg: in potato, in grapes and wine, and in grape bunches and raisins. In all studies, two additional fragment ions (HPLC-MS) were monitored for confirmation purposes. These primary methods are supported by two independent laboratory validations (ILV) performed in several commodities: the first one in potato, grape bunches and wine, the second one in grapes, raisins, tomato paste and grape juice (EFSA, 2013).

Even though not needed under the current review, an analytical method using HPLC-MS/MS technique was also validated in high oil content and dry commodities (wheat and rapeseeds) with an LOQ of 0.01 mg/kg, and supported by an ILV (Hungary, 2013).

During the completeness check, the EURLs provided QuEChERS multi-residue analytical method using HPLC-MS/MS, LC-QqQ-MS/MS and GC-MS/MS, with a default LOQ of 0.01 mg/kg for the routine analysis of valifenalate in high water content, high acid content, high oil content and dry commodities. Even lower levels were successfully validated in high water and high acid commodities (down to 0.005 mg/kg) and in dry commodities (down to 0.0005 mg/kg). According to the EURLs, it was observed...
that the two isomers had a similar detection response. This would mean that the isomeric mixture would be suitable for accurate quantification and that there is no need for having analytical standards of the individual isomers (EURLs, 2020).

It can be concluded that sufficiently validated analytical methods are available for the enforcement of all commodities under assessment (high water content and high acid content commodities).

1.1.5. Stability of residues in plants

The storage stability of valifenalate and its metabolite IR5839 was investigated in the framework of the peer review (EFSA, 2013) in high water/high starch content (potato), high acid content (grape) commodities and processed products (wine). It was also investigated under a previous MRL application (EFSA, 2009) for valifenalate in high water content commodities (tomato, lettuce).

The available studies demonstrated storage stability for valifenalate and IR5839 (individually) in high water content, high starch content and high acid content commodities, for a period of at least 2 years when stored at -20°C. It is noted, however, that metabolite IR5839 is not currently included in the residue definition (see Section 1.1.6).

1.1.6. Proposed residue definitions

The metabolism of valifenalate was similar in all crops assessed and the ratio of the isomers was shown to be unchanged. The metabolism in rotational crops is similar to the metabolism observed in primary crops and, although studies on the nature of residues in processed commodities are not available, the processing of valifenalate is not expected to modify the nature of residues.

As the parent compound was found to be a sufficient marker in fruits, leafy vegetables and roots, and the most relevant compound to consider, residue definition for enforcement and risk assessment is proposed as valifenalate only (EFSA, 2013). Specific residue definitions are not required in rotational crops nor processed commodities (see also Sections 1.1.2 and 1.1.3).

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in all matrix groups is available (EFSA, 2013; Hungary, 2013). According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses in all matrix groups. The analytical standard for valifenalate is commercially available as an equimolar mixture of the two diastereomers and experiments showed that there is no need for having analytical standards of the individual isomers (EURLs, 2020).

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 GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report (Hungary, 2020). All residue trial samples considered in this framework were stored in compliance with the conditions for which storage stability of residues was demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

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).

For all crops under assessment, available residue trials are sufficient to derive (tentative) MRL and risk assessment values, taking note of the following considerations:

- Table grape: although MRL and risk assessment values can be derived from the southern data set, four trials compliant with the northern GAP are still required.
- Potato: The number of residue trials supporting the northern outdoor GAP is not compliant with the data requirements for this crop. However, the reduced number of residue trials is considered acceptable in this case because all results were below the LOQ and considering the metabolism study, no residues above the LOQ are expected. Further residue trials are therefore not required.
- Onion: Although tentative MRL and risk assessment values can be derived from the southern limited data set, eight trials compliant with the northern GAP are still required. In addition, the number of residue trials supporting the southern GAP is not compliant with the data requirements for this crop. However, the reduced number of residue trials is considered
acceptable in this case because all results were below the LOQ. Further residue trials supporting the southern GAP are therefore not required.

- Shallots: Although MRL and risk assessment values can be derived from the southern data set, four trials compliant with the northern GAP are still required.
- Tomato: Tentative MRL and risk assessment values can be derived from the southern limited data set; however, one additional trial compliant with the southern GAP is required to confirm the MRL.

1.2.2. Magnitude of residues in rotational crops

There were no studies investigating the magnitude of residues in rotational crops available for this review. However, since valifenalate has low potential to accumulate in soil, no studies on rotational crop are required (see also Section 1.1.2).

Based on the confined rotational crop study available, considering the overdosing factor of this study and the fact that the active substance was applied to a bare soil (interception of active substance by the plants is expected in practice), it is confirmed that valifenalate residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that the active substance is applied in compliance with the GAPs reported in Appendix A.

1.2.3. Magnitude of residues in processed commodities

The effect of industrial processing and/or household preparation was assessed on studies conducted on grapes (EFSA, 2013; Hungary, 2013) and tomatoes (Hungary, 2020). An overview of all available processing studies is available in Appendix B.1.2.3. Robust processing factors (fully supported by data) could be derived for all processed products of grape bunches (wet pomace, must, juice, bottled wine, unbottled wine), while limited processing factors (not fully supported by data) were derived for processed tomato (ketchup, canned tomato, juice, sauce and paste).

Further processing studies are not required as they are not expected to affect the outcome of the risk assessment. However, if more robust processing factors were to be required by risk managers, in particular for enforcement purposes, additional processing studies would be needed.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive (tentative) MRL proposals as well as risk assessment values for all commodities under evaluation. The MRL proposal for tomato is tentative since an additional trial is still required to support the southern GAP.

2. Residues in livestock

Valifenalate is authorised for use on potatoes that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. The input values for all relevant commodities are summarised in Appendix D.

Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg dry matter (DM), further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Even though not needed, the metabolism of valifenalate residues in livestock was investigated in lactating goats at dose rate covering the maximum dietary burdens calculated in this review. This study performed with valifenalate radiolabelled in the chlorophenyl ring of the molecule was assessed in the framework of the peer review (EFSA, 2013; Hungary, 2013).

The study performed on lactating goats indicates that transfer of residues in all matrices was very limited. Total radioactive residues in muscle and milk were negligible (0.003 mg eq/kg) and very low in fat (0.011 mg eq/kg). Highest residue levels were found in kidney (0.045 mg eq/kg) and liver (0.109 mg eq/kg) (EFSA, 2013). The main compounds identified were unchanged valifenalate in fat (64% TRR; 0.007 mg eq/kg) and milk (53%; 0.0016 mg eq/kg) and metabolite IR5839 in liver (63% TRR; 0.066 mg eq/kg) and kidney (51% TRR; 0.023 mg eq/kg).

EFSA concludes that the metabolism of valifenalate in livestock is adequately elucidated, and parent valifenalate and its acid (IR5839) are the most relevant components of the residues in livestock commodities. Although valifenalate acid (IR5839) is not of toxicological concern, available toxicological data are not sufficient to conclude whether parent valifenalate and its acid share the same toxicity.
Therefore, a residue definition for enforcement and risk assessment in ruminants is proposed as valifenalate and valifenalate acid (IR5839) (EFSA, 2013). In case additional uses were to be granted in the future triggering the need to set MRLs in livestock commodities, additional toxicological data would be required to confirm the proposed residue definition.

A fully validated analytical method for enforcement in animal matrices was not available for this review and not required. Nevertheless, the EURLs provided data for an enforcement method. According to the EURLs, default LOQs of 0.01 mg/kg for valifenalate and of 0.02 mg/kg for IR5839 are achievable in liver and milk by using the QuEChERS method in routine analyses. Based on the experience gained, the EURLs concluded that these LOQs should be also achievable in other matrix groups (e.g. muscle, kidney, fat). In addition, screening validation data generated by the EURL-AO for commodities of animal origin show that valifenalate can be monitored in milk and honey with a screening detection limit (SDL) of 0.005 mg/kg, and in muscle with an SDL of 0.01 mg/kg. However, it is noted that the analytical standard for IR5839 is, to the best knowledge of the EURLs, not commercially available yet (EURLs, 2020).

The storage stability of valifenalate and IR5839 was not investigated and is not required under this review. No feeding studies are available and are not required since livestock is not expected to be exposed to significant levels of valifenalate residues.

3. Consumer risk assessment

In the framework of this review, only the uses of valifenalate reported by the RMS in Appendix A were considered. The use of valifenalate was also assessed by the JMPR (FAO, 2020); however, the residue levels derived for valifenalate by the JMPR are not yet adopted by the CAC. Therefore, these values are not considered under this review.

Chronic exposure calculations for all crops reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018a, 2019). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for those commodities where a (tentative) MRL could be derived by EFSA in the framework of this review, input values were derived according to the internationally agreed methodologies (FAO, 2009). All input values included in the exposure calculations are summarised in Appendix D. Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance.

The exposure values calculated were compared with the toxicological reference value derived for valifenalate (European Commission, 2014). The highest chronic exposure was calculated for the diet ‘PT General’ representing 0.7% of the ADI. This calculation indicates that the uses assessed under this review result in a consumer exposure lower than the toxicological reference value. Although uncertainties remain due to the data gaps identified in the previous sections, this indicative exposure calculation did not indicate a risk to consumer’s health.

Conclusions

The metabolism of valifenalate in plants was investigated in primary crops, and according to the results of the metabolism studies, the residue definition for enforcement and risk assessment can be proposed as valifenalate. Although a metabolism study is available for rotational crops, a specific residue definition for these crops is not deemed necessary considering the very low persistence of valifenalate in the soil. No residue definition is deemed necessary neither for processed commodities. Fully validated analytical methods are available for the enforcement of the proposed residue definition in high water content, high acid content, high oil content and dry commodities at the LOQ of 0.01 mg/kg. According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation, except for tomato where a tentative MRL was derived.

Valifenalate is authorised for use on crops that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg DM, further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.
Nevertheless, the metabolism of valifenalate residues in livestock was investigated in lactating goats at dose rate covering the maximum dietary burdens calculated in this review. According to the results of this study, a residue definition for enforcement and risk assessment is proposed as valifenalate and valifenalate acid (IR5839). If new uses were to be granted in the future triggering the need to set MRLs in livestock commodities, additional toxicological data on valifenalate acid would be required to confirm this residue definition. An analytical method for the enforcement of the proposed residue definition is not available. However, according to the EURLs, the LOQs of 0.01 mg/kg for valifenalate and 0.02 mg/kg for IR5839 are achievable by using the QuEChERS method in routine analyses in milk and liver and should be achievable also in other matrix groups (e.g. kidney, muscle, fat). The analytical standard of valifenalate acid (IR5839) is not commercially available.

Chronic consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure represented 0.7% of the ADI (‘PT General’ diet). Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance. This indicative exposure calculation did not indicate a risk to consumer’s health.

**Recommendations**

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 2). All MRL values listed as ‘Recommended’ in the table are sufficiently supported by data and are therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL value listed in the table is not recommended for inclusion in Annex II because it requires further consideration by risk managers (see Table 2 footnotes for details). In particular, this tentative MRL needs to be confirmed by the following data:

1) One additional residue trial supporting the southern outdoor GAP on tomato.

