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Modification of the existing maximum residue level for metalaxyl-M in gooseberries

European Food Safety Authority (EFSA)

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS), the United Kingdom, received an application from the UK Agriculture and Horticulture Development Board to modify the existing maximum residue level (MRL) for the active substance metalaxyl-M in gooseberries. In order to accommodate for the intended use of metalaxyl-M, the United Kingdom proposed to raise the existing MRL from the limit of quantification to 0.3 mg/kg. The United Kingdom 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 EFSA. According to EFSA the data are sufficient to derive a MRL proposal of 0.3 mg/kg for the proposed use on gooseberries. Adequate analytical enforcement methods are available to control the residues of metalaxyl-M in gooseberries. Based on the risk assessment results, EFSA concludes that the proposed use of metalaxyl-M on gooseberries will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a health risk to consumers.

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Keywords: metalaxyl, metalaxyl-M, gooseberries, 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), the United Kingdom, received an application from the UK Agriculture and Horticulture Development Board to modify the existing maximum residue level (MRL) for the active substance metalaxyl-M in gooseberries. In order to accommodate for the intended use of metalaxyl-M, the United Kingdom proposed to raise the existing MRL from the limit of quantification (LOQ) to 0.3 mg/kg. The United Kingdom 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 5 March 2015.

EFSA bases its assessment on the evaluation report submitted by the EMS, the renewal assessment report (RAR) (and its addenda) prepared under Regulation (EC) No 1141/2010, the Commission review report on metalaxyl-M, the conclusion on the peer review of the pesticide risk assessment of the active substance metalaxyl-M, as well as the conclusions from previous EFSA opinions on metalaxyl-M.

The toxicological profile of metalaxyl-M was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.08 mg/kg bw per day and an acute reference dose (ARfD) of 0.5 mg/kg bw.

The metabolism of metalaxyl-M in primary crops was investigated in the fruit and leafy crop groups following foliar application and the cereals group following seed treatment. From these studies the peer review established the residue definitions for enforcement and for risk assessment as metalaxyl (including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)). For the use on gooseberries, EFSA concludes that the metabolism of metalaxyl-M in primary crops has been sufficiently addressed and that the residue definitions derived are applicable.

EFSA concludes that the submitted supervised residue trials are sufficient to derive an MRL proposal of 0.3 mg/kg on gooseberries. Adequate analytical enforcement methods are available to monitor the residues of metalaxyl-M in gooseberries at the validated LOQ of 0.01 mg/kg.

Standard hydrolysis studies simulating the effect on the nature and magnitude of metalaxyl-M residues under processing conditions representative of pasteurisation, boiling and sterilisation were assessed in the conclusion of the peer review and it was concluded that the compound is hydrolytically stable under the representative conditions. Thus, for processed commodities, the same residue definition as for raw agricultural commodities (RAC) is applicable. Several processing factors were derived during the MRL review including a factor for strawberries.

As the proposed use of metalaxyl-M is on permanent crops, investigations of residues in rotational crops are not required.

Residues of metalaxyl-M in commodities of animal origin were not assessed, since gooseberries are normally not fed to livestock.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). In the framework of the review of the existing MRLs for metalaxyl-M according to Article 12 of Regulation (EC) No 396/2005, a comprehensive long-term exposure assessment was performed taking into account the existing uses at the EU level and the acceptable CXLs. EFSA has updated this risk assessment with the median values for gooseberries derived from the residue trials conducted on strawberries and blackcurrants.

Long-term consumer intake concerns were not identified for any of the European diets incorporated in the EFSA PRIMo. The total chronic intake calculated accounted for up to 23 % of the ADI (DE child). The contribution of gooseberries to the total intake was insignificant (< 0.1 %).

An acute consumer risk was not identified in relation to the MRL proposal for gooseberries. The maximum exposure calculated was 0.2 % of the ARfD.

EFSA concludes that the proposed use of metalaxyl-M on gooseberries will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a health risk to consumers.

EFSA proposes to amend the existing MRL 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: Metalaxyl and metalaxyl-M (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)) ^(F)				
154040	Gooseberries	0.05*	0.3	Extrapolation from strawberries and blackcurrants NEU residue trials.

