REASONED OPINION

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

European Food Safety Authority (EFSA)

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS), Spain, received an application from the company Industrias Químicas del Vallés to modify the existing maximum residue levels (MRLs) for the active substance metalaxyl in oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves'. Spain proposed to maintain the MRL in strawberries at the level of 0.5 mg/kg and to raise the existing EU MRLs for the other crop commodities. According to EFSA, the submitted residue trials are sufficient to derive MRL proposals for all crops under consideration. In addition, as the residues transferred in citrus pomace used to fed livestock result in an increase in animal burdens, MRLs were proposed for animal matrices considering two possible enforcement residue definitions. Based on the risk assessment results, EFSA concludes that the proposed use of metalaxyl on oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves' will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

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Keywords: metalaxyl, oranges, grapefruits, strawberries, Brussels sprouts, spinaches and similar leaves, MRL application, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS), Spain, received an application from the company Industrias Químicas del Vallés to modify the existing maximum residue levels (MRLs) for the active substance metalaxyl in oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves'. The EMS Spain proposed to maintain the MRL at the level of 0.5 mg/kg in strawberries and to raise the existing European Union (EU) MRLs in the other crop commodities. Spain 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 9 November 2015.

It is highlighted that metalaxyl is a racemic mixture of *R*- and *S*-enantiomers, the single *R*-enantiomer being also an active substance available on the market as metalaxyl-M. Therefore, data available for both active substances were considered in this evaluation. The assessment was mostly based on the updated evaluation report submitted by the EMS, the draft assessment reports (DARs) prepared for both active substances under Directive 91/414/EEC, the Commission review report on metalaxyl, the conclusions from the peer review of the pesticide risk assessment of metalaxyl-M and EFSA opinions on the review of the existing MRLs according to Regulation (EC) No 396/2005 (hereafter Article 12 MRL review) of metalaxyl and metalaxyl-M.

In the framework of the peer review, data were sufficient to derive an acceptable daily intake (ADI) of 0.08 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.5 mg/kg bw, applicable to both metalaxyl and metalaxyl-M.

The metabolism of metalaxyl and metalaxyl-M in primary crops was evaluated in the framework of the peer review and under the Article 12 MRL review. The residue definition for enforcement and risk assessment were proposed as 'metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)'. For the uses on the crops under consideration, EFSA concludes that the metabolism of metalaxyl is sufficiently addressed and the above residue definition for enforcement and risk assessment is applicable.

EFSA concludes that the submitted residue trials are sufficient to derive MRL proposals for all crops under consideration. Adequate analytical enforcement methods are available to monitor metalaxyl residues in the plant matrices under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg.

Studies on residues in processed commodities have not been submitted and are not required as for each crop, the individual theoretical maximum daily intake (TMDI) is below 10% of the ADI.

The metabolic pathway of metalaxyl in rotational crops is similar to that in primary crops. Based on the available field studies, it is concluded that significant residues are unlikely to occur in rotational crops, provided that metalaxyl is used according to the proposed good agricultural practice (GAP).

Based on the Organisation for Economic Co-operation and Development (OECD) feedstuff table, residues in citrus pulp (pomace) resulting from the uses on oranges and grapefruits result in an increase in the animal burdens. Therefore, the setting of MRLs in products of animal origin was considered. Since not relevant for the representatives uses, residue definitions for animal products were not proposed in the framework of the peer review. Based on the available data, two optional MRL values are proposed for animal products, considering the two following possible residue definitions for enforcement:

1) 'sum of metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl' as proposed under the Article 12 MRL review;
2) 'metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)' as currently reported under Regulation (EC) No 396/2005, and considering that such a definition is set by default as metalaxyl is extensively metabolised and not observed in the goat and poultry metabolism studies (except eggs but accounting for very low proportions).

EFSA proposes to the risk managers to decide which of these two options should be taken into consideration for the setting of residue definitions and MRLs in animal products.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). The long-term exposure assessment performed under the Article 12 MRL review was updated with the median residue levels (STMR) derived from the residue trials conducted on the crops under consideration and the STMR proposed for animal commodities. Additionally, the STMR reported for gooseberries in the previous EFSA opinion was included in the calculation. The food commodities,

for which no uses were reported in the framework of the Article 12 MRL review, were excluded from the calculation, assuming that there is no use of metalaxyl on these crops.

Consumer intake concerns were not identified for any of the European diets incorporated in the EFSA PRIMo, as the highest chronic intake was calculated to be 21% of the ADI (DE child) and the highest acute exposure 3% of the ARfD (spinach, BE child). EFSA concludes that the intended use of metalaxyl on oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves' will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a concern for public health. EFSA proposes to amend the existing MRLs as reported in the summary table below.

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition (plant commodities): Metalaxyl and metalaxyl-M (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)				
0110010	Grapefruits	0.5	0.7	SEU, based on trials on oranges
0110020	Oranges	0.5	0.7	
0152000	Strawberries	0.5	0.6	Indoor, soil drip applications
0242010	Brussels sprouts	0.05*	0.15	SEU
0252000	Spinaches and similar leaves	–	1.5	Extrapolated to the whole group from SEU trials on open leaf varieties of lettuce
0252010	Spinaches	0.05*		
0252020	Purslanes	1.0		
0252030	Chards/beet leaves	0.05*		
Option 1: Enforcement residue definition (animal commodities): Sum of metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl				
101X010	Swine/sheep/goat: Meat	(b)	0.01*	LOQ of 0.01 mg/kg (meat, fat) and of 0.05 mg/kg (liver, kidney) based on the LOQs achieved by the available validated analytical methods
101X020	Swine/sheep/goat: Fat	(b)	0.01*	
101X030	Swine/sheep/goat: Liver	(b)	0.05*	
101X040	Swine/sheep/goat: Kidney	(b)	0.2	
1012010	Bovine: Meat	(b)	0.01*	
1012020	Bovine: Fat	(b)	0.01*	
1012030	Bovine: Liver	(b)	0.05*	
1012040	Bovine: Kidney	(b)	0.3	
10160X0	Poultry: Meat and fat	(b)	0.01*	
10160X0	Poultry: Liver and kidney	(b)	0.05*	
1020000	Milk	(b)	0.01*	
1030000	Birds' eggs	(b)	0.01*	
Option 2: Enforcement residue definition (animal commodities): Metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers) (current residue definition under Reg. 2016/486)				
101X0X0	All species: All matrices	0.05*	0.02*	Default MRL. Metalaxyl not expected to be present in animal matrices

EU: European Union; MRL: maximum residue level; SEU: southern Europe.

