Adopted: 18 December 2023

DOI: 10.2903/j.efsa.2024.8546

efsa JOURNAL

REASONED OPINION

Modification of the existing maximum residue level for clopyralid in honey

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Corteva Agriscience International Sàrl submitted a request to the competent national authority in Finland to modify the existing maximum residue levels (MRLs) for the active substance clopyralid in honey. The data submitted in support of the request were found to be sufficient to derive MRL proposals for honey. Adequate analytical methods for enforcement are available to control the residues of clopyralid (including potential conjugates) in honey at the validated limit of quantification (LOQ) of 0.001 mg/kg. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of clopyralid residues in honey, resulting from the authorised use of clopyralid on oilseed rape notified in the present MRL assessment, is unlikely to present a risk to consumer health.

KEYWORDS

clopyralid, consumer risk assessment, honey, MRL, pesticide

CONTENTS

SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, Corteva Agriscience International Sàrl submitted an application to the competent national authority in Finland (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance clopyralid in honey.

The application, alongside the dossier containing the supporting data in IUCLID format, was submitted through the EFSA Central Submission System on 25 July 2022. The appointed EMS Finland assessed the dossier and declared its admissibility on 5 October 2022. Subsequently, following the implementation of the EFSA's confidentiality decision, the non-confidential version of the dossier was published by EFSA and a public consultation was launched on the dossier. The consultation aimed to consult stakeholders and the public on the scientific data, studies and other information part of, or supporting, the submitted application, in order to identify whether other relevant scientific data or studies are available. The consultation ran from 13 February 2023 to 6 March 2023. No additional data or comments were submitted in the framework of the consultation.

At the end of the commenting period, the EMS proceeded with drafting the 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 9 March 2023. To accommodate clopyralid residues in honey from the authorised use on oilseed rape (identified by the applicant as the critical GAP for residues in honey), the EMS proposed to raise the existing MRLs in honey from the limit of quantification (LOQ) of 0.05 to 0.15 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified data gaps which needed further clarification and requested the EMS to address them. On 28 September 2023, the applicant provided the requested information in an updated IUCLID dossier. The additional information was duly considered by the EMS who submitted a revised evaluation report to EFSA on 30 September 2023, which replaced the previously submitted evaluation report.

Based on the conclusions derived by EFSA in the framework of Regulation (EC) No 1107/2009, the data evaluated under previous MRL assessments and the additional data provided by the EMS in the framework of this application, the following conclusions are derived.

The metabolism of clopyralid following foliar treatment was investigated in crops belonging to the groups of leafy crops, cereals, pulses/oilseeds and root crops. Regarding pulses/oilseeds and root crops, two new metabolism studies have been submitted within the current application. The results of new studies showed that a significant part of the residues corresponds to less polar compounds, not properly identified, but which are readily converted to free parent after basic hydrolysis. This was also the finding of the cereal study assessed in a previous application. Therefore, it can be concluded that clopyralid (free, conjugated or any forms readily converted to free clopyralid after basic hydrolysis) is the only relevant compound in the different investigated crops and thus is the main residue to which bees are exposed. Nevertheless, the current wording of the existing residue definition for enforcement (clopyralid) might need to be reassessed in the framework of the MRL review to better reflect the nature of clopyralid residues in plants. A proposal as 'clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid)' was already reported in previous assessments.

The rotational crop metabolism studies which were assessed in the framework of the EU pesticides peer review allowed to conclude that the same metabolic pattern is expected across all rotational crops and that this corresponds with the findings in primary crops. A new field rotational crop study submitted under the present assessment indicated possible residue uptakes in cereals (grain and straw) at all investigated plant back intervals (PBIs), as well as in root crops (roots and tops) and in aerial parts of oilseed plants (only at short PBIs). Regarding leafy crops or oilseed (seed parts), the available results indicate that no residues uptakes are expected. Data indicate that clopyralid residues might be present in rotational crops foraged by bees. However, the potential residues from rotational crops are not expected to significantly impact the value of the MRL for honey assessed in the present opinion.

Studies investigating the effect of processing on the nature of clopyralid (hydrolysis studies) demonstrated that the active substance is stable under standard processing conditions.

In the absence of specific metabolism studies on honey, the studies investigating the nature of residues in primary and rotational crops and studies investigating the degradation of the active substance during pasteurisation were considered to derive conclusions on the nature of clopyralid in honey. The nature of residue in plants has been sufficiently depicted to support the present MRL request for honey. The residue definition for honey for monitoring (RD-Mo) and risk assessment (RD-RA) is proposed as 'clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid)'. The wording of this residue definition might still need to be reassessed in the framework of the art 12 MRL review, but a revised wording is not expected on the MRLs and risk assessment values derived in the present opinion because the analytical methods proposed for enforcement of clopyralid in honey and the methods used to analyse residue trial samples of honey were found to extract the conjugates of clopyralid potentially present in honey, using a caustic-methanol solvent.

A new analytical method for enforcement of clopyralid residues in honey, based on gas chromatography with negative ion electrospray ionisation mass spectrometry (GC/NCI–MS), and its independent laboratory validation (ILV) were submitted and deemed sufficiently validated. This method can quantify clopyralid residues in honey, nectar and pollen in line with the proposed enforcement residue definition. Because of the basic treatment applied to the samples, the method is expected to release free clopyralid from its different conjugated forms. The methods enable the quantification of residues at or above 0.001 mg/kg in honey (LOQ).

Specific studies investigating the magnitude of clopyralid residues in processed commodities as well as investigations on the residues of clopyralid in commodities of animal origin were not required for the present MRL application on honey.

In support of the MRL application, a new study on the storage stability of clopyralid in honey, nectar and pollen samples was submitted. This study was deemed valid and demonstrated that clopyralid was stable for at least 18 months when stored at −18°C in honey, nectar and pollen.

In support of the MRL application, two studies investigating the magnitude of clopyralid residues in honey following an application of clopyralid to oilseed rape plants were submitted and assessed. The first study is a GLP study meeting the requirements of the current guidelines. There are six semi-field trials performed with an application pattern in line with the critical GAP on winter oilseed rape proposed in the present MRL request. Therefore, this study was considered valid and sufficient to derive an MRL proposal of 0.15 mg/kg for honey. The second study is a non-GLP study for which several deficiencies were identified. Therefore, EFSA agreed with the conclusion of the EMS that this second study was not suitable to derive an MRL in honey.

The toxicological profile of clopyralid was assessed in the framework of the EU pesticides peer review under Regulation (EC) No 1107/2009 and the data were sufficient to derive an acceptable daily intake (ADI) of 0.15 mg/kg bw per day and an acute reference dose (ARfD) of 0.17 mg/kg bw.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The short-term exposure assessment was performed for honey based on the highest residue (HR) derived from six relevant supervised semi-field trials assessed in the present application. The short-term exposure did not exceed the ARfD for honey (0.1% ARfD). Regarding the long-term exposure, the median value derived for honey in the present opinion was considered. For the crops and animal commodities that were assessed in previous MRL applications, the corresponding supervised trials median residue (STMR) values could be used. In the absence of an MRL review completed at the time of the present assessment, the existing EU MRLs for all remaining commodities were considered in the risk assessment. The estimated long-term dietary intake was in the range of 2% of the ADI (IE child) to 29% of the ADI (NL toddler). The highest contribution of residues in honey was < 0.001% of the ADI (DE child).

EFSA concluded that the proposed MRL for clopyralid in honey as derived on the basis of the authorised use of clopyralid on oilseed rape, will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

Nevertheless, it should be noted that the chronic dietary risk assessment for the existing MRLs shall be updated in the framework of the MRL review (article 12 of Reg (EU) 396/2005), where further information on the authorised uses and their supporting data are expected to be provided.

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 to D.

Code[a]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Existing residue definition: Clopyralid **Proposed enforcement residue definition:** Sum of clopyralid, its salts and conjugates, expressed as clopyralid				
1040000	Honey and other apiculture products[b]	0.05*	**0.15**	MRL proposal based on a single honey residue study conducted by Applicant. The proposal is supported by sufficient data, no consumer risks are identified

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

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

[b]According to Regulation (EC) No 396/2005 MRLs are not applicable to other apiculture products until individual products have been identified and listed within this group.

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

ASSESSMENT

The European Food Safety Authority (EFSA) received an application to modify the existing MRL for clopyralid in honey. The current MRL application is not linked to one specific good agricultural practice (GAP) but is related to the existing uses in crops that might be attractive to bees and that are a potential source for residues of clopyralid in honey. The worst-case GAP was identified by the applicant (Finland, 2023).

