Modification of the existing maximum residue level for phenmedipham in celeriac

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant UPL Europe Ltd. submitted an application to the competent national authority in Germany (evaluating Member State, EMS) to raise the existing maximum residue level (MRL) to 0.15 mg/kg for the active substance phenmedipham in celeriac. The submitted residue trials are sufficient to derive a tentative MRL of 0.15 mg/kg, pending further investigation of nature of phenmedipham residues in root crops. For this assessment EFSA considered that the available sugar beet metabolism data can be extrapolated to celeriac on a tentative basis. The acceptability of such proposal shall be further considered by risk managers. Adequate analytical methods for enforcement are available to control the residues of phenmedipham in celeriac at the validated limit of quantification (LOQ) of 0.01 mg/kg. Since the current MRL application was submitted before the finalisation of the EU pesticides peer review of the renewal of the approval of phenmedipham, the consumer exposure assessment was performed according to the conclusions on the toxicity of phenmedipham from the first approval under Directive 91/414/EEC. Accordingly, the long-term intake of residues of phenmedipham resulting from the existing and the intended uses does not indicate a risk to consumer health. The present assessment does not consider the data gaps identified in the context of the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009 which prevented experts to derive toxicological reference values (TRVs) for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites.

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, UPL Europe Ltd. submitted an application to the competent national authority in Germany (evaluating Member State, EMS) to raise the existing maximum residue level (MRL) to 0.15 mg/kg for the active substance phenmedipham in celeriac. 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 13 January 2020. To accommodate for the intended northern Europe (NEU) use of phenmedipham, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.01 to 0.15 mg/kg in celeriac.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. During the assessment, EFSA identified data gaps which needed further clarification, which were requested from the EMS. On 22 January 2021, the EMS proposed EFSA to resume the assessment on phenmedipham, despite the pending open point identified during the European Union (EU) pesticides peer review on the renewal of the approval of phenmedipham concerning the genotoxic potential of the active substance, as this was not yet applicable at time of submission of the MRL application. EFSA resumed the assessment, based on the available information.

Since the current MRL application was submitted before the finalisation of the EU pesticides peer review on the renewal of the approval of phenmedipham, the current assessment is based on the conclusions derived in the first approval of phenmedipham according to Directive 91/414/EEC and in the framework of the review of existing phenmedipham MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review), acknowledging the new scientific data available for the EU pesticides peer review.

The metabolism of phenmedipham in primary crops has been investigated in the MRL review and in the framework of the renewal of the approval following foliar application on root crops (sugar beet) and fruits (strawberries). Based on the data available for the MRL review on sugar beet, it was concluded that the available studies are insufficient and new metabolism study on root crop is required. The EU peer review assessed additional new studies on sugar beet and concluded that phenmedipham and its conjugates are the predominant compounds of the total residues in sugar beet, but the study is valid only for the use on sugar beet. Due to significant proportions of unknown compounds and low rate of metabolites’ identification, the EU pesticides peer review concluded that the fate of phenmedipham should be further investigated in case of new intended uses on other root crops with further characterisation and identification of the radioactive residues in roots.

EFSA received an MRL application on celeriac, representing the root crop group, for which the data gaps related to a need for an adequate metabolism study are applicable and have not been addressed. In response to this data gap, the EMS noted that the MRL application on celeriac was submitted (April 2015) before the EU pesticides peer review was completed and requested EFSA to assess the MRL application emphasising that celeriac is a minor crop and proposing to extend residue definitions from sugar beet to celeriac on tentative basis, until more metabolism studies are available. EFSA thus proceeded with the assessment of the MRL application on celeriac considering the arguments of the EMS, the data gaps identified by the MRL review and the EU pesticides peer review and noting that the proposal to extrapolate results of the sugar beet metabolism study to celeriac is supported on a tentative basis and shall be further considered by the risk managers.

In the MRL review, a hydrolysis study to address the effect of processing on the nature of phenmedipham residues, was not required, considering low chronic exposure to phenmedipham residues. Such studies were assessed for the renewal of the approval demonstrating that the active substance degraded partially into 3-methylaniline (m-toluidine) and methyl (3-hydroxyphenyl) carbamate (MHPC) at baking/brewing and boiling and completely into 3-methylaniline (m-toluidine) under sterilisation conditions. Under pasteurisation conditions phenmedipham is considered stable. The EU pesticides peer review in the context of the renewal of approval set a data gap for the toxicity of 3-methylaniline and proposed that for MHPC the toxicological reference values (TRVs) of phenmedipham, or the lack thereof, are applicable.

As the intended use of phenmedipham is on annual crop, investigation of residues in rotational crops is required. Based on the results of metabolism studies, the EU pesticides peer review concluded that the metabolism of phenmedipham in rotational crops proceeds in a different pathway than in primary crops, with phenmedipham and MHPC being the relevant residues. The field studies assessed confirm the results of metabolism studies that residues of phenmedipham and MHPC are not expected...
to occur above 0.01 mg/kg in rotational crops. The same conclusion is thus applicable for the intended phenmedipham use on celeriac.

The MRL review proposed to define the enforcement residue definition in plant commodities as ‘phenmedipham’ on tentative basis. The residue definition for the risk assessment was proposed as ‘phenmedipham’ for fruit crops only and is tentative for leafy and root primary crops and rotational crops, pending additional metabolism studies. The EU peer review of the renewal of approval proposed the enforcement residue definition as ‘phenmedipham’ only for root and fruit crops. The risk assessment residue definition in fruit crops could not be derived and the residue definition as ‘phenmedipham (free and glucoside conjugates)’ is applicable to sugar beet only. Thus, there is currently no risk assessment residue definition that would be applicable for celeriac. Upon the request of the EMS and considering the intended use refers to a minor crop, for this assessment EFSA considered that the sugar beet metabolism could be extrapolated to celeriac on a tentative basis. The acceptability of such proposal shall be further considered by risk managers.

Sufficiently validated analytical enforcement methods are available to quantify residues in celeriac at the validated LOQ of 0.01 mg/kg. Sufficient number of residue trials has been submitted to derive an MRL of 0.15 mg/kg in support of the NEU use of phenmedipham on celeriac. The calculated MRL is tentative, pending new metabolism study on root crops or further characterisation/identification of residues from available sugar beet metabolism study.