*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.

(b): MRLs not listed according to the proposed residue definition in the EU legislation.

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Background

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

Spain, hereafter referred to as the evaluating Member State (EMS), received an application from the company Industrias Químicas del Vallés[4] to modify the existing MRLs for the active substance metalaxyl in oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves'. This application was notified to the European Commission and the European Food Safety Authority (EFSA) and was subsequently evaluated by the EMS in accordance with Article 8 of the Regulation. After completion, the evaluation report was submitted to the European Commission and to EFSA on 9 November 2015. The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2015-00698 and the following subject:

Metalaxyl – Application to modify the existing MRLs in various crops.

Spain proposed to raise the existing MRLs to 0.6 mg/kg in grapefruits and oranges, to 0.15 mg/kg in Brussels sprouts and to 1.5 mg/kg in 'spinaches and similar leaves'. For strawberries, no modification of the existing MRL of 0.5 mg/kg was proposed.

EFSA proceeded with the assessment of the application and the evaluation report as required by Article 10 of the Regulation. In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the EMS, provide a reasoned opinion on the risks to the consumer associated with the application.

An updated evaluation report, addressing the data requirements set by EFSA (Spain, 2016) 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.

In accordance with Article 11 of the Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within 3 months (which may be extended to 6 months if more detailed evaluations need to be carried out) from the date of receipt of the application. If EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

The active substance and its use pattern

Metalaxyl is the ISO common name for methyl *N*-(methoxyacetyl)-*N*-(2,6-xylyl)-DL-alaninate (IUPAC) and is a racemic mixture of *R*- and *S*-enantiomers, the single *R*-enantiomer being also an active substance available on the market as metalaxyl-M. The chemical structures of the active substances and its main metabolites are reported in Appendix B.

Metalaxyl was evaluated in the framework of Directive 91/414/EEC with Portugal designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Directive 2010/28/EU[5] which entered into force on 1 July 2010 for use as fungicide only. In accordance with Regulation (EU) No 540/2011[6], metalaxyl is approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC. The representative uses evaluated in the peer review were foliar applications on potatoes and tomatoes. The draft assessment report (DAR) was not peer reviewed by EFSA and therefore no EFSA conclusion is available. In 2015, the peer review for the renewal of the approval of the active

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

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

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

[4] Industrias Químicas del Vallés, S.A., Av. Rafael Casanova, 81, 08100 Mollet del Vallés, Barcelona, Spain.

[5] Commission Directive 2010/28/EU of 23 April 2010 amending Council Directive 91/414/EEC to include metalaxyl as active substance. OJ L 104, 24.4.2010, p. 57–59.

[6] Commission Implementing Regulation (EU) No 540/2011 of 23 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.

substance metalaxyl-M (active *R*-enantiomer of metalaxyl racemate) according to the Regulation (EU) No 1141/2010 was finalised (EFSA, 2015a).

Common EU MRLs to cover the uses of metalaxyl and metalaxyl-M have been established in Annex II of Regulation (EC) No 396/2005, according to a common residue definition for enforcement reported as 'metalaxyl, including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)'. Since the entry into force of this regulation, EFSA has issued several reasoned opinions on the modification of MRLs related to the uses of metalaxyl-M, but none for metalaxyl. The review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 has been initially conducted separately for metalaxyl-M (EFSA, 2011) and metalaxyl (EFSA, 2014). These assessments have been reconsidered in 2015 taking into account a combined review of the MRLs applicable to metalaxyl and metalaxyl-M (hereafter Article 12 MRL review) (EFSA, 2015b). These proposals, however, have not been considered yet in the EU legislation. The MRL changes reported for metalaxyl/metalaxyl-M in the EU legislation since the Article 12 MRL reviews are summarised in Table 1.

Table 1: Overview of the MRL changes after the Article 12 MRL reviews

Procedure	Considered by Regulation	Remarks
Art. 10 (EFSA, 2012)	(EU) No 441/2012	Lettuce, other salad plants (metalaxyl-M)
Art. 10 (EFSA, 2013)	(EU) No 36/2014	Currants (metalaxyl-M)
Art. 43 (EFSA, 2015b)	Not yet implemented	Combined review of MRLs applicable to metalaxyl and metalaxyl-M
Art. 10 (EFSA, 2015c)	(EU) 2016/486	Gooseberries (metalaxyl-M)

MRL: maximum residue level; EU: European Union.

Codex Alimentarius has established maximum residue limits (CXLs) according to a monitoring residue definition set as metalaxyl, for a wide range of commodities including for some of the crops under consideration: 5 mg/kg citrus fruits (post-harvest treatment), 0.2 mg/kg Brussels sprouts and 2 mg/kg spinaches.

The details of the intended good agricultural practices (GAPs) for metalaxyl are given in Appendix A.

Assessment

EFSA has based its assessment on the updated evaluation report submitted by the EMS (Spain, 2016), the DAR prepared under Directive 91/414/EEC (Portugal, 2000), the Commission review report on metalaxyl (European Commission, 2010a), the conclusions from the peer review of the pesticide risk assessment of the active substance metalaxyl-M (EFSA, 2015a) and EFSA opinions on the Article 12 MRL reviews of metalaxyl and metalaxyl-M (EFSA, 2011, 2014, 2015b). 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[7] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a–g, 2000, 2010a,b, 2015; OECD, 2011, 2013).

