Setting of an import tolerance for mandipropamid in cocoa beans

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

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Syngenta Agro GmbH submitted a request to the competent national authority in Austria to set a maximum residue level (MRL) for the active substance mandipropamid in cocoa beans imported from Nigeria and Cameroon. The data submitted in support of the request were found to be sufficient to derive a MRL proposal of 0.06 mg/kg. Adequate analytical methods for enforcement are available to control the residues of mandipropamid 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 long-term intake of residues resulting from the use of mandipropamid according to the reported agricultural practice is unlikely to present a risk to consumer health. The consumer risk assessment is affected by non-standard uncertainties related to the pending hazard characterisation for the metabolite SYN 500003, which is expected to occur in root crops.

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Correspondence: pesticides.mrl@efsa.europa.eu
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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta Agro GmbH submitted an application to the competent national authority in Austria (evaluating Member State (EMS)) to set import tolerance for the active substance mandipropamid in cocoa beans. 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 11 July 2018. The EMS proposed to establish a maximum residue level (MRL) for cocoa beans imported from Nigeria and Cameroon at the level of 0.06 mg/kg.

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

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under the review of the existing maximum residue levels for mandipropamid according to Article 12 of Regulation (EC) No 396/2005 and the additional data provided by the EMS in the framework of this application, the following conclusions were derived.

The metabolism of mandipropamid following foliar applications showed to be similar in fruit and leafy crops, while in root crops metabolism was more extensive and significant amounts of the metabolite SYN 500003 were observed. Studies investigating the effect of processing on the nature of mandipropamid (hydrolysis studies) demonstrated that the active substance was stable. As the proposed use of mandipropamid is on a permanent crop and for an import application, investigations of residues in rotational crops are not required.

Based on the results of the metabolism studies, the hydrolysis studies and the capability of the currently available enforcement analytical method (not stereoselective), in the framework of the MRL review the residue definition for enforcement was proposed as ‘mandipropamid (any ratio of constituent isomers)’. The residue definition for enforcement in Regulation (EC) No 396/2005 is substantially identical. For risk assessment, the same residue definition as ‘parent compound (any ratio of constituent isomers)’ was established for fruit and leafy crops. The residue definition for risk assessment in root crops was tentatively proposed as ‘sum of mandipropamid and SYN 500003’, pending the submission of toxicological information on the metabolite SYN 500003.

EFSA concluded that for the crop assessed in this application, the metabolism of mandipropamid in primary crops and the possible degradation in processed products have been sufficiently addressed and that the previously derived residue definitions are applicable.

Sufficiently validated analytical methods are available to quantify residues of mandipropamid in cocoa beans. The methods enable quantification of residues at or above 0.01 mg/kg (limit of quantification (LOQ)).

The available residue trials were sufficient to derive a MRL proposal of 0.06 mg/kg for cocoa beans imported from Nigeria and Cameroon.

From two processing studies, tentative processing factors were derived. Because of the limited data set, they are not recommended to be included in Annex VI of Regulation (EC) No 396/2005.

Residues of mandipropamid in rotational crops and commodities of animal origin were not assessed in the framework of this application for use on a permanent crop, which imported beans are not normally fed to livestock.

The toxicological profile of mandipropamid was assessed in the framework of the EU pesticides peer review and the data were sufficient to derive an acceptable daily intake (ADI) of 0.15 mg/kg body weight (bw) per day. An acute reference dose (ARfD) was deemed unnecessary. The data available were not sufficient to define the toxicological profile of the plant metabolite SYN 500003 provisionally included in the residue definition for risk assessment of root crops.

Provided that the active substance contained as an ingredient in plant protection products used in third countries complies with the European Union (EU) approval conditions for the technical material, i.e. it does not contain the impurity SYN545038, which is a suspected genotoxic carcinogen, in higher concentration than 0.1 g/kg, the risk assessment can be based on the toxicological reference values derived in the EU pesticides peer review for parent mandipropamid.