It is highlighted, however, that some of the MRLs derived result from a GAP in one climatic zone only, whereas other GAPs reported by the RMS were not fully supported by data. EFSA therefore identified the following data gaps which are not expected to impact on the validity of the MRLs derived but which might have an impact on national authorisations:

2) Four residue trials supporting the northern outdoor GAP on table grapes;
3) Eight residue trials supporting the northern outdoor GAP on onions;
4) Four residue trials supporting the northern outdoor GAP on shallots.

If the above reported data gaps are not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level.

**Table 2: Summary table**

| Code number | Commodity          | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review          | Comment                  |
|-------------|-------------------|------------------------|---------------------|-------------------------------|-------------------------|
| 151010      | Table grapes      | 0.2                    | –                   | 1 Recommended*(a)             |                         |
| 151020      | Wine grapes       | 0.2                    | –                   | 1 Recommended*(a)             |                         |
| 211000      | Potatoes          | 0.01*                  | –                   | 0.01* Recommended*(a)         |                         |
| 220020      | Onions            | 0.5                    | –                   | 0.01* Recommended*(a)         |                         |
| 220030      | Shallots          | 0.5                    | –                   | 0.01* Recommended*(a)         |                         |
| 231010      | Tomatoes          | 0.8                    | –                   | 0.15 Further consideration needed(b) | Data gap #1 |
| 231030      | Aubergines (eggplants) | 0.8                  | –                   | 0.15 Recommended*(a)          |                         |
| –           | Other commodities of plant and/or animal origin | See Reg. (EU) 2019/50 | –                   | – Further consideration needed(c) |                         |

MRL: maximum residue level; CXL: codex maximum residue limit.
*: Indicates that the MRL is set at the limit of quantification.
(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E).
(b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E).

(c): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).

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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 
CAC Codex Alimentarius Commission 
CAS Chemical Abstract Service 
CCPR Codex Committee on Pesticide Residues 
CF conversion factor for enforcement residue definition to risk assessment residue definition 
CIPAC Collaborative International Pesticide Analytical Council 
CIRCA (EU) Communication & Information Resource Centre Administrator 
CIRCABC Communication and Information Resource Centre for Administrations, Businesses and Citizens 
CS capsule suspension 
CV coefficient of variation (relative standard deviation) 
CXL codex maximum residue limit 
DALA days after last application 
DAR draft assessment report 
DAT days after treatment 
DB dietary burden 
DM dry matter 
DS powder for dry seed treatment 
DT$_{90}$ period required for 90% dissipation (define method of estimation) 
DTU Danish Technical University 
EC emulsifiable concentrate 
ECD electron capture detector 
EDI estimated daily intake 
EMA European Medicines Agency (former EMEA) 
EMS evaluating Member State 
eq residue expressed as a.s. equivalent 
ESI electrospray ionisation 
EURLs European Union Reference Laboratories for Pesticide Residues (former CRLs)
| Abbreviation | Full Form |
|--------------|-----------|
| FAO          | Food and Agriculture Organization of the United Nations |
| GAP          | Good Agricultural Practice |
| GC           | gas chromatography |
| GC-MS/MS     | gas chromatography with tandem mass spectrometry |
| GR           | Granule |
| GS           | growth stage |
| HPLC         | high-performance liquid chromatography |
| HPLC-MS      | High-performance liquid chromatography with mass spectrometry |
| HPLC-MS/MS   | High-performance liquid chromatography with tandem mass spectrometry |
| HR           | highest residue |
| IEDI         | international estimated daily intake |
| ILV          | independent laboratory validation |
| ISO          | International Organisation for Standardization |
| IUPAC        | International Union of Pure and Applied Chemistry |
| JMPR         | Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues) |
| LC           | liquid chromatography |
| LC-QqQ-MS/MS | liquid chromatography with triple-quadrupole tandem mass spectrometry |
| LOQ          | limit of quantification |
| Mo           | Monitoring |
| MRL          | maximum residue level |
| MS           | Member States |
| MS/MS        | tandem mass spectrometry detector |
| MW           | molecular weight |
| NEDI         | national estimated daily intake |
| NTMDI        | national theoretical maximum daily intake |
| OECD         | Organisation for Economic Co-operation and Development |
| PBI          | plant back interval |
| PF           | processing factor |
| PHI          | preharvest interval |
| ppm          | parts per million \((10^{-6})\) |
| PRIMo        | (EFSA) Pesticide Residues Intake Model |
| PROFile      | (EFSA) Pesticide Residues Overview File |
| QuEChERS     | Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| RA           | risk assessment |
| RAC          | raw agricultural commodity |
| RD           | residue definition |
| RMS          | rapporteur Member State |
| SANCO        | Directorate-General for Health and Consumers |
| SC           | suspension concentrate |
| SEU          | southern European Union |
| SMILES       | simplified molecular-input line-entry system |
| SG           | water soluble granule |
| SL           | soluble concentrate |
| SP           | water soluble powder |
| STMR         | supervised trials median residue |
| TMDI         | theoretical maximum daily intake |
| TRR          | total radioactive residue |
| WG           | water dispersible granule |
| WHO          | World Health Organization |
### Appendix A – Summary of authorised uses considered for the review of MRLs