Clopyralid is the ISO common name for 3,6-dichloropyridine-2-carboxylic acid or 3,6-dichloropicolinic acid (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Clopyralid was first evaluated in the framework of Directive 91/414/EEC[1] with Finland designated as rapporteur Member State (RMS) for the representative uses as post-emergence applications on cereals, pasture, oilseed rapes and sugar beets. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2005). Clopyralid was

[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, pp. 1–32.

approved for the use as a herbicide on 1 May 2007.[2] In 2018, clopyralid was evaluated for renewal of the approval in the framework of Regulation (EC) No 1107/2009[3] with Finland designated as RMS for the representative uses as a foliar treatment on winter cereals and grassland. The renewal assessment report (RAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2018c). The decision on the renewal of clopyralid entered into force on 19 July 2021. [4]

The EU MRLs for clopyralid are established in Annex IIIA of Regulation (EC) No 396/2005.[5] The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has not yet been performed. After completion of the renewal of the first approval, EFSA has issued one reasoned opinion on the modification of MRLs for clopyralid (EFSA, 2021). The proposals from this reasoned opinion have been considered in recent MRL regulations.[6]

In accordance with Article 6 of Regulation (EC) No 396/2005 and following the provisions set by the 'Transparency Regulation' (EU) 2019/1381,[7] the applicant Corteva Agriscience International Sàrl submitted on 25 July 2022 an application to the competent national authority in Finland to modify the clopyralid MRL in honey, alongside the dossier containing the supporting data using the IUCLID format.

Furthermore, EFSA was notified of certain studies submitted to support this MRL application, which were commissioned or carried out after 27 March 2021 and therefore subject to the obligation of notification of studies in accordance with Article 32b of the GFL Regulation.[8] The list of notified studies for the concerned application is considered as background information to this reasoned opinion and therefore made publicly available.

The appointed EMS Finland assessed the dossier and declared its admissibility on 5 October 2022. Subsequently, following the implementation of the EFSA's confidentiality decision, the non-confidential version of the dossier was published by EFSA and a public consultation was launched on the dossier. The consultation aimed to consult stakeholders and the public on the scientific data, studies and other information part of, or supporting, the submitted application, in order to identify whether other relevant scientific data or studies are available. The consultation ran from 13 February 2023 to 6 March 2023. No additional data or comments were submitted in the framework of the consultation.

At the end of the commenting period, the EMS proceeded with drafting the 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 9 March 2023. To accommodate clopyralid residues in honey from the authorised use on oilseed rape (identified by the applicant as the critical GAP for residues in honey), the EMS proposed to raise the existing MRLs in honey from the limit of quantification (LOQ) of 0.05 to 0.15 mg/kg.

EFSA identified data gaps which needed further clarification and requested the EMS to address them. On 28 September 2023, the applicant provided the requested information in an updated IUCLID dossier. The additional information was duly considered by the EMS who submitted a revised evaluation report to EFSA on 30 September 2023 (Finland, 2023), which replaced the previously submitted evaluation report.

EFSA based its assessment on the evaluation report submitted by the EMS (Finland, 2023), the RAR (and its revision) (Finland, 2017, 2018) prepared under Regulation (EC) 1107/2009, the Commission renewal report on clopyralid (European Commission, 2021b), the conclusions on the peer review of the pesticide risk assessment of the active substance clopyralid (EFSA, 2005, 2018c), as well as the conclusions from previous EFSA opinions on clopyralid (EFSA, 2011, 2018b, 2021).

For this application, the data requirements established in Regulation (EU) No 283/2013[9] and the guidance documents applicable at the date of submission of the IUCLID application are applicable (European Commission, 2010, 2018, 2020, 2021a, 2023; OECD, 2007a, 2007b, 2007c, 2007d, 2007e, 2007f, 2009a, 2009b, 2011, 2016, 2018). 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.[10]

As the review of the existing MRLs under Article 12 of Regulation 396/2005 has not yet been carried out, the conclusions reported in this reasoned opinion may need to be reconsidered in light of the outcome of the MRL review to be launched in the future.

[2]Commission Directive 2006/64/CE of 18 July 2006 amending Council Directive 91/414/EEC to include clopyralid, cyprodinil, fosetyl and trinexapac as active substances. OJ L 206, 27.7.2006, pp. 107–111.

[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, pp. 1–50.

[4]Commission Implementing Regulation (EU) 2021/1191 of 19 July 2021 renewing the approval of the active substance clopyralid 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 540/201OJ L 258, 20.7.2021, pp. 37–41.

[5]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, pp. 1–16.

[6]For an overview of all MRL Regulations on this active substance, please consult: https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=search.as.

[7]Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC, PE/41/2019/REV/1. OJ L 231, 6.9.2019, pp. 1–28.

[8]'In accordance with Article 32b of the GFL Regulation, both potential applicants and laboratories/testing facilities commissioning or carrying out studies as of 27 March 2021 in view of an MRL application have the obligation to notify EFSA' (For further details see EFSA Administrative guidance on Peer-review of pesticide active substances and MRL applications; EFSA, 2021).

[9]Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, 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. OJ L 93, 3.4.2013, pp. 1–84.

[10]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, pp. 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, is presented in Appendix B.

The evaluation report submitted by the EMS (Finland, 2023) 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

In the framework of the EU pesticide peer review for the renewal of the active substance clopyralid, three GLP and guideline compliant metabolism studies with foliar application of radiolabelled clopyralid were assessed (leafy vegetables, pulses/oilseeds and root crops) (EFSA, 2018c).

In the study performed with leafy vegetables (**head cabbage**) an extraction with caustic methanol resulted in the identification of free clopyralid at maturity up to 92% and 99% total radioactive residue (TRR) in all samples. No other significant fractions or metabolites were found in cabbage.

Regarding the studies performed on **oilseed rape** and **sugar beet**, two extraction steps (neutral + basic hydrolysis) were performed. In samples taken at day zero, free clopyralid was the major compound retrieved. However, it significantly decreased in the samples taken at maturity where a 'polar form' of clopyralid was found at significant levels: 39% TRR in sugar beet roots; 28% TRR in rape seeds. Furthermore, in oilseed rape, an unknown metabolite B was found up to 29% and 18% TRR in mature straw and mature seed, respectively. It was suggested that metabolite B was potentially a conjugate of clopyralid, but this was not demonstrated. The conclusion of the peer review was that further clarifications on the observed results were needed. Clarification on the nature of the unknown metabolite B and whether it is identical with the polar form of clopyralid and clopyralid conjugates was required. Furthermore, an explanation of why the polar form of clopyralid was only observed in mature samples of sugar beet and oilseed rape was required (EFSA, 2018c). These data gaps have not been addressed so far.

A GLP metabolism study covering the group of cereals (**wheat**) was assessed in a previous MRL application (EFSA, 2021). Free clopyralid was the only identified residue in straw and grain, ranging between 20% and 28% TRR. A multitude of less polar compounds were reported accounting for 30% to 45% TRR. These less polar fractions were not identified. However, when the plant extracts were subjected to a base treatment, these compounds were found to release free clopyralid. Therefore, these compounds were characterised as base labile. Because of this lack of further identification, it was concluded that the study did not fulfil the requirements of OECD Guideline 501 (OECD, 2007a).

In the framework of the present application, the applicant submitted two new GLP and guidelines-compliant metabolism studies: one on oilseed rape and one on sugar beet (Finland, 2023). Both studies are performed with application patterns similar to the studies assessed in the peer review (foliar application at an early growth stage at the rate of 200 or 300 g a.s./ha).

In the study performed with **oilseed rape**, the TRR was 0.069 mg eq./kg in mature **seeds**. After the first extraction was performed with a neutral solvent (ACN:H_2O), 40.8% of the TRR could be extracted. A satisfactory level of extraction could then be achieved after subsequent extractions performed with methanol: 10N NaOH (basic hydrolysis) and further extractions with 0.5 M NaOH. In seeds, the chromatograms obtained with HPLC revealed the presence of free clopyralid (29% TRR; 0.02 mg/kg) and of a multitude of less polar regions. The less polar regions were not identified but, after hydrolysis treatment performed with base, the major part of the less polar regions was converted to free clopyralid (41.3% TRR in total; 0.028 mg eq./kg). The results of a methylation experiment did not demonstrate that these regions correspond to clopyralid conjugates. Instead, the study authors and the EMS formulated the hypothesis that clopyralid may undergo interaction with endogenous plant matrix, in the form of weak chelation effects or electrostatic interactions. These interactions are readily broken upon treatment with base. In seeds, a remaining 20% of TRR was characterised but not analysed by high performance liquid chromatography (HPLC). However, given the overall rate of identification/characterisation in seeds and since it only corresponds to 0.014 mg eq./kg, this is deemed as a minor deficiency for seeds. From the same study, samples were also performed on **forage** parts, where the TRR represented 1.84 mg eq/kg. In forage, 100% of the TRR was identified: 30% of the TRR corresponded to free clopyralid and the remainder corresponded to less polar regions which, after hydrolysis treatment performed with base, converted to free clopyralid. Similar findings were also reported in the analysis performed in **anthers** and **pollen,** where 85% to 100% of the TRR was also identified as clopyralid (free or released after basic hydrolysis).