The consumer risk assessment was performed with revision 3 of the EFSA Pesticide Residues Intake Model (PRIMO). No acute risk evaluation was performed as the setting of an ARfD was considered not necessary for mandipropamid. EFSA concluded that the long-term intake of residues resulting from the use of mandipropamid according to the reported agricultural practice is unlikely to present a risk to consumer health. The consumer risk assessment is affected by non-standard uncertainties related to the pending hazard characterisation for the metabolite SYN 500003, which is expected to occur in root crops.
EFSA proposes to amend the existing MRL 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 (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|----------------|------------|------------------------|------------------------|-----------------------|
| **Enforcement residue definition** (existing): Mandipropamid |  |  |  |
| 0640000 | Cocoa beans | 0.02* | 0.06 | The submitted data are sufficient to derive an import tolerance (Nigeria and Cameroon GAP). No MRL value is established in the exporting countries. Residues of mandipropamid in cocoa beans related to the use assessed are unlikely to pose a consumer risk. Due to the pending hazard characterisation for metabolite SYN 500003, which is expected to occur in root crops, the risk assessment is affected by non-standard uncertainties. |

MRL: maximum residue level; GAP: Good Agricultural Practice.
\(^{*}\): Indicates that the MRL is set at the limit of analytical quantification (LOQ).
\(^{(a)}\): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
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Assessment

Mandipropamid is authorised for use on cocoa in Cameroon and marketed in Nigeria, but no maximum residue level (MRL) value is established for cocoa beans in the countries of origin. The detailed description of the use of mandipropamid in Cameroon and Nigeria in cocoa, which is the basis for the current MRL application, is 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)acetam (IUPAC). Mandipropamid is a racemic mixture of a pair of enantiomers and contains a relevant impurity, SYN545038, which is a suspected genotoxic carcinogen. According to the European Union (EU) approval conditions, this impurity was restricted to a maximum concentration of 0.1 g/kg in the technical material (European Commission, 2013). No FAO specifications for mandipropamid were developed so far and the European Food Safety Authority (EFSA) could not verify if the active substance used in the exporting countries complies with this limit for impurity.

The chemical structures of the active substance and its main metabolite 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 spraying against fungi on greenhouse crops of melon, tomato, lettuce and cucumber and field crops of potato, tomato, melon, cucumber, lettuce and grapes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (2012). Mandipropamid was approved in accordance with Regulation (EC) No 1107/2009 for the use as a fungicide on 1 August 2013.

The EU MRLs for mandipropamid are established in Annex III of Regulation (EC) No 396/2005. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 has been performed (EFSA, 2018b); the proposed modifications have not yet been implemented in the EU MRL legislation.

In accordance with Article 6 of Regulation (EC) No 396/2005, Syngenta Agro GmbH submitted an application to the competent national authority in Austria (evaluating Member State (EMS)) to set a MRL for the active substance mandipropamid in cocoa beans imported from Nigeria and Cameroon. 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 EFSA on 11 July 2018. The EMS proposed to set the MRL for cocoa beans at 0.06 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 (Austria, 2018), the DAR and its addendum (Austria, 2006, 2012) prepared under Directive 91/414/EEC, the 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) as well as the EFSA opinion on the review of the existing maximum residue levels for mandipropamid according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2018b).

For this application, the data requirements established in Regulation (EU) No 544/2011 and the guidance documents applicable at the date of submission of the application to the EMS are applicable (European Commission, 1997a-g, 2000, 2010a,b, 2017; OECD, 2011, EFSA, 2018a). 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.

1 Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32.
2 Commission Implementing Regulation (EU) No 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. OJ L 62, 6.3.2013, p. 13–16.
3 Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.
4 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.
5 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.
6 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.
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.

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

1. **Residues in plants**

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

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

The metabolism of mandipropamid after foliar applications was investigated in fruit, leafy and root crops in the framework of the EU pesticides peer review (EFSA, 2012). The metabolism of mandipropamid in fruit and leafy crops showed to be similar with the parent compound being the major component of the residues (53–94% of total radioactive residue (TRR)). In root crops, metabolism was more extensive, with the metabolite SYN 500003 present in significant percentage (7–14% TRR).

For the crop under assessment, EFSA concluded that the metabolism in primary crops is sufficiently addressed. Nevertheless, 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 available (EFSA, 2018b).

1.1.2. **Nature of residues in rotational crops**

Not relevant for a permanent crop and for an import application.