Specific studies investigating the magnitude of phenmedipham residues in processed celeriac are not required in the context of the current assessment given the low contribution of residues in celeriac to the total theoretical maximum daily intake (TMDI). Residues of phenmedipham in commodities of animal origin were not assessed since celeriac are normally not fed to livestock.

The toxicological profile of phenmedipham was assessed in the framework of the first approval under Directive 91/414/EEC and the data were considered sufficient to derive an acceptable daily intake (ADI) of 0.03 mg/kg body weight (bw) per day; setting of an acute reference dose (ARfD) was considered not necessary. Since the current MRL application was submitted before the finalisation of the EU peer review on the renewal of the approval of phenmedipham, the consumer exposure assessment was undertaken in line with conclusions of the MRL review and the first approval of phenmedipham under Directive 91/414/EEC. It is noted that during the renewal of the approval process the TRVs for phenmedipham could not be derived since a genotoxic potential for phenmedipham could not be excluded; also the toxicity of the degradation product 3-methylaniline remains a data gap.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). A short-term dietary risk assessment was not required. In the framework of the MRL review a comprehensive long-term exposure assessment was performed taking into account the existing uses at EU level. EFSA updated the calculation with the STMR value derived from the residue trials on celeriac as submitted in support of this MRL application as well as with the risk assessment value for strawberries from a recent EFSA assessment. A provisional conversion factor of 1.4 as derived by the EU peer review for sugar beet root was applied to account for potential phenmedipham conjugates in celeriac root. Crops on which no uses were reported in the MRL review or for which the MRL proposals were not implemented in the MRL legislation (sugar beet) were excluded from the calculation.

The estimated long-term dietary intake of phenmedipham residues accounted for up to 11% of the ADI (NL toddler diet). The highest contribution of residues in celeriac to the overall long-term exposure is 0.07% of the ADI for the GEMS/Food G11 diet. EFSA concluded that, according to the conclusions on the toxicity of phenmedipham from the first approval under Directive 91/414/EEC, the long-term intake of residues of phenmedipham resulting from the existing and the intended uses is unlikely to present a risk to consumer health.

EFSA notes that on the basis of new scientific data available for the renewal of the approval process of phenmedipham under Regulation (EC) No 1107/2009, various data gaps with regard to the toxicological profile of phenmedipham and its metabolites were identified, which prevented experts to derive TRVs for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites. The conclusions of this assessment are thus provisional pending the finalisation of the renewal of the approval process of phenmedipham.

Considering the above-mentioned outstanding issues, the proposal for amendment of the existing MRL as reported in the summary table below requires further risk management considerations.

Full details of all endpoints 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                                                                 |
|-----------|-----------------------------------|------------------------|-------------------------|----------------------------------------------------------------------------------------|
| 0213030   | Celeriacs/turnip rooted celeries  | 0.01*                  | (0.15)                  | The submitted data are sufficient to derive an MRL proposal in support of the intended NEU use. The MRL proposal is considered tentative, pending the availability of a metabolism study in primary root crops, allowing to derive a risk assessment residue definition in root crops other than sugar beet. Upon the request of the evaluating Member State (EMS) and considering the intended use refers to a minor crop, for this assessment EFSA extrapolated the sugar beet metabolism data to celeriac on a tentative basis. The acceptability of such proposal shall be further considered by the risk managers. Risk to consumers unlikely, according to the conclusions on the toxicity of phenmedipham from the first approval of the active substance under Directive 91/414/EEC. The present assessment does not consider the data gaps identified in the context of the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009 which prevented experts to derive toxicological reference values (TRVs) for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites. |

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

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
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Modification of the existing maximum residue level for phenmedipham in celeriac
Assessment

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

Phenmedipham is the ISO common name for 3-[(methoxycarbonyl)amino]phenyl(3-methylphenyl) carbamate (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Phenmedipham was evaluated in the framework of Directive 91/414/EEC1 with Finland being the designated rapporteur Member State (RMS). The representative use supported for the peer review process was the outdoor foliar application on sugar beet, fodder beet and beetroot in both northern and southern Europe. According to Regulation (EU) No 540/20112, phenmedipham is deemed to have been approved under Regulation (EC) No 1107/20093. This approval is restricted to uses as herbicide. EFSA was not involved in the first peer review of phenmedipham.

The EU peer review in the context of the renewal of the approval of phenmedipham according to Regulation (EC) No 1107/2009 has been completed (EFSA, 2018b), but the renewal decision has not been taken yet, pending the assessment of endocrine-disrupting (ED) properties of phenmedipham. Finland was designated as RMS and Denmark as co-RMS, evaluating the representative uses of phenmedipham as a post-emergence treatment on sugar beet/fodder beet. The renewal assessment report (RAR) has been peer reviewed by EFSA (2018b). The approval of phenmedipham was extended until 31 July 2021 by Regulation (EU) 2020/8694, pending the assessment of ED properties.

The EU MRLs for phenmedipham are established in Annex II of Regulation (EC) No 396/20055. The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been completed (EFSA, 2014) and the proposed modifications for all crops, except sugar beet, have been implemented in the MRL legislation.6 There are no Codex maximum limits (CXLs) established for phenmedipham.

In accordance with Article 6 of Regulation (EC) No 396/2005, UPL Europe Ltd. submitted an application to the competent national authority in Germany (EMS) to raise the existing MRL to 0.15 mg/kg for the active substance phenmedipham in celeriac. 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 13 January 2020. To accommodate for the intended NEU use of phenmedipham, the EMS proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.01 to 0.15 mg/kg in celeriac.

During the assessment, EFSA identified data gaps which needed further clarification, which were requested from the EMS. On 22 January 2021 the EMS proposed EFSA to resume the assessment on phenmedipham despite the pending open points identified during EU pesticides peer review on the renewal of the approval of phenmedipham concerning the genotoxic potential of the active substance and the lack of metabolism studies in root crops, as this was not yet applicable at time of submission of the MRL application. EFSA agreed to resume the assessment, based on the available information.