#### A.1. Authorised outdoor uses in northern EU

| Crop and/or situation | MS or country | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|---------------|-------------|-------------|--------------------------------|------------|---------|
| **Table grapes**      | SI, CZ        | Foliar      | Treatment – general (see also comment field) | 53–70 | 2 | 10 | – | – | 120 g a.s./ha | 70 | CZ: 60 g a.s./ha up to BBCH 61, 120 g a.s./ha after BBCH 61 |
| **Wine grapes**       | HU, CZ        | Foliar      | Treatment – general (see also comment field) | 15–83 | 3 | 10 | – | – | 120 g a.s./ha | 28 | CZ: 60 g a.s./ha up to BBCH 61, 120 g a.s./ha after BBCH 61 |
| **Potatoes**          | FR            | Foliar      | Treatment – broadcast spraying | 17–91 | 4 | 5 | – | – | 150 g a.s./ha | 7 |
| **Onions**            | AT            | Foliar      | Treatment – broadcast spraying | 40–47 | 2 | 10 | – | – | 120 g a.s./ha | 28 |
| **Shallots**          | AT            | Foliar      | Treatment – broadcast spraying | 40–47 | 2 | 10 | – | – | 120 g a.s./ha | 28 |

**MS:** Member State; **a.s.:** active substance; **WG:** water dispersible granules; **BBCH:** growth stages of mono- and dicotyledonous plants.

(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).

(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system. 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.

(c): PHI – minimum preharvest interval.
## A.2. Authorised outdoor uses in southern EU

| Crop and/or situation | MS or country  | F G or I<sup>(a)</sup> | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)<sup>(d)</sup> | Remarks |
|-----------------------|----------------|------------------------|-----------------------------------|-------------|------------|--------------------------------|-----------------|---------|
| Table grapes          | IT F           |                        | Plasmopara viticola               | WG 60 g/kg  | Foliar treatment – broadcast spraying | 13–81 3 10 – – 120 g a.s./ha | 28     |
| Wine grapes           | IT, EL F       |                        | Plasmopara viticola               | WG 60 g/kg  | Foliar treatment – broadcast spraying | 15–83 3 10 – – 120 g a.s./ha | 28     |
| Potatoes              | EL F           |                        | Late blight of potato             | WG 60 g/kg  | Foliar treatment – broadcast spraying | 17–91 6 5 – – 150 g a.s./ha | 7      |
| Onions                | IT, EL, BG F   |                        | Peronospora destructor            | WG 60 g/kg  | Foliar treatment – broadcast spraying | 21–48 3 7 – – 150 g a.s./ha | 3      |
| Shallots              | IT, BG F       |                        | Peronospora destructor            | WG 60 g/kg  | Foliar treatment – broadcast spraying | 21–48 3 7 – – 150 g a.s./ha | 3      |
| Tomatoes              | ES, IT, PT, FR, EL, BG F |          | Late blight of tomato             | WG 60 g/kg  | Foliar treatment – broadcast spraying | 17–85 3 7 – – 150 g a.s./ha | 3      |
| Aubergines            | ES, IT, FR, BG F |          | Late blight of tomato             | WG 60 g/kg  | Foliar treatment – broadcast spraying | 17–85 1–3 7 – – 150 g a.s./ha | 3      |

MS: Member State; a.s.: active substance; WG: water dispersible granules.

(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system. 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.

(c): 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          | Foliar, 4 x 150 mg a.s./L or 4 x 750 mg a.s./L | 74             | [chlorophenyl-14C]-valifenalate (EFSA, 2013; Hungary, 2013) |
| Root crops                       | Potato           | Foliar, 3 x 150 g a.s./ha                        | 21             | [chlorophenyl-14C]-valifenalate (EFSA, 2013; Hungary, 2013) |
| Leafy crops                      | Vine leaves      | Foliar, 1 x 150 mg a.s./L                         | 0, 1, 3, 8, 14, 23, 30 | [chlorophenyl-14C]-valifenalate Translocation to new leaves grown after the treatment was studied (EFSA, 2013; Hungary, 2013) |
|                                  | Tomato leaves    | Foliar, 1 x 250 mg a.s./L                         | 0, 1, 3, 7, 14, 21, 28 | [chlorophenyl-14C]-valifenalate Translocation to new leaves grown after the treatment was studied (EFSA, 2013; Hungary, 2013) |
|                                  | Potato leaves    | Foliar, 1 x 250 mg a.s./L                         | 0, 1, 3, 7, 14, 21, 28 | [chlorophenyl-14C]-valifenalate Translocation to new leaves grown after the treatment was studied (EFSA, 2013; Hungary, 2013) |
|                                  | Lettuce          | Foliar, 3 x 150 g a.s./ha                         | 7              | [chlorophenyl-14C]-valifenalate (EFSA, 2013; Hungary, 2013) |

| Rotational crops (available studies) | Crop groups     | Crop(s)     | Application(s) | PBI (DAT) | Comment/Source                                      |
|-------------------------------------|-----------------|-------------|----------------|-----------|-----------------------------------------------------|
| Root/tuber crops                    | Carrots         | Bare soil, 1.44 kg a.s./ha                        | 30, 120, 365  | [chlorophenyl-14C]-valifenalate (EFSA, 2009)         |
| Leafy crops                         | Lettuce         | Bare soil, 1.44 kg a.s./ha                         | 30, 120, 365  | [chlorophenyl-14C]-valifenalate (EFSA, 2009)         |
| Cereal (small grain)                | Wheat           | Bare soil, 1.44 kg a.s./ha                         | 30, 120, 365  | [chlorophenyl-14C]-valifenalate (EFSA, 2009)         |

| Processed commodities (hydrolysis study) | Conditions                  | Stable? | Comment/Source |
|------------------------------------------|-----------------------------|---------|----------------|
|                                          | Pasteurisation (20 min, 90°C, pH 4) | Not triggered | – |
|                                          | Baking, brewing and boiling (60 min, 100°C, pH 5) | Not triggered | – |
|                                          | Sterilisation (20 min, 120°C, pH 6) | Not triggered | – |
|                                          | Other processing conditions | –       | – |

