Modification of the existing maximum residue level for ametoctradin in honey

EFSA (European Food Safety Authority)

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant BASF SE submitted a request to the competent national authority in the Netherlands to modify the existing maximum residue level (MRL) for the active substance ametoctradin in honey. The data submitted in support of the request were found to be sufficient to derive an MRL proposal for honey. Adequate analytical methods for enforcement are available to control the residues of ametoctradin in the commodity under consideration at the validated screening detection limit (SDL) of 0.0025 mg/kg. Based on the risk assessment results, EFSA concluded that the dietary intake of residues in food of plant and animal origin (including honey) resulting from the use of ametoctradin according to the existing agricultural practices is unlikely to present a risk to consumer health.

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, BASF SE submitted an application to the competent national authority in the Netherlands (evaluating Member State, EMS) to modify the existing maximum residue level (MRL) for the active substance ametoctradin in honey. The EMS drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 29 June 2021. The EMS proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.05 to 5 mg/kg.

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

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

The metabolism of ametoctradin following foliar application was investigated in crops belonging to the groups of fruit, leafy and root crops. In the crops tested, the parent compound was the main residue, with evident presence of metabolites M650F03 and M650F04 in root crops from soil uptake.

Studies investigating the effect of processing on the nature of ametoctradin (hydrolysis studies) demonstrated that the active substance is stable.

In rotational crops, the major residues identified were the soil metabolites M650F03 and M650F04, with occasional detection of the parent.

In the context of the MRL review, the residue definition for enforcement was proposed as ‘ametoctradin’ for all plant commodities; the residue definition for risk assessment was proposed as ‘ametoctradin’ for primary crops and processed commodities and as ‘sum of ametoctradin, M650F03 and M650F04, expressed as ametoctradin’ for rotational crops.

In the absence of specific metabolism studies on honey and considering the possible transfer of residues from floral nectar collected from primary and rotational crops to honey, EFSA proposed the following residue definitions for honey:

- residue definition for enforcement: ametoctradin
- residue definition for risk assessment: sum of ametoctradin, M650F03 and M650F04, expressed as ametoctradin

Sufficiently validated analytical methods based on LC-MS-Q-ToF (QuEChERS method) are available to quantify residues in honey according to the enforcement residue definition. The methods enable the quantification of residues at or above the screening detection limit (SDL) of 0.0025 mg/kg in honey.

The applicant provided residue trials for honey, where ametoctradin was applied to buckwheat under semi-field conditions in tunnels. The bee colonies were placed in the tunnels and produced honey which was collected when it reached its commercial maturity. The trials are considered sufficiently representative for the authorised EU uses of ametoctradin and are therefore appropriate to derive an MRL proposal for honey (5 mg/kg).

Specific studies investigating the magnitude of ametoctradin residues in processed honey are not required, considering that the overall dietary exposure is expected to be below 10% of the acceptable daily intake (ADI).

Residues of ametoctradin in commodities of animal origin were not assessed since honey is not used for feed purposes.

The toxicological profile of ametoctradin was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 10 mg/kg body weight (bw) per day. An acute reference dose (ARfD) was deemed unnecessary. During the peer review, it was concluded that the metabolites included in the residue definition are of similar toxicity to the parent active substance.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The highest estimated long-term dietary intake accounted for 0.2% of the ADI (NL toddler diet). An acute reference dose (ARfD) was deemed unnecessary. During the peer review, it was concluded that the metabolites included in the residue definition are of similar toxicity to the parent active substance.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The highest estimated long-term dietary intake accounted for 0.2% of the ADI (NL toddler diet). An acute reference dose (ARfD) was deemed unnecessary. During the peer review, it was concluded that the metabolites included in the residue definition are of similar toxicity to the parent active substance.

The risk assessment is affected by minor, non-standard uncertainties (lack of information on residue levels of the metabolites M650F03 and M650F04 taken up from soil in rotational crops and transferred to honey, lack of validation of analytical methods regarding extraction efficiency and the data gaps...
identified in the context of the MRL review). Overall, EFSA concluded that despite these minor uncertainties, the exposure calculation provides sufficient evidence that the proposed MRL for honey and existing MRLs derived in previous assessments are unlikely to pose a risk to consumers’ health.

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

| Code<sup>(a)</sup> | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|------------------|-----------|------------------------|-------------------------|-----------------------|
| 1040000          | Honey     | 0.05*                  | 5                       | The submitted data are sufficient to derive an MRL proposal for honey which sufficiently reflects the uses of ametoctradin authorised in the EU. Risk for consumers unlikely. |

Enforcement residue definition: ametoctradin<sup>(F)</sup>

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe; GAP: Good Agricultural Practice.

*: 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.

(F): Fat soluble.
Table of contents

Abstract ................................................................................................................................................... 1
Summary ............................................................................................................................................... 3
Assessment .......................................................................................................................................... 6
1. Residues in plants .......................................................................................................................... 7
   1.1. Nature of residues and methods of analysis in plants ............................................................... 7
      1.1.1. Nature of residues in primary crops ...................................................................................... 7
      1.1.2. Nature of residues in rotational crops ..................................................................................... 7
      1.1.3. Nature of residues in processed commodities ......................................................................... 7
      1.1.4. Nature of residues in honey .................................................................................................... 8
      1.1.5. Methods of analysis in plants and honey ............................................................................... 8
      1.1.6. Storage stability of residues in honey ...................................................................................... 8
      1.1.7. Proposed residue definition ..................................................................................................... 8
   1.2. Magnitude of residues in plants and honey ............................................................................... 9
      1.2.1. Magnitude of residues in primary crops .................................................................................. 9
      1.2.2. Magnitude of residues in rotational crops .............................................................................. 9
      1.2.3. Magnitude of residues in honey .............................................................................................. 9
      1.2.4. Magnitude of residues in processed commodities .................................................................. 10
      1.2.5. Proposed MRLs ....................................................................................................................... 10
2. Residues in livestock ....................................................................................................................... 10
3. Consumer risk assessment .............................................................................................................. 11
4. Conclusion and Recommendations ................................................................................................. 11
References ......................................................................................................................................... 11
Abbreviations .................................................................................................................................... 12
Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs .......... 14
Appendix B – List of end points ......................................................................................................... 15
Appendix C – Pesticide Residue Intake Model (PRIMo) ..................................................................... 21
Appendix D – Input values for the exposure calculations .................................................................. 23
Appendix E – Used compound codes ............................................................................................... 24
Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue levels (MRLs) for ametoctradin in honey. The current MRL application is not linked to one specific good agricultural practice (GAP) but is related to the existing uses assessed in the framework of the review of MRLs according to Art. 12 of Regulation (EC) No 396/2005 (EFSA, 2020), where numerous GAPs were reported for crops that might be attractive to bees and that are a potential source for residues of ametoctradin in honey.

