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Modification of the existing maximum residue levels for isofetamid in certain salad plants

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Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant ISK Biosciences Europe N.V. submitted a request to the competent national authority in Belgium to modify the existing maximum residue levels (MRLs) for the active substance isofetamid in certain salad plants. The data submitted in support of the request were found to be sufficient to derive MRL proposals for lamb's lettuces/corn salads, escaroles/broad leaved endives, cresses and other sprouts and shoots, land cresses, Roman rocket/rucola, red mustards, baby leaf crops (including brassica species) and other lettuces and salad plants. An adequate analytical method for enforcement is available to enforce the residues of isofetamid on the commodities under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the uses of isofetamid according to the reported agricultural practices is unlikely to present a risk to consumer health.

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, ISK Biosciences Europe N.V. submitted an application to the competent national authority in Belgium (evaluating Member State, EMS) to modify the existing maximum residue levels (MRLs) for the active substance isofetamid in certain salad plants.

The application, alongside the dossier containing the supporting data in IUCLID format, was submitted through the European Food Safety Authority (EFSA) Central Submission System on 8 July 2022. The appointed EMS Belgium assessed the dossier and declared its admissibility on 20 September 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 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 run from 24 March 2023 to 14 April 2023. No additional data nor comments were submitted in the framework of the consultation.

At the end of the commenting period, the EMS proceeded 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 EFSA on 3 May 2023. To accommodate for the intended uses of isofetamid, the EMS proposed to raise the existing MRLs from the limit of quantification (LOQ) to 20 mg/kg.

EFSA assessed the application and the evaluation report as required by Article 10 of the MRL regulation. EFSA identified points which needed further clarification, which were requested from the EMS. On 12 June 2023, the applicant provided the requested information in an updated IUCLID dossier. The additional information was previously duly considered by the EMS who submitted a revised evaluation report to EFSA on 08 June 2023 (Belgium, 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 isofetamid following foliar application was investigated in crops belonging to the groups of fruit crops (grape), leafy crops (lettuce) and pulses/oilseeds (French bean). In rotational crops metabolism was qualitative similar as in primary crops. Studies investigating the effect of processing on the nature of isofetamid (hydrolysis studies) demonstrated that the active substance is stable.

Based on the metabolic pattern identified in metabolism studies, hydrolysis studies, the toxicological significance of metabolite, the residue definitions for plant products were proposed by the EU pesticides peer review as 'isofetamid' for enforcement and 'sum of isofetamid and metabolite GPTC, expressed as isofetamid', for risk assessment. These residue definitions are applicable to primary crops, rotational crops, processed products.

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

A sufficiently validated analytical method based on liquid chromatography–tandem mass spectrometry detector (LC–MS/MS) is available to quantify residues in the crops assessed in this application according to the enforcement residue definition. The method enables quantification of residues at or above 0.01 mg/kg in the crops assessed (LOQ). Extraction efficiency of the analytical enforcement method has not been proven. EFSA would recommend that data on extraction efficiency for all types of matrices are further considered and confirmed.

The available residue trials are sufficient to derive MRL proposals of 20 mg/kg for lamb's lettuces/corn salads, escaroles/broad leaved endives, cresses and other sprouts and shoots, land cresses, Roman rocket/rucola, red mustards, baby leaf crops (including brassica species) and other lettuces and salad plants.

Lettuce can be grown in rotation with other plants. The possible occurrence of residues in succeeding crops resulting from the use on primary crops was investigated during the EU pesticides peer review for the approval of the active substance. Based on field rotational crop studies and despite the shortcoming in the application rate tested, EFSA confirms previous conclusions that residues of isofetamid and GPTC are unlikely to be present at significant levels (> 0.01 mg/kg) in rotational crops.

Specific studies investigating the magnitude of isofetamid residues in processed commodities are not required, as the crop under consideration are either eaten raw or their individual contribution (Escaroles/broad-leaved endives) are below 10% acceptable daily intake (ADI).

Residues of isofetamid in commodities of animal origin were not assessed since the crops under consideration in this MRL application are normally not fed to livestock.

The toxicological profile of isofetamid 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 ADI of 0.02 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 1 mg/kg bw. The metabolite GPTC included in the residue definition for risk assessment in plants is of similar toxicity as the parent active substance.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). The estimated short-term exposure was performed only for the crops under consideration and did not exceed the ARfD for any of the crops assessed in this application. There are no specific data for the acute and chronic consumption of land cresses and baby leaf crops. However, their contribution to the overall dietary exposure is of minor relevance.

For the calculation of the chronic exposure, EFSA used the median residue values (STMR) as derived from the residue trials submitted and the STMRs available from previously issued EFSA opinions, including the STMR related to the Codex MRLs (CXLs) implemented in the EU regulation. Since the CXL STMRs refer to parent compound only, conversion factors for risk assessment were included in the exposure calculation, when available. No long-term consumer intake concerns were identified for any of the European diets incorporated in EFSA PRIMo. The highest estimated long-term dietary intake accounted for 29% of the ADI (NL toddler diet). The contributions of residues expected in the commodities assessed in the present MRL application to the overall long-term exposure accounted for a maximum of 0.32% (Escaroles/broad-leaved endives).

EFSA concluded that the proposed uses of isofetamid on the salad plants under assessment will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a risk to consumers' health. It is noted that the chronic consumer exposure shall be considered indicative because for several commodities for which the existing EU MRL is based on the CXL residue data according to the EU risk assessment residue definition are not available and, therefore, the exposure to the plant metabolite GPTC might be underestimated.

EFSA proposes to amend the existing MRLs as reported in the summary table below.

Full details of all end points and the consumer risk assessment can be found in Appendices B–D.

Code ^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/justification
Enforcement residue definition: Isofetamid				
0251010	Lamb's lettuces/corn salads	0.01*	20	The submitted data are sufficient to derive an MRL proposal for the intended NEU, SEU and indoor use by extrapolation from trials on lettuces (open leaf varieties). The MRL proposal reflects the more critical residue situation represented by the intended indoor EU use. Risk for consumers unlikely.
0251030	Escaroles/broad-leaved endives			
0251040	Cresses and other sprouts and shoots			
0251050	Land cresses			
0251060	Roman rocket/rucola			
0251070	Red mustards			
0251080	Baby leaf crops (including brassica species)			
0251990	Others			

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe.

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

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

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Assessment

The European Food Safety Authority (EFSA) received an application to modify the existing maximum residue levels (MRLs) for isofetamid in certain commodities included in the group of lettuces and salad plants. The detailed description of the intended uses of isofetamid, which are the basis for the current MRL application, is reported in Appendix A.

Isofetamid is the ISO common name for *N*-[1,1-dimethyl-2-(4-isopropoxy-*o*-tolyl)-2-oxoethyl]-3-methylthiophene-2-carboxamide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Isofetamid was evaluated in the framework of Regulation (EC) No 1107/2009¹ with Belgium designated as rapporteur Member State (RMS) for the representative field uses on peaches, plums, apricots, cherries, grapes, strawberries, lettuces and oilseed rapes and glasshouse uses on strawberries and lettuces. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2015). Isofetamid was approved² for the use as fungicide on 15 September 2016. The process of renewal of the first approval has not yet been initiated.

The EU MRLs for isofetamid are established in Annex II of Regulation (EC) No 396/2005³. Proposals for setting MRLs covering the representative uses according to good agricultural practices (GAP) in the EU were assessed during the approval of isofetamid under Regulation (EC) No 1107/2009 and implemented in Regulation in accordance with Article 11(2) of the Regulation (EC) No 1107/2009. Since the EU pesticides peer review (EFSA, 2015), EFSA has issued two reasoned opinions on the modification of MRLs for isofetamid in several fruiting vegetables (EFSA, 2018b) and on the modification of MRLs in raspberries, blackberries and dewberries (EFSA, 2021a). The proposals from these reasoned opinions have been considered in recent MRL regulations⁴. EFSA also has issued three scientific reports in support of preparing the EU position in the Sessions of the Codex Committee on Pesticide Residues (CCPR) (EFSA, 2017, 2019b, 2021b). CXLs have been taken over in the EU MRL legislation.^{5,6,7}

In accordance with Article 6 of Regulation (EC) No 396/2005 and following the provisions set by the 'Transparency Regulation' (EU) 2019/1381⁸, the applicant ISK Biosciences Europe N.V. submitted on 8 July 2022 an application to the competent national authority in Belgium, alongside the dossier containing the supporting data using the IUCLID format.