(a): Commodity code number according to Annex I of Regulation (EC) 396/2005

(*): indicates that the MRL is set at the limit of analytical quantification (LOQ)

(F): fat soluble

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Background

Regulation (EC) No 396/2005¹ 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, when appropriate, an application to modify a MRL in accordance with the provisions of Article 7 of the Regulation.

The United Kingdom, hereafter referred to as the evaluating Member State (EMS), received an application from the UK Agriculture and Horticulture Development Board⁴ to modify the existing MRL for the active substance metalaxyl-M in gooseberries. 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 5 March 2015.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2015-00153 and the following subject:

Metalaxyl-M: Modification MRLs in gooseberries

The United Kingdom proposed to raise the existing MRL of metalaxyl-M in gooseberries from the limit of quantification (LOQ) of 0.05 mg/kg to 0.3 mg/kg.

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.

In accordance with Article 11 of the Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six 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). Metalaxyl-M, is the ISO common name for methyl *N*-(methoxyacetyl)-*N*-(2,6-xylyl)-D-alaninate (IUPAC). Metalaxyl is the racemic mixture of metalaxyl-M and its *S*-enantiomer and both compounds are recognised as pesticide active substances. The chemical structures of the active substance and its main metabolites are reported in appendix C. Metalaxyl-M has been approved for use as a fungicide.

Metalaxyl-M was included in Annex I to Directive 91/414/EEC by means of Commission Directive 2002/64/EC,⁵ entering into force on 1 October 2002, and is deemed to have been approved under Regulation (EC) No 1107/2009 by means of Regulation (EU) No 540/2011. This approval is restricted to use only as a fungicide. Metalaxyl-M was also evaluated for renewal of approval in the framework of Commission Regulation (EU) No 1141/2010 with Belgium being the designated RMS. The

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, 16.03.2005, 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, 19.08.1991, 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 UK Agriculture and Horticulture Development Board, Stoneleigh Park, Kenilworth, Warwickshire, CV8 2TL, United Kingdom

⁵ Commission Directive 2002/64/EC of 15 July 2002 amending Council Directive 91/414/EEC to include cinidon-ethyl, cyhalofop butyl, famoxadone, florasulam, metalaxyl-M and picolinafen as active substances. OJ L 189, 18.7.2002, p. 27–32.

representative uses supported at EU level were as a seed treatment to field grown spinach and sunflower and an outdoor spray application to tomatoes and grape vines. EFSA published its conclusion on the peer review of the pesticide risk assessment of the active substance metalaxyl-M on 3 March 2015 (EFSA, 2015a). A final decision concerning the renewal of approval under Regulation (EC) No 1107/2009 had not been taken when this opinion was finalised.

The EU MRLs for metalaxyl (including other mixtures of constituent isomers including metalaxyl-M, (sum of isomers)) are established in Annexes II and IIIB of Regulation (EC) No 396/2005. An overview of the MRL changes that occurred since the entry into force of the abovementioned regulation is provided in Table 1.

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

Procedure ^(a)	Considered by Regulation	Remarks
Art. 12 metalaxyl-M (EFSA, 2011)	–	Not yet legally implemented pending a combined assessment for metalaxyl and metalaxyl-M.
Art. 10 (EFSA, 2012)	Reg. (EU) No 441/2012	Modification of the existing MRL in lettuce and other salad plants.
Art. 10 (EFSA, 2013)	Reg. (EU) No 36/2014	Modification of the existing MRL in currants.
Art. 12 metalaxyl (EFSA, 2014)	–	Not yet legally implemented pending a combined assessment for metalaxyl and metalaxyl-M.
Art. 43 Combining MRL reviews of metalaxyl and metalaxyl-M (EFSA, 2015)	–	Not yet legally implemented

(a): Art. 10: Assessment of MRL application according to Article 6 to 10 of Regulation (EC) No 396/2005

Art. 12: Review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005

Art. 43: EFSA scientific opinion according to Article 43 of Regulation (EC) No 396/2005

CXLs have not been established for metalaxyl-M in gooseberries.

The details of the intended/authorised GAP for metalaxyl-M is given in Appendix A.