Ametoctradin is the ISO common name for 5-ethyl-6-octyl[1,2,4]triazolo[1,5-a]pyrimidin-7-amine (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Ametoctradin was evaluated in the framework of Directive 91/414/EEC with the Netherlands designated as rapporteur Member State (RMS); the representative uses were foliar treatments on potatoes and tomatoes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2012). Ametoctradin was approved for the use as fungicide on 1 August 2013.

The EU MRLs for ametoctradin are established in Annexes II of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2020). The proposed modifications have been recently implemented in the EU MRL legislation, which will become applicable as from 27 January 2022. Certain Codex maximum residue limits (CXLs) have been taken over in the EU MRL legislation.

In accordance with Article 6 of Regulation (EC) No 396/2005, BASF SE submitted an application to the competent national authority in the Netherlands (evaluating Member State, EMS) to modify the existing maximum residue level (MRL) for the active substance ametoctradin in honey. 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 EFSA on 29 June 2021. The EMS proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.05 to 5 mg/kg.

EFSA based its assessment on the evaluation report submitted by the EMS (Netherlands, 2021), the draft assessment report (DAR) and its addendum (Netherlands, 2010, 2012) prepared under Council Directive 91/414/EEC, the Commission review report on ametoctradin (European Commission, 2013), the conclusion on the peer review of the pesticide risk assessment of the active substance ametoctradin (EFSA, 2012), as well as the reasoned opinion on the MRL review according to Article 12 of Regulation No 396/2005 (EFSA, 2020).

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, 2010, 2017, 2018, 2021; 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 this MRL application including the end points of relevant studies assessed previously is presented in Appendix B.

The evaluation report submitted by the EMS (Netherlands, 2021) and the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo) are considered as supporting documents to

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1 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.
2 Commission Implementing Regulation (EU) No 200/2013 of 8 March 2013 approving the active substance ametoctradin, 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 67, 9.3.2013, p. 1–5.
3 Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.
4 Commission Regulation (EU) 2021/1110 of 6 July 2021 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 ametoctradin, bixafen, fenazaquin, spinetoram, tefluthrin and thiacarbazone-methyl in or on certain products. OJ L 239, 7.7.2021, p. 4–21.
5 For an overview of all MRL Regulations on this active substance, please consult: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=search.as
6 Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.
7 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of ametoctradin (BAS 650 F) was investigated after foliar treatment in fruits (tomatoes), leafy vegetables (lettuces) and root crops (immature and mature potato tubers) (EFSA, 2012). All studies were performed with 2,7-14C-labelled and 2,5,7-13C-labelled ametoctradin in combination.

In the crops tested, the parent compound was the main residue, accounting for 67–99.1% of the total radioactive residues (TRR), except in mature potato tuber where ametoctradin was only 3.6% of the TRR and the main residues were the metabolites M650F03 and M650F04 representing the 40% and 27% TRR, respectively (EFSA, 2012, 2020).

As ametoctradin was the only compound found in treated commodities, besides metabolites M650F03 and M650F04 found in mature tubers, it was assumed that these two metabolites are taken up from the soil (EFSA, 2020). It was therefore concluded, in line with the peer review (EFSA, 2012), that the metabolism of ametoctradin was similar in all three crops, with the parent being hardly taken up and not translocated via leaves or fruits of plants and poorly metabolised following foliar applications. In root crops, uptake of soil metabolites M650F03 and M650F04 was evident (EFSA, 2020).

An additional study with non-standard study design was performed with radiolabelled 5-14C-M650F03 or 5-14C-M650F04 to investigate the metabolite uptake by tomato plants from aqueous nutrient solution. However, the study did not provide clear information whether there is uptake of the metabolites via the roots and translocation to aerial parts of the crop and it is considered as additional information only.

The metabolic behaviour in primary crops is sufficiently addressed.

1.1.2. Nature of residues in rotational crops

Ametoctradin is authorised on several annual crops that can be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review, the field DT90 of ametoctradin is 13.3 days; the DT90 values of the main soil metabolites M650F03 and M650F04 are above 100 days (EFSA, 2012). Thus, further studies investigating the nature of residues in rotational crops are triggered (European Commission, 1997c).

In the framework of the EU pesticides peer review and MRL review, the metabolism of ametoctradin was investigated in a confined rotational crop study on root crops (white radishes), leafy crops (lettuces) and cereals (spring wheat) at plant back intervals (PBIs) of 30, 120 and 365 days (EFSA, 2012, 2020).

In the rotational crop metabolism studies, significant residues of soil metabolites M650F03 and M650F04 were observed up to a PBI of 120 days after treatment (DAT) in lettuce and in radish roots and at a PBI of 365 DAT in wheat straw, forage and grain. The parent was only detected in lettuce at a PBI of 30 DAT and in wheat forage and straw at a PBI of 120 DAT (EFSA, 2020).

It was concluded that the metabolism of ametoctradin in rotational crops is dissimilar to the metabolism observed in primary crops where the parent was the main residue. In rotational crops, main soil metabolites M650F03 and M650F04 were found with occasional detection of the parent.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of ametoctradin was investigated in the framework of the EU pesticides peer review and MRL review (EFSA, 2012, 2020).

