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## Modification of the existing maximum residue level for acrinathrin in lettuce

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### Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Cheminova A/S submitted a request to the competent national authority in Spain to modify the existing maximum residue level (MRL) for the active substance acrinathrin in lettuce. The data submitted in support of the request were found to be sufficient to derive an MRL proposal for lettuce. Adequate analytical methods for enforcement are available to control the residues of acrinathrin on the commodity under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of acrinathrin according to the reported agricultural practice and the current approval restrictions of acrinathrin is unlikely to present a risk to consumer health. However, uncertainties remain, particularly on the toxicological profile of the different isomers. Hence, the consumer risk assessment is considered tentative.

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## Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Cheminova A/S submitted an application to the competent national authority in Spain (Evaluating Member State, EMS) to modify the existing maximum residue level (MRL) for the active substance acrinathrin in lettuce. 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 18 March 2020. To accommodate for the intended SEU use of acrinathrin, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) to 0.1 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 Regulation (EC) No 1107/2009, the conclusions on the review of the existing EU MRLs of acrinathrin according to Article 12 of Regulation (EU) No 396/2005 (MRL review) and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of acrinathrin following foliar application was investigated during the EU pesticides review in crops belonging to the groups of fruits and leafy vegetables. In the framework of the current assessment, the applicant submitted a new metabolism study on lettuce. Among all available metabolism studies, only the metabolism study in grapes (which detects the enantiomeric pair of isomers but not acrinathrin enantiomer) and the newly provided metabolism study in lettuce (which detects the enantiomeric pair of isomers as well as acrinathrin enantiomer) could be considered valid to address the metabolism in primary crops.

Standard hydrolysis studies investigating the stability of acrinathrin under conditions representative for pasteurisation, boiling/cooking and sterilisation are not available and are not required, considering low contribution of residues in lettuce to the total theoretical maximum daily intake (TMDI).

In rotational crops, a significant translocation of residues is not expected (total residue less than 0.01 mg/kg) if crops are grown in rotation with lettuce, which were treated according to the intended good agricultural practice (GAP).

Based on the metabolic pattern identified in grape metabolism study, the toxicological significance of metabolites and the capabilities of analytical enforcement methods, the residue definitions for fruit crops were proposed by the EU pesticides peer review as acrinathrin and its enantiomer for enforcement and acrinathrin and all isomers for the risk assessment. The risk assessment residue definition has been proposed on a provisional basis, pending the investigation of the toxicological profile of the 15 acrinathrin isomers. Now with a new lettuce metabolism study available, the residue definitions can be extended also for leafy crop group. However, since the toxicological profile of all 15 acrinathrin isomers is not fully addressed yet, the revision of the existing provisional residue definition for risk assessment is not proposed in the framework of the current assessment.

According to the EU pesticides peer review, for rotational crops, there is no need to set a specific residue definition due to low residues expected.

EFSA concluded that for lettuce, metabolism of acrinathrin has been sufficiently addressed and that the previously derived residue definitions are still applicable. A conversion factor of 1.1 was derived on the basis of the grape metabolism study and in the absence of adequate metabolism studies covering crop groups other than fruits and leafy vegetables, the proposed residue definition and conversion factor has been tentatively applied to all crops as a worst-case assumption to conduct the consumer risk assessment.

Sufficiently validated analytical methods based on GC/MS are available to quantify residues in lettuce according to the enforcement residue definition. The methods enable quantification of residues at or above 0.01 mg/kg in the crop assessed (LOQ).

The available residue trials are sufficient to derive an MRL proposal of 0.1 mg/kg for lettuce in support of the intended SEU use of acrinathrin.

Specific studies investigating the magnitude of acrinathrin residues in processed commodities have not been provided and are not necessary since lettuce is normally consumed raw.

Residues of acrinathrin in commodities of animal origin were not assessed since lettuce is normally not fed to livestock.

The toxicological profile of acrinathrin was assessed in the framework of the EU pesticides peer review under Regulation (EC) No 1107/2009 and the data were sufficient to derive an acceptable daily intake (ADI) of 0.01 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.01 mg/kg bw. However, a data gap was set by the EU pesticides peer review for the investigation of the toxicological

profile of all 15 acrinathrin isomers and translated into confirmatory data to be submitted by the applicant 2 years after adoption of the specific guidance. In the framework of the current assessment, the applicant has provided additional toxicity studies and information, which allow to conclude that acrinathrin isomers are not genotoxic, three of them are expected to be less acutely neurotoxic than the parent, but for the other 12 isomers, no conclusion can be made regarding their general toxicity. In lettuce, according to metabolism studies, none of these isomers, including enantiomer of acrinathrin, were present at relevant concentrations. Therefore, the data gap set by the EU pesticides review regarding the toxicological profile of acrinathrin isomers is not relevant for lettuce.

It is also noted that only few of the existing uses – on grapes and some lettuces – were maintained after the MRL review. It can therefore be concluded that for the existing uses of acrinathrin and the proposed use on lettuce, isomers other than acrinathrin and its enantiomer will be of no concern. Nevertheless, pending the assessment of the toxicological profile of acrinathrin isomers, the consumer exposure assessment is considered tentative.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMO). The exposure assessment was performed taking into account the supervised trials median residue (STMR) and HR values derived for lettuce from the residue trials submitted in the framework of the current assessment, multiplied by the conversion factor of 1.1 for the risk assessment, as derived by the MRL review. In the chronic assessment, for the remaining commodities covered by the MRL regulation, the median residue levels derived in the MRL review were used as input values, multiplied by the conversion factor of 1.1 for the risk assessment. Those crops on which authorised uses were not reported for the MRL review or were not supported after the MRL review (i.e. the commodities where the GAPs were not compliant with the restriction of use of acrinathrin) were not included in the exposure calculation. No long-term and short-term consumer intake concerns were identified for the crop under assessment; the calculated long-term exposure accounted for a maximum of 2% of the ADI (PT general diet) and the short-term exposure for lettuce accounted for a maximum of 21% of the ARfD in children and 7% of the ARfD in adults.

EFSA concludes that, although uncertainties remain, particularly on the toxicological profile of the different isomers, this tentative exposure calculation did not indicate a risk to consumer health from the existing uses of acrinathrin and the intended use on lettuce. Nevertheless, as soon as the toxicity of acrinathrin isomers is addressed, the risk assessment residue definition shall be confirmed and the consumer exposure updated.

EFSA proposes to amend the existing MRL 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 <sup>(a)</sup>  | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification   |
|--|-----------|-------------------------|-------------------------|---|
| <b>Enforcement residue definition: Acrinathrin<sup>(F)</sup></b> |           |                         |                         |   |
| 251020   | Lettuce   | 0.02*                   | 0.1                     | The submitted data are sufficient to derive an MRL proposal for the intended SEU use. Risk for consumers unlikely |

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

MRL: maximum residue level; SEU: southern Europe.

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

(F): Fat soluble.