Assessment

EFSA bases its assessment on the Review Report on metalaxyl-M (European Commission, 2002), the previous EFSA reasoned opinion on combined MRLs review of metalaxyl and metalaxyl-M (EFSA, 2015b), and the EFSA conclusion on metalaxyl-M prepared in the framework of Regulation (EC) No 1107/2009 (EFSA, 2015a). 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 546/2011⁶ and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 1997a–g, 2000, 2010b, c, 2011; OECD, 2011).

1. Method of analysis

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

Analytical methods for the determination of metalaxyl-M residues in plant commodities were detailed in the previous assessments during the peer review and combined MRL review for metalaxyl and metalaxyl-M in high water, high acid, high oil content and dry commodities. These methods are based

⁶ Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.06.2011, p. 127–175.

on the QuEChERS and DGF S19 and they were considered appropriate for enforcement of metalaxyl in plant commodities with a LOQ of 0.01 mg/kg (EFSA, 2015a,b).

As the gooseberries belong to high acid commodity group, EFSA concludes that sufficiently validated analytical methods are available for enforcing the proposed MRL for metalaxyl-M in gooseberries.

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

Analytical methods for the determination of metalaxyl-M in food of animal origin are not assessed in the current application, since gooseberries are normally not fed to livestock.

2. Mammalian toxicology

The toxicological profile of the active substance metalaxyl-M was first assessed in the framework of the peer review under Directive 91/414/EEC (Belgium, 1999) where the toxicological reference values set out below were derived; these values were confirmed during the recent peer review under Regulation (EC) 1107/2009 (EFSA, 2015a). Both metalaxyl-M and metalaxyl have the same toxicological reference values as set out in Table 2.

Table 2: Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
Metalaxyl and metalaxyl-M					
ADI	EC	2002, 2010a	0.08 mg/kg bw per day	Dog studies with metalaxyl (90 days, 6 months, 1 year and 2 years)	100
ARfD	EC	2002, 2010a	0.5 mg/kg bw	Developmental rat study with metalaxyl-M	100

3. Residues

3.1. Nature and magnitude of residues in plants

3.1.1. Primary crops

3.1.1.1. Nature of residues

The metabolism of metalaxyl-M in primary crops was evaluated in the framework of the MRL review in (EFSA, 2011) in the leafy crop group and during the peer review of Regulation (EC) No 1107/2009 in the fruit and cereal crop groups (EFSA, 2015a). An overview of the available metabolism studies is presented in Table 3.

Table 3: Summary of available metabolism studies in plants

Crop group	Crops	Application	Sampling ^(a) (DAT)	Comments
Fruit	Tomato	Foliar (3 × 160 g/ha)	3, 14	EFSA, 2015a
Leafy	Lettuce	Foliar (3 × 200 g/ha,	21	EFSA, 2011
Cereals	Wheat	Seed (19.3 g/100 kg seeds)	83, 127	EFSA, 2015a
		Seed (157 g/100 kg seeds)	83, 127	EFSA, 2015a

(a): DAT_x, days after treatment x, e.g. DAT₂: day after 2nd treatment.

Based on these metabolism studies, the residue definition for enforcement and risk assessment was proposed as metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers). 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 gooseberries, EFSA concludes that the metabolism of metalaxyl-M is sufficiently addressed and the residue definitions agreed during the peer review (EFSA, 2015a) and confirmed under article 43 MRL review are applicable (EFSA, 2015b).

3.1.1.2. Magnitude of residues

In support of the MRL application, the EMS referred to eight residue trials (four on blackcurrants and four on strawberries) to support the extrapolation to gooseberries as proposed in the 7525/VI/95 guideline. The field residue trials on currants were conducted in line with the intended NEU GAP (2 × 75g/ha; PHI 42 days) using a mixture of chlorotalonil and metalaxyl-M (ratio 13:1), while the residue trials on strawberries were conducted with a higher application rate (1 × 188 g/ha; PHI 42 days) using metalaxyl-M. Although the application rate on strawberries was higher, the results were considered usable in the context of no residues having been detected in strawberries and as the application rate was ca. +25 % compared to the maximum total dose being assessed. All samples were analysed for metalaxyl-M. The residue results were lower than 0.02 mg/kg for strawberries, and ranged between 0.02 – 0.17 mg/kg for currants.