These studies showed that ametoctradin is hydrolytically stable under standard processing conditions of pasteurisation, baking/brewing/boiling and sterilisation.

Hydrolysis studies for the metabolites M650F03 and M650F04, found in significant amounts in rotational crops, are not available. Considering the overall low intake of ametoctradin and its metabolites compared to the ADI (below 1%), the lack of studies investigating the hydrolytic stability
of M650F03 and M650F04 is considered a minor deficiency and it is not expected to have an impact on the outcome of the risk assessment (EFSA, 2020).

1.1.4. Nature of residues in honey

Honey is a product produced by bees from sugary secretions of plants (floral nectar mainly) through regurgitation, enzymatic conversion and water evaporation and followed by storage in the bee hives for a certain time period.

In the absence of specific metabolism studies with honey bees, studies investigating the nature of residues in primary crops and rotational crops and studies investigating the degradation during pasteurisation should be considered to determine the nature of residues in honey (European Commission, 2018). It is likely that the nature of residues in pollen and nectar collected from primary and rotational crops, as well as in honey (resulting from the residues in floral nectar), is the same as in primary and rotational crops.

Considering that sufficient data investigating the metabolic profile in primary and rotational crops and the degradation of the active substance (a.s.) under standard hydrolysis conditions are available, no further information is required for the current application according to the guidelines. However, it would be desirable to further investigate whether enzymatic processes involved in the production of honey occurring in the bee gut or during the storage in the beehive have an impact on the nature of residues in honey.

1.1.5. Methods of analysis in plants and honey

Several enforcement methods have been previously assessed for different plant matrices in the context of the peer review and MRL review (EFSA, 2012, 2020).

Analytical methods for the determination of residues of ametoctradin in honey were assessed during the MRL review (EFSA, 2020). The LC–MS–Q–ToF (QuEChERS method) is sufficiently validated for the determination of residues of ametoctradin, according to the residue definition for enforcement, at or above the screening detection limit (SDL) of 0.0025 mg/kg in honey.

Information on extraction efficiency of the analytical methods applied for enforcement and used for the residue trials is not available. However, since the existing guidance document on extraction efficiency (European Commission, 2017) cannot be applied for the honey matrix and since no other guidance on how to investigate extraction efficiency is available, the lack of evidence of extraction efficiency is not considered to be a major data gap.

1.1.6. Storage stability of residues in honey

Information on the stability of residues in frozen samples of honey was submitted with the current application (Netherlands, 2021). It was demonstrated that in honey, residues of ametoctradin and metabolites M650F03 and M650F04 were stable for at least 6 months when stored at –18°C.

1.1.7. Proposed residue definitions

In the framework of the MRL review, the following residue definitions were derived (EFSA, 2020):

- residue definition for enforcement: ametoctradin;
- residue definition for risk assessment in primary crops and processed commodities: ametoctradin;
- residue definition for risk assessment for rotational crops: sum of ametoctradin, M650F03 and M650F04, expressed as ametoctradin.

In the absence of specific metabolism studies on honey, the studies investigating the nature of residues in primary and rotational crops and studies investigating the degradation of the active substance during pasteurisation are considered to derive the residue definitions for honey; the following residue definitions are proposed for honey:

- residue definition for enforcement: ametoctradin;
- residue definition for risk assessment: sum of ametoctradin, M650F03 and M650F04, expressed as ametoctradin.
It is noted that the EMS proposed the residue definition for risk assessment for honey as ametoctradin only. However, EFSA is of the opinion that the inclusion of the soil metabolites M650F03 and M650F04 is appropriate, taking into account the following considerations:

- due to their persistence, the two soil metabolites have the potential to accumulate in soil;
- there is evidence that the metabolites are taken up from the soil by crops grown as rotational crops;
- the transfer to the metabolites to aerial plant parts is expected, leading to residues in leaves;
- lacking specific data, the transfer to nectar and a carry-over into honey cannot be excluded.

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical with the above-mentioned residue definition for enforcement.

1.2. Magnitude of residues in plants and honey

1.2.1. Magnitude of residues in primary crops

As the current MRL application is on honey, investigations of residues in primary crops are not required.

1.2.2. Magnitude of residues in rotational crops

The magnitude of residues in rotational crops was assessed in the framework of the EU pesticide peer review and MRL review (EFSA, 2012, 2020). Based on two field rotational crop studies performed on wheat, carrot, cauliflower and lettuce, it was concluded that the soil metabolites M650F03 and M650F04 are the only residues observed in significant concentrations in the mature crops, following application of ametoctradin at 960 g a.s./ha to bare soil. The data indicate that at plant back intervals of 120 days, most of the crop parts for human consumption are not expected to contain residues above the LOQ with exception of cereal grains. In addition, in one rotational field crop trial, maximum residues (measured according to the residue definition for risk assessment) of 0.03 mg/kg in carrot roots and wheat grain and 0.036 mg/kg in cauliflower were measured at a PBI of 360 DAT (See Section B.1.2.2).

For the purpose of this application, further information on the possible transfer of the metabolites M650F03 and M650F04 from the soil to the flowers and floral nectar of rotational crops would be desirable, especially for crops belonging to the group of fruiting vegetables as these crops are relevant melliferous crop (i.e. solanaceae and cucurbits).

1.2.3. Magnitude of residues in honey

In support of the MRL application, the applicant submitted four independent residue trials where ametoctradin was applied to buckwheat under semi-field conditions (tunnel trials) during the growing season of 2020 in Germany. The bee colonies were placed in the tunnels. During the time of application, the bee hives were covered to protect the bees from overspray. All colonies were visually assessed prior to introduction into the tunnels and at the end of the trial. Colonies were in good health (Netherlands, 2021).

