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REASONED OPINION

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# Setting of import tolerances for hexythiazox in blackberries and raspberries

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## Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the applicant Gowan Crop Protection Limited submitted a request to the competent national authority in Finland to set an import tolerance for the active substance hexythiazox in blackberries and raspberries. The data submitted in support of the request were found to be sufficient to derive maximum residue level (MRL) proposals of 3 mg/kg for raspberries and blackberries. Adequate analytical methods for enforcement are available to control the residues of hexythiazox in the plant matrices under consideration at the validated limit of quantification (LOQ) of 0.01 mg/kg. Based on the risk assessment results, EFSA concluded that the intake of residues resulting from the use of hexythiazox according to the reported agricultural practices is unlikely to present a risk to consumer health.

**KEYWORDS**

blackberries, consumer risk assessment, hexythiazox, MRL, pesticide, raspberries

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## SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, Gowan Crop Protection Limited submitted an application to the competent national authority in Finland (Rapporteur Member State, RMS) to set the import tolerances for the active substance hexythiazox in raspberries and blackberries.

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 16 February 2023. The appointed RMS Finland assessed the dossier and declared its admissibility on 21 April 2023. 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 4 July 2023 to 25 July 2023. No additional data nor comments were submitted in the framework of the consultation.

At the end of the commenting period, the RMS 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 15 January 2024. The RMS proposed to establish maximum residue levels (MRLs) for raspberries and blackberries imported from the USA at the level of 3 mg/kg.

The European Commission sent a mandate to EFSA on 1 February 2024 to assess the application and the evaluation report as required by Article 10 of MRL regulation. EFSA identified data gaps and points which needed further clarification and requested the RMS to address them. On 24 July 2024, the applicant provided the requested information in an updated IUCLID dossier. The additional information was duly considered by the RMS who submitted a revised evaluation report to EFSA on 11 September 2024, which replaced the previously submitted evaluation report.

Based on the conclusions derived by EFSA in the framework of Directive 91/414/EEC, the data evaluated under previous MRL assessment, and the additional data provided by the RMS in the framework of this application, the following conclusions are derived.

The metabolism of hexythiazox in primary crops was sufficiently investigated in fruit crops and leafy crops following foliar and local applications. A general residue definition for all plant commodities could not be established as other commodity groups were not investigated. The residue definitions were defined as hexythiazox (any ratio of constituent isomers) for both enforcement and risk assessment purposes for fruit and leafy crops, and tentatively for the other commodity groups. A validated analytical quick, easy, cheap, effective, rugged, and safe (QuEChERS) method using high performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) is available for the enforcement of this residue definition for the crops under assessment. The method enable quantification of residues at or above 0.01 mg/kg (LOQ).

As the proposed uses of hexythiazox are on imported crops, investigations of residues in rotational crops are not required.

Hexythiazox was stable under pasteurisation and baking, brewing and boiling processes but not under sterilisation. Under sterilisation, the parent compound degrades to PT-1-3 and cyclohexylamine. The MRL review concluded, based on processing studies and toxicological data related to metabolite PT-1-3, that the same residue definition used for primary crops could be applied to processing studies for enforcement and risk assessment purposes. However, this conclusion did not contemplate the potential formation of metabolite cyclohexylamine, for which no toxicological information was provided. Consequently, further toxicological data and additional information on the transfer of cyclohexylamine during processing may be needed to establish a comprehensive residue definition for hexythiazox in processed commodities. Nevertheless, since sterilisation is uncommon for low pH commodities such as raspberries and strawberries and processing trials performed on strawberries did not indicate a significant occurrence of cyclohexylamine in processed products (canned fruits and jam), the uncertainty around cyclohexylamine is considered minor for the commodities under assessment. EFSA concluded that for the crops assessed in this application, the metabolism of hexythiazox in primary crops and the possible degradation in processed products have been sufficiently addressed, and the previously derived residue definitions are applicable.

The available residue trials performed on raspberries are sufficient to derive an MRL proposal of 3 mg/kg for blackberries and raspberries based on the most critical GAP identified in the dossier: a foliar application of emulsion in water (EW) formulation at the rate 280 g a.s./ha.

Processing factors (PF) for the crops under assessment were updated, considering the previously submitted processing studies in strawberries provided in the context of the MRL review and the new studies reported in the current application. The updated median PFs can be considered for inclusion in Annex VI of Regulation (EC) No 396/2005 as follows:

– Strawberries/ jam: 0.52
– Strawberries/ canned: 0.48

Residues of hexythiazoxin 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 hexythiazox was assessed in the framework of the EU pesticides peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.03 mg/kg bw per day. An acute reference dose (ARfD) was deemed unnecessary.

The consumer risk assessment was performed with revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo). Considering the toxicological profile of the active substance, a short-term dietary risk assessment was not required. EFSA updated the chronic risk assessment conducted in the framework of the MRL review with the median residue (STMR) value derived from the residue trials submitted in support of this MRL application for blackberries and raspberries. The estimated long-term dietary intake accounted for a maximum of 12% of ADI (NL toddler diet). The individual contribution of residues expected in blackberries and raspberries to the overall long-term exposure accounted for below 1% of the ADI.

EFSA concluded that the proposed use of hexythiazox on raspberries and blackberries will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a risk to consumers' health.

It is noted that the above assessment does not consider the possible impact of plant and livestock metabolism on the isomer ratio of hexythiazox. However, the potential change of isomer ratios of hexythiazox in the final residue in the current assessment is not considered a concern due to the large margin of safety observed in the consumer risk assessment. In case future uses of hexythiazox would lead to higher consumer exposure, further information regarding the impact of plant and livestock metabolism on the isomer ratio might be required.

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:** hexythiazox (any ratio of constituent isomers)[(F)] | | | | |
| 0153010 | Blackberries | 0.01* | 3 | The submitted data are sufficient to derive an import tolerance (US GAP). MRL set in the USA for blackberries and raspberries is 3 mg/kg. Risk for consumers is unlikely |
| 0153030 | Raspberries (red and yellow) | 0.01* | 3 | |

Abbreviations: (F), fat soluble; GAP, Good Agricultural Practice; MRL, maximum residue level.

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

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

# ASSESSMENT

The European Food Safety Authority (EFSA) received an application to set an import tolerance for the active substance hexythiazoxin in raspberries and blackberries. The detailed description of the existing uses of hexythiazox authorised in the USA in raspberries and blackberries, which are the basis for the current MRL application, is reported in Appendix A.

Hexythiazox is the ISO common name for (4*RS*,5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxothiazolidine-3-carboxamide (IUPAC). The chemical structures of the active substance and its main metabolites are reported in Appendix E.

Hexythiazox was evaluated in the framework of Directive 91/414/EEC[1] with Finland designated as rapporteur Member State (RMS) for the representative uses as a foliar treatment on oranges, mandarins, pome fruits and grapes. The draft assessment report (DAR) prepared by the RMS has been peer reviewed by EFSA (EFSA, 2010). Hexythiazox was approved[2] for the use as acaricide on 1 June 2011. The EU MRLs for hexythiazox are established in Annexe IIIA of Regulation (EC) No 396/2005.[3] The review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (MRL review) has been performed (EFSA, 2019a) and the proposed modifications have been implemented in the MRL legislation.[4]

In accordance Article 6 of Regulation (EC) No 396/2005 and following the provisions set by the 'Transparency Regulation' (EU) 2019/1381,[5] the applicant Gowan Crop Protection Limited submitted on 16 February 2023 an application to the competent national authority in Finland, alongside the dossier containing the supporting data using the IUCLID format.

The appointed RMS Finland assessed the dossier and declared its admissibility on 21 April 2023. 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 4 July 2023 to 25 July 2023. No additional data nor comments were submitted in the framework of the consultation.

At the end of the commenting period, the RMS 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 15 January 2024. The RMS proposed to establish maximum residue levels (MRLs) for raspberries and blackberries imported from the USA at the level of 3 mg/kg.

The European Commission sent a mandate to EFSA on 1 February 2024 to assess the application and the evaluation report as required by Article 10 of MRL regulation. EFSA identified data gaps and points which needed further clarification and requested the RMS to address them. On 24 July 2024, the applicant provided the requested information in an updated IUCLID dossier. The additional information was duly considered by the RMS who submitted a revised evaluation report to EFSA on 11 September 2024 (Finland, 2024), which replaced the previously submitted evaluation report.