In the study performed with **sugar beet**, the total recovered radioactivity (TRR) was 2.1 mg eq./kg in immature roots and 0.48 mg eq./kg in mature roots. After an extraction performed with a neutral solvent (ACN:H_2O), 100% of the TRR could be extracted from mature roots. Based on HPLC analysis, free clopyralid accounted for 22.6% of the TRR (0.11 mg/kg) in mature roots. As in oilseeds, less polar regions were observed on the chromatogram, some of them exceeding 10% TRR and 0.05 mg eq/kg. However, following a base hydrolysis with methanol:10N NaOH (at ambient temperature), free clopyralid accounted for a total of 71.7% of the TRR in mature roots and only one unidentified region still accounted for more

than 10% TRR and 0.05 mg eq/kg (region 4: 11.3% TRR; 0.055 mg eq/kg). Further attempts were then performed to explain the nature of these less polar regions. An experiment using enzymatic extraction (B-glucosidase) indicated that the less polar regions did not correspond to sugar conjugates of clopyralid. However, further analysis of the unidentified regions was performed by high resolution accurate mass liquid chromatography tandem mass spectrometry (LC–HRMS/MS). This analysis showed the presence of characteristic fragment ions found in the MS/MS spectra of clopyralid indicating that each component might be a conjugate of clopyralid. A total of six components were observed to be conjugates of clopyralid, corresponding to a total of 73.1% TRR in mature roots. Based on the mass spectra produced by the six compounds, the study authors were able to propose molecular formulas and structures. The compounds were assigned as different types of conjugates (glucaric acid, methylated glucaric acid, amino sugar, methylated amino sugar, bis-methylated glucaric acid and bis-methylated amino sugar). All these compounds undergo deconjugation after hydrolysis under basic conditions. However, an explanation is still needed as to why these conjugated forms of clopyralid eluted after the parent compound under reversed phase HLPC.

The results of a new study on oilseed rape showed similar results compared to the previously assessed study on wheat, with a significant part of the TRR corresponding to compounds less polar than clopyralid, not properly identified, but which are readily converted to free parent after basic hydrolysis. In both cases, an impact on the magnitude of residues in samples analysed in the residue trials and in monitoring is not expected, provided that the analytical methods used to generate the data also apply basic hydrolysis in order to convert all the relevant residues to clopyralid (EFSA, 2021).

Information on the nature of residues in primary crops is relevant to support the present MRL application in honey (see Section 3.1). EFSA concludes that the nature of residues in plants (and in plant parts foraged by bees) has been sufficiently depicted to support the present MRL request for honey. The available studies submitted after the EU peer review indicate that clopyralid (free, conjugated or any forms readily converted to free clopyralid after basic hydrolysis) is the only relevant compound found in oilseed rape, wheat and sugar beet. However, a conclusion on the metabolism of clopyralid in plants shall be taken in the MRL review according to Article 12 of Regulation (EC) No 396/2005 where all available plant metabolism studies will be reassessed.

1.1.2 | Nature of residues in rotational crops

From the rotational crop metabolism studies which were assessed in the framework of the EU pesticides peer review, it was concluded that the same metabolic pattern is observed across all rotational crops and that this corresponds with the findings in primary crops with clopyralid and conjugated clopyralid being the major residues (EFSA, 2018c).

These metabolism studies also showed that radioactive residues above 0.01 mg/kg might be expected in soybeans (seed and plant) and wheat straw at a plant back interval of 125 days. Therefore, it was concluded that rotational crop field trials should be submitted to support uses on non-permanent crops.

1.1.3 | Nature of residues in processed commodities

The effect of processing on the nature of clopyralid was investigated in the framework of the EU pesticides peer review. The study showed that clopyralid is hydrolytically stable under standard processing conditions (EFSA, 2018c).

1.1.4 | Analytical methods for enforcement purposes in plant commodities

An analytical method for enforcement analysis for clopyralid, its salts and conjugates was assessed during the EU pesticides peer review (EFSA, 2018c).

The method (based on LC–MS/MS) is sufficiently validated for the determination of residues of clopyralid, its salts and conjugates in the four main plant matrices. The enforcement method quantifies residues at or above the LOQ of 0.01 mg/kg for the total residue (sum of clopyralid, its salts and conjugates) in the four main plant matrices.

The assessment of extraction efficiency in plant matrices is not relevant for the current application on honey (see also Section 3.1.1) but could be further investigated for the plant matrices of concern under the future MRL review. It is recommended to verify whether the sample preparation conditions are expected to release free clopyralid from its various conjugated forms and to confirm the extraction efficiency according to the requirements of the extraction efficiency Guidance, SANTE 2017/10632 GD (European Commission, 2023).

1.1.5 | Storage stability of residues in plants

Two new storage stability studies of clopyralid in strawberries and in dry beans were submitted in the present MRL dossier (Finland, 2023). However, these studies were not further assessed as they are not relevant for the setting of an MRL in honey (see also Section 3.1.2).

1.1.6 | Proposed residue definitions

A general residue definition for primary and rotational crops was derived in the EU assessment of the renewal of clopyralid as follows (EFSA, 2018c):

- Residue definition for risk assessment: clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid).
- Residue definition for enforcement: clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid).

Data gaps were identified in the EFSA conclusion on the peer review of clopyralid regarding the nature of polar residues found in sugar beet and oilseed rape metabolism studies.[11] Furthermore, it was also noted that the characterisation of metabolism in leafy crops was limited because of a direct extraction performed with caustic methanol. However, the above residue definition was confirmed for cereal crops after the evaluation of a new metabolism study performed on wheat and submitted in a previous MRL assessment (EFSA, 2021).

It should be noted that the residue definition for enforcement currently set in Regulation (EC) No 396/2005 is 'clopyralid' alone. However, provided the analytical method used for enforcement and for generating data for risk assessment includes a hydrolysis step comparable to the one applied in the metabolism studies, it is expected that free clopyralid and clopyralid moiety released from its different conjugated forms would be analysed. A change of the wording of the existing enforcement residue definition might need to be proposed in the framework of the MRL review (art 12 of Reg (EU) 396/2005) to better reflect these aspects of the nature of clopyralid residues in plants.

Furthermore, whether this residue definition is also applicable to crops other than cereals also needs to be concluded in the framework of the MRL review. The two new studies submitted and assessed in the framework of the present application indicate that clopyralid (free, conjugated or any forms readily converted to free clopyralid after basic hydrolysis) is the only relevant compound found in oilseed rape and sugar beet. No further metabolites were identified, thus a different degradation of the parent compound in these crops is not expected compared to wheat. In the new sugar beet study, the presence of clopyralid conjugates could be demonstrated. In the new oilseed rape study, however, the authors could only formulate the hypothesis that clopyralid may undergo interaction with endogenous plant matrix, in the form of weak chelation effects or electrostatic interactions. Nevertheless, in both cases, an impact on the magnitude of residues in samples analysed in monitoring, or in the residue trials, is not expected provided that the analytical methods used to generate the data also apply basic hydrolysis to convert all the relevant residues to clopyralid.

Consequently, in the framework of the present MRL application, EFSA concludes that the nature of residues in plants (and in plant parts foraged by bees) has been sufficiently depicted to support the present MRL request for honey.

1.2 | Magnitude of residues in plants

1.2.1 | Magnitude of residues in primary crops

The assessment of the magnitude of residues in primary crops is not relevant as the present MRL request is for honey (see Section 3.2).

1.2.2 | Magnitude of residues in rotational crops

Based on the findings in the rotational crop metabolism studies (see Section 1.1.2), residues of clopyralid cannot be excluded in succeeding crops, and therefore, the magnitude of clopyralid residues in rotational crops should be further investigated. A new field study investigating the magnitude of clopyralid residues in rotational crops was submitted in the framework of the present application and the EMS assessed this study in its evaluation report (Finland, 2023). A summary of the study parameters and main results is reported in this section.

A total of six rotational crop trials (3 NEU and 3 SEU) were performed over two different growing seasons (2019 and 2020). According to the EMS, the trials were considered independent. The closest sites were in Poland (ca. 50 km distance) and in Spain (ca. 100 km distance).

In all trials, the protocol started with one application of clopyralid on bare soil. In each trial, different application rates were tested (60, 80 or 125 g a.s./ha). The application on bare soil was followed by planting crops (radish, cabbage, oilseed rape, wheat, barley and sunflower) at different plant back intervals (30, 90, 125 and 270–365 days).

Samples of radish, cabbage, oilseed rape, wheat, barley and sunflower were harvested at maturity. The samples were stored deep frozen within a time period for which storage stability of clopyralid has been demonstrated in the respective

[11] Clarification on the nature of the unknown metabolite B and whether it is identical with the polar form of clopyralid and clopyralid conjugates and an explanation of why the polar form of clopyralid was only observed in mature samples of sugar beet and oilseed rape were required (EFSA, 2018c).

plant matrices, except for radishes, in one trial, where the samples were stored for 601–605 days (20 months) while the storage stability of clopyralid in high-water content matrices has been demonstrated for 17 months.

Procedural recoveries of the analytical method were within the range of 70%–110% and max 20% RSD in all matrices.