The appointed EMS Belgium assessed the dossier and declared its admissibility on 20 September 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 launched on the dossier. The consultation aimed to consult stakeholders and the public on the scientific data, studies

¹ 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.

² Commission Implementing Regulation (EU) 2016/1425 of 25 August 2016 approving the active substance isofetamid in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and amending the Annex to Commission Implementing Regulation (EU) No 540/2011. OJ L 231, 26.8.2016, p. 30–33.

³ 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.

⁴ For an overview of all MRL Regulations on this active substance, please consult: <https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls>

⁵ Commission Regulation (EU) 2018/687 of 4 May 2018 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acibenzolar-S-methyl, benzovindiflupyr, bifenthrin, bixafen, chlorantraniliprole, deltamethrin, flonicamid, fluazifop-P, isofetamid, metrafenone, pendimethalin and teflubenzuron in or on certain products. C/2018/2627. OJ L 121, 16.5.2018, p. 63–104.

⁶ Commission Regulation (EU) 2020/856 of 9 June 2020 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for cyantraniliprole, cyazofamid, cyprodinil, fenpyroximate, fludioxonil, fluxapyroxad, imazalil, isofetamid, kresoxim-methyl, lufenuron, mandipropamid, propamocarb, pyraclostrobin, pyriofenone, pyriproxyfen and spinetoram in or on certain products. C/2020/3608. OJ L 195, 19.6.2020, p. 9–51.

⁷ Commission Regulation (EU) 2022/1324 of 28 July 2022 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for benzovindiflupyr, boscalid, fenazaquin, fluazifop-P, flupyradifurone, fluxapyroxad, fosetyl-Al, isofetamid, metaflumizone, pyraclostrobin, spirotetramat, thiabendazole and tolclofos-methyl in or on certain products. C/2022/5316. OJ L 200, 29.7.2022, p. 68–108.

⁸ 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, p. 1–28.

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 run from 24 March 2023 to 14 April 2023. No additional data nor comments were submitted in the framework of the consultation.

EFSA based its assessment on the evaluation report submitted by the EMS (Belgium, 2023), the DAR and its addendum (Belgium, 2014, 2015) prepared under Regulation (EC) 1107/2009, the Commission review report on isofetamid (European Commission, 2020b), the conclusion on the peer review of the pesticide risk assessment of the active substance isofetamid (EFSA, 2015), as well as the conclusions from previous EFSA outputs on isofetamid (EFSA, 2017, 2018b, 2019b, 2021a,b).

For this application, the data requirements established in Regulation (EU) No 544/2011⁹ and the guidance documents applicable at the date of submission of the IUCLID application are applicable (European Commission, 1997a–g, 2010, 2017, 2020a, 2021; 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 546/2011¹⁰.

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 (Belgium, 2023) and the exposure calculations using the PRIMo are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.¹¹

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 isofetamid in primary crops belonging to the group of fruit crops (grape), leafy crops (lettuce) and pulses/oilseeds (bean) has been investigated in the framework of the EU pesticides peer review (EFSA, 2015). In the crops tested, parent compound was the main residue, accounting for 18–73% of the total radioactive residues (TRR), except in bean seeds at harvest, where isofetamid was only 1% of the TRR and the residues mainly composed of polar fractions representing all 22–51% TRR. The metabolic pathway was seen to be similar in the three plant groups. Isofetamid is primarily metabolised by *O*-dealkylation to the 4HP metabolite with subsequent conjugations leading to its glucose conjugate GPTC¹². Metabolite GPTC was observed up to 10% TRR in grape and lettuce, all other identified metabolites being below 7% TRR (EFSA, 2015).

For the intended uses on the crops belonging to the group of lettuces and salad plants under consideration, the metabolic behaviour in primary crops is sufficiently addressed.

1.1.2. Nature of residues in rotational crops

Isofetamid is proposed to be used on crops that can be grown in rotation with other crops. According to the soil degradation studies evaluated in the framework of the EU pesticides peer review, the DT₉₀ value of isofetamid ranged from 96 to 174 days (EFSA, 2015). The trigger value of 100 days was exceeded, and therefore, studies investigating the nature and magnitude of residues in rotational crops are required.

In the confined rotational crop studies assessed in the framework of the EU pesticides peer review, parent isofetamid was detected in lower amounts and proportions than in primary crops and the residues mainly composed of the metabolites GPTC and GPTC-malonyl, accounting together up to ca 40% TRR in carrot roots and up to ca 60% TRR in lettuce at the 120-day plant back interval (EFSA, 2015). Overall, the peer review concluded that the metabolic pathways in rotational crops are similar to those observed in primary crops.

For the proposed uses assessed in the present application, no further information is required.

⁹ 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.

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, p. 127–175.

¹¹ Background documents to this reasoned opinion are published on OpenEFSA portal and are available at the following link: <https://open.efsa.europa.eu/study-inventory/EFSA-Q-2022-00583>

¹² N-{1-[4-(D-glucopyranosyloxy)-2-methylphenyl]-2-methyl-1-oxopropan-2-yl}-3-methylthiophene-2-carboxamide.

1.1.3. Nature of residues in processed commodities

The effect of processing on the nature of isofetamid was investigated in the framework of the EU pesticides peer review (EFSA, 2015). It was concluded that under standard hydrolysis conditions simulating pasteurisation, baking/brewing/boiling and sterilisation, isofetamid was stable and no degradation was observed.

The metabolite GPTC, included together with isofetamid in the plant residue definition for risk assessment, is a glucoside conjugate of isofetamid, and therefore, possible hydrolytic decomposition of GPTC to the aglycone is covered by the available hydrolysis studies on isofetamid (EFSA, 2018b).

1.1.4. Analytical methods for enforcement purposes in plant commodities

Analytical methods for the determination of residues of isofetamid in food/feed of plant origin were assessed during the framework of the EU pesticide peer review (EFSA, 2015). The assessed method was fully validated (including independent laboratory validation), in accordance with the EU guideline SANCO/825/00 rev.8 applicable at that time. The LC-MS/MS method allows the quantification of residues at or above the limit of quantification (LOQ) of 0.01 mg/kg in crops belonging to the high acid, high water content and to dry matrices (EFSA, 2015). New data were not submitted in the present application. EFSA concludes that analytical method assessed in the EU peer review is fully validated according to the guidance SANTE/2020/12830 Rev. 1 (European Commission, 2021) in the crops under consideration in the present MRL application.

According to the EMS, extraction efficiency of the analytical enforcement method has been sufficiently demonstrated according to the guidance SANTE/2017/10632 (European Commission, 2017) in the context of the draft assessment report (DAR) (Belgium, 2014), and remains relevant for this application. However, the study was performed before the implementation of the guidance, and its compliance to the guidance was not assessed in the Evaluation Report (Belgium, 2023). Therefore, EFSA is not in the position to endorse the EMS conclusion and would recommend that data on extraction efficiency for all types of matrices are further considered and confirmed.

1.1.5. Storage stability of residues in plants

The storage stability of isofetamid and the metabolite GPTC in plants stored under frozen conditions was investigated in the framework of the EU pesticides peer review (EFSA, 2015). It was demonstrated that for the crops assessed in the framework of this application, residues were stable for at least 12 months when stored at -20°C .

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolite, the following general residue definitions were proposed by the EU pesticides peer review (EFSA, 2015):

- residue definition for risk assessment: sum of isofetamid and metabolite GPTC, expressed as isofetamid;
- residue definition for enforcement: isofetamid.