EFSA based its assessment on the evaluation report submitted by the RMS (Finland, 2024), the DAR and its addenda (Finland, 2006, 2009, 2010) prepared under Council Directive 91/414/EEC, the Commission review report on hexythiazox (European Commission, 2014), the conclusion on the peer review of the pesticide risk assessment of the active substance hexythiazox (EFSA, 2010), the JMPR reports (FAO, 2009a, 2009b, 2011), as well as the conclusions of previous EFSA opinion on hexythiazox (EFSA, 2012), and the reasoned opinion on the MRL review according to Article 12 of Regulation No 396/2005 (EFSA, 2019a).

For this application, the data requirements established in Regulation (EU) No 544/2011[6] and the guidance documents applicable at the date of submission of the IUCLID application are applicable (European Commission, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2010, 2020, 2021, 2023; OECD, 2011, 2013). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011.[7]

A selected list of end points of the studies assessed by EFSA in the framework of this MRL application including the end points of relevant studies assessed previously, is presented in Appendix B.

The evaluation report submitted by the RMS (Finland, 2024) and the exposure calculations using the EFSA PRIMo are considered as supporting documents to this reasoned opinion and, thus, are made publicly available as background documents to this reasoned opinion.[8]

[1]Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, pp. 1–32.

[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, pp. 1–186.

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

[6]Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, pp. 1–66.

[7]Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, pp. 127–175.

[8]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-2023-00283.

# 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 hexythiazox in fruit crops (grapes, citrus, pears and apples) and leafy crops (tea) was investigated in the framework of the EU pesticides peer review and the MRL review after foliar application of $^{14}$C-hexythiazox labelled on the thiazolidine moiety (EFSA, 2010, 2019a). The reported studies indicated that the metabolism of hexythiazox in primary crops is limited.

Hexythiazox molecule has two different rings: thiazolidine and cyclohexyl. All available studies were performed with the same $^{14}$C-hexythiazox, labelled on the thiazolidine moiety. However, degradation of the parent compound is very limited, and no cleavage of the molecule is observed. Consequently, additional primary crops studies performed with another labelling were not required (EFSA, 2010, 2019a).

In the metabolism studies, the possible changes in the stereochemistry of the active substance were not investigated and subsequently, a data gap was identified on the preferential metabolism of the two hexythiazox enantiomers in plants during the peer review process (EFSA, 2010). This data gap has not been addressed yet. EFSA would recommend considering this point according to the guidance document on the risk assessment of compounds that may have stereoisomers (EFSA, 2019c) in the framework of the peer review for the renewal of approval of hexythiazox.

Since the crops under consideration belong to the fruit crop group and since the applications patterns tested in the metabolism studies cover the application rate of the critical GAP under assessment, EFSA concluded that the metabolic behaviour in primary crops is sufficiently addressed, and further studies are not required for the intended uses.

### 1.1.2 | Nature of residues in rotational crops

Investigations of residues in rotational crops are not required for imported crops.

### 1.1.3 | Nature of residues in processed commodities

The effect of industrial processing on the nature of the residues was investigated in the framework of the peer review (EFSA, 2010). A hydrolysis study with $^{14}$C-hexythiazox labelled on the thiazolidine moiety showed that hexythiazox is relatively stable under conditions simulating pasteurisation (90°C, pH 4, 20 min), baking, brewing and boiling (100°C, pH 5, 60 min), with up to 20% of hydrolysis occurring (20% and 13% of total radioactive residue (TRR), respectively). In contrast, under sterilisation conditions (120°C, pH 6, 20 min), degradation to the metabolite PT-1-3 accounted for up to 48.7% of the TRR, roughly the same amount as the non-hydrolysed parent compound. The formation of metabolite PT-1-3 was not significant under pasteurisation and baking, brewing and boiling (≤ 2% of TRR).

In the current application, a new hydrolysis study performed with $^{14}$C-hexythiazox labelled on the cyclohexyl ring was submitted (Finland, 2024). Similarly to the hydrolysis study evaluated in the peer review, hexythiazox was stable under pasteurisation and baking, brewing and boiling processes but not under sterilisation. In the assay simulating sterilisation process, the parent compound was identified as the main component (54.4% TRR) and cyclohexylamine (43.5% TRR) as the major degradation compound. This study completes the overall picture of the metabolic degradation of hexythiazox under sterilisation: the parent compound is hydrolysed into two main metabolites: PT-1-3 and cyclohexylamine.

As PT-1-3 was shown to be more acutely toxic than the parent, additional toxicological information was requested on its toxicological relevance and its possible transfer and level in processed commodities during the peer review (EFSA, 2010). Additional toxicological studies were assessed by the RMS and submitted to the European Commission as confirmatory data following the peer review (Finland, 2014). Based on this additional information received, the Standing Committee on the Food Chain and Animal Health agreed that the toxicity of metabolite PT-1-3 was well addressed, and its mutagenicity could be ruled out (European Commission, 2014).

No information was submitted on the toxicity of metabolite cyclohexylamine in the context of the current application (Finland, 2024). Cyclohexylamine is only expected to be formed during sterilisation process and this condition is not a common practice for low pH commodities (European Commission, 1997d). Therefore, for the two commodities under assessment in the present opinion (raspberries and blackberries), this uncertainty is only considered as minor and data gaps were not identified by EFSA for the present application. Nevertheless, given the significant formation of this metabolite during sterilisation processes, EFSA recommend addressing the toxicological relevance of cyclohexylamine in the framework of the peer review for the renewal of approval of hexythiazox as this may be relevant for several commodities which can undergo sterilisation before being consumed.

### 1.1.4 | Analytical methods for enforcement purposes in plant commodities

During the peer review, a multi-residue analytical method (DFG-S19) using high performance liquid chromatography with ultra-violet detector (HPLC–UV) or gas chromatography with electron capture detector (GC–ECD) was validated for the determination of hexythiazox in high-water, high-acid and high-oil content commodities with a limit of quantification (LOQ) of 0.05 mg/kg (EFSA, 2010).

In the framework of confirmatory data assessment following the peer review and the MRL review, a fully validated quick, easy, cheap, effective, rugged, and safe (QuEChERS) methods using high performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) for the detection of hexythiazox was provided for high acid, high oil, high water and dry commodities with a LOQ of 0.01 mg/kg (EFSA, 2019a; Finland, 2014). Furthermore, in the context of the MRL review, validated methods in matrices considered difficult to analyse (hops, tea) with a LOQ of 0.01 mg/kg using HPLC-MS/MS were provided (EFSA, 2019a). These methods are also suitable and validated for the detection of the hexythiazox metabolite PT-1-3 if deemed necessary (EFSA, 2019a; Finland, 2014). Additionally, during the MRL review, it was concluded from the information provided by the EURL that hexythiazox can be monitored using the QuEChERS method in high acid, high oil and dry commodities at an LOQ of 0.01 mg/kg and at an LOQ of 0.005 mg/kg in high-water content commodities (EFSA, 2019a; EURL, 2017).

In the current application, the applicant submitted a cross-validation study to address the extraction efficiency of the QuEChERS method proposed for enforcement against the method used in the metabolism studies in grapes and citrus (high-acid matrices).[9] The total extracted radioactivity with the extraction solvent used in the metabolism studies (methanol/water 80/20) was high (> 93% TRR in grapes; 70% TRR in citrus at PHI 21–30). On the other hand, the solvent system, used in the QuEChERS procedure was acetonitrile/acetic acid 99.9:0.1%. The assessment of the extraction efficiency was conducted by comparing the residues from incurred samples in grapes and strawberries, after extraction with methanol/water 80/20 solvent ('solvent system of the metabolism studies') or with acetonitrile/acetic acid 99.9:0.1% ('QuEChERS solvent'). Residues of hexythiazox were determined by HPLC–MS/MS monitoring two ion mass transitions. The amount of residues extracted from the samples analysed with the QuEChERS solvent system differed by less than 30% compared to the extraction solvent system of the metabolism studies. Therefore, the suitability of the extraction solvent of the QuEChERS method was sufficiently validated according to the extraction efficiency Technical Guideline (European Commission, 2023).

