REASONED OPINION

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

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicants Syngenta Crop Protection B.V. and Agriculture and Horticulture Development Board (AHDB) submitted, respectively, a request to the competent national authorities in the Netherlands and United Kingdom to modify the existing maximum residue levels (MRLs) for the active substance mandipropamid in various crops. The data submitted in support of the request were found to be sufficient to derive MRL proposals for beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes. Adequate analytical methods for enforcement are available to control the residues of mandipropamid in plant matrices under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the intake of residues resulting from the use of mandipropamid according to the reported agricultural practices is unlikely to present a risk to consumer health.

Keywords: mandipropamid, beetroot, Brussels sprouts, cauliflower, globe artichoke, peas, radish, witloof, Belgian endive, pesticide, MRL, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta Crop Protection B.V. submitted an application to the competent national authority in the Netherlands (evaluating Member State, EMS-NL) to modify the existing maximum residue levels (MRLs) for the active substance mandipropamid in various crops. In addition, the applicant AHDB submitted an application to the competent national authority in the United Kingdom (evaluating Member State, EMS-UK) to modify the existing maximum residue level (MRL) for the active substance mandipropamid in beetroots. The EMS-NL and the EMS-UK each drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which were submitted to the European Commission and forwarded to the European Food Safety Authority (EFSA) on 2 August 2016 and 23 January 2017, respectively. To accommodate for the intended uses of mandipropamid, the EMS-NL proposed to raise the existing MRLs from the limit of quantification (LOQ) 0.01 to 0.3 mg/kg in radishes, 0.15 mg/kg in cauliflowers, 0.2 mg/kg in Brussels sprouts, 0.15 mg/kg in witloofs/Belgian endives, 0.3 mg/kg in peas (without pods) and 0.3 mg/kg in globe artichokes. The EMS-UK proposed to raise the existing MRL from the limit of quantification (LOQ) 0.01 to 0.1 mg/kg for beetroots.

For reasons of efficiency, EFSA combined both applications in a single reasoned opinion. EFSA based its assessment on the evaluation reports submitted by the EMSs, the draft assessment report (DAR) (and its addendum) prepared under Council Directive 91/414/EEC, the European Commission review report on mandipropamid, the conclusion on the peer review of the pesticide risk assessment of the active substance mandipropamid, the Joint Meeting on Pesticide Residues (JMPR) evaluation reports, as well as the conclusions from previous EFSA opinions on mandipropamid.

The metabolism of mandipropamid following foliar application was investigated in crops belonging to the groups of fruit crops, leafy crops and root crops.

Studies investigating the effect of processing on the nature of mandipropamid (hydrolysis studies) demonstrated that the active substance is hydrolytically stable. Metabolisms in rotational crops showed similar pathways as in primary crops.

Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies and the capabilities of enforcement analytical methods, the MRL review proposed the residue definition for enforcement as: 'mandipropamid (any ratio of constituent isomers)'. The residue definition for enforcement set in Regulation (EC) No 396/2005 is equivalent to the above mentioned residue definition, although it does not detail that it covers any ratio of constituent isomers.

The residue definition for risk assessment was proposed by the MRL review for fruits and leafy vegetables as: 'mandipropamid (any ratio of constituent isomers)'. The MRL review proposed a tentative residue definition for risk assessment for root crops as: 'sum of mandipropamid and SYN 500003', pending on the submission of toxicological information for hazard characterisation of the metabolite SYN 500003.

The tentative residue definition for risk assessment for root crop commodities was used for the root category crops assessed in the present MRL application. The lack of toxicological data on the metabolite SYN 500003 is not relevant to the intended uses in root crops assessed in the present application because there is sufficient evidence that SYN 500003 is not present at significant levels in the treated crops if mandipropamid is used according to the intended good agricultural practice (GAPs).

Sufficiently validated analytical methods based on liquid chromatography with tandem mass spectrometry (LC–MS/MS) are available to quantify residues in the crops assessed in this application according to the enforcement residue definition. The methods enable quantification of residues at or above 0.01 mg/kg in the crops assessed (LOQ).

The available residue trials are sufficient to derive MRL proposals of 0.1 mg/kg for beetroots 0.3 mg/kg for radishes, 0.15 mg/kg for cauliflowers, 0.2 mg/kg for Brussels sprouts, 0.15 mg/kg for witloofs/Belgian endives, 0.3 mg/kg for peas (without pods) and 0.3 mg/kg in globe artichokes.

Specific studies investigating the magnitude of mandipropamid residues in processed commodities are not required due to the low dietary exposure, which is below the trigger value of 10% of the acceptable daily intake (ADI).

The occurrence of mandipropamid residues in rotational crops was investigated in the framework of the EU pesticides peer review. Based on the available information on the nature and magnitude of residues, it was concluded that significant residue levels are unlikely to occur in rotational crops, provided that the active substance is used according to the proposed GAP.

Residues of mandipropamid in commodities of animal origin were not assessed since the crops under consideration in these MRL applications and their by-products are not intended to be fed to livestock.

The toxicological profile of mandipropamid was assessed in the framework of the European Union (EU) pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.15 mg/kg body weight (bw) per day. Based on the toxicological profile of mandipropamid, the derivation of an acute reference dose (ARfD) was not considered necessary.

For the plant metabolite SYN 500003, included in the tentative residue definition for risk assessment for root crops, data were submitted and the new toxicological information was discussed at the EFSA experts' meeting on mammalian toxicology in November 2018, where the experts agreed with the view of the EMSs that the metabolite is unlikely to be genotoxic. Regarding general toxicity, further toxicological data are currently not available. Thus, according to EFSA, data addressing the general toxicity of metabolite SYN 500003 are still required in order to confirm whether SYN 500003 is of lower, similar or higher toxicity in comparison with the parent mandipropamid or whether specific reference values should be set. However, considering that the metabolite was not present at significant levels in the residue trials for beetroots and radishes submitted in support of the present MRL applications, the lack of a complete toxicological characterisation of SYN 500003 is not considered as a relevant data gap for the crops under consideration in the present MRL applications.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). Considering the toxicological profile of the active substance, a short-term dietary risk assessment was not required.

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 Codex maximum residue limits (CXLs). EFSA updated the calculation with the relevant supervised trials median residue (STMR) values derived from the residue trials submitted in support of this MRL application for beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes; and the STMR for cocoa beans derived in an EFSA opinion published after the MRL review. The risk assessment is based on the assumption that SYN 500003 is of similar toxicity as the parent compound.

The estimated long-term dietary intake was in the range from 0.3% to 4.6% of the ADI. EFSA concluded that the proposed use of mandipropamid on beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes will not result in a consumer exposure exceeding the toxicological reference value for mandipropamid.

The risk assessment is affected by non-standard uncertainty related to the lack of hazard characterisation of the metabolite SYN 500003. The overall risk might be underestimated due to the contribution of other root and tuber vegetables for which this metabolite might be of relevance (i.e. potatoes, onions and spring onions) if the metabolite SYN 500003 possesses a higher toxicity than the parent.

The risk assessment was performed disregarding the possible impact of plant or livestock metabolism on the isomer ratio of parent compound and its relevant metabolite. EFSA is of the opinion that this issue is not of concern considering the wide margin between the calculated exposure and the ADI.

Based on the risk assessment results, EFSA concluded that the intake of residues resulting from the use of mandipropamid according to the reported agricultural practices is unlikely to present a risk to consumer health.