EFSA based its assessment on the evaluation report submitted by the EMS (Germany, 2021), the Draft Assessment Report (DAR) prepared under Council Directive 91/414/EEC (Finland, 1999), the RAR (Finland, 2016) prepared under Regulation (EC) 1107/2009, the Commission review report on phenmedipham (European Commission, 2004), the conclusion on the peer review of the pesticide risk

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 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.
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 Commission Implementing Regulation (EU) 2020/869 of 24 June 2020 amending Implementing Regulation (EU) No 540/2011 as regards the extension of the approval periods of the active substances beflubutiram, benalaxyl, bethiavacarb, bifenazate, boscalid, bromoxynil, captan, cyazofamid, dimethomorph, ethephon, etoxazole, fenamiphos, flumioxazin, fluoxastrobin, folpet, fortementate, metribuzin, milbemectin, Paecilomyces lilacinus strain 251, phenmedipham, phosmet, pirimiphos-methyl, propamocarb, prothioconazole and S-metolachlor. OJ L 201, 25.6.2020, p. 7–9.
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, p. 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
assessment of the active substance phenmedipham (EFSA, 2018b), as well as the conclusions from EFSA opinion on the review of existing MRLs for phenmedipham according to Article 12 of Regulation (EC) 396/2005 (EFSA, 2014).

For this application, the data requirements established in Regulation (EU) No 544/2011\(^7\) 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). 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\(^8\).

A selected list of end points from the renewal of approval process of phenmedipham, is presented in Appendix B.

The evaluation report submitted by the EMS (Germany, 2021) 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.

EFSA notes that new scientific data have become available for the renewal process of phenmedipham under Regulation (EC) No 1107/2009, as provided in the RAR (Finland, 2016) and assessed in the conclusion on the peer review of the pesticide risk assessment of the active substance phenmedipham (EFSA, 2018b). However, since the present MRL application was submitted before the finalisation of the EU pesticides peer review in the context of the renewal of the approval of phenmedipham, the current assessment is based on the conclusions derived in the first approval of phenmedipham according to Directive 91/414/EEC and in the framework of the review of existing phenmedipham MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review), acknowledging the new scientific data available from the EU pesticides peer review. The conclusions of this assessment are thus provisional pending the finalisation of the renewal of the approval process of phenmedipham.

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 phenmedipham in primary crops has been investigated in the framework of the MRL review (EFSA, 2014) and in the renewal of approval process (EFSA, 2018b) following foliar application on root crops (sugar beet) with both [amino-phenyl-UL-\(^{14}\)C] and [phenyl-methyl-UL-\(^{14}\)C] phenmedipham and in fruits (strawberries) only with [amino-phenyl-UL-\(^{14}\)C] radiolabelled phenmedipham (Finland, 1999, 2016). Since the finalisation of the MRL review, additional new metabolism study on sugar beet was provided, addressing the uncertainties identified in the MRL review, i.e. "none of the studies on sugar beet were performed according to the GLP principles and studies do not give information about the metabolism of phenmedipham in mature crop parts and consequently new metabolism data covering the currently authorised European uses and performed on crops representative for root and tuber vegetables is required" (EFSA, 2014).

Based on the new and old available studies on sugar beet, the EU pesticides peer review concluded that phenmedipham and its conjugates were the predominant compounds of the total residues in immature and mature sugar beet leaves (95% total radioactive residue (TRR) and 51% TRR, respectively). In sugar beet root, phenmedipham and its conjugates were detected at a low level (6.6% TRR) while a major unknown fraction accounted for ca. 26% TRR in roots and 14% TRR in mature leaves. This fraction was generated only from the amino phenol moiety and consisted of several polar minor metabolite fractions (EFSA, 2018b).

In strawberries, phenmedipham was the main compound recovered in fruits (58% TRR) while 3-acetamidophenol accounted for 13% TRR. 3-Acetamidophenol is a rat metabolite and was not recovered in the sugar beet metabolism study. However, since only one label was investigated in strawberry metabolism studies, the EU pesticide peer review could not conclude on the relevant

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\(^7\) 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.

\(^8\) 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.
residues for the risk assessment in fruit crops and, in addition, set a data gap for the toxicity of 3-acetamidophenol (EFSA, 2018b).

During the expert meeting, the validity of the metabolism studies provided on sugar beet (old and new) was discussed considering the significant proportions of unknown compounds/low rate of metabolites’ identification and whether these data are compliant with the current OECD recommendations (only 29% TRR identified in mature sugar beet leaves, 6% TRR identified in mature root). The characterised fraction accounted for 34% and 32% TRR in mature sugar beet leaves and root, respectively. The meeting agreed that the available metabolism data on sugar beet are considered acceptable to support the representative use on sugar beet only. The meeting was also of the opinion that the fate of phenmedipham should be further investigated in case of uses on other root crops with further characterisation and identification of the radioactive residues in root, as the high extracted polar fraction as sugar, cannot necessarily be extrapolated to other root crops (EFSA, 2018b). It is noted that the data gap for a new metabolism study on root crops was already identified in the framework of the MRL review (EFSA, 2014).

EFSA received an MRL application on celeriac, representing the root crop group. According to the conclusions of the MRL review, a new use on root crop is not supported by metabolism study. According to the EU pesticides peer review, which addressed the data gaps of the MRL review, a new use on root crop (except sugar beet), would need to be supported by an adequate metabolism study on a root crop or further characterisation/identification of radioactive residues from the available metabolism studies would be required.

Upon receipt of the MRL application on celeriac, a need for an adequate metabolism study in root crops was identified as a data gap. In response to the EFSA request for additional data and noting that the MRL application on celeriac was submitted to the EMS (April 2015) before the EU pesticides peer review was completed, the EMS asked EFSA to assess the MRL application emphasising that celeriac is a minor crop and proposing to extend residue definitions on a tentative basis to celeriac, until more metabolism studies are available for other crops/groups.

EFSA thus proceeded with the assessment of the MRL application on celeriac considering the arguments of the EMS, the data gaps identified by the MRL review (EFSA, 2014) and the EU pesticides peer review (EFSA, 2018b) and noting that the proposal to extrapolate results of the sugar beet metabolism study to celeriac is supported on a tentative basis and shall be further considered by the risk managers.

1.1.2. Nature of residues in rotational crops

Celeriac can be grown in rotation with other crops. The fate and behaviour of phenmedipham in soil was investigated in the EU pesticides peer review and studies indicated that in soil laboratory incubations under aerobic conditions in the dark, phenmedipham exhibited low to high persistence, forming the metabolite methyl (3-hydroxyphenyl)carbamate (MHPC) (max. 14% applied radioactivity (AR)), which exhibited low to moderate persistence (EFSA, 2018b). Thus, the nature and magnitude of phenmedipham residues in rotational crops was investigated further.