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

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

Taking into account the proposed uses assessed in this application, EFSA concluded that the previously derived residue definitions are applicable and no further information is required.

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

In support of the MRL application, the applicant submitted residue trials performed on open leaf lettuce compliant (25% tolerance rule) with the intended uses. The trials were conducted over three seasons and 14 of them (more than half) were designed as decline trials.

A total of 19 outdoor residue trials were conducted on open leaf lettuce in northern Europe (10 trials, including 1 replicate trial) and southern Europe (nine trials, seven of which were considered for

MRL calculation). A total of 13 indoor trials, 10 of which were considered for MRL calculations, were conducted on open leaf lettuce throughout Europe. Overall, the lettuce residue trial data package provided comprises the lettuce trials on open leaves that were already evaluated in the framework of the EU pesticides peer review (EFSA, 2015) plus additional six trials (three indoor, two NEU, one SEU).

The samples of these residue trials were stored under conditions for which integrity of the samples has been demonstrated. The samples were analysed for the parent compound and the metabolite GPTC, in accordance with the requirements of the residue definitions for enforcement (isofetamid) and risk assessment (sum of isofetamid and GPTC, expressed as isofetamid). According to the assessment of the EMS, the methods used were sufficiently validated and fit for purpose (Belgium, 2023). However, extraction efficiency has not been assessed.

According to the technical guidance SANTE/2019/12752 (European Commission, 2020a), the residue data on open leaf varieties available are sufficient to derive an MRL proposal for the intended indoor and NEU outdoor uses by extrapolation to the whole group of lettuces and salad plants. The SEU outdoor use is also supported, since the extrapolation is proposed to a group of minor crops only and the minimum four trials are sufficient (European Commission, 2020a). The residue data from the supervised residue trials in primary crops are summarised in Appendix B.1.2.1.

1.2.2. Magnitude of residues in rotational crops

The possible transfer of isofetamid residues to crops that are grown in crop rotation has been assessed in EU pesticides peer review (EFSA, 2015).

Based on field rotational crop studies (2×400 g/ha) using lettuce as primary crop, residues of isofetamid and GPTC are unlikely to be present at significant levels (> 0.01 mg/kg) in rotational crops and residues of GPTC-malonyl are expected to be negligible (≤ 0.02 mg/kg, expressed as GPTC) in edible crop parts. The field rotational crop studies assessed in the EU pesticides peer review are under-dosed (0.33 N based on the annual application rate of the intended indoor uses assessed in this application for three growing cycles). Nevertheless, since isofetamid and GPTC were barely detected (limit of detection [LOD] = 0.004 mg/kg) and mostly below the LOQ (0.01 mg/kg) in the tested rotational crops, EFSA endorsed the previous conclusion of the EU pesticides peer review reached for the same annual application rate of the representative use on lettuces (2×400 g/ha, 3 cycles per year) that this under-dosing is not considered to be of any concern and there is no need to set MRLs in rotational crop commodities.

1.2.3. Magnitude of residues in processed commodities

No new processing data are provided in the framework of this MRL application. This is considered acceptable as processing studies are not normally required for the leafy crops under consideration, which are mostly eaten raw, except for escaroles/broad-leaved endives. However, processing studies are not required as the theoretical maximum daily intake (TMDI) contribution of escaroles/broad-leaved endives is expected to be less than 10% of the acceptable daily intake (ADI) (European Commission, 1997d).

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposal of 20 mg/kg as well as risk assessment values for the commodities under evaluation (see Appendix B.4). The MRL proposal is driven by the more critical residue situation observed in the indoor trials.

In Section B.3, EFSA assessed whether residues on these crops resulting from the intended uses are likely to pose a consumer health risk.

2. Residues in livestock

Not relevant as salad plants are not used for feed purposes. No further consideration of residues in livestock is required.

3. Consumer risk assessment

EFSA performed a dietary risk assessment using revision 3.1 of the EFSA PRIMo (EFSA, 2018a, 2019a). 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, 2016a). There are no specific data for the acute and chronic consumption of land cresses and baby leaf crops. However, the contribution of land cresses and baby leaf crops to the overall dietary exposure is of minor relevance.

The toxicological reference values for isofetamid used in the risk assessment (i.e. ADI and acute reference dose (ARfD) values) were derived in the framework of the EU pesticide peer review (European Commission, 2020b). The toxicological reference values for isofetamid are considered to be applicable to the metabolite GPTC included in the risk assessment residue definition for plants (EFSA, 2015).

Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed for the commodities assessed in this application in accordance with the internationally agreed methodology (FAO, 2016a). The calculations were based on the highest residue (HR) values according to the residue definition for risk assessment expected in the raw agricultural commodity derived from supervised field trials. The complete list of input values can be found in Appendix D.1.

The estimated short-term exposure did not exceed the ARfD for any of the crops assessed in this application. The acute consumer exposure accounted for a maximum of 47.4% of ARfD (escaroles/broad-leaved endives) and is presented in more details in Appendix B.3.

Long-term (chronic) dietary risk assessment

The long-term exposure assessment was performed taking into account the median residue values (STMR) derived from supervised trials for the commodities assessed in this application. For the remaining commodities covered by the MRL regulation, the STMR values derived in the EU pesticides peer review (EFSA, 2015), in previous MRL applications (EFSA, 2018b, 2021b), and for the acceptable CXLs implemented in the MRL regulation (EFSA, 2017, 2019b, 2021a) as derived in the evaluations by the Joint FAO/WHO Meetings on Pesticide Residues (JMPR) (FAO, 2016b, 2019, 2020) selected as input values. The commodities of animal origin were also considered in the exposure calculation even though MRLs are set at the LOQ.

To be noted that for those commodities for which the existing EU MRL is set on a basis of the CXL, the residue data according to the EU risk assessment residue definition are not available. Lacking specific information, EFSA applied previously derived conversion factor (CF) for risk assessment when available. For certain commodities derived based on the CXL a CF was not available which may lead to an underestimation of residue levels. For these commodities the risk assessment is considered indicative.

The complete list of input values is presented in Appendix D.1.

The highest estimated long-term dietary intake accounted for a maximum of 29% of the ADI (NL toddler diet). The contributions of residues expected in the commodities assessed in the present MRL application to the overall long-term exposure accounted for a maximum of 0.32% of the ADI (Escaroles/broad-leaved endives) and is presented in more details in Appendix B.3.

EFSA concluded that the long-term intake of residues of isofetamid resulting from the existing and the intended uses is unlikely to present a risk to consumer health. It is also noted that the chronic consumer exposure shall be considered indicative because for several commodities for which the existing EU MRL is based on the CXL residue data according to the EU risk assessment residue definition are not available and therefore the exposure to the plant metabolite GPTC might incur a minor underestimation.

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

4. Conclusion and Recommendations

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for lamb's lettuces/corn salads, escaroles/broad leaf endives, cresses and other sprouts and shoots, land cresses, Roman rocket/rucola, red mustards, baby leaf crops (including brassica species) and other lettuces and salad plants.

EFSA concluded that the proposed uses of isofetamid will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a risk to consumers' health. It is noted that the chronic consumer exposure shall be considered indicative because for

several commodities for which the EU MRL is based on the CXL residue data according to the EU risk assessment residue definition are not available and therefore the exposure to the plant metabolite GPTC might incur a minor level of underestimation.

The MRL recommendations are summarised in Appendix B.4.

