The evaluation of new MRLs and the review of MRLs for hexythiazox in or on various commodities

UK Competent Authority Evaluation Report and Draft Reasoned Opinion

- Prepared under Articles 6 (3) and 8 of Assimilated Regulation 396/2005 and Data Requirements of Assimilated Regulation 544/2011
- Application Reference Number: COP 2023/00222

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Contents

Summary

This assessment is a draft only and outlines proposed recommendations for the MRLs for the active substance hexythiazox.

According to Article 6(3) of Assimilated Regulation 396/2005, HSE considered the need to review the MRLs for hexythiazox in or on various commodities:

- HSE identified chronic intake concerns when considering all of the current GB MRLs, with the main contribution being from citrus fruit, apples and pears.

Additionally, in accordance with Article 6 of Assimilated Regulation 396/2005,[1] HSE received an application from Gowan Crop Protection Limited on 20 February 2023 to set import tolerances for the active substance hexythiazox in or on raspberries and blackberries. This was to accommodate authorisations in USA.

The applicant submitted a dossier in accordance with the data requirements outlined in Assimilated Regulation 544/2011.

In accordance with Article 8 of Assimilated Regulation 396/2005, HSE evaluated the dossier in accordance with the uniform principles as outlined in Article 29(6) of Assimilated Regulation 1107/2009.[2]

Based on the assessment HSE prepared an Evaluation Report that included its Reasoned Opinion on the risk to consumers associated with amending the MRLs. HSE also took into account the data assessed for the approval of the active substance and previous Reasoned Opinions.

Sufficiently validated analytical methods for the determination of hexythiazox in products of plant origin, in line with the residue definition for enforcement, are available to support the uses under consideration in the import tolerance application.

Toxicological reference values were established for the approval of the active substance: an ADI of 0.03 mg/kg bw/day and no ARfD allocated or required.

The metabolism of hexythiazox in primary crops was investigated in fruits (grape, pear citrus, apple) and miscellaneous crops (tea) following foliar applications for the approval of the active substance (EFSA, 2010). The crops included in this import tolerance application

[1] Assimilated Regulation No 396/2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin

[2] Assimilated Regulation No 1107/2009 concerning the placing of plant protection products on the market

belong to the fruit commodity group and are, therefore, covered by the metabolism studies available.

The residue definition for risk assessment (RD-RA) in plants has been agreed as:

- Hexythiazox

The residue definition for enforcement (RD-Enf) in plants has been agreed as:

- Hexythiazox

Five outdoor trials on raspberries conducted in the USA were submitted to support MRLs for raspberries and blackberries. The trials are supported by validated analytical methods and storage stability data.

Hydrolysis of hexythiazox under representative conditions of pasteurisation, baking, brewing, boiling and sterilisation was evaluated for the approval of the active substance. The hydrolysis data from the approval of the active substance (thiazolidine radiolabel), demonstrate that hexythiazox is stable under standard conditions of pasteurisation and baking, boiling and brewing with formation of the PT-1-3 metabolite shown to be not significant. Under sterilisation conditions, hexythiazox is degraded to PT-1-3 (48% TRR). New hydrolysis data (cyclohexyl radiolabel) demonstrates that hexythiazox is stable under standard conditions of pasteurisation and baking, boiling and brewing, whereas under sterilisation conditions, hexythiazox is degraded to cyclohexylamine (43.5% TRR). Specific residue definitions for processed commodities of raspberries and blackberries are not required as residues of PT-1-3 and cyclohexylamine were shown to be <LOQ in the relevant processed commodities and sterilisation is not routinely performed for cane fruit due to their low pH.

No consideration of rotational crops was made as the impact of residues in rotational crops on the import tolerances was not required.