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Can a general residue definition be proposed for primary crops? | Yes | Similar metabolic pathway in three different groups (fruits, leafy crops and roots).
---|---|---
Rotational crop and primary crop metabolism similar? | Yes | A residue definition for rotational crops is not required. However, a study is available showing that the only significant compound is parent valifenalate.
Residue pattern in processed commodities similar to residue pattern in raw commodities? | Not applicable | A residue definition for processed commodities is not required.
Plant residue definition for monitoring (RD-Mo) | Valifenalate | Valifenalate
Plant residue definition for risk assessment (RD-RA) | Valifenalate | Valifenalate
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

**Matrices with high water content and high acid content (Hungary, 2013; EFSA, 2013):**
- HPLC-MS/MS, LOQ 0.01 mg/kg in potatoes, grapes and wine
  ILV available (potato, grape bunches and wine)
- HPLC–MS/MS, LOQ 0.01 mg/kg in grape bunches and raisins
  ILV available (grape, raisins, tomato paste and grape juice)

**Matrices with high oil content and dry matrices (Hungary, 2013):**
- HPLC–MS/MS, LOQ 0.01 mg/kg in wheat and rapeseeds
  ILV available (wheat and rapeseeds)

**Matrices with high water content, high acid content, high oil content and dry commodities (EURLs, 2020):**
- QuEChERS (LC–QqQ–MS/MS, GC–MS/MS or HPLC–MS/MS) for enforcement in routine analysis, default LOQ 0.01 mg/kg
- Even lower levels (down to 0.005 mg/kg in high water and high acid commodities and down to 0.0005 mg/kg in dry commodities) were successfully validated.

a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LC–QqQ–MS/MS: liquid chromatography with triple-quadrupole tandem mass spectrometry; GC–MS/MS: gas chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe.
B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category | Commodity | T (°C) | Stability period Value | Unit | Compounds covered | Comment/Source                  |
|-----------------------------------|----------|-----------|--------|------------------------|------|-------------------|--------------------------------|
| High water/high starch content    | Potato   | –20       | 24     | Months                 |      | Valifenalate; valifenalate acid (IR5839) | EFSA (2013), Hungary (2013) |
| High water content                | Tomato   | –20       | 24     | Months                 |      | Valifenalate       | Hungary (2009), EFSA (2009) |
|                                    | Lettuce  | –20       | 24     | Months                 |      | Valifenalate       | Hungary (2009), EFSA (2009) |
| High acid content                 | Grape    | –20       | 24     | Months                 |      | Valifenalate; valifenalate acid (IR5839) | EFSA (2013), Hungary (2013) |
| Processed products                | Wine     | –20       | 24     | Months                 |      | Valifenalate; valifenalate acid (IR5839) | EFSA (2013), Hungary (2013) |

B.1.2. Magnitude of residues in plants

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

| Commodity       | Region(a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 | Calculated MRL (mg/kg) | HR(b) (mg/kg) | STMR(c) (mg/kg) |
|-----------------|-----------|-----------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|---------------|-----------------|
| Table grapes    | NEU       | –                                                              | No GAP compliant trials available.                                             | –                      | –             | –               |
| Table grapes    | SEU       | < 0.01; 0.013; 0.014; 0.019; 0.067; 0.095; 0.11; 0.18; 0.22; 0.26; 0.29; 0.39; 0.59; 0.62 | Trials on table grapes compliant with GAP (Hungary, 2020). Extrapolation to wine grapes is acceptable. MRL_OECD = 1.03 | 1.00                   | 0.62          | 0.15            |
| Wine grapes     | NEU       | 0.04; 0.045; 0.051; 0.058; 0.069; 0.073; 0.085; 0.086; 0.087; 0.095; 2 × 0.12; 0.121; 0.129; 0.18; 0.19; 0.22; 0.36 | Trials on wine grapes compliant with GAP (Hungary, 2020). MRL_OECD = 0.43 | 0.50                   | 0.36          | 0.09            |
| Potatoes        | NEU       | 2 × < 0.01                                                    | Trials on potato compliant with the GAP (Hungary, 2020). Reduced number of trials is sufficient since, also considering metabolism studies in roots, no residues above the LOQ are expected. MRL_OECD = – | 0.01*                 | 0.01          | 0.01            |
|                 | SEU       | 8 × < 0.01                                                   | Trials on potato compliant with the GAP (Hungary, 2020). MRL_OECD = 0.01 | 0.01*                 | 0.01          | 0.01            |
### Commodity Region (a) Residue levels observed in the supervised residue trials (mg/kg) Comments/Source Calculated MRL (mg/kg) HR (b) (mg/kg) STMR (c) (mg/kg)

| Commodity                  | Region (a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source                                                                 | Calculated MRL (mg/kg) | HR (b) (mg/kg) | STMR (c) (mg/kg) |
|----------------------------|------------|------------------------------------------------------------------|---------------------------------------------------------------------------------|------------------------|----------------|-----------------|
| Onions                     | NEU        | –                                                                | No GAP compliant trials available.                                             | 0.01*                  | 0.01           | 0.01            |
| Shallots                   | SEU        | 4 × 0.01                                                         | Trials on onions compliant with GAP (Hungary, 2020). Reduced number of residue trials is considered acceptable because all results are < LOQ. Extrapolation to shallots is applicable. MRL<sub>OECD</sub> = 0.01 | 0.15 (tentative for tomato<sup>(d)</sup>) | 0.08           | 0.04            |
| Shallots                   | NEU        | –                                                                | No GAP compliant trials available.                                             | 0.15 (tentative for tomato<sup>(d)</sup>) | 0.08           | 0.04            |
| Tomatoes                   | SEU        | 0.020; 0.024; 0.032; 0.036; 0.039; 0.074; 0.077                 | Trials on tomato compliant with GAP (Hungary, 2020). Extrapolation to aubergines is applicable. MRL<sub>OECD</sub> = 0.14 | 0.15 (tentative for tomato<sup>(d)</sup>) | 0.08           | 0.04            |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level.