EFSA proposes to amend the existing MRLs as 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[a]	Commodity	Existing EU MRL[b]/MRL recommended in MRL review[c] (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition (existing): Mandipropamid **Enforcement residue definition** (proposed): Mandipropamid (any ratio of constituent isomers)				
0213010	Beetroots	0.01*/–	**0.1**	The submitted data are sufficient to derive an MRL for the intended NEU use. Risk for consumers unlikely

Code[a]	Commodity	Existing EU MRL[b]/MRL recommended in MRL review[c] (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
0213080	Radishes	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL for the intended NEU and SEU uses. Risk for consumers unlikely
0241020	Cauliflowers	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the NEU and SEU use. Risk for consumers unlikely
0242010	Brussels sprouts	0.01*/–	**0.2**	The submitted data are sufficient to derive an MRL proposal for the intended NEU use. Risk for consumers unlikely
0255000	Witloofs/ Belgian endives	0.01*/25[d]	**0.15**	The submitted data are sufficient to derive an MRL proposal for the intended indoor use at forcing stage. Risk for consumers unlikely
0260040	Peas (without pods)	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the intended NEU use. Risk for consumers unlikely
0270050	Globe artichokes	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the intended SEU use. Risk for consumers unlikely

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Existing EU MRL Commission Regulation (EU) 2015/845.
(c): MRL recommendations derived in the framework of the MRL review, which have not yet been legally implemented. No MRL recommendations were derived where no GAP was notified to EFSA, indicated by '–'.
(d): The MRL Review included the Codex CXL for mandipropamid in leafy vegetables of 25 mg/kg in the EU MRL proposals for witloofs/Belgian endives; however, the CXL for leafy vegetables is not applicable to witloof and therefore the MRL proposal for witloofs/Belgian endives derived in the MRL Review has to be withdrawn.

Table of contents

Assessment

The applicants requested the modification of the existing maximum residue levels (MRLs) for mandipropamid in beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes. The detailed description of the intended uses of mandipropamid, which are the basis for the current MRL applications, are reported in Appendix A.

Mandipropamid is the ISO common name for (*RS*)-2-(4-chlorophenyl)-*N*-[3-methoxy-4-(prop-2-ynyloxy)phenethyl]-2-(prop-2-ynyloxy)acetamide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Mandipropamid was evaluated in the framework of Directive 91/414/EEC with Austria designated as rapporteur Member State (RMS) for the representative uses as foliar applications on potato, tomato, melon, cucumber, lettuce and vines. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by European Food Safety Authority (EFSA, 2012). Mandipropamid was approved[1] for the use as a fungicide on 1 August 2013.

The European Union (EU) MRLs for mandipropamid are established in Annex III of Regulation (EC) No 396/2005[2]. Certain Codex maximum residue limits (CXLs) for mandipropamid established by the Codex Alimentarius Commission (CAC) have been implemented in the EU MRL legislation by Commission Regulation (EU) No 459/2010[3] and Commission Regulation (EU) 2015/845[4]. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2018a), but the proposed modifications have not yet been implemented in the EU MRL legislation. After completion of the MRL review, EFSA has issued one reasoned opinion on the modification of MRLs for cocoa beans (EFSA, 2018b). The proposed MRL for cocoa beans has not yet been implemented in the EU MRL legislation.[5]

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Syngenta Crop Protection B.V. submitted an application to the competent national authority in the Netherlands, hereafter referred to as the evaluating Member State-Netherlands (EMS-NL), to modify the existing MRLs for the active substance mandipropamid in various crops. In addition, a second applicant, the United Kingdom Agriculture and Horticulture Development Board (AHDB) submitted an application to the competent national authority in the United Kingdom, hereafter referred to as the evaluating Member State-United Kingdom (EMS-UK), to modify the existing MRL for the active substance mandipropamid in beetroots. These applications were notified to the European Commission and EFSA and were subsequently evaluated by the EMSs in accordance with Article 8 of the MRL regulation.

The EMS-NL and the EMS-UK each drafted an evaluation report in accordance with Article 8 of the Regulation, which were submitted to the European Commission and forwarded to EFSA on 2 August 2016 and 23 January 2017, respectively. To accommodate for the intended uses of mandipropamid, the EMS-NL proposed to raise the existing MRLs from the limit of quantification (LOQ) 0.01 mg/kg to: 0.3 mg/kg in radishes, 0.15 mg/kg in cauliflowers, 0.2 mg/kg in Brussels sprouts, 0.15 mg/kg in witloofs/Belgian endives, 0.3 mg/kg in peas (without pods) and 0.3 mg/kg in globe artichokes. The EMS-UK proposed to raise the existing MRL in beetroots from the LOQ 0.01 to 0.1 mg/kg. EFSA assessed the applications and the evaluation reports as required by Article 10 of the Regulation and identified points which needed further information, which were requested from the EMS-NL and the EMS-UK. The applicant Syngenta Crop Protection B.V. partially addressed the identified open issues by submitting new toxicological information for the plant metabolite SYN 500003, which was assessed by the EMS-NL. EFSA resumed the assessment based on the information provided in the revised

[1] Commission Implementing Regulation (EU) No 188/2013 of 5 March 2013 approving the active substance mandipropamid, 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 T. OJ L 62, 6.3.2013, p. 13–16.

[2] 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.

[3] Commission Regulation (EU) No 459/2010 of 27 May 2010 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for certain pesticides in or on certain products. OJ L 129, 28.5.2010, p. 1–47.

[4] Commission Regulation (EU) 2015/845 of 27 May 2015 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for azoxystrobin, chlorantraniliprole, cyantraniliprole, dicamba, difenoconazole, fenpyroximate, fludioxonil, glufosinate-ammonium, imazapic, imazapyr, indoxacarb, isoxaflutole, mandipropamid, penthiopyrad, propiconazole, pyrimethanil, spirotetramat and trinexapac in or on certain products. OJ L 130, 4.6.2015, p. 1–69.

[5] For an overview of all MRL Regulations on this active substance, please consult: http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=pesticide.residue.selection&language=EN

evaluation reports submitted to EFSA on 10 September 2018 (Netherlands, 2016) and 9 October 2018 (United Kingdom, 2016).

EFSA based its assessment on the evaluation reports submitted by the EMSs (Netherlands, 2016; United Kingdom, 2016), the DAR (and its addendum) prepared under Directive 91/414/EEC (Austria, 2006, 2012), the European Commission review report on mandipropamid (European Commission, 2013), the conclusion on the peer review of the pesticide risk assessment of the active substance mandipropamid (EFSA, 2012), the JMPR evaluation reports (FAO, 2008, 2014), the EFSA reasoned opinion the review of the existing maximum residue levels (MRLs) for mandipropamid according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2018a) as well as the conclusion from a previous EFSA opinion on mandipropamid (EFSA, 2018b).

For this application, the data requirements established in Regulation (EU) No 544/2011[6] 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, 2015; 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[7].

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, submitted in support of the current MRL application, are presented in Appendix B.

The evaluation reports submitted by the EMSs (Netherlands, 2016; United Kingdom 2016), the exposure calculations using the EFSA Pesticide Residues Intake Model (PRIMo), together with the report of the experts' meeting on mammalian toxicology regarding mandipropamid (EFSA, 2018c), are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents.

1. Mammalian toxicology

The toxicological profile of mandipropamid was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive a toxicological reference value for acceptable daily intake (ADI) of 0.15 mg/kg body weight (bw) per day. Based on the toxicological profile of mandipropamid, the derivation of an acute reference dose (ARfD) was not considered necessary (EFSA, 2012).

In the metabolism study in root crops, metabolite SYN 500003 was identified (see Section 2.1.1); this plant metabolite was included in the tentative residue definition for risk assessment for root crops.

The pesticides peer review concluded that the plant metabolite SYN 500003 was shown to be more acutely toxic than mandipropamid (oral LD_{50} 1049 mg/kg bw) and negative in an Ames test. However, the data were found insufficient to conclude on the genotoxic potential of SYN 500003 and to derive toxicological reference values for the consumer risk assessment. Additional data were requested to address the data gaps identified, including also a request to conclude on the relative toxicity of the isomers of the metabolite (EFSA, 2012). The data gap for toxicological information on the metabolite SYN 500003 relevant for root crops was subsequently confirmed by the MRL review (EFSA, 2018a).

Additional genotoxicity data on SYN 500003 were provided in the context of the present MRL application. In addition, new information on a bioanalytical method for SYN 500003 and a bone marrow exposure study for SYN 500003 were submitted, in order to support the interpretation of a previous mouse micronucleus study with regard to the genotoxic potential of SYN 500003. The new information was evaluated by the EMS-NL in the revised evaluation report (Netherlands, 2016).

Taking into account the new information, the EMS considered SYN 500003 unlikely to be genotoxic. The new toxicological information was discussed at the EFSA experts' meeting on mammalian toxicology held on 21–22 November 2018 where the experts agreed with the view of the EMS that SYN 500003 is unlikely to be genotoxic (EFSA, 2018c).