1.1.3. **Nature of residues in processed commodities**

Studies investigating the nature of residues in processed commodities were assessed in the framework of the EU pesticides peer review (EFSA, 2012). Mandipropamid was stable to hydrolysis under standard conditions of pasteurisation, baking/brewing/boiling and sterilisation.

1.1.4. **Methods of analysis in plants**

Mandipropamid can be enforced with a limit of quantification (LOQ) of 0.01 mg/kg in high water content, high acid content, high oil content and dry commodities (EFSA, 2018b). In the framework of this application, further validation data for the liquid chromatography with tandem mass spectrometry (LC–MS/MS) (QuEChERS) method in several matrices, including cocoa beans, were provided (Austria, 2018). It is noted that the analytical methods available are not stereo-selective.

1.1.5. **Stability of residues in plants**

Mandipropamid was demonstrated to be stable for a period of 24 months at –20°C in high oil content matrices to which group the crop under assessment belongs (EFSA, 2018b).

1.1.6. **Proposed residue definitions**

Based on the results of the metabolism studies, the hydrolysis studies and the capability of the currently available enforcement analytical methods (see Section 1.1.4), in the framework of the MRL review the residue definition for enforcement was proposed as ‘mandipropamid (any ratio of constituent isomers)’.

The residue definition for enforcement in Regulation (EC) No 396/2005 is substantially identical as the above-mentioned, although it does not detail that it covers any ratio of its constituents.

For risk assessment, the same residue definition as parent compound (any ratio of constituent isomers) was established for fruit and leafy crops, whereas the residue definition for risk assessment in root crops was proposed as ‘sum of mandipropamid and SYN 500003’. The residue definition for root crops is tentative pending the submission of toxicological information on the metabolite SYN 500003 (EFSA, 2012, 2018b).
1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the MRL application, the applicant submitted eight decline residue trials performed in Ivory Coast and Ghana over a single season on cocoa trees compliant with the Nigerian and Cameroon good agricultural practice (GAP). The results obtained from these West Africa cocoa production areas were combined in a single data set, since cocoa trees are expected to grow only in regions with similar climatic conditions; furthermore, a statistical analysis was performed (Mann–Whitney U-Test; FAO, 2016) that demonstrated that the data belong to a similar population. The data are sufficient to derive a MRL proposal for cocoa beans, which is a major crop according to the EU crop classification (European Commission, 2017).

According to the EMS, samples of fermented dried beans were analysed for the parent compound with a sufficiently validated analytical method and stored for up to 6 months, under conditions for which integrity was demonstrated (Austria, 2018).

1.2.2. Magnitude of residues in rotational crops

Not relevant for the current assessment (see Section 1.1.2).

1.2.3. Magnitude of residues in processed commodities

Two processing studies on cocoa beans were provided. The unprocessed cocoa beans were derived from residue trials performed with a higher application rate compared to the GAP reported in Appendix A (about five times the application rate and a shorter preharvest interval (PHI) of 3 days). A reduction of mandipropamid residues was observed in roasted nibs, cocoa butter and powder and chocolate. Due to the limited data set, indicative processing factors were derived.

1.2.4. Proposed MRLs

The submitted data are sufficient to derive a MRL proposal of 0.06 mg/kg for the reported use on cocoa in Nigerian and Cameroon as well as risk assessment values. According to the EMS, no MRL value is established in the exporting countries (Austria, 2018).

2. Residues in livestock

Not relevant. Cocoa beans are not used as feed items.

3. Consumer risk assessment

The consumer risk assessment was performed with revision 3 of the EFSA Pesticide Residues Intake Model (PRiMo). This exposure assessment model contains the relevant European food consumption data for different subgroups of the EU population (EFSA, 2018a).

The estimated exposure was then compared with the acceptable daily intake (ADI) of 0.15 mg/kg body weight (bw) per day derived for mandipropamid. An acute reference dose (ARfD) was deemed unnecessary (European Commission, 2013). The plant metabolite SYN 500003 is relevant for root crops and it was not identified in the rat metabolism (EFSA, 2012). The data available were not sufficient to derive toxicological reference values for the consumer risk assessment and further information has been requested (EFSA, 2012, 2018b).