Furthermore, the analytical method used in this study (method 120610) includes a hydrolysis step performed with basic methanol solvent (methanol:10N sodium hydroxide; 100:1) prior to analysis. This extraction is expected to extract all clopyralid residues potentially bound to the matrix (conjugates or other), which were characterised in a series of less polar compounds in the metabolism studies (Finland, 2023). This extraction efficiency has been demonstrated for oilseed rape and sugar beet matrices in the new metabolism studies performed on these crops. Comparisons of the quantitation of clopyralid residue obtained with the analytical method 120610 with the TRR results of the metabolism studies in different matrices show that the analytical method is expected to extract the same amounts of clopyralid (and bound clopyralid) as in the metabolism studies.

In head cabbage (leafy crop) and in oilseed rape and sunflower seeds (oilseed crops), no residues above LOQ were found in any trials (at any PBIs, any application rates). However, in oilseed rape (whole plant) and sunflower (rest of plant), residues were detected at a PBI of 30 days (up to 0.21 mg/kg).

In radish root (root crop), residues above LOQ were detected only at PBI of 30 days (up to 0.042 mg/kg). In radish tops, residues were detected at PBI of 30 days (up to 0.63 mg/kg) and 90 days (0.025 mg/kg). The highest residue values were found at 30-day PBI with an application rate of 125 g a.s/ha.

In barley and wheat grains (cereals), residues above LOQ were detected at all PBIs. The highest values were found at 30-day PBI (0.17 mg/kg with an application rate of 125 g a.s/ha). It is noted that in the trials performed with PBI of 270–365 days, detectable residues were still found up to 0.025–0.037 mg/kg. In cereal straws, residues above LOQ were found at 30-day PBI (up to 0.28 mg/kg) and at 270- to 365-day PBI (0.036 mg/kg).

It is noted that the highest application rate tested (125 g a.s./ha) corresponds to the critical GAP on oilseed rape, identified by the applicant as the worst-case authorised GAP with respect to residues in honey. Overall, residue uptakes were found in cereals (grain and straw) at all investigated PBIs, as well as in root crops (roots and tops) and in aerial parts of oilseed plants (only at short PBIs). Regarding leafy crops or oilseed (seed parts), the available results indicate that no residues uptakes are expected, even at the shortest PBI (30 days) and highest investigated application rate (125 g a.s./ha on bare soil).

As clopyralid residues might occur in plants grown on soil previously treated with 125 g a.s./ha, it is concluded that residues from rotational crops can also be relevant for melliferous crops and consequently for honey. However, it is noted that the maximal value of the residue uptakes observed in aerial parts of oilseed plants (0.21 mg/kg at a short PBI of 30 days) is lower compared to the residue concentrations found in oilseed plant samples taken from the tunnel trials assessed in Section 3.2 of the present opinion (0.69–2.33 mg/kg at PHI 0 day; 0.34–2.12 at PHI 10–12 days). Also considering that the crop interception is expected to occur in real conditions (compared to bare soil study), it is concluded that the potential residues from rotational crops will not significantly impact the value of the MRL for honey assessed in the present opinion. EFSA considers that the tunnel trials assessed in Section 3.2 of the present opinion are representative of the worst-case conditions regarding MRL in honey.

Regarding the potential residue uptakes in cereals and root crops, the need for deriving MRLs or implementing risk mitigation measures (as proposed by EMS) should be assessed in the framework of the MRL review to be carried out under Article 12 of Reg (EU) 396/2005.

1.2.3 | Magnitude of residues in processed commodities

Specific processing studies for honey are not available and are not required (see also Section 3.1).

1.2.4 | Proposed MRLs

The present MRL request is for honey for which a detailed assessment is reported in Section 3 of the present opinion.

2 | RESIDUES IN LIVESTOCK

The assessment of residues in livestock is not relevant as the present MRL request is for honey.

3 | RESIDUES IN HONEY

Based on a critical use on winter oilseed rape authorised in the EU (Foliar application 1 × 125 g a.s./ha; BBCH 30–51), identified by the applicant as the worst-case authorised GAP with respect to residues in honey, the applicant requested a new MRL in honey for clopyralid. Therefore, an assessment of the nature and magnitude of residues in honey is necessary.

3.1 | Nature of residues in honey

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

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

The available data investigating the metabolic profile in primary and rotational crops indicate that clopyralid (free, conjugated or any forms readily converted to free clopyralid after basic hydrolysis) is the only relevant compound found in wheat, oilseed rape and sugar beet. According to the detailed description of the analytical method used in the tunnel trials performed to generate residue data on honey, the treatment applied to the samples is expected to release clopyralid moiety from its different conjugated forms (Finland, 2023). The same applies to the analytical methods for enforcement in honey (see Section 3.1.1).

It would still be recommended to further investigate whether enzymatic processes involved in the production of honey occurring in the bee gut or during the storage in the beehive have an impact on the nature of residues in honey.

3.1.1 | Analytical methods for enforcement in honey

In the framework of the present assessment, a new method for enforcement of clopyralid residues in honey and its independent laboratory validation (ILV) were submitted by the applicant and assessed by the EMS (Finland, 2023).

The analytical method is based on gas chromatography with negative ion electrospray ionisation mass spectrometry (GC/NCI–MS) and was successfully validated for the determination of clopyralid in honey, nectar and pollen. The method is sufficiently validated according to the current guidance document on pesticide analytical methods SANTE/2020/12830, rev.1 (European Commission, 2021a). An LOQ of 0.001 mg/kg was demonstrated to be achievable in honey.

It is noted that the analytical method includes a hydrolysis step performed with caustic methanol, similar to those performed in the new metabolism studies performed on oilseed rape and sugar beet: clopyralid is extracted from the honey matrix with a mixture of methanol containing 10N sodium hydroxide. The extracts are left overnight at room temperature. The use of caustic methanol is expected to simultaneously extract and hydrolyse the potential conjugates. Consequently, this analytical method is expected to cover all the compounds relevant for the enforcement residue definition, including potential conjugates of clopyralid or any clopyralid residues potentially bound to the matrix, which was characterised in a series of less polar compounds in the metabolism studies (Finland, 2023).

An independent validation was also successfully completed (Finland, 2023).

Further information on the extraction efficiency of the analytical method applied for enforcement of residues in honey is not available. However, since the existing guidance document on extraction efficiency (European Commission, 2023) cannot be applied to the honey matrix and since no other guidance on how to investigate extraction efficiency in honey is available, demonstration of extraction efficiency in honey matrix is not required for the present assessment.

3.1.2 | Storage stability of residues in honey

The storage stability of clopyralid in honey, nectar and pollen samples was investigated in the current MRL application (Finland, 2023). The study is acceptable and fulfils the requirement of OECD Guideline 506.

It was demonstrated that clopyralid was stable for at least 18 months when stored at –18°C in honey, nectar and pollen.

3.1.3 | Proposed residue definitions

In the absence of specific metabolism studies on honey, the studies investigating the nature of clopyralid residues in primary and rotational crops and studies investigating the degradation of the active substance during pasteurisation are considered to address the nature of clopyralid in honey. The available studies demonstrate that clopyralid (free or released after basic hydrolysis) is the main residue in plants.

Therefore, the residue definition for honey for monitoring (RD-Mo) and risk assessment (RD-RA) is proposed as 'clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid)'.

The analytical methods used for enforcement of clopyralid in honey and used in the submitted tunnel trials (used to generate data for risk assessment and to derive an MRL proposal in honey) are expected to extract the conjugates of clopyralid potentially present in honey, using a caustic-methanol solvent. Because of the basic treatment applied to the samples, these methods are expected to release free clopyralid from its different conjugated forms (Finland, 2023).

Consequently, EFSA concluded that an appropriate residue definition is available for the intended MRL on honey. The wording of the residue definitions might still be reassessed in the framework of the art 12 MRL review, but an impact on the MRLs and risk assessment values derived in the present opinion is not expected (see also Section 1.1.6).

3.2 | Magnitude of residues in honey

In support of the MRL application, two studies investigating the magnitude of clopyralid residues in honey following an application of clopyralid to oilseed rape plants were submitted and assessed by the EMS (Finland, 2023). The first study is a GLP study generated by the applicant. The second study is a non-GLP study published by the Danish Environmental Protection Agency.

Study 1

In this GLP study, 6 independent trials were performed under semi-field conditions (tunnel trial) according to the technical guideline SANTE/11956/2016 rev. 9 (European Commission, 2018). The trials were all conducted in 2020 in 6 different sites in Germany, Romania, The Netherlands, France and Spain. Oilseed rape was used as a surrogate crop. A foliar treatment of one application at 125 g a.s./ha was performed on oilseed rape before flowering (growth stage corresponding to BBCH 55). Clopyralid being a systemic substance, application before flowering is expected to lead to significant residues in nectar and honey. Furthermore, the parameters applied in these trials are fully compliant with the critical GAP on winter oilseed rape identified in the present MRL request (Foliar application 1 × 125 g a.s./ha; BBCH 30–51).

