Modification of the existing maximum residue levels for emamectin in leafy brassica and beans and peas with pods

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

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta France SAS submitted a request to the competent national authority in France to modify the existing maximum residue levels (MRLs) for the active substance emamectin in leafy brassica and beans and peas with pods. The data submitted in support of the request were found to be sufficient to derive MRL proposals for the crops under consideration. An adequate analytical method for enforcement is available to control the residues of emamectin in the commodities under consideration. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of emamectin benzoate according to the reported agricultural practices is unlikely to present a risk to consumer health. The reliable end points, appropriate for use in regulatory risk assessment are presented.

© 2018 European Food Safety Authority. EFSA Journal published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: emamectin, leafy brassica, beans and peas with pods, pesticide, MRL, consumer risk assessment

Requestor: European Commission
Question number: EFSA-Q-2015-00155
Correspondence: pesticides.mrl@efsa.europa.eu
Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta France SAS submitted an application to the competent national authority in France (evaluating Member State (EMS)) to modify the existing maximum residue levels (MRLs) for the active substance emamectin in leafy brassica and beans and peas with pods. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA). EFSA identified data gaps or points which needed further clarification, which were addressed by the EMS in a revised evaluation report. The evaluation was based on data belonging to the variant emamectin benzoate. To accommodate for the intended uses, the EMS proposed to raise the existing MRLs to 0.03 mg/kg.

EFSA based its assessment on the evaluation report submitted by the EMS, the draft assessment report (DAR) and its final addendum prepared under Directive 91/414/EEC, the Commission review report on emamectin, the conclusion on the peer review of the pesticide risk assessment of the active substance emamectin, the Joint Meeting on Pesticide Residues (JMPR) evaluation reports as well as the conclusions from previous EFSA opinions and scientific reports on emamectin benzoate.

The metabolism of emamectin following foliar applications was investigated in primary crops belonging to the groups of the fruit crops, leafy crops and cereals/grass and in rotational crops in root/tuber crops, leafy crops and cereals during the EU pesticides peer review. Studies investigating the effect of processing on the nature of emamectin residues showed limited degradation under standard hydrolysis conditions.

Based on the metabolic pattern identified in metabolism studies and the additional studies on the toxicological significance of the photodegradation metabolites, the residue definition for enforcement applied to primary crops, including the crops under assessment is emamectin B1a benzoate, expressed as emamectin, which corresponded to the residue definition currently set in the EU legislation. For risk assessment, the residue definition was provisionally proposed during the EU pesticides review as sum of emamectin B1ar, emamectin B1br, 8,9-Z-MAB1a plus 3 times AB1a plus 3 times MFB1a and 3 times FAB1ar, expressed as emamectin, pending the MRL review.

The toxicological profile of emamectin was assessed in the framework of the EU pesticides peer review and the data were sufficient to derive an acceptable daily intake (ADI) of 0.0005 mg/kg bw per day and an acute reference dose (ARFD) of 0.01 mg/kg bw. Based on the additional studies assessed in this MRL application, the photodegradation metabolites included in the risk assessment residue definition were considered to be of the same or higher potency in comparison to the parent compound.

Sufficiently validated analytical methods are available to quantify residues in leafy brassica and beans and peas with pods according to the enforcement residue definition at or above the limit of quantification (LOQ) of 0.001 mg/kg. The available residue trials were sufficient to derive a MRL proposal of 0.03 mg/kg for leafy brassica and beans and peas with pods. Having regard to the low residue levels observed in the residue trials, no processing studies were provided. No significant residues are expected in rotational crops, provided that emamectin benzoate is applied to the crops under assessment according to the intended good agricultural practices. Therefore, further considerations are not necessary.

As kale leaves may be used as a feed product, a potential carry-over into food of animal origin was assessed. The dietary burdens derived did not exceed the trigger value of 0.1 mg/kg dry matter (DM) for all relevant groups of livestock. Since the existing MRLs in products of animal origin are derived based on higher livestock intakes estimated by Codex, they do not need to be revised.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMO). For the calculation of the chronic exposure, EFSA used the median residue values derived according to the residue definition proposed for risk assessment for the commodities assessed in this MRL application. For the remaining commodities of plant and animal origin, the available median residue derived for emamectin and the MRL values set at the LOQ were included in the calculation. The short-term risk assessment was performed only for the crops under consideration according to the residue definition proposed for risk assessment.

Based on the available information, EFSA concluded that the proposed uses of emamectin benzoate on leafy brassica and beans and peas with pods will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a risk to consumers’ health.

EFSA emphasised that the chronic risk assessment is indicative as it does not take into consideration the contribution of the photodegradation metabolites and their relative potency for the existing uses of emamectin benzoate. A more realistic long-term consumer risk assessment will be
performed in the framework of the ongoing MRL review, when full information on authorised uses and residue data will be available to EFSA. Additionally, no information was available on the possible preferential degradation/metabolism in plants, animals and the environment of each enantiomer of the two emamectin components B_{1a} and B_{1b}. The consequent impact on the consumer risk assessment and further investigation on this matter would in principle be required. Since guidance on how to address the dietary risk assessment of isomer mixtures is not yet implemented, EFSA recommended that this issue is reconsidered when such guidance is available.

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

EFSA proposes to amend the existing MRLs as reported in the summary table below. Full details of all endpoints and the consumer risk assessment can be found in Appendices B–D.

| Code(a) | Commodity                  | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification                                      |
|--------|---------------------------|-------------------------|-------------------------|------------------------------------------------------------|
| 0243010 | Chinese cabbage/pe-tsai   | 0.01*                   | 0.03                    | NEU use supported by extrapolation from residue data on kale. SEU use not supported. Risk for consumers unlikely |
| 0243020 | Kales                     | 0.01*                   | 0.03                    | Risk for consumers unlikely                                 |
| 0243990 | Others leafy brassica     | 0.01*                   | 0.03                    | NEU, SEU and indoor use supported by extrapolation from data on beans. The MRL proposal reflects the more critical indoor use. Risk for consumers unlikely |
| 0260010 | Beans with pods           | 0.01*                   | 0.03                    | Risk for consumers unlikely                                 |
| 0260030 | Peas with pods            | 0.01*                   | 0.03                    | Risk for consumers unlikely                                 |

Enforcement residue definition: Emamectin B_{1a} benzoate, expressed as emamectin

MRL: maximum residue level; NEU: northern Europe; 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.
# Table of contents

Abstract ................................................................................................................................................... 1  
Summary ................................................................................................................................................. 3  
Background ............................................................................................................................................. 6  
The active substance and its use pattern ................................................................................................... 7  
Assessment .............................................................................................................................................. 7  
1. Mammalian toxicology ....................................................................................................................... 8  
2. Residues in plants ............................................................................................................................... 8  
   2.1. Nature of residues and methods of analysis in plants ................................................................. 8  
   2.1.1. Nature of residues in primary crops ....................................................................................... 8  
   2.1.2. Nature of residues in rotational crops ................................................................................... 9  
   2.1.3. Nature of residues in processed commodities ..................................................................... 9  
   2.1.4. Methods of analysis in plants ............................................................................................. 9  
   2.1.5. Stability of residues in plants .............................................................................................. 9  
   2.1.6. Proposed residue definitions ............................................................................................... 9  
2.2. Magnitude of residues in plants .................................................................................................... 9  
   2.2.1. Magnitude of residues in primary crops .............................................................................. 9  
   2.2.1.1. Leafy brassica ................................................................................................................ 10  
   2.2.1.2. Beans and peas with pods ............................................................................................ 10  
   2.2.2. Magnitude of residues in rotational crops ........................................................................ 10  
   2.2.3. Magnitude of residues in processed commodities ............................................................ 10  
   2.2.4. Proposed MRLs ............................................................................................................... 10  
3. Residues in livestock ....................................................................................................................... 10  
4. Consumer risk assessment .............................................................................................................. 11  
   4.1. Short-term (acute) dietary risk assessment .............................................................................. 11  
   4.2. Long-term (chronic) dietary risk assessment ........................................................................... 11  
Conclusions and recommendations ........................................................................................................ 11  
References ............................................................................................................................................... 12  
Abbreviations ........................................................................................................................................... 13  
Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs ............... 15  
Appendix B – List of selected end points ............................................................................................. 16  
Appendix C – Input values for the exposure calculations ..................................................................... 22  
Appendix D – Used compound codes ............................................................................................... 24
Background

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

The applicant Syngenta France SAS submitted an application to the competent national authority in France, hereafter referred to as the evaluating Member State (EMS), to modify the existing MRLs for the active substance emamectin in leafy brassica and beans and peas with pods. This application was notified to the European Commission and the European Food Safety Authority (EFSA) and was subsequently evaluated by the EMS in accordance with Article 8 of the MRL regulation.