Each trial consisted of two plots (control and treatment). The active substance was applied on buckwheat (treated plot) in three foliar applications at a rate of 390 g a.s./ha. The first application was performed at BBCH 55–59 (before flowering); the following two applications were performed during flowering, at BBCH 61–63 and 63–65, respectively. Since ametoctradin is not a systemic substance, the applications contributing to the residue carry-over from the plant to honey are considered to be the ones performed at BBCH 61–65. The application rate tested in the residue trials is considered sufficiently representative of the worst-case GAP with respect to residues in honey, identified among the GAPs notified in the context of the EU MRL review (i.e. NEU GAP on wine grapes: 3 × 480 g ametoctradin/ha, 10 day-interval between applications, BBCH from 53 to 83, RTI of 10 days, preharvest interval (PHI) of 35 days) (EFSA, 2020), also considering that during flowering a maximum number of two application might be expected.

Honey samples were collected when honey reached its commercial maturity (water content in honey from control and treated plots below 20%), 7–14 days after the last application. The sampled honey amount ranged from 21.2 to 56.5 g.
The samples were stored under conditions for which integrity of the samples has been demonstrated and were analysed for the parent compound and the metabolites included in the residue definitions for risk assessment. The method used in the analysis of samples in the context of the residue trials is based on LC-MS/MS and enables the quantification of residues of parent ametoctradin, M650F03 and M650F04 at or above the LOQ of 0.01 mg/kg for each analyte in the commodity assessed. According to the assessment of the EMS, the method used was sufficiently validated and fit for purpose (Netherlands, 2021).

The residue levels in honey, measured as the ‘sum of the parent ametoctradin, M650F03 and M650F04, expressed as ametoctradin’, ranged from 0.102 to 1.825 mg/kg; the metabolites were in concentrations below the LOQ, except in one trial where M650F04 occurred at a level of 0.078 mg/kg. Data on residues in pollen and inflorescences of buckwheat were also presented in the evaluation report (Netherlands, 2021). According to Commission Regulation (EU) 2018/628, MRLs are currently established only for honey; therefore, these additional results in pollen and inflorescences of buckwheat are considered as supplementary information only. No residues of ametoctradin, M650F03 and M650F04 were found at or above the LOQ in honey samples collected from untreated plots.

EFSA noted the following minor deficiencies for the studies:

- The amount of honey harvested in the trials was below the recommended honey amount of at least 100 g honey (European Commission, 2018). However, it is commonly acknowledged that this sample size is difficult to obtain under semi-field conditions. This is therefore considered only as a minor deviation not affecting the validity of the trials.
- The extraction efficiency of the analytical method used in the residue trials was not investigated, due to the lack of an appropriate guidance for this type of matrix; this minor deficiency of the trials may lead to an additional, minor uncertainty for the results on the analysis.
- The trials were not designed to account for residues of soil metabolites (M650F03 and M650F04) taken up from preceding crops planted on aged soil previously treated with ametoctradin. Therefore, the residue levels of the two metabolites may be underestimated, compared to the level in honey produced under real field conditions, where bees are foraging on crops grown on soil containing residues of M650F03 and M650F04 from previous treatments.

Overall, the use conditions tested in the residue trials are considered sufficiently representative of the most critical GAP authorised in the EU assessed in the MRL review (EFSA, 2020) in view of residues in honey, i.e. the GAP on wine grapes in NEU (3 × 480 g ametoctradin/ha, 10-day interval between applications, BBCH: 53–83, PHI: 35 days), also considering a maximum number of two applications performed during flowering. EFSA concluded that the residue trials were valid to derive an MRL proposal and risk assessment values for honey.

### 1.2.4. Magnitude of residues in processed commodities

Specific processing studies for the commodity under assessment are not available and are not required, considering that the overall dietary exposure is expected to be below 10% of the ADI (European Commission, 2013).

### 1.2.5. Proposed MRLs

The available data are considered sufficient to derive an MRL proposal as well as risk assessment values for honey (see Appendix B.1.2.1). In Section 3, EFSA assessed whether residues on this commodity resulting from the existing uses of ametoctradin are likely to pose a consumer health risk.

### 2. Residues in livestock

Not relevant as honey and other apiculture products are not used for feed purposes.

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8 Commission Regulation (EU) 2018/62 of 17 January 2018 replacing Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council. C/2018/0138. OJ L 18, 23.1.2018, p. 1–73.
3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo (EFSA, 2018, 2019). This exposure assessment model contains food consumption data for different subgroups 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 toxicological reference value for ametoctradin used in the risk assessment (i.e. ADI value) was derived in the framework of the EU pesticides peer review (European Commission, 2013). The metabolites included in the risk assessment residue definition were considered to be of similar toxicity to the parent compound.

Short-term (acute) dietary risk assessment

Considering the toxicological profile of the active substance, a short-term dietary risk assessment was not required.

Long-term (chronic) dietary risk assessment

In the framework of the MRL review, a comprehensive long-term exposure assessment was performed, taking into account the existing uses at EU level and the acceptable CXLs (EFSA, 2020). EFSA updated the calculation with the relevant STMR value derived from the residue trials submitted in support of this MRL application for honey. The input values used in the exposure calculations are summarised in Appendix D.11.

The highest estimated long-term dietary intake accounted to 0.2% of the ADI (NL toddler diet). The contribution of residues expected in honey to the overall long-term exposure is insignificant (< 0.01% ADI in the DE child diet) (see Appendix B.3).

The risk assessment is affected by additional, minor, non-standard uncertainties related to the lack of information on residue levels of the metabolites M650F03 and M650F04 taken up from soil in rotational crops and transferred to honey, as well as minor deficiencies regarding the validation of analytical methods (extraction efficiency) and the data gaps identified in the context of the MRL review (EFSA, 2020). Overall, EFSA concluded that despite these minor uncertainties, the exposure calculation provides sufficient evidence that the proposed MRL for honey and existing MRLs derived in previous assessments are unlikely to pose a risk to consumers’ health.

For further details on the exposure calculations, a screenshot of the Report sheet of the PRIMo is presented in Appendix C.

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for honey.