EFSA concluded that for the crops under consideration in the present MRL applications (concerning high-acid content matrices), sufficiently validated analytical methods are available.

### 1.1.5 | Storage stability of residues in plants

The storage stability of hexythiazox in plants stored under frozen conditions was investigated in the framework of the EU pesticides peer review and the MRL review (EFSA, 2010, 2019a). In high-acid content matrices, to which group the crops under assessment belong, hexythiazox residues were stable for at least 24 months when stored at −20°C.

In addition, as part of the confirmatory data following the peer review, storage stability data for hexythiazox and PT-1-3 in processed commodities were also provided. Storage stability was demonstrated for each substance for 1 year in processed apple (juice, puree, canned fruit, pomace), grapes (wine, juice, raisins and pomace), citrus (juice, marmalade, canned fruit, pomace) stored at −18°C (EFSA, 2019a; Finland, 2014).

In the current application, additional storage stability studies were submitted. The stability of hexythiazox (analysed as the sum of the parent compound and all metabolites containing the PT-1-3 moiety) was demonstrated for at least 73 days in citrus whole fruit, dried pulp and citrus oil when stored frozen at −17°C. This result is of limited value for the present assessment. Furthermore, hexythiazox and PT-1-3 were demonstrated to be stable in strawberry jam for up to 1 year when stored frozen at −18°C (Finland, 2024).

Finally, two other new storage stability studies[10] were submitted in which the stability of the metabolite cyclohexylamine was demonstrated in high-water, dry/high-protein, dry/high-starch and high-acid content plant matrices for up to 14 months and in oily plant matrices for up to 18 months when stored frozen at ≤ −18°C. According to the OECD Guideline 506 (OECD, 2007), if there is no observed decline of residues across the range of the five different commodity categories, then specific freezer storage stability data for processed foods will not be needed.

### 1.1.6 | Proposed residue definitions

Based on the metabolism in primary crops, the residue definition for enforcement and risk assessment was set in the MRL review as hexythiazox (any ratio of constituent isomers) in leafy crops and fruit crops (EFSA, 2019a).

[9] EFSA did not consider the cross-validation data for apples (high-water content matrix) included in the study submitted since they are out of scope in the present MRL request.

[10] These studies also assessed the storage stability of other compounds that EFSA did not consider in the current application since there are out of scope in the present MRL request. Nevertheless, it is noted that these studies have been submitted in the context of the renewal of the active substance.

In the absence of metabolism studies on cereals and oil seeds, tentatively the same residue definition was used for the relevant authorised uses on these crops and a data gap was identified on at least one additional metabolism study with a third group to confirm the applicability of the residue definition for these crops (EFSA, 2019a).

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical to the above-mentioned residue definition. The same residue definitions for primary crops are also applicable to rotational crops.

Based on the available hydrolyses studies performed with two different radiolabels, hexythiazox is deemed stable under pasteurisation and under baking, brewing, boiling but not under sterilisation conditions, where it is significantly degraded to the metabolites PT-1-3 and cyclohexylamine. Thus, the possible inclusion of these metabolites in the residue definitions for processed commodities should be further discussed. Regarding the residue definition for enforcement, the parent compound can still be considered a sufficient marker for enforcement as concluded in the framework of the MRL review. Regarding the residue definition for risk assessment however, a conclusion can only be drawn after further considerations on the toxicity of the two metabolites. The toxicity of metabolite PT-1-3 was well addressed, and its mutagenicity was ruled out (European Commission, 2014). Furthermore, no significant formation of PT-1-3 was observed in the available processing studies. Moreover, considering that the chronic consumer exposure to hexythiazox from the existing uses was relatively low (13.2% of the ADI), the MRL review concluded that PT-1-3 was not relevant for the risk assessment residue definition (EFSA, 2019a). The toxicological characterisation of cyclohexylamine was not addressed. Therefore, EFSA recommends addressing the toxicological relevance of cyclohexylamine in the framework of the peer review for the renewal of approval of hexythiazox, where a conclusion on the residue definition for risk assessment in process commodities should be drawn.

For the two commodities under assessment in the present opinion (raspberries and blackberries), the lack on conclusion for metabolite cycloxylamine is considered as a minor uncertainty because these commodities are not expected to undergo sterilisation conditions under processing operations (European Commission, 1997d).

EFSA concluded that the metabolic behaviour in the plants and processed commodities is sufficiently addressed for the context of the present application.

## 1.2 | Magnitude of residues in plants

### 1.2.1 | Magnitude of residues in primary crops

*GAP 1: Raspberries/blackberries (US outdoor, Foliar spray application): 1 × 280 g a.s./ha; pre-harvest interval (PHI): 3 days. Formulation type: Emulsion in water (EW).*
*GAP 2: Raspberries/blackberries (US outdoor, Foliar spray application): 1 × 210 g a.s./ha; pre-harvest interval (PHI): 3 days. Formulation type: Water-dispersible granule (WG).*

Two GAPs with different formulation types and different application rates are triggering the present MRL assessment. In support of the current MRL application, the applicant provided five residue trials on raspberries conducted in the USA. The trials include a bridging assessment with side-by-side plots comparing residues on raspberry fruit treated with a formulation type EW and WG, both at 0.280 kg a.s./ha and at a lower rate of 0.262 kg a.s./ha. Statistical analysis (Mann–Whitney *U*-test) showed that residue samples from the two different formulations at the same application rate are not statistically different. Trials performed with the formulation type EW at 0.280 kg a.s./ha are compliant with GAP 1. Regarding GAP2, the submitted residue trials performed with WG formulation are overdosed (260 g a.s./ha) and cannot be used to derive MRL from GAP 2. However, considering that the bridging study showed no differences between both formulation types (EW and WG) and considering that the application rate of GAP 2 (210 a.s. g/ha) is less critical that GAP 1 (280 g a.s./ha), it can be concluded that GAP 2 is less critical than GAP 1. Consequently, only GAP 1 was retained for the MRL assessment and further data were not required in support of GAP 2.

The trials were conducted following U.S. EPA test guidelines and several deviations from the EU data requirement[11] were noted. More specifically, the trials were performed only during one growing season in 2018 and none of the trials had a decline design. Nevertheless, the trials were performed in three different U.S. EPA Regions, which is deemed to cover seasonal variability. In addition, studies that indicated decline over time were assessed in the MRL review on different crops, including strawberries (Finland, 2012). Therefore, these deviations are considered as minor. Finally, it should be noted that a non-ionic surfactant was added to the tank mix before spraying. However, it was clarified that this is a common practice among growers to increase surface tension and product adherence and, therefore, it represents a realistic scenario of application method (Finland, 2024).

According to the RMS, the samples of these residue trials were stored under conditions for which the integrity of the samples has been demonstrated (Finland, 2024). It should be noted that the residue definition for enforcement in the USA, hexythiazox and its metabolites containing the (4-chlorophenyl)-4-methyl-2-oxo-3-thiazolidine moiety, calculated as the stoichiometric equivalent of hexythiazox, is wider than the residue definition set in the EU. Consequently, the analytical method used to analyse samples was based on a common moiety and, the parent was analysed as the sum of the parent compound and all metabolites containing PT-1-3. However, overestimation of the residues is not expected, as based on the metabolism studies, the parent compound is not metabolised significantly at short PHIs: parent ≥ 93% of the TRR in fruit at

[11]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, pp. 1–186.

PHIs 5 (pears), 7 (citrus) and 21 (grape). In addition, the extraction efficiency was demonstrated, as the extraction solvent of the method used in the residue trials, (methanol/water (70:30, v/v)) varies less than 20 vol.-% from the solvent used in the metabolism studies (methanol/water (80:20, v/v)); hence they can be considered identical according to the technical GD SANTE/2017/10632 (European Commission, 2023).

According to the technical guidance (European Commission, 2020), extrapolation from raspberries to blackberries is acceptable and both crops are considered minor. Therefore, the number of trials is sufficient to derive an MRL proposal of 3 mg/kg for the intended uses of hexythiazox on raspberries and blackberries.

### 1.2.2 | Magnitude of residues in rotational crops

Investigations of residues in rotational crops are not required for imported crops.

### 1.2.3 | Magnitude of residues in processed commodities

Based on the hydrolysis studies, hexythiazox was considered relatively stable, except under sterilisation conditions where the formation of metabolite PT-1-3 and cyclohexylamine is expected (see Section 1.1.3).