The nature of phenmedipham in rotational crops was investigated in the MRL review and in the EU pesticides peer review (EFSA, 2014, 2018b). A study was conducted with the amino-phenyl-UL-14C phenmedipham (1.1 kg/ha) on lettuce, sugar beet and wheat at 30, 120 and 365 plant-back intervals (PBIs). The metabolic pattern was consistent throughout all PBIs with phenmedipham and MHPC being the only identified metabolite in rotational crops. In wheat straw, phenmedipham (20% TRR) and MHPC (25% TRR) were the major compounds of the TRR (0.95 mg eq./kg). The same metabolic pattern was observed in cereal forage. A significant decline of the total residues from the first to the third rotation interval was observed.

In the framework of the EU pesticides peer review (EFSA, 2018b), a new confined rotational crop study was conducted on wheat, turnip and chard with an application of 1.28 kg phenyl-methyl-UL-14C phenmedipham/ha at 30, 164 and 305 days PBIs. Although some deficiency was noted (low rate of identification) as in the first study, the metabolism pattern was considered sufficiently addressed because of the expected low residue levels in all edible parts.

The EU pesticides peer review concluded that the metabolism of phenmedipham in rotational crops proceeds in a different pathway than in primary crops, with phenmedipham and MHPC being the relevant residues (EFSA, 2018b).
1.1.3. Nature of residues in processed commodities

In the MRL review, no studies were assessed or required to address the effect of processing on the nature of phenmedipham residues, considering low chronic exposure to phenmedipham residues (EFSA, 2014).

The nature of phenmedipham residues during processing (standard hydrolysis study) was investigated in the framework of the renewal of approval process (EFSA, 2018b). Under standard hydrolysis conditions when investigated with phenyl-methyl labelling, phenmedipham degraded partially into 3-methylaniline (m-toluidine) under conditions representative of baking/brewing and boiling (86% AR) and completely into 3-methylaniline (m-toluidine) under sterilisation conditions. Under these conditions, it can reasonably be assumed that the formation of aniline can be excluded. For the amino phenol labelling form, a complete degradation of phenmedipham to MHPC was observed under conditions representative of baking/brewing and boiling and also under conditions representative of sugar production. Under pasteurisation conditions, phenmedipham is considered stable for both labelled forms (82–87% of AR). The EU pesticides peer review on the renewal of the approval concluded that the nature of phenmedipham residues in raw and processed commodities is different (EFSA, 2018b).

1.1.4. Methods of analysis in plants

Analytical methods for the determination of phenmedipham residues in plant matrices were assessed during the renewal of approval process (EFSA, 2018b). Phenmedipham residues can be monitored in food and feed of plant origin by the multiresidue method DFG S19 (extended revision) using liquid chromatography with tandem mass spectrometry (LC-MS/MS) with a limit of quantification (LOQ) of 0.01 mg/kg in all commodity groups. In addition, there is QuEChERS method using gas chromatography-mass spectrometry (GC-MS) and/or LC-MS/MS for all plant commodities with LOQs in the range 0.01–0.05 mg/kg.

In the framework of the EU pesticides peer review on the renewal of approval, a specific residue definition for monitoring was proposed in processed commodities of plant origin. In case a specific MRL for these commodities is set, monitoring methods for the components included in the residue definition might be required (EFSA, 2018b).

It is concluded that sufficiently validated analytical enforcement methods are available to control phenmedipham residues in celeriac.

1.1.5. Storage stability of residues in plants

The storage stability of phenmedipham and metabolite MHPC in plant matrices stored under frozen conditions was assessed in the framework of the renewal of approval process (EFSA, 2018b). Storage stability data demonstrated that phenmedipham and MHPC residues are stable up to 24 months in high water- high oil-, high protein-, high starch- and high acid-content commodities, when stored at ≤–18°C. Thus, in high-water content commodities (relevant for celeriac) residues of phenmedipham and of its metabolite MHPC are stable for at least 24 months when stored at ≤–18°C.

1.1.6. Proposed residue definitions

The MRL review, based on metabolism studies in primary and rotational crops, the toxicological significance of metabolites and the capabilities of analytical enforcement methods, proposed the following residue definitions in primary crops and processed commodities (EFSA, 2014):

- residue for risk assessment: ‘phenmedipham’ (fruits and fruiting crops; tentative for other crops, pending additional metabolism studies on leafy and root primary crops and rotational crops).
- residue definition for enforcement: ‘phenmedipham’ (tentative, pending additional metabolism studies on leafy and root primary crops and rotational crops).

The EU pesticides peer review in the framework of the renewal of approval of the active substance, based on the metabolic pattern identified in primary and rotational crop metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and degradation products, the capabilities of enforcement analytical methods, proposed the following residue definitions (EFSA, 2018b):
• residue for risk assessment:
  – ‘phenmedipham (free and glucoside conjugates)’ (RAC: restricted to sugar beet),
  – ‘sum of phenmedipham and MHPC, and their conjugates, expressed as phenmedipham’ (RAC: rotational crops),
  – ‘sum of phenmedipham and MHPC, expressed as phenmedipham’ and ‘m-toluidine’ (provisional, processed commodities).

• residue definition for enforcement:
  – ‘phenmedipham’ (RAC: root and fruit crops),
  – ‘sum of phenmedipham and MHPC, expressed as phenmedipham’ (processed commodities).

Provisional conversion factors (CFs) for risk assessment of 1.4 (root) and 1.2 (leaves) were derived from the metabolism studies; these data would still need to be confirmed by residue trials (EFSA, 2018b).

Since the present MRL application was submitted to the EMS (April 2015) before the EU pesticides peer review on the renewal of approval was completed, EFSA assessed this application according to the MRL setting procedure at the time of the submission of MRL application, though acknowledging the new scientific information that has become available during the EU pesticides peer review. Upon the request of the EMS and considering the minor intended use on celeriac, for this assessment EFSA considered the conclusions of the sugar beet metabolism extrapolated to celeriac on a tentative basis. The acceptability of such proposal shall be further considered by risk managers.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the intended NEU use of phenmedipham on celeriac, the applicant submitted five residue trials on celeriac, which were performed in Germany in 2012 and 2013. One trial was performed with one instead of two applications, but, as the residue value was within the same range as in other trials and would not affect the MRL proposal, this trial was accepted. The remaining four trials were all GAP compliant.