1. Method of analysis

1.1. Methods for enforcement of residues in food of plant origin

Analytical methods for the determination of metalaxyl (sum of isomers) in plant commodities were assessed during the combined Article 12 MRL review, where it was concluded that metalaxyl residues can be enforced at an limit of quantification (LOQ) of 0.01 mg/kg in high water, high acid and high oil content commodities as well as in dry commodities (EFSA, 2015b).

As the crops under consideration in this MRL application belong to the high acid and high water groups, EFSA concludes validated analytical methods are available to enforce metalaxyl residues at the LOQ of 0.01 mg/kg.

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

1.2. Methods for enforcement of residues in food of animal origin

Since not required in support to the representative uses, analytical methods for the determination of metalaxyl residues in animal matrices were not assessed in the framework of the peer review. An assessment of the available methods was conducted during the Article 12 MRL review (EFSA, 2015b), based on an enforcement residue definition proposed as 'sum of metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl'. This proposal differs from the current enforcement residue definition established in Regulation (EC) No 396/2005 as 'metalaxyl, including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)'.

A high-performance liquid chromatography (HPLC) method using a tandem mass spectrometry (MS/MS) detection was concluded to be validated for the determination of metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety at an LOQ of 0.01 mg/kg in muscle, fat, milk and eggs and of 0.05 mg/kg in liver and kidney. An independent laboratory validation (ILV) was only provided for eggs, liver and milk and is still missing for fat. Furthermore, the efficiency of the extraction, hydrolysis and derivatisation steps could not be demonstrated and further information was requested under the combined Article 12 MRL review (EFSA, 2015b).

Additionally, and considering the monitoring residue definition currently reported in the EU legislation, it was concluded that an analytical method using liquid chromatography with tandem mass spectrometry (LC–MS/MS) and its ILV were evaluated and validated in food of animal origin for the determination of metalaxyl (sum of isomers) at an LOQ of 0.02 mg/kg in eggs, fat, meat and milk (EFSA, 2014).

2. Mammalian toxicology

The toxicological profile of the active substance metalaxyl was assessed in the framework of the peer review under Directive 91/414/EEC and toxicological reference values were established for the active substance (European Commission, 2010a). In the framework of the renewal of the approval of the active substance metalaxyl-M, animal metabolism studies and toxicity studies conducted with both active substances were considered and it was concluded that the toxicological reference values initially proposed for metalaxyl apply also to metalaxyl-M (EFSA, 2015a,b). The toxicological reference values applicable to both active substances are compiled in Table 2.

Table 2: Overview of the toxicological reference values

	Source	Year	Value	Study	Safety factor
Metalaxyl and metalaxyl-M					
ADI	EC/EFSA	2010/2015a	0.08 mg/kg bw per day	Dog, 2-year study[(a)]	100
ARfD	EC/EFSA	2010/2015a	0.5 mg/kg bw	Rat, developmental study[(b)]	100

ADI: acceptable daily intake; ARfD: acute reference dose; EC: European Commission; EFSA: European Food Safety Authority; bw: body weight.
(a): Study performed with metalaxyl.
(b): Study performed with metalaxyl-M.

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

The metabolism of metalaxyl in primary crops was initially assessed during the peer review under Directive 91/414/EEC (Portugal, 2000). Further studies with metalaxyl-M were evaluated under the renewal of the approval of metalaxyl-M (EFSA, 2015a). All available data were considered together during the Article 12 MRL review to derive conclusions on the metabolism of metalaxyl and metalaxyl-M in primary crops (EFSA, 2015b). An overview of the available metabolism studies is presented in Table 3.

Table 3: Summary of available metabolism studies in plants

Crop groups	Crops	Applications	Sampling (DAT)	Comments
Fruit	Grape	Foliar: 7 × 500 g/hL	52 DAT_7	Metalaxyl
	Tomato	Foliar: 3 × 160 g/ha	3, 14 DAT_3	Metalaxyl-M
Root	Potato	Foliar: 1) 4 × 62.5 g/ha 2) 6 × 426 g/ha 3) 6 × 1,280 g/ha	1) 37 DAT_4 2) 7 DAT_6 3) 7 DAT_6	Metalaxyl
Leafy	Lettuce	Foliar: 2 × 250 g/ha	14 DAT_2	Metalaxyl
		Foliar: 3 × 200 g/ha	21 DAT_3	Metalaxyl and metalaxyl-M
	Tobacco	Soil: 1) 1 × 280 g/ha 2) 1 × 560 g/ha 3) 1 × 3,530 g/ha	21–140 DAT	Metalaxyl
Cereals/grass	Wheat	Seed: 1) 19.3 g/100 kg seeds 2) 157 g/100 kg seeds	83, 127 DAT	Metalaxyl-M

DAT: days after treatment.

The metabolic patterns were concluded to be similar in the different crop groups and no preferential metabolism is expected for the *R*- and *S*-enantiomers. Based on these studies and considering that metalaxyl constitute the most relevant part of the residues, the residue definition for enforcement and risk assessment was proposed as 'metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)' (EFSA, 2014, 2015a,b).

The current residue definition set in Regulation (EC) No 396/2005 is identical to the residue definition for enforcement derived in the peer review.

For the uses on the crops under consideration, EFSA concludes that the metabolism of metalaxyl is sufficiently addressed and the residue definitions for enforcement and risk assessment agreed during the Article 12 MRL review and the peer review are applicable.