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## Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue level (MRL) for acrinathrin in lettuce. The detailed description of the intended SEU use of acrinathrin in lettuce, which is the basis for the current MRL application, is reported in Appendix A.

Acrinathrin is the ISO common name for (*S*)- $\alpha$ -cyano-3-phenoxybenzyl (*Z*)-(1*R*,3*S*)-2,2-dimethyl-3-[2-(2,2,2-trifluoro-1-trifluoromethylethoxycarbonyl)vinyl]cyclopropanecarboxylate or (*S*)- $\alpha$ -cyano-3-phenoxybenzyl(*Z*)-(1*R*)-cis-2,2-dimethyl-3-[2-(2,2,2-trifluoro-1trifluoromethylethoxycarbonyl)vinyl] cyclopropanecarboxylate (IUPAC name).

The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Acrinathrin was evaluated in the framework of Regulation (EC) No 1107/2009<sup>1</sup> with France designated as rapporteur Member State (RMS) for the representative uses as an insecticide and acaricide on wine grapes, table grapes and ornamentals. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2010, 2013). Acrinathrin was approved<sup>2</sup> for the use as insecticide and acaricide on 1 January 2012.

The EU MRLs for acrinathrin are established in Annex II of Regulation (EC) No 396/2005<sup>3</sup>. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2015) and the proposed modifications have been implemented in the MRL legislation only for the commodities where the GAPs are compliant with the current approval restrictions of acrinathrin (authorised at rates not exceeding 22.5 g/ha per application).

In accordance with Article 6 of Regulation (EC) No 396/2005, Cheminova A/S submitted an application to the competent national authority in Spain (evaluating Member State, EMS) to modify the existing maximum residue level (MRL) for the active substance acrinathrin in lettuce. 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 18 March 2020. To accommodate for the intended use of acrinathrin, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) to 0.1 mg/kg.

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

EFSA based its assessment on the evaluation report submitted by the EMS (Spain, 2020), the draft assessment report (DAR) and its addenda (France, 2007, 2010, 2012, 2013) prepared under Regulation (EC) 1107/2009, the Commission review report on acrinathrin (European Commission, 2017a), the conclusions on the peer review of the pesticide risk assessment of the active substance acrinathrin (EFSA, 2013) and the MRL review (EFSA, 2015).

For this application, the data requirements established in Regulation (EU) No 544/2011<sup>4</sup> 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, 2017b; OECD, 2011, 2013). 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<sup>5</sup>.

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, are presented in Appendix B.

<sup>1</sup> 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.

<sup>2</sup> Commission Implementing Regulation (EU) No 974/2011 of 29 September 2011 approving the active substance acrinathrin, 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 and Commission Decision 2008/934/EC. OJ L 255, 1.10.2011, p. 1–5.

<sup>3</sup> 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.

<sup>4</sup> 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.

<sup>5</sup> 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.



The evaluation report submitted by the EMS (Spain, 2020) 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 as background documents to this reasoned opinion.

## 1. Residues in plants

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

Acrinathrin is an enantiomerically pure synthetic pyrethroid having three stereogenic centres and a double bond in a defined configuration. Having three stereogenic centres and a double bond, a total of 16 possible isomers – which comprise eight pairs of enantiomers – exist. It is important to note that except for acrinathrin and its own enantiomer, reference standards of only one compound of each enantiomeric pair were synthesised. The chemical structure of acrinathrin is provided in Appendix E. The complete list of acrinathrin isomers is reported in the Evaluation Report (Spain, 2020). It should be further noted that under natural sunlight, and in common with other pyrethroids, acrinathrin has the potential to isomerise, which could lead to formation of isomers on crops.

#### 1.1.1. Nature of residues in primary crops

The metabolism of acrinathrin on fruit crops (grapes, apples, cucumbers and oranges) and on leafy crops (cabbage) has been investigated in the framework of the EU pesticides peer review (EFSA, 2013) and the MRL review (EFSA, 2015). During the peer review and MRL review, it was concluded that, since the levels of each of the isomers or enantiomeric pairs of isomers present had not been quantified in apples, cabbage, cucumbers and oranges, these studies were considered insufficient to determine the nature of acrinathrin residues in primary crops.

Therefore, based on the metabolism study in grapes, which was the only study analysing all pairs of isomers, it was concluded that isomerisation could occur as part of the normal metabolic process and the isomer profile is dependent on the PHI. It should be, however, noted that this study did not use chiral high-performance liquid chromatography (HPLC) method and it was therefore not able to distinguish between acrinathrin and its own enantiomer. Based on the grape metabolism study, EFSA concluded that following foliar application, the residue definition proposed for risk assessment is acrinathrin and all 15 isomers (as long as the toxicity of the individual isomers including enantiomers has not been addressed by eligible data), and for monitoring is acrinathrin and its enantiomer (EFSA, 2013).

New metabolism studies representing fruit crops (tomato) and leafy crops (lettuce) were submitted in support of the current MRL application (Spain, 2020) and results are reported in Appendix B. The study on tomato was not assessed as not relevant for the current application.

The new metabolism study in lettuce is considered valid to address the nature of acrinathrin in this commodity. Moreover, this study was performed with the specific intention to further evaluate isomerisation and the presence of the different isomers of acrinathrin. Reverse-phase HPLC analysis was used to separate acrinathrin from its metabolic transformation products, normal-phase HPLC analysis was used to separate enantiomeric pairs of acrinathrin from each other and, where appropriate, chiral HPLC analysis was also used to separate enantiomers from each other.

In lettuce, acrinathrin was the most prominent component detected from both radiolabelled samples (cyclopropyl- $1-^{14}\text{C}$  and phenoxy- $\text{U-}^{14}\text{C}$ ) and accounted for 37.2–64.5% of total radioactive residue (TRR) (0.103–1.197 mg/kg). The results of normal-phase and chiral HPLC analysis showed no significant photo-isomerisation of acrinathrin and no detection of the acrinathrin enantiomer. Only a low level of the R-acrinathrin and/or its enantiomer was detected in phenoxy 3 and 7 days after last application (DALA) rinses (equivalent to 1% of TRR, 0.019 mg/kg in 3 DALA lettuce and 0.8% of TRR, 0.009 mg/kg in 7 DALA lettuce). No other isomers of acrinathrin were present in lettuce at relevant levels. Other identified metabolites were detected at individual levels ranging from 0.4% to 8.0% of TRR (0.003–0.064 mg/kg). Moreover, other unassigned components were also detected, the few above 10% TRR (after 3 and 7 DALA) were shown to consist of multiple compounds by TLC with all individual compounds below 10% TRR and no unassigned components in the raw agricultural commodity 14 DALA above 10% of TRR and 0.05 mg/kg.