Samples of oilseed rape (plants, pollen and nectar) and of honey were collected in control and treated tunnels. Samples were transferred to deep frozen conditions at less than −18°C within less than 12 h after sampling. The storage period of the samples was up to 313 days, therefore below the demonstrated storage stability period (18 months).

The analytical method 120610, used in the trials, was validated in all sampled matrices according to the requirements of SANCO/3029/99, rev. 4. The LOQ of the analytical method was 0.01 mg/kg for all matrices. The hydrolysis of the samples performed with basic methanol solvent (methanol:10N sodium hydroxide; 100:1) prior to analysis is expected to extract all clopyralid residues potentially bound to the matrix (conjugates or other), which were characterised in a series of less polar compounds in the metabolism studies (Finland, 2023). All relevant residues considered in the residue definition are expected to be released as clopyralid during the sample preparation and therefore have been taken into account in the analysis. Within the new metabolism studies performed on oilseed rape and sugar beet, experiments were made to demonstrate the extraction efficiency of the analytical method 120610 on these different plant matrices. Comparisons of the quantitation of clopyralid residue obtained with the analytical method 120610 with the TRR results of the metabolism studies in different matrices show that the analytical method is expected to extract the same amounts of clopyralid (and bound clopyralid) as in the metabolism studies.

The main study parameters are compliant with the technical guideline. The following minor deviations were reported but overall acceptable: in trial 2, a positive control sample was found (0.018 mg/kg); the sample weight was generally less than the guideline of 100 g; the moisture percentage of the honey sample was above 20% in three trials.

Residues above the LOQ were quantified in nectar and pollen. In the honey residues of clopyralid analysed according to the residue definition ranged from 0.01 mg/kg (LOQ) to 0.07 mg/kg.

Study 2

This non-GLP study was conducted in 2019 and 2020 at the University of Copenhagen, using the experimental fields of the Højbakkegaard research facility in Denmark. The study has been published in 2022 (Hansted et al., 2022).

Winter oilseed rape was treated with one application of clopyralid at the rate of 80 g a.s./ha up to BBCH 55. Hives were then placed field side when oilseed rape reached the growth stage of BBCH 61 according to local commercial practice. From these hives, 10 pollen and 10 honey samples were collected each year (2019 and 2020). The pollen present in honey samples was identified, to determine whether the bees were visiting the clopyralid-treated fields. Honey samples were collected from the field-side hives until alternative pollen sources became available.

The trials were located in two different places only (Jutland and Zealand) and trials in each geographic location were considered as replicates. Therefore, only four independent trial values were considered. The results ranged between 0.084 and 0.158 mg/kg. The study confirmed that a significant transfer of clopyralid residues to pollen and honey is occurring. Furthermore, the residue levels found in this study are higher compared to the GLP-study results.

However, this study presents some deficiencies regarding the requirements for field trial designs in SANTE/11956/2016 rev. 9. It is noted that all trials were performed in Denmark, that no control samples were taken and that there is no evidence that honey sampled for analysis corresponded to mature honey. Furthermore, no validation of the analytical methods was provided and there is no evidence that the samples were analysed according to the full residue definition (including conjugates and salts). Furthermore, the parameters applied in these trials are not compliant with the critical GAP on winter oilseed rape which was proposed by the applicant in the present MRL request. For these reasons, the EMS concluded that the study is to be considered as supporting information only. Therefore, the results should not be used to derive an MRL in honey.

Magnitude of residues from EU national monitoring programme

In the framework of Article 32 of Regulation (EC) No 396/2005 (official national control programmes), monitoring data were submitted to EFSA. Considering all samples available from 2009 to 2022, a total of 274 samples are available, 207 of them originating from EU Member States. All available honey samples analysed resulted in clopyralid residue levels below the LOQ (ranging between 0.005 and 0.05 mg/kg). No MRL exceedance has therefore been observed in the available data. The data indicate that the clopyralid concentrations found in honey in the available valid semi-field/tunnel residue trials are higher than the residues found in market samples of honey.

MRL proposal

Based on the six GAP-compliant trials from the GLP study, an MRL of 0.15 mg/kg can be proposed for clopyralid in honey using the OECD MRL calculator. It should be noted that currently, MRLs set for honey are not applicable to other apicultural products following Commission Regulation (EU) 2018/62.[12]

4 | CONSUMER RISK ASSESSMENT

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo (EFSA, 2018a, 2019). This exposure assessment model contains food consumption data for different sub-groups of the EU population and allows the acute and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016).

The toxicological reference values for clopyralid used in the risk assessment (i.e. ADI and ARfD values) were derived in the framework of the renewal of approval of clopyralid (European Commission, 2021b). The ADI value is 0.15 mg/kg bw/day and the ARfD value is 0.17 mg/kg bw.

Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed for honey in accordance with the internationally agreed methodology (FAO, 2016). The calculations were based on the HR derived from supervised semi-field trials and the complete list of input values can be found in Appendix D.1.

The short-term exposure did not exceed the ARfD for honey (see Appendix B.4).

Long-term (chronic) dietary risk assessment

In the framework of the previous MRL assessment, the long-term exposure assessment was performed with EFSA PRIMo 3.1 (EFSA, 2021). EFSA updated this calculation, taking into account the STMR value derived for honey in the present opinion. For the crops that were assessed in previous MRL applications (EFSA, 2011, 2018c, 2021), the STMR values were used. For animal commodities, the STMR values as derived in 2021 were used (EFSA, 2021). For milk, the input value was multiplied by the conversion factor of 1.3 for risk assessment (EFSA, 2021).

For all remaining crops, the existing EU MRLs were considered in the risk assessment in the absence of detailed information and data on the currently authorised uses of clopyralid; this corresponds to the 'normal mode' calculation option in PRIMo rev. 3.1. The complete list of input values is presented in Appendix D.1.

The estimated long-term dietary intake was in the range of 2% of the ADI (IE child) to 29% of the ADI (NL toddler). The highest contribution of residues in honey was < 0.001% of the ADI (DE child). The detailed results are available in Appendix B.4.

EFSA concluded that the long-term intake of residues of clopyralid at the levels of existing MRLs and at the proposed MRL on honey is unlikely to present a risk to consumer health. Nevertheless, it should be noted that the chronic dietary risk assessment for the existing MRLs shall be updated in the framework of the MRL review (Article 12 of Reg (EU) 396/2005), where further information on the authorised uses and their supporting data are expected to be provided.

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 this MRL application were found to be sufficient to derive an MRL proposal for honey.

EFSA concluded that the proposed MRL for honey, resulting from the authorised use of clopyralid on oilseed rape notified in the present MRL assessment, will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a risk to consumers' health.

[12]Commission Regulation (EU) 2018/62 of 17 January 2018 replacing Annex I to Regulation (EC) No 396/2005 of the European Parliament and of the Council. C/2018/0138. OJ L 18, 23.1.2018, pp. 1–73.

Furthermore, it was noted that the residue definition for enforcement, which is currently set in Regulation (EC) No 396/2005 is 'clopyralid' alone, might need to be reworded to better reflect the nature of clopyralid residues in plants and honey. This should be assessed in the framework of the MRL review to be carried out under Article 12 of Reg (EU) 396/2005.

The MRL recommendations are summarised in Appendix B.5.

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
cGAP	critical GAP
CV	coefficient of variation (relative standard deviation)
CXL	Codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{90}	period required for 90% dissipation (define method of estimation)
dw	dry weight
EC	emulsifiable concentrate
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
ESI	electrospray ionisation
EURL	EU Reference Laboratory (former Community Reference Laboratory (CRL))
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GC	gas chromatography
GC/NCI–MS	gas chromatography with negative ion electrospray ionisation mass spectrometry
GLP	Good Laboratory Practice
GR	granule
GS	growth stage
HPLC	high performance liquid chromatography
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	independent laboratory validation
IPCS	International Programme of Chemical Safety
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_{oc}	organic carbon adsorption coefficient
LC	liquid chromatography
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry detector
MW	molecular weight
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PBI	plant back interval
PF	processing factor
PHI	pre-harvest interval
P_{ow}	partition coefficient between n-octanol and water
PRIMo	(EFSA) Pesticide Residues Intake Model
RA	risk assessment
RAC	raw agricultural commodity
RD	residue definition
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers
SC	suspension concentrate

SEU	southern Europe
STMR	supervised trials median residue
TRR	total radioactive residue
WHO	World Health Organization

ACKNOWLEDGEMENTS

EFSA wishes to thank: Stathis Anagnos, Mavriou Galini, Matteo Lazzari and Elena Taglianini for the support provided to this opinion.