The EMS summarised the data provided by the applicant in an evaluation report which was submitted to the European Commission and forwarded to EFSA on 5 March 2015. The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2015-00155 and the following subject:

*Emamectin benzoate: Setting new MRLs in leafy brassica, bean and peas with pods (fresh)*

France proposed to raise existing MRLs of emamectin in leafy brassica, beans and peas with pods (fresh) from the limit of quantification (LOQ) of 0.01 to 0.03 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps or points which needed further clarification, which were requested from the EMS. On 18 October 2016 and 6 February 2018, the EMS submitted the requested information. The last revision of the evaluation report (France, 2018) replaced the previously submitted versions.

Terms of Reference

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

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

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

The revised evaluation report submitted by the EMS (France, 2018) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available.

The active substance and its use pattern

The detailed description of the intended uses of emamectin formulated as benzoate salt in leafy brassica and beans and peas with pods which are the basis for the current MRL application is reported in Appendix A.

---

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

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

\(^3\) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.
Emamectin is the ISO common name for a mixture of emamectin B$_1$$_8$ ($\geq$ 90%) and emamectin B$_2$$_9$ ($\leq$ 10%): (10E,14E,16E)-(1R,4S,5'S,6'S,R,8'R,12'S,13'S,20'R,21'R,24'S)-6'-(5'-sec-butyl)-21,24-dihydroxy-5',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetraacyclo[15.6.1.1$^4$,$^8$]6$^2$0.24$^6$]pentacos-10,14,16,22-tetraene)-6-spiro-2'-(5',6'$^4$-dihydro-2'H-pyran)-12-yl 2,6-dideoxy-3-O-methyl-4-O-(2,4,6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexapyranosyl)-α-L-arabino-hexapyranoside; and (10E,14E,16E)-(1R,4S,5'S,6'S,R,8'R,12'S,13'S,20'R,21'R,24'S)-21,24-dihydroxy-6'-isopropyl-5',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetraacyclo[15.6.1.1$^4$,$^8$]6$^2$0.24$^6$]pentacos-10,14,16,22-tetraene)-6-spiro-2'-(5',6'$^4$-dihydro-2'H-pyran)-12-yl 2,6-dideoxy-3-O-methyl-4-O-(2,4,6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexapyranosyl)-α-L-arabino-hexapyranoside; respectively (IUPAC).

It should be noted that the evaluation was based on data belonging to the variant emamectin benzoate. The chemical structures of the active substance, its main components and metabolites are reported in Appendix D.

Emamectin was evaluated in the framework of Directive 91/414/EEC in accordance with Commission Regulation (EU) No 188/2011$^4$ with the Netherlands designated as rapporteur Member State (RMS) for the representative use as an insecticide after foliar applications on grapes, tomatoes, peppers, cucurbits andlettuce, outdoor and/or indoor, depending on the vegetable. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2012b).

Emamectin was approved in accordance with Regulation (EC) No 1107/2009 by Commission Regulation (EU) No 828/2013$^5$ for the use as insecticide on 1 May 2014. The process of renewal of the first approval has not yet been initiated.

The EU MRLs for emamectin are established in Annexes IIIA of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has not yet been completed. EFSA has issued a number of reasoned opinions on the modification of MRLs for emamectin. The proposals from these reasoned opinions have been considered in regulations$^6,7$ for EU MRL legislation. Certain Codex MRLs (CXLs) adopted by Codex Alimentarius Commission (CAC) in 2012 were implemented in the EU legislation.$^8$

Emamectin is included in Regulation (EU) No 37/2010$^9$ for use in veterinary medicine. The MRL of 0.1 mg/kg is set in fin fishes (muscle and skin in natural proportions).

**Assessment**

EFSA has based its assessment on the revised evaluation report submitted by the EMS (France, 2018), the DAR and its final addendum prepared under Directive 91/414/EEC (Netherlands, 2008, 2012), the European Commission review report on emamectin (European Commission, 2013), the conclusion on the peer review of the pesticide risk assessment of the active substance emamectin (EFSA, 2012b), the JMPR Evaluation reports (FAO, 2011) and EFSA scientific reports and reasoned opinions (EFSA, 2009, 2011, 2012a, 2015).

---

$^4$ 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.

$^5$ Commission Implementing Regulation (EU) No 828/2013 of 29 August 2013 approving the active substance emamectin, 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 232, 30.8.2013, p. 23-28.

$^6$ Commission Regulation (EC) No 1050/2009 of 28 August 2009 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 azoxystrobin, acetamiprid, clomazone, cyflufenamid, emamectin benzoate, famoxadone, fenbutatin oxide, flufenoxuron, fluopicolide, indoxacarb, ipoxynil, mepanpyrim, prothioconazole, pyridachlor and trifloxystrobin in or on certain products. OJ L 290, 6.11.2009, p. 7-55.

$^7$ Commission Regulation (EU) No 813/2011 of 11 August 2011 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 acequinocyl, emamectin benzoate, ethametsulfuron-methyl, flubendiamide, fludioxonil, kresoxim-methyl, methoxyfenozide, novaluron, thiacloprid and trifloxystrobin in or on certain products. OJ L 208, 13.8.2011, p. 23-79.

$^8$ Commission Regulation EU No 293/2013 of 20 March 2013 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 emamectin benzoate, etofenprox, etoxazole, fluoroacetofen, glyphosate, phosmet, pencycuron, spinoad and spirotetramat in or on certain products. OJ L 96, 5.4.2013, p. 1-30.

$^9$ Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. OJ L 015 20.1.2010, p. 1-72.
For this application, the data requirements established in Regulation (EU) No 544/2011 and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a-g, 2000, 2010a,b, 2017; OECD, 2011). 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.

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

1. Mammalian toxicology

In the framework of the current MRL application the EMS assessed additional studies on metabolites MFB1a, FAB1a, AB1a, and 8,9-Z MAB1a. An additional comparative 2-week neurotoxicity study in dogs with emamectin hydrochloride and the metabolite AB1a was also assessed (France, 2018).

Metabolites MFB1a, FAB1a, AB1a, and 8,9-Z MAB1a were not mutagenic in the Ames Test. Clastogenicity/aneugenicity endpoints have not been addressed by in vitro tests. The EMS addressed clastogenicity/aneugenicity endpoints on the basis of QSAR (i.e. DEREK). However EFSA considered that QSAR should not be used for read-across. QSAR prediction should be complemented with read-across (EFSA PPR Panel, 2016). EFSA performed a read-across analysis using mechanistic and endpoint-specific profilers in the OECD QSAR toolbox (version 3.4). The analysis indicated an additional alert for metabolite MFB1a (mechanistic profiler DNA binding by OECD/iminium ion formation) and for metabolite FAB1a (mechanistic profiler DNA binding by OECD/acylation) compared to parent. However, no additional alerts for protein binding for chromosome aberration or endpoint-specific profiler (i.e. in vivo MN test) were found. On the basis of available data, in particular negative Ames tests EFSA considered that metabolites MFB1a, FAB1a, 8,9-Z MAB1a, and AB1a are unlikely to be DNA-reactive.