In the framework of the MRL review, a comprehensive chronic exposure assessment was performed, taking into account the existing uses and acceptable Codex MRLs. To address the lack of information as regards the amount of metabolite SYN 500003 occurring in root crops, a conversion factor of 2 was applied to root crops, based on the levels of mandipropamid and SYN 500003 from residue trials on potatoes (EFSA, 2018b). This exposure assessment was updated with the median residue value (STMR) derived for cocoa beans from the residue trials submitted. The input values used for the dietary exposure calculation are summarised in Appendix D. Considering the fact that the hazard characterisation for metabolite SYN 500003 is not finalised, the risk assessment shall be regarded as indicative. However, in cocoa beans the metabolite is not expected to occur.
No long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated chronic intake accounted for up to 5% of the ADI, with very low maximum contribution of the residues on the crop under consideration (0.004% of ADI).

Due to the high margin of safety observed in the consumer risk assessment, the possible impact of each individual mandipropamid enantiomer was considered acceptable (EFSA, 2012, 2018b).

An acute risk assessment was not necessary since no ARfD was derived for the active substance. 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 a MRL proposal for cocoa beans imported from Nigeria and Cameroon.

EFSA concluded that the long-term intake of residues resulting from the use of mandipropamid according to the reported agricultural practice is unlikely to present a risk to consumer health. The consumer risk assessment is affected by non-standard uncertainties related to the pending hazard characterisation for the metabolite SYN 500003, which is expected to occur in root crops.

The MRL recommendation is summarised in Appendix B.4.

References

Austria, 2006. Draft Assessment Report (DAR) on the active substance mandipropamid prepared by the rapporteur Member State Austria in the framework of Directive 91/414/EEC, November 2006. Available online: www.efsa.europa.eu

Austria, 2012. Final Addendum to Draft Assessment Report on mandipropamid, compiled by EFSA, July 2012. Available online: www.efsa.europa.eu

Austria, 2018. Evaluation report on the setting of an import tolerance for mandipropamid in cocoa. June 2018, 36 pp.

EFSA (European Food Safety Authority), 2012. Conclusion on the peer review of the pesticide risk assessment of the active substance mandipropamid. EFSA Journal 2012;10(11):2935, 76 pp. https://doi.org/10.2903/j.efsa.2012.2935.

EFSA (European Food Safety Authority), Brancato A, Brocca D, Ferreira L, Greco L, Jarrah S, Leuschner R, Medina P, Miron I, Nougadere A, Pedersen R, Reich H, Santos M, Stanek A, Tarazona J, Theobald A and Villamar-Bouza L, 2018a. Guidance document on use of EFSA Pesticide Residue Intake Model (EFSA PRIMo revision 3). EFSA Journal 2018;16(1):5147, 50 pp. https://doi.org/10.2903/j.efsa.2018.5147

EFSA (European Food Safety Authority), Brancato A, Brocca D, De Lentdecker C, Ferreira L, Greco L, Jarrah S, Kardassi D, Leuschner R, Lythgo C, Medina P, Miron I, Molnar T, Nougadere A, Pedersen R, Reich H, Sacchi A, Santos M, Stanek A, Sturma J, Tarazona J, Theobald A, Vagenende B, Verani A and Villamar-Bouza L, 2018b. Review of the existing maximum residue levels for mandipropamid according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2018;16(5):5284, 46 pp. https://doi.org/10.2903/j.efsa.2018.5284

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

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

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

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

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

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

European Commission, 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VII/95-rev. 5, 22 July 1997. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010, finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23–24 March 2010.

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

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

European Commission, 2010b. Residue analytical methods. For post-registration control. SANCO/825/00-rev. 8.1, 16 November 2010.
European Commission, 2013. Final Review report for the active substance mandipropamid finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 1 February 2013 in view of the approval of mandipropamid as active substance in accordance with Regulation (EC) No 1107/2009. SANCO/12991/2012 rev 4, 1 February 2013, revised in 23 March 2018.

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

FAO (Food and Agriculture Organization of the United Nations), 2016. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed. Pesticide Residues. 3rd Edition. FAO Plant Production and Protection Paper 225, 298 pp.