EFSA concluded that the current authorised EU uses of ametoctradin on crops that are foraged by bees to produce honey will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a risk to consumers’ health.

EFSA notes that this assessment presents some minor, non-standard uncertainties related to the lack of information on the transfer of residues of the metabolites M650F03 and M650F04 from rotational crops to honey via soil uptake and on the extraction efficiency of the analytical methods, along with the data gaps identified in the context of the MRL review (EFSA, 2020).

The MRL recommendations are summarised in Appendix B.4.

References

EFSA (European Food Safety Authority), 2012. Conclusion on the peer review of the pesticide risk assessment of the ametoctradin (BAS 650 F). EFSA Journal 2012;10(11):2921, 84 pp. https://doi.org/10.2903/j.efsa.2012.2921

EFSA (European Food Safety Authority), Brancato A, Brocca D, Ferreira L, Greco L, Jarrah S, Leuschner R, Medina P, Miron I, Nougadere A, Pedersen R, Reich H, Santos M, Stanek A, Tarazona J, Theobald A and Villamar-Bouza L, 2018. Guidance on use of EFSA Pesticide Residue Intake Model (EFSA PRIMo revision 3). EFSA Journal 2018;16(1):5147, 43 pp. https://doi.org/10.2903/j.efsa.2018.5147

EFSA (European Food Safety Authority), Anastassiadou M, Brancato A, Carrasco Cabrera L, Ferreira L, Greco L, Jarrah S, Kazocina A, Leuschner R, Magrans JO, Miron I, Pedersen R, Raczyk M, Reich H, Ruocco S, Sacchi A, Santos M, Stanek A, Tarazona J, Theobald A and Verani A, 2019. Pesticide Residue Intake Model- EFSA PRIMo revision 3.1 (update of EFSA PRIMo revision 3). EFSA supporting publication 2019;EN-1605, 15 pp. https://doi.org/10.2903/sp.efsa.2019.en-1605
EFSA (European Food Safety Authority), Anastassiadou M, Bernasconi G, Brancato A, Carrasco Cabrera L, Greco L, Jarrah S, Kazocina A, Leuschner R, Magrans JO, Miron I, Nave S, Pedersen R, Reich H, Rojas A, Sacchi A, Santos M, Stanek A, Theobald A, Vagenende B and Verani A, 2020. Reasoned Opinion on the review of the existing maximum residue levels for ametoctradin according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2020;18(1):5990, 74 pp. https://doi.org/10.2903/j.efsa.2020.5990

EURL (European Union Reference Laboratories for Pesticide Residues), 2018. Evaluation report prepared under Article 12 of Regulation (EC) No 396/2005. Analytical methods validated by the EURLs and overall capability of official laboratories to be considered for the review of the existing MRLs for ametoctradin. October 2018. Updated November 2019. Available online: www.efsa.europa.eu

European Commission, 1997a. Appendix A. Metabolism and distribution in plants. 7028/VI/95-rev.3, 22 July 1997. 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, 2010. 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, 2013. Review report for the active substance ametoctradin (BAS 650 F). Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 1 February 2013 in view of the inclusion of ametoctradin (BAS 650 F) in Annex I of Council Directive 91/414/EEC. SANCO/12977/2012 rev 2-Final, 01 February 2013. European Commission, 2017. Technical Guideline on the Evaluation of Extraction Efficiency of Residue Analytical Methods. SANTE 2017/10632, Rev. 3, 22 November 2017. European Commission, 2018. Technical guidelines for determining the magnitude of pesticide residues in honey and setting Maximum Residue Levels in honey. SANTE/2016/11956, Rev. 9, 14 September 2018. European Commission, 2021. Guidance Document on Pesticide Analytical Methods for Risk Assessment and Post-approval Control and Monitoring Purposes. SANTE/2020/12830, Rev.1 24. February 2021. 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. Netherlands, 2010. Draft assessment report on the active substance ametoctradin prepared by the rapporteur Member State the Netherlands in the framework of Council Directive 91/414/EEC, December 2010. Netherlands, 2012. Final Addendum to the draft assessment report on the active substance ametoctradin prepared by the rapporteur Member State the Netherlands in the framework of Council Directive 91/414/EEC, September 2012. Netherlands, 2021. Evaluation report on the modification of MRLs for ametoctradin in honey and other apiculture products. June 2021, 31 pp. Available online: www.efsa.europa.eu 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

**Abbreviations**

| a.s. | active substance |
| ADI | acceptable daily intake |
| ARFD | acute reference dose |
| BBCH | growth stages of mono- and dicotyledonous plants |
| bw | body weight |
| CF | conversion factor for enforcement to risk assessment residue definition |
| CXL | Codex maximum residue limit |
| DAR | draft assessment report |
| DAT | days after treatment |
| DT$_{90}$ | period required for 90% dissipation (define method of estimation) |
Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

In the framework of the review of existing MRLs according to Art. 12 of EU Regulation 396/2005 (EFSA, 2020), numerous GAPs were reported for crops that might be attractive to bees for food foraging and that might contribute to the final residues of ametoctradin and its metabolites M650F03 and M650F04 in honey. However, since the MRL application is not linked to one specific GAP and applies to honey as food item for consumers, this Appendix is not relevant for the given application.9

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9 The use pattern of ametoctradin in buckwheat, which was tested in the residue trials, was reported in the GAP table in the MRL application and in the evaluation report (Netherlands, 2021). However, the applicant clarified that a use in buckwheat is not intended for ametoctradin.
## Appendix B – List of end points