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Abbreviations

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CCPR	Codex Committee on Pesticide Residues
CF	conversion factor for enforcement to risk assessment residue definition
CXL	Codex maximum residue limit
DAR	draft assessment report
DAT	days after treatment
DT ₉₀	period required for 90% dissipation (define method of estimation)
EC	emulsifiable concentrate
EMS	evaluating Member State
eq	residue expressed as a.s. equivalent
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
HR	highest residue
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
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	liquid chromatography
LOD	limit of detection
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
PRIMo	(EFSA) Pesticide Residues Intake Model
RA	risk assessment
RAC	raw agricultural commodity
RMS	rapporteur Member State
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 or I ^(a)	Pests or Group of pests controlled	Preparation		Application				Application rate per treatment				PHI (days) ^(d)	Remarks
				Type ^(b)	Conc. a.s. (g/L)	Method kind	Range of growth stages and season ^(c)	Number min–max	Interval between application (days) min–max	g a.s./hL min–max	Water (L/ha) min–max	Rate min–max	Unit		
Lamb's lettuces/ corn salads, Escaroles/broad-leaved endives, Cresses and other sprouts and shoots, Land cresses, Roman rocket/rucola, Red mustards, Baby leaf crops (including brassica species), Others	NEU	F	Botrytis disease/ sclerotinia disease	SC	400	Tractor mounted or pulled boom sprayer/ knapsack sprayer	BBCH 12-until PHI	2	10 ± 1	50–200	200–800	400	g a.s./ha	21	2 applications and 1 crop cycle for outdoor uses.
	SEU	F	Botrytis disease/ sclerotinia disease	SC	400	Broadcast foliar spray/ Air compressed backpack boom sprayer	BBCH 12-until PHI	2	10 ± 1	50–200	200–800	400	g a.s./ha	21	2 applications and 1 crop cycle for outdoor uses.
	EU	G	Botrytis disease/ sclerotinia disease	SC	400	Broadcast foliar spray/ Air compressed backpack boom sprayer	BBCH 12-until PHI	2	10 ± 1	50–200	200–800	400	g a.s./ha	21	2 applications and 3 crop cycles (6 applications per season) for glasshouse uses.

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 pre-harvest interval.

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

Primary crops (available studies)	Crop groups	Crops	Applications	Sampling (DAT)	Comment/Source
	Fruit crops	Grapes	3 × 750 g/ha foliar spray, 13–14 days interval, BBCH 67–69, 71–75 and 77–79	14, 43	Radiolabelled active substance: [¹⁴ C-phenyl]-isofetamid or [¹⁴ C-(C2)-thiophene]-isofetamid (EFSA, 2015)
	Leafy crops	Lettuce	3 × 750 g/ha foliar spray, 14 days interval	7, 18	Radiolabelled active substance: [¹⁴ C-phenyl]-isofetamid or [¹⁴ C-(C2)-thiophene]-isofetamid (EFSA, 2015)
	Pulses/oilseeds	French bean	3 × 750 g/ha foliar spray, 8 days interval, first application at BBCH 60–61	0, 14, 68	Radiolabelled active substance: [¹⁴ C-phenyl]-isofetamid or [¹⁴ C-(C2)-thiophene]-isofetamid (EFSA, 2015)
Rotational crops (available studies)	Crop groups	Crops	Application	PBI (DAT)	Comment/Source
	Root/tuber crops	Carrot	1 × ca 2,150 g/ha, bare soil application	30, 120 and 365	Radiolabelled active substance: [¹⁴ C-phenyl]-isofetamid or [¹⁴ C-(C2)-thiophene]-isofetamid (EFSA, 2015)
	Leafy crops	Lettuce			
	Cereal (small grain)	Wheat			
Processed commodities (hydrolysis study)	Conditions		Stable?	Comment/Source	
	Pasteurisation (20 min, 90°C, pH 4)		Yes	EFSA (2015)	
	Baking, brewing and boiling (60 min, 100°C, pH 5)		Yes	EFSA (2015)	
	Sterilisation (20 min, 120°C, pH 6)		Yes	EFSA (2015)	

Can a general residue definition be proposed for primary crops?	Yes	EFSA (2015)
Rotational crop and primary crop metabolism similar?	Yes	Rotational crop metabolism similar but more extensive with further conjugation than in primary crops (EFSA, 2015).
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes	Isofetamid stable under standard hydrolysis conditions (EFSA, 2015).

Plant residue definition for monitoring (RD-Mo)	Isofetamid
Plant residue definition for risk assessment (RD-RA)	Sum of isofetamid and metabolite GPTC, expressed as isofetamid (EFSA, 2015)
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)	<p>Isofetamid: Matrices with high water content, high acid content and dry matrices (EFSA, 2015):</p> <ul style="list-style-type: none"> • LC–MS/MS, LOQ 0.01 mg/kg (individually) • ILV available • Extraction efficiency not verified.

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

Plant products (available studies)	Category	Commodity	T (°C)	Stability period		Compounds covered	Comment/ Source
				Value	Unit		
	High-water content	Lettuces	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	High-water content/ high-starch content	Potatoes	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	High-oil content	Almonds	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	High-oil content	Rapeseeds	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	High-protein content	Beans	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	High-acid content	Grapes	–20	12	Month	Isofetamid, GPTC	EFSA (2015)
	Processed products	–	–	–	–	–	–

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)
Lamb's lettuces/ corn salads, Escaroles/broad- leaved endives, Cresses and other sprouts and shoots, Land cresses, Roman rocket/rucola, Red mustards, Baby leaf crops (including brassica species), Others	Indoor (EU)	Mo: < 0.01; 0.01; <u>0.018</u> ; 0.02; <u>0.036</u> ; <u>0.42</u> ; 2.56; 3.70; 4.02; 11.7 RA ^(f) : 2 × < 0.02; 0.026; <u>0.03</u> ; <u>0.043</u> ; 0.47; 2.58; 3.78; 4.04; 11.8	Residue trials on open leaf lettuce varieties compliant with GAP. Underlined values: new trials not previously assessed (EFSA, 2015) Extrapolation to the subgroup of lettuces and salad plants possible, excluding lettuces, which is the only major crop of this group.	20	Mo: 11.7 RA: 11.8	Mo: 0.23 RA: 0.26	1.07
	NEU	Mo: < 0.01; < <u>0.01</u> ; 2 × 0.03; <u>0.095</u> ; 0.10; 0.22; 0.29; 0.45 ^(e) RA ^(f) : < 0.02; < <u>0.02</u> ; 0.04; 0.05; <u>0.10</u> ; 0.16; 0.30; 0.34; 0.47 ^(e)		0.8	Mo: 0.45 RA: 0.47	Mo: 0.10 RA: 0.10	1.33
	SEU	Mo: 3 × < 0.01; < <u>0.01</u> ; 0.02; 0.04; 0.05 RA ^(f) : 2 × < 0.02; < <u>0.02</u> ; 0.03; 0.03; 0.05; 0.06		0.09	Mo: 0.05 RA: 0.06	Mo: 0.01 RA: 0.03	1.20

MRL: maximum residue level; GAP: Good Agricultural Practice; Mo: monitoring; RA: risk assessment.

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, EU: indoor 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.

(e): Two NEU trials were co-located (not independent); EFSA selected the worst-case residue value from the two trials for derivation of the MRL for outdoor NEU trials.

(f): RA: Sum of isofetamid and GPTC, expressed as isofetamid. Residues of GPTC (479.5 g/mol) when above the LOQ are converted to isofetamid (359.5 g/mol) equivalents using a molecular weight conversion factor of 0.75 (i.e. 359.5 g/mol ÷ 479.5 g/mol) prior to be summed up to isofetamid residues; When below LOQ, they were summed as such (combined LOQ of 0.02 mg/kg).

B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?	Yes	Following soil application of isofetamid at ca 2,150 g/ha, parent isofetamid in succeeding crops was detected in lower amounts and proportions than in primary crops and the residues mainly composed of the GPTC and GPTC-malonyl metabolites accounting together up to ca 40% TRR in carrot roots (0.02 mg/kg) and up to ca 60% TRR in lettuce (0.06 mg/kg) at the 120-day plant-back interval (EFSA, 2015).
Residues in rotational and succeeding crops expected based on field rotational crop study?	No	The field rotational crop studies reported in the peer review were under-dosed (0.33N based on the annual application rate on the salad plants under assessment (indoor use)). Since isofetamid and GPTC were barely detected (LOD = 0.004 mg/kg) and mostly below the LOQ (0.01 mg/kg) in rotational crops, EFSA confirms previous conclusion reached for of the representative use on lettuces (same seasonal application rate) during the EU pesticides peer review that this under-dosing is not considered to be of any concern and there is no need to set MRLs in rotational crop commodities (EFSA, 2015).