3.1.1.2. Magnitude of residues

Oranges, grapefruits (southern Europe (SEU) GAP: 3 × 200 g/ha, preharvest interval (PHI) 14 days)

The applicant submitted eight GAP-compliant residue trials on oranges, performed in Italy, Spain and Greece over the growing seasons of 2011 and 2012. Samples were analysed for the whole fruit when collected from 0 to 7 days after application and for peel and pulp separately when harvested at longer intervals (residues in whole fruit derived by calculation). Except for one sample, residues in pulp were all below the LOQ of 0.01 mg/kg. Based on residue levels in the range of 0.03–0.30 mg/kg, an MRL proposal of 0.7 mg/kg is derived from the trials conducted on orange and extrapolated to grapefruit.

This proposal is higher than the MRL proposed by the EMS Spain (0.6 mg/kg), since the EMS did not apply the Organisation for Economic Co-operation and Development (OECD) approach as currently required for the estimation of the MRL values (OECD, 2011), but the former EU methodology (European Commission, 1997g).

Strawberries (Indoor GAP: 3 × 380 g/ha, drip applications, PHI 14 days)

The applicant submitted eight indoor GAP-compliant residue trials, performed in Italy, Spain and Portugal over the growing seasons of 2011 and 2012, where the active substance was applied by soil drip applications according to the proposed GAP. Residue data are sufficient to derive an MRL proposal of 0.6 mg/kg.

As previously proposed, the lower MRL proposal (0.5 mg/kg) suggested by the EMS, results from the use of the EU methodology instead of the agreed OECD approach.

Brussels sprouts (SEU GAP: 3 × 200 g/ha, PHI 14 days)

The applicant submitted four GAP-compliant residue trials on Brussels sprouts, performed in Spain, Italy and Greece over the growing seasons of 2011 and 2012. The residue data are sufficient to derive an MRL proposal of 0.15 mg/kg.

Spinaches and similar leaves (SEU GAP: 3 × 200 g/ha, PHI 14 days)

The applicant submitted eight GAP-compliant residue trials on lettuce (open leaf varieties), performed in Italy, Spain, France, Greece and Portugal over the growing seasons of 2011 and 2012 and proposes to extrapolate these data to the whole group 'spinach and similar leaves'. According to EU guidance document, such an extrapolation is acceptable and an MRL of 1.5 mg/kg is proposed for the 'spinach and similar leaves' group.

The results of the residue trials, the highest (HR) and median (STMR) residue level and the MRL proposals are summarised in Table 4.

Table 4: Overview of the available residues trials data

Crop (GAP)	NEU/SEU indoor[a]	Residue levels observed in the supervised residue trials[b] (mg/kg)	Recommendations/ comments[c]	MRL proposal (mg/kg)	HR[d] (mg/kg)	STMR[e] (mg/kg)
Oranges (3 × 200 g/ha PHI 14 days)	SEU	0.03; 2 × 0.10; 0.18; 0.26; 0.28; 0.29; 0.30 Pulp: 7 × < 0.01; 0.02	• Underlined values: higher residues at a longer PHI of 21 or 28 days. • MRL_{OECD}: 0.61/0.70 • **Bold** values: Extrapolation to grapefruits	**0.7**	0.30 Pulp: 0.02	0.22 Pulp: 0.01
Strawberries (3 × 380 g/ha PHI 14 days)	Indoor	0.08; 0.11; 0.12; 0.16; 2 × 0.17; 0.25; 0.30 (Trial conducted with drip irrigation applications)	• Underlined value: higher residues at a longer PHI of 21 days. MRL_{OECD}: 0.51/0.60	**0.6**	0.30	0.17
Brussels sprouts (3 × 200 g/ha PHI 14 days)	SEU	2 × 0.03; 0.05; 0.07	MRL_{OECD}: 0.14/0.15	**0.15**	0.07	0.04
Lettuce (3 × 200 g/ha PHI 14 days)	SEU	0.05; 0.07; 0.12; 0.15; 0.17; 0.36; 0.71; 0.74	MRL_{OECD}: 1.42/1.5 • **Bold** values: Extrapolation to the whole group 'spinach and similar leaves'	**1.5**	0.74	0.16

GAP: good agricultural practice; MRL: maximum residue level; PHI: preharvest interval; OECD: Organisation for Economic Co-operation and Development.

(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): Individual residue levels considered for MRL calculation are reported in ascending order (2 × < 0.01, 0.01, 6 × 0.02, 0.04, 0.08, 2 × 0.10, 0.15, 0.17).

(c): Any information/comment supporting the decision and OECD MRL calculation (unrounded/rounded values).

(d): HR: Highest residue level according to the residue definition for risk assessment.

(e): STMR: Median residue level according to residue definition for risk assessment.

The stability of metalaxyl residues in plant matrices under storage conditions prior to analysis was assessed during the peer review of metalaxyl-M (EFSA, 2015a). Residues of metalaxyl were found to be stable at $\leq -18°C$ for up to 24 months in high water (tomato), high water/starch (potato), high oil (rapeseed), high acid (orange) and dry/starch (cereals) matrices (EFSA, 2015a,b). As the trial samples were stored for a maximum period of 10 months under conditions for which integrity of the samples was demonstrated, it is concluded that the residue data are valid with regard to storage stability.

According to the EMS, the analytical methods used to analyse the residue trial samples have been sufficiently validated and were proven to be fit for purpose (Spain, 2016).

EFSA concludes that the data are sufficient to derive the following MRL proposals:

- 0.7 mg/kg oranges and grapefruits in SEU (trials on oranges);

- 0.6 mg/kg strawberries, indoor EU;
- 0.15 mg/kg Brussels sprouts in SEU;
- 1.5 mg/kg spinaches and similar leaves in SEU (extrapolation from trials on open leaf varieties of lettuce).

3.1.1.3. Effect of industrial processing and/or household preparation

Standard hydrolysis studies simulating the effect on the nature of metalaxyl residues under processing conditions representative of pasteurisation, boiling and sterilisation were assessed in the peer review of metalaxyl-M and under the Article 12 MRL review (EFSA, 2014, 2015a,b). It was concluded that metalaxyl is hydrolytically stable and that the residue definitions derived for primary crops are also applicable to processed commodities.