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

**Abbreviations**

a.s. active substance  
ADI acceptable daily intake  
AR applied radioactivity  
ARfD acute reference dose  
BBCH growth stages of mono- and dicotyledonous plants  
bw body weight  
CF conversion factor for enforcement to risk assessment residue definition  
DALA days after last application  
DAR draft assessment report  
DAT days after treatment  
EMS evaluating Member State  
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  
LC liquid chromatography  
LOQ limit of quantification  
MRL maximum residue level  
MS/MS tandem mass spectrometry detector  
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  
QuEChERS Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)  
RA risk assessment  
RAC raw agricultural commodity  
RD residue definition  
RMS rapporteur Member State  
SANCO Directorate-General for Health and Consumers  
SEU southern Europe  
SMILES simplified molecular-input line-entry system  
STMR supervised trials median residue  
TRR total radioactive residue  
WG water-dispersible granule
### Appendix A – Summary of reported GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, MS or country | Pests or Group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|--------------------------|-----------------------------------|-------------|-------------|-------------------------------|------------|---------|
|                       |                          |                                   | Type(b)     | Conc. a.s.  | Method kind                   | Range of growth stages & season(c) | Number min-max | Interval between application (min) | g a.s./hL min-max | Water L/ha min-max | Rate | Unit | |
| Cocoa bean            | CM                       | F Black pod disease               | WG          | 125 g/kg   | Foliar                        | 4–6        | 14–21 days                      | 25          | 90 g/ha       | 14    | 30 g product/15 L water (Knapsack sprayers) |
|                       | NG                       | F Black pod disease               | WG          | 125 g/kg   | Foliar                        | 4–6        | 21 days                         | 25          | 90 g/ha       | 14    |

MRL: maximum residue level; GAP: Good Agricultural Practice; NEU: northern European Union; SEU: southern European Union; MS: Member State; NG: Nigeria; CM: Cameroon; a.s.: active substance; WG: water-dispersible granule.

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

(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide 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 (DALA) | Comment/Source |
|-----------------------------------|-------------|---------|----------------|----------------|----------------|
| Fruit crops                       |             |         |                |                |                |
|                                   |             | Grapes  | Foliar, 6 × 143–150 g/ha | 0, 14, 28 | Radiolabelled a.s.: chlorophenyl-14C- or methoxyphenyl-14C-mandipropamid (EFSA, 2012) |
|                                   |             |         | Foliar, 6 × 411–464 g/ha | 28 |                |
|                                   |             | Tomato  | Foliar, 4 × (149–276) g/ha | 0, 3, 7, 14, 28 | Radiolabelled a.s.: 1-C14-mandipropamid (EFSA, 2012) |
| Root crops                        |             |         |                |                |                |
|                                   |             | Potato  | Foliar, 6 × 46–158 g/ha | 7, 21 | Radiolabelled a.s.: chlorophenyl-14C- or methoxyphenyl-14C-mandipropamid (EFSA, 2012) |
|                                   |             |         | Foliar, 6 × 418–458 g/ha |                |                |
| Leafy crops                       |             | Lettuce | Foliar, 2 × 156–160 g/ha | 3, 14 | Radiolabelled a.s.: chlorophenyl-14C- or methoxyphenyl-14C-mandipropamid (EFSA, 2012) |
|                                   |             |         | Foliar, 2 × 418–458 g/ha |                |                |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
|--------------------------------------|-------------|---------|----------------|-----------|----------------|
|                                     | Root/tuber crops | Radish | Bare soil, 1 × 900 g/ha | 29, 58, 120, 365 | Radiolabelled a.s.: chlorophenyl-14C- or methoxyphenyl-14C-mandipropamid (EFSA, 2012) |
|                                     | Leafy crops  | Lettuce | Bare soil, 1 × 900 g/ha | 29, 58, 120, 36 |                |
|                                     | Cereal (small grain) | Spring wheat | Bare soil, 1 × 900 g/ha | 29, 58, 120, 36 |                |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|---------|----------------|
|                                          | Pasteurisation (20 min, 90°C, pH 4) | yes | Radiolabelled a.s.: chlorophenyl-14C- or methoxyphenyl-14C-mandipropamid (EFSA, 2012) |
|                                          | Baking/brewing/boiling (60 min, 100°C, pH 5) | yes |                |
|                                          | Sterilisation (20 min, 120°C, pH 6) | yes |                |
Can a general residue definition be proposed for primary crops?

| Residue pattern in processed commodities similar to residue pattern in raw commodities? |
| No | EFSA (2012) |
| Yes | EFSA (2012) |