The reference values of emamectin were based on dog studies (EFSA, 2012b). Most studies submitted under the current application were performed with CD-1 and CF-1 mice. However, available studies allow a comparison between the toxicity of the metabolites and the toxicity of emamectin.

Toxicity studies on metabolites MFB1a, FAB1a, AB1a, and 8,9-Z MAB1a indicated that their toxicological profile is qualitatively similar to parent but that there are potency differences. MFB1a appears to be 3 times more toxic than the parent considering acute and chronic endpoints. FAB1a is more acutely toxic than parent but is less acutely toxic than MFB1a. AB1a is slightly more acutely toxic than parent and seems to be more neurotoxic than parent. AB1a accounted for 2–22% (faeces) and 4–26% (organs) of the radioactivity in metabolism studies in rats with emamectin (Netherlands, 2008). 8,9-Z MAB1a is less acutely toxic and less neurotoxic than parent and MFB1a (France, 2018).

In line with the EMS assessment, EFSA concluded that a relative potency factor (RPF) of approximately 3 can be established for metabolites MFB1a, FAB1a, and AB1a and a RPF of 1 for metabolite 8,9-Z MAB1a in comparison to the parent. The RPFs can be used for both the acute and chronic risk assessment.

2. Residues in plants

2.1. Nature of residues and methods of analysis in plants

2.1.1. Nature of residues in primary crops

The metabolism of emamectin following foliar application was investigated in crops belonging to the groups of fruit crops, leafy crops and cereals/grass in the framework of the EU pesticides peer review (EFSA, 2012b). Emamectin B1a was largely metabolised, with photo-degradation more extensively observed in leafy crops (lettuces and cabbages). Emamectin B1a was the predominant compound (3–22% of total radioactive residue (TRR), at preharvest interval (PHI) ≤ 1 day) but the different photodegradation metabolites (‘mectin-like’ fraction, with formation of the primary metabolites 8,9-Z-
which individually were in low levels, represented significant amounts altogether (up to 20% of TRR). Details of the metabolism studies are presented in Appendix B.

2.1.2. Nature of residues in rotational crops

Emamectin is proposed for use on crops that can be grown in rotation with other crops. Confined rotational crop studies were submitted and assessed in the framework of EU pesticides peer review (EFSA, 2012b). Neither emamectin B1a benzoate nor the ‘mectin-like’ metabolites could be detected. Details of the studies are presented in Appendix B.

2.1.3. Nature of residues in processed commodities

The effect of processing on the nature of emamectin benzoate B1a component was investigated in the framework of the EU pesticides peer review (EFSA, 2012b). The compound was seen to be significantly degraded under standard hydrolysis condition (ca. 20%) to MSB1a, AB1a and several unknown compounds.

2.1.4. Methods of analysis in plants

The EU pesticide peer review concluded that an analytical method using liquid chromatography with tandem mass spectrometry (LC-MS/MS) was sufficiently validated for one ion transition on high water, high acid and high oil content matrices, dry commodities and wheat straw. Confirmatory methods were missing and independent laboratory validation (ILV) was provided only for high water content commodities (EFSA, 2012b). A confirmatory method was submitted with the current MRL application (France, 2018).

EFSA concluded that sufficiently validated analytical methods are available for the determination of emamectin B1a benzoate in the crops under consideration, which belong to the high water content group. The methods allow quantifying residues at or above the LOQ of 0.001 mg/kg.

2.1.5. Stability of residues in plants

The storage stability of emamectin (B1a and B1b) and its relevant photodegradation metabolites in plants stored under frozen conditions was investigated in the framework of the EU pesticides peer review (EFSA, 2012b). It was demonstrated that in the group to which the crops assessed in this application belong, residues were stable during frozen storage for 18 months.

2.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies and the capability of enforcement analytical methods, the following residue definition was proposed during the EU pesticides peer review.

- residue definition for enforcement: emamectin B1a and its salts, expressed as emamectin B1a benzoate.

The residue definition applies to rotational crops and processed products.

It is noted that the residue definition for enforcement in Regulation (EC) No 396/2005 refers to ‘emamectin B1a benzoate, expressed as emamectin’ (free base). In the framework of this MRL application, EFSA applied the residue definition for enforcement currently set in the EU legislation.

Taking into account the additional toxicological information provided with this MRL application, EFSA confirmed the inclusion of the photodegradation metabolites in the residue definition for risk assessment as proposed during the EU pesticides peer review. These compounds share a common toxicological mode of action but with different potencies. Pending the MRL review, EFSA agreed with the EMS to express residues as follow:

- residue definition for risk assessment: ‘sum of emamectin B1a, emamectin B1b, 8,9-Z-MAB1a plus 3 times AB1a plus 3 times MFB1a and 3 times FAB1a, expressed as emamectin’.

2.2. Magnitude of residues in plants

2.2.1. Magnitude of residues in primary crops

In support of the MRL application, GAP-compliant residue trials conducted with emamectin benzoate on kale and beans with pods were submitted. Samples were analysed for emamectin B1a
benzoate, emamectin B₁b, benzoate, 8,9-Z-MAB₁a, AB₁a, MFB₁a and FAB₁a. Photometabolites were quantifiable only in few samples collected just after the last application and after one day; at the intended PHI of 3 days (and up to 10 and 14 days in kale and beans, respectively) levels were below the LOQ (0.001 mg/kg per analyte).

According to the assessment of the EMS, the analytical method used was sufficiently validated and the trial samples were stored for up to 10 months under conditions for which integrity was demonstrated.

### 2.2.1. Leafy brassica

Northern Europe (NEU): Four GAP-compliant residue trials on kale conducted during two seasons were provided. In accordance with the EU extrapolation rules (European Commission, 2017), four trials on kale are sufficient to extrapolate the results to the other representative crop of the group of leafy brassica, which is Chinese brassica. The MRL of 0.03 mg/kg is proposed to leafy brassica.

Southern Europe (SEU): Not supported by data.

### 2.2.1.2. Beans and peas with pods

NEU: Eight GAP-compliant residue trials on beans with pods conducted during two seasons were provided and are sufficient to derive a MRL proposal.

SEU: Eight GAP-compliant residue trials on beans with pods conducted during two seasons were provided. Two trials were concluded not to be independent as the plots were about 21 km apart and the three applications were given on the same days resulting in seven valid trials. Beans are major crops in SEU and at least eight independent trials should be available to derive the MRL proposal. Since the indoor use of emamectin benzoate showed to provide higher residue levels, the deficiency was considered as minor and further data were not requested.

EU (indoor): Eight GAP-compliant indoor residue trials on beans with pods conducted during two seasons were provided. Samples were harvested from October to February, except one, which was sampled in June.

According to the EU guidance (European Commission, 2017), extrapolation from residues on beans with pods (at least eight trials) to peas with pods is acceptable. The MRL proposal of 0.03 mg/kg reflects the more critical residue situation of the indoor use.

### 2.2.2. Magnitude of residues in rotational crops

Studies on the magnitude of emamectin residues in rotational crops are not available. Based on the results of the rotational crops studies under confined conditions (at about 17N the maximum total application rate for the crops under assessment), EFSA concluded that significant residues are not expected in rotational crops, provided that the emamectin benzoate is applied in primary crops according to the intended GAPs.