New studies to assess the magnitude of residues in the processed commodities have not been submitted and are not necessary as for each individual commodity, the total theoretical maximum daily intake (TMDI) amounts for less than 10% of the ADI (European Commission, 1997d). However, processing studies on citrus, grape and strawberry have been assessed during the Article 12 MRL review and processing factors (PFs) have been proposed (EFSA, 2014).

3.1.2. Rotational crops

Most of the crops under consideration can be grown in rotation with other plants and therefore the possible occurrence of residues in succeeding crops resulting from the use on primary crops has to be assessed. The soil degradation studies for metalaxyl and metalaxyl-M resulted in maximum period required for 90% dissipation (field method; DT_{90f}) values of 289 and 103 days, respectively, which are above the trigger value of 100 days for both compounds (EFSA, 2015a). Thus, further studies on rotational crops are required (European Commission, 1997c).

3.1.2.1. Nature of residues

The metabolism of metalaxyl and metalaxyl-M in rotational crops has been investigated in the framework of the Article 12 MRL review (EFSA, 2014) and in the framework of the peer review (EFSA, 2015a), respectively. Based on the available studies, it was concluded that the metabolic pathway of metalaxyl and metalaxyl-M in rotational crops is similar to that in primary crops but with a greater proportion of sugar conjugates (EFSA, 2014, 2015a).

3.1.2.2. Magnitude of residues

Rotational crop field studies performed with metalaxyl-M were assessed during the Article 12 MRL review (EFSA, 2014) and in the peer review for metalaxyl-M (EFSA, 2015a).

The Article 12 MRL review for metalaxyl assessed three rotational crop field trials, where metalaxyl-M was applied to potatoes at 700–1,000 g/ha and rotational crops (carrot, lettuce, cauliflower/broccoli and wheat/barley) planted at plant-back interval (PBI) of 27–30 days. Residues were all below the LOQ of 0.02 mg/kg, except in one trial where residues in immature lettuce and immature broccoli were measured at levels of 0.03–0.11 mg/kg (EFSA, 2014).

Four additional field trials were considered during the peer review of metalaxyl-M, where the active substance was applied to bare soil at 600 g/ha and rotational crops (carrot, spinach and wheat/barley) planted at PBIs of 30, 60, 180, 365 and 465, depending on the crop. Residues were generally found to be below the LOQ of 0.01 mg/kg, except for the two shortest PBIs where residues up to 0.03 mg/kg were observed in spinach, up to 0.023 mg/kg in carrot tops, up to 0.12 mg/kg in cereal forage and up to 0.06 mg/kg in cereal straw (EFSA, 2015a).

The seasonal application rates reported for metalaxyl for the crops under consideration range from 600 to 1,140 g/ha. Considering that the mostrecent rotational crop field trials include applications to a bare soil (overestimation of residues is expected and confirmed by the older trials), EFSA concludes that significant residues are not expected in rotational crops provided that metalaxyl on primary crops is applied in compliance with the intended GAPs.

3.2. Nature and magnitude of residues in livestock

Citrus fruit by-products can be fed to livestock and therefore the nature and magnitude of metalaxyl residues in livestock shall be further assessed (European Commission, 1996).

3.2.1. Dietary burden of livestock

The most recent dietary burden for livestock was calculated by EFSA during the combined Article 12 MRL review (EFSA, 2015b) considering the existing uses of metalaxyl and metalaxyl-M and the European methodology and feedstuff table reported in the EU guideline 7031/VI/95 rev. 4 (European Commission, 1996).

EFSA now updated the animal burden calculations according to the OECD feedstuff table and methodology reported in the OECD guidance documents (OECD, 2009, 2013), taking into account metalaxyl residues in citrus fruits from the new intended uses. As no information was provided, a default PF of 10 was applied to estimate the transfer of residues in dried citrus pulp (pomace). In addition, as carrots are now listed in the OECD feedstuff table, this crop was added to the livestock dietary burden calculations.

It is noted that the OECD list of feed commodities comprises additional by-products of the plant commodities on which the uses of metalaxyl/metalaxyl-M have been authorised according to the Article 12 MRL review, but for which no residue data are available: forage/silage/by-products of maize, pea hay/silage, lupin seed meal, dried pulp and process waste of potato. In addition, according to the combined Article 12 MRL review, there are authorised uses on apples and soya bean but no residue data are available (EFSA, 2015b).

The input values for the dietary burden calculation are summarised in Table 5. Default PFs have been added to this table within brackets.

Table 5: Input values for the dietary burden calculation

Feed commodity	Median dietary burden		Maximum dietary burden	
	Input (mg/kg)	Comment	Input (mg/kg)	Comment
Citrus dried pulp	2.2	STMR (0.22) × PF (10)	2.2	STMR (0.22) × PF (10)
Carrot	0.02	STMR (EFSA, 2015b)	0.07	HR (EFSA, 2015b)
Cabbage, kale, rape forage, maize grain, pulses, potato, rapeseed meal, linseed meal, sunflower seed meal	See Table 8 of the EFSA reasoned opinion on the combined Article 12 MRL review for metalaxyl and metalaxyl-M (EFSA, 2015b)			

STMR: supervised trials median residue; PF: processing factor; EFSA: European Food Safety Authority; HR: highest residue.

The estimated animal dietary intakes taking into account the feed commodities listed in Table 5 and including the crops under consideration in this MRL application are summarised in Table 6.