The low levels of isomers found in the new metabolism study in lettuce suggested that in lettuce, the main component of the residues is parent acrinathrin only. Other isomers, for which the data gap regarding their toxicological profile was set in the peer review and the MRL review, are not present at significant amounts. Although metabolism studies in lettuce and grapes indicate low extent of isomerisation, it was also noted in the peer review, that isomerisation varies between crops and depends

on the PHI. Thus, on the basis of two studies in grapes and lettuce and, pending the assessment of the toxicological profile for all acrinathrin isomers, a final conclusion on the need for revision of existing risk assessment residue definition cannot be taken. Thus, as a worst scenario, the consumer risk assessment is still performed using the existing residue definition for risk assessment in force.

For the intended use on lettuce, the metabolic behaviour in primary crops is sufficiently addressed.

### 1.1.2. Nature of residues in rotational crops

Acrinathrin is authorised or is proposed to be used on several crops that can be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the peer review (EFSA, 2013), the  $DT_{90}$  value of acrinathrin and its enantiomer and their relevant soil metabolites ranged from 0.5 to 887 days. The trigger value of 100 days was exceeded, and therefore, further studies investigating the nature and magnitude of residues in rotational crops were required.

The metabolism of acrinathrin in rotational crops (wheat, spinach, carrots and kohlrabi) has been evaluated during the peer review (EFSA, 2013) with  $^{14}C$ -labelled acrinathrin (cyclopropyl-1- $^{14}C$  and  $^{14}C$ -benzyl). The residues were partitioned into organo-soluble and water-soluble fractions but could not be further identified due to the very low amount detected. Therefore, a specific residue definition for rotational crops was not deemed necessary due to the very low residue levels expected.

For the proposed use assessed in this application, no further information was provided.

### 1.1.3. Nature of residues in processed commodities

Standard hydrolysis studies regarding the stability of acrinathrin under conditions representative for pasteurisation, boiling/cooking and sterilisation are not available. Such studies are not required, considering low contribution of residues in lettuce to the total theoretical maximum daily intake (TMDI).

### 1.1.4. Methods of analysis in plants

Analytical methods for the determination of acrinathrin residues were assessed during the MRL review (EFSA, 2015). Sufficiently validated methods are available for the determination of residues of acrinathrin in lettuce. However, these methods are not stereoselective and allow quantifying residues of acrinathrin together with its enantiomer at an LOQ of 0.02 mg/kg in crops belonging to the group of high-water content commodity.

In addition, a new analytical method has been validated with an associated independent laboratory validation (ILV) in crop matrices with high acid content (strawberry), high water content (sweet pepper, tomato), high oil content (soybean) and high starch content (wheat grain) with a lower LOQ of 0.01 mg/kg. Since chiral analysis was not employed, also for this analytical method the acrinathrin peak could include its enantiomer. This new analytical method has been validated in lettuce and used to analyse residues of acrinathrin in the supervised crop residue trials provided in this application.

### 1.1.5. Storage stability of residues in plants

The storage stability of acrinathrin in plants stored under frozen conditions was investigated in the framework of the pesticides peer review demonstrating storage stability for acrinathrin in high water content commodities up to 24 months (EFSA, 2013). During the EU pesticides peer review and the MRL review, a data gap regarding the freezer storage stability in high acid content crop matrices was noted (EFSA, 2013, 2015).

### 1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the toxicological significance of metabolites, the capabilities of enforcement analytical methods, the following residue definitions were tentatively proposed in the context of the pesticide peer review and MRL review (EFSA, 2013, 2015):

- residue for risk assessment: acrinathrin and all isomers (as long as the toxicity of the individual isomers including enantiomers has not been addressed by eligible data)
- residue definition for enforcement: acrinathrin and its enantiomer

This residue definition is limited to the use on fruit crops. The MRL review concluded, that in order to extend the residue definition to other crop groups, representative metabolism studies are required.



As long as studies representative for relevant crop groups are not available, the MRL review proposed to tentatively extend proposed enforcement and risk assessment residue definitions to other crop groups (EFSA, 2015).

Now with a new and reliable lettuce metabolism study available, the residue definitions can be confirmed also for leafy crop group. It is noted, however, that the inclusion of the isomers in the residue definition for risk assessment could eventually be reviewed due to the very low amount of isomers found in the new metabolism study in lettuce. However, considering the uncertainty in the previous metabolism studies in grapes, where no chiral analysis was performed, and the absence of metabolism studies on other crop categories (root, cereals and pulses/oilseed), the revision of the existing risk assessment residue definition is not proposed in the framework of the current assessment. Moreover, the data gap identified by the pesticides peer review regarding the toxicological profile of acrinathrin isomers still remains.

On the basis of grape metabolism study, the peer review derived a tentative conversion factor of 1.1 from enforcement to risk assessment, which, in order to account for a worst-case scenario, is applied to all crops in the consumer risk assessment. A specific residue definition for rotational crops was not deemed necessary due to the very low residue levels expected.

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

## 1.2. Magnitude of residues in plants

### 1.2.1. Magnitude of residues in primary crops

In support of the intended SEU use, the applicant submitted residue trials on lettuce. The samples were analysed for the parent compound including its enantiomer as in the residue definition for enforcement.

In total, eight supervised crop residue trials compliant with the intended SEU GAP and the current approval restrictions of acrinathrin (authorised at rates not exceeding 22.5 g/ha per application) were submitted. The eight trials in the SEU included four harvest and four decline trials and were conducted on open leaf lettuce from April to September 2016 by using five different varieties in eight different geographical locations, thus demonstrating the independency of these trials.

The applicant submitted also four residue trials on lettuce representing NEU, but these were not considered under the current assessment, since no GAP has been reported for acrinathrin on lettuce in the NEU.

EFSA agrees with the approach proposed by the EMS, concluding that the eight residue trials conducted in the SEU region are considered acceptable according to the proposed SEU GAP and the current approval restrictions of acrinathrin and therefore could be considered to derive a new MRL of 0.1 mg/kg.

According to the assessment of the EMS, the methods used were sufficiently validated using an LOQ of 0.01 mg/kg and the samples of all these residue trials were stored under conditions for which integrity of the samples has been demonstrated.

### 1.2.2. Magnitude of residues in rotational crops

The possible transfer of acrinathrin residues to crops that are grown in crop rotation has been assessed in the EU pesticides peer review (EFSA, 2013). The available studies demonstrated that significant residues (above 0.01 mg/kg) are not expected in succeeding crops when planted in soil treated at 0.113–0.158 kg a.s./ha.

Since the application rate for the crop under consideration (i.e. 0.0225 kg a.s./ha) is lower than the application rate tested in the rotational crop studies, it is concluded that no residues are expected in following crops grown in rotation with lettuce, provided that the active substance is applied according to the proposed GAP.

### 1.2.3. Magnitude of residues in processed commodities

Specific processing studies for the crop under assessment are not available and not deemed necessary as lettuce is not a crop expected to undergo further processing.

#### 1.2.4. Proposed MRLs

The available data are considered sufficient to derive an MRL proposal as well as risk assessment values for lettuce in support of the intended SEU use of acrinathrin. In Section 3, EFSA assessed whether residues on crops resulting from the intended uses are likely to pose a consumer health risk.