CONFLICT OF INTEREST

If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR

European Commission

QUESTION NUMBER

EFSA-Q-2022-000622

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How to cite this article: EFSA (European Food Safety Authority), Bellisai, G., Bernasconi, G., Carrasco Cabrera, L., Castellan, I., del Aguila, M., Ferreira, L., Santonja, G. G., Greco, L., Jarrah, S., Leuschner, R., Mioč, A., Nave, S., Pedersen, R., Reich, H., Ruocco, S., Scarlato, A. P., Szot, M., Theobald, A., Tiramani, M., & Verani, A. (2024). Modification of the existing maximum residue level for clopyralid in honey. *EFSA Journal*, *22*(1), e8546. https://doi.org/10.2903/j.efsa.2024.8546

APPENDIX A

Summary of GAP triggering the amendment of existing EU MRLs

Since the MRL application is not linked to a specific intended GAP and applies to honey as food item for consumers, this appendix is not relevant for the given application.[13]

[13]The critical authorised EU GAP in winter oilseed rape (foliar application 1 × 125 g a.s./ha; BBCH 30–51), identified by the EMS to derive MRL in honey and tested in the residue trials, was reported in the GAP table in the MRL application and the evaluation report (Finland, 2023).

APPENDIX B

List of end points

B.1 | RESIDUES IN PLANTS

B.1.1 | Nature of residues and analytical methods for enforcement purposes in plant commodities

B.1.1.1 | Metabolism studies, analytical methods and residue definitions in plants

	Crop groups	Crop(s)	Application(s)	Sampling (DAT)	Comment/source
Primary crops (available studies)	Fruit crops	–	–	–	–
	Root crops	Sugar beet	Foliar, 1 × 300 g/ha, at BBCH 36	0, 28, 105 days (maturity)	GLP and guideline compliant study conducted with radiolabelled clopyralid (EFSA, 2005, 2018c)
			Foliar, 1 × 300 g/ha, BBCH 17–19	21 (immature whole plant) 110 days (mature foliage and mature roots)	New GLP and guideline compliant study conducted with radiolabelled clopyralid (Finland, 2023)
	Leafy crops	Cabbage	Foliar, 1 × 420 g/ha, at 8–10 leaf stage BBCH 31	0, 5, 38 days	GLP and guideline compliant study conducted with radiolabelled clopyralid (EFSA, 2005, 2018c)
	Cereals/grass	Wheat	Foliar, 1 × 125 g a.s./ha, BBCH 39	3 (forage) 23 (hay) 92 (straw, grain)	GLP and guideline compliant study conducted with radiolabelled clopyralid (EFSA, 2021)
	Pulses/oilseeds	Oilseed rape	Foliar, 1 × 300 g/ha, at BBCH 36	0, 28, 77 days (maturity)	GLP and guideline compliant study conducted with radiolabelled clopyralid (EFSA, 2005, 2018c)
			Foliar, 1 × 200 g/ha, BBCH 30	23 (forage), 94 (trash and seeds)	New GLP and guideline compliant study conducted with radiolabelled clopyralid (Finland, 2023)
	Miscellaneous	Pasture	1.121 kg a.s./ha	7, 14, 28,56, 126	Non-GLP and non-guideline compliant study on pasture grass, supportive only (EFSA, 2005, 2018c)

	Crop groups	Crop(s)	Application(s)	PBI (DAT)	Comment/source
Rotational crops (available studies)	Root/tuber crops	Turnip	1 × 0.28 kg/ha to bare soil	125 or 319 days	Radiolabelled 3,6-dichloro-2-6-^{14}C-2-pyridinecarboxylic acid In rotational crops, clopyralid was metabolised in a similar pathway as in primary crops (EFSA, 2011, 2018c) The 30 DAT mature cabbage was harvested at 128 days (9+ leaves/head; heads failed to fully close due to heat, BBCH 53)
		Radish	1 × 0.3 kg/ha to bare soil	30 days	
	Leafy crops	Lettuce	1 × 0.28 kg/ ha to bare soil	125 or 319 days	
		Cabbage	1 × 0.3 kg/ha to bare soil	30 days	
	Cereal (small grain)	Wheat	1 × 0.3 kg/ha to bare soil (30 days) 1 × 0.28 kg/ha to bare soil (125 and 319 days)	30, 125, 319 days	
	Other	Soybean	1 × 0.28 kg/ha to bare soil	125 days	
		Green bean	1 × 0.28 kg/ha to bare soil	319 days	

	Conditions	Stable?	Comment/source
Processed commodities (hydrolysis study)	Pasteurisation (20 min, 90°C, pH 4)	Yes	Radiolabelled 3,6-dichloro-2-6-^{14}C-2-pyridinecarboxylic acid. Clopyralid was stable (99.3, 96.9, 97.1% TRR, respectively) (EFSA, 2018c)
	Baking, brewing and boiling (60 min, 100°C, pH 5)	Yes	
	Sterilisation (20 min, 120°C, pH 6)	Yes	
	Other processing conditions	–	–

Can a general residue definition be proposed for primary crops?	Inconclusive	Metabolism studies are available for four different crop groups. Clopyralid (free or bound to the plant matrix), released after mild-base hydrolysis) is the common residue in all crops. However, conjugation and interaction in plant matrices vary between crops.
Rotational crop and primary crop metabolism similar?	Yes	EFSA (2018c)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes	EFSA (2018c)
Plant residue definition for monitoring (RD-Mo)	Cereals: Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) (EFSA, 2021) Existing residue definition of Regulation (EC) No 396/2005: clopyralid [Wording of the existing residue definition and extension to other crop groups to be assessed in the MRL review].	
Plant residue definition for risk assessment (RD-RA)	Cereals: Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid) (EFSA, 2021) [Wording of the existing residue definition and extension to other crop groups to be assessed in the MRL review].	
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	LC–MS/MS (EFSA, 2018c): - Validated for residues of clopyralid, its salts and conjugates in high water, high acid, high oil content and dry/starch commodities. - LOQ 0.01 mg/kg - ILV available - This method involves a hydrolysis step that releases free clopyralid from its conjugates.	

DAT: days after treatment; PBI: plant-back interval; BBCH: growth stages of mono- and dicotyledonous plants; a.s.: active substance; MRL: maximum residue level; LC-MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.

B.1.1.2 | Stability of residues in plants

	Category	Commodity	*T* (°C)	Stability period		Compounds covered	Comment/ source
				Value	Unit		
Plant products (available studies)	High-water content	Pasture	–20	17	Months	Clopyralid[a]	EFSA (2018c)
		Maize forage/fodder	–20	13	Months	Clopyralid[a]	EFSA (2018c)
	High-oil content	Rape seed	–20	24	Months	Clopyralid[a]	EFSA (2018c)
		Olive (fruit and oil)	–18	10	Months	Clopyralid[a]	EFSA (2018c)
	High-protein content	–	–	–	–	–	–
	Dry/high starch	Maize grain	–20	13	Months	Clopyralid[a]	EFSA (2018c)
	High-acid content	Orange	–18	10	Months	Clopyralid[a]	EFSA (2018c)
	Processed products	–	–	–	–	–	–
	Others						

[a]Any possible decline of conjugates of clorpyralid during storage is only expected to release clopyralid. Therefore, conjugates are also deemed covered by this endpoint.

B.1.2 | Magnitude of residues in plants

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

Not relevant.

B.1.2.2 | Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	Yes	In rotational crop majority of the residue identified at PBI 30 days was clopyralid conjugates (up to 81% TRR) and unconjugated clopyralid (10–50% TRR) in all crop parts except radish roots. In total, 81–99% of the extractable radioactivity was attributed to clopyralid and its conjugate (EFSA, 2018c).
Residues in rotational and succeeding crops expected based on field rotational crop study?	Yes	The new field rotational crop study indicates possible residue uptakes in cereals (grain and straw) at all investigated PBIs, as well as in root crops (roots and tops) and in aerial parts of oilseed plants (only at short PBIs). Regarding leafy crops or oilseed (seed parts), the available results indicate that no residues uptakes are expected (Finland, 2023).

B.1.2.3 | Processing factors

No processing studies were submitted in the framework of the present MRL application and this was not required.

B.2 | RESIDUES IN LIVESTOCK

Not relevant

B.3 | RESIDUES IN HONEY

B.3.1 | Nature of residues and analytical methods for enforcement purposes in honey

B.3.1.1 | Metabolism studies, analytical methods and residue definitions in honey

Metabolism studies in honey	Metabolism studies in honey are not available. The nature of the residues in honey is based on the major components of the residue detected in primary crops, rotational crops and processed commodities.
Honey residue definition for monitoring (RD-Mo)	Sum of clopyralid, its salts and conjugates expressed as clopyralid (wording to be adapted during the MRL review)
Honey residue definition for risk assessment (RD-RA)	Sum of clopyralid, its salts and conjugates expressed as clopyralid (wording to be adapted during the MRL review).
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	GC/NCI–MS (Finland, 2023): - Validated for the determination of clopyralid in honey, nectar and pollen. - LOQ = 0.001 mg/kg - Hydrolysis step performed with methanol containing 10 N sodium hydroxide is expected to cover all the compounds relevant for the enforcement residue definition, including potential conjugates of clopyralid or any clopyralid residues potentially bound to the matrix. - An ILV also successfully completed.

GC/NCI–MS, Gas chromatography with negative ion electrospray ionization mass spectrometry; LOQ, limit of quantification; ILV, independent laboratory validation.