Table 6: Results of the dietary burden calculation

Animals	Median burden (mg/kg bw)	Maximum burden (mg/kg bw)	Above 0.1 mg/kg DM	Maximum burden[(a)] (mg/kg DM)	Highest contributor[(b)]	Previous assessment (max. burden)
Beef cattle	0.005	0.012	Yes	0.50	Citrus dried pulp	0.61 mg/kg DM
Dairy cattle	0.023	**0.033**	Yes	**0.86**	Citrus dried pulp	0.59 mg/kg DM
Ram/ewe	0.003	0.009	Yes	0.27	Kale leaves	Bovine intake taken into account
Lamb	0.004	0.012	Yes	0.27	Kale leaves	
Pig breeding	0.010	**0.015**	Yes	**0.66**	Citrus dried pulp	0.32 mg/kg DM
Pig finishing	0.002	0.005	Yes	0.17	Carrot culls	
Poultry broiler	0.003	0.006	No	0.08	Carrot culls	0.12 mg/kg DM
Poultry layer	0.003	0.006	No	0.09	Carrot culls	
Turkey	0.003	0.006	No	0.08	Carrot culls	

bw: body weight; DM: dry matter.
(a): Values in bold indicate animal intakes higher than those listed in the previous assessment (EFSA, 2015b).
(b): Considering the maximum dietary animal burden.

Compared to the previous assessment (EFSA, 2015b), residues in citrus pulp and the use of the OECD methodology increase the dietary burden for dairy cattle and swine. Therefore, a need for the modification of the MRLs has to be considered for ruminant and porcine products.

3.2.2. Nature of residues

Residue definitions for animal matrices were not proposed in the conclusion of the peer review of metalaxyl/metalaxyl-M, since not required in support of the representative uses. In the framework of the Article 12 MRL review, based on the available metabolism studies on hen and goat, the residue definition for enforcement and risk assessment was proposed as 'sum metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl'.

Additionally and taking into account that metalaxyl isomers cannot be appropriate markers of the residues in animal matrices, since not present in the goat metabolism and mostly not detected in hen (except eggs 5–8% total radioactive residue (TRR)), it was suggested to limit the residue definition to metabolite CGA107955 in animal tissues and to metabolite CGA67869 in milk. However, analytical methods and livestock feeding studies supporting such a simplified residue definition are currently not available and would be necessary to apply this proposal (EFSA, 2015b).

The existing enforcement residue definition in Regulation (EC) No 396/2005 is set as for plants as 'metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)'. As mentioned previously, this residue definition should be considered set by default, since metalaxyl isomers were not identified animal matrices (except eggs).

3.2.3. Magnitude of residues

The feeding study conducted on cows and submitted in the framework of the peer review (EFSA, 2015a) was considered under the combined Article 12 MRL review. Cows were dosed with metalaxyl at 0.07, 0.36 and 0.68 mg/kg bw for 14, 21 and 28 consecutive days, representing a 2 N, 11 N and 21 N dose rates, respectively, when referring the estimated dairy cow intake. Samples were analysed using a common moiety method taking into account metalaxyl and metabolites containing the 2,6-dimethylaniline moiety. In addition, liver and kidney samples were reanalysed for metalaxyl only (sum of isomers).

The highest (HR), median (STMR) residue levels and the MRL proposals derived from this feeding study and considering the intakes of 0.033, 0.012 and 0.015 mg/kg bw calculated according to the OECD methodology for dairy cattle, sheep and pig, respectively, are reported in Table 7. For muscle and fat, although analysed with a method achieving an LOQ of 0.05 mg/kg, MRL, STMR and HR were proposed at the value of 0.01 mg/kg taking into account the following:

- Residues in muscle and fat were all below the LOQ of 0.05 mg/kg at all feeding levels, including the highest ones (21 N for dairy cattle and 59 N for ewe).
- A validated analytical method is available to analyse metalaxyl residues in fat, muscle, eggs and milk at the LOQ of 0.01 mg/kg according to the proposed residue definition (see Section 1.2).

It is highlighted that these MRL proposals refer to a residue definition including metalaxyl isomers and the metabolites containing the 2,6-dimethylaniline moiety. These proposals are similar to the values proposed for ruminant and pig products in the framework of the combined Article 12 MRL review (EFSA, 2015b), except for swine kidney where the value is increased from 0.15 to 0.20 mg/kg.

A poultry study was submitted and assessed in the framework of the peer review (EFSA, 2015a). In the samples analysed according to the common moiety method for metalaxyl and metabolites containing the 2,6-dimethylaniline moiety, residues were all below the LOQ of 0.05 mg/kg (except liver: 0.18 mg/kg) at the lowest feeding levels of 10 mg/kg DM (*ca.* 100 N). It is concluded that metalaxyl residues are not expected to be present in poultry matrices. Therefore, MRLs are proposed at the LOQ of 0.01 mg/kg in muscle, fat and eggs and 0.05 mg/kg in liver and kidney. Considering that residues were almost all below or close to the LOQ at the lowest feeding level (*ca.* 100 N), STMR and HR are proposed at the value of 0.01 mg/kg.