Regarding general toxicity, further toxicological data are currently not available. Thus, according to EFSA, data addressing the general toxicity of metabolite SYN 500003 are still required in order to confirm whether SYN 500003 is of lower, similar or higher toxicity in comparison with the parent mandipropamid or whether specific reference values should be set. However, considering that the

[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.

metabolite was not present at significant levels in the residue trials for beetroots and radishes submitted in support of the present MRL applications, the lack of a complete toxicological characterisation of SYN 500003 is not considered as a relevant data gap for the crops under consideration.

2. Residues in plants

2.1. Nature of residues and methods of analysis in plants

2.1.1. Nature of residues in primary crops

The metabolism of mandipropamid in fruit crops (grapevine, tomato), leafy crops (lettuce) and root crops (potato) was investigated in the framework of the EU pesticides peer review (EFSA, 2012). No further studies on the metabolism of mandipropamid in primary crops were submitted in the present MRL applications.

The studies on grapes, lettuce and potatoes were conducted with ^{14}C–mandipropamid labelled at either the methoxyphenyl- or chlorophenyl-ring. The metabolism study on tomato was conducted with [1-^{14}C]–mandipropamid (radiolabel on the carbon chain). The metabolism of mandipropamid in fruit crops and leafy crops was shown to be similar, with the parent compound being the major component of the residues in grape, tomato and lettuce, accounting for 53–94% of the total radioactive residues (TRR) in all samples collected 3–28 days after last application (DALA), the other fractions or identified metabolites representing mostly less than 2% TRR and less than 0.02 mg/kg (EFSA, 2012).

In contrast, the metabolism was more extensive in potato, with a higher number of fractions observed, each below 10% TRR, with the exception of the metabolite SYN 500003 which was present at levels up to 10.1% TRR (0.0042 mg eq/kg) in peel and 14.2% TRR (0.0062 mg eq/kg) in flesh of potato tubers (foliar application at 1N rate: 6 × 146–158 g a.s./ha; 10- to 12-day intervals; at 7 days after treatment (DAT)). The parent mandipropamid was not detected in the flesh of potato tubers and was only detected in peel, at levels up to 13% TRR (0.0075 mg eq/kg at 21 DAT) (EFSA, 2012).

The metabolite SYN 500003 was present at significant levels only in the tubers of potato in the available primary crop metabolism studies. In potato leaves, mandipropamid was the major fraction (40–61% TRR) and all other metabolites were below 2% TRR (Austria, 2012), indicating limited translocation of metabolite SYN 500003 to the aerial parts of the plant. Furthermore, it is noted that the metabolite SYN 500003 was not identified as a relevant soil metabolite (occurring at max. 0.2% applied radioactivity) and has a low $DT_{50\ Soil}$ (up to 4 days) under aerobic conditions (EFSA, 2012).

The metabolic pathways observed in potato tuber are not consistent with the routes of degradation observed in primary crops of the fruit and leafy crop-group categories or in the leaves or potato plant, specifically with regard to the occurrence of the metabolite SYN 500003. However, the absolute levels of residues in the primary crop metabolism studies were low, and the experimental design time periods from first application to harvest were shorter in metabolism studies conducted with grapevine (up to 52 days), lettuce (up to 21 days) and tomatoes (up to 35 days) than in the metabolism study conducted with potato (59 and 73 days) (Austria, 2012), which indicated that the extent of metabolism observed in the studies may be influenced by the overall length of time period from first application to sampling of the crop.

For the intended uses on beetroots and radishes (root vegetables category), cauliflowers, Brussels sprouts, witloofs/Belgian endives and globe artichokes (leafy crops category) the metabolic behaviour in primary crops is sufficiently addressed.

For the intended use on pea (legume vegetables in the pulses and oilseeds category), no specific metabolism study is available. Considering that the metabolic pathways in fruit and leafy crops are not consistent with the metabolic pathways observed in the available root crop metabolism study, the setting of a general residue definition for all crops is not appropriate. Peas are a leguminous vegetable formed as pod fruit from the aerial parts of the plant and, for the specific good agricultural practice (GAP) on fresh peas harvested as succulent green seeds, the available metabolism studies conducted on leafy crops and fruit crops are considered sufficiently representative to address the metabolic behaviour expected in peas. Therefore, the metabolic behaviour in primary crop is considered sufficiently addressed for the specific intended use on fresh peas (without pods).

Information on the possible impact of plant metabolism on the isomer ratio of mandipropamid was not provided and further investigation would in principle be required. Since guidance on the consideration of isomer ratios in the consumer risk assessment is not yet available, EFSA recommended reconsidering this issue when such guidance is finalised and implemented.

2.1.2. Nature of residues in rotational crops

Mandipropamid 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, the DT_{90} value of mandipropamid ranged up to 240 days (EFSA, 2012). The trigger value of 100 days was exceeded and therefore studies investigating the nature and magnitude of residues in rotational crops are required. No new rotational crops studies were submitted in the present MRL applications.

A confined rotational crop study was assessed in the framework of the EU peer review (EFSA, 2012). Mandipropamid was applied to bare soil at a rate of 900 g a.s./ha and lettuce, radish and wheat were sown at plant-back intervals (PBI) of 29, 58, 120 and 365 days. The major metabolites formed were also identified in primary plant metabolism studies as well as in soil metabolism studies. Based on the results of the confined rotational crop study, it was concluded that metabolism in rotational crops is similar to the pathways observed in primary crops (EFSA, 2012, 2018a).

2.1.3. Nature of residues in processed commodities

The effect of processing on the nature of mandipropamid was investigated in the framework of the EU pesticides peer review (EFSA, 2012). These studies showed that the mandipropamid is hydrolytically stable under standard processing conditions representative of pasteurisation, baking/brewing/boiling and sterilisation.

2.1.4. Methods of analysis in plants

Analytical methods for the determination of mandipropamid residues were assessed during the EU pesticides peer review (EFSA, 2012). The methods based on liquid chromatography with tandem mass spectrometry (LC–MS/MS) are sufficiently validated for residues of mandipropamid in the crops under consideration. The methods allow quantifying residues at or above the LOQ of 0.01 mg/kg for crops belonging to the groups of high water content, high oil content, high acid content and dry matrices. It is noted that the available analytical methods are not stereoselective.

2.1.5. Stability of residues in plants

The storage stability of mandipropamid in plants stored under frozen conditions was investigated in the framework of the EU pesticides peer review (EFSA, 2012). Furthermore, the storage stability of the metabolite SYN 500003 in frozen samples of crops classified as matrices with high water content (potatoes) stored under frozen conditions was investigated in the framework of the MRL review (EFSA, 2018a). Information on the stability of the metabolite SYN 500003 in frozen samples of potato tubers, potato granules/flakes, potato chips and potato wet peel was also submitted with the current application (Netherlands, 2016). It was demonstrated that in matrices relevant for this application, residues were stable for at least 24 months when stored at –20°C.

2.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies and the capabilities of enforcement analytical methods, the MRL review proposed the residue definition for enforcement as: 'mandipropamid (any ratio of constituent isomers)' (EFSA, 2018a). The residue definition for enforcement set in Regulation (EC) No 396/2005 is equivalent to the above mentioned residue definition, although it does not detail that it covers any ratio of constituent isomers.

The residue definition for risk assessment was proposed by the MRL review for fruits and leafy vegetables as: 'mandipropamid (any ratio of constituent isomers)'. The MRL review proposed a tentative residue definition for risk assessment for root crops as: 'sum of mandipropamid and SYN 500003' pending on the submission of toxicological information for hazard characterisation of the metabolite SYN 500003 (EFSA, 2018a).

The tentative residue definition for risk assessment for root crop commodities was used for the root category crops assessed in the present MRL applications. The lack of toxicological data on the metabolite SYN 500003 is not relevant to the intended uses in root crops assessed in the present applications because there is sufficient evidence that SYN 500003 is not present at significant levels in the treated crops if mandipropamid is used according to the intended GAPs.

For the proposed use on fresh peas without pods assessed in this application, EFSA considered the residue definition for risk assessment and enforcement for fruits and leafy vegetables as appropriate.

However, it should be highlighted that EFSA does not recommend extrapolation of the residue definition to the whole category of pulses and oilseeds crops; if in future additional uses in pulses and oilseeds are intended to be authorised, the submission of a metabolism study in a crop belonging to the crop category of pulses and oilseeds will be required, since the conditions tested in metabolism studies in fruit crops and leafy crops do not cover the typical longer vegetation period and the crop characteristics of pulses and oilseeds (dry matter content, fat content).