## 2. Residues in livestock

Not relevant as lettuce is not used for feed purposes.

## 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 (EFSA, 2019).

The toxicological reference values for acrinathrin used in the risk assessment were derived in the framework of the EU pesticides peer review where an ADI of 0.01 mg/kg body weight (bw) per day and an ARfD of 0.01 mg/kg bw were set (EFSA, 2013). During the EU pesticides peer review, the data gap regarding the further assessment of the toxicological profile of the 15 isomers of acrinathrin was established (EFSA, 2013). For the MRL review, the assessment of the toxicological profile of all isomers was still missing, and therefore, the MRL review proposed to consider the toxicological reference values set for acrinathrin tentatively valid also for the other isomers and to use a conversion factor for risk assessment of 1.1 based on the grape metabolism study. The applicant in the framework of the current assessment has provided additional information, which allows to conclude that isomers included in the residue definition are not genotoxic and three of these acrinathrin isomers are expected to be less acutely neurotoxic than the parent, but for the other 12 isomers, no conclusion can be made regarding their general toxicity (high, equal, less acutely neurotoxic than the parent). The acute toxicity of acrinathrin enantiomer has not been addressed, but it is not of concern in lettuce as this enantiomer was not detected in the metabolism study.

As reported in the nature of residues in primary crops section, the very low levels of isomers found in the new metabolism study in lettuce suggests that the exposure to the acrinathrin isomers in lettuce is very low. However, since this evidence is only based on metabolism study in lettuce and only partially confirmed by the metabolism study in grapes (with the uncertainty regarding the presence of the enantiomer), the residue definition for risk assessment currently in force and conversion factor of 1.1 as proposed by the MRL review is still applied for consumer exposure assessment. It is also noted that only few of the existing uses – on grapes and some lettuces – were maintained after the MRL review. It can therefore be concluded that for the existing uses of acrinathrin and the proposed use on lettuce, isomers other than acrinathrin and its enantiomer will be of no concern. Nevertheless, pending the assessment of toxicity of acrinathrin isomers the consumer exposure assessment is considered tentative.

### *Short-term (acute) dietary risk assessment*

The short-term exposure assessment was performed for lettuce only in accordance with the internationally agreed methodology (EFSA, 2019).

The calculations were based on the highest residue level in lettuce as derived from the submitted residue trials, multiplied by the conversion factor for the risk assessment. The complete list of input values can be found in Appendix D.1.

The short-term exposure did not exceed the ARfD for the crop assessed in this application, accounting for a maximum of 21% of the ARfD in children and 7% of the ARfD in adults; therefore, EFSA concludes that the use of acrinathrin according to the reported agricultural practice is unlikely to present a short-term (acute) risk to consumer health.

### *Long-term (chronic) dietary risk assessment*

The long-term exposure assessment was performed, taking into account the median residue levels expected in lettuce as derived from the submitted residue trials, multiplied by the conversion factor for the risk assessment as derived by the MRL review. For the remaining commodities covered by the MRL regulation, the median residue levels derived in the MRL review were selected, multiplied by the conversion factor for the risk assessment. Those crops on which authorised uses were not reported for

the MRL review or were not supported after the MRL review (i.e. the commodities where the GAPs were not compliant with the restriction of use of acrinathrin) were not included in the exposure calculation. The complete list of input values can be found in Appendix D.1.

The estimated long-term dietary intake accounted for a maximum of 2% of the ADI (PT general diet). The contribution of residues expected in lettuce to the overall long-term exposure accounted for a maximum of 0.6% of the ADI.

EFSA concludes, that although uncertainties remain, particularly on the toxicological profile of the different isomers, this tentative exposure calculation did not indicate a risk to consumer health from the existing uses of acrinathrin and the intended use on lettuce. Nevertheless, as soon as the toxicological profile of acrinathrin isomers is addressed, the risk assessment residue definition shall be confirmed and the consumer exposure updated.

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 lettuce in support of the intended SEU use of acrinathrin.

EFSA concluded that the proposed use of acrinathrin on lettuce will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

However, it should be noted that uncertainties remain particularly on the toxicological profile of the different isomers and on the metabolism in different crop groups. Hence, the consumer risk assessment is considered tentative only.

The MRL recommendations are summarised in Appendix B.4.

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## Abbreviations

|                  |   |
|------------------|---|
| a.s.             | active substance  |
| ADI              | acceptable daily intake   |
| ARfD             | acute reference dose  |
| BBCH             | growth stages of mono- and dicotyledonous plants                        |
| bw               | body weight   |
| CAC              | Codex Alimentarius Commission   |
| CAS              | Chemical Abstract Service   |
| CF               | conversion factor for enforcement to risk assessment residue definition |
| cGAP             | critical GAP  |
| CIRCA            | (EU) Communication & Information Resource Centre Administrator          |
| CS               | capsule suspension  |
| CV               | coefficient of variation (relative standard deviation)                  |
| DALA             | days after last application   |
| DAR              | draft assessment report   |
| DAT              | days after treatment  |
| DM               | dry matter  |
| DP               | dustable powder   |
| DS               | powder for dry seed treatment   |
| DT <sub>90</sub> | period required for 90% dissipation (define method of estimation)       |
| EC               | emulsifiable concentrate  |
| EDI              | estimated daily intake  |
| EMS              | evaluating Member State   |
| eq               | residue expressed as a.s. equivalent                                    |
| EW               | emulsion, oil in water  |
| FID              | flame ionisation detector   |
| GAP              | Good Agricultural Practice  |
| GC               | gas chromatography  |
| GC-FID           | gas chromatography with flame ionisation detector                       |
| GC-MS            | gas chromatography with mass spectrometry                               |
| GC-MS/MS         | gas chromatography with tandem mass spectrometry                        |

|            |  |
|------------|--|
| GS         | growth stage   |
| HPLC       | high-performance liquid chromatography                               |
| HPLC-MS    | high-performance liquid chromatography with mass spectrometry        |
| HPLC-MS/MS | high-performance liquid chromatography with tandem mass spectrometry |
| HR         | highest residue  |
| IEDI       | international estimated daily intake                                 |
| IESTI      | international estimated short-term intake                            |
| ILV        | independent laboratory validation                                    |
| ISO        | International Organisation for Standardisation                       |
| IUPAC      | International Union of Pure and Applied Chemistry                    |
| LOQ        | limit of quantification  |
| MRL        | maximum residue level  |
| MS         | Member States  |
| MS         | mass spectrometry detector   |
| MS/MS      | tandem mass spectrometry detector                                    |
| MW         | molecular weight   |
| NEU        | northern Europe  |
| OECD       | Organisation for Economic Co-operation and Development               |
| PBI        | plant back interval  |
| PF         | processing factor  |
| PHI        | preharvest interval  |
| PRIMo      | (EFSA) Pesticide Residues Intake Model                               |
| RA         | risk assessment  |
| RD         | residue definition   |
| RMS        | rappporteur Member State   |
| SANCO      | Directorate-General for Health and Consumers                         |
| SC         | suspension concentrate   |
| SEU        | southern Europe  |
| SL         | soluble concentrate  |
| SP         | water-soluble powder   |
| STMR       | supervised trials median residue                                     |
| TAR        | total applied radioactivity  |
| TLC        | Thin layer chromatography  |
| TMDI       | theoretical maximum daily intake                                     |
| TRR        | total radioactive residue  |
| UV         | ultraviolet (detector)   |
| WHO        | World Health Organization  |

## Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, MS or country | F G or I <sup>(a)</sup> | Pests or group of pests controlled | Preparation         |                | Application                           |  |                | Application rate per treatment     |                   |                    | Unit  | PHI (days) <sup>(d)</sup> | Remarks |  |
|-----------------------|-------------------------|-------------------------|------------------------------------|---------------------|----------------|---------------------------------------|--|----------------|------------------------------------|-------------------|--------------------|-------|---------------------------|---------|--|
|                       |                         |                         |                                    | Type <sup>(b)</sup> | Conc. a.s. g/L | Method kind                           | Range of growth stages & season <sup>(c)</sup> | Number min–max | Interval between application (min) | G a.s./hL min–max | Water L/ha min–max |       |                           |         | Rate   |
| Lettuces              | SEU                     | F                       | Red mites and thrips               | EW                  | 75.0           | Foliar treatment – broadcast spraying | From BBCH 10                                   | 1–2            | 10                                 |                   | 500–700            | 22.50 | g a.s./ha                 | 14      | Against mobile forms. At first signs of pest 40–60 mL fp/hL (max. 0.3 L fp/ha) |

MRL: maximum residue level; GAP: Good Agricultural Practice; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; EW: emulsion, oil in water.

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

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

(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 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                       | Grape vines |         | Foliar, F <sup>(a)</sup><br>2 × 0.0225 kg a.s./ha (both radiolabelled samples)<br>2 × 0.225 kg a.s./ha ( <sup>14</sup> C-gem-dimethyl sample only) | 0, 13, 27, 41  | 13 day sample just prior to second application<br>Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C and <sup>14</sup> C-benzyl (EFSA, 2015)   |
|                                   | Apples      |         | Foliar, F <sup>(a)</sup><br>1 × 45-91 µg per fruit, 52-145 µg per leaf <sup>(b)</sup> (both radiolabelled samples)                                 | 0, 7, 14, 21, 28, 42, 56 <sup>(c)</sup><br>0, 28 <sup>(d)</sup>                                  | Supportive, not fully valid (EFSA, 2015)<br>Application by brush to individual fruits and leaves<br>Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C and <sup>14</sup> C-benzyl      |
|                                   | Oranges     |         | Foliar, F <sup>(a)</sup><br>2 × 0.09 kg a.s./ha (all radiolabelled samples)  | 21   | Identification of individual isomers not undertaken (EFSA, 2015)<br>Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C, <sup>14</sup> C-benzyl and <sup>14</sup> C-hexafluoroisopropyl |
|                                   | Cucumbers   |         | Foliar, F <sup>(a)</sup><br>2 × 0.078 kg a.s./ha (all radiolabelled samples)   | 0, 14, 42  | Study invalid due to photo-isomerisation (EFSA, 2015)<br>Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C, <sup>14</sup> C-benzyl and <sup>14</sup> C-hexafluoroisopropyl            |
|                                   | Tomato      |         | Foliar, F <sup>(a)</sup><br>3 × 0.060 kg a.s./ha (both radiolabelled samples)  | 3, 7, 14   | Radiolabelled active substance: Cyclopropyl-1- <sup>14</sup> C and phenoxy-U- <sup>14</sup> C (Spain, 2020)  |
|                                   | Leafy crops | Cabbage |  | Foliar, F <sup>(a)</sup><br>2 × 587-679 µg per plant <sup>(b)</sup> (both radiolabelled samples) | 0, 28, 56 <sup>(c)</sup><br>0, 14, 28 <sup>(d)</sup>   |
| Let tuce                          |             |         | Foliar, F <sup>(a)</sup><br>2 × 0.060 kg a.s./ha (both radiolabelled samples)  | 3, 7, 14   | Radiolabelled active substance: Cyclopropyl-1- <sup>14</sup> C and phenoxy-U- <sup>14</sup> C (Spain, 2020)  |

| <b>Rotational crops</b><br>(available studies) | <b>Crop groups</b>   | <b>Crop(s)</b>    | <b>Application(s)</b>  | <b>PBI (DAT)</b> | <b>Comment/Source</b>   |
|--|----------------------|-------------------|------------------------|------------------|---|
|  | Root/tuber crops     | Carrots, kohlrabi | 0.113–0.158 kg a.s./ha | 29, 70           | Treatment to bare soil Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C and <sup>14</sup> C-benzyl (EFSA, 2013) |
|  | Leafy crops          | Spinach           | 0.113–0.158 kg a.s./ha | 29, 70           | Treatment to bare soil Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C and <sup>14</sup> C-benzyl (EFSA, 2013) |
|  | Cereal (small grain) | Wheat             | 0.113–0.158 kg a.s./ha | 29, 70           | Treatment to bare soil Radiolabelled active substance: cyclopropyl-1- <sup>14</sup> C and <sup>14</sup> C-benzyl (EFSA, 2013) |

| <b>Processed commodities</b><br>(hydrolysis study) | <b>Conditions</b>                                 | <b>Stable?</b> | <b>Comment/Source</b>           |
|--|---|----------------|---------------------------------|
|  | Pasteurisation (20 min, 90°C, pH 4)               | n/a            | Hydrolysis study not available. |
|  | Baking, brewing and boiling (60 min, 100°C, pH 5) | n/a            |                                 |
|  | Sterilisation (20 min, 120°C, pH 6)               | n/a            |                                 |
|  | Other processing conditions                       | –              |                                 |

(a): Outdoor/field application (F) or glasshouse/protected/indoor application (G).

(b): Total applied radioactivity (TAR) for each sample.

(c): Application 8 weeks before normal harvest.