Table 7: STMR, HR and MRL values derived from the livestock feeding studies

Residue levels expressed as 'sum metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl'						
Bovine						
Closest level[(a)] 0.07 mg/kg bw 21 N (Dairy cattle) 59 N (Beef cattle)	**Residues at the closest feeding level (mg/kg)**		**Estimated value at 1 N level**		**MRL proposal (mg/kg)**	**MRL proposal (Art. 12 MRL review)**
	Mean	**Highest**	**STMR[(b)] (mg/kg)**	**HR (mg/kg)**		
Meat	–	–	0.01[(c)]	0.01[(c)]	–	–
Muscle	< 0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	0.01*
Fat	< 0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	0.01*
Liver	0.10	0.11	0.03	0.05	0.05*	0.05*
Kidney	0.19	0.21	0.18	0.20	0.3	0.3
Milk	< 0.01	< 0.01	< 0.01	< 0.01	0.01*	0.01*
Sheep						
Closest level[(a)] 0.07 mg/kg bw 6.1 N Lamb 7.7 N Ewe	**Residues at the closest feeding level (mg/kg)**		**Estimated value at 1 N level**		**MRL proposal (mg/kg)**	**MRL proposal (Art. 12 MRL review)**
	Mean	**Highest**	**STMR[(b)] (mg/kg)**	**HR (mg/kg)**		
Meat	–	–	0.01[(c)]	0.01[(c)]	–	No specific proposals for sheep (MRLs for bovine applicable to ovine)
Muscle	< 0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	
Fat	0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	
Liver	0.10	0.11	0.01	0.02	0.05*	
Kidney	0.19	0.21	0.17	0.18	0.2	
Milk	< 0.01	< 0.01	0.01	0.01	0.01*	
Swine						
Closest level[(a)] 0.07 mg/kg bw 6.1 N Breeding 13.9 N Finishing	**Residues at the closest feeding level (mg/kg)**		**Estimated value at 1 N level**		**MRL proposal (mg/kg)**	**MRL proposal (Art. 12 MRL review)**
	Mean	**Highest**	**STMR[(b)] (mg/kg)**	**HR (mg/kg)**		
Meat	–	–	0.01[(c)]	0.01[(c)]	–	–
Muscle	< 0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	0.01*
Fat	0.05	< 0.05	0.01[(c)]	0.01[(c)]	0.01*,[(c)]	0.01*
Liver	0.10	0.11	0.015	0.024	0.05*	0.05*
Kidney	0.19	0.21	0.18	0.18	0.2	0.15

STMR: supervised trials median residue; HR: highest residue; MRL: maximum residue level; bw: body weight.
*Indicates that the MRL is proposed at the limit of quantification.
(a): Closest feeding level and N dose rate related to the maximum dietary burden (Table 6).
(b): Mean dietary burden considered to derive the STMR values at the 1 N dose rate.
(c): MRLs, STMR and HR proposed at 0.01 mg/kg, since all residues < 0.05 mg/kg at the highest feeding levels in the range of 21 N for dairy cattle to 59 N for ewe.

Alternatively, taking into account the animal monitoring residue definition reported in Regulation (EU) No 2016/486 as 'metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)', it can be proposed to set the MRLs for animal products at the LOQ Level achieved by the available analytical method, since:

- At the highest feeding levels (21 N dairy cattle and 100 N laying hen), residues were all below the LOQ (0.01 or 0.05 mg/kg) in the fat, muscle, milk and egg samples analysed for total residues (metalaxyl and metabolites containing the 2,6-dimethylaniline moiety).

- Residues were below the LOQ of 0.05 mg/kg in cow liver and kidney when reanalysed for metalaxyl only (except liver at the 21 N dose level, 0.06 mg/kg).

As an analytical method is available to analyse metalaxyl (sum of isomers) at an LOQ of 0.02 mg/kg (see Section 1.2), it is proposed to set all MRLs for all animal products at the LOQ value of 0.02 mg/kg. The setting of MRL values at the LOQ, confirm the results of the animal metabolism studies where it was concluded that metalaxyl alone (sum of isomers) cannot be a correct marker for the residues in animal matrices.

EFSA proposes to the risk managers to decide which of these two options should be taken into consideration for the setting of residue definitions and MRLs in animal products.

4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population[8] (EFSA, 2007).

In the framework of the combined Article 12 MRL review a comprehensive long-term exposure assessment was performed taking into account the existing uses of metalaxyl and metalaxyl-M (EFSA, 2015b). This risk assessment was now updated with the median residue levels (STMR) derived from the trials conducted on the crops under consideration (Table 4). Additionally, the STMR reported for gooseberries in the most recent EFSA opinion (EFSA, 2015c) was included in the calculation. For animal commodities, the STMR and HR reported in Table 6 were considered. The food commodities, for which no uses were reported in the framework of the combined Article 12 review, were excluded from the calculation, assuming that there is no use of metalaxyl on these crops. As CXLs for metalaxyl are currently not implemented in the EU legislation, these values were not considered.

The acute exposure assessment was performed only with regard to the commodities under consideration, assuming the consumption of a large portion of the food items containing residues at the highest (HR) level (Table 4). A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation, when required (EFSA, 2007). The input values used for the dietary exposure calculation are summarised in Table 8.

Table 8: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input (mg/kg)	Comment	Input (mg/kg)	Comment
Risk assessment residue definition; plant commodities: Metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)				
Oranges, grapefruits	0.01	STMR pulp (Table 4)	0.02	HR pulp (Table 4)
Strawberries	0.17	STMR (Table 4)	0.30	HR (Table 4)
Brussels sprouts	0.04	STMR (Table 4)	0.07	HR (Table 4)
Spinach and similar leaves	0.16	STMR (Table 4)	0.74	HR (Table 4)
Gooseberries	0.02	STMR (EFSA, 2015c)	Acute risk assessment undertaken only with regard to the crops under consideration	
Other food commodities of plant origin	STMR	Table 11 of EFSA reasoned opinion on combined Article 12 MRL review (EFSA, 2015b)		
Risk assessment residue definition; animal commodities (Article 12 review proposal): Sum of metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl				
Other food commodities of plant origin	STMR and HR reported in Table 7 for ruminant and pig products 0.01 mg/kg for poultry products (see Section 3.2.3)			

STMR: supervised trials median residue; EFSA: European Food Safety Authority; HR: highest residue.

[8] The calculation of the long-term exposure (chronic exposure) is based on the mean consumption data representative for 22 national diets collected from MS surveys plus 1 regional and 4 cluster diets from the World Health Organization Global Environment Monitoring System (WHO GEMS) Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys are used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

The estimated exposure was compared with the toxicological reference values derived for metalaxyl (Table 2). The results of the intake calculation using the PRIMo model is a key supporting document and is made publicly available as a background document to this reasoned opinion.

A long-term consumer intake concern was not identified for any of the European diets incorporated in the PRIMo model. The highest chronic intake was calculated to be 21% of the ADI (DE child). The individual contribution of the crops under consideration to the total consumer exposure accounted for a maximum of 0.1% of the ADI for strawberries (FR toddler).