B.3.1.2 | Storage stability of residues in honey

	Category	Commodity	*T* (°C)	Stability period		Compounds covered	Comment/source
				Value	Unit		
Products of animal origin (available studies)	–	Pollen Nectar Honey	–18	18	Months	Clopyralid[a]	New study (Finland, 2023)

[a]Any possible decline of conjugates of clorpyralid during storage is only expected to release clopyralid. Therefore, conjugates are also deemed covered by this endpoint.

B.3.2 | Magnitude of residues in honey

B.3.2.1 | Summary of residues data from the supervised residue trials

Commodity	Region[a]	Residue levels observed in the supervised residue trials (mg/kg)	Comments/source	Calculated MRL (mg/kg)	HR[b] (mg/kg)	STMR[c] (mg/kg)	CF[d]
Proposed residue definition for enforcement and risk assessment: The sum of clopyralid, its salts and conjugates, expressed as clopyralid							
Relevant data used to support the MRL proposal							
Honey	NEU SEU	3× < 0.01; 0.027 < 0.01; 0.07	Six semi-field trials performed with application on oilseed rape according to cGAP (1 × 125 g a.s./ha, BBCH 55) (Finland, 2023) Residues analysed for clopyralid and its conjugates Four NEU + two SEU trials can be merged to derive an MRL in honey	0.15	0.07	< 0.01	n.a.
Additional data (supportive only)							
Honey	DK	Residues after application at 1 × 80 g a.s./ha: 0.082; 0.084; 0.158; 0.160	Four field trials performed with application on oilseed rape at 1 × 80 g a.s./ha, BBCH 55 Non-GLP and non-guideline compliant study, published (Hansted et al., 2022). Also reported by EMS (Finland, 2023)	–	–	–	n.a.
		Residues scaled to 1 × 125 g a.s./ha: 0.128; 0.131; 0.247; 0.250	Residues analysed for clopyralid only. Study considered supportive due to major deficiencies, thus not used to derive MRL in honey	(0.6)	(0.25)	(0.25)	n.a.

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

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

[b]Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.

[c]Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.

[d]Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.

B.4 | CONSUMER RISK ASSESSMENT

ARfD	0.17 mg/kg bw (European Commission, 2021b)
Highest IESTI, according to EFSA PRIMo	Honey: 0.1% of ARfD
Assumptions made for the calculations	The calculation is based on the highest residue level expected in the raw agricultural commodity under consideration (i.e., honey) based on the six relevant semi-field trials assessed in the present application. Calculations performed with PRIMo revision 3.1 (normal mode).

ADI	0.15 mg/kg bw per day (European Commission, 2021b)
Highest IEDI, according to EFSA PRIMo	29% ADI (NL toddler) Contribution of crops assessed: Honey: <0.001% of ADI (DE child)
Assumptions made for the calculations	The calculation is based on the median residue level for honey as derived from submitted residue trials. For the crops that were assessed in previous MRL applications (EFSA, 2011, 2018b, 2021), the STMR values were used. For animal commodities the STMR values were used; for milk, the input value was multiplied by the conversion factor of 1.3 for risk assessment (EFSA, 2021). For all remaining commodities, existing EU MRLs were considered in the risk assessment in the absence of information and data on the currently authorised uses. Calculations performed with PRIMo revision 3.1 (normal mode).

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

B.5 | RECOMMENDED MRLS

Code[a]	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Existing residue definition: Clopyralid **Proposed enforcement residue definition:** Sum of clopyralid, its salts and conjugates, expressed as clopyralid				
1040000	Honey and other apiculture products[b]	0.05*	**0.15**	MRL proposal based on a single honey residue study conducted by Applicant. The proposal is supported by sufficient data, no consumer risks are identified.

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

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

[b]According to Regulation (EC) No 396/2005 MRLs are not applicable to other apiculture products until individual products have been identified and listed within this group.

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

APPENDIX C

Pesticide Residue Intake Model (PRIMo)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Clopyralid

LOQs (mg/kg) range from: 0.01 to: 0.05

Toxicological reference values

ADI (mg/kg bw per day):	0.15	ARfD (mg/kg bw):	0.17
Source of ADI:	EC	Source of ARfD:	EC
Year of evaluation:	2021	Year of evaluation:	2021

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	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	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	29%	NL toddler	43.27	9%	Maize/corn	4%	Apples	2%	Wheat	0.0%	4%
	15%	GEMS/Food G06	21.99	3%	Wheat	2%	Rice	2%	Maize/corn	0.1%	4%
	14%	DE child	21.68	4%	Apples	2%	Wheat	1%	Oranges	0.0%	3%
	13%	NL child	19.49	2%	Wheat	2%	Sugar beet roots	2%	Apples	0.0%	4%
	11%	IE adult	17.00	2%	Sweet potatoes	1%	Wheat	0.8%	Potatoes	0.0%	2%
	11%	GEMS/Food G10	16.90	2%	Wheat	2%	Rice	1%	Soyabeans	0.0%	2%
	10%	GEMS/Food G08	14.93	2%	Wheat	1%	Potatoes	0.7%	Soyabeans	0.1%	3%
	10%	GEMS/Food G15	14.85	2%	Wheat	1%	Potatoes	0.9%	Maize/corn	0.0%	3%
	10%	GEMS/Food G11	14.69	2%	Wheat	1%	Potatoes	1%	Soyabeans	0.1%	2%
	10%	GEMS/Food G07	14.61	2%	Wheat	1%	Potatoes	0.6%	Soyabeans	0.1%	2%
	10%	FR child 3 15 yr	14.59	2%	Wheat	1%	Oranges	0.9%	Sugar beet roots	0.0%	3%
	10%	DK child	14.43	3%	Rye	2%	Wheat	0.8%	Potatoes		5%
	9%	RO general	14.10	2%	Wheat	1%	Maize/corn	1%	Potatoes		3%
	9%	PT general	13.34	2%	Wheat	2%	Potatoes	1%	Rice		2%
	8%	UK infant	12.67	1%	Maize/corn	1%	Wheat	1%	Potatoes	0.0%	2%
	8%	IT toddler	12.35	3%	Wheat	2%	Other cereals	0.5%	Tomatoes		3%
	8%	FR toddler 2 3 yr	12.16	1%	Wheat	1%	Apples	0.8%	Rice	0.0%	3%
	8%	UK toddler	12.05	2%	Wheat	1%	Potatoes	0.8%	Rice	0.0%	3%
	8%	SE general	11.48	2%	Wheat	1%	Potatoes	0.6%	Bananas		2%
	8%	ES child	11.26	2%	Wheat	0.7%	Oranges	0.6%	Rice	0.0%	2%
	7%	DE women 14-50 yr	10.16	1%	Sugar beet roots	1%	Wheat	0.9%	Apples	0.0%	3%
	7%	FI 3 yr	9.81	2%	Potatoes	0.7%	Rice	0.6%	Wheat		1%
	6%	DE general	9.58	1.0%	Sugar beet roots	0.9%	Wheat	0.8%	Apples	0.0%	3%
	6%	NL general	9.15	0.9%	Wheat	0.8%	Potatoes	0.7%	Sugar beet roots	0.0%	2%
	6%	IT adult	8.45	2%	Wheat	0.9%	Other cereals	0.4%	Tomatoes		2%
	5%	FI 6 yr	7.69	1%	Potatoes	0.6%	Rice	0.5%	Wheat		1.0%
	5%	ES adult	7.14	1%	Wheat	0.4%	Oranges	0.3%	Rice	0.0%	1%
	5%	FR adult	7.02	1%	Wheat	0.8%	Wine grapes	0.3%	Apples	0.0%	1%
	5%	FI adult	6.77	2%	Coffee beans	0.4%	Potatoes	0.3%	Rye		0.6%
	4%	UK vegetarian	6.39	1.0%	Wheat	0.5%	Rice	0.5%	Potatoes	0.0%	1%
	4%	LT adult	6.26	1%	Potatoes	0.6%	Apples	0.5%	Rye		1%
	4%	FR infant	5.87	0.6%	Potatoes	0.6%	Apples	0.4%	Wheat	0.0%	1.0%
	4%	UK adult	5.37	0.8%	Wheat	0.5%	Rice	0.5%	Potatoes	0.0%	1%
	3%	DK adult	4.91	0.5%	Wheat	0.4%	Potatoes	0.3%	Apples		0.9%
	3%	PL general	4.87	1%	Potatoes	0.7%	Apples	0.3%	Tomatoes		0.1%
	2%	IE child	2.55	0.6%	Wheat	0.4%	Rice	0.2%	Potatoes		0.6%

Conclusion:

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of Clopyralid is unlikely to present a public health concern.

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

Acute risk assessment/children	Acute risk assessment/adults/general population
Details - acute risk assessment/children	Details - acute risk assessment/adults

The acute risk assessment is based on the ARfD. DISCLAIMER: Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.
The calculation is based on the large portion of the most critical consumer group.