The same residue definitions for primary crops are also applicable to rotational crops and processed products.

2.2. Magnitude of residues in plants

2.2.1. Magnitude of residues in primary crops

In support of the MRL applications, the applicants submitted residue trials performed in beetroot, radish, broccoli, cauliflower, Brussels sprouts, witloofs/Belgian endives, fresh peas (without pods) and globe artichoke. The root category vegetables (beetroot and radish) were analysed for the parent compound in accordance with in the residue definition for enforcement and the metabolite SYN 500003 included in the residue definition for risk assessment. The samples on leafy category crops (broccoli, cauliflower, Brussels sprouts, witloofs/Belgian endives and globe artichoke) and on peas (in the pulses and oilseeds category crops) were analysed for the parent compound only, in accordance with in the residue definitions for enforcement and risk assessment. According to the assessment of the EMS, the methods of analysis used were sufficiently validated and fit for purpose, with individual LOQs of 0.01 mg/kg for each component of the residue definitions, except for the metabolite SYN 500003 in the residue trials on radish, where the LOQ for SYN 500003 in radish root was 0.005 mg/kg. The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated.

2.2.1.1. Beetroot

In support of the proposed northern Europe (NEU) GAP, eight GAP-compliant residue decline trials were conducted on beetroot in the United Kingdom in 2014 and 2015 (150 g a.s./ha, two applications, 14-day preharvest interval (PHI)) (United Kingdom, 2016). Trials were conducted at geographically independent sites. Applications were performed at growth stages BBCH 30–49, with the exception of one trial where the first application was reported to be at BBCH 15. In one trial, the first application was overdosed (130%) however total application rates were within the acceptable range. Sampling was performed at PHI or PHI–1 day (one trial). Overall, the trials are sufficiently compliant with the GAP.

The residue levels of parent mandipropamid in beetroots ranged from 0.01 to 0.05 mg/kg. Residue levels of the metabolite SYN 500003 in beetroot were below the LOQ of 0.01 mg/kg in all trials (including decline samples taken at up to 20- to 22-day PHI). A conversion factor to recalculate residues according to the residue definition for monitoring to the tentative residue definition for risk assessment for root category vegetables is not proposed because levels of the metabolite SYN 500003 were below the LOQ in all trials.

The number and quality of the trials is sufficient to derive an MRL proposal of 0.1 mg/kg for beetroots on the basis of the intended NEU GAP.

2.2.1.2. Radish

In support of the proposed NEU and southern Europe (SEU) GAP, a total of eight GAP-compliant residue trials were conducted on radish (150 g a.s./ha, two applications, 7-day PHI) (Netherlands, 2016). Four trials were conducted in NEU (northern France and the United Kingdom) in 2013 and 2014, and four trials were conducted in SEU (southern France, Italy and Spain) in 2013 and 2014. First applications were performed at growth stages BBCH 14–49 (NEU trials) or BBCH 43–48 (SEU trials), in compliance with the proposed GAP (BBCH 12–49). Sampling was performed at PHI or PHI–1 day (two trials in SEU). Radish is a minor use crop in the EU and a minimum of four trials are required for each zone. The residue trials are representative of the intended GAP for residues of mandipropamid in radishes at harvest.

The residue levels of parent mandipropamid ranged from 0.02 to 0.15 mg/kg in radish roots. Residue levels of the metabolite SYN 500003 in radish root were below the LOQ of 0.005 mg/kg in all trials (sampling at up to 7-day PHI only). A conversion factor to recalculate residues according to the residue definition for monitoring to the tentative residue definition for risk assessment for root

category vegetables is not proposed because levels of the metabolite SYN 500003 were below the LOQ in all trials.

The NEU and SEU trials data belong to the same statistical population according to the Mann–Whitney U-test, and therefore, the residue trials were combined to derive the MRL proposal. Overall, the number and quality of the trials is sufficient to derive an MRL proposal of 0.3 mg/kg for radishes.

2.2.1.3. Cauliflower

In support of the proposed NEU and SEU GAP on cauliflower, a total of 16 GAP-compliant residue decline trials were conducted on broccoli and cauliflower (150 g a.s./ha, two applications, 14-day PHI) (Netherlands, 2016).

Trials on broccoli were performed in NEU (northern France, Germany and the United Kingdom; four trials) in 2013 and 2014, and in SEU (southern France, Italy and Spain; four trials) in 2013 and 2014. Trials on broccoli were performed with application intervals of 10–12 days and with applications at growth stages BBCH 39–49 (NEU) or 41–48 (SEU), with the exception of one trial SEU where first application was performed at BBCH 19. Sampling was performed at PHI or PHI+1 day (one trial).

Trials on cauliflower were performed in NEU (Germany and the United Kingdom; four trials) in 2013 and 2014, and in SEU (southern France, Italy and Spain; four trials) in 2013 and 2014. Trials on cauliflower were performed with application intervals of 10–11 days and applications at growth stages BBCH 39–47 (NEU) or 31–47 (SEU). Sampling was performed at PHI–1 day (three trials), at PHI or at PHI+1 day (one trial).

Cauliflower is a major crop in the EU and a minimum of eight trials in each zone are required to support the proposed use. In accordance with the EU extrapolation rules (European Commission, 2015), it is possible to combine the results on broccoli and cauliflower to derive a MRL for the whole subgroup of flowering brassica. The NEU and SEU trials data on broccoli and cauliflower belong to the same statistical population according to the Mann–Whitney U-test and therefore the residue trials were combined to derive the MRL proposal. Overall, the number and quality of the trials on broccoli and cauliflower is sufficient to derive an MRL proposal of 0.3 mg/kg for cauliflower.

2.2.1.4. Brussels sprouts

In support of the proposed NEU GAP, four GAP-compliant residue decline trials were conducted on Brussels sprouts in northern France, Hungary, Poland and the United Kingdom in 2014 (150 g a.s./ha, two applications, 14-day PHI) (Netherlands, 2016). Trials were conducted at sites widely distributed in the NEU zone and therefore trials performed over one season are acceptable. Trials were performed with application intervals of 10–12 days at growth stages BBCH 43–48. Overall, the trials are sufficiently GAP compliant. Brussels sprouts are a minor crop in the EU and a minimum of four trials are sufficient to support the proposed use. The number and quality of the trials is sufficient to derive an MRL proposal of 0.2 mg/kg for Brussels sprouts on the basis of the intended NEU GAP.

2.2.1.5. Witloof/Belgian endive

In support of the proposed indoor GAP, four GAP-compliant residue trials were conducted on witloof in northern France in 2014 (0.125 g/m^2, one application, 21-day PHI) (Netherlands, 2016). Residue trials were conducted at the same location. Normally indoor trials conducted at the same facility would be considered to be experimental replicates. However, considering that the environmental conditions in commercial practice for forcing of witloof are controlled within a narrow range, the limited independence of the residue trials locations is a minor deviation. The number and quality of the trials is sufficient to derive an MRL of 0.15 mg/kg for witloofs/Belgian endives on the basis of the proposed indoor GAP.

2.2.1.6. Peas (without pods)

In support of the proposed NEU GAP, 10 residue decline trials were conducted on pea in northern France, Belgium and the United Kingdom in 2014 (150 g a.s./ha, two applications, 14-day PHI) (Netherlands, 2016). Trials were conducted at sites widely distributed in the NEU zone and therefore trials performed over one season are considered acceptable. Trials were performed with an application interval of 13 days (one trial) or 14 days. Sampling was performed by harvesting fresh peas as succulent green seeds at PHI–1 day (three trials), at PHI or at PHI+1 day (one trial).

Residue trials were performed with first applications at growth stages BBCH 51–66 (inflorescence emergence to flowering) and second applications at BBCH 65–77 (flowering to development of fruit), which are later growth stages than the proposed use GAP (applications at BBCH 35–59). Application at

later growth stages may be expected to represent a slightly more critical residue situation. Although the residue trials are not fully compliant with the GAP, they are accepted since for the proposed use on fresh peas without pods, the PHI is expected to be the most critical parameter of the GAP influencing the residue level in the harvested product and the specific growth stage at application may be considered of lesser importance (OECD, 2009). The application interval and PHI in the submitted trials are sufficiently compliant with the GAP, and therefore, although the growth stages at application are not fully compliant, the trials are considered sufficiently representative for the intended GAP. An MRL proposal of 0.3 mg/kg for peas (without pods) was derived on the basis of the proposed NEU GAP.