### 2.2.3. Magnitude of residues in processed commodities

Having regard to the low residue levels observed in the residue trials for the crops under assessment (highest value according to the residue definition for risk assessment was 0.03 mg/kg for beans and peas with pods), no processing studies were provided. Nevertheless, accounting for the high acute toxicity and the low acceptable daily intake (ADI) of emamectin and the currently estimated overall long-term dietary intake of 91% of the ADI (see Section 4) further information to refine consumer intake assessments by consideration of processed commodities would be desirable.

### 2.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals based on the residue definition for enforcement in Regulation (EC) No 396/2005. Conversion factors from enforcement to risk assessment were also calculated. In Section 4, EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumer health risk.

### 3. Residues in livestock

Kale leaves may be used for feed purposes. Livestock dietary burdens were calculated for different groups of livestock according to OECD guidance (OECD, 2013). The input values are summarised in Appendix C.1. The contribution of the photo-degradation metabolites could not be considered for head cabbages, citrus and apple by-products. The results of the calculations are presented in Appendix B.3.
The dietary burdens derived did not exceed the trigger value of 0.1 mg/kg dry matter (DM) for all relevant groups of livestock; however, actual residues in feed items may potentially be underestimated. Since the existing MRLs in products of animal origin were derived based on higher livestock intakes estimated by Codex, they do not need to be revised.

4. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different sub-groups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016). The complete list of input values can be found in Appendix C.2.

The toxicological reference values for emamectin used in the risk assessment (i.e. ADI and acute reference dose (ARfD) values) were derived in the framework of the EU pesticides peer review (European Commission, 2013). Based on the additional studies assessed in this MRL application, the photodegradation metabolites included in the risk assessment residue definition were considered to be of same or higher potency in comparison to the parent (see Section 2).

4.1. Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed for the commodities assessed in this MRL application in accordance with the internationally agreed methodology (FAO, 2016). The calculations were based on the highest residue (HR) derived according to the proposed residue definition for risk assessment. The short-term exposure did not exceed the ARfD for any of the crops assessed in this application (see Appendix B.4).

4.2. Long-term (chronic) dietary risk assessment

The long-term exposure assessment was performed taking into account the median residue (supervised trials median residue (STMR)) values derived according to the proposed residue definition for risk assessment for leafy brassica, peas and beans with pods. For the remaining commodities of plant and animal origin, the STMRs derived in previous EFSA reasoned opinions (EFSA, 2009, 2011), the STMRs derived for the acceptable CXLs (FAO, 2011; EFSA, 2012a) plus the MRL values set at the LOQ were included in the calculation. For the existing uses, the contribution of the photodegradation metabolites and their relative toxicity was not considered in the chronic risk assessment. Their levels in plants depend on several factors and differ among commodities. No significant contribution was observed for the representative uses on grapes, tomatoes, peppers and cucurbits assessed during the EU pesticide peer review. In contrast on lettuces, all metabolites were systematically observed (EFSA, 2012b).

The estimated long-term dietary intake was 91% of the ADI. The contribution of residues expected in the commodities assessed in this MRL application to the overall long-term exposure is presented in more detail in Appendix B.4.

Based on the available information, EFSA concluded that the long-term intake of residues resulting from the intended uses on emamectin benzoate on leafy brassica and beans and peas with pods is unlikely to present a risk to consumer health.

Conclusions and recommendations

The data submitted in support of this MRL application were found to be sufficient to derive MRL proposals for leafy brassica, beans with pods and peas with pods according to the residue definition for enforcement in Regulation (EC) No 396/2005.

Based on the available information, EFSA concluded that the proposed uses of emamectin benzoate in the crops under assessment will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a risk to consumers’ health.

EFSA emphasised that the chronic risk assessment is indicative as it does not take into consideration the contribution of the photodegradation metabolites and their relative potency for the existing uses of emamectin benzoate. A more realistic long-term consumer risk assessment will be performed in the framework of the ongoing MRL review, when full information on authorised uses and residue data will be available to EFSA. Additionally, no information was available on the possible

12 Maximum dietary burden of 0.19 mg/kg DM for cattle based on the Australian feeding diet (FAO, 2011).
preferential degradation/metabolism in plants, animals and the environment of each enantiomer of the two emamectin components B1a and B1b. The consequent impact on the consumer risk assessment and further investigation on this matter has in principle to be addressed. Since guidance on how to address the dietary risk assessment of isomer mixtures is not yet implemented, EFSA recommended that this issue is reconsidered when such guidance is available.

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

The MRL recommendations are summarised in Appendix B.5.

References

EFSA (European Food Safety Authority), 2007. Reasoned opinion on the potential chronic and acute risk to consumers’ health arising from proposed temporary EU MRLs. EFSA Journal 2007;5(3):32r, 1141 pp. https://doi.org/10.2903/j.efsa.2007.32r

EFSA (European Food Safety Authority), 2009. Reasoned opinion on the setting of new MRLs for emamectin benzoate in various crops. EFSA Journal 2009;7(6):290r, 89 pp. https://doi.org/10.2903/j.efsa.2009.290r

EFSA (European Food Safety Authority), 2011. Modification of the existing MRLs for emamectin benzoate in plums, apricots and citrus fruit. EFSA Journal 2011;9(1):1974, 37 pp. https://doi.org/10.2903/j.efsa.2011.1974

EFSA (European Food Safety Authority), 2012a. Scientific support for preparing an EU position in the 44th Session of the Codex Committee on Pesticide Residues (CCPR). EFSA Journal 2012;10(7):2859, 155 pp. https://doi.org/10.2903/j.efsa.2012.2859

EFSA (European Food Safety Authority), 2012b. Conclusion on the peer review of the pesticide risk assessment of the active substance emamectin. EFSA Journal 2012;10(11):2955, 89 pp. https://doi.org/10.2903/j.efsa.2012.2955

EFSA (European Food Safety Authority), 2015. Scientific support for preparing an EU position in the 47th Session of the Codex Committee on Pesticide Residues (CCPR). EFSA Journal 2015;13(7):4208, 178 pp. https://doi.org/10.2903/j.efsa.2015

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2016. Guidance on the establishment of the residue definition for dietary risk assessment. EFSA Journal 2016;14(12):4549, 129 pp. https://doi.org/10.2903/j.efsa.2016.4549

European Commission, 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev., 22 July 1996.

European Commission, 1997b. Appendix B. General recommendations for the design, preparation and realization of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev. 6, 22 July 1997.

European Commission, 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev. 2, 22 July 1997.

European Commission, 1997d. Appendix E. Processing studies. 7035/VI/95-rev. 5, 22 July 1997.

European Commission, 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev. 3, 22 July 1997.

European Commission, 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev. 5, 22 July 1997.

European Commission, 1997g. Appendix I. Calculation of maximum residue level and safety intervals.7039/VI/95 22 July 1997. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010, finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23–24 March 2010.

European Commission, 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414. SANCO/3029/99-rev. 4.

European Commission, 2010a. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010-rev. 0, Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23–24 March 2010.

European Commission, 2010b. Residue analytical methods. For post-registration control. SANCO/825/00-rev. 8.1, 16 November 2010.

European Commission, 2013. Report on the active substance active substance. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 16 July 2013 i in view of the approval of emamectin as active substance in accordance with Regulation (EC) No 1107/2009. SANCO/11454/2013 rev 2. 16 July 2013.

European Commission, 2017. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev. 10.3, 13 June 2017.

FAO (Food and Agriculture Organization of the United Nations), 2011. Emamectin benzoate. In: Pesticide residues in food –2011 Joint meeting of the FAO Panel of Experts on Pesticide Residues in food and the Environment and the WHO Core Assessment Group. Evaluations, Part I, Residues. FAO Plant Production and Protection Paper 212, pp. 231–404.
FAO (Food and Agriculture Organization of the United Nations), 2016. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed. Pesticide Residues. 3rd Edition. FAO Plant Production and Protection Paper 225, 298 pp.