The effect of industrial processing and/or household preparation was investigated in the context of the peer review, the confirmatory data assessment following the peer review and in the MRL review. Studies conducted on citrus, apples, grapes, strawberries and hops are available (EFSA, 2010, 2019a; Finland, 2014). Several of these studies included heat treatment processes (pasteurisation/sterilisation). Overall, residues of hexythiazox decreased compared to the RAC in all processed commodities, except for wet and dry pomace and raisins. In addition, residues of PT-1-3 were only formed in dry pomace, at low levels. No residues of PT-1-3 were detected in processing studies on strawberries and orange jam following sterilisation. The possible formation of cyclohexylamine was not investigated in these studies.

Robust processing factors could be derived for processing of citrus fruits (peeling, juice, marmalade, wet and dry pomace), apple (pasteurised juice; purée; canned fruit; wet and dry pomace), grapes (raisin; wine; must; pasteurised juice; wet and dry pomace), strawberry (jam, canned fruits) and hops (beer) (EFSA, 2019a).

In the present application, two new processing studies in strawberries (canned, jam) were submitted. The studies were considered valid according to the applicable guidance (European Commissions, 1997d) and confirm that accumulation of hexythiazox in processed products of strawberries (canned fruits and jam) is not expected, as the derived processing factors were below 1. The studies also provided data for metabolites PT-1-3 and cyclohexylamine. These compounds were not quantified above the LOQ in strawberries processed fractions following application of hexythiazox at a 1.8× rate. According to the assessment of the RMS, the analytical methods used were sufficiently validated and fit for purpose and samples were stored under conditions for which integrity of the samples has been demonstrated (Finland, 2024). In addition, the enantiomers (4S, 5S) and (4R, 5R) were analysed separately for hexythiazox and metabolite PT-1-3.

The results of the new processing studies were considered together with the previously assessed processing studies in strawberries (canned/ jam) (EFSA, 2019a) deriving a new median processing factor of 0.52 for jam and 0.48 for canned strawberries.

It is noted that the new processing studies provided on strawberries do not cover sterilisation conditions and that the formation of metabolite cyclohexylamine might occur following this kind of treatment. Nevertheless, acidic berries are generally not sterilised/heated in high temperatures (European Commission, 1997d). Furthermore, in previous processing studies performed with sterilised strawberries and orange jam, the metabolite PT-1-3 was not quantified above the LOQ of 0.01 and 0.015 mg/kg respectively. Consequently, a significant formation of cyclohexylamine in processed strawberries, which would also result from the cleavage of the parent compound, is not expected.

EFSA concluded that the effect of industrial processing and/or household preparation is sufficiently studied for the crops under assessment. Nevertheless, processing studies simulating the critical conditions with a sterilisation step where metabolite cyclohexylamine is analysed would be desirable to get a complete picture of the magnitude of cyclohexylamine residues in processed products. If additional uses will be granted in the future, additional processing studies may be required.

### 1.2.4 | Proposed MRLs

The available data are considered sufficient to derive an MRL proposal as well as risk assessment values for the commodities under evaluation (see Appendix B.1.2.1). The MRL proposal is the same as the MRL set in the USA for raspberries and blackberries (3 mg/kg).[12] This MRL proposal is derived from the most critical GAP identified in the dossier: a foliar application of EW formulation at the application rate of 280 g a.s./ha. In Section 3. EFSA assessed whether residues resulting from the intended uses are likely to pose a consumer health risk.

[12]https://www.ecfr.gov/current/title-40/chapter-I/subchapter-E/part-180/subpart-C/section-180.448.

## 2 | RESIDUES IN LIVESTOCK

Not assessed, as the crops under assessment are not considered as the relevant feed items to livestock according to the current guidance (OECD, 2013).

## 3 | CONSUMER RISK ASSESSMENT

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

The toxicological reference value for hexythiazox used in the risk assessment (i.e. ADI of 0.03 mg/kg body weight per day) was derived in the framework of the EU pesticides peer review while an acute reference dose (ARfD) was not allocated as considered not necessary (European Commission, 2014).

*Short-term (acute) dietary risk assessment*

Considering the toxicological profile of the active substance, a short-term dietary risk assessment was not required.

*Long-term (chronic) dietary risk assessment*

The long-term exposure assessment was performed taking into account the STMR value derived for the raspberries and blackberries in this application; for the remaining commodities covered by the MRL regulation, the STMR derived in the framework of the MRL review and Codex MRLs (EFSA, 2019a; FAO, 2009a, 2009b, 2011) were used. The complete list of input values used in the exposure calculations is presented in Appendix D.

Exceedances of the ADI are not indicated for any of the consumer groups. The highest estimated long-term dietary exposure is reported for the NL toddler diet, representing up to 12% of the ADI of hexythiazox. The contribution of residues expected in the commodities assessed in this application to the overall long-term exposure is very low (< 1% of the ADI) and is presented in more detail in Appendix B.3.

It is noted that hexythiazox is a mixture of two enantiomers. A data gap on the possible impact of the preferential degradation and/or conversion of the mixture of isomers was identified during the peer review and the MRL review (EFSA, 2010). This data gap was confirmed by approval decision, Commission Implementing Directive 2011/46/EU,[13] where it is further stated that information is to be submitted 2 years after the adoption of specific guidance and has not been addressed yet.

In addition to the two enantiomers, which are the only constituents of the racemate active substance (i.e. (4R, 5R)-hexythiazox and (4S, 5S)- hexythiazox), two other diastereoisomers ((4R, 5S)- hexythiazox and (4S, 5R)- hexythiazox) can potentially be formed. In the two processing studies on strawberries submitted in this application, the enantiomers (4S, 5S) and (4R, 5R) were analysed separately within the study and the enantiomers change % was < 10%. Nevertheless, this information is not sufficient to draw an overall conclusion on the isomeric shift of hexythiazox in plant matrices. In addition, no information on the two other diastereoisomers was reported in the studies.

The above risk assessment was performed disregarding the possible impact of the isomer ratio due to plant or livestock metabolism. To mitigate the data gap on the possible impact of the preferential degradation and/or conversion of the mixture of isomers, the risk assessment was re-calculated by using an uncertainty factor of 2. This simulates a worst-case situation in which a change in the isomer ratio would lead to a duplication of the toxicological burden of the residue. The total intake can be estimated to account for up to 24% of the ADI with a contribution of blackberries and raspberries of around 1.2% of the ADI. Considering that up to four isomers could be potentially formed a more conservative uncertainty factor of 4 could even be considered according to the technical guidance on stereoisomers (EFSA, 2019c). EFSA, is of the opinion that an uncertainty factor of 2 is sufficient in the context of the current application. Nevertheless, it is noted that the margin of safety would still be sufficiently large with an uncertainty factor of 4. EFSA concludes that the potential change of isomer ratios of hexythiazox in the final residue will not be of concern for the proposed uses assessed in the framework of this application. In case future uses of hexythiazox would lead to higher consumer exposure, further information regarding the impact of plant and livestock metabolism on the isomer ratio might be required.

The indicative long-term intake of residues of hexythiazox resulting from the existing and the reported uses in the USA is unlikely to present a risk to consumer health.

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

[13]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, pp. 1–186.

## 4 | CONCLUSION AND RECOMMENDATIONS

The data submitted in support of this MRL application were found to be sufficient to derive an MRL proposal for blackberries and raspberries. EFSA concluded that the uses of hexythiazox reported to be authorised in the USA in blackberries and raspberries will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a risk to consumers' health.

In the current application, the metabolite cyclohexylamine was identified as a potential degradation product during sterilisation conditions, but its toxicity was not addressed. Processing trials performed on strawberries did not indicate a significant occurrence of cyclohexylamine in processed products (canned fruits and jam). Furthermore, since sterilisation is uncommon for low pH commodities, the uncertainty regarding cyclohexylamine toxicity is considered minor for the commodities under assessment. However, given its significant formation during sterilisation, the toxicological profile and occurrence of cyclohexylamine might need to be addressed in future evaluations, particularly for products that may undergo sterilisation.