TRR: total radioactive residue; LOQ: limit of quantification; MRL; maximum residue level.

B.1.2.3. Processing factors

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

B.2. Residues in livestock

Not relevant.

B.3. Consumer risk assessment

ARfD

Highest IESTI, according to EFSA PRIMo

1 mg/kg bw (European Commission, 2020b)
Lamb’s lettuces: 3.3% of ARfD Escaroles: 47.4% of ARfD Cresses and other sprouts and shoots: 0.3% of ARfD Roman rocket: 3.2% of ARfD Red mustards: 6.3% of ARfD Land cresses: no acute risk assessment Baby leaf crops: no acute risk assessment

Assumptions made for the calculations

Calculations performed with PRIMo revision 3.1

The calculation is based on the highest residue levels expected in raw agricultural commodities under assessment (HR values) according to the risk assessment residue definition derived from the residue trials.

ADI

0.02 mg/kg bw per day (European Commission, 2020b)

Highest IEDI, according to EFSA PRIMo

29% ADI (NL toddler diet)

Contribution of crops assessed:
 Lamb's lettuces: 0.11% of ADI (GEMS diet)
 Escaroles: 0.32% of ADI (NL toddler diet)
 Cresses and other sprouts and shoots: 0.08% of ADI (GEMS diet)
 Roman rocket: 0.04% of ADI (GEMS diet)
 Red mustards: 0.002% of ADI (GEMS diet)
 Other lettuces and other salad plants: 0.21% of ADI (IT adult diet)
 Land cresses: no chronic risk assessment
 Baby leaf crops: no chronic risk assessment

Assumptions made for the calculations

Calculations performed with PRIMo revision 3.1

The calculation is based on the median residue levels derived for raw agricultural commodities (STMR values) according to the risk assessment residue definition for the salads under assessment.

For the remaining commodities covered by the MRL regulation, the STMR values derived in the EU pesticides peer review (EFSA, 2015), in previous MRL applications (EFSA, 2018b, 2021b) and, where relevant, those derived in the evaluations of Codex MRLs (CXLs,) implemented in the EU legislation (FAO, 2016b, 2019, 2020) were selected as input values). The commodities of animal origin were also considered in the exposure calculation even though MRLs are set at the LOQ.

For those commodities, for which the existing EU MRLs are set on the basis of CXLs, the residue data according to the EU risk assessment residue definition are not available. Thus, in order to estimate the contribution of the plant metabolite GPTC, EFSA applied the conversion factor (CF) of 1.1 for risk assessment previously derived (EFSA, 2015) for peaches, apricots, plums blueberries, currants, gooseberries, rose hips and other small fruit and berries (EFSA 2019b, 2021a). For rape seeds, mustard seeds and gold of pleasure, the combined LOQ of 0.017 mg/kg was used as input value for the risk assessment (EFSA, 2017). For other commodities derived from CXLs - almonds, pome fruits, cherries, strawberries, cranberries, blackberries, dewberries, raspberries, other cane fruits, azarole, kaki, beans (with pods), peas (with pods), pulses- a conversion

factor was not available which may lead to an underestimation of residue levels. For these commodities the risk assessment is considered indicative.

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level; 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
Enforcement residue definition: Isofetamid				
0251010	Lamb's lettuces/corn salads	0.01*	20	The submitted data are sufficient to derive an MRL proposal for the intended NEU, SEU and indoor use by extrapolation from trials on lettuces (open leaf varieties). The MRL proposal reflects the more critical residue situation represented by the intended indoor EU use. Risk for consumers unlikely.
0251030	Escaroles/broad-leaved endives			
0251040	Cresses and other sprouts and shoots			
0251050	Land cresses			
0251060	Roman rocket/rucola			
0251070	Red mustards			
0251080	Baby leaf crops (including brassica species)			
0251990	Other lettuces and salad plants			

MRL: maximum residue level; NEU: northern Europe; SEU: southern Europe.

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

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

Appendix C – Pesticide Residue Intake Model (PRIMo)



Isofetamid			
LOQs (mg/kg) range from:	0.01	to:	0.05
Toxicological reference values			
ADI (mg/kg bw per day):	0.02	ARLD (mg/kg bw):	1
Source of ADI:	EC	Source of ARLD:	EC
Year of evaluation:	2020	Year of evaluation:	2020

Input values	
Details – chronic risk assessment	Supplementary results – chronic risk assessment
Details – acute risk assessment/children	Details – acute risk assessment/adults

Comments:											
Refined calculation mode											
Chronic risk assessment: JMPR methodology (IEDI/TMDI)											
No of diets exceeding the ADI : ---											
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)		2nd contributor to MS diet (in % of ADI)		3rd contributor to MS diet (in % of ADI)		Exposure resulting from MRLs set at the LOQ (in % of ADI)	
				MS diet (in % of ADI)	Commodity/group of commodities	MS diet (in % of ADI)	Commodity/group of commodities	MS diet (in % of ADI)	Commodity/group of commodities	MS diet (in % of ADI)	Commodity/group of commodities
TMDI/IEDI calculation (based on average food consumption)	29%	NL toddler	5.84	7%	Apples	5%	Table grapes	3%	Milk: Cattle	3%	29%
	26%	DE child	5.21	8%	Apples	5%	Table grapes	2%	Tomatoes	1%	26%
	19%	GEMS/Food G06	3.82	9%	Tomatoes	4%	Table grapes	1%	Sweet peppers/bell peppers	0.2%	19%
	17%	NL child	3.44	4%	Apples	4%	Table grapes	2%	Raspberries (red and yellow)	1%	17%
	17%	RO general	3.35	6%	Wine grapes	5%	Tomatoes	1%	Sweet peppers/bell peppers	0.7%	17%
	15%	PT general	3.08	9%	Wine grapes	2%	Tomatoes	1%	Peaches		15%
	13%	GEMS/Food G15	2.68	4%	Wine grapes	3%	Tomatoes	2%	Sweet peppers/bell peppers	0.5%	13%
	13%	IE adult	2.63	4%	Wine grapes	1%	Blackberries	1%	Peaches	0.3%	13%
	13%	GEMS/Food G07	2.52	5%	Wine grapes	3%	Tomatoes	1%	Table grapes	0.5%	13%
	13%	FR adult	2.51	8%	Wine grapes	1%	Tomatoes	0.5%	Peaches	0.3%	13%
	13%	GEMS/Food G08	2.51	4%	Wine grapes	3%	Tomatoes	1%	Table grapes	0.5%	13%
	12%	DE women 14-50 yr	2.33	3%	Wine grapes	2%	Tomatoes	2%	Apples	0.7%	12%
	11%	GEMS/Food G11	2.18	4%	Wine grapes	2%	Tomatoes	1%	Table grapes	0.6%	11%
	11%	DE general	2.16	3%	Wine grapes	2%	Apples	2%	Tomatoes	0.7%	11%
	10%	FR child 3 15 yr	2.03	2%	Tomatoes	1%	Wine grapes	1%	Table grapes	-1%	10%
	10%	GEMS/Food G10	2.00	3%	Tomatoes	1%	Wine grapes	1%	Table grapes	0.5%	10%
	8%	IT toddler	1.65	3%	Tomatoes	1%	Peaches	0.6%	Apples		8%
	8%	FI 3 yr	1.61	2%	Raspberries (red and yellow)	1%	Tomatoes	0.9%	Strawberries		8%
	8%	UK toddler	1.56	1%	Tomatoes	1%	Raspberries (red and yellow)	1%	Apples	1%	8%
	8%	FR toddler 2 3 yr	1.53	2%	Apples	1%	Milk: Cattle	1%	Tomatoes	2%	8%
	8%	DK adult	1.53	3%	Wine grapes	1%	Tomatoes	0.6%	Apples	0.4%	8%
	8%	NL general	1.52	2%	Wine grapes	1%	Tomatoes	1.0%	Apples	0.5%	8%
	8%	IT adult	1.52	3%	Tomatoes	2%	Peaches	0.5%	Apples		8%
	8%	DK child	1.52	2%	Apples	1%	Tomatoes	1%	Cucumbers	0.9%	8%
	7%	ES adult	1.42	2%	Tomatoes	1%	Wine grapes	0.9%	Peaches	0.4%	7%
	7%	SE general	1.40	2%	Tomatoes	0.7%	Apples	0.6%	Milk: Cattle	0.9%	7%
	7%	ES child	1.37	2%	Tomatoes	0.8%	Peaches	0.8%	Apples	0.9%	7%
	6%	UK infant	1.30	2%	Milk: Cattle	1%	Apples	0.9%	Tomatoes	2%	6%
	6%	UK vegetarian	1.29	3%	Wine grapes	1%	Tomatoes	0.4%	Apples	0.2%	6%
	6%	UK adult	1.27	4%	Wine grapes	1%	Tomatoes	0.3%	Apples	0.2%	6%
6%	PL general	1.26	2%	Tomatoes	1%	Apples	1%	Table grapes		6%	
6%	FI 6 yr	1.19	2%	Raspberries (red and yellow)	1%	Tomatoes	0.7%	Strawberries		6%	
5%	FI adult	0.93	1%	Tomatoes	1%	Wine grapes	0.5%	Raspberries (red and yellow)		5%	
4%	LT adult	0.80	1%	Tomatoes	1%	Apples	0.3%	Cucumbers	0.3%	4%	
4%	FR infant	0.78	1%	Apples	0.8%	Milk: Cattle	0.4%	Strawberries	0.9%	4%	
1%	IE child	0.21	0.2%	Apples	0.2%	Table grapes	0.2%	Milk: Cattle	0.2%	1%	