Plant residue definition for monitoring (RD-Mo)

- Plant residue definition for risk assessment (RD-RA)

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

| Matrices with high water content, high oil content, high acid content and dry matrices: LC–MS/MS, LOQ 0.01 mg/kg ILV available (EFSA, 2012) |

B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category | Commodity | T (°C) | Stability period | Compounds covered | Comment/Source |
|-----------------------------------|----------|-----------|--------|-----------------|------------------|----------------|
| High water content                | Tomatoes, Lettuces, Cucumbers, Potatoes | -20 | 24 Months | Parent | EFSA (2018b) |
| High water content                | Potatoes | -20 | 32 Months | SYN 500003 | EFSA (2018b) |
| High oil content                  | Soyabees | -20 | 24 Months | Parent | EFSA (2018b) |
| Dry / High starch                 | Wheat | -20 | 24 Months | Parent | EFSA (2018b) |
| High acid content                 | Grapes | -20 | 24 Months | Parent | EFSA (2018b) |
### B.1.2. Magnitude of residues in plants

#### B.1.2.1. 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\(^{(d)}\) |
|--------------|--------------------------|---------------------------------------------------------------|-----------------|------------------------|---------------------|----------------------|----------|
| Cocoa beans  | NG, CM                   | < 0.01; 4 × 0.01; 0.02; 2 × 0.03                              | Residue trials conducted on cocoa trees in Ivory Coast and Ghana compliant with the GAP MRL\(_{OECD}\) = 0.05 (unrounded) | 0.06                   | 0.03                 | 0.01                 | NA       |

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

\(^{(a)}\): 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. NA, not applicable.
### B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Not triggered | Imported crop |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | Not triggered | Imported crop |

### B.1.2.3. Processing factors

| Processed commodity                  | Number of valid studies\(^{(a)}\) | Processing Factor (PF) | CF\(_P^{(b)}\) | Comment/Source |
|--------------------------------------|----------------------------------|------------------------|----------------|----------------|
|                                      |                                  | Individual values       | Median PF      |                |
| Cacao bean, roasted nibs             | 2                                | 0.40; 0.56              | 0.48           | N/A            | Tentative\(^{(c)}\) |
| Cacao beans, powder                  | 2                                | 0.40; 0.56              | 0.48           | N/A            | Tentative\(^{(c)}\) |
| Cocoa bean, butter                   | 2                                | 0.40; 0.66              | 0.53           | N/A            | Tentative\(^{(c)}\) |
| Cocoa bean, chocolate                | 2                                | 0.50; 0.70              | 0.61           | N/A            | Tentative\(^{(c)}\) |

\(^{(a)}\): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).  
\(^{(b)}\): Conversion factor for risk assessment in the processed commodity. N/A, not applicable.  
\(^{(c)}\): A tentative PF is derived based on a limited data set.

### B.2. Residues in livestock

Not relevant.

### B.3. Consumer risk assessment

| ARfD                                  | Not necessary (European Commission, 2013) |
|---------------------------------------|-------------------------------------------|
| ADI                                   | 0.15 mg/kg bw per day (European Commission, 2013) |
| Highest IEDI, according to EFSA PRIMo 3 | 5% of ADI (NL toddler diet)               |
| Contribution of the crop assessed:    | Cocoa beans: 0.004% of ADI (Spanish diet) |
| Assumptions made for the calculations | The calculation is based on the median residue levels derived for raw agricultural cocoa beans and the median residue values derived in the framework of the MRL review. A tentative conversion factor for risk assessment of 2 was applied to root crops. The contributions of commodities where no GAP and safe Codex MRLs was reported in the framework of the MRL review were not included in the calculation |

ARfD: acute reference dose; bw: body weight; ADI: acceptable daily intake; IEDI: international estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; MRL: maximum residue level; GAP: Good Agricultural Practice.
### B.4. Recommended MRLs

| Code\(^{(a)}\) | Commodity   | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|----------------|-------------|-------------------------|-------------------------|------------------------|
| 0640000        | Cocoa beans | 0.02*                   | 0.06                    | The submitted data are sufficient to derive an import tolerance (Nigeria and Cameroon GAP). No MRL value is established in the exporting countries. Residues of mandipropamid in cocoa beans related to the use assessed are unlikely to pose a consumer risk. Due to the pending hazard characterisation for metabolite SYN 500003, which is expected to occur in root crops, the risk assessment is affected by non-standard uncertainties. |

**Enforcement residue definition** (existing): Mandipropamid

**Enforcement residue definition** (proposed): Mandipropamid (any ratio of constituent isomers)

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MRL: maximum residue level; GAP: Good Agricultural Practice.