Furthermore, EFSA emphasises that the above assessment does not consider the possible impact of plant and livestock metabolism on the isomer ratio of hexythiazox. However, the potential change of isomer ratios of hexythiazox in the final residue in the current assessment is not considered a concern due to the large margin of safety observed in the consumer risk assessment. In case future uses of hexythiazox would lead to higher consumer exposure, further information regarding the impact of plant and livestock metabolism on the isomer ratio might be required.

The MRL recommendation is summarised in Appendix B.4.

### ABBREVIATIONS

| | |
|---|---|
| a.s. | active substance |
| ADI | acceptable daily intake |
| ARfD | acute reference dose |
| BBCH | growth stages of mono- and dicotyledonous plants |
| bw | body weight |
| CAS | Chemical Abstract Service |
| CXL | codex maximum residue limit |
| DAR | draft assessment report |
| DAT | days after treatment |
| DM | dry matter |
| dw | dry weight |
| EMS | evaluating Member State |
| EURL | EU Reference Laboratory (former Community Reference Laboratory (CRL)) |
| FAO | Food and Agriculture Organization of the United Nations |
| GAP | Good Agricultural Practice |
| GC-ECD | gas chromatography with electron capture detector |
| GLP | Good Laboratory Practice |
| HPLC-MS/MS | high performance liquid chromatography with tandem mass spectrometry |
| HPLC-UVD | high performance liquid chromatography with ultra-violet detector |
| HR | highest residue |
| IEDI | international estimated daily 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 |
| LOD | limit of detection |
| LOQ | limit of quantification |
| MRL | maximum residue level |
| MS | Member States |
| 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 |
| 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 |
| SEU | southern Europe |
| SG | water-soluble granule |
| SL | soluble concentrate |
| SP | water-soluble powder |
| STMR | supervised trials median residue |
| TRR | total radioactive residue |
| UV | ultraviolet (detector) |
| WG | water-dispersible granule |
| WHO | World Health Organization |
| WP | wettable powder |

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## REQUESTOR
European Commission

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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# APPENDIX A

## Summary of intended GAP triggering the amendment of existing EU MRLs

| | | | | Preparation | | Application | | | | Application rate per treatment | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Crop and/or situation | NEU, SEU, MS or country | F G or I[a] | Pests or group of pests controlled | Type[b] | Conc. a.s. | 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 | PHI (days) | Remarks |
| Blackberries<br>Raspberries (red and yellow) | USA | F | Pacific mite<br>Yellow spider mite<br>McDaniel spider mite<br>Two-spotted spider mite | EW | 120 g a.s./L | spraying on foliage/ plant | At infestation | 1 | – | Ground Application: 56–150<br>Air Application: 225–600 | Ground Application: 187<br>Air Application: 47 | 105–280 | g a.s./ha | 3 | App. equipment: Ground and air application. Only ground sprayer and aerial applications are permitted<br>Restrictions: 1. Do not make more than one application per year. 2. Treatment of the bushes after collection of the fruit may be made |
| Blackberries<br>Raspberries (red and yellow) | USA | F | | WG | 500 g a.s./L | spraying on foliage/ plant | At infestation | 1 | – | 300–450 | 47 | 140–210 | g a.s./ha | 3 | |

Abbreviations: a.s., active substance; EW, Emulsion in water; GAP, Good Agricultural Practice; MS, Member State; NEU, northern European Union; PHI, minimum pre-harvest interval; SEU, southern European Union; WG, Water-dispersible granule.

[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.

# APPENDIX B

## List of end points

## B.1 | RESIDUES IN PLANTS

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

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

| | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/source |
|---|---|---|---|---|---|
| **Primary crops** (available studies) | Fruit crops | Grapes | Local application corresponding to 210 g a.s./ha | Fruits: 0, 14, 21, 41 Leafs: 0, 14, 28 and 56 | Thiazolidine-5-$^{14}$C hexythiazox. Due to the limited degradation of parent compound, additional label was not considered necessary (EFSA, 2010) |
| | | | Local application corresponding to 2 × 100 g a.s./ha | 21 | |
| | | Citrus | Local leaves and fruit: 5.3 g a.s./hL | 0, 7, 14, 30, 60 and 91 | |
| | | Pears | Local application on leaves and fruit: 5 g a.s./hL | 0, 5, 10, 20, 30 and 60 | |
| | | Apples | Local application on leaves and fruit: 5 g a.s./hL | 10, 20, 30 and 50 | |
| | Leafy crops | Tea | Foliar, 200 g a.s./ha | 0, 7, 14, 21 | |
| | Cereals/grasses | – | – | – | Data gap identified in the context of the MRL review (EFSA, 2019a) |
| | Pulses/oilseeds | | | | |
| | **Crop groups** | **Crop(s)** | **Application(s)** | **PBI (DAT)** | **Comment/source** |
| **Rotational crops** (available studies) | Root/tuber crops | Turnips | Bare soil, 280 g a.s./ha or 560 g a.s./ha | 30 or 122 | Thiazolidine-5-$^{14}$C hexythiazox (EFSA, 2010) |
| | Leafy crops | Lettuce | Bare soil, 280 g a.s./ha or 560 g a.s./ha | 30 or 122 | |
| | Cereal (small grain) | Wheat | Bare soil, 280 g a.s./ha or 560 g a.s./ha | 30 or 122 | |
| | **Conditions** | | **Stable?** | | **Comment/source** |
| **Processed commodities** (hydrolysis study) | Pasteurisation (20 min, 90°C, pH 4) | | Yes | | Studies performed with thiazolidine-5-$^{14}$C hexythiazox (EFSA, 2010) and cyclohexyl-U-$^{14}$C hexythiazox label (Finland, 2024) |
| | Baking, brewing and boiling (60 min, 100°C, pH 5) | | Yes | | |
| | Sterilisation (20 min, 120°C, pH 6) | | No | | Studies performed with thiazolidine-5-$^{14}$C hexythiazox (EFSA, 2010) and cyclohexyl-U-$^{14}$C hexythiazox label (Finland, 2024) Hexythiazox is degraded to PT-1-3 and to cyclohexalidine |
| | | | – | | – |

| | | |
|---|---|---|
| Can a general residue definition be proposed for primary crops? | no | Metabolism studies performed on fruit and leafy crops indicated that the metabolism of hexythiazox in primary crops is limited. However, metabolism studies for cereals and for pulses and oil seeds were not available. In the absence of metabolism studies on cereals and oil seeds tentatively the same residue definition was used for the relevant authorised uses on these crops in the MRL review. Nonetheless, a data gap is identified and at least one additional metabolism study with a third group is required (EFSA, 2019a) |
| Rotational crop and primary crop metabolism similar? | yes | - |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | no | Under sterilisation (120°C, pH 6, 20 min) hexythiazox is degraded to PT-1-3 (48.7 % TRR) and to cyclohexylamine (43.5% TRR) (EFSA, 2010; Finland, 2024).<br>The mutagenicity of PT-1-3 has been ruled out and its occurrence is expected to be low based on the available processing studies (European Commission, 2014). No information on the toxicological profile of cyclohexylamine was submitted in the current application and the occurrence of this metabolite in process commodities was only investigated under pasteurization conditions. Additional toxicological information and additional data on the formation of cyclohexylamine in processed commodities might be required to conclude a residue definition for hexythiazox in processed commodities. |
| Plant residue definition for monitoring (RD-Mo) | Fruits and leafy crops: hexythiazox (any ratio of constituent isomers) [tentative for cereals and oil seeds]<br>Processed commodities: hexythiazox (any ratio of constituent isomers) | |
| Plant residue definition for risk assessment (RD-RA) | Fruits and leafy crops: hexythiazox (any ratio of constituent isomers) [tentative for cereals and oil seeds]<br>Processed commodities: hexythiazox (any ratio of constituent isomers) [tentative pending further assessment on the toxicity and occurrence of cyclohexylamine] | |
| Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) | <u>High acid, high water, high oil content, dry and difficult to analyse matrices (tea, hops):</u><br>• QuEChERS, HPLC-MS/MS;<br>• LOQ: 0.01 mg/kg (EFSA, 2019a);<br>• ILV available (EFSA, 2019a);<br>QuEChERS (HPLC-MS/MS) for enforcement in routine analysis, LOQ 0.01 mg/kg in high acid, high oil and dry commodities; LOQ 0.005 mg/kg for high water content commodities (EFSA, 2019a).<br><br>Extraction efficiency in high acid matrices demonstrated | |

DAT: days after treatment; PBI: plant-back interval; a.s.: active substance; MRL: maximum residue level; HPLC-MS/MS: high performance liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; ILV: independent laboratory validation.