France, 2018. Evaluation report on the modification of MRLs for emamectin benzoate in leafy brassica, beans and peas with pods (fresh). September, 2016, revised on 1 February 2018, 149 pp.

Netherlands, 2008. Draft assessment report on the active substance emamectin prepared by the rapporteur Member State Netherlands in the framework of Council Directive 91/414/EEC, March 2008.

Netherlands, 2012. Final addendum to the draft assessment report on the active emamectin, October, 2012.

OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: http://www.oecd.org

OECD (Organisation for Economic Co-operation and Development), 2013. Guidance document on residues in livestock. In: Series on Pesticides No 73. ENV/JM/MONO(2013)8, 4 September 2013.

**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
- **CCPR**  Codex Committee on Pesticide Residues
- **CF**  conversion factor for enforcement to risk assessment residue definition
- **CXL**  Codex maximum residue limit
- **DAR**  draft assessment report
- **DAT**  days after treatment
- **DM**  dry matter
- **EMS**  evaluating Member State
- **eq**  residue expressed as a.s. equivalent
- **FAO**  Food and Agriculture Organization of the United Nations
- **GAP**  Good Agricultural Practice
- **HR**  highest residue
- **IEEDI**  international estimated daily intake
- **IESTI**  international estimated short-term intake
- **ILV**  independent laboratory validation
- **ISO**  International Organisation for Standardisation
- **IUPAC**  International Union of Pure and Applied Chemistry
- **JMPR**  Joint FAO/WHO Meeting on Pesticide Residues
- **LC**  liquid chromatography
- **LOAEL**  lowest observed adverse effect level
- **LOQ**  limit of quantification
- **Mo**  monitoring
- **MRL**  maximum residue level
- **MS**  mass spectrometry detector
- **MS/MS**  tandem mass spectrometry detector
- **MW**  molecular weight
- **NEU**  northern Europe
- **NOAEL**  no observed adverse effect level
- **OECD**  Organisation for Economic Co-operation and Development
- **PBI**  plant-back interval
- **PF**  processing factor
- **PHI**  preharvest interval
- **PRIMO (EFSA)**  Pesticide Residues Intake Model
- **QSAR**  quantitative structure-activity relationship
- **RA**  risk assessment
- **RAC**  raw agricultural commodity
- **RD**  residue definition
## Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation                | NEU, SEU, MS or country | F G I(a) | Pests or group of pests controlled                                      | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-------------------------------------|-------------------------|----------|------------------------------------------------------------------------|-------------|-------------|--------------------------------|----------------|---------|
|                                     |                         |          |                                                                        | Type(b)     | Conc. a.s.  | Method kind                  | Range of growth stages and season(c) | Number min-max | Interval between application (min) | g a.s./hL min-max | g a.s./ha min-max |         |
| Leafy brassica                      | NEU (BE, DE, HU, NL, PL, SI) | F        | Pieris spp., Plutella spp., Plusia spp., Heliothis spp.               | SG          | 9.5 g/kg   | Foliar spray                | BBCH 39-49                  | 3                   | 7 days                  | 200–1,000       | 15      | 3       |
| NEU (BE, DE, HU, NL, PL, SI)       | F                       |          |                                                                        |             |            |                              |                            |                      |                         |                   |         |
| SEU (BG, FR)                        | G                       |          |                                                                        |             |            |                              |                            |                      |                         |                   |         |
| EU                                  | I                       |          |                                                                        |             |            |                              |                            |                      |                         |                   |         |
| Beans and peas with pods (fresh)    | NEU (BE, DE, HU, NL, PL, SI) | F        | Heliothis spp., Ostrinia nubilalis                                     | SG          | 9.5 g/kg   | Foliar spray                | BBCH 71–89                  | 3                   | 7 days                  | 200–1,000       | 20      | 3       |
| SEU (CY, GR, PT, FR)                |                         |          |                                                                        |             |            |                              |                            |                      |                         |                   |         |
| EU                                  | I                       |          |                                                                        |             |            |                              |                            |                      |                         |                   |         |

NEU: northern European Union; SEU: southern European Union; MS: Member State. a.s.: the concentration of the formulation and the application rates are expressed as emamectin benzoate; SG: water-soluble granule.

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

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

(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

(d): PHI: minimum preharvest interval.
Appendix B – List of selected end points

B.1. Mammalian toxicology

Other toxicological studies

Supplementary studies on the active substance

- Acute oral toxicity (CD-1 mouse): NOAEL = 40 mg/kg bw (EFSA, 2012b)
- 15-day neurotoxicity (CF-1 mouse): NOAEL = 0.1 mg/kg bw per day and LOAEL = 0.3 mg/kg bw per day (EFSA, 2012b)
- 2-week (dog): NOAEL < 1.5 mg/kg bw per day

Studies performed on metabolites or impurities

| Compound | Ames test | Acute oral toxicity (CD-1 mouse) | 15-day neurotoxicity (CF-1 mouse) | RPF |
|----------|-----------|---------------------------------|----------------------------------|-----|
| MFB₁₅ | negative | NOAEL < 25 mg/kg bw | NOAEL = 0.075 mg/kg bw per day | 3 |
| FAB₁₅ | negative | NOAEL < 50 mg/kg bw | NOAEL > 0.3 mg/kg bw per day | 3 |
| AB₁₅ | negative | NOAEL < 50 mg/kg bw | NOAEL < 1.5 mg/kg bw per day | 3 |
| 8,9-Z MAB₁₅ | negative | NOAEL > 200 mg/kg bw | NOAEL > 0.3 mg/kg bw per day | 1 |

Reference: France (2018)
### B.2. Residues in plants

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

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

| Primary crops (available studies) | Crop groups | Crops | Applications | Sampling |
|-----------------------------------|-------------|-------|--------------|----------|
| Fruit crops                       | Pears       | Foliar, 3 x 16.8 or 168 g/ha, interval 7 days | 2 DAT1, 14, 28 DAT3 |
| Leafy crops                       | Lettuce     | Foliar, 8 x 16.8 or 84 g/ha, interval 7 days | 2 DAT1, 1, 3, 7, 10 DAT8 |
|                                  |            | Head cabbage | Foliar, 8 x 16.8 or 84 g/ha, interval 7 days | 2 DAT1, 1, 3, 7, 10 DAT8 |
| Cereals/grass                     | Maize       | Foliar, 6 x 16.8 or 84 g/ha, interval 3-5 days | 2 DAT1, 1, 3, 7 DAT6 |

Comments: [3, 7, 11, 13, 23-14C]-emamectin B1a benzoate or [23-14C]-emamectin B1a benzoate (pear study) variant
Reference: EFSA (2012b)

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) |
|--------------------------------------|-------------|---------|----------------|-----------|
| Root/tuber crops                     | Carrots     | Bare soil, 6 x 168 g/ha, interval 7 days | 30, 141, 365 |
| Leafy crops                          | Lettuce     | Bare soil, 6 x 168 g/ha, interval 7 days | 30, 120, 365 |
| Cereal (small grain)                 | Barley      | Bare soil, 6 x 168 g/ha, interval 7 days | 30, 141, 365 |

Comments: [3, 7, 11, 13, 23-14C]-emamectin B1a benzoate variant
Reference: EFSA (2012b)

| Processed commodities (hydrolysis study) | Conditions | Investigated |
|------------------------------------------|------------|--------------|
|                                         | Pasteurisation (20 min, 90°C, pH 4) | Yes |
|                                         | Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes |
|                                         | Sterilisation (20 min, 120°C, pH 6) | Yes |

Comment: [23-14C]-emamectin B1a benzoate variant. Reference: EFSA (2012b)
Emamectin B1a benzoate underwent hydrolysis (ca 20%) forming the monosaccharide MSB1a (pH 5, 100°C and pH 6, 120°C), aglycone milbemectin B (pH 6, 120°C) and AB1a (pH 6, 120°C). All degradation products were individually < 10% of applied radioactivity.