Conclusion:
 The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
 The long-term intake of residues of Isofetamid 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				Results for adults			
	No. of commodities for which ARfD/ADI is exceeded (IESTI):				No. of commodities for which ARfD/ADI is exceeded (IESTI):			
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IESTI				IESTI				
Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)	
47%	Escaroles/broad-leaved	20/11.8	474	24%	Escaroles/broad-leaved	20/11.8	238	
43%	Lettuces	20/11.38	433	22%	Chards/beet leaves	20/11.38	215	
26%	Spinaches	20/11.38	257	14%	Lettuces	20/11.38	138	
23%	Table grapes	4/3.13	228	11%	Table grapes	4/3.13	106	
18%	Peaches	3/1.87	178	7%	Wine grapes	4/3.13	74	
18%	Chards/beet leaves	20/11.38	178	6%	Red mustards	20/11.8	63	
10%	Sweet peppers/bell peppers	3/1.66	99	5%	Spinaches	20/11.38	46	
7%	Apricots	3/1.87	65	4%	Blueberries	4/4.4	40	
6%	Pears	0.6/0.42	58	4%	Peaches	3/1.87	35	
5%	Tomatoes	1.5/0.94	55	3%	Cherries (sweet)	4/3.4	34	
5%	Strawberries	4/3.1	51	3%	Blackberries	7/3.75	31	
5%	Apples	0.6/0.42	45	3%	Currants (red, black and	4/4.4	29	
4%	Cherries (sweet)	4/3.4	42	3%	Strawberries	4/3.1	29	
4%	Blackberries	7/3.75	40	3%	Sweet peppers/bell peppers	3/1.66	27	
4%	Cucumbers	1/0.56	37	3%	Aubergines/egg plants	1.5/0.94	25	
3%	Currants (red, black and	4/4.4	35	2%	Lamb's lettuce/corn salads	20/11.8	22	
3%	Raspberries (red and	7/3.75	35	2%	Purslanes	20/11.38	22	
3%	Lamb's lettuce/corn salads	20/11.8	33	2%	Apricots	3/1.87	20	
3%	Roman rocket/rucola	20/11.8	32	2%	Raspberries (red and	7/3.75	20	
3%	Wine grapes	4/3.13	29	2%	Gooseberries (green, red	4/4.4	20	
3%	Blueberries	4/4.4	26	2%	Cucumbers	1/0.56	16	
3%	Courgettes	1/0.56	26	1%	Tomatoes	1.5/0.94	15	
3%	Gooseberries (green, red	4/4.4	26	1%	Roman rocket/rucola	20/11.8	14	
2%	Aubergines/egg plants	1.5/0.94	24	1%	Parsley	20/11.38	14	
2%	Kaki/Japanese persimmons	0.6/0.42	20	1%	Courgettes	1/0.56	13	
2%	Plums	0.8/0.43	18	1%	Pears	0.6/0.42	13	
1%	Chervil	20/11.38	15	1%	Apples	0.6/0.42	12	
1%	Cranberries	4/3.1	14	1.0%	Rose hips	4/4.4	9.7	
1%	Parsley	20/11.38	12	0.9%	Kaki/Japanese persimmons	0.6/0.42	9.2	
1%	Quinces	0.6/0.42	10	0.8%	Plums	0.8/0.43	7.6	
0.9%	Chives	20/11.38	9.3	0.6%	Quinces	0.6/0.42	6.4	
0.9%	Sage	20/11.38	8.6	0.5%	Dewberries	7/3.75	5.4	
0.8%	Basil and edible flowers	20/11.38	8.3	0.4%	Cress and other sprouts and	20/11.8	4.5	
0.7%	Dewberries	7/3.75	6.6	0.4%	Celery leaves	20/11.38	3.7	
0.6%	Medlar	0.6/0.42	5.8	0.4%	Cranberries	4/3.1	3.5	
0.5%	Celery leaves	20/11.38	5.5	0.3%	Gherkins	1/0.56	3.4	
0.4%	Beans (with pods)	0.6/0.36	4.1	0.3%	Medlar	0.6/0.42	2.9	
0.3%	Cress and other sprouts	20/11.8	3.5	0.3%	Beans (with pods)	0.6/0.36	2.8	
0.3%	Peas (with pods)	0.6/0.36	2.9	0.2%	Sage	20/11.38	2.3	
0.2%	Gherkins	1/0.56	1.6	0.2%	Chives	20/11.38	1.9	
0.1%	Milk: Cattle	0.01/0.01	1.2	0.1%	Basil and edible flowers	20/11.38	1.4	
0.07%	Thyme	20/11.38	0.68	0.1%	Peas (with pods)	0.6/0.36	1.2	
0.04%	Azarole/Mediterranean	0.6/0.42	0.38	0.1%	Rosemary	20/11.38	1.1	
0.03%	Rosemary	20/11.38	0.34	0.1%	Rosemary	20/11.38	1.1	
0.02%	Milk: Goat	0.01/0.01	0.24	0.1%	Rosemary	20/11.38	1.1	
0.02%	Beans	0.09/0.01	0.18	0.1%	Rosemary	20/11.38	1.1	
0.02%	Poultry: Muscle/meat	0.01/0.01	0.17	0.09%	Chervil	20/11.38	0.92	
0.01%	Eggs: Chicken	0.01/0.01	0.12	0.04%	Milk: Cattle	0.01/0.01	0.39	
0.01%	Swine: Muscle/meat	0.01/0.01	0.12	0.02%	Milk: Goat	0.01/0.01	0.18	
0.01%	Laurel/bay leaves	20/11.38	0.11	0.02%	Milk: Sheep	0.01/0.01	0.15	
0.01%	Bovine: Liver	0.01/0.01	0.08	0.01%	Poultry: Muscle	0.01/0.01	0.12	
0.01%	Bovine: Edible offals (other	0.01/0.01	0.07	0.01%	Beans	0.09/0.01	0.07	
0.01%	Bovine: Muscle/meat	0.01/0.01	0.07	0.01%	Lentils	0.09/0.01	0.06	
0.01%	Other farmed animals:	0.01/0.01	0.07	0.01%	Bovine: Muscle	0.01/0.01	0.06	
0.01%	Lentils	0.09/0.01	0.07	0.01%	Other farmed animals:	0.01/0.01	0.06	
0.01%	Peas	0.09/0.01	0.07	0.00%	Swine: Muscle/meat	0.01/0.01	0.05	
0.01%	Equine: Muscle/meat	0.01/0.01	0.06	0.00%	Equine: Muscle/meat	0.01/0.01	0.05	
0.01%	Sheep: Muscle/meat	0.01/0.01	0.05	0.00%	Sheep: Muscle/meat	0.01/0.01	0.05	
0.00%	Bovine: Kidney	0.01/0.01	0.04	0.00%	Poultry: Liver	0.01/0.01	0.05	
0.00%	Milk: Sheep	0.01/0.01	0.04	0.00%	Eggs: Chicken	0.01/0.01	0.04	
0.00%	Swine: Edible offals (other	0.01/0.01	0.03	0.00%	Bovine: Liver	0.01/0.01	0.04	
0.00%	Almonds	0.01/0.01	0.03	0.00%	Peas	0.09/0.01	0.03	
0.00%	Rapeseeds/canola seeds	0.02/0.02	0.02	0.00%	Bovine: Edible offals (other	0.01/0.01	0.03	