### B.1.1.2 | Stability of residues in plants

| | Category | Commodity | T (°C) | Stability period | | Compounds covered | Comment/ source |
|---|---|---|---|---|---|---|---|
| | | | | Value | Unit | | |
| **Plant products** (available studies) | High-water content | Apples | −20 | 24 | Month | Hexythiazox | EFSA (2010) |
| | | Spinaches | −18 | 14 | Month | Cyclohexylamine | Finland (2024) |
| | High-oil content | Almonds nutmeat | −10 | 7[a] | Month | Hexythiazox | EFSA (2019a) |
| | | Sunflower seeds | −18 | 18 | Month | Cyclohexylamine | Finland (2024) |
| | Dry/high-protein content | Dry beans | −18 | 14 | Month | Cyclohexylamine | Finland (2024) |
| | Dry/high starch | Stover | −10 | 8[a] | Month | Hexythiazox | EFSA (2019a) |
| | | Barley grain | −18 | 14 | Month | Cyclohexylamine | Finland (2024) |
| | High-acid content | Strawberries | −20 | 24 | Month | Hexythiazox | EFSA (2010) |
| | | Grapes | −18 | 14 | Month | Cyclohexylamine | Finland (2024) |
| | Processed products | Processed apple (juice, puree, canned fruit, pomace), grapes (wine, juice, raisins and pomace), citrus (juice, marmalade, canned fruit, pomace) | −18 | 12 | Month | Hexythiazox PT-1-3 | Finland (2014), EFSA (2019a) |
| | Others | Tea (dry) | −30 | 4 | Month | Hexythiazox | EFSA (2010) |

[a]Common moiety method used, which is not compliant with the EU residue definition for enforcement. For these commodities storage stability data is supporting trials using common moiety method only.

## B.1.2 | Magnitude of residues in plants

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

| Commodity | Region[a] | Residue levels observed in the supervised residue trials (mg/kg) | Comments/source | Calculated MRL (mg/kg) | HR[b] (mg/kg) | STMR[c] (mg/kg) | CF[d] |
|---|---|---|---|---|---|---|---|
| Raspberries | USA | 0.486, 0.893, 1.035, 1.090, 1.655 | Residue trials performed on raspberries compliant with GAP with application rate of 280 g a.s./ha and a formulation type EW (Finland, 2024). Extrapolation to blackberries possible | 3 | 1.655 | 1.035 | NA |
| Blackberries | | | | | | – | |

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

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

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

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

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

#### B.1.2.2 | Residues in rotational crops

| | | |
|---|---|---|
| Residues in rotational and succeeding crops expected based on confined rotational crop study? | no | Residues are not expected at significant levels in succeeding crops based on the studies assessed during the MRL review (EFSA, 2019a). |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | no | A field rotational study following bare soil applications (1.3N compared to the most critical GAP) supports that significant residues are not expected in succeeding crops (EFSA, 2019a). |

#### B.1.2.3 | Processing factors

| Processed commodity | Number of valid studies[a] | Processing factor (PF) | | $CF_P$[b] | Comment/source |
|---|---|---|---|---|---|
| | | Individual values | Median PF | | |
| Strawberries, jam | 6 | 0.5[c]; 0.54[c]; 0.79[c]; 1.07[c]; 0.32; 0.32 | 0.52 | NA | EFSA (2019a), Finland (2024) |
| Strawberries, canned | 6 | 0.36[c]; 0.4[c], 0.52[c], 0.99[c]; 0.39; 0.55 | 0.48 | NA | Residues of PT-1-3 and cyclohexylamine were < LOQ |

Abbreviations: NA, not applicable; PF, processing factor.

[a]Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).

[b]Conversion factor for risk assessment in the processed commodity; median of the individual conversion factors for each processing residues trial.

[c]Study evaluated in the framework of the MRL review (EFSA, 2019a).

### B.2 | Residues in livestock

Not relevant.

### B.3 | Consumer risk assessment

Not relevant since no ARfD has been considered necessary.

| | |
|---|---|
| ADI | 0.03 mg/kg bw per day (European Commission, 2014) |
| Highest IEDI, according to EFSA PRIMo | 12% ADI (NL toddler)<br><br>Contribution of crops assessed:<br><br>Blackberries: 0.4% of ADI (IE adult diet)<br>Raspberries: 0.64% of ADI (FI 3 yr diet) |
| Assumptions made for the calculations | The calculation is based on the median residue levels derived for blackberries and raspberries from the submitted residue trials in the framework of the current application, and from STMRs derived in the MRL review and from CXLs (EFSA, 2019a; FAO, 2009, 2011).<br><br>The above risk assessment was performed disregarding the possible impact of the isomer ratio due to plant or livestock metabolism.<br><br>Calculations performed with PRIMo revision 3.1 |

ARfD: acute reference dose; bw: body weight; 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:** hexythiazox (any ratio of constituent isomers)[(F)] | | | | |
| 0153010 | Blackberries | 0.01* | 3 | The submitted data are sufficient to derive an import tolerance (US GAP). MRL set in the USA for blackberries and raspberries is 3 mg/kg. Risk for consumers is unlikely |
| 0153030 | Raspberries (red and yellow) | 0.01* | 3 | |

Abbreviations: (F), fat soluble; GAP, Good Agricultural Practice; MRL, maximum residue level.

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

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

# APPENDIX C

## Pesticide Residue Intake Model (PRIMo)

European Food Safety Authority

EFSA PRIMo revision 3.1; 2021/01/06

### Hexythiazox (F)

| | | | |
|---|---|---|---|
| LOQs (mg/kg) range from: | 0.01 | to: | 3.0 |
| **Toxicological reference values** | | | |
| ADI (mg/kg bw/day): | 0.03 | ARfD (mg/kg bw): | Not relevant |
| Source of ADI: | European Commission | Source of ARfD: | |
| Year of evaluation: | 2014 | Year of evaluation: | |