The results of the residue trials, the related risk assessment input values (highest residue, median residue) and the MRL proposal(s) are summarised in Table 4.

The stability of metalaxyl-M residues in plant matrices under storage conditions prior to analysis was assessed during the peer review under Regulation (EC) No 1107/2009 (EFSA, 2015a). Residues of metalaxyl-M were found to be stable at –18 °C for at least 24 months in high water-, high acid- and high oil content matrices as well as in dry matrices. As the trial samples were stored for less than one month under proper conditions, 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 (United Kingdom, 2015).

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

- 0.3 mg/kg gooseberries in NEU (extrapolation from trials on blackcurrant and strawberries)

Table 4: Overview of the available residues trials data

Crop (GAPs)	Region/ Indoor ^(a)	Residue levels observed in the supervised residue trials ^(b) (mg/kg)	Recommendations/comments ^(c)	MRL proposal (mg/kg)	HR ^(d) (mg/kg)	Median residue ^(e) (mg/kg)
Blackcurrants and strawberries → gooseberries GAP (2× 75 g/ha, PHI 42 d)	NEU for outdoor trials. (UK)	6× <0.02, 0.024, 0.17	Extrapolation from strawberries and blackcurrants residue trials. MRL _{OECD} (0.25/0.3)	0.3	0.17	0.02

(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

(c): Any information/comment supporting the decision and OECD MRL calculation (e.g. MRL_{OECD}: unrounded/rounded values)

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

(e): Median value of the individual trial results according to the residue definition for risk assessment

3.1.1.3. Effect of industrial processing and/or household preparation

Standard hydrolysis studies simulating the effect on the nature of metalaxyl-M residues under processing conditions representative of pasteurisation, boiling and sterilisation were assessed in the conclusion of the peer review (EFSA, 2015a) and it was concluded that the compound is hydrolytically stable under the representative conditions. Thus, for processed commodities, the same residue definition as for raw agricultural commodities (RAC) is applicable.

Studies on the magnitude of metalaxyl-M were presented during the MRL review and processing factors were derived for several commodities, including strawberries (EFSA 2015b).

3.1.2. Rotational crops

As the proposed use of metalaxyl-M being assessed is on a permanent crop, the investigation of residues in rotational crops is not required and therefore was not considered in this reasoned opinion.

3.2. Nature and magnitude of residues in livestock

As gooseberries are normally not fed to livestock, the nature and magnitude of metalaxyl-M residues in livestock was not assessed in the framework of this application (European Commission, 1996).

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 sub-groups of the EU population⁷ (EFSA, 2007).

In the framework of the reviews of the existing MRLs for metalaxyl-M and metalaxyl according to Article 12 of Regulation (EC) No 396/2005, a comprehensive long-term exposure assessment was performed taking into account the existing uses at the EU level and the acceptable CXLs (EFSA, 2011, 2014, 2015b). EFSA updated this risk assessment with the median residue levels (STMR) derived from the residue trials conducted to support the MRL proposal in gooseberries in this MRL application (see Table 4). The food commodities for which no uses were reported in the framework of the Article 12 reviews were excluded from the exposure calculation, assuming that there is no use of metalaxyl-M on these crops.

The acute exposure assessment was performed only with regard to gooseberries, assuming the consumption of a large portion of the food items as reported in the national food surveys and that these items contained residues at the highest residue level (HR) as observed in supervised field trials (see 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 5.

Table 5: 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: metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)				
Gooseberries	0.02	STMR	0.17	HR
Other commodities assessed during the combined MRL review	See Table 11 in EFSA Reasoned Opinion on combined review of the existing MRLs for metalaxyl and metalaxyl-M under article 43 of Regulation (EC) 396/2005 (EFSA, 2015b)			

⁷ 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 WHO GEMS Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

The estimated exposure was then compared with the toxicological reference values derived for metalaxyl-M (see Table 1). The results of the intake calculation are presented in Appendix B of this reasoned opinion.