Following estimations of dietary exposures related to the proposed MRLs for raspberries and blackberries, and current GB MRLs for all other commodities, HSE identified chronic intake concerns associated with current MRLs. The highest UK NEDI was 136% of the ADI (toddler). The highest PRIMo IEDI was 127% of the ADI (NL toddler). Therefore, a chronic intake concern has been identified from exposure to hexythiazox from all dietary sources. Consideration of acute exposure was not required as the active substance is not acutely toxic and an ARfD has not been allocated.

For the UK NEDI, two diets had exceedances of the ADI (toddler (136%) and infant (107%)). For the PRIMo IEDI, one diet showed an exceedance of the ADI (NL toddler (127%)). For the toddler diet in the UK NEDI and the NL toddler diet in the PRIMo IEDI calculation, raspberries and blackberries are not the main contributors to the exceedances

of the ADI. The main contributors are citrus fruit, apples and pears (contribute up to 76%, 36% and 15% of the ADI respectively).

For citrus fruit, apples and pears, there are CXLs available which are lower than the current GB MRLs, and which contribute significantly less to chronic exposures. Additionally, the CXLs accommodate the authorised GB uses on apples and pears and there are no GB authorisations for citrus fruit. No health effects are expected. Therefore, HSE recommends that the GB MRLs for citrus fruit, apples and pears are lowered and the CXLs for these commodities adopted.

The CXLs for strawberries, teas and eggs are higher than the current GB MRLs. For cane fruits and eggs, new CXLs have been adopted in 2025 which are higher than the current GB MRLs. These CXLs are acceptable; they do not contribute significantly to chronic exposures and no health effects are expected. Therefore, HSE recommends that the CXLs for strawberry, tea, eggs and cane fruit can be adopted in GB.

Consideration of the chronic risk assessment was performed for the proposed MRLs for raspberries and blackberries, lowering of the GB MRLs for citrus fruit, apples and pears to the CXLs, adoption of the CXLs for strawberries, teas, eggs and other cane fruit, and all other current GB MRLs. The highest UK NEDI was 86% of the ADI (infant). The highest PRIMo IEDI was 73% of the ADI (NL toddler). Therefore, no health effects due to chronic exposure are expected from the consumption of commodities treated with hexythiazox.

HSE concludes that sufficient data has been provided to support the setting of new MRLs for raspberries and blackberries. HSE also recommends that the GB MRLs for citrus fruit, apples and pears are lowered to the CXLs, and that the CXLs for strawberries, tea, eggs and cane fruit are adopted. The MRLs considered will not result in consumer exposures exceeding the toxicological reference values and therefore these MRLs are unlikely to have harmful effects on human health.

HSE recommends that the MRLs outlined in Table 0.1 are amended in the GB MRL Statutory Register. A full list of all MRLs is outlined in Table 8.1.

Table 0.1 MRLs proposed by HSE for hexythiazox

Product code	Product	Existing GB MRL (mg/kg)	New or amended GB MRL (mg/kg)	Comments
Enforcement residue definition for products of plant and animal origin: **Hexythiazox**				
0110010	Grapefruits	1.0	0.5	The MRL is based on the CXL. No health effects are expected.
0110020	Oranges	1.0	0.5	The MRL is based on the CXL. No health effects are expected.
0110030	Lemons	1.0	0.5	The MRL is based on the CXL. No health effects are expected.
0110040	Limes	1.0	0.5	The MRL is based on the CXL. No health effects are expected.
0110050	Mandarins	1.0	0.5	The MRL is based on the CXL. No health effects are expected.
0110990	Others – citrus fruit	1.0	0.5	The MRL is based on the CXL. No health effects are expected.

Product code	Product	Existing GB MRL (mg/kg)	New or amended GB MRL (mg/kg)	Comments
Enforcement residue definition for products of plant and animal origin: **Hexythiazox**				
0130010	Apples	1.0	0.4	The MRL is based on the CXL. No health effects are expected.
0130020	Pears	1.0	0.4	The MRL is based on the CXL. No health effects are expected.
0152000	Strawberries	0.5	6	The MRL is based on the CXL. No health effects are expected.
0153010	Blackberries	0.5	4	The MRL is derived by extrapolation of residue trials on raspberries. No health effects are expected. The MRL is line with the CXL adopted in 2025.
0153020	Dewberries	0.5	4	The MRL is line with the CXL adopted in 2025. No health effects are expected.