2.2.1.7. Globe artichoke

In support of the proposed SEU GAP, four GAP-compliant residue decline trials were conducted on globe artichoke in southern France and Spain in 2014 (150 g a.s./ha, two applications, 7-day PHI) (Netherlands, 2016). Trials were conducted at geographically independent sites distributed over the SEU zone and therefore trials performed over one season are considered acceptable. Trials were performed with application intervals of 6–7 days at growth stages BBCH 41–47. Sampling was performed at PHI–1 day (one trial) or at PHI. Globe artichoke is a minor crop in the EU and a minimum of four trials are sufficient to support the proposed use. The number and quality of the trials is sufficient to derive an MRL proposal of 0.3 mg/kg for globe artichokes on the basis of the proposed SEU GAP.

2.2.2. Magnitude of residues in rotational crops

The possible transfer of mandipropamid residues to crops that are grown in crop rotation has been assessed in the EU pesticides peer review (EFSA, 2012). The confined rotational crop study assessed in the framework of the EU peer review demonstrated that no significant residues (residues below 0.01 mg/kg) are expected in succeeding crops (lettuce, radish and wheat) planted in soil treated at 900 g a.s./ha at PBI of 29, 58, 120 or 365 days. Since the maximum annual application rate for the crops under consideration is 900 g a.s./ha per year (i.e. radish maximum 6 applications per year at 150 g a.s./ha), which is equal to the total annual application rate tested in the rotational crop study, it is concluded that no residues are expected, provided that the active substance is applied according to the proposed GAPs.

2.2.3. Magnitude of residues in processed commodities

Specific processing studies for the crops under assessment are not available and are not necessary because the total theoretical maximum daily intake (TMDI) is less than 10% of the ADI.

2.2.4. Proposed MRLs

The available data are sufficient to derive MRL proposals as well as risk assessment values for beetroot, radish, cauliflower, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichoke (see Appendix B.5). For beetroot and radish, the risk assessment values refer to the tentative residue definition for risk assessment for root category crops (EFSA, 2018a). In Section 4, EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumer health risk.

3. Residues in livestock

The commodities beetroot, radish, cauliflower, Brussels sprouts, witloof/Belgian endive, peas without pods and globe artichoke are not used for feed purposes. Pea vines, hay and silage may be used as a fodder crop; however, the EMS-NL clarified that for the intended GAP on fresh peas (without pods), the by-products are not destined for use as animal feed. Therefore the calculation of the livestock dietary exposure and an assessment of a modification of MRLs for food of animal origin is not required in the present MRL applications.

4. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different sub-groups of the EU

population and allows the chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2009).

The toxicological reference value for mandipropamid used in the risk assessment (i.e. ADI value) was derived on the basis of an enantiomeric racemate in the framework of the EU pesticides peer review (EFSA, 2012). Based on the toxicological profile of mandipropamid, the peer review concluded that derivation of an ARfD was not necessary (EFSA, 2012). Considering the toxicological profile of the active substance, a short-term dietary risk assessment was not needed.

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, 2018a). EFSA updated the calculation with the relevant STMR values derived from the residue trials submitted in support of this MRL application for beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/ Belgian endives, peas (without pods) and globe artichokes; and the STMR for cocoa beans derived in an EFSA opinion published after the MRL review (EFSA, 2018b). The risk assessment is based on the assumption that SYN 500003 is of similar toxicity as the parent compound.

The input values used in the exposure calculations are summarised in Appendix D.1.

The estimated long-term dietary intake was in the range from 0.3% to 4.6% of the ADI. The contribution of residues expected in the commodities assessed in this application to the overall long-term exposure is presented in more detail in Appendix B.4.

It is noted by EFSA that the above risk assessment was performed disregarding the possible impact of the isomer ratio due to plant or livestock metabolism. Considering, however, that the active substance consists of enantiomers which are applied as a racemic mixture and that the toxicological studies were carried out according to these specifications (EFSA, 2012), a change of isomer ratio in the residue might, in the worst case situation, lead to a duplication of the toxicological burden of the residue. Since the exposure calculations represent less than 50% of the ADI, EFSA concludes that the potential change of isomer ratios in the final residue will not be of concern for the proposed uses assessed in the framework of these applications. In case future uses of mandipropamid would lead to a higher consumer exposure, further information regarding the impact of plant and livestock metabolism on the isomer ratio might be required.

The risk assessment is affected by non-standard uncertainty related to the lack of hazard characterisation of the metabolite SYN 500003. However, considering that in none of the residue trials submitted in support of the MRL application for beetroots and radishes the metabolite was found in quantifiable concentrations, the lack of a complete toxicological characterisation of SYN 500003 is not considered as a relevant data gap for the present MRL application.

The overall risk might be underestimated due to the contribution of other root and tuber vegetables for which this metabolite might be of relevance (i.e. potatoes, onions and spring onions) if the metabolite SYN 500003 possesses a higher toxicity than the parent.

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

5. Conclusion and Recommendations

The data submitted in support of the present MRL applications were found to be sufficient to derive MRL proposals for all crops under consideration (beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes).

Adequate analytical methods for enforcement are available to control the residues of mandipropamid in plant matrices under consideration.

EFSA concluded that the proposed use of mandipropamid on beetroots, radishes, cauliflowers, Brussels sprouts, witloofs/Belgian endives, peas (without pods) and globe artichokes will not result in a consumer exposure exceeding the toxicological reference value for mandipropamid.

The risk assessment is affected by non-standard uncertainty related to the lack of hazard characterisation of the metabolite SYN 500003. However, considering that the metabolite was not present at significant levels in the residue trials for beetroots and radishes submitted in support of the present MRL application, the lack of a complete toxicological characterisation of SYN 500003 is not considered as a relevant data gap for the crops under consideration.

The risk assessment was performed disregarding the possible impact of plant or livestock metabolism on the isomer ratio of parent compound and its relevant metabolite. EFSA is of the opinion that this issue is not of concern considering the wide margin between the calculated exposure and the ADI.

Based on the risk assessment results, EFSA concluded that the intake of residues resulting from the use of mandipropamid according to the reported agricultural practices is unlikely to present a risk to consumer health.

The MRL recommendations are summarised in Appendix B.5.

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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
CF	conversion factor for enforcement to risk assessment residue definition
CXL	Codex maximum residue limit
DALA	days after last application
DAR	draft assessment report
DAT	days after treatment
DT_{50}	period required for 50% dissipation (define method of estimation)
DT_{90}	period required for 90% dissipation (define method of estimation)
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
HR	highest residue
IEDI	international estimated daily intake
ILV	independent laboratory validation
InChiKey	International Chemical Identifier Key
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LC–MS/MS	liquid chromatography with tandem mass spectrometry
LOQ	limit of quantification
Mo	monitoring
MRL	maximum residue level
MS	Member States
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant-back interval
PHI	preharvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
RA	risk assessment
RD	residue definition
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SC	suspension concentrate
SEU	southern Europe
SMILES	simplified molecular-input line-entry system
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization

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[a]	Pests or group of pests controlled	Preparation		Application				Application rate per treatment			Unit	PHI (days)[d]	Remarks
				Type[b]	Conc. a.s.	Method kind	Range of growth stages & season[c]	Number min–max	Interval between appl. (min)	g a.s./hL min–max	Water L/ha min–max	Rate			
Beetroot	NEU	F	Downy mildew	SC	250 g/L	Foliar spray	See PHI	2 per crop	7	75	Min 200 L	150	g a.s./ha	14	7 day intervals between applications Use as a preventative fungicide at first sign of disease or when environmental conditions suggest that disease pressure will be elevated. Estimated period of use: June–October
Radish	NEU SEU	F	*Peronospora brassicae*	SC	250 g/L	Foliar spray	BBCH 12–49	2	7	25–75	200–600	150	g a.s./ha	7	2 application per crop, Max 6 apps per year (i.e. 3 cycles)
Broccoli	NEU SEU	F	*Peronospora brassicae*	SC	250 g/L	Foliar spray	BBCH 16–49	2	10	18.8–75	200–800	150	g a.s./ha	14	
Cauliflower	NEU SEU	F	*Peronospora brassicae*	SC	250 g/L	Foliar spray	BBCH 16–49	2	10	18.8–75	200–800	150	g a.s./ha	14	
Brussels sprout	NEU	F	*Peronospora brassicae*	SC	250 g/L	Foliar spray	BBCH 16–49	2	10	18.8–75	200–800	150	g a.s./ha	14	
Witloof chicory	EU	I	*Phytophthora cryptogea*	SC	250 g/L	Foliar spray	BBCH 40	1	–	–	1–2 L/m^2	0.125	g/m^2	21	Appl. on the forcing tray in 1–2 L water/m^2