*: Indicates that the MRL is proposed at the limit of quantification.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, EU: indoor EU trials or Country code: if non-EU trials.

(b): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(c): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

(d): MRL is tentative for tomato because one additional residue trial is required.

### B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?

| Not triggered | Considering the DT<sub>90</sub> of valifenalate and main soil metabolites (far below 100 days), investigation of residues in rotational crops is not required. In addition, the available study confirmed that no residues are expected in rotational crops. |

Residues in rotational and succeeding crops expected based on field rotational crop study?

| Not triggered | – |

DT<sub>90</sub>: period required for 90% dissipation (define method of estimation).
### B.1.2.3. Processing factors

| Processed commodity                  | Number of valid studies<sup>(a)</sup> | Processing Factor (PF)                           | Median PF | Comment/Source                  |
|--------------------------------------|--------------------------------------|--------------------------------------------------|-----------|---------------------------------|
| *Grape bunches, wet pomace*          | 7                                    | 1.13; 1.2; 1.68; 2.23; 2.74; 3; 4.35              | 2.23      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, must*                | 7                                    | 0.68; 0.71; 0.72; 0.77; 1.17; 1.36; 1.76         | 0.77      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, white wine (unbottled)* | 7                                    | 0.53; 0.54; 0.55; 0.57; 0.80; 0.89; 1.32        | 0.57      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, red wine (unbottled)* | 7                                    | 0.37; 0.45; 0.74; 0.76; 0.80; 0.84; 0.89         | 0.76      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, bottled white wine*  | 7                                    | 0.27; 0.48; 0.49; 0.50; 0.57; 0.84; 1.32        | 0.50      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, bottled red wine*    | 7                                    | 0.23; 0.37; 0.67; 0.71; 0.75; 0.86; 0.94        | 0.71      | Hungary (2013), EFSA (2013)     |
| *Grape bunches, juice*               | 10                                   | 0.26; 0.37; 0.43; 0.46; 0.48; 0.53; 0.63; 0.64; 0.75; 0.77 | 0.51      | Hungary (2013), EFSA (2013)     |
| *Tomato, juice*                      | 2                                    | 0.29; 0.39                                      | 0.34      | Tentative<sup>(b)</sup>         |
|                                       |                                      |                                                  |           | Hungary (2020)                  |
| *Tomato, ketchup*                    | 2                                    | 0.25; 0.36                                      | 0.31      | Tentative<sup>(b)</sup>         |
|                                       |                                      |                                                  |           | Hungary (2020)                  |
| *Tomato, canned*                     | 2                                    | 0.25; 0.36                                      | 0.31      | Tentative<sup>(b)</sup>         |
|                                       |                                      |                                                  |           | Hungary (2020)                  |
| *Tomato, sauce*                      | 2                                    | 0.46; 0.61                                      | 0.54      | Tentative<sup>(b)</sup>         |
|                                       |                                      |                                                  |           | Hungary (2020)                  |
| *Tomato, paste*                      | 2                                    | 0.81; 0.82                                      | 0.82      | Tentative<sup>(b)</sup>         |
|                                       |                                      |                                                  |           | Hungary (2020)                  |

PF: Processing factor (~Residue level in processed commodity expressed according to RD-Mo/Residue level in raw commodity expressed according to RD-Mo).  
<sup>(a)</sup>: Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).  
<sup>(b)</sup>: A tentative PF is derived based on a limited data set.
### B.2. Residues in livestock

| Relevant groups (subgroups) | Dietary burden expressed in | Most critical subgroup<sup>(a)</sup> | Most critical commodity<sup>(b)</sup> | Trigger exceeded (Y/N) | Comments |
|---------------------------|-----------------------------|-------------------------------------|-------------------------------------|------------------------|----------|
|                           | mg/kg bw per day | mg/kg DM |                          |                         |          |
|                           | Median   | Maximum | Median   | Maximum |                          |          |
| Cattle (all diets)        | 0.002    | 0.002   | 0.05     | 0.05    | Dairy cattle             | Potato, process waste | N        | –        |
| Cattle (dairy only)       | 0.002    | 0.002   | 0.04     | 0.04    | Dairy cattle             | Potato, process waste | N        | –        |
| Sheep (all diets)         | 0.002    | 0.002   | 0.05     | 0.05    | Ram/Ewe                  | Potato, process waste | N        | –        |
| Sheep (ewe only)          | 0.002    | 0.002   | 0.05     | 0.05    | Ram/Ewe                  | Potato, process waste | N        | –        |
| Swine (all diets)         | 0.001    | 0.001   | 0.04     | 0.04    | Swine (breeding)         | Potato, process waste | N        | –        |
| Poultry (all diets)       | 0.001    | 0.001   | 0.01     | 0.01    | Turkey                   | Potato, culls         | N        | –        |
| Poultry (layer only)      | 0.000    | 0.000   | 0.01     | 0.01    | Poultry layer            | Potato, culls         | N        | –        |

bw: body weight; DM: dry matter.