(d): Application 4 weeks before normal harvest.

|  |  |  |
|--|--|--|
| Can a general residue definition be proposed for primary crops?                          | No   | The residue definition is limited to fruit crop group (EFSA, 2013, 2015) and, based on new metabolism study in lettuce, can be extended to leafy crops |
| Rotational crop and primary crop metabolism similar?                                     | n/a  | A specific residue definition for rotational crops was not deemed necessary due to the very low residue levels expected (EFSA, 2015)                   |
| Residue pattern in processed commodities similar to residue pattern in raw commodities?  | n/a  |  |
| Plant residue definition for monitoring (RD-Mo)  | Acrinathrin and its enantiomer (EFSA, 2013, 2015)  |  |
| Plant residue definition for risk assessment (RD-RA)                                     | Acrinathrin and its 15 isomers (tentative, as long as the toxicity of the individual isomers including enantiomers has not been addressed by eligible data) (EFSA, 2013, 2015)   |  |
| Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) | <p>Matrices with high water content,: GC–MS, LOQ 0.02 mg/kg, ILV available. The methods are not stereoselective and therefore the methods determine the sum of acrinathrin and its enantiomer (EFSA, 2015)</p> <p>Matrices with high water content, high oil content, high acid content and starch matrices: GC–MS, LOQ 0.01 mg/kg, ILV available. The methods are not stereoselective and therefore the methods determine the sum of acrinathrin and its enantiomer (Spain, 2020)</p> |  |

DAT: days after treatment; a.s.: active substance; PBI: plant-back interval; n/a: not applicable; GC–MS: gas chromatography with mass spectrometry; ILV: independent laboratory validation; LOQ: limit of quantification.

### B.1.1.2. Stability of residues in plants

| Plant products<br>(available studies) | Category           | Commodity                   | T (°C) | Stability period |        | Compounds covered | Comment/Source  |
|---------------------------------------|--------------------|-----------------------------|--------|------------------|--------|-------------------|---|
|                                       |                    |                             |        | Value            | Unit   |                   |   |
|                                       | High water content | Cucumber, whole green beans | -18°C  | 24               | months | Acrinathrin       | EFSA (2013)<br>From available study is not clear if the enantiomer was tested |

## B.1.2. Magnitude of residues in plants

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

| Commodity | Region/<br>Indoor <sup>(a)</sup> | Residue levels observed in<br>the supervised residue<br>trials (mg/kg) | Comments/Source  | Calculated<br>MRL<br>(mg/kg) | HR <sup>(b)</sup><br>(mg/kg)    | STMR <sup>(c)</sup><br>(mg/kg)  | CF <sup>(d)</sup> |
|-----------|----------------------------------|--|--|------------------------------|---------------------------------|---------------------------------|-------------------|
| Lettuce   | SEU                              | <b>Mo:</b> 6 × < 0.01, 2 × 0.05<br><b>RA:</b> –                        | Residue trials on lettuce compliant with GAP.<br>Sufficient number of trials to derive an MRL for the SEU<br>Residue trial samples were analysed for acrinathrin and its enantiomer. Samples were not analysed for other isomers since these were not present or were present at insignificant levels, according to lettuce metabolism study | <b>0.1</b>                   | <b>Mo:</b> 0.05<br><b>RA:</b> – | <b>Mo:</b> 0.01<br><b>RA:</b> – | n/a               |

MRL: maximum residue level; GAP: Good Agricultural Practice; Mo: monitoring; RA: risk assessment; n/a: not applicable.

(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): 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 monitoring to the residue definition for risk assessment.

### B.1.2.2. Residues in rotational crops

|   |     |   |
|---|-----|---|
| Residues in rotational and succeeding crops expected based on confined rotational crop study? | No  | <p>The metabolism of acrinathrin in rotational crops (wheat, spinach, carrots and kohlrabi) has been evaluated during the peer review (EFSA, 2013) with <sup>14</sup>C-labelled acrinathrin (cyclopropyl-1-<sup>14</sup>C and <sup>14</sup>C-benzyl) with a single application to bare soil at 3N compared to the cGAP for lettuce</p> <p>Translocation of residues in crops growing in the following season is not expected to be significant (total residue less than 0.01 mg/kg) for the representative uses</p> |
| Residues in rotational and succeeding crops expected based on field rotational crop study?    | n/a | No residues are expected in rotational crops, provided that the active substance is applied according to the proposed GAPs.   |

cGAP: critical Good Agricultural Practice; GAP: Good Agricultural Practice.

### 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.

## B.3. Consumer risk assessment

|  |   |
|--|---|
| ARfD                                   | 0.01 mg/kg bw (EFSA, 2013)  |
| Highest IESTI, according to EFSA PRIMo | Lettuce: 21% of ARfD for children and 7% of ARfD for adults.  |
| Assumptions made for the calculations  | <p>The calculation is based on the highest residue levels expected in lettuce and multiplied by the conversion factor of 1.1 for risk assessment, as derived by the MRL review. The exposure assessment is considered tentative, pending the toxicological profile of all acrinathrin isomers to be addressed</p> <p>Calculations performed with PRIMo revision 3.1</p> |

|                                       |   |
|---------------------------------------|---|
| ADI                                   | 0.01 mg/kg bw per day (EFSA, 2013)  |
| Highest IEDI, according to EFSA PRIMo | 2% ADI (PT general diet)<br>Contribution of crop assessed: 0.06% of ADI   |
| Assumptions made for the calculations | The calculation is based on the median residue levels in lettuce as derived from the submitted residue trials, multiplied by the conversion factor of 1.1 for the risk assessment, as derived by the MRL review. For the remaining commodities covered by the MRL regulation on which the existing uses were supported after the MRL review (grapes, lamb's lettuce, escarole, cresses, Roman rocket, red mustard), the median residue levels derived in the MRL review were selected as input value, multiplied by the conversion factor of 1.1 for risk assessment. |
|                                       | The exposure assessment is considered tentative, pending the toxicological profile of all acrinathrin isomers to be addressed   |
|                                       | Calculations performed with PRIMo revision 3.1.   |

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.

#### B.4. Recommended MRLs

| Code <sup>(a)</sup>   | Commodity | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification   |
|---|-----------|-------------------------|-------------------------|---|
| <b>Enforcement residue definition:</b> Acrinathrin <sup>(F)</sup> |           |                         |                         |   |
| 251020  | Lettuce   | 0.02*                   | 0.1                     | The submitted data are sufficient to derive an MRL proposal for the intended SEU use. Risk for consumers unlikely |

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

MRL: maximum residue level; SEU: southern Europe.

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

(F): Fat soluble.



### Appendix C – Pesticide Residue Intake Model (PRIMo)



| Acrinathrin                    |  |                     |                       |
|--------------------------------|--|---------------------|-----------------------|
| LOCs (mg/kg) range from:       |  | 0.01                | to: 0.05              |
| Toxicological reference values |  |                     |                       |
| ADI (mg/kg bw per day):        |  | 0.01                | ARID (mg/kg bw): 0.01 |
| Source of ADI:                 |  | Source of ARID:     |                       |
| Year of evaluation:            |  | Year of evaluation: |                       |