0.00%	Bovine: Fat tissue	0.01/0.01	0.02	0.00%	Swine: Other products	0.01/0.01	0.03
0.00%	Linseeds	0.01/0.02	0.02	0.00%	Sheep: Liver	0.01/0.01	0.03
0.00%	Mustard seeds	0.01/0.02	0.02	0.00%	Swine: Edible offals (other	0.01/0.01	0.03
0.00%	Swine: Fat tissue	0.01/0.01	0.02	0.00%	Swine: Kidney	0.01/0.01	0.02
0.00%	Swine: Kidney	0.01/0.01	0.01	0.00%	Bovine: Kidney	0.01/0.01	0.02
0.00%	Swine: Liver	0.01/0.01	0.01	0.00%	Swine: Fat tissue	0.01/0.01	0.02
0.00%	Poultry: Liver	0.01/0.01	0.01	0.00%	Bovine: Other products	0.01/0.01	0.02
0.00%	Poultry: Fat tissue	0.01/0.01	0.00	0.00%	Goat: Muscle	0.01/0.01	0.02
				0.00%	Almonds	0.01/0.01	0.01
				0.00%	Swine: Liver	0.01/0.01	0.01
				0.00%	Eggs: Quail	0.01/0.01	0.01
				0.00%	Poultry: Kidney	0.01/0.01	0.01
				0.00%	Poppy seeds	0.01/0.02	0.01
				0.00%	Poppy seeds	0.01/0.02	0.01
				0.00%	Bovine: Fat tissue	0.01/0.01	0.01
				0.00%	Rapeseeds/canola seeds	0.02/0.02	0.01
				0.00%	Linseeds	0.01/0.02	0.01
				0.00%	Sheep: Edible offals (other	0.01/0.01	0.01
				0.00%	Eggs: Goose	0.01/0.01	0.01
				0.00%	Poultry: Fat tissue	0.01/0.01	0.00
				0.00%	Sheep: Kidney	0.01/0.01	0.00
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

Processed commodities	Results for children				Results for adults			
	No of processed commodities for which ARfD/ADI is exceeded (IESTI):				No of processed commodities for which ARfD/ADI is exceeded (IESTI):			
	---				---			
	IESTI				IESTI			
	Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL/input for RA (mg/kg)	Exposure (µg/kg bw)
	78%	Escaroles/broad-leaved endi	20/11.8	782	24%	Escaroles/broad-leaved	20/11.8	241
	35%	Chards/beet leaves/boiled	20/11.38	354	14%	Chards/beet leaves/boiled	20/11.38	142
	16%	Spinaches/frozen; boiled	20/11.38	158	9%	Spinaches/frozen; boiled	20/11.38	94
	5%	Peaches/canned	3/1.87	49	5%	Purslanes/boiled	20/11.38	47
	3%	Wine grapes/juice	4/0.71	31	3%	Wine grapes/wine	4/3.13	30
	3%	Raspberries/juice	7/2.45	29	2%	Table grapes/raisins	4/14.71	18
	2%	Courgettes/boiled	1/0.56	20	2%	Peaches/canned	3/1.87	15
	1%	Peaches/juice	3/0.84	14	1%	Wine grapes/juice	4/0.71	15
	1%	Gherkins/pickled	1/0.56	13	1%	Courgettes/boiled	1/0.56	13
	1.0%	Currants (red, black and whi	4/0.34	9.7	0.4%	Apples/juice	0.6/0.14	4.5
	0.9%	Tomatoes/juice	1.5/0.48	9.1	0.4%	Currants (red, black and	4/0.34	4.3
	0.7%	Apples/juice	0.6/0.14	7.3	0.4%	Tomatoes/sauce/puree	1.5/0.48	3.9
	0.5%	Tomatoes/sauce/puree	1.5/0.48	4.6	0.3%	Okra, lady's fingers/boiled	3/1.66	2.7
	0.5%	Beans (with pods)/boiled	0.6/0.36	4.5	0.1%	Peas (with pods)/boiled	0.6/0.36	1.2
	0.4%	Pears/juice	0.6/0.14	4.4	0.04%	Rose hips/jam	4/0.34	0.43
	0.3%	Cranberries/juice	4/0.49	2.8	0.04%	Cranberries/dried	4/0.49	0.37
	0.2%	Plums/juice	0.8/0.19	1.8	0.02%	Quinces/jam	0.6/0.14	0.17
	0.1%	Rose hips/jam	4/0.34	1.0	0.01%	Beans/canned	0.09/0.01	0.07
	0.1%	Azarole (mediterranean med	0.6/0.14	0.75	0.00%	Peas/canned	0.09/0	0.03
	0.0%	Quinces/jam	0.6/0.14	0.41				
	0.0%	Lentils/boiled	0.09/0.01	0.08				
	0.0%	Peas/canned	0.09/0	0.07				
	0.0%	Rapeseeds/oils	0.02/0.03	0.01				
Expand/collapse list								

Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short-term intake of residues of isofetamid 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 for product of plant origin: Sum of isofetamid and metabolite GPTC, expressed as isofetamid						
Lamb's lettuce/ corn salads	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Escaroles/broad- leaved endives	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Cress and other sprouts and shoots	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Land cress	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Roman rocket/ rucola	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Red mustards	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Baby leaf crops (including brassica species)	20	Proposed MRL	0.26	STMR-RAC	11.8	HR-RAC
Other lettuce and other salad plants	20	Proposed MRL	0.26	STMR-RAC		
Almonds	0.01*	FAO (2016b)	0.01	STMR-RAC	0.01	HR-RAC
Apples	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Pears	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Quinces	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Medlar	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Loquats/ Japanese medlars	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Other pome fruit	0.6	FAO (2019)	0.135	STMR-RAC		
Apricots	3	FAO (2019)	0.836	STMR-RAC (0.760) × CF (1.1) (EFSA, 2019b)	1.870	HR-RAC (1.700) × CF (1.1) (EFSA, 2019b)
Cherries (sweet)	4	FAO (2019)	1.100	STMR-RAC	3.400	HR-RAC
Peaches	3	FAO (2019)	0.836	STMR-RAC (0.760) × CF (1.1) (EFSA, 2019b)	1.870	HR-RAC (1.700) × CF (1.1) (EFSA, 2019b)
Plums	0.8	FAO (2019)	0.193	STMR-RAC (0.175) × CF (1.1) (EFSA, 2019b)	0.429	STMR-RAC (0.390) × CF (1.1) (EFSA, 2019b)
Table grapes	4	EFSA (2015)	0.710	STMR-RAC	3.130	HR-RAC
Wine grapes	4	EFSA (2015)	0.710	STMR-RAC	3.130	HR-RAC
Strawberries	4	FAO (2016b)	0.490	STMR-RAC	3.100	HR-RAC
Blackberries	7	EFSA (2021b)	2.450	STMR-RAC	3.750	HR-RAC
Dewberries	7	EFSA (2021b)	2.450	STMR-RAC	3.750	HR-RAC
Raspberries (red and yellow)	7	EFSA (2021b)	2.450	STMR-RAC	3.750	HR-RAC
Other cane fruit	7	EFSA (2021b)	2.450	STMR-RAC		