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

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

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

#### B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

| Livestock (available studies) | Animal | Dose (mg/kg bw/d) | Duration (days) | Comment/Source |
|-------------------------------|--------|-------------------|-----------------|----------------|
| Lactating ruminants           |        | 0.32              | 5               | Goat, [chlorophenyl-<sup>14</sup>C]-valifenalate (EFSA, 2013; Hungary, 2013) |
### Time needed to reach a plateau concentration in milk and eggs (days)

|          | Milk: 8 hours after administration | Eggs: – |
|----------|-----------------------------------|---------|
|          |                                   | No study available on poultry |

### Metabolism in rat and ruminant similar

|          | Yes |
|----------|-----|
|          | –   |

### Can a general residue definition be proposed for animals?

|          | Not applicable |
|----------|----------------|
|          | Although a study is available, a residue definition is not required under this review. |

### Animal residue definition for monitoring (RD-Mo)

|          | Ruminants: Valifenalate and valifenalate acid (IR5839) |
|----------|-------------------------------------------------------|
|          | If required in the future, this residue definition would need to be confirmed by additional toxicological data on valifenalate acid. |

### Animal residue definition for risk assessment (RD-RA)

|          | Ruminants: Valifenalate and valifenalate acid (IR5839) |
|----------|-------------------------------------------------------|
|          | If required in the future, this residue definition would need to be confirmed by additional toxicological data on valifenalate acid. |

### Fat soluble residues

|          | No |
|----------|----|
|          | –  |

### Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

|          | No analytical methods available for this review, and not required. However, a method described below was provided by the EURLs. |
|----------|-------------------------------------------------------------------------------------------------------------------|
|          | Liver, milk, muscle, kidney, fat (EURLs, 2020): |
|          | QuEChERS (HPLC–MS/MS) validated in liver and milk |
|          | LOQ 0.01 mg/kg for valifenalate and LOQ 0.02 mg/kg for IR5839. |

Based on the experience gained for liver and milk, an LOQ of 0.01 mg/kg for valifenalate and an LOQ of 0.02 mg/kg for IR5839 are supposed to be achievable for other animal products as well (e.g. muscle, kidney, fat).

Screening validation data generated by the EURL-AO for commodities of animal origin show that valifenalate can be monitored in milk and honey with an SDL of 0.005 mg/kg, and in muscle with an SDL of 0.01 mg/kg.

The analytical standard of the valifenalate metabolite IR5839 is not commercially available yet.

bw: body weight; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; SDL: screening detection limit; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe.

### B.2.1.2. Stability of residues in livestock

No studies available and not required under this review.
B.2.1.3. Magnitude of residues in livestock

Not relevant under this review as no MRLs are needed in animal commodities.

B.3. Consumer risk assessment

An ARfD has not been considered necessary; therefore, no acute exposure calculation was performed.

| ADI | 0.07 mg/kg bw per day (European Commission, 2014) |
| TMDI according to EFSA PRIMo | Not assessed in this review. |
| NTMDI, according to (to be specified) | Not assessed in this review. |
| Highest IEDI, according to EFSA PRIMo (rev.3.1) | Scenario EU: 0.7% ADI (PT general) |
| NEDI (% ADI) | Not assessed in this review. |
| Assumptions made for the calculations | |

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003)

| Metabolite(s) | Not assessed in this review. |
| ADI (mg/kg bw per day) | Not assessed in this review. |
| Intake of groundwater metabolites (% ADI) | Not assessed in this review. |

B.4. Proposed MRLs

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review |
|-------------|-----------|-------------------------|----------------------|-----------------------|
|             |           |                         |                      | MRL (mg/kg) | Comment |
| 151010      | Table grapes | 0.2 | – | 1 | Recommended(a) |
| 151020      | Wine grapes | 0.2 | – | 1 | Recommended(a) |
| 211000      | Potatoes | 0.01* | – | 0.01* | Recommended(a) |
| 220020      | Onions | 0.5 | – | 0.01* | Recommended(a) |
| 220030      | Shallots | 0.5 | – | 0.01* | Recommended(a) |
| 231010      | Tomatoes | 0.8 | – | 0.15 | Further consideration needed(b) |
|             |           | | | | |
| 231030      | Aubergines (eggplants) | 0.8 | – | 0.15 | Recommended(a) |
|             | Other commodities of plant nd/or animal origin | See Reg. (EU) 2019/50 | – | – | Further consideration needed(c) |

MRL: maximum residue level; CXL: codex maximum residue limit.

*: Indicates that the MRL is set at the limit of quantification.
(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E).
(b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E).
(c): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
### Appendix C – Pesticide Residue Intake Model (PRIMo)

#### Valifenalate

| Commodity | Input values | Calculated exposure (% of ADI) | Exposure resulting from the LOQ (MS diet) (% of ADI) | Details – acute risk assessment/children | Details – acute risk assessment/adults |
|-----------|--------------|--------------------------------|-------------------------------------------------|------------------------------------------|-----------------------------------------|
| Table grapes | 0.7% 0.49 0.5% 0.1% 0.1% | | | | |
| Potatoes | 0.6% 0.39 0.3% 0.1% 0.1% | | | | |
| Tomatoes | 0.5% 0.38 0.5% 0.0% 0.0% | | | | |
| Wine grapes | 0.5% 0.34 0.3% 0.1% 0.1% | | | | |
| Table grapes | 0.5% 0.33 0.2% 0.2% 0.0% | | | | |
| Tomatoes | 0.4% 0.31 0.3% 0.0% 0.0% | | | | |
| Wine grapes | 0.4% 0.3 0.2% 0.1% 0.0% | | | | |
| Table grapes | 0.4% 0.28 0.2% 0.1% 0.1% | | | | |
| Tomatoes | 0.4% 0.26 0.3% 0.1% 0.0% | | | | |
| Wine grapes | 0.4% 0.25 0.2% 0.0% 0.0% | | | | |
| Table grapes | 0.4% 0.24 0.2% 0.0% 0.0% | | | | |