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

\(^{(a)}\): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
### Appendix C – Pesticide Residue Intake Model (PRIMo)

**Mandipropamid**

| ADI (mg/kg bw/day) | ARfD (mg/kg bw): |
|-------------------|-----------------|
| Not necessary     |                 |

#### Toxicoological reference values

- **LOQs (mg/kg)** range from: 0.02 to: 0.15
- **Details – chronic risk**
  - ADI (mg/kg bw/day): 0.02
  - ARfD (mg/kg bw): 0.02

#### Input values

- Source of ADI: 2013
- Year of evaluation: 2013
- EFSA PRIMo revision 3.1; 2018/08/18

#### Chronic risk assessment: JMPR methodology (IEDI/TMDI)

| Commodity/ group of commodities | Exposure resulting from commodities not under assessment | No of diets exceeding the ADI: --- |
|---------------------------------|--------------------------------------------------------|----------------------------------|
| Source:                        | Calculated exposure (µg/kg bw per diet)                  |                                    |
|                                | (in % of ADI)                                           |                                    |

#### Conclusion:

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

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

### IESTI new calculations:

The calculation is performed with the MRL, and the peeling/processing factor (PF) taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations, a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.

Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.

### Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)

#### Results for children

| Commodity | No. of commodities for which ARfD/ADI is exceeded (IESTI) | Highest % of ARfD/ADI | MRL for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|----------------------------------------------------------|-----------------------|-------------------|---------------------|

#### Results for adults

| Commodity | No. of commodities for which ARfD/ADI is exceeded (IESTI) | Highest % of ARfD/ADI | MRL for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|----------------------------------------------------------|-----------------------|-------------------|---------------------|

### Total number of commodities found exceeding the ARfD/ADI in children and adult diets (IESTI new calculation)

#### Results for children

| Commodity | No. of commodities for which ARfD/ADI is exceeded (IESTI new) | Highest % of ARfD/ADI | MRL for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|---------------------------------------------------------------|-----------------------|-------------------|---------------------|

#### Results for adults

| Commodity | No. of commodities for which ARfD/ADI is exceeded (IESTI new) | Highest % of ARfD/ADI | MRL for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------|---------------------------------------------------------------|-----------------------|-------------------|---------------------|

### Conclusion:

Setting of an import tolerance for mandipropamid in cocoa beans
Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

Not applicable.