Long-term consumer intake concerns were not identified for any of the European diets incorporated in the EFSA PRIMo. The total chronic intake calculated accounted for up to 23.3 % of the ADI (DE child). The contribution of residues in gooseberries to the total consumer intake was insignificant (< 0.1 %).

An acute consumer risk was not identified in relation to the MRL proposal for gooseberries. The highest acute consumer exposure calculated was 0.2 % of the ARfD (DE child).

EFSA concludes that the intended use of metalaxyl-M on gooseberries 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 derive the MRL proposals summarised in the table below:

Code ^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/Justification
Enforcement residue definition: Metalaxyl and metalaxyl-M (metalaxyl including other mixtures of constituent isomers including metalaxyl-M (sum of isomers)) ^(F)				
154040	Gooseberries	0.05*	0.3	Extrapolation from strawberries and blackcurrants NEU residue trials.

(a): Commodity code number according to Annex I of Regulation (EC) 396/2005

(*): indicates that the MRL is set at the limit of analytical quantification (LOQ)

(F): fat soluble

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CXL	Codex maximum residue limit (Codex MRL)
d	day
DAR	draft assessment report
DAT	days after treatment
EMS	evaluating Member State
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly International Group of National Associations of Manufacturers of Agrochemical Products (GIFAP))
HR	highest residue
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry detector
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RAC	raw agricultural commodity
RAR	renewal assessment report
RD	residue definition
RMS	rapporteur Member State
SC	suspension concentrate

Appendix A – Good Agricultural Practice (GAPs)

Crop and/or situation ^(a)	MS or NEU/SEU or Country	F G or I ^(b)	Pest or group of pests controlled ^(c)	Formulation		Application				Application rate per treatment		PHI ^(l) (days)	Remarks ^(m)	
				type ^(d-f)	conc. a.s. ⁽ⁱ⁾	Method kind ^(f-h)	Growth stage & season ^(j)	Number min-max ^(k)	Interval min-max	g/hL min-max	Water L/ha min-max			g/ha min-max
Blueberries, cranberries, gooseberries and other ribes species (outdoor bush fruit)	UK	F	Fungicide	SC	500 g/L chlorothalonil and 37.4 g/L metalaxyl-M	Foliar spray		2			200	1000 g/ha chlorothalonil and 75 g/ha metalaxyl-M	42	

Remarks:

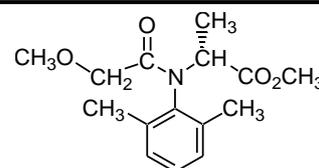
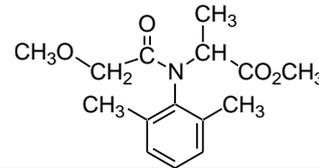
- (a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the usage situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
- (c) e.g. biting and sucking insects, soil-born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), water soluble granule (WG)
- (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
- (f) all abbreviations must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants. type of equipment used must be indicated

- (i) g/kg or g/L
- (j) Growth stage at last treatment (Meier U, 2001. Growth Stages of mono- and dicotyledonous plants. BBCH Monograph, 2nd Ed., Federal Biological Research Centre of Agriculture and Forestry, Braunschweig, Germany, 2001), including where relevant, information on season at time of application
- (k) The minimum and maximum number of application possible under practical conditions of use must be provided
- (l) PHI - minimum pre-harvest interval
- (m) Remarks may include: Extent of use/economic importance/restrictions

Appendix B – Pesticide Residue Intake Model (PRIMO)