The number of trials is sufficient to derive the risk assessment values and the MRL proposal of 0.15 mg/kg for phenmedipham in celeriac in support of the intended NEU use. The calculated MRL is tentative according to the proposal of the EMS Germany (Germany, 2021), pending new metabolism study on root crops or further characterisation/identification of residues from the available metabolism study in sugar beet.

Under the assumption that for celeriac the same risk assessment residue definition is applicable as for sugar beet roots (e.g. phenmedipham (free and glucoside conjugates)), in order to derive risk assessment values, a provisional conversion factor of 1.4 as proposed by the EU pesticides peer review (EFSA, 2018b) from enforcement to risk assessment in sugar beet root, was applied also for the celeriac root.

According to the assessment of the EMS, the analytical methods used to analyse residue trial samples were sufficiently validated and were fit for purpose. The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated (Germany, 2021).

1.2.2. Magnitude of residues in rotational crops

The magnitude of phenmedipham in rotational crops was investigated in the framework of the EU pesticides peer review (EFSA, 2018b). Phenmedipham was applied either on a bare soil or target crop sugar beet at an application rate of 0.96 kg/ha, followed by planting of rotational crops lettuce, carrots, turnips, wheat and barley. The results confirm the conclusions of the confined study, that residues of phenmedipham and MHPC do not occur above the level of 0.01 mg/kg in the rotational crops studied. The same conclusion is thus applicable for the intended phenmedipham use on celeriac.

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9 Pending confirmation of the toxicity of m-toluidine (EFSA, 2018b).
1.2.3. Magnitude of residues in processed commodities

Specific processing studies for celeriac are not available and are not required in the context of the current assessment, considering low consumer exposure to phenmedipham residues (see Section 3).

1.2.4. Proposed MRLs

Based on five celeriac trials, an MRL of 0.15 mg/kg is derived in support of the intended NEU GAP of phenmedipham. The calculated MRL is tentative, pending a new metabolism study on root crops or further characterisation/identification of residues from the available metabolism study in sugar beet.

In Section 3, EFSA assessed whether residues in celeriac resulting from the intended use are likely to pose a consumer health risk.

2. Residues in livestock

Not relevant as celeriac is not used for feed purposes.

3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo. 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 (EFSA, 2018a, 2019).

Since the current MRL application was submitted prior to the finalisation of the EU peer review of the pesticide risk assessment in the context of the renewal of the approval of phenmedipham, the consumer exposure assessment was undertaken in line with the first approval of phenmedipham and the conclusions of the MRL review (European Commission, 2004; EFSA, 2014). Thus, the toxicological reference value (TRV) for phenmedipham used in the risk assessment (i.e. acceptable daily intake (ADI) value of 0.03 mg/kg body weight (bw) per day) was the one derived in the first peer review in the framework of the approval of the active substance under Directive 91/414/EEC; the setting of an acute reference dose (ARfD) was considered not necessary (European Commission, 2004).

It is noted that in the framework of the EU peer review in the context of the renewal of the approval of phenmedipham, the TRVs for parent compound could not be derived since a genotoxic potential for phenmedipham could not be excluded (EFSA, 2018b). In addition, data gaps for the assessment of toxicity were set for the processing degradation product 3-methylaniline (m-toluidine) and the plant metabolite 3-acetamidophenol (EFSA, 2018b).

Short-term (acute) dietary risk assessment

Considering the outcome of the assessment of the toxicological profile of the active substance in the framework of the approval of the active substance phenmedipham under Directive 91/414/EEC, a short-term dietary risk assessment was not required (European Commission, 2004).

Long-term (chronic) dietary risk assessment

In the framework of the MRL review a comprehensive long-term exposure assessment was performed, taking into account the existing uses at EU level (EFSA, 2014). Recently an assessment of the phenmedipham use on strawberries (EFSA, 2021) was carried out by EFSA and therefore considered in the exposure assessment. EFSA updated the calculation with the STMR value derived from the residue trials on celeriac submitted in support of the current MRL application. A provisional conversion factor of 1.4, as derived by the EU pesticides peer review for sugar beet root, was applied to account for potential phenmedipham conjugates in celeriac root. Crops for which no uses were reported in the MRL review were excluded from the calculations. The use on sugar beet has been assessed in the MRL review, resulting in a tentative MRL proposal, which was not implemented in the MRL legislation. Thus, sugar beet was excluded from the exposure assessment, assuming there are no authorised uses in the EU. A provisional conversion factor of 1.4 as derived by the EU pesticides peer review for sugar beet roots was also applied for the input values of beetroot.

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

The estimated long-term dietary intake of phenmedipham residues accounted for up to 11% of the ADI (NL toddler diet), considering the proposed use on celeriac, and the reported uses of phenmedipham in the MRL review and the new intended use recently assessed on strawberries. The
highest contribution of residues in celeriac to the overall long-term exposure is 0.07% of the ADI for the GEMS/Food G11 diet.

EFSA concluded that, according to the conclusions on the toxicity of phenmedipham from the first approval of phenmedipham under Directive 91/414/EEC, the long-term intake of residues of phenmedipham resulting from the existing and the intended uses is unlikely to present a risk to consumer health.

EFSA notes that on the basis of new scientific data available in the process for the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009, various data gaps with regard to the toxicological profile of phenmedipham and its metabolites were identified, which prevented experts to derive TRVs for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites.

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

Based on five celeriac trials, an MRL of 0.15 mg/kg is derived in support of the intended NEU use of phenmedipham. The calculated MRL is tentative, pending new metabolism study on root crops or further characterisation/identification of residues from available sugar beet metabolism study.

Since the current MRL application was submitted prior to the finalisation of the EU peer review of the pesticide risk assessment (EFSA, 2018b) in the context of the renewal of the approval of phenmedipham, the consumer exposure assessment was performed in line with the conclusions of the first approval of phenmedipham and the MRL review. EFSA concluded that according to the conclusions on the toxicity of phenmedipham from the first approval of phenmedipham under Directive 91/414/EEC, the long-term intake of phenmedipham residues resulting from the existing and the intended uses is unlikely to present a risk to consumer health.

EFSA notes that on the basis of new scientific data available in the process for the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009, various data gaps with regard to the toxicological profile of phenmedipham and its metabolites were identified, which prevented experts to derive TRVs for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites.

The conclusions of this assessment are thus provisional pending the finalisation of the process for the renewal of the approval of phenmedipham.