DAT1, DATn: days after the first, the n treatment; PHI: plant-back interval.
Can a general residue definition be proposed for primary crops?

Yes

Rotational crop and primary crop metabolism similar?

No

Degradation products in rotational crops were characterised as natural products only: Parent or ‘mectin-like’ degradates were not detected

Residue pattern in processed commodities similar to residue pattern in raw commodities?

No

Different degradation profile

Plant residue definition for monitoring (RD-Mo)

Emamectin B$_{1a}$ and its salts expressed as emamectin (Regulation (EU) No 396/2005)

Plant residue definition for risk assessment (RD-RA)

Sum of emamectin B$_{1a}$, emamectin B$_{1b}$, 8,9-Z-MAB$_{1a}$ plus 3 times AB$_{1a}$, plus 3 times MFB$_{1a}$ and 3 times FAB$_{1a}$, expressed as emamectin (provisionally, pending MRL review)

Conversion factor (monitoring to risk assessment)

Kale: 3
Beans/peas with pods: 2.5

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

Matrices with high water, high oil and high acid content and dry matrices: LC–MS/MS, LOQ of 0.001 mg/kg emamectin B$_{1a}$ benzoate (EFSA, 2012b)
ILV available for high water content matrices (EFSA, 2012b)
Confirmatory method available for high water content matrices (France, 2018)

B.2.1.2. Stability of residues in plants

| Plant products (available studies) | Category | Commodity | T (°C) | Stability (months) |
|-----------------------------------|----------|-----------|--------|-------------------|
|                                   | High water content | Tomato Beans with pod | –20 | 18 |
|                                   | High oil content |                         |      |                  |
|                                   | High protein content |                         |      |                  |
|                                   | High starch content | Potato                  | –20 | 18 |
|                                   | High acid content |                         |      |                  |

Comment: Compounds covered by storage data are emamectin B$_{1a}$ benzoate, emamectin B$_{1b}$ benzoate, 8,9-Z MAB$_{1a}$, AB$_{1a}$, MFB$_{1a}$, and FAB$_{1a}$
Reference: EFSA (2012b)
## B.2.2. Magnitude of residues in plants

### B.2.2.1. Summary of residues data from the supervised residue trials

| Crop                             | Region/indoor(a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments (OECD calculations)(b)                                                                                     | MRL proposals (mg/kg) | HR_Mo(c) (mg/kg) | STMR_Mo(d) (mg/kg) | CF(e) |
|----------------------------------|------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|-----------------------|------------------|-------------------|-------|
| Kale                             | NEU              | Mo: 0.002: 0.004; 0.009; 0.011; RA: 0.013; 0.015; 0.019; 0.021 | Residue trials on kale compliant with the GAP MRL<sub>OECD</sub>: 0.023 (unrounded) EMA B<sub>1b</sub> benzoate, 8,9-Z-MBA<sub>1a</sub>, AB<sub>1a</sub>, MFB<sub>1a</sub>, FaB<sub>1a</sub>: 4 × < 0.001 mg/kg Extrapolation to Chinese cabbage | 0.03                  | 0.011            | 0.006             | 3     |
|                                  | SEU              | –                                                               | No trials submitted. Use not supported                                                                           | –                     | –                | –                 | –     |
| Beans and peas with pod          | NEU              | Mo: 4 × < 0.001; 3 × 0.001; 0.009; RA: 4 × < 0.012; 3 × 0.012; 0.019 | Residue trials on beans with pods compliant with the GAP MRL<sub>OECD</sub>: 0.013 (NEU, unrounded) MRL<sub>OECD</sub>: 0.003 (SEU, unrounded) | 0.02                  | 0.009            | 0.001             | 2.1   |
|                                  | SEU              | Mo: 5 × < 0.001; 0.001; 0.002; RA: 5 × < 0.012; 0.012; 0.013 | MRL proposal derived from the more critical indoor use with samples collected in winter, except one (underlined value) EMA B<sub>1b</sub> benzoate, 8,9-Z-MBA<sub>1a</sub>, AB<sub>1a</sub>, MFB<sub>1a</sub>, FaB<sub>1a</sub>: 23 < 0.001 mg/kg | 0.01*                 | 0.002            | 0.001             | –     |
| Indoor                           |                  | Mo: < 0.001; 0.003: 0.005; 0.006; 0.007; 0.008; 0.012; 0.018 | Extrapolation to peas with pods | 0.03                  | 0.018            | 0.006             | 2.5   |

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

*: Indicates that the MRL is set below the (default) limit of quantification (LOQ).

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

(b): Mo: Individual residue values of emamectin (EMA) B<sub>1b</sub> benzoate were recalculated to emamectin (free base) using a conversion factor (CF) of 0.97 (EFSA, 2009).

RA: Individual residue values of EMA B<sub>1b</sub> benzoate were recalculated to EMA B<sub>1a</sub> using a molecular weight (MW) CF of 0.88. Since the MW CF for EMA B<sub>1b</sub> is 0.88 and for the photodegradation metabolites ranged from 0.95 to 1, the individual residues (all < LOQ) of EMA B<sub>1b</sub> benzoate, 8,9-Z-MBA<sub>1a</sub>, AB<sub>1a</sub>, MFB<sub>1a</sub>, FaB<sub>1a</sub> were not adjusted to express them as emamectin equivalents prior to be summed up.

(c): Highest residue according to the current residue definition for monitoring in Regulation (EU) No 396/2005 (emamectin benzoate B<sub>1b</sub> expressed as emamectin). Under brackets according to the residue definition for risk assessment (HR<sub>RA</sub>).

(d): Supervised trials median residue according to the current residue definition for monitoring in Regulation (EU) No 396/2005. Under brackets according to the residues definition for risk assessment (STMR<sub>RA</sub>).

(e): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment. Samples with residues at or close to the LOQ were disregarded from the calculation.
B.2.2.2. Residues in succeeding crops

**Confined rotational crop study** (quantitative aspect)

Rotational crop matrices (barley, lettuce, carrot) at plant-back intervals of 30, 120–141 and 365 days, total radioactivity ranged from < 0.003 to 0.030 mg eq/kg. No parent compound (emamectin B1a benzoate) and no ‘mectin-like’ degradates could be detected. Reference: EFSA (2012b)

**Field rotational crop study**

Not triggered

B.2.2.3. Processing factors

| Processed commodity | Number of valid studies\(^{(a)}\) | Processing factor (PF) | \(C_{F_P}\)\(^{(b)}\) |
|---------------------|----------------------------------|------------------------|------------------|
|                     |                                  | Individual values      | Median PF        |
| Not triggered (residues < 0.1 mg/kg) |                                  |                        |                  |

\(^{(a)}\) Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).

\(^{(b)}\) Conversion factor for risk assessment in the processed commodity if residue definition in raw commodities is different.

B.3. Residues in livestock

| Relevant groups          | Dietary burden expressed in | Most critical diet\(^{(a)}\) | Most critical commodity\(^{(a)}\) | Trigger exceeded (Y/N) |
|--------------------------|-----------------------------|-------------------------------|----------------------------------|------------------------|
|                          | mg/kg bw per day            | mg/kg DM                      |                                  |                        |
|                          | Median                      | Maximum                       | Median                          | Maximum                |
| Cattle (all diets)       | 0.0034                      | 0.0036                        | 0.0886                          | 0.0939                 | Dairy cattle Citrus, dry pulp N |
| Cattle (dairy only)      | 0.0034                      | 0.0036                        | 0.0886                          | 0.0939                 | Dairy cattle Citrus, dry pulp N |
| Sheep (all diets)        | 0.0007                      | 0.0009                        | 0.0176                          | 0.0203                 | Lamb Kale, leaves N |
| Sheep (ewe only)         | 0.0006                      | 0.0007                        | 0.0176                          | 0.0203                 | Ram/Ewe Kale, leaves N |
| Swine (all diets)        | 0.0014                      | 0.0015                        | 0.0608                          | 0.0635                 | Swine (breeding) Citrus, dry pulp N |
| Poultry (all diets)      | 0.00002                     | 0.00005                       | 0.00033                         | 0.00067                | Poultry layer Cabbage, heads N |
| Poultry (layer only)     | 0.00002                     | 0.00005                       | 0.00033                         | 0.00067                | Poultry layer Cabbage, heads N |

bw: body weight; DM: dry matter.