Crop and/or situation	NEU, SEU, MS or country	F G or I[a]	Pests or group of pests controlled	Preparation		Application				Application rate per treatment			Unit	PHI (days)[d]	Remarks
				Type[b]	Conc. a.s.	Method kind	Range of growth stages & season[c]	Number min–max	Interval between appl. (min)	g a.s./hL min–max	Water L/ha min–max	Rate			
Peas (without pods)	NEU	F	*Peronospora brassicae*	SC	250 g/L	Foliar spray	BBCH 35–59	2	14	18.8–75	200–800	150	g a.s./ha	14	
Globe artichoke	SEU	F	*Bremia lactucae*	SC	250 g/L	Foliar spray	BBCH 15–55	2	7	15–50	200–1,000	150	g a.s./ha	7	

GAP: Good Agricultural Practice; MRL: maximum residue level; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; SC: suspension concentrate.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system. SC: Suspension concentrate.
(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. Mammalian toxicology

Other toxicological studies (Regulation (EU) No 283/2013, Annex Part A, point 5.8)

Studies performed on metabolites or impurities	**SYN 500003**
Rat LD_{50} oral	1,049 mg/kg bw (EFSA, 2012)
In vitro studies	–Ames test: negative (±S9) (EFSA, 2012) –Mammalian cell gene mutation test: negative (±S9) –Mammalian chromosome aberration test: positive (–S9)
In vivo studies	–Micronucleus Test (OECD TG 474): negative (plasma analysis: proof of bone marrow exposure)
Potential for genotoxicity	Unlikely to be genotoxic *in vivo*.
Threshold of toxicological concern	Cramer class III

	Value (mg/kg bw per day)	Study	Uncertainty factor
Acceptable daily intake (ADI)	Not sufficient data available.	–	–
Acute reference dose (ARfD)	Not sufficient data available.	–	–

bw: body weight; OECD: Organisation for Economic Co-operation and Development.

B.2. Residues in plants

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

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

Primary crops (available studies)	**Crop groups**	**Crop (s)**	**Application(s)**	**Sampling (DAT)**	**Comment/source**
	Fruit crops	Grapes	Foliar, 6 ×, 143–151 g a.s./ha	0, 14, 28	Radiolabelled a.s.: methoxyphenyl-(U)-^{14}C or chlorophenyl-(U)-^{14}C labelled mandipropamid (Austria, 2006; EFSA, 2012)
			Foliar, 6 ×, 411–464 g a.s./ha	28	
		Tomato	Foliar, 266 + 295 + 147 + 149 g a.s./ha	0, 3, 7, 14, 28	Radiolabelled a.s.: [1-^{14}C]-labelled mandipropamid (Austria, 2006; EFSA, 2012)
	Root crops	Potato	Foliar, 6 ×, 146–158 g a.s./ha	7, 21	Radiolabelled a.s.: methoxyphenyl-(U)-^{14}C or chlorophenyl-(U)-^{14}C labelled mandipropamid (Austria, 2006; EFSA, 2012)
			Foliar, 6 ×, 418–458 g a.s./ha	21	
	Leafy crops	Lettuce	Foliar, 2 ×, 140–160 g a.s./ha	3, 14	Radiolabelled a.s.: methoxyphenyl-(U)-^{14}C or chlorophenyl-(U)-^{14}C labelled mandipropamid (Austria, 2006; EFSA, 2012)

Rotational crops (available studies)	**Crop groups**	**Crop(s)**	**Application(s)**	**PBI (DAT)**	**Comment/Source**
	Root/tuber crops	Radish	Bare soil, 1 × 900 g a.s./ha	29, 58, 120	Radiolabelled a.s.: methoxyphenyl-(U)-^{14}C or chlorophenyl-(U)-^{14}C labelled mandipropamid (Austria, 2006; EFSA, 2012)
	Leafy crops	Lettuce	Bare soil, 1 × 900 g a.s./ha	29, 58, 120, 365	
	Cereal (small grain)	Spring wheat	Bare soil, 1 × 900 g a.s./ha	29, 58, 120, 365	
Processed commodities (hydrolysis study)	**Conditions**		**Stable?**		**Comment/Source**
	Pasteurisation (20 min, 90°C, pH 4)		Yes		EFSA (2012)
	Baking, brewing and boiling (60 min, 100°C, pH 5)		Yes		EFSA (2012)
	Sterilisation (20 min, 120°C, pH 6)		Yes		EFSA (2012)
	Other processing conditions		–		–

Can a general residue definition be proposed for primary crops?	No	EFSA (2012)
Rotational crop and primary crop metabolism similar?	Yes	EFSA (2012)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes	EFSA (2012)
Plant residue definition for monitoring (RD-Mo)	Enforcement residue definition (existing): mandipropamid (Commission Regulation (EU) 2015/845) Enforcement residue definition (proposed by EFSA): mandipropamid (any ratio of constituent isomers) (EFSA, 2018a)	
Plant residue definition for risk assessment (RD-RA)	Fruits and leafy crops: mandipropamid (any ratio of constituent isomers) (EFSA, 2018a) Root crops: sum of mandipropamid and SYN 500003 (tentative, pending the submission of toxicological information on SYN 500003) (EFSA, 2018a)	
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: LC–MS/MS, LOQ 0.01 mg/kg ILV available (EFSA, 2012)	

DAT: days after treatment; a.s.: active substance; PBI: plant-back interval; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.

B.2.1.2. Stability of residues in plants

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/ Source
				Value	Unit		
	High water content	Tomatoes, lettuce, cucumber	−20	24	Months	Parent	EFSA (2018a)
	High water content	Potatoes	−20	32	Months	SYN 500003	EFSA (2018a)
	High oil content	Soya beans	−20	24	Months	Parent	EFSA (2018a)
	Dry/High starch	Wheat	−20	24	Months	Parent	EFSA (2018a)
	High acid content	Grapes	−20	24	Months	Parent	EFSA (2018a)

B.2.2. Magnitude of residues in plants

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

Commodity	Region/ indoor[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[e]
Residue definition for enforcement: mandipropamid (any ratio of constituent isomers) **Residue definition for risk assessment**: sum of mandipropamid and SYN 500003 [tentative, pending on information on the toxicological profile of metabolite SYN 500003]							
Beetroot	NEU	**Mo:** 0.01, 0.02, 0.03, 0.03[f], 0.03, 0.04, 0.04[f], 0.05[f] **RA[g]:** 0.02, 0.03, 0.04, 0.04[f], 0.04, 0.05, 0.05[f], 0.06[f]	Residue trials on beetroot compliant with GAP SYN 500003: 8 × < 0.01 mg/kg (LOQ)	**0.1**	**Mo:** 0.05 **RA:** 0.06	**Mo:** 0.03 **RA:** 0.04	–[h]
Radish	NEU	**Mo:** 0.02, 0.06, 0.08, 0.12 **RA[g]:** 0.03, 0.07, 0.09, 0.13	Residue trials on radish compliant with GAP SYN 500003: 4 × < 0.005 mg/kg (LOQ) NEU and SEU trials data belong to the same statistical population according to the Mann–Whitney U-test and therefore residue trials were combined to derive MRL and risk assessment values	**0.3**	**Mo:** 0.15 **RA:** 0.16	**Mo:** 0.07 **RA:** 0.07	–[h]
	SEU	**Mo:** 0.04, 0.06, 0.07, 0.15 **RA[g]:** 0.05, 0.07, 0.08, 0.16					
Residue definition for enforcement: mandipropamid (any ratio of constituent isomers) **Residue definition for risk assessment**: mandipropamid (any ratio of constituent isomers)							
Cauliflower	NEU	Cauliflower trials: 2 × 0.01*, 0.01, 0.03 Broccoli trials: 0.01*, 0.07, 0.08, 0.14	Residue trials on broccoli and cauliflower compliant with NEU and SEU GAPs for cauliflower NEU and SEU trials data belong to the same statistical population according to the Mann–Whitney U-test and therefore residue trials were combined to derive MRL and risk assessment values	**0.3**	0.17	0.05	–
	SEU	Cauliflower trials: 2 × 0.01*, 2 × 0.06 Broccoli trials: 0.02, 0.08, 0.12, 0.17					–
Brussels sprouts	NEU	0.01*, 0.03, 0.04, 0.08	Residue trials on Brussels sprouts compliant with GAP	**0.2**	0.08	0.04	–
Witloofs/ Belgian endives	Indoor	0.01*, 0.01*, 0.02, 0.07	Residue trials on witloof compliant with indoor GAP for application at forcing stage	**0.15**	0.07	0.02	–
Peas (without pods)	NEU	0.01, 4 × 0.02, 0.04, 2 × 0.05, 0.07, 0.15	Residue trials on peas compliant with GAP	**0.3**	0.15	0.03	–