**Conclusion:**

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of valifenalate is unlikely to present a public health concern.
As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

### Show results for all crops

| Unprocessed commodities | Processed commodities |
|-------------------------|-----------------------|
|                         |                       |

#### Details – acute risk assessment/children

| Results for children | Results for adults |
|----------------------|--------------------|
| No of commodities for which ARfDADI is exceeded (IESTI): | No of commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |             |                           |                     |
|                       |             |                           |                     |

#### Conclusion:

Total number of commodities exceeding the ARfDADI in children and adult diets

Details – acute risk assessment/adults/general population

| Results for children | Results for adults |
|----------------------|--------------------|
| No of processed commodities for which ARfDADI is exceeded (IESTI): | No of processed commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | Processed commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |                       |                           |                     |
|                       |                       |                           |                     |

Details – acute risk assessment/children

| Results for children | Results for adults |
|----------------------|--------------------|
| No of commodities for which ARfDADI is exceeded (IESTI): | No of commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |             |                           |                     |
|                       |             |                           |                     |

Details – acute risk assessment/adults/general population

| Results for children | Results for adults |
|----------------------|--------------------|
| No of processed commodities for which ARfDADI is exceeded (IESTI): | No of processed commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | Processed commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |                       |                           |                     |
|                       |                       |                           |                     |

Details – acute risk assessment/children

| Results for children | Results for adults |
|----------------------|--------------------|
| No of commodities for which ARfDADI is exceeded (IESTI): | No of commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |             |                           |                     |
|                       |             |                           |                     |

Details – acute risk assessment/adults/general population

| Results for children | Results for adults |
|----------------------|--------------------|
| No of processed commodities for which ARfDADI is exceeded (IESTI): | No of processed commodities for which ARfDADI is exceeded (IESTI): |
| Highest % of ARfDADI | Processed commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) |
|                       |                       |                           |                     |
|                       |                       |                           |                     |
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 |
| Potato culls            | 0.01*                | STMR                   | 0.01*               | HR      |
| Potato process waste    | 0.01*                | STMR\(^{(a)}\)         | 0.01*               | STMR\(^{(a)}\) |
| Potato dried pulp       | 0.01*                | STMR\(^{(a)}\)         | 0.01*               | STMR\(^{(a)}\) |

Risk assessment residue definition: valifenalate

STMR: supervised trials median residue; HR: highest residue.
*: Indicates that the input value is proposed at the limit of quantification.
(a): For processed commodities of potato, no default processing factor was applied because valifenalate residues are expected to be below the LOQ. Concentration of residues in these commodities is therefore not expected.

D.2. Consumer risk assessment

| Commodity            | Chronic risk assessment |
|----------------------|-------------------------|
|                      | Input value (mg/kg)     | Comment               |
| Table grapes         | 0.15                    | STMR                  |
| Wine grapes          | 0.15                    | STMR                  |
| Potatoes             | 0.01*                   | STMR                  |
| Onions               | 0.01*                   | STMR                  |
| Shallots             | 0.01*                   | STMR                  |
| Tomatoes             | 0.04                    | STMR (tentative)      |
| Aubergines/egg plants| 0.04                    | STMR                  |

Risk assessment residue definition: valifenalate

STMR: supervised trials median residue.
*: Indicates that the input value is proposed at the limit of quantification.
Appendix E – Decision tree for deriving MRL recommendations
### Appendix F – Used compound codes

| Code/trivial name | IUPAC name/SMILES notation/InChiKey\(^{(a)}\) | Structural formula\(^{(b)}\) |
|------------------|---------------------------------------------|-----------------------------|
| Valifenalate (IRS885), formerly valiphenal | Methyl (3RS)-3-(4-chlorophenyl)-N-[N-((isopropoxycarbonyl)-L-valyl]-β-alaninate | ![Structural formula](image1) |
|                  | DBXFMOWZRXXBRN-LWKPJOBUSA-N                |                             |
|                  | Clc1ccc(cc1)C(NC(=O)[C@@H](NC(=O)OC(C)C(C)CC(=O)=O) |                             |
| Valifenate acid (IRS839) | 3-(4-chlorophenyl)-3-[[N-{{(propan-2-yl)oxy}carbonyl}-L-valyl]amino]propanoic acid | ![Structural formula](image2) |
|                  | Clc1ccc(cc1)C(NC(=O)[C@@H](NC(=O)OC(C)C(C)CC(=O)=O) |                             |
|                  | QRSGZUTWBYAKHI-WMCAAGNKSA-N                |                             |
| Valifenate acid glucosyl ester | 1-O-[3-(4-chlorophenyl)-3-[[2S]-3-methyl-2-{{(propan-2-yl)oxy}carbonyl}amino]butanoyl]amino]propanoyl]-β-D-glucopyranose (One example of several possible glycoside structures) | ![Structural formula](image3) |
|                  | O=C[C@@H]10[C@H](CO)[C@@H](O)[C@H][O][C@H][O][C@H](OC(=O)OC(C)C(C)C1ccc(Cl)cc1KFYQZVQJOZGLV-GZLHUZQISA-N |                             |
| β-4-chlorophenylalanine | 3-amino-3-(4-chlorophenyl)propanoic acid | ![Structural formula](image4) |
|                  | NC(CC(=O)O)C1ccc(Cl)cc1 |                             |
|                  | BXGDBHAMDMMNO-UHFFFAOYSA-N |                             |

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.

\(^{(a)}\): ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).

\(^{(b)}\): ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version C05H41, Build 111302, 27 August 2019).