An acute consumer risk was not identified in relation to the MRL proposals for the crops under consideration. The highest acute consumer exposure was calculated to be 3% of the ARfD for spinaches, and was lower for other crops under consideration.

EFSA concludes that the intended use of metalaxyl on oranges, grapefruits, strawberries, Brussels sprouts and the group 'spinaches and similar leaves' will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a concern for public health.

Conclusions and recommendations

The information submitted was sufficient to propose the MRLs summarised in the table below:

Code[(a)]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition (plant commodities): Metalaxyl and metalaxyl-M (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)				
0110010	Grapefruits	0.5	0.7	SEU, based on trials on oranges
0110020	Oranges	0.5	0.7	
0152000	Strawberries	0.5	0.6	Indoor
0242010	Brussels sprouts	0.05*	0.15	Supported by SEU trials
0252000	Spinaches and similar leaves	–	1.5	Extrapolated to the whole group from SEU trials on open leaf varieties of lettuce
0252010	Spinaches	0.05*		
0252020	Purslanes	1.0		
0252030	Chards/beet leaves	0.05*		
Option 1: Enforcement residue definition (animal commodities): Sum of metalaxyl (sum of isomers) and its metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl				
101X010	Swine/sheep/goat: Meat	(b)	0.01*	LOQ of 0.01 mg/kg (meat, fat) and of 0.05 mg/kg (liver, kidney) based on the LOQs achieved by the available validated analytical methods
101X020	Swine/sheep/goat: Fat	(b)	0.01*	
101X030	Swine/sheep/goat: Liver	(b)	0.05*	
101X040	Swine/sheep/goat: Kidney	(b)	0.2	
1012010	Bovine: Meat	(b)	0.01*	
1012020	Bovine: Fat	(b)	0.01*	
1012030	Bovine: Liver	(b)	0.05*	
1012040	Bovine: Kidney	(b)	0.3	
10160X0	Poultry: Meat and fat	(b)	0.01*	
10160X0	Poultry: Liver and kidney	(b)	0.05*	
1020000	Milk	(b)	0.01*	
1030000	Birds' eggs	(b)	0.01*	
Option 2: Enforcement residue definition (animal commodities): Metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers) (current residue definition under Reg. 2016/486)				
101X0X0	All species: All matrices	0.05*	0.02*	Default MRL. Metalaxyl not expected to be present in animal matrices

EU: European Union; MRL: maximum residue level; SEU: southern Europe.

*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.

(b): No MRLS listed according to the proposed residue definition in Regulation.

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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
BE	Belgium
bw	body weight
CXL	Codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DE	Germany
DM	dry matter
DT_{90f}	period required for 90% dissipation (field method)
EMS	evaluating Member State
FAO	Food and Agriculture Organization of the United Nations
FR	France
GAP	good agricultural practice
GEMS	Global Environment Monitoring System
GS	growth stage
HPLC–MS/MS	high-performance liquid chromatography with tandem mass spectrometry
HR	highest residue
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
LOQ	limit of quantification
MRL	maximum residue level
MS	Member State
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant-back interval
PF	processing factor
PHI	preharvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
RD	residue definition
RMS	rapporteur Member State
SEU	southern Europe
SMILES	Simplified Molecular Input Line Entry System
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization
WP	wettable powder

Appendix A – Good agricultural practice

Crop	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	BBCH stages & season[c]	Number min–max	Interval between application	g/hL min–max	Water L/ha min–max	g/ha min–max		
Spinach and similar (leaves)	Spain (SEU)	F	Lettuce downy mildew (*Bremia lactucae*)	WP	25	Foliar	14–69	3	10		400–100	200	14	
Oranges, grapefruit	Spain (SEU)	F	Phytophthora (*Phytophthora* spp.)	WP	25	Foliar	19–85	3	14		1,000–2,000	200	14	
Strawberries	Spain (SEU)	G	Phytophthora (*Phytophthora* spp.)	WP	25	Drip irrigation	13–71	3	10			380	14	
Brussels sprouts	Spain (SEU)	F	Downy mildew (*Hyaloperonospora brassicae*)	WP	25	Foliar spray	13–63	3	10		400–1,000	200	14	

a.s.: active substance; BBCH: growth stages of mono- and dicotyledonous plants; NEU: northern European Union; SEU: southern European Union; MS; Member State; WP: wettable powder.

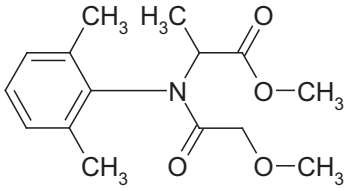
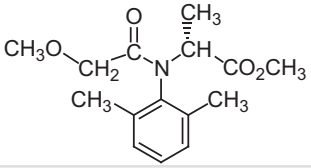
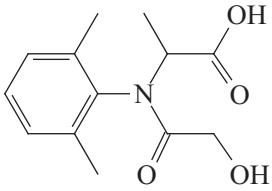
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).

(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.

(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 – Used compound codes

Code/trivial name	Chemical name/SMILES notation	Structural formula
Metalaxyl, (*R*, *S*-enantiomers racemic)	Methyl *N*-(methoxyacetyl)-*N*-2,6-xylyl-alaninate CC(N(C(=O)COC)c1c(C)cccc1C)C(=O)OC	
Metalaxyl-M (*R*-enantiomer)	Methyl *N*-(methoxyacetyl)-*N*-2,6-xylyl-D-alaninate MW = 279.3	
CGA107955	*N*-(2,6-Dimethylphenyl)-*N*-(hydroxyacetyl)alanine CC(N(C(=O)CO)c1c(C)cccc1C)C(=O)O	
CGA67869	*N*-(2,6-Dimethylphenyl)-*N*-(hydroxyacetyl)alanine methylester	