Commodity	Region/ indoor[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[e]
Globe artichoke	SEU	2 × 0.05, 0.06, 0.12	Residue trials on globe artichoke compliant with GAP	**0.3**	0.12	0.06	–

MRL: maximum residue level; GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; LOQ: limit of quantification.
*: Indicates that the MRL is proposed at the limit of quantification.
(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): Supervised trials median residue according to the residue definition for monitoring.
(e): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.
(f): Peak residue detected in residue decline studies after the minimum PHI defined in the GAP.
(g): Residue values for risk assessment calculated without molecular weight conversion according to the tentative residue definition for risk assessment and rounded to two decimal places.
(h): Conversion factors to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment are not proposed because levels of the metabolite SYN 500003 were below the LOQ in all trials.

B.2.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	No residues are expected in rotational crops.	EFSA (2018a)
Residues in rotational and succeeding crops expected based on field rotational crop study?	Not available and not required.	EFSA (2018a)

B.2.2.3. Processing factors

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

B.3. Residues in livestock

Not relevant to the proposed use GAPs supported in the present MRL applications.

B.4. Consumer risk assessment

ARfD	Not necessary (EFSA, 2012)
ADI	0.15 mg/kg bw per day (EFSA, 2012)
Highest IEDI, according to EFSA PRIMo	4.6% ADI (WHO Cluster diet B) Contribution of crops assessed: Beetroots: < 1% of ADI (all diets) Radishes: < 1% of ADI (all diets) Cauliflowers: < 1% of ADI (all diets) Brussels sprouts: < 1% of ADI (all diets) Witloofs/Belgian endives: < 1% of ADI (all diets) Peas: < 1% of ADI (all diets) Globe artichokes: < 1% of ADI (all diets)
Assumptions made for the calculations	The calculation is based on the median residue levels derived for raw agricultural commodities assessed in the framework of the MRL review and the current application. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation For the root category crops assessed in the MRL Review (potatoes, onions and spring onions), the calculation is based on the median residue levels derived for raw agricultural commodities multiplied by the conversion factor for risk assessment derived in a previous EFSA assessment (EFSA, 2018a)

ARfD: acute reference dose; ADI: acceptable daily intake; bw: body weight; IEDI: international estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; MRL: maximum residue level; GAP: Good Agricultural Practice.

B.5. Recommended MRLs

Code[a]	Commodity	Existing EU MRL[b]/MRL recommended in MRL review[c] (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition (existing): Mandipropamid **Enforcement residue definition** (proposed): Mandipropamid (any ratio of constituent isomers)				
0213010	Beetroots	0.01*/–	**0.1**	The submitted data are sufficient to derive an MRL for the intended NEU use. Risk for consumers unlikely
0213080	Radishes	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL for the intended NEU and SEU uses. Risk for consumers unlikely
0241020	Cauliflowers	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the NEU and SEU use. Risk for consumers unlikely
0242010	Brussels sprouts	0.01*/–	**0.2**	The submitted data are sufficient to derive an MRL proposal for the intended NEU use. Risk for consumers unlikely
0255000	Witloofs/ Belgian endives	0.01*/25[d]	**0.15**	The submitted data are sufficient to derive an MRL proposal for the intended indoor use at forcing stage. Risk for consumers unlikely
0260040	Peas (without pods)	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the intended NEU use. Risk for consumers unlikely
0270050	Globe artichokes	0.01*/–	**0.3**	The submitted data are sufficient to derive an MRL proposal for the intended SEU use. Risk for consumers unlikely

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe.
*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Existing EU MRL Commission Regulation (EU) 2015/845.
(c): MRL recommendations derived in the framework of the MRL review, which have not yet been legally implemented. No MRL recommendations were derived where no GAP was notified to EFSA, indicated by '–'.
(d): The MRL Review included the Codex CXL for mandipropamid in leafy vegetables of 25 mg/kg in the EU MRL proposals for witloofs/Belgian endives; however, the CXL for leafy vegetables is not applicable to witloof and therefore the MRL proposal for witloofs/Belgian endives derived in the MRL Review has to be withdrawn.

Appendix C – Pesticide Residue Intake Model (PRIMo)

Mandipropamid			
Status of the active substance:		Code no.	
LOQ (mg/kg bw):	0.01	Proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw per day):	**0.15**	ARfD (mg/kg bw):	**n.n.**
Source of ADI:	**EFSA**	Source of ARfD:	**EFSA**
Year of evaluation:	**2012**	Year of evaluation:	**2012**

14/11/2018 MRL Review proposals updated for CXLs in witloof and fresh herbs. Updated EFSA_Q_2018_00579, Q-2016-00498, Q-2017-00066.

Chronic risk assessment – refined calculations

	TMDI (range) in % of ADI minimum – maximum
	0 – 5
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity/ group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity/ group of commodities	pTMRLs at LOQ (in % of ADI)
4.6	WHO Cluster diet B	1.3	Lettuce	0.7	Tomatoes	0.6	Wine grapes	0.0
4.3	NL child	1.4	Spinach	0.8	Scarole (broad-leaf endive)	0.6	Kale	0.0
3.6	IT adult	1.4	Lettuce	0.6	Other lettuce and other salad plants	0.4	Spinach	0.0
3.4	FR toddler	2.7	Spinach	0.2	Scarole (broad-leaf endive)	0.2	Tomatoes	0.0
3.1	IE adult	0.8	Other leafy brassica	0.5	Spinach	0.4	Wine grapes	0.0
3.1	ES adult	2.0	Lettuce	0.3	Beet leaves (chard)	0.3	Spinach	0.0
3.0	WHO regional European diet	1.4	Lettuce	0.3	Head cabbage	0.2	Tomatoes	0.0
2.9	WHO cluster diet D	0.7	Chinese cabbage	0.3	Kale	0.3	Kale	0.0
2.9	FR all population	1.4	Wine grapes	0.7	Other lettuce and other salad plants	0.3	Lettuce	0.0
2.9	IT kids/toddler	1.1	Lettuce	0.4	Other lettuce and other salad plants	0.3	Tomatoes	0.0
2.6	NL general	0.5	Spinach	0.5	Lettuce	0.4	Scarole (broad-leaf endive)	0.0
2.6	ES child	1.6	Lettuce	0.3	Spinach	0.3	Beet leaves (chard)	0.0
2.5	DE child	0.8	Spinach	0.4	Table grapes	0.2	Lettuce	0.0
2.4	WHO cluster diet E	0.5	Wine grapes	0.3	Lettuce	0.2	Head cabbage	0.0
2.4	WHO Cluster diet F	1.1	Lettuce	0.2	Chinese cabbage	0.2	Head cabbage	0.0
2.2	SE general population 90th percentile	0.8	Chinese cabbage	0.5	Head cabbage	0.3	Spinach	0.0
1.9	FR infant	1.7	Spinach	0.1	Broccoli	0.1	Potatoes	0.0
1.5	UK vegetarian	0.5	Lettuce	0.3	Wine grapes	0.1	Tomatoes	0.0
1.3	PT General population	0.8	Wine grapes	0.2	Tomatoes	0.1	Table grapes	
1.3	UK Adult	0.4	Lettuce	0.4	Wine grapes	0.1	HOPS (dried),	0.0
0.9	DK child	0.5	Lettuce	0.1	Tomatoes	0.1	Table grapes	0.0
0.9	PL general population	0.3	Head cabbage	0.2	Tomatoes	0.1	Table grapes	0.0
0.8	DK adult	0.5	Wine grapes	0.1	Tomatoes	0.1	Chinese cabbage	0.0
0.8	LT adult	0.3	Head cabbage	0.2	Lettuce	0.1	Tomatoes	
0.8	FI adult	0.3	Lettuce	0.1	Chinese cabbage	0.1	Wine grapes	0.0
0.6	UK Toddler	0.1	Tomatoes	0.1	Spinach	0.1	Table grapes	0.0
0.3	UK Infant	0.1	Tomatoes	0.1	Head cabbage	0.0	Potatoes	0.0

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Mandipropamid is unlikely to present a public health concern.