Product code	Product	Existing GB MRL (mg/kg)	New or amended GB MRL (mg/kg)	Comments
Enforcement residue definition for products of plant and animal origin: **Hexythiazox**				
0153030	Raspberries (red and yellow)	0.5	4	The MRL is sufficiently supported by data. No health effects are expected. The MRL is line with the CXL adopted in 2025.
0153990	Others – Cane fruit	0.5	4	The MRL is line with the CXL adopted in 2025. No health effects are expected.
0610000	Teas	4.0	15	The MRL is based on the CXL. No health effects are expected.
1030010	Chicken - eggs	0.02*	0.05	The MRL is line with the CXL adopted in 2025. No health effects are expected.
1030020	Duck – eggs	0.02*	0.05	The MRL is line with the CXL adopted in 2025. No health effects are expected.

Product code	Product	Existing GB MRL (mg/kg)	New or amended GB MRL (mg/kg)	Comments
Enforcement residue definition for products of plant and animal origin: **Hexythiazox**				
1030030	Geese – eggs	0.02*	0.05	The MRL is line with the CXL adopted in 2025. No health effects are expected.
1030040	Quail – eggs	0.02*	0.05	The MRL is line with the CXL adopted in 2025. No health effects are expected.
1030990	Others – Birds' eggs	0.02*	0.05	The MRL is line with the CXL adopted in 2025. No health effects are expected.

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

This is not a full MRL review and does not replace the full MRL review of all GB MRLs that may be initiated under Article 12 of Assimilated Regulation 396/2005.

Proposed Recommendations

The proposed recommendations are outlined in Table 8.1.

HSE identified chronic intake concerns when considering all of the current GB MRLs, with the main contribution being from citrus fruit, apples and pears. For citrus fruit, apples and pears, there are CXLs available which are lower than the current GB MRLs, and which contribute significantly less to chronic exposures. Therefore, HSE recommends that the CXLs for citrus fruits, apples and pears are adopted as GB MRLs.

The CXLs for strawberry, tea, eggs and cane fruits are also recommended for adoption as GB MRLs.

HSE concludes that sufficient data have been provided to support the setting of new MRLs for the proposed uses of hexythiazox on raspberries and blackberries.

The new MRLs for raspberries and blackberries and the CXLs recommended for adoption will not result in consumer exposures exceeding the toxicological reference values and therefore harmful effects on human health are not expected.

Notification of the proposed MRLs

To meet the UK's international trade obligations, the measures have been notified to the World Trade Organization (WTO). The WTO/SPS notification can be found at the following link and searching for hexythiazox and United Kingdom as the notifying member:

Home - ePing SPS&TBT platform (epingalert.org)

- **There may be a delay between publication of this draft RO and the notification appearing in the Sanitary and Phytosanitary Information Management System**
- **The notification includes the proposed date of adoption/publication and the proposed date of entry in force of the new MRLs.**

Background

Assimilated Regulation 396/2005 outlines the rules for setting MRLs in GB. This Evaluation Report and Reasoned Opinion covers:

- The review of the current MRLs for various commodities
- The evaluation of import tolerance requests

Review of the MRLs for various commodities

HSE considered the need to review the current GB MRLs for hexythiazox due to chronic intake concerns associated with the current MRLs. In accordance with Article 6 (3) of Assimilated Regulation 396/2005, HSE compiled and evaluated additional information that was publicly available.

HSE identified a chronic intake concern for hexythiazox, with citrus fruits, apples and pears being the main contributors to chronic exposures, therefore HSE reviewed the GB MRLs for these commodities. The review also considered the adoption of CXLs which are higher than the current GB MRLs in force. This review is the basis of HSE's draft Reasoned Opinion.