The MRL recommendations are summarised in Appendix B.4.

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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
CXL Codex maximum residue limit
DAR draft assessment report
DAT days after treatment
EMS evaluating Member State
eq residue expressed as a.s. equivalent
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
GC-MS gas chromatography with mass spectrometry
HR highest residue
IEDI international estimated daily intake
| Acronym | Description |
|---------|-------------|
| InChiKey | International Chemical Identifier Key |
| ILV     | independent laboratory validation |
| ISO     | International Organisation for Standardisation |
| IUPAC   | International Union of Pure and Applied Chemistry |
| JMPR    | Joint FAO/WHO Meeting on Pesticide Residues |
| LC-MS/MS| liquid chromatography with tandem mass spectrometry |
| LOQ     | limit of quantification |
| MRL     | maximum residue level |
| MS      | Member States |
| 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 |
| PROFile | (EFSA) Pesticide Residues Overview File |
| 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 |
| SC      | suspension concentrate |
| SEU     | southern Europe |
| STMR    | supervised trials median residue |
| TMDI    | theoretical maximum daily intake |
| TRR     | total radioactive residue |
| WHO     | World Health Organization |
### Appendix A – Summary of intended GAP triggering the amendment of existing EU MRLs

| Crop and/or situation | NEU, SEU, MS or country | F | G | I | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|-------------------------|---|---|---|-----------------------------------|-------------|-------------|---------------------------------|------------|---------|
|                       |                         |   |   |   | **Crop**                          | **Type**<sup>(b)</sup> | **Conc. a.s.** | **Method kind** | **Range of growth stages & season**<sup>(c)</sup> | **Number min-max** | **Interval between application (min)** | **g a.s./hl min-max** | **Water L/ha min-max** | **Rate** | **Unit** | **Remarks** |
| Celeriac              | DE                      | F |   |   | Annual dicotyledonous weeds       | SC          | 160 g/L     | Spraying From BBCH 13         | 2          | 7 days                           | 96-480     | 100-500  | 480      | g a.s./ha | 35       |

**MRL:** maximum residue level; **GAP:** Good Agricultural Practice; **NEU:** northern European Union; **SEU:** southern European Union; **MS:** Member State; **a.s.:** active substance; **SC:** Suspension concentrate.

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

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

(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

(d): PHI: minimum preharvest interval.
## Appendix B – List of end points

### B.1. Residues in plants

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

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

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/Source |
|-----------------------------------|-------------|---------|----------------|----------------|----------------|
| Fruit crops                       | Strawberries | Foliar BBCH 42; 1 × 0.96 kg/ha (1 × 2.88 kg/ha; supporting trial) | 49 | Radiolabelled active substance: [14C-amino-phenyl]-phenmedipham (Finland, 2016; EFSA, 2014, 2018b) |
| Root crops                        | Sugar beet 1 × 1 kg/ha, and 1 × 5 kg/ha (old study) | 5, 10, 20, 30, and 40 | Radiolabelled active substance: [14C-amino-phenyl]-phenmedipham or [14C-phenyl-methyl]-phenmedipham (Finland, 2016; EFSA, 2018b; old studies: Finland, 1999; EFSA, 2014) |
|                                  |            | Foliar: 1 × 1.066 kg/ha (BBCH 14) | 0, 3, 7, 14, 21, and 28, 19, and 137 |
|                                  |            | Foliar: 1 × 1.044 kg/ha (BBCH 14) | |
| Leafy crops                      | –          | –       | –              | –             |
| Cereals/grass                    | –          | –       | –              | –             |
| Pulses/oilseeds                  | –          | –       | –              | –             |
| Miscellaneous                    | –          | –       | –              | –             |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
|------------------------------------|-------------|---------|----------------|-----------|----------------|
| Root/tuber crops                   | Sugar beet  | Soil    | 30, 120, 365   | From 1.1 to 1.3 kg/ha on bare soil. From 1.1 to 1.3 kg/ha on bare soil. |
|                                    | Turnips     | Soil    | 30, 164, 305   | Both radiolabelled [14C-amino-phenyl]-phenmedipham or [14C-phenyl-methyl]-phenmedipham (Finland, 2016; EFSA, 2018b) |
| Leafy crops                        | Lettuce     | Soil    | 30, 120, 365   |       |
|                                    | Swiss chard | Soil    | 30, 164, 305   |       |
| Cereal (small grain)               | Wheat       | Soil    | 30, 120, 365   |       |
| Other                              | –           | –       | –              | –             |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|--------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)     | Yes        |        | Under standard condition simulating pasteurisation phenmedipham degrades into m-toluidine for 13% AR and MHPC 18% AR, while for other processing conditions phenmedipham degrades completely into m-toluidine and/or MHPC (EFSA, 2018b) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | No        |        |
| Sterilisation (20 min, 120°C, pH 6)     | No         |        |
| Other processing conditions           | –          | –      |
Can a general residue definition be proposed for primary crops?

| Yes/No | Explanation |
|--------|-------------|
| No     | Root and fruit crops only (EFSA, 2018b). |

Rotational crop and primary crop metabolism similar?

| Yes/No | Explanation |
|--------|-------------|
| No     | In rotational crops, besides phenmedipham, MHPC (soil metabolite) occurs in significant level (25% TRRs in straw) (EFSA, 2018b). |

Residue pattern in processed commodities similar to residue pattern in raw commodities?

| Yes/No | Explanation |
|--------|-------------|
| No     | Under standard condition simulating pasteurisation phenmedipham is considered stable, while for other processing conditions phenmedipham degrades completely into m-toluidine and/or MHPC (EFSA, 2018b). |

Plant residue definition for monitoring (RD-Mo)

| MRL review (EFSA, 2014), Regulation (EC) No 396/2005: phenmedipham (tentative) |
| EU pesticides peer review (EFSA, 2018b): Root and fruit crops: phenmedipham. Processed commodities: sum of phenmedipham and MHPC, expressed as phenmedipham. |

Plant residue definition for risk assessment (RD-RA)

| MRL review (EFSA, 2014): phenmedipham (fruits and fruiting crops; tentative for other crops). |
| EU pesticides peer review (EFSA, 2018b):  
**Primary crops**: phenmedipham (free and glucoside conjugates) restricted to sugar beet.  
**Rotational crops**: sum of phenmedipham and MHPC, and their conjugates, expressed as phenmedipham.  
**Processed commodities** (provisional):  
1) sum of phenmedipham and MHPC expressed as phenmedipham.  
2) m-toluidine, pending upon confirmation of the toxicity of m-toluidine. |