Acute risk assessment/children – refined calculations	Acute risk assessment/adults/general population – refined calculations

Acute risk assessment is not necessary.

For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.

In the **IESTI 1** calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002); for lettuce a variability factor of 5 was used.

In the **IESTI 2** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variabilty factor of 3.

Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100% of the ARfD.

Unprocessed commodities

No of commodities for which ARfD/ADI is exceeded (IESTI 1): ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 1):** ---			**No of commodities for which ARfD/ADI is exceeded (IESTI 2):** ---		
IESTI 1 *)		**)	**IESTI 2** *)		**)	**IESTI 1** *)		**)	**IESTI 2** *)		**)
Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
No of critical MRLs (IESTI 1) ---						**No of critical MRLs (IESTI 2)** ---					

Processed commodities

No of commodities for which ARfD/ADI is exceeded: ---				**No of commodities for which ARfD/ADI is exceeded:** ---			
		***)				***)	
Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	

*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

**) pTMRL: provisional temporary MRL.

***) pTMRL: provisional temporary MRL for unprocessed commodity.

Conclusion:

As no ARfD was considered necessary, it is concluded that the short-term intake of Mandipropamid residues is unlikely to present a pulbic health concern.

Appendix D – Input values for the exposure calculations

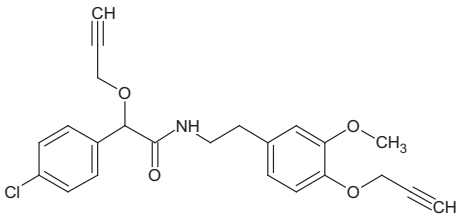
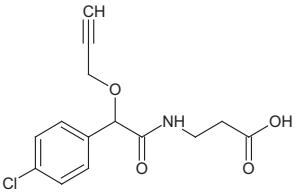
D.1. Consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Residue definition for risk assessment: sum of mandipropamid and SYN 500003 [tentative, pending on information on the toxicological of metabolite SYN 500003]				
Beetroots	0.04	STMR (tentative)	Considering the toxicological profile of the active substance, an acute risk assessment was not needed as the setting of an ARfD for the active substance was considered not necessary (EFSA, 2012). A short-term dietary risk assessment may be required, pending on the submission of toxicological information for the metabolite SYN 500003	
Radishes	0.07	STMR (tentative)		
Potatoes	0.02	STMR (tentative) × CF (EFSA, 2018a)		
Onions	0.02	STMR (CXL, tentative) × CF (EFSA, 2018a)		
Spring onions	0.96	STMR (CXL, tentative) × CF (EFSA, 2018a)		
Residue definition for risk assessment: mandipropamid (any ratio of constituent isomers)				
Cauliflowers	0.01	STMR	Considering the toxicological profile of the active substance, an acute risk assessment was not needed as the setting of an ARfD for the active substance was considered not necessary (EFSA, 2012)	
Brussels sprouts	0.04	STMR		
Witloofs/ Belgian endives	0.02	STMR		
Peas (without pods)	0.03	STMR		
Globe artichokes	0.06	STMR		
Table grapes	0.51	STMR (CXL) (EFSA, 2018a)		
Wine grapes	0.51	STMR (CXL) (EFSA, 2018a)		
Tomatoes	0.34	STMR (EFSA, 2018a)		
Peppers	0.12	STMR (CXL) (EFSA, 2018a)		
Aubergines/ eggplants	0.34	STMR (EFSA, 2018a)		
Cucumbers	0.02	STMR (CXL) (EFSA, 2018a)		
Courgettes	0.04	STMR (CXL) (EFSA, 2018a)		
Melons	0.12	STMR (CXL) (EFSA, 2018a)		
Pumpkins	0.07	STMR (EFSA, 2018a)		
Broccoli	0.44	STMR (CXL) (EFSA, 2018a)		
Head cabbage	1.21	STMR (CXL) (EFSA, 2018a)		
Chinese cabbage	5.65	STMR (CXL) (EFSA, 2018a)		
Kale	5.65	STMR (CXL) (EFSA, 2018a)		
Lamb's lettuces/corn salads	5.65	STMR (CXL) (EFSA, 2018a)		
Lettuces	5.65	STMR (CXL) (EFSA, 2018a)		
Escaroles/ broad-leaved endives	5.65	STMR (CXL) (EFSA, 2018a)		
Cresses and other sprouts and shoots	5.65	STMR (CXL) (EFSA, 2018a)		
Land cresses	5.65	STMR (CXL) (EFSA, 2018a)		

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Roman rocket/ rucola	5.65	STMR (CXL) (EFSA, 2018a)		
Red mustards	5.65	STMR (CXL) (EFSA, 2018a)		
Baby leaf crops (including brassica species)	5.65	STMR (CXL) (EFSA, 2018a)		
Spinaches	5.65	STMR (CXL) (EFSA, 2018a)		
Purslanes	5.65	STMR (CXL) (EFSA, 2018a)		
Chards/beet leaves	5.65	STMR (CXL) (EFSA, 2018a)		
Vine leaves (grape leaves)	5.65	STMR (CXL) (EFSA, 2018a)		
Water cress	5.65	STMR (CXL) (EFSA, 2018a)		
Chervil	5.65	STMR (CXL) (EFSA, 2018a)		
Chives	5.65	STMR (CXL) (FAO, 2008)		
Celery leaves	5.65	STMR (CXL) (FAO, 2008)		
Parsley	5.65	STMR (CXL) (FAO, 2008)		
Sage	5.65	STMR (CXL) (FAO, 2008)		
Rosemary	5.65	STMR (CXL)(FAO, 2008)		
Thyme	5.65	STMR (CXL) (FAO, 2008)		
Basil and edible flowers	5.65	STMR (CXL)(FAO, 2008)		
Laurel/bay leave	5.65	STMR (CXL) (FAO, 2008)		
Tarragon	5.65	STMR (CXL) (FAO, 2008)		
Celery	2.70	STMR (CXL) (EFSA, 2018a)		
Cocoa beans	0.01	STMR (EFSA, 2018b)		
Hops	28.50	STMR (EFSA, 2018a)		

STMR: supervised trials median residue; CXL: Codex maximum residue limit; CF: conversion factor for enforcement to risk assessment residue definition; ARfD: acute reference dose.

Appendix E – Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/ InChiKey[b]	Structural formula[c]
Mandipropamid	(*RS*)-2-(4-chlorophenyl)-N-[3-methoxy-4-(prop-2-ynyloxy)phenethyl]-2-(prop-2-ynyloxy)acetamide Clc1ccc(cc1)C(OCC#C)C(=O)NCCc2ccc(OCC#C)c(OC)c2 KWLVWJPJKJMCSH-UHFFFAOYSA-N	
SYN 500003 R740990 EZA15629 CA 4013 U1 U29b	*N*-{(2*RS*)-2-(4-chlorophenyl)-2-[(prop-2-yn-1-yl)oxy]acetyl}-β-alanine Clc1ccc(cc1)C(OCC#C)C(=O)NCCC(=O)O ZNNAJYNLYSBVRG-UHFFFAOYSA-N	

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 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).
(c): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).