Import Tolerance

Article 6 covers the submission of applications for MRLs, including the parties which can submit an application. Article 7 outlines that a dossier in accordance with the data requirements of Assimilated Regulation 1107/2009 must be provided.

On 20 February 2023, HSE accepted an application from Gowan Crop Protection Limited to set new import tolerances for hexythiazox in or on raspberries and blackberries.

Overall

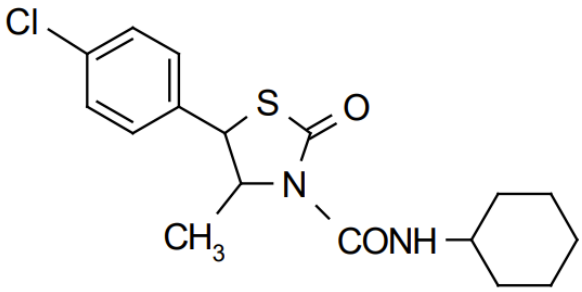
HSE evaluated the information submitted to uniform principles, as defined by Article 8 of Assimilated Regulation 396/2005 and prepared an Evaluation Report. HSE also took into account EFSA Reasoned Opinions and Conclusions on the peer review relating to decisions implemented in GB.

The Evaluation Report is the basis of HSE's draft Reasoned Opinion.

The active substance and its use pattern

Information on the active substance hexythiazox is outlined in Table 0.2.

Table 0.2 Information on the active substance

Common name (ISO)	Hexythiazox
Chemical name (IUPAC)	(4RS,5RS)-5-(4-chlorophenyl)-N-cyclohexyl-4- methyl-2-oxo-1,3-thiazolidine-3-carboxamide
CAS number	78587-05-0
Structural formula	
Molecular formula	$C_{17}H_{21}ClN_2O_2S$
Molecular mass	352.9 g/mol

Hexythiazox is an approved active substance in GB. An EFSA Conclusion is available (EFSA, 2010). MRLs are established for hexythiazox in Part 3a of the GB MRL Statutory Register.

A copy of the current national legislation in the exporting country related to the MRLs under consideration and evidence of the authorisation of the respective uses of the plant protection product in USA was provided by the applicant and is summarised in Appendix E.

Appendix A outlines the GAPs (Good Agricultural Practices) supported in this application.

Consideration of CXLs

The following CXLs are available for hexythiazox (Codex Pesticide Residues in food online database).

The CXL database is available at the following link:

http://www.fao.org/fao-who-codexalimentarius/codex-texts/dbs/pestres/en/

Table 0.3 CXLs relevant to the proposed uses

Codex commodity description	GB commodity description (GB commodity code)	CXL (mg/kg)	Comments	Year of adoption
Citrus fruits (group)	Citrus fruits (0110000)	0.5	The CXL is lower than the current GB MRL. Citrus fruits are the main contributor to chronic intake concerns based on the current GB MRLs. The CXL can be adopted as a GB MRL for citrus fruits; no health effects are expected.	2010
Date	Dates (0161010)	2	The CXL is the basis of the current GB MRL.	2010
Edible offal (mammalian)	Edible offal – Swine, Bovine, Sheep, Goat, Equine, Other farmed terrestrial animals (various)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Eggplant	Aubergines/ eggplants (0231030)	0.1	The CXL is lower than the current GB MRL and therefore no further consideration is required.	2010
Eggs	Birds eggs (1030000)	0.05	This CXL was revoked in November 2025; see	2010