\(^{(a)}\) Calculated for the maximum dietary burden.

B.3.1. Nature of residues and methods of analysis in livestock

B.3.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

Not required.

B.3.1.2. Stability of residues in livestock

Not required.

B.3.2. Magnitude of residues in livestock

Not required.
B.4. Consumer risk assessment

**ARfD**
0.01 mg/kg bw per day (European Commission, 2013)

Highest IESTI, according to EFSA PRIMo
Beans (with pods): 35% of ARfD
Peas (with pods): 11% of ARfD
Kale: 14% of ARfD
Chinese cabbages: 8% of ARfD

Assumptions made for the calculations
The calculation is based on the highest residue levels expected in leafy brassica, beans and peas with pods

**ADI**
0.0005 mg/kg bw per day (European Commission, 2013)

Highest IEDI, according to EFSA PRIMo
91% of the ADI (WHO Cluster diet B)

Contribution of crops assessed:
Beans (with pods): 3.8% of ADI
Peas (with pods): 0.8 of ADI
Chinese cabbages: 0.7% of ADI
Kale: 0.5% of ADI

Contribution of the crops at < 0.01 mg/kg: 64% of ADI (WHO Cluster diet B)

Assumptions made for the calculations
The calculation is based on the median residue levels expected in leafy brassica, beans and peas with pods.
For the remaining commodities of plant and animal origin, the STMRs derived in previous EFSA opinions and for the acceptable CXLs plus the existing MRL values (LOQs) were included in the calculation. For the existing uses, the contribution of the photo-degradation metabolites and their relative toxicity was not considered in the chronic risk assessment

B.5. Recommended MRLs

| Code(a) | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------|-----------|------------------------|-------------------------|-----------------------|
| 0243010 | Chinese cabbage/pe-tsai | 0.01* | 0.03 | NEU use supported by extrapolation from residue data on kale. SEU use not supported. Risk for consumers unlikely |
| 0243020 | Kales | 0.01* | 0.03 | |
| 0243990 | Others leafy brassica | 0.01* | 0.03 | |
| 0260010 | Beans with pods | 0.01* | 0.03 | NEU, SEU and indoor use supported by extrapolation from data on beans. The MRL proposal reflects the more critical indoor use. Risk for consumers unlikely |
| 0260030 | Peas with pods | 0.01* | 0.03 | |

**Enforcement residue definition:** Emamectin B₁₉ benzoate, expressed as emamectin

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

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
# Appendix C – Input values for the exposure calculations

## C.1. Livestock dietary burden calculations

| Feed commodity          | Median dietary burden (Input value (mg/kg)) | Maximum dietary burden (Input value (mg/kg)) |
|-------------------------|---------------------------------------------|---------------------------------------------|
|                         | Comment                                     | Comment                                     |
| **Risk assessment residue definition:** Sum of emamectin B_{1a}, emamectin B_{1b}, 8,9-Z-MAB_{1a} plus 3 times A{B_{1a}} plus 3 times MFB_{1a} and 3 times FAB_{1a}, expressed as emamectin (provisional) |                                             |                                             |
| Kale leaves              | 0.017 STMR RA                                | 0.021 HR RA                                 |                                             |
| Apple pomace, wet        | 0.030 STMR Mo (EFSA, 2009) × PF(b)           | –                                            |                                             |
| Citrus, dry pulp         | 0.300 STMR Mo (EFSA, 2011) × PF(b)           | –                                            |                                             |
| Head cabbage             | 0.001 STMR Mo (EFSA, 2009)                   | 0.002 HR Mo (EFSA, 2009)                    |                                             |

STMR: supervised trials median residue; HR: highest residue; PF: processing factor; Mo: monitoring.

(a): For head cabbages, apple and citrus by-products, the input values (STMR_{Mo}/HR_{Mo}) refer to emamectin (free base). The contribution of the photometabolites was not considered in the chronic risk assessment as residue data were not available.

(b): For apple pomace and citrus dry pulp, in the absence of a processing factor supported by data, the default processing factors of 5 and 10 (respectively) was included in the calculation.

## C.2. Consumer risk assessment

| Commodity                  | Chronic risk assessment | Acute risk assessment |
|---------------------------|-------------------------|-----------------------|
|                           | Input value (mg/kg)     | Comment(a)            | Input value (mg/kg) | Comment |
| Citrus fruits             | 0.003                   | STMR_{Mo} (EFSA, 2011)| 0.021               | HR_{RA} |
| Pome fruits               | 0.005                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Apricots                  | 0.008                   | STMR_{Mo} (EFSA, 2011)|                     |        |
| Peaches                   | 0.0095                  | STMR_{Mo} (FAO, 2011)|                     |        |
| Plums                     | 0.003                   | STMR_{Mo} (EFSA, 2011)|                     |        |
| Grapes                    | 0.0025                  | STMR_{Mo} (FAO, 2011)|                     |        |
| Strawberries              | 0.009                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Tomatoes                  | 0.006                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Peppers                   | 0.003                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Aubergines                | 0.002                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Cucurbits (edible peel)   | 0.001                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Cucurbits (inedible peel) | 0.002                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Broccoli, Cauliflowrs     | 0.001                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Head cabbages             | 0.001                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Chinese cabbage           | 0.017                   | STMR_{RA}             | 0.021               | HR_{RA} |
| Kale                      | 0.017                   | STMR_{RA}             | 0.021               | HR_{RA} |
| Lettuces and salad plants except scarole | 0.272 | STMR_{Mo} (EFSA, 2009)|                     |        |
| Scarole                   | 0.030                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Herbs and edible flowers  | 0.272                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Beans (with pods)         | 0.017                   | STMR_{RA}             | 0.031               | HR_{RA} |
| Peas with pods            | 0.017                   | STMR_{RA}             | 0.031               | HR_{RA} |
| Globe artichokes          | 0.027                   | STMR_{Mo} (EFSA, 2009)|                     |        |
| Mammalian meat            | 0.002                   | STMR_{Mo} (FAO, 2011)|                     |        |
| Mammalian fat             | 0.002                   | STMR_{Mo} (FAO, 2011)|                     |        |
| Mammalian liver           | 0.006                   | STMR_{Mo} (FAO, 2011)|                     |        |
| Mammalian kidney          | 0.006                   | STMR_{Mo} (FAO, 2011)|                     |        |
| Mammalian edible offal    | 0.006                   | STMR_{Mo} (FAO, 2011)|                     |        |
### Commodity Risk Assessment

| Commodity                                      | Chronic risk assessment | Acute risk assessment |
|------------------------------------------------|-------------------------|-----------------------|
| Milk and cream products                        | Input value (mg/kg)     | STMR<sub>Mo</sub> (FAO, 2011) |
| Other food commodities of plant and animal origin | MRL                    | Regulation (EU) No 293/2013 |

**STMR**: supervised trials median residue; **HR**: highest residue; **Mo**: monitoring; **RA**: risk assessment.

(a): For several commodities, the median residues (STMR<sub>Mo</sub>) refer to emamectin (free base). The contribution of the photo-metabolites was not considered in the chronic risk assessment as residue data were not available.