### B.1. Residues in plants

#### B.1.1. Nature of residues and methods of analysis in plants

#### B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s) | Application (s) | Sampling (DAT) | Comment/Source |
|------------------------------------|-------------|---------|-----------------|----------------|----------------|
| Fruit crops                        | Tomatoes    | Foliar (post-emergence): 3 × 300 g a.i./ha | 1              | Radiolabelled mixture of 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; post-emergence; three foliar treatments of tomato plants 47, 54 and 61 days after planting (EFSA, 2020) |
|                                    | Tomatoes    | 30 μg/L | 8               | Radiolabelled 5-\textsuperscript{14}C-M650F03 or 5-\textsuperscript{14}C-M650F04 in nutrient solution; tomato plants transferred to flask with nutrient solution and test item placed in greenhouse (EFSA, 2020); Supporting information only. |
| Root crops                         | Potatoes    | Foliar (post-emergence): 3 × 441 g a.i./ha | 7, 14           | Radiolabelled mixture of 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; post-emergence; three foliar treatments of potato plants 35, 21 and 7 days prior to harvest (EFSA, 2020) |
| Leafy crops                        | Lettuces    | Foliar (post-emergence): 3 × 223 g a.i./ha | 7               | Radiolabelled mixture of 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; post-emergence; three foliar treatments of lettuce plants 21, 31 and 39 days after planting (EFSA, 2020) |
| Rotational crops (available studies) | Crop groups | Crop(s) | Application (s) | PBI (DAT) | Comment/Source |
|                                    | Root/tuber crops | White radishes | Bare soil: 1 × 1.44 kg a.i./ha | 30, 120, 365 | Radiolabelled mixture of non-radiolabelled, 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; soil treatment; harvested 89–91 days after planting and separated into edible parts (root) and remaining green parts (top) (EFSA, 2020) |
|                                    | Leafy crops  | Lettuces | Bare soil: 1 × 1.44 kg a.i./ha | 30, 120, 365 | Radiolabelled mixture of non-radiolabelled, 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; soil treatment; harvested 28–35 and 56–63, respectively (EFSA, 2020) |
|                                    | Cereals (small grain) | Wheat | Bare soil: 1 × 1.44 kg a.i./ha | 30, 120, 365 | Radiolabelled mixture of non-radiolabelled, 2,7-\textsuperscript{14}C-ametoctradin and 2,5,7-\textsuperscript{13}C-ametoctradin; soil treatment; immature green plants (wheat forage) were harvested 48–56 days after planting for PBIs of 120 and 365 days only; mature wheat was harvested 110–125 days after planting (EFSA, 2020) |
| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|                                    | Pasteurisation (20 min, 90°C, pH 4) | Yes | Radiolabelled ametoctradin, label not specified (EFSA, 2020) |
### Baking, brewing and boiling (60 min, 100°C, pH 5)

- **Yes**
- Radiolabelled ametoctradin, label not specified (EFSA, 2020)

### Sterilisation (20 min, 120°C, pH 6)

- **Yes**
- Radiolabelled ametoctradin, label not specified (EFSA, 2020)

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| Question                                                                 | Yes | EFSA (2020) |
|--------------------------------------------------------------------------|-----|-------------|
| Can a general residue definition be proposed for primary crops?           |     |             |
| Rotational crop and primary crop metabolism similar?                     | No  |             |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | Yes |             |
| Plant residue definition for monitoring (RD-Mo)                          |     |             |
| Plant residue definition for risk assessment (RD-RA)                     |     |             |
| Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) |     |             |
|                                                                          |     |             |
| Matrices with high water content, high oil content, high acid content and dry matrices: |     |             |
| HPLC–MS/MS, LOQ 0.01mg/kg for each compound (ametoctradin, M650F03 and M650F04) |     |             |
| Confirmatory method and ILV available (EFSA, 2012).                      |     |             |
| Applicability and validation of method for hops, however validation data for dried hop cones needed (data gap) (EFSA, 2020) |     |             |
| EURs (EURs, 2018; EFSA, 2020) provided for routine analyses following methods for ametoctradin in the following matrices: |     |             |
| High water and acid content commodities:                                |     |             |
| - LC–MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.005 mg/kg; |     |             |
| Dry matrices:                                                            |     |             |
| - LC–QqQ-MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.005 mg/kg; |     |             |
| High oil content matrices:                                               |     |             |
| - LC–MS/MS method (QuEChERS-method EN 15662:2008) with a LOQ 0.005 mg/kg; |     |             |
| Honey:                                                                  |     |             |
| - LC–MS–Q–ToF QuEChERS method with a screening detection limit (SDL) of 0.0025 mg/kg |     |             |

DAT: days after treatment; PBI: plant-back interval; BBCH: growth stages of mono- and dicotyledonous plants; a.s.: active substance; MRL: maximum residue level; GC–MS: gas chromatography with mass spectrometry; LC–MS/MS: liquid chromatography with tandem mass spectrometry; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; ILV: independent laboratory validation.
### B.1.1.2. Storage stability of residues in plants and honey

| Plant products (available studies) | Category                  | Commodity      | Stability period | Compounds covered | Comment/Source                                           |
|------------------------------------|---------------------------|----------------|------------------|-------------------|----------------------------------------------------------|
|                                    |                           |                | **T (°C)**       | **Value** | **Unit** | **Compounds covered** | **Comment/Source**                                           |
| **High water content**             | Tomato fruit             | –20            | 24 Months        | ametoctradin     | Metabolism studies (EFSA, 2020)                           |
|                                    | Lettuces                 | –20            | 36 months        | ametoctradin     | Metabolism studies (EFSA, 2020)                           |
|                                    | Tomatoes                 | –20            | 36 Months        | ametoctradin     | Stability study with parent (EFSA, 2020)                  |
|                                    |                          | –20            | 24 Months        | M650F03, M650F04 | Storage of spiked samples of rotational crop study (EFSA, 2020) |
|                                    | Wheat forage             | –20            | 24 Months        | Ametoctradin     | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
|                                    | Lettuces                 | –20            | 24 Months        | Ametoctradin     | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
|                                    | Potatoes                 | –20            | 24 Months        | Ametoctradin     | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
| **High protein content**           | Pea(1)                   | –20            | 24 Months        | Ametoctradin, M650F03, M650F04 | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
| **High starch content**            | Wheat grain(1)           | –20            | 24 Months        | Ametoctradin     | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
|                                    | Grape                    | –20            | 16 Months        | Ametoctradin     | Stability study with parent (EFSA, 2020)                  |
|                                    |                          | –20            | 24 Months        | M650F03, M650F04 | Storage of spiked samples of rotational crop study (EFSA, 2020) |
| **Others**                         | Wheat straw(1)           | –20            | 24 Months        | Ametoctradin     | Stability study with parent; in spiked samples of rotational crop study metabolites M650F03, M650F04 (EFSA, 2020) |
| **Products of animal origin**      | Honey                    | –18            | 6 Months         | Ametoctradin     | Netherlands (2021)                                       |