Input values

- Details – chronic risk assessment
- Supplementary results – chronic risk assessment
- Details – acute risk assessment/children
- Details – acute risk assessment/adults

| Chronic risk assessment: JMPR methodology (IEDI/TMDI) |                   |                             |  |                                 |  |                                 |  |                                |                                   |  |                         |
|---|-------------------|-----------------------------|--|---------------------------------|--|---------------------------------|--|--------------------------------|-----------------------------------|--|-------------------------|
| No of diets exceeding the ADI :                       |                   |                             |  |                                 |  |                                 |  |                                |                                   |  | Exposure resulting from |
| Calculated exposure (% of ADI)                        | MS Diet           | Exposure (µg/kg bw per day) | Highest contributor to MS diet (in % of ADI) |                                 | 2nd contributor to MS diet (in % of ADI) |                                 | 3rd contributor to MS diet (in % of ADI) |                                | MRLs set at the LOO (in % of ADI) | commodities not under assessment (in % of ADI) |                         |
|   |                   |                             | Commodity/ group of commodities              | Commodity/ group of commodities | Commodity/ group of commodities          | Commodity/ group of commodities |  |                                |                                   |  |                         |
| 2%  | PT general        | 0.15                        | 1%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 2%   |                         |
| 1%  | FR adult          | 0.13                        | 1%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Lamb's lettuce/corn salads     |                                   | 1%   |                         |
| 1%  | GEMS/Food G07     | 0.10                        | 0.8%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 1%   |                         |
| 1%  | RD general        | 0.10                        | 0.9%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 1%   |                         |
| 0.9%  | NL toddler        | 0.09                        | 0.9%   | Table grapes                    | 0.1%                                     | Escaroles/broad-leaved endives  | 0.0%                                     | Lettuces                       |                                   | 0.9%   |                         |
| 0.8%  | IE adult          | 0.08                        | 0.7%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.8%   |                         |
| 0.8%  | GEMS/Food G11     | 0.08                        | 0.6%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lamb's lettuce/corn salads     |                                   | 0.8%   |                         |
| 0.8%  | GEMS/Food G08     | 0.08                        | 0.6%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.8%   |                         |
| 0.8%  | DE child          | 0.08                        | 0.8%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Wine grapes                    |                                   | 0.8%   |                         |
| 0.8%  | GEMS/Food G15     | 0.08                        | 0.6%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.8%   |                         |
| 0.6%  | DE women 14-50 yr | 0.06                        | 0.5%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.6%  | GEMS/Food G06     | 0.06                        | 0.6%   | Table grapes                    | 0.0%                                     | Wine grapes                     | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.6%  | UK adult          | 0.06                        | 0.6%   | Wine grapes                     | 0.0%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.6%  | DK adult          | 0.06                        | 0.5%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.6%  | DE general        | 0.06                        | 0.5%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.6%  | NL child          | 0.06                        | 0.6%   | Table grapes                    | 0.0%                                     | Escaroles/broad-leaved endives  | 0.0%                                     | Lettuces                       |                                   | 0.6%   |                         |
| 0.5%  | UK vegetarian     | 0.05                        | 0.4%   | Wine grapes                     | 0.0%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.5%   |                         |
| 0.5%  | NL general        | 0.05                        | 0.3%   | Wine grapes                     | 0.1%                                     | Table grapes                    | 0.0%                                     | Escaroles/broad-leaved endives |                                   | 0.5%   |                         |
| 0.4%  | GEMS/Food G10     | 0.04                        | 0.2%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.4%   |                         |
| 0.4%  | FR child 3-15 yr  | 0.04                        | 0.2%   | Wine grapes                     | 0.2%                                     | Table grapes                    | 0.0%                                     | Lamb's lettuce/corn salads     |                                   | 0.4%   |                         |
| 0.3%  | ES adult          | 0.03                        | 0.2%   | Wine grapes                     | 0.1%                                     | Lettuces                        | 0.0%                                     | Table grapes                   |                                   | 0.3%   |                         |
| 0.2%  | FI adult          | 0.02                        | 0.2%   | Wine grapes                     | 0.0%                                     | Table grapes                    | 0.0%                                     | Lettuces                       |                                   | 0.2%   |                         |
| 0.2%  | PL general        | 0.02                        | 0.2%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Lettuces                       |                                   | 0.2%   |                         |
| 0.2%  | UK toddler        | 0.02                        | 0.1%   | Table grapes                    | 0.0%                                     | Wine grapes                     | 0.0%                                     | Lettuces                       |                                   | 0.2%   |                         |
| 0.1%  | FR toddler 2-3 yr | 0.01                        | 0.1%   | Wine grapes                     | 0.0%                                     | Table grapes                    | 0.0%                                     | Lamb's lettuce/corn salads     |                                   | 0.1%   |                         |
| 0.1%  | FI 3 yr           | 0.01                        | 0.1%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Wine grapes                    |                                   | 0.1%   |                         |
| 0.1%  | IT adult          | 0.01                        | 0.1%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Escaroles/broad-leaved endives |                                   | 0.1%   |                         |
| 0.1%  | DK child          | 0.01                        | 0.1%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Escaroles/broad-leaved endives |                                   | 0.1%   |                         |
| 0.1%  | FI 6 yr           | 0.01                        | 0.1%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Wine grapes                    |                                   | 0.1%   |                         |
| 0.1%  | IT toddler        | 0.01                        | 0.1%   | Table grapes                    | 0.0%                                     | Lettuces                        | 0.0%                                     | Escaroles/broad-leaved endives |                                   | 0.1%   |                         |
| 0.1%  | ES child          | 0.01                        | 0.0%   | Lettuces                        | 0.0%                                     | Table grapes                    | 0.0%                                     | Wine grapes                    |                                   | 0.1%   |                         |
| 0.0%  | SE general        | 0.00                        | 0.0%   | Lettuces                        |  | FRUIT AND TREE NUTS             |  |                                |                                   | 0.0%   |                         |
| 0.0%  | IE child          | 0.00                        | 0.0%   | Table grapes                    | 0.0%                                     | Lettuces                        |  |                                |                                   | 0.0%   |                         |
| 0.0%  | UK infant         | 0.00                        | 0.0%   | Table grapes                    | 0.0%                                     | Wine grapes                     |  |                                |                                   | 0.0%   |                         |
| 0.0%  | FR infant         | 0.00                        | 0.0%   | Wine grapes                     | 0.0%                                     | Table grapes                    |  |                                |                                   | 0.0%   |                         |
| 0.0%  | LT adult          | 0.00                        | 0.0%   | Table grapes                    | 0.0%                                     | Lettuces                        |  |                                |                                   | 0.0%   |                         |

**Conclusion:**  
 The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.  
 The long-term intake of residues of Acrinathrin is unlikely to present a public health concern.

|  |   |
|--|---|
| <b>Acute risk assessment /children</b>   | <b>Acute risk assessment /adults / general population</b> |
| Details - acute risk assessment/children | Details - acute risk assessment/adults                    |

The acute risk assessment is based on the ARfD.  
The calculation is based on the large portion of the most critical consumer group.