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)
Blueberries	4	FAO (2020)	0.341	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)	4.400	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)
Cranberries	4	FAO (2016b)	0.490	STMR-RAC	3.100	HR-RAC
Currants (red, black and white)	4	FAO (2020)	0.341	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)	4.400	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)
Gooseberries (green, red and yellow)	4	FAO (2020)	0.341	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)	4.400	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)
Rose hips	4	FAO (2020)	0.341	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)	4.400	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)
Azarole/ Mediterranean medlar	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Other small fruit & berries	4	FAO (2020)	0.341	STMR-RAC (0.310) × CF (1.1) (EFSA, 2021b)		
Kaki/Japanese persimmons	0.6	FAO (2019)	0.135	STMR-RAC	0.420	HR-RAC
Tomatoes	1.5	EFSA (2018b)	0.480	STMR-RAC	0.940	HR-RAC
Sweet peppers/ bell peppers	3	EFSA (2018b)	0.570	STMR-RAC	1.660	HR-RAC
Aubergines/egg plants	1.5	EFSA (2018b)	0.480	STMR-RAC	0.940	HR-RAC
Okra/lady's fingers	3	EFSA (2018b)	0.570	STMR-RAC	1.660	HR-RAC
Cucumbers	1	EFSA (2018b)	0.130	STMR-RAC	0.560	HR-RAC
Gherkins	1	EFSA (2018b)	0.130	STMR-RAC	0.560	HR-RAC
Courgettes	1	EFSA (2018b)	0.130	STMR-RAC	0.560	HR-RAC
Other cucurbits - edible peel	1	EFSA (2018b)	0.130	STMR-RAC	0.560	HR-RAC
Lettuces	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Spinaches	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Purslanes	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Chards/beet leaves	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Other spinach and similar	20	EFSA (2015)	0.047	STMR-RAC		
Chervil	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Chives	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Celery leaves	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Parsley	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Sage	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Rosemary	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Thyme	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Basil and edible flowers	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC

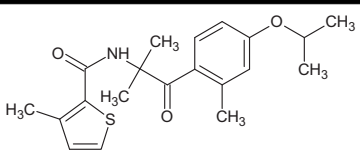
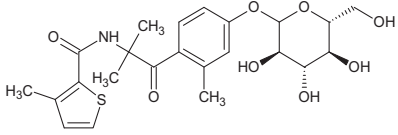
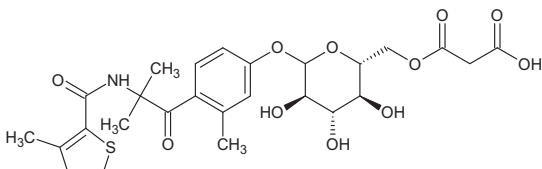
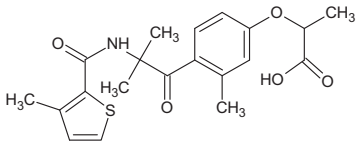
Commodity	Existing/ Proposed MRL (mg/kg)	Source	Chronic risk assessment		Acute risk assessment	
			Input value ^(a) (mg/kg)	Comment	Input value ^(a) (mg/kg)	Comment ^(b)
Laurel/bay leaves	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Tarragon	20	EFSA (2015)	0.047	STMR-RAC	11.380	HR-RAC
Other herbs	20	EFSA (2015)	0.047	STMR-RAC		
Beans (with pods)	0.6	FAO (2019)	0.096	STMR-RAC	0.360	HR-RAC
Peas (with pods)	0.6	FAO (2019)	0.096	STMR-RAC	0.360	HR-RAC
Beans	0.09	FAO (2020)	0.01	STMR-RAC	0.01	HR-RAC
Lentils	0.09	FAO (2020)	0.01	STMR-RAC	0.01	HR-RAC
Peas	0.09	FAO (2020)	0.01	STMR-RAC	0.01	HR-RAC
Lupins/lupini beans	0.09	FAO (2020)	0.01	STMR-RAC	0.01	HR-RAC
Other pulses	0.09	FAO (2020)	0.01	STMR-RAC		
Linseeds	0.01*	EFSA (2015)	0.017	STMR-RAC	0.017	HR-RAC
Poppy seeds	0.01*	EFSA (2015)	0.017	STMR-RAC	0.017	HR-RAC
Rapeseeds/ canola seeds	0.015	FAO (2016b)	0.017	STMR-RAC	0.017	HR-RAC
Mustard seeds	0.01*	EFSA (2015)	0.017	STMR-RAC	0.017	HR-RAC
Gold of pleasure seeds	0.01*	EFSA (2015)	0.017	STMR-RAC	0.017	HR-RAC
Risk assessment residue definition for products of animal origin Sum of isofetamid and PPA, expressed as isofetamid (provisional) (EFSA, 2015)						
Commodities of animal origin	0.01*	Reg. (EU) 2022/93	0.01	MRL (LOQ)	0.01	MRL (LOQ)

STMR-RAC: supervised trials median residue in raw agricultural commodity; HR-RAC: highest residue in raw agricultural commodity.

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

- (a): Figures in the table are rounded to three 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. The conversion factor (CF) of 1.1 for risk assessment derived for peaches, plums, grapes (EFSA, 2015) was used for the calculation of input values derived by JMPR for peaches, apricots, plums, blueberries, currants, gooseberries, rose hips and other small fruit and berries. For rape seeds, mustard seeds and gold of pleasure, the combined LOQ of 0.017 mg/kg was used as input value for the risk assessment. The chronic risk assessment was performed using the STMR expressed as isofetamid (only) derived by the JMPR for almonds, pome fruits, strawberries, cranberries blackberries, dewberries, raspberries, other cane fruits, azaroles, kaki, beans (with pods), peas (with pods) and pulses.
- (b): Input values for the commodities which are not under consideration for the acute risk assessment are reported in grey.

Appendix E – Used compound codes

Code/trivial name	IUPAC name/SMILES notation/ InChIKey ^(a)	Structural formula ^(b)
Isofetamid IKF-5411	<i>N</i> -[1,1-dimethyl-2-(4-isopropoxy- <i>o</i> -tolyl)-2-oxoethyl]-3-methylthiophene-2-carboxamide O=C(NC(C)(C)C(=O)c1ccc(OC(C)C)cc1C)c2sccc2C WMKZDPFZIZQROT-UHFFFAOYSA-N	
GPTC	<i>N</i> -{1-[4-(D-glucopyranosyloxy)-2-methylphenyl]-2-methyl-1-oxopropan-2-yl]-3-methylthiophene-2-carboxamide O=C(NC(C)(C)C(=O)c2ccc(O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O)cc2C)c3sccc3C AJMFCWXRIDCDDN-XHCNLMPIISA-N	
GPTC-malonyl	3-methyl-4-[2-methyl- <i>N</i> -(3-methylthiophene-2-carbonyl)alanyl]phenyl 6- <i>O</i> -(carboxyacetyl)-D-glucopyranoside O=C(NC(C)(C)C(=O)c2ccc(OC1O[C@H](COC(=O)CC(=O)O)[C@@H](O)[C@H](O)[C@H]1O)cc2C)c3sccc3C HAKKTWCXWDYAPF-VVHFXJRLSA-N	
PPA	(2 <i>RS</i>)-2-{3-methyl-4-[2-methyl- <i>N</i> -(3-methylthiophene-2-carbonyl)alanyl]phenoxy}propanoic acid O=C(NC(C)(C)C(=O)c1ccc(OC(C)C(=O)O)cc1C)c2sccc2C CFZWEHRXSMYLPD-UHFFFAOYSA-N	

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

(a): The 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, 7 July 2021).

(c): ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021).