Show results for all crops

Unprocessed commodities

Results for children
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
48%	Cauliflowers	3/1.42	82
45%	Potatoes	0.5/0.5	77
45%	Melons	0.5/0.5	76
41%	Pears	0.5/0.5	69
40%	Head cabbages	3/1.52	67
39%	Oranges	0.5/0.5	66
36%	Watermelons	0.5/0.5	61
34%	Beetroots	1/1	57
32%	Apples	0.5/0.5	54
30%	Pineapples	0.5/0.5	51
29%	Bananas	0.5/0.5	49
28%	Peaches	0.5/0.5	48
26%	Kales	1/1	44
24%	Swedes/rutabagas	1.5/0.8	41
23%	Mangoes	0.5/0.5	39

Expand/collapse list

Results for adults
No. of commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
38%	Head cabbages	3/1.52	64
19%	Cauliflowers	3/1.42	33
17%	Yams	1/1	28
16%	Swedes/rutabagas	1.5/0.8	27
15%	Chinese cabbages/pe-tsai	1/1	25
14%	Beetroots	1/1	23
12%	Sweet potatoes	1/1	21
12%	Watermelons	0.5/0.5	20
12%	Melons	0.5/0.5	20
11%	Kales	1/1	19
11%	Chards/beet leaves	1/1	19
10%	Broccoli	1.5/0.73	17
10%	Rice	2/2	17
10%	Table grapes	0.5/0.5	17
9%	Oranges	0.5/0.5	15

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

Processed commodities

Results for children
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
58%	Cauliflowers/boiled	3/1.42	99
34%	Broccoli/boiled	1.5/0.73	58
30%	Sweet potatoes/boiled	1/1	50
27%	Potatoes/fried	0.5/0.5	47
27%	Maize/oil	2/50	47
26%	Pumpkins/boiled	0.5/0.5	44
26%	Witloofs/boiled	0.5/0.5	44
26%	Beetroots/boiled	1/1	44
24%	Turnips/boiled	1.5/0.8	41
23%	Sugar beets (root)/sugar	1/4.2	39
19%	Escaroles/broad-leaved endives/boiled	0.5/0.5	33
18%	Chards/beet leaves/boiled	1/1	31
17%	Potatoes/dried (flakes)	0.5/2.3	30
16%	Kales/boiled	1/1	28
16%	Apples/juice	0.5/0.5	27

Expand/collapse list

Results for adults
No of processed commodities for which ARfD/ADI is exceeded (IESTI): ---

IESTI

Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
35%	Cauliflowers/boiled	3/1.42	59
23%	Beetroots/boiled	1/1	39
16%	Pumpkins/boiled	0.5/0.5	28
15%	Maize/oil	2/50	25
11%	Cassava roots/boiled	1/1	19
10%	Broccoli/boiled	1.5/0.73	18
10%	Celeries/boiled	0.5/0.5	17
10%	Apples/juice	0.5/0.5	17
9%	Sweet potatoes/boiled	1/1	15
9%	Sugar beets (root)/sugar	1/4.2	15
9%	Turnips/boiled	1.5/0.8	15
7%	Chards/beet leaves/boiled	1/1	13
7%	Courgettes/boiled	0.5/0.5	11
6%	Parsnips/boiled	0.5/0.5	11
6%	Kohlrabies/boiled	0.5/0.5	11

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

APPENDIX D

Input values for the exposure calculations

D.1 | CONSUMER RISK ASSESSMENT

Commodity	Existing/ proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value[a] (mg/kg)	Comment	Input value[a] (mg/kg)	Comment[b]
Risk assessment residue definition: Clopyralid common moiety (sum of clopyralid, its salts and conjugates expressed as clopyralid)						
Swedes/rutabagas	1.5	EFSA (2011)	0.35	STMR-RAC	0.8	HR-RAC
Turnips	1.5	EFSA (2018b)	0.35	STMR-RAC	0.8	HR-RAC
Broccoli	1.5	EFSA (2011)	0.3	STMR-RAC	0.73	HR-RAC
Cauliflowers	3	EFSA (2011)	0.29	STMR-RAC	1.42	HR-RAC
Head cabbages	3	EFSA (2011)	0.23	STMR-RAC	1.52	HR-RAC
Leeks	0.7	EFSA (2018b)	0.18	STMR-RAC	0.43	HR-RAC
Linseeds	20	EFSA (2011)	4.46	STMR-RAC	4.46	STMR-RAC
Barley	2	EFSA (2021)	0.33	STMR-RAC	0.33	STMR-RAC
Oat	3	EFSA (2021)	0.72	STMR-RAC	0.72	STMR-RAC
Rye	3	EFSA (2021)	0.72	STMR-RAC	0.72	STMR-RAC
Wheat	3	EFSA (2021)	0.72	STMR-RAC	0.72	STMR-RAC
Sugar beet roots	1	EFSA (2011)	0.35	STMR-RAC	0.8	HR-RAC
Swine muscle/meat	0.01*	EFSA (2021)	0.01	STMR-RAC	0.01	HR-RAC
Swine: Fat tissue	0.05	EFSA (2021)	0.01	STMR-RAC	0.05	HR-RAC
Swine: Liver	0.05	EFSA (2021)	0.02	STMR-RAC	0.05	HR-RAC
Swine: Kidney	0.6	EFSA (2021)	0.2	STMR-RAC	0.54	HR-RAC
Bovine: muscle/meat	0.03	EFSA (2021)	0.01	STMR-RAC	0.03	HR-RAC
Bovine: Fat tissue	0.15	EFSA (2021)	0.05	STMR-RAC	0.14	HR-RAC
Bovine: Liver	0.15	EFSA (2021)	0.06	STMR-RAC	0.13	HR-RAC
Bovine: Kidney	1.5	EFSA (2021)	0.72	STMR-RAC	1.45	HR-RAC
Sheep: Muscle/meat	0.04	EFSA (2021)	0.02	STMR-RAC	0.03	HR-RAC
Sheep: Fat tissue	0.2	EFSA (2021)	0.06	STMR-RAC	0.17	HR-RAC
Sheep: Liver	0.2	EFSA (2021)	0.06	STMR-RAC	0.17	HR-RAC
Sheep: Kidney	2	EFSA (2021)	0.87	STMR-RAC	1.81	HR-RAC
Goat: Muscle/meat	0.04	EFSA (2021)	0.02	STMR-RAC	0.03	HR-RAC
Goat: Fat tissue	0.2	EFSA (2021)	0.06	STMR-RAC	0.17	HR-RAC
Goat: Liver	0.2	EFSA (2021)	0.06	STMR-RAC	0.17	HR-RAC
Goat: Kidney	2	EFSA (2021)	0.87	STMR-RAC	1.81	HR-RAC
Poultry: Muscle/meat	0.01*	EFSA (2021)	0.01	STMR-RAC	0.01	HR-RAC
Poultry: Fat tissue	0.01*	EFSA (2021)	0.01	STMR-RAC	0.01	HR-RAC
Poultry: Liver	0.03	EFSA (2021)	0.01	STMR-RAC	0.02	HR-RAC
Milk: Cattle	0.015	EFSA (2021)	0.013	STMR-RAC×CF (1.3)	0.013	STMR-RAC×CF (1.3)
Milk: Sheep	0.015	EFSA (2021)	0.013	STMR-RAC×CF (1.3)	0.013	STMR-RAC×CF (1.3)
Eggs: Chicken	0.01*	EFSA (2021)	0.01	STMR-RAC	0.01	HR-RAC
Honey and other apiculture products	0.15	Proposed	0.01	STMR-RAC	0.07	HR-RAC
Other crops/commodities	–	Regulation (EU) 2021/1807	–	EU MRL	–	EU MRL

Abbreviations: CF, conversion factor; HR-RAC, highest residue in raw agricultural commodity; PeF, Peeling factor; STMR-RAC, supervised trials median residue in raw agricultural commodity.

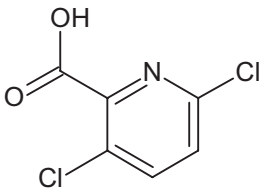
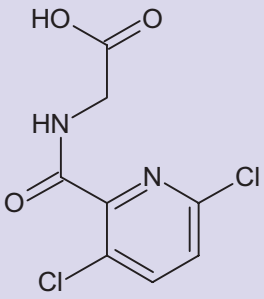
[a]Figures in the table are rounded to two digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce dietary burden calculations, the unrounded values need to be used.

[b]Input values for the commodities which are not under consideration for the acute risk assessment are reported in grey.

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

APPENDIX E

Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Clopyralid	3,6-dichloropyridine-2-carboxylic acid or 3,6-dichloropicolinic acid O=C(C1=NC(Cl)=CC=C1Cl)O HUBANNPOLNYSAD-UHFFFAOYSA-N	
X36538 **clopyralid glycine conjugate**	*N*-(3,6-dichloropyridine-2-carbonyl)glycine Clc1ccc(Cl)nc1C(=O)NCC(=O)O QONCEWHCVBAIBS-UHFFFAOYSA-N	

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

[a]The metabolite name in bold is the name used in the conclusion.

[b]ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 07 Jul 2021).

[c]ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 Aug 2021).