**Show results for all crops**

|   |  |             |                          |                     |  |             |                        |                     |
|---|--|-------------|--------------------------|---------------------|--|-------------|------------------------|---------------------|
| Unprocessed commodities   | <b>Results for children</b>                                |             |                          |                     | <b>Results for adults</b>                                  |             |                        |                     |
|   | No. of commodities for which ARfD/ADI is exceeded (IESTI): |             |                          |                     | No. of commodities for which ARfD/ADI is exceeded (IESTI): |             |                        |                     |
|   | ---  |             |                          |                     | ---  |             |                        |                     |
|   | <b>IESTI</b>   |             |                          |                     | <b>IESTI</b>   |             |                        |                     |
|   | Highest % of ARfD/ADI                                      | Commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI                                      | Commodities | MRL/put for RA (mg/kg) | Exposure (µg/kg bw) |
| 40%   | Table grapes   | 0.05/0.06   | 4.0                      | 19%                 | Table grapes   | 0.05/0.06   | 1.9                    |                     |
| 21%   | Lettuces   | 0.1/0.06    | 2.1                      | 16%                 | Wine grapes  | 0.1/0.07    | 1.6                    |                     |
| 13%   | Escaroles/broad-leaved endives                             | 0.06/0.03   | 1.3                      | 7%                  | Lettuces   | 0.1/0.06    | 0.67                   |                     |
| 6%  | Wine grapes  | 0.1/0.07    | 0.61                     | 7%                  | Escaroles/broad-leaved endives                             | 0.06/0.03   | 0.67                   |                     |
| 0.9%  | Lamb's lettuce/corn salads                                 | 0.06/0.03   | 0.09                     | 2%                  | Red mustards   | 0.06/0.03   | 0.18                   |                     |
| 0.9%  | Roman rocket/rucola  | 0.06/0.03   | 0.09                     | 0.6%                | Lamb's lettuce/corn salads                                 | 0.06/0.03   | 0.06                   |                     |
| 0.10%   | Cress and other sprouts and shoots                         | 0.06/0.03   | 0.01                     | 0.4%                | Roman rocket/rucola  | 0.06/0.03   | 0.04                   |                     |
|   |  |             |                          | 0.1%                | Cress and other sprouts and shoots                         | 0.06/0.03   | 0.01                   |                     |
| <a href="#">Expand/collapse list</a>  |  |             |                          |                     |  |             |                        |                     |
| <b>Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)</b> |  |             |                          |                     |  |             |                        |                     |

|                                      |   |                       |                          |                     |   |                       |                          |                     |
|--------------------------------------|---|-----------------------|--------------------------|---------------------|---|-----------------------|--------------------------|---------------------|
| Processed commodities                | <b>Results for children</b>   |                       |                          |                     | <b>Results for adults</b>   |                       |                          |                     |
|                                      | No of processed commodities for which ARfD/ADI is exceeded (IESTI): |                       |                          |                     | No of processed commodities for which ARfD/ADI is exceeded (IESTI): |                       |                          |                     |
|                                      | ---   |                       |                          |                     | ---   |                       |                          |                     |
|                                      | <b>IESTI</b>  |                       |                          |                     | <b>IESTI</b>  |                       |                          |                     |
|                                      | Highest % of ARfD/ADI   | Processed commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI   | Processed commodities | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
| 24%                                  | Wine grapes/juice   | 0.1/0.06              | 2.4                      | 11%                 | Wine grapes/juice   | 0.1/0.06              | 1.1                      |                     |
| 22%                                  | Escaroles/broad-leaved endives/boiled                               | 0.06/0.03             | 2.2                      | 7%                  | Escaroles/broad-leaved endives/boiled                               | 0.06/0.03             | 0.67                     |                     |
|                                      |   |                       |                          | 6%                  | Wine grapes/wine  | 0.1/0.07              | 0.62                     |                     |
|                                      |   |                       |                          | 3%                  | Table grapes/raisins  | 0.1/0.26              | 0.32                     |                     |
| <a href="#">Expand/collapse list</a> |   |                       |                          |                     |   |                       |                          |                     |

**Conclusion:**  
No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short-term intake of residues of Acrinathrin is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.

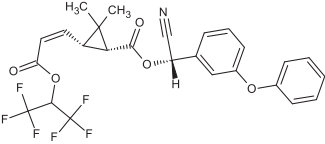
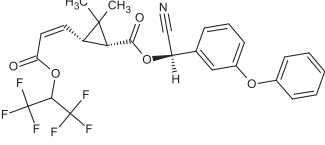
## Appendix D – Input values for the exposure calculations

### D.1. Consumer risk assessment

| Commodity                          | Chronic risk assessment |                        | Acute risk assessment  |                      |
|------------------------------------|-------------------------|------------------------|--|----------------------|
|                                    | Input value (mg/kg)     | Comment                | Input value (mg/kg)  | Comment              |
| Lettuce                            | 0.011                   | STMR proposed MRL × CF | 0.055  | HR proposed MRL × CF |
| Table grapes                       | 0.055                   | STMR MRL review × CF   | Acute exposure was performed only for the crop under consideration |                      |
| Wine grapes                        | 0.055                   | STMR MRL review × CF   |  |                      |
| Lamb's lettuce/corn salads         | 0.022                   | STMR MRL review × CF   |  |                      |
| Escaroles/broadleaved endives      | 0.022                   | STMR MRL review × CF   |  |                      |
| Cress and other sprouts and shoots | 0.022                   | STMR MRL review × CF   |  |                      |
| Roman rocket/rucola                | 0.022                   | STMR MRL review × CF   |  |                      |
| Red mustards                       | 0.022                   | STMR MRL review × CF   |  |                      |

MRL: maximum residue level; STMR: supervised trials median residue; HR: highest residue; CF: conversion factor.

## Appendix E – Used compound codes

| Code/trivial name <sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey <sup>(b)</sup>   | Structural formula <sup>(c)</sup>   |
|----------------------------------|--|---|
| Acrinathrin                      | <p><b>(S)-cyano(3-phenoxyphenyl)methyl (1R,3S)-3-{{(1Z)-3-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-3-oxoprop-1-en-1-yl}}-2,2-dimethylcyclopropane-1-carboxylate</b></p> <p>CC1(C)[C@@H]([C@@H]1\C=C/C(=O)OC(C(F)(F)F)C(F)(F)F)C(=O)O[C@H](C#N)c1cccc(Oc2ccccc2)c1</p> <p>YLFSVIMMRPNPFK-WEQBUNFVSA-N</p> |  |
| R-Acrinathrin                    | <p><b>(R)-cyano(3-phenoxyphenyl)methyl (1R,3S)-3-{{(1Z)-3-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-3-oxoprop-1-en-1-yl}}-2,2-dimethylcyclopropane-1-carboxylate</b></p> <p>CC1(C)[C@@H]([C@@H]1\C=C/C(=O)OC(C(F)(F)F)C(F)(F)F)C(=O)O[C@H](C#N)c1cccc(Oc2ccccc2)c1</p> <p>YLFSVIMMRPNPFK-UTFPDPTSA-N</p>  |  |

The complete list of acrinathrin isomers is reported in the Evaluation Report (Spain, 2020).

(a): The metabolite name in bold is the name used in the conclusion.

(b): ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 Jul 2018).

(c): ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 07 Dec 2018).