(1): According to the recently published guidance document (European Commission, 2021), peas, wheat grain and wheat straw belong to the ‘dry commodities’ group. The classification reported in Table B.1.1.2 is based on the previous crop classification which follows OECD GD 39 and which was also used in PROFile prepared in the MRL review (EFSA, 2020).
### B.1.2. Magnitude of residues in primary crops/honey

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

| Commodity | Region\(^{(a)}\) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source | Calculated MRL (mg/kg) | HR\(^{(b)}\) (mg/kg) | STMR\(^{(c)}\) (mg/kg) | CF\(^{(d)}\) |
|-----------|-----------------|---------------------------------------------------------------|-----------------|------------------------|------------------|-------------------|------------|
| Honey     | NEU             | Mo: 0.077; 0.079; 1.2; 1.8 RA\(^{(e)}\): 0.102; 0.104; 1.290; 1.825 | Semi-field (tunnel) trials on buckwheat treated with 3 × 390 g ametoctradin/ha at BBCH 55–65\(^{(f)}\) via foliar application. The number of trials is sufficient to derive an MRL in honey. | 5 | Mo: 1.80 RA: 1.83 | Mo: 0.64 RA: 0.70 | 1.2 |

MRL: maximum residue level; GAP: Good Agricultural Practice; Mo: monitoring; RA: risk assessment.

\(^{(a)}\): Indicates that the MRL is proposed at the limit of quantification.

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

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

\(^{(d)}\): Conversion factor to recalculate residues according to the residue definition for risk assessment. Calculated as the median value of the CFs derived for each trial.

\(^{(e)}\): Residue levels measured in the trials according to the risk assessment residue definition as ‘sum of ametoctradin, M650F03 and M650F04, expressed as parent’, following foliar applications.

\(^{(f)}\): Considering that treatment 1 (T\(_1\)) was performed before the flowering stage (at BBCH between 55 and 59) and that ametoctradin is not a systemic substance, the treatments contributing to the residue carry-over from the plant to honey are T\(_2\) and T\(_3\), performed during flowering at BBCH 61–65.
B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Yes |
|---|---|
| **Yes** | Metabolism of ametoctradin investigated in a confined rotational crop study on root crops (white radishes), leafy crops (lettuces) and cereals (spring wheat) at plant-back intervals (PBIs) of 30, 120 and 365 days (EFSA, 2012, 2020) |
| | Significant residues of soil metabolites M650F03 and M650F04 up to a PBI of 120 DAT in lettuce and in radish roots and at a PBI of 365 DAT in wheat straw, forage and grain. The parent was detected in lettuce at a PBI of 30 DAT and in wheat forage and straw at a PBI of 120 DAT (EFSA, 2020). |

| Residues in rotational and succeeding crops expected based on field rotational crop study? | Yes |
|---|---|
| **Yes** | Two field rotational crop studies: - on wheat with PBI of 120 DAT; - on wheat, carrot, cauliflower and lettuce with-(PBIs) of 30, 120 and 360 days after treatment (DAT). Mainly residues of metabolites M650F03 and M650F04 were found (highest concentration at PBI 30 days, in all commodities analysed, which decreased at longer PBIs); residues of metabolites above the LOQ were measured at PBI of 120 and 360 DAT in products used for animal feed (M650F03 and M650F04) and in cereal grains (M650F04), and at PBI of 360 DAT in cereal grains (M650F03), cauliflower inflorescence and carrot roots (M650F03 and M650F04); no residues above the LOQ were observed at PBI of 120 DAT in cereal grains (M650F03 only), cauliflower inflorescence and carrot roots, and at PBI of 120 and 360 DAT in lettuce (EFSA, 2012, 2020); parent compound only at PBI of 30 days in wheat straw and cauliflower inflorescence. |

LOQ: limit of quantification.

B.1.2.3. Processing factors

No processing studies were submitted in the framework of the present MRL application.

B.2. Residues in livestock

Not relevant as honey and apiculture products are not expected to contribute to the livestock dietary burden.
B.3. Consumer risk assessment

Acute consumer risk assessment not relevant since no ARfD has been considered necessary (European Commission, 2013).

| ADI | 10 mg/kg bw per day (European Commission, 2013) |
| Highest IEDI, according to EFSA PRIMo | 0.2% ADI (NL toddler diet) |

Contribution of commodities assessed:
Honey and other apiculture products: <0.01% of ADI (DE child diet)

Assumptions made for the calculations
Calculations were performed with PRIMo revision 3.1.
The calculation is based on the median residue level (STMR value) derived from residue trials in honey according to the proposed risk assessment residue definition for honey.
For the remaining commodities covered by the MRL regulation, the STMR values derived in the MRL review were selected as input values (EFSA, 2020).
The crops for which no uses have been reported in the MRL review (EFSA, 2020), were not included in the exposure calculation.
The risk assessment is affected by minor, non-standard uncertainties (lack of information on residue levels of the metabolites M650F03 and M650F04 taken up from soil in rotational crops and transferred to honey, lack of validation of analytical methods regarding extraction efficiency and the data gaps identified in the context of the MRL review.

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level; STMR: supervised trials median residue; CXL: codex maximum residue limit.