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 : ---

**TMDI/NEDI/IEDI calculation (based on average food consumption)**

| Calculated exposure (% of ADI) | MS Diet | Expsoure (µg/kg bw per day) | Highest contributor to MS diet (in % of ADI) | Commodity / group of commodities | 2nd contributor to MS diet (in % of ADI) | Commodity / group of commodities | 3rd contributor to MS diet (in % of ADI) | Commodity / group of commodities | Exposure resulting from MRLs set at the LOQ (in % of ADI) | Exposure resulting from commodities not under assessment (in % of ADI) |
|---|---|---|---|---|---|---|---|---|---|---|
| 12% | NL toddler | 3.67 | 4% | Apples | 2% | Milk: Cattle | 2% | Pears | | 12% |
| 10% | DE child | 3.15 | 5% | Apples | 1% | Oranges | 0.9% | Table grapes | | 10% |
| 10% | GEMS/Food G11 | 2.92 | 6% | Soyabeans | 0.7% | Wine grapes | 0.6% | Tea (dried leaves of Camellia sinensis | | 10% |
| 8% | GEMS/Food G10 | 2.52 | 5% | Soyabeans | 0.5% | Tea (dried leaves of Camellia sinensis) | 0.3% | Oranges | | 8% |
| 7% | NL child | 2.12 | 2% | Apples | 0.8% | Milk: Cattle | 0.7% | Table grapes | | 7% |
| 7% | GEMS/Food G07 | 2.05 | 3% | Soyabeans | 1.0% | Wine grapes | 0.7% | Tea (dried leaves of Camellia sinensis | | 7% |
| 7% | GEMS/Food G08 | 1.99 | 3% | Soyabeans | 0.7% | Wine grapes | 0.4% | Apples | | 7% |
| 7% | GEMS/Food G06 | 1.98 | 2% | Soyabeans | 0.8% | Tea (dried leaves of Camellia sinensis) | 0.7% | Table grapes | | 7% |
| 6% | GEMS/Food G15 | 1.85 | 3% | Soyabeans | 0.7% | Wine grapes | 0.4% | Apples | | 6% |
| 6% | IE adult | 1.80 | 2% | Tea (dried leaves of Camellia sinens | 0.8% | Wine grapes | 0.4% | Blackberries | | 6% |
| 5% | FR adult | 1.51 | 2% | Tea (dried leaves of Camellia sinens | 2% | Wine grapes | 0.3% | Apples | | 5% |
| 4% | FR child 3 15 yr | 1.34 | 0.9% | Oranges | 0.8% | Milk: Cattle | 0.6% | Apples | | 4% |
| 4% | DE women 14-50 yr | 1.27 | 0.9% | Apples | 0.6% | Wine grapes | 0.5% | Oranges | | 4% |
| 4% | UK infant | 1.20 | 1% | Milk: Cattle | 0.9% | Tea (dried leaves of Camellia sinensis) | 0.6% | Apples | | 4% |
| 4% | DE general | 1.19 | 0.9% | Apples | 0.6% | Wine grapes | 0.5% | Tea (dried leaves of Camellia sinensis | | 4% |
| 4% | FR toddler 2 3 yr | 1.15 | 1% | Apples | 1.0% | Milk: Cattle | 0.4% | Oranges | | 4% |
| 4% | PT general | 1.09 | 2% | Wine grapes | 0.5% | Soyabeans | 0.4% | Apples | | 4% |
| 4% | UK toddler | 1.08 | 0.7% | Milk: Cattle | 0.6% | Apples | 0.5% | Oranges | | 4% |
| 3% | RO general | 1.04 | 1% | Wine grapes | 0.5% | Apples | 0.4% | Milk: Cattle | | 3% |
| 3% | NL general | 0.94 | 0.5% | Apples | 0.5% | Tea (dried leaves of Camellia sinensis) | 0.4% | Wine grapes | | 3% |
| 3% | DK child | 0.81 | 0.9% | Apples | 0.4% | Milk: Cattle | 0.3% | Cucumbers | | 3% |
| 2% | ES child | 0.75 | 0.6% | Oranges | 0.4% | Apples | 0.4% | Milk: Cattle | | 2% |
| 2% | FI 3 yr | 0.73 | 0.7% | Strawberries | 0.6% | Raspberries (red and yellow) | 0.3% | Apples | | 2% |
| 2% | UK vegetarian | 0.72 | 0.8% | Tea (dried leaves of Camellia sinens | 0.5% | Wine grapes | 0.2% | Oranges | | 2% |
| 2% | UK adult | 0.70 | 0.8% | Tea (dried leaves of Camellia sinens | 0.7% | Wine grapes | 0.2% | Apples | | 2% |
| 2% | SE general | 0.68 | 0.4% | Milk: Cattle | 0.4% | Apples | 0.3% | Strawberries | | 2% |
| 2% | DK adult | 0.62 | 0.6% | Wine grapes | 0.4% | Apples | 0.2% | Milk: Cattle | | 2% |
| 2% | FR infant | 0.58 | 0.6% | Apples | 0.6% | Milk: Cattle | 0.3% | Strawberries | | 2% |
| 2% | ES adult | 0.58 | 0.3% | Oranges | 0.3% | Apples | 0.3% | Wine grapes | | 2% |
| 2% | FI 6 yr | 0.55 | 0.5% | Strawberries | 0.5% | Raspberries (red and yellow) | 0.2% | Apples | | 2% |
| 2% | IT toddler | 0.50 | 0.3% | Apples | 0.2% | Tomatoes | 0.2% | Strawberries | | 2% |
| 2% | PL general | 0.47 | 0.7% | Apples | 0.2% | Table grapes | 0.2% | Cherries (sweet) | | 2% |
| 1% | IT adult | 0.41 | 0.3% | Apples | 0.2% | Tomatoes | 0.2% | Peaches | | 1% |
| 1% | LT adult | 0.39 | 0.7% | Apples | 0.1% | Milk: Cattle | 0.1% | Tomatoes | | 1% |
| 1% | FI adult | 0.38 | 0.2% | Strawberries | 0.2% | Apples | 0.2% | Wine grapes | | 1% |
| 0.5% | IE child | 0.14 | 0.1% | Milk: Cattle | 0.1% | Apples | 0.0% | Strawberries | | 0.5% |

**Conclusion:**
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Hexythiazox (F) 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

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**<br>No. of commodities for which ARfD/ADI is exceeded (IESTI): | | | --- | **Results for adults**<br>No. of commodities for which ARfD/ADI is exceeded (IESTI): | | | --- |
|---|---|---|---|---|---|---|---|
| **IESTI** | | | | **IESTI** | | | |
| Highest % of ARfD/ADI | Commodities | MRL / input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodities | / input for | Exposure (µg/kg bw) |
| Expand/collapse list | | | | | | | |
| **Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)** | | | | | | | |

**Processed commodities**

| **Results for children**<br>No of processed commodities for which ARfD/ADI is exceeded (IESTI): | | | --- | **Results for adults**<br>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) |
| 42% | Peaches / canned | 0.7 / 0.48 | 12 | 13% | Peaches / canned | 0.7 / | 3.9 |
| 40% | Raspberries / juice | 3 / 1.03 | 12 | 11% | Pumpkins / boiled | 0.07 | 3.3 |
| 18% | Pumpkins / boiled | 0.07 / 0.06 | 5.3 | 10% | Hops / beer | 3 / | 2.9 |
| 12% | Pears / juice | 0.4 / 0.11 | 3.6 | 4% | Courgettes / boiled | 0.05 | 1.1 |
| 8% | Peaches / juice | 0.7 / 0.14 | 2.3 | 3% | Tea (dried leaves of Camellia | 15 / | 0.92 |
| 7% | Soyabeans / soya drink | 0.5 / 0.5 | 2.1 | 3% | Table grapes / raisins | 1 / | 0.82 |
| 6% | Courgettes / boiled | 0.05 / 0.05 | 1.8 | 2% | Apples / juice | 0.4 / | 0.73 |
| 5% | Tea (dried leaves of | 15 / 0.05 | 1.6 | 1% | Tomatoes / sauce/puree | 0.1 / | 0.41 |
| 4% | Apples / juice | 0.4 / 0.02 | 1.2 | 1% | Wine grapes / juice | 1 / | 0.33 |
| 4% | Gherkins / pickled | 0.05 / 0.05 | 1.1 | 0.8% | Maize / oil | 0.02 | 0.25 |
| 3% | Tomatoes / juice | 0.1 / 0.05 | 0.95 | 0.8% | Oranges / juice | 0.5 / | 0.24 |
| 3% | Oranges / juice | 0.5 / 0.02 | 0.84 | 0.8% | Wine grapes / wine | 1 / | 0.23 |
| 2% | Soyabeans / boiled | 0.5 / 0.2 | 0.73 | 0.6% | Grapefruits / juice | 0.5 / | 0.17 |
| 2% | Wine grapes / juice | 1 / 0.02 | 0.70 | 0.5% | Quinces / jam | 0.4 / | 0.14 |
| 2% | Plums / juice | 0.7 / 0.07 | 0.66 | 0.4% | Currants (red, black and | 0.01 | 0.13 |
| Expand/collapse list | | | | | | | |

**Conclusion:**
No exceedance of the toxicological reference value was identified for any unprocessed commodity.
A short term intake of residues of Hexythiazox (F) 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