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:  
DFG S19 (extended revision) LC–MS/MS, LOQ: 0.01 mg/kg (phenmedipham)  
QuEChERS GC–MS and/or LC–MS/MS, LOQ: 0.01-0.05 mg/kg (phenmedipham)  
ILV available. (EFSA, 2018b) |

DAT: days after treatment; BBCH: growth stages of mono- and dicotyledonous plants; PBI: plant-back interval; a.s.: active substance; AR: applied radioactivity; TRR: total radioactive residue; MRL: maximum residue level; LOQ: limit of quantification; LC-MS/MS: liquid chromatography with tandem mass spectrometry; GC-MS: gas chromatography with mass spectrometry; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; ILV: independent laboratory validation.
### 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        | Sugar beet leaves*    | ≤ -20  | 24 Months        | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   | Lettuce                   | ≤ -18                 | 24     | Months           | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   | High oil content          | Sunflower seed        | ≤ -18  | 24 Months        | Parent, MHPC       | MHPC: 25% decline after 24 months (EFSA, 2018b)                               |
|                                   | High protein content      | Dry pea (seed)        | ≤ -18  | 24 Months        | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   | High starch               | Wheat (grain)         | ≤ -18  | 24 Months        | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   |                           | Sugar beet root       | ≤ -20  | 24 Months        | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   | High acid content         | Orange                | ≤ -18  | 24 Months        | Parent, MHPC       | EFSA (2018b)                                                                 |
|                                   | Others                    | –                     | –      | –                | –                  | –                                                                             |

*: Analysed by common moiety method (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) |
|-----------|-------------------|---------------------------------------------------------------|----------------|------------------------|----------------|-----------------|-------|
| Celeriac  | NEU               | <0.01; 0.042; 0.044; 0.051(e); 0.053                           | Residue trials on celeriac compliant with the GAP. The risk assessment residue definition originally derived for sugar beet, tentatively extrapolated to celeriac. The calculated MRL proposal is tentative, pending new metabolism study on root crops or further characterisation/identification of residues from available sugar beet metabolism study. | 0.15 (tentative) | 0.053 | 0.04 | 1.4(f) |

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

(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 monitoring refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue. The median residue for monitoring 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.
(e): Residue trial with one application instead of two applications as in the intended GAP.
(f): Derived for sugar beet root from sugar beet metabolism studies (EFSA, 2018b).
B.1.2.2. Residues in rotational crops

| Question                                                                 | Answer                                                                 |
|-------------------------------------------------------------------------|------------------------------------------------------------------------|
| Residues in rotational and succeeding crops expected based on confined rotational crop study? | No. Confined rotational crops conducted with radiolabelled \[^{14}\text{C-}
\text{amino-phenyl}\] or \[^{14}\text{C-phenyl-methyl}\]\-phenmedipham in sugar beet, turnips, lettuce, Swiss chard, wheat (from 1.1 kg a.s./ha to 1.3 kg a.s./ha, on bare soil). No residues are expected in edible commodities above 0.01 mg/kg (EFSA, 2018b). |

| Question                                                                 | Answer                                                                 |
|-------------------------------------------------------------------------|------------------------------------------------------------------------|
| Residues in rotational and succeeding crops expected based on field rotational crop study? | No. In the field rotational crop studies (0.96 kg phenmedipham/soil), no residues of phenmedipham >0.01 mg/kg were found in the edible crops at any plant-back intervals (PBI) (EFSA, 2018b). |

a.s.: active substance

B.1.2.3. Processing factors

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

B.2. Residues in livestock

Not relevant.
B.3. **Consumer risk assessment**

Acute exposure assessment: Not relevant since no ARfD has been considered necessary (European Commission, 2004).

| ADI | 0.03 mg/kg bw per day (European Commission, 2004) |
| --- | --- |
| Highest IEDI, according to EFSA PRIMo | 11% of ADI (NL toddler diet) |
| Contribution of crops assessed: | Celeriac: 0.07% of ADI (GEMS/Food 11 diet) |

**Assumptions made for the calculations**

The calculation is based on the median residue level derived for celeriac and multiplied by a provisional conversion factor of 1.4 as derived by the EU pesticides peer review (EFSA, 2018b) for sugar beet root. For the remaining commodities, the input values were as derived from a previous EFSA assessment (EFSA, 2021) and from the MRL review (EFSA, 2014). Crops for which no uses were reported in the MRL review were excluded from the calculations. For sugar beet a tentative MRL was derived in the MRL review but not implemented in the MRL legislation and therefore sugar beet, was excluded from the exposure calculation assuming there are no authorized EU uses on this crop. For beetroot as well a provisional conversion factor of 1.4 was applied.

Since the current MRL application was submitted before the finalization of the EU peer review of the renewal of the approval of phenmedipham, the consumer exposure assessment was undertaken in line with conclusions on the toxicity of phenmedipham from the first approval and the MRL review (European Commission, 2004; EFSA, 2014).

It is reiterated that the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009, could not establish toxicological reference values for phenmedipham, since its genotoxicity potential was not clarified. Consequently, the non-dietary exposure assessment could not be conducted in the absence of toxicological reference values (EFSA, 2018b).

Calculations performed with PRIMo revision 3.1.

**ARfD**: acute reference dose; **ADI**: acceptable daily intake; **bw**: body weight; **IEDI**: international estimated daily intake; **PRIMo**: (EFSA) Pesticide Residues Intake Model; **MRL**: maximum residue level; **STMR**: supervised trials median residue; **CXL**: codex maximum residue limit.
### B.4. Recommended MRLs

| Code\(^{(a)}\) | Commodity                           | Existing EU MRL (mg/kg) | Proposed EU MRL (mg/kg) | Comment/justification |
|--------------|-------------------------------------|-------------------------|-------------------------|-----------------------|
| 0213030      | Celeriacs/turnip rooted celeries    | 0.01*                   | (0.15)                  | Further risk management considerations required |

**Enforcement residue definition:** Phenmedipham

The submitted data are sufficient to derive an MRL proposal in support of the intended NEU use. The MRL proposal is considered tentative, pending the availability of a metabolism study in primary root crops, allowing to derive a risk assessment residue definition in root crops other than sugar beet.