B.4. Recommended MRLs

| Code(a) | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|---------|-----------|------------------------|------------------------|-----------------------|
| 1040000 | Honey     | 0.05*                  | 5                      | The submitted data are sufficient to derive an MRL proposal for honey which sufficiently reflects the uses of ametoctradin authorised in the EU. Risk for consumers unlikely. |

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe; GAP: Good Agricultural Practice.
*: 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.
(F): Fat soluble.
Appendix C – Pesticide Residue Intake Model (PRIMO)

Please insert here the MRLs of COM database (use ‘paste values’ function) (F)

| Input values | Supplementary results - chronic risk assessment | Details - acute risk assessment/children |
|--------------|-----------------------------------------------|----------------------------------------|

**Toxicological reference values**

- EC, 2013
- Source of ADI: EC, 2013
- Year of evaluation: EC, 2013

**EFSA PRIMO revision 3.1; 2021/01/06**

**Pesticide Residue Intake Model (PRIMo)**

**Revised parameters**

- Chronic risk assessment: JMPR methodology (IEDI/TMDI)
- Exposure: Refined calculation mode
- Calculation: Chronic risk assessment - JMPR methodology (IEDI/TMDI)
- Details - chronic risk assessment
- Details - acute risk assessment/children

**Please insert here the MRLs of COM database (use ‘paste values’ function) (F)**

**Supplementary results - LOQs (mg/kg) range from:**

- 0.01 to:
- 0.05

**Toxicological reference values**

- ARfD (mg/kg bw):
- Source of ARfD:
- Details - acute risk
- Details - chronic risk assessment

**Refined calculation mode**

**Chronic risk assessment - JMPR methodology (IEDI/TMDI)**

**Calculate exposure to ADI (mg/kg bw per day)**

- Calculation of exposure: Refined calculation mode
- Chronic risk assessment: JMPR methodology (IEDI/TMDI)
- No of diets exceeding the ADI: ---

**Exposure resulting from**

- Commodity:
- MS Diet:
- Exposure (mg/kg bw per day)
- Highest contributor to MS diet in % of ADI
- 2nd contributor to MS diet in % of ADI
- Toxicological reference values

- MRLs set at the LOQ
- MRLs not necessary

**Conclusion:**

The estimated long-term dietary intake (TMDI/SENDI/IEDI) was below the ADI. The long-term intake of residues of Please insert here the MRLs of COM database (use ‘paste values’ function) (F) is unlikely to present a public health concern.

**DISCLAIMER:** Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.

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As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

### Results for all crops

|                | ARfD/ADI is exceeded (IESTI): | ARfD/ADI is exceeded (IESTI): |
|----------------|-------------------------------|-------------------------------|
| Unprocessed commodities |                                |                                |
| Highest % of ARfD/ADI | Commodities                  | Highest % of ARfD/ADI          |
| MRL / input for RA (mg/kg) | Exposure (µg/kg bw)           | MRL / input for RA (mg/kg)   |
| Exposure (µg/kg bw)       |                               | Exposure (µg/kg bw)           |

|                | ARfD/ADI is exceeded (IESTI): | ARfD/ADI is exceeded (IESTI): |
|----------------|-------------------------------|-------------------------------|
| Processed commodities |                                |                                |
| Highest % of ARfD/ADI | Processed commodities          | Highest % of ARfD/ADI          |
| MRL / input for RA (mg/kg) | Exposure (µg/kg bw)           | MRL / input for RA (mg/kg)   |
| Exposure (µg/kg bw)       |                               | Exposure (µg/kg bw)           |

**Conclusion:**
Appendix D – Input values for the exposure calculations

D.1. Consumer risk assessment

| Commodity                          | Existing/proposed MRL (mg/kg) | Source      | Chronic risk assessment | Acute risk assessment |
|------------------------------------|-------------------------------|-------------|-------------------------|-----------------------|
|                                    |                               |             | Input value (mg/kg)     | Comment(a)            |
|                                    |                               |             |                         | Input value (mg/kg)   | Comment                  |
| Risk assessment residue definition for honey: sum of ametoctradin, M650F03 and M650F04, expressed as ametoctradin(F) |
| Honey                              | 5                             | MRL proposal| 0.7                     | STMR-RAC              |
|                                    |                               |             |                         | Not performed since no ARFD was established and it was not considered necessary (European Commission, 2013) |
| Other products of plant and animal origin | See EFSA (2020)              |             |                         |                       |

STMR-RAC: supervised trials median residue in raw agricultural commodity; PeF: Peeling factor.
*: Indicates that the input value is proposed at the limit of quantification (LOQ).
(F): The residue definition is fat soluble.
(a): Residue levels of the soil metabolites M650F03 and M650F04, included in the risk assessment residue definition, were only accounted for potential residue carry-over from crops via foliar uptake and not via soil uptake. This may result in an underestimation of the STMR value in honey.
## Appendix E – Used compound codes

| Code/trivial name(a) | IUPAC name/SMILES notation/InChiKey(b) | Structural formula(c) |
|---------------------|--------------------------------------|-----------------------|
| **Ametoctrandin** (BAS 650 F) | 5-ethyl-6-octyl[1,2,4]triazolo[1,5-a]pyrimidin-7-amine  
Nc1c(CCCCCCCC)c(nc2ncnn12)CC  
GGKQIOFASHYUJZ-UHFFFAOYSA-N | ![Structural formula](image1) |
| M650F03 | (7-amino-5-ethyl[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)acetic acid  
O=CC(C)c1c(N)n2ncnc2nc1CC  
FLMGQFFLZHIWOW-UHFFFAOYSA-N | ![Structural formula](image2) |
| M650F04 | 7-amino-5-ethyl[1,2,4]triazolo[1,5-a]pyrimidine-6-carboxylic acid  
O=CC(C)c1c(N)n2ncnc2nc1CC  
IAKVACUHWXCBHI-UHFFFAOYSA-N | ![Structural formula](image3) |

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

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2020.2.1 ACD/Labs 2020 Release (File version N15E41, Build 116563, 15 June 2020).
(c): ACD/ChemSketch 2020.2.1 ACD/Labs 2020 Release (File version C25H41, Build 121153, 22 March 2021).