| 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 |
| **Risk assessment residue definition: hexythiazox (any ratio of constituent isomers)** | | | | | | |
| Grapefruits | 0.5 | FAO (2009a, 2009b) | 0.08 | STMR-Pulp (CXL) | Considering the toxicological profile of the active substance, an acute risk assessment was not needed as the setting of an ARfD for the active substance was considered not necessary. | |
| Oranges | 0.5 | FAO (2009a, 2009b) | 0.08 | STMR-Pulp (CXL) | | |
| Lemons | 0.5 | FAO (2009a, 2009b) | 0.08 | STMR-Pulp (CXL) | | |
| Limes | 0.5 | FAO (2009a, 2009b) | 0.08 | STMR-Pulp (CXL) | | |
| Mandarins | 0.5 | FAO (2009a, 2009b) | 0.08 | STMR-Pulp (CXL) | | |
| Almonds | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Brazil nuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Cashew nuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Chestnuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Coconuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Hazelnuts/cobnuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Macadamia | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Pecans | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Pine nut kernels | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Pistachios | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Walnuts | 0.05 | FAO (2009a, 2009b) | 0.02 | STMR-RAC (CXL) | | |
| Apples | 0.4 | FAO (2009a, 2009b) | 0.11 | STMR-RAC (CXL) | | |
| Pears | 0.4 | FAO (2009a, 2009b) | 0.11 | STMR-RAC (CXL) | | |
| Quinces | 0.4 | FAO (2009a, 2009b) | 0.11 | STMR-RAC (CXL) | | |
| Medlar | 0.4 | FAO (2009a, 2009b) | 0.11 | STMR-RAC (CXL) | | |
| Loquats/Japanese medlars | 0.4 | FAO (2009a, 2009b) | 0.11 | STMR-RAC (CXL) | | |
| Apricots | 0.7 | EFSA (2019a) | 0.14 | STMR-RAC | | |
| Cherries (sweet) | 1.5 | EFSA (2019a) | 0.52 | STMR-RAC | | |
| Peaches | 0.7 | EFSA (2019a) | 0.14 | STMR-RAC | | |
| Plums | 0.7 | EFSA (2019a) | 0.07 | STMR-RAC | | |
| Table grapes | 1 | FAO (2009a, 2009b) | 0.2 | STMR-RAC (CXL) | | |
| Wine grapes | 1 | FAO (2009a, 2009b) | 0.2 | STMR-RAC (CXL) | | |
| Strawberries | 6 | FAO (2011) | 0.54 | STMR-RAC (CXL) | | |
| Blackberries | 3 | **Proposed MRL** | 1.03 | STMR-RAC | | |
| Dewberries | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Raspberries (red and yellow) | 3 | **Proposed MRL** | 1.03 | STMR-RAC | | |
| Blueberries | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Cranberries | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Currants (red, black and white) | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Gooseberries (green, red and yellow) | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Rose hips | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Mulberries (black and white) | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Azarole/Mediteranean medlar | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Elderberries | 0.01 | EFSA (2019a) | 0.01 | STMR-RAC | | |
| Dates | 2 | FAO (2009a, 2009b) | 0.26 | STMR-RAC (CXL) | | |

(Continues)

(Continued)

| Commodity | Existing/ proposed MRL (mg/kg) | Source | Chronic risk assessment: Input value[a] (mg/kg) | Chronic risk assessment: Comment | Acute risk assessment: Input value[a] (mg/kg) | Acute risk assessment: Comment |
|---|---|---|---|---|---|---|
| Tomatoes | 0.1 | FAO (2009a, 2009b) | 0.05 | STMR-RAC (CXL) | | |
| Sweet peppers/bell peppers | 0.09 | EFSA (2019a) | 0.05 | STMR-RAC | | |
| Aubergines/egg plants | 0.1 | FAO (2009a, 2009b) | 0.05 | STMR-RAC (CXL) | | |
| Cucumbers | 0.05 | EFSA (2019a) | 0.05 | STMR-RAC | | |
| Gherkins | 0.05 | EFSA (2019a) | 0.05 | STMR-RAC | | |
| Courgettes | 0.05 | EFSA (2019a) | 0.05 | STMR-RAC | | |
| Melons | 0.07 | EFSA (2019a) | 0.05 | STMR-Pulp | | |
| Pumpkins | 0.07 | EFSA (2019a) | 0.05 | STMR-Pulp | | |
| Watermelons | 0.07 | EFSA (2019a) | 0.05 | STMR-Pulp | | |
| Soyabeans | 0.5 | EFSA (2019a) | 0.5 | MRL | | |
| Maize/corn | 0.02 | EFSA (2019a) | 0.02 | STMR-RAC | | |
| Tea (dried leaves of Camellia sinensis) | 15 | FAO (2011) | 4.55 | STMR-RAC (CXL) | | |
| HOPS (dried) | 3 | FAO (2011) | 0.79 | STMR-RAC (CXL) | | |
| Products of animal Origin-terrestrial Animals Swine: Swine-, bovine-, equine-, sheep-, goat-, other farm animals-Muscle/ meat[b] | 0.05 | FAO (2009a, 2009b) | 0.01[c] | STMR (CXL) | | |
| Products of animal Origin –terrestrial Animals Swine: Swine-, bovine-, equine-, sheep-, goat-, other farm animals – fat tissue, liver, kidney, other edible offal | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |
| Poultry: Muscle/meat[b] | 0.05 | FAO (2009a, 2009b) | 0.01[c] | STMR (CXL) | | |
| Poultry: Fat tissue | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |
| Poultry: Liver | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |
| Poultry: Kidney | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |
| Poultry: Edible offal (other than liver and kidney) | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |
| Milk: Cattle, sheep, goat, horse | 0.05 | FAO (2009a, 2009b) | 0.01 | STMR (CXL) | | |

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

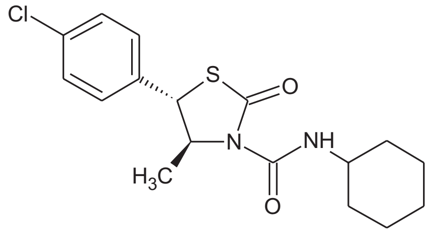
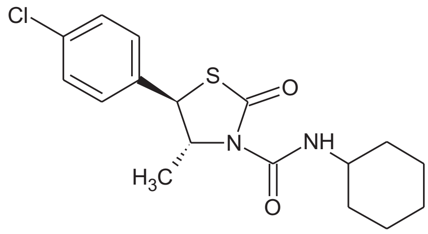
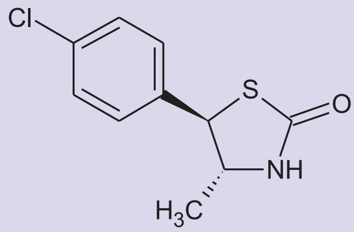
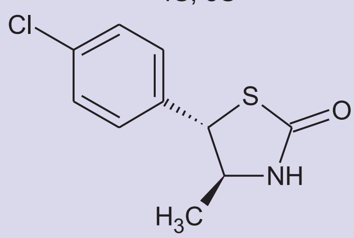
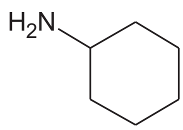
[a]Figures in the table are rounded to two digits, but the calculations are normally performed with the actually calculated values (which may contain more digits). To reproduce dietary burden calculations, the unrounded values need to be used.

[b]Consumption figures in the EFSA PRIMo are expressed as meat. Since the a.s. is a fat-soluble pesticides, STMR and HR residue values were calculated considering a 80%/90% muscle and 20%/10% fat content for mammal/poultry meat respectively (FAO, 2016).

[c]The input value is proposed at the limit of quantification, therefore no correction for fat solubility was done.

## APPENDIX E

### Used compound codes

| Code/trivial name[a] | IUPAC name/SMILES notation/InChiKey[b] | Structural formula[c] |
|---|---|---|
| **Hexythiazox** | (4*RS*,5*RS*)-5-(4-chlorophenyl)-*N*-cyclohexyl-4-methyl-2-oxothiazolidine-3-carboxamide<br>O=C1S[C@@H](c2ccc(Cl)cc2)[C@H](C)N1C(=O)NC1CCCCC1.O=C1S[C@H](c2ccc(Cl)cc2)[C@@H](C)N1C(=O)NC1CCCCC1<br>KYOUEHWYDNYHAL-IOORBXIBSA-N | <br>and<br> |
| **PT-1-3** | (4*R*,5*R*)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one<br>O=C1S[C@H](c2ccc(Cl)cc2)[C@@H](C)N1<br>IPCDQNZFHKSICG-MUWHJKNJSA-N<br>(4*S*,5*S*)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one<br>O=C1S[C@@H](c2ccc(Cl)cc2)[C@H](C)N1<br>IPCDQNZFHKSICG-IMTBSYHQSA-N | 4*R*, 5*R*<br><br>4*S*, 5*S*<br> |
| **Cyclohexylamine** | Cyclohexanamine<br>PAFZNILMFXTMIY-UHFFFAOYSA-N<br>NC1CCCCC1 |  |

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

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

[b]ACD/Name 2023.2.4 ACD/Labs 2023.2.4 (File Version N25E41, Build 137185, 31 Jan 2024).

[c]ACD/ChemSketch 2023.2.4 ACD/Labs 2024.2.4 (File Version C45H41, Build 137017, 18 Jan 2024).