Upon the request of the Evaluating Member State (EMS) and considering the intended use refers to a minor crop, for this assessment EFSA extrapolated the sugar beet metabolism data to celeriac on a tentative basis. The acceptability of such proposal shall be further considered by the risk managers.

Risk to consumers unlikely, according to the conclusions on the toxicity of phenmedipham from the first approval of the active substance under Directive 91/414/EEC.

The present assessment does not consider the data gaps identified in the context of the renewal of the approval of phenmedipham under Regulation (EC) No 1107/2009 which prevented experts to derive toxicological reference values (TRVs) for phenmedipham, to derive the risk assessment residue definition for root crops other than sugar beet and to conclude on the toxicity of relevant metabolites.

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\(^{(*)}\): 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.

MRL: maximum residue level; NEU: northern Europe; GAP: Good Agricultural Practice.
Appendix C – Pesticide Residue Intake Model (PRIMo)

### Phenmedipham

**Input values**
- Source of ADI: EFSA PRIMo revision 3.1; 2019/03/19
- Source of ARfD: EFSA PRIMo revision 3.1; 2019/03/19

**Refined calculation mode**

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

| Commodity/group of commodities | % of ADI | MS Diet | Highest contributor to ADI | % of ADI | MS Diet | 2nd contributor to ADI | % of ADI | MS Diet | 3rd contributor to ADI | % of ADI | MS Diet |
|--------------------------------|----------|---------|---------------------------|----------|---------|------------------------|----------|---------|------------------------|----------|---------|
| Swine: Muscle/meat             | 11%      | Milk: Cattle | Bovine: Muscle/meat | 10%      | Milk: Cattle | Bovine: Muscle/meat | 0.1%    | Milk: Cattle | Strawberries | 0.1% | Milk: Cattle |
| Bovine: Muscle/meat            | 7%       | Milk: Cattle | Bovine: Muscle/meat | 6%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Bovine: Muscle/meat            | 6%       | Milk: Cattle | Bovine: Muscle/meat | 5%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |
| Swine: Muscle/meat             | 5%       | Milk: Cattle | Bovine: Muscle/meat | 4%       | Milk: Cattle | Bovine: Muscle/meat | 0.2%    | Milk: Cattle | Bovine: Muscle/meat | 0.2% | Milk: Cattle |

**Summary:** The estimated chronic dietary intake (TMDI/IEDI/TMDI) were below the ADI. The long-term residues of phenmedipham is unlikely to present a public health concern.
## Appendix D – Input values for the exposure calculations

### D.1. Consumer risk assessment

| Commodity | Existing/Proposed MRL (mg/kg) | Source/type of MRL | Chronic risk assessment | Acute risk assessment |
|-----------|-------------------------------|--------------------|------------------------|-----------------------|
| Celeriac  | 0.15                          | Intended use; New tentative MRL proposal | 0.074 STMR-RAC (tentative) $\times$ CF$^a$ (1.4) (EFSA, 2018b) | Acute risk assessment not undertaken, as an ARfD was considered not necessary (European Commission, 2004). |
| Strawberries | 0.7                           | EFSA (2021)        | 0.11 STMR-RAC           |                        |
| Beetroot  | 0.15                          | EFSA (2014)        | 0.07 STMR-RAC (tentative) $\times$ CF$^a$ (1.4) (EFSA, 2018b) |                        |
| Spinach, beet leaves (chard), tarragon | 0.3                           | EFSA (2014)        | 0.01 STMR-RAC (tentative) |                        |
| Herbs and edible flowers, except tarragon | 7                             | EFSA (2014)        | 0.22 STMR-RAC (tentative) |                        |
| Sugar beet roots | 0.05*                         | EFSA (2014)        | _$^b$ (B) –            |                        |
| Meat, fat, liver, kidney of ruminants and swine; Poultry muscle, fat, liver; Eggs; Milk | 0.05*                         | EFSA (2014)        | 0.05 STMR-RAC (tentative) |                        |
| Other crops/commodities | –                             | –                  | –                      | –                     |

**Tentative** residue definition for risk assessment: phenmedipham (EFSA, 2014) or phenmedipham (free and glucoside conjugates) (EFSA, 2018b). The risk assessment residue definition originally derived for sugar beet, tentatively extrapolated to celeriac.

STMR-RAC: supervised trials median residue in raw agricultural commodity; CF: conversion factor.

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

(a): A provisional conversion factor of 1.4, as derived for sugar beet root from sugar beet metabolism studies during the EU pesticides peer review (EFSA, 2018b), was applied to root crops to account for potential formation of phenmedipham glucoside conjugates.

(b): Sugar beet use was assessed in the MRL review (EFSA, 2014), resulting in tentative MRL of 0.15 mg/kg, which was not implemented in the MRL regulation. The existing MRL is set at the LOQ, therefore assuming that there are no uses of phenmedipham authorized on sugar beet in EU, EFSA did not consider sugar beet in this exposure calculation.
### Appendix E – Used compound codes

| Code/trivial name       | IUPAC name/SMILES notation/InChiKey<sup>(a)</sup> | Structural formula<sup>(b)</sup> |
|-------------------------|--------------------------------------------------|----------------------------------|
| phenmedipham            | 3-[[[methoxycarbonyl]amino]phenyl (3-methylphenyl)carbamate O-C(Oc1cccc(c1)NC(=O)OC)c1 | ![Structural formula](image) |
|                         | IDOWTHOLJBTAI-UHFFFAOYSA-N                      |                                  |
| 3-methylaniline m-toluidine | 3-methylaniline CC1=CC=CC(N)=C1              | ![Structural formula](image) |
|                         | JJYPMNFTHTTDI-UHFFFAOYSA-N                      |                                  |
| MHPC                    | methyl (3-hydroxyphenyl)carbamate Oc1cccc(NC(=O)OC)c1 | ![Structural formula](image) |
|                         | FFQQCJGNKKIRMD-UHFFFAOYSA-N                     |                                  |
| 3-acetamidophenol       | N-(3-hydroxyphenyl)acetamide Oc1cccc(NC(=O)c1   | ![Structural formula](image) |
|                         | QLNWXBAGRTUKKI-UHFFFAOYSA-N                    |                                  |

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

<sup>(a)</sup> ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).

<sup>(b)</sup> ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version CH5H41, Build 111302, 27 August 2019).