		Metalaxyl and metalaxyl-M				Prepare workbook for refined calculations						
Status of the active substance:		Included		Code no.								
LOQ (mg/kg bw):				proposed LOQ:								
		Toxicological end points				Undo refined calculations						
ADI (mg/kg bw/day):		0.08		ARfD (mg/kg bw):		0.5						
Source of ADI:		EC		Source of ARfD:		EC						
Year of evaluation:		2002		Year of evaluation:		2002						
Chronic risk assessment - refined calculations												
		TMDI (range) in % of ADI minimum - maximum										
		2 ---										
		No of diets exceeding ADI:				---						
Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRs at LOQ (in % of ADI)				
23.3	DE child	15.1	Apples	3.2	Table grapes	2.4	Oranges					
14.7	NL child	7.9	Apples	1.9	Oranges	1.9	Table grapes					
8.2	WHO Cluster diet B	2.2	Wine grapes	1.3	Apples	0.9	Table grapes					
7.3	FR all population	5.0	Wine grapes	0.6	Apples	0.3	Table grapes					
7.2	FR toddler	3.3	Apples	1.3	Oranges	0.5	Table grapes					
6.9	IE adult	1.6	Wine grapes	1.0	Apples	0.8	Pears					
6.7	PT General population	3.1	Wine grapes	1.3	Apples	0.7	Table grapes					
5.7	DK child	2.9	Apples	0.8	Pears	0.5	Table grapes					
5.4	FR infant	3.1	Apples	0.6	Oranges	0.4	Pears					
5.3	WHO cluster diet E	2.0	Wine grapes	1.1	Apples	0.4	Table grapes					
5.3	UK Toddler	2.1	Apples	1.2	Oranges	0.6	Table grapes					
5.2	NL general	1.5	Apples	0.9	Oranges	0.8	Wine grapes					
4.8	ES child	1.4	Apples	1.4	Oranges	0.6	Pears					
4.3	PL general population	2.6	Apples	0.8	Table grapes	0.4	Pears					
4.2	UK Infant	2.0	Apples	0.8	Oranges	0.5	Milk and cream,					
4.2	ES adult	1.0	Apples	0.8	Oranges	0.7	Lettuce					
3.8	DK adult	1.7	Wine grapes	1.0	Apples	0.3	Pears					
3.8	WHO regional European diet	0.8	Apples	0.5	Lettuce	0.4	Table grapes					
3.8	WHO Cluster diet F	0.8	Apples	0.7	Wine grapes	0.5	Oranges					
3.7	SE general population 90th percentile	1.3	Apples	0.5	Oranges	0.4	Pears					
3.4	UK vegetarian	1.0	Wine grapes	0.7	Apples	0.5	Oranges					
3.2	WHO cluster diet D	0.8	Apples	0.5	Table grapes	0.5	Wine grapes					
3.2	IT kids/toddler	1.1	Apples	0.4	Pears	0.4	Lettuce					
3.1	IT adult	1.0	Apples	0.5	Lettuce	0.3	Table grapes					
3.0	LT adult	2.3	Apples	0.2	Pears	0.1	Lettuce					
3.0	UK Adult	1.4	Wine grapes	0.5	Apples	0.4	Oranges					
2.2	FI adult	0.6	Oranges	0.5	Apples	0.4	Wine grapes					
Conclusion:												
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRs were below the ADI.												
A long-term intake of residues of Metalaxyl and metalaxyl-M is unlikely to present a public health concern.												
Acute risk assessment /children - refined calculations					Acute risk assessment / adults / general population - refined calculations							
The acute risk assessment is based on the ARfD.												
For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.												
In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.												
In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variability factor of 3.												
Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.												
Unprocessed commodities	No of commodities for which ARfD/ADI is exceeded (IESTI 1):			No of commodities for which ARfD/ADI is exceeded (IESTI 2):			No of commodities for which ARfD/ADI is exceeded (IESTI 1):			No of commodities for which ARfD/ADI is exceeded (IESTI 2):		
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	IESTI 1	*)	**)	IESTI 2	*)	**)	IESTI 1	*)	**)	IESTI 2	*)	**)
	Highest % of ARfD/ADI	Commodities	pTMR/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMR/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMR/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMR/ threshold MRL (mg/kg)
	0.2	Gooseberries	0.17 / -	0.2	Gooseberries	0.17 / -	0.1	Gooseberries	0.17 / -	0.1	Gooseberries	0.17 / -

Appendix C – Used compound code(s)

Code/Trivial name	Chemical name ^(a)	Structural formula ^(a)
metalaxyl-M	methyl <i>N</i> -(methoxyacetyl)- <i>N</i> -(2,6-xylyl)-D-alaninate MW: 279.3 g/mol	
metalaxyl	methyl <i>N</i> -(methoxyacetyl)- <i>N</i> -(2,6-xylyl)-DL-alaninate	

(a): ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).