D.2. Consumer risk assessment

| Commodity               | Chronic risk assessment | Comment                                      |
|-------------------------|-------------------------|----------------------------------------------|
|                         | Input value (mg/kg)     |                                              |
| Potatoes                | 0.02                    | STMR × CF (EFSA, 2018b)                      |
| Onions                  | 0.02                    | STMR × CF (EFSA, 2018b)                      |
| Spring onions           | 0.96                    | STMR × CF (EFSA, 2018b)                      |
| Table grapes            | 0.51                    | STMR (EFSA, 2018b)                          |
| Wine grapes             | 0.51                    | STMR (EFSA, 2018b)                          |
| Tomatoes                | 0.34                    | STMR (EFSA, 2018b)                          |
| Peppers                 | 0.12                    | STMR (EFSA, 2018b)                          |
| Aubergines/eggplants    | 0.34                    | STMR (EFSA, 2018b)                          |
| Cucumbers               | 0.02                    | STMR (EFSA, 2018b)                          |
| Courgettes              | 0.04                    | STMR (EFSA, 2018b)                          |
| Melons                  | 0.12                    | STMR (EFSA, 2018b)                          |
| Pumpkins                | 0.07                    | STMR (EFSA, 2018b)                          |
| Broccoli                | 0.44                    | STMR (EFSA, 2018b)                          |
| Head cabbage            | 1.21                    | STMR (EFSA, 2018b)                          |
| Chinese cabbage         | 5.65                    | STMR (EFSA, 2018b)                          |
| Kale                    | 5.65                    | STMR (EFSA, 2018b)                          |
| Lamb’s lettuces/com salads | 5.65                | STMR (EFSA, 2018b)                          |
| Lettuces                | 5.65                    | STMR (EFSA, 2018b)                          |
| Escaroles/broad-leaved endives | 5.65      | STMR (EFSA, 2018b)                          |
| Cresses and other sprouts and shoots | 5.65 | STMR (EFSA, 2018b)                          |
| Land cresses            | 5.65                    | STMR (EFSA, 2018b)                          |
| Roman rocket/rucola     | 5.65                    | STMR (EFSA, 2018b)                          |
| Red mustards            | 5.65                    | STMR (EFSA, 2018b)                          |
| Baby leaf crops         | 5.65                    | STMR (EFSA, 2018b)                          |
| Spinaches               | 5.65                    | STMR (EFSA, 2018b)                          |
| Purslanes               | 5.65                    | STMR (EFSA, 2018b)                          |
| Chards/beet leaves      | 5.65                    | STMR (EFSA, 2018b)                          |
| Vine leaves (grape leaves) | 5.65                | STMR (EFSA, 2018b)                          |
| Water cress             | 5.65                    | STMR (EFSA, 2018b)                          |
| Witloof                 | 5.65                    | STMR (EFSA, 2018b)                          |
| Chervil                 | 5.65                    | STMR (EFSA, 2018b)                          |
| Chives                  | 5.15                    | STMR (EFSA, 2018b)                          |
| Celery leaves           | 5.15                    | STMR (EFSA, 2018b)                          |
| Parsley                 | 5.15                    | STMR (EFSA, 2018b)                          |
| Sage                    | 5.15                    | STMR (EFSA, 2018b)                          |
| Rosemary                | 5.15                    | STMR (EFSA, 2018b)                          |
| Thyme                   | 5.15                    | STMR (EFSA, 2018b)                          |
| Basil and edible flowers | 5.15                 | STMR (EFSA, 2018b)                          |

Risk assessment residue definition: sum of mandipropamid and metabolite SYN 500003 [tentative; pending the submission of toxicological information on SYN 500003]
### Commodity

| Commodity          | Input value (mg/kg) | Comment                  |
|--------------------|---------------------|--------------------------|
| Laurel/bay leave   | 5.15                | STMR (EFSA, 2018b)       |
| Tarragon           | 5.15                | STMR (EFSA, 2018b)       |
| Celery             | 2.70                | STMR (EFSA, 2018b)       |
| **Cocoa beans**    | 0.01                | STMR                     |
| Hops               | 28.50               | STMR (EFSA, 2018b)       |

STMR: supervised trials median residue; CF: conversion factor.
## Appendix E – Used compound codes

| Code/trivial name | IUPAC name/SMILES notation/InChiKey<sup>a</sup> | Structural formula<sup>b</sup> |
|-------------------|-----------------------------------------------|-------------------------------|
| mandipropamid     | (RS)-2-(4-chlorophenyl)-N-[3-methoxy-4- (prop-2-ynyloxy)phenethyl]-2-(prop-2-ylynoxy)acetamide Clc1ccc(cc1)C(OCC#C)C(=O)NCCc2ccc (OCC#C)c(OC)c2 KWLVWPJKMJCSH-UHFFFAOYSA-N | ![Structural formula](image1.png) |
| SYN 500003        | N-((2RS)-2-(4-chlorophenyl)-2-[(prop-2-yn-1-yl)oxy]acetyl]-l-alanine Clc1ccc(cc1)C(OCC#C)C(=O)NCc1ccc(OCC(=O)C)c1 ZNNAJYNLSBVRG-UHFFFAOYSA-N | ![Structural formula](image2.png) |
| SYN 545038        | (2RS)-2-(4-chlorophenyl)-N-2-[[2-chloroprop-2-en-1-yl]oxy]-3-methoxyphenyl)ethyl]-2-(prop-2-yn-1-yloxy)acetamide Clc1ccc(cc1)C(OCC#C)C(=O)NCCc1ccc(OCC(=O)C)c1 MDGSWMXCTICBST-UHFFFAOYSA-N | ![Structural formula](image3.png) |

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

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

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