(b): Mammalians: swine, bovine, sheep, goats, equine, other farmed animals.
## Appendix D – Used compound codes

| Code/trivial name | IUPAC name/SMILES notation/InChIKey(a) | Structural formula(b) |
|-------------------|----------------------------------------|-----------------------|
| **emamectin B1a** | (10E,14E,16E)-(1R,4S,5S,6S,6'R,8R,12S,13S,20R,21R,24S)-6'-(5'-sec-butyl)-21,24-dihydroxy-5',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2'-((5',6'-dihydro-2'H-pyran)-12-yl 2,6-dideoxy-3-O-methyl-4-O-(2,4,6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexopyranosyl)-α-L-arabino-hexopyranoside | ![Structural formula for emamectin B1a](Image) |
| **emamectin B1b** | (10E,14E,16E)-(1R,4S,5S,6S,6'R,8R,12S,13S,20R,21R,24S)-21,24-dihydroxy-6'-isopropyl-5',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2'-(5',6'-dihydro-2'H-pyran)-12-yl 2,6-dideoxy-3-O-methyl-4-O-(2,4,6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexopyranosyl)-α-L-arabino-hexopyranoside | ![Structural formula for emamectin B1b](Image) |
| **emamectin B1a benzoate** | (10E,14E,16E)-(1R,4S,5S,6S,6'R,8R,12S,13S,20R,21R,24S)-6'-(5'-sec-butyl)-21,24-dihydroxy-5',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2'-(5',6'-dihydro-2'H-pyran)-12-yl 2,6-dideoxy-3-O-methyl-4-O-(2,4,6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexopyranosyl)-α-L-arabino-hexopyranosidebenzoate | ![Structural formula for emamectin B1a benzoate](Image) |

(a) **InChIKey** is a unique identifier for each compound.

(b) **Structural formulas** are provided in the image.
| Name                        | IUPAC name/SMILES notation/InChiKey(a)                                      | Structural formula(b) |
|-----------------------------|---------------------------------------------------------------------------|-----------------------|
| emamectin B₁b benzoate      | 10E, 14E, 16E)-(1R, 4S, 5S, 6S, 6R, 8R, 12S, 13S, 20R, 21R, 24S)-21, 24-dihydroxy-6'-isopropyl-5', 11, 13, 22-tetramethyl-2-oxo-(3', 7, 19-trioxatetracyclo[15.6.1.1^4, 8, 0^20, 24]pentacosa-10, 14, 16, 22-tetraene)-6'-spiro-2', 5', 6'-dihydro-2'H-pyran)-12-yl 2, 6-dideoxy-3-O-methyl-4-O-(2, 4, 6-trideoxy-3-O-methyl-4-methylamino-α-L-lyxo-hexopyranosyl)-α-L-arabino-hexopyranoside benzoate | ![Structure of emamectin B₁b benzoate](image) |
| 8,9-Z-MAB₁a NOA 438376     | (1'R, 25'S, 5'S, 6'R, 10'E, 12'S, 13'R, 14'E, 16E, 20R, 21'R, 24S')-6'-(6-{(25)-butan-2-yl}-21', 24'-dihydroxy-5', 11', 13', 22'-tetramethyl-2'-oxo-5, 6-dihydrospiro[pyran-2, 6']-3', 7, 19'-tioxatetracyclo[15.6.1.1^4, 8, 0^20, 24]pentacosa-10, 14, 16, 22-tetraene)-6'-spiro-2', 5', 6'-dihydro-2'H-pyran)-12'yl 2, 6-dideoxy-3-O-methyl-4-O-{[2, 4, 6-trideoxy-3-O-methyl-4-(methylamino)-a-L-lyxo-hexopyranosyl]-a-L-arabino-hexopyranoside | ![Structure of 8,9-Z-MAB₁a NOA 438376](image) |
| FAB₁a NOA 415693           | (1'R, 25'S, 5'S, 6'R, 10'E, 12'S, 13'S, 14'E, 16E, 20R, 21'R, 24S')-6'-(6-{(25)-butan-2-yl}-21', 24'-dihydroxy-5', 11', 13', 22'-tetramethyl-2'-oxo-5, 6-dihydrospiro[pyran-2, 6']-3', 7, 19'-tioxatetracyclo[15.6.1.1^4, 8, 0^20, 24]pentacosa-10, 14, 16, 22-tetraene)-6'-spiro-2', 5', 6'-dihydro-2'H-pyran)-12'yl 2, 6-dideoxy-3-O-methyl-4-O-{[2, 4, 6-trideoxy-3-O-methyl-a-L-lyxo-hexopyranosyl]-α-L-arabino-hexopyranoside | ![Structure of FAB₁a NOA 415693](image) |
| Code/trivial name | IUPAC name/SMILES notation/InChiKey(a) | Structural formula(b) |
|------------------|---------------------------------------|----------------------|
| MFB1a NOA 415692 | (1'R,2S,4'S,5S,6R,8'R,10'E,12'S,13'S,14' E,16'E,20'R,21'R,24'S)-6-{(25S)-butan-2-yl}-21',24'-dihydroxy-5,11',13',22'-tetramethyl-2'-oxo-5,6-dihydrospiro[pyran-2,6'-[3,7,19]trioxatetracyclo[15.6.1.1^{9,8,0^{20,24}}]pentacosa[10,14,16,22]tetraen]-12'-yl 4,6-dideoxy-3-O-methyl-4-O-{2,4,6-trideoxy-4-[formyl(methyl) amino]-3-O-methyl-a-L-lyxo-hexopyranosyl}-a-L-arabino-hexopyranoside | ![Structural formula for MFB1a](image) |
| AB1a NOA 438309 | (1'R,2S,4'S,5S,6R,8'R,10'E,12'S,13'S,14' E,16'E,20'R,21'R,24'S)-6-{(25S)-butan-2-yl}-21',24'-dihydroxy-5,11',13',22'-tetramethyl-2'-oxo-5,6-dihydrospiro[pyran-2,6'-[3,7,19]trioxatetracyclo[15.6.1.1^{9,8,0^{20,24}}]pentacosa[10,14,16,22]tetraen]-12'-yl 4-O-([4-amino-2,4,6-trideoxy-3-O-methyl-a-L-arabino-hexopyranosyl]-2,6-dideoxy-3-O-methyl-a-L-arabino-hexopyranoside | ![Structural formula for AB1a](image) |
| MSB1a NOA 419150 | (1'R,25,4'S,5S,6R,8'R,10'E,12'S,13'S,14' E,16'E,20'R,21'R,24'S)-6-{(25S)-butan-2-yl}-21',24'-dihydroxy-5,11',13',22'-tetramethyl-2'-oxo-5,6-dihydrospiro[pyran-2,6'-[3,7,19]trioxatetracyclo[15.6.1.1^{9,8,0^{20,24}}]pentacosa[10,14,16,22]tetraen]-12'-yl 2,6-dideoxy-3-O-methyl-a-L-arabino-hexopyranoside | ![Structural formula for MSB1a](image) |
| Code/trivial name | IUPAC name/SMILES notation/InChiKey<sup>a</sup> | Structural formula<sup>b</sup> |
|------------------|---------------------------------------------|--------------------------------|
| Aglycone milbemectin B NOA 419153 | (1'R,2S,4'S,5S,6R,8'R,10'E,12'S,13'S,14'E,16'E,20'R,21'R,24'S)-6-[(2S)-butan-2-yl]-12',21',24'-trihydroxy-5,11',13',22'-tetramethyl-5,6-dihydro-2'H-spiro[pyran-2,6'-[3,7,19]trioxatetracyclo[15.6.1.1<sup>4,8</sup>,0<sup>20,24</sup>]]pentacosa[10,14,16,22]tetraen]-2'-one | ![Structural formula](image) |

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

<sup>a</sup> ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).

<sup>b</sup> ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).