			Table 0.4 for new CXL adopted.	
Fruiting vegetables, cucurbits (group; except watermelon)	Cucurbits with edible peel (0232000), cucurbits with inedible peel (0233000) (excluding watermelons (0233030)	0.05	The CXL is lower than the current GB MRL and therefore no further consideration is required.	2010
Grapes	Grapes (0151000)	1	The CXL is equivalent to the current GB MRL for grapes. Therefore, no further consideration is required.	2010
Grapes dried (currants, raisins and sultanas)	N/A	1	GB MRLs are not currently set on processed products.	2010
Grape pomace, dried	N/A	15	GB MRLs are not currently set on processed products.	2010
Hops, dry	Hops (0700000)	3	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2012
Mammalian fats (except milk fats)	Fat - Swine, Bovine, Sheep, Goat, Equine, Other farmed terrestrial animals (various)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010

Meat (group of muscle)† (from mammals other than marine mammals)	Muscle - Swine, Bovine, Sheep, Goat, Equine, Other farmed terrestrial animals (various)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Milk fats	N/A	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Milks	Milk (1020000)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Pome fruits (group)	Pome fruits (0130000)	0.4	The CXL is lower than the current GB MRL. An MRL of 1.0 mg/kg is currently applicable in GB for apples and pears which are the main contributors to chronic intake concerns based on the current GB MRLs. The CXL can be adopted as a GB MRL for apples and pears; no health effects are expected. For other pome fruits, the current GB MRL is 0.5 mg/kg. As no chronic intake concerns were linked to these commodities, and the current GB MRL is higher, HSE recommends the CXL	2010

			is not adopted for the following commodities: Quinces (0130030) Medlars (0130040) Loquats/Japanese medlars (0130050) Others – pome fruit (0130990)	
Poultry meat (group of avian muscle) †	Muscle - poultry (1016010)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Poultry, edible offals (group of avian, edible offal of) †	Edible offals (other than liver and kidney) – poultry (1016050)	0.05	This CXL was revoked in November 2025; see Table 0.4 for new CXL adopted.	2010
Stone fruits (group)	Stone fruits (0140000)	0.3	The CXL is lower than the current GB MRL and therefore no further consideration is required.	2010
Strawberry	Strawberries (0152000)	6	The CXL is higher than the current GB MRL for strawberry. The CXL can be adopted as a GB MRL; no health effects are expected.	2013
Tea, green, black (black, fermented and dried)	Teas (0610000)	15	The CXL is higher than the current GB MRL for tea. The CXL can be adopted as a GB MRL; no health effects are expected.	2012
Tomato	Tomatoes (0231010)	0.1	The CXL is lower than the current GB MRL and	2010

			therefore no further consideration is required.	
Tree nuts (group)	Tree nuts (0120000)	0.05*	The CXL is lower than the current GB MRL and therefore no further consideration is required.	2010

† New commodity group title adopted by CCPR 2025.

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

The CXLs outlined in Table 0.4 have been adopted as new international food standards at the 48th Session of the Codex Alimentarius Commission, November 2025.[3] They do not yet appear in the online CXL database.

Table 0.4 CXLs adopted in 2025

Codex commodity description	GB commodity description (GB commodity code)	CXL (mg/kg)	Comments	Year of adoption
Cane berries, subgroup of (group)	Cane fruits (0153000)	4	The CXL is higher than the current GB MRL. The CXL can be adopted as a GB MRL; no health effects are expected.	2025
Group of avian fats	Fat - poultry (1016020)	0.05	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025
Group of avian muscle	Muscle – poultry (1016010)	0.05*	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025
Group of avian, edible offal of	Edible offals (other than liver and kidney) –	0.05	The CXL adopted in 2025 is equivalent to the current GB MRL.	2025

[3] Report of the 48th Session of the Codex Alimentarius Commission

	poultry (1016050)		Therefore, no further consideration is required.	
Group of edible offal (mammalian)	All mammals - edible offals (other than liver and kidney)† (1011050 1012050 1013050 1014050 1015050 1017050)	0.05	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025
Group of eggs	Birds eggs (1030000)	0.05	The CXL adopted in 2025 is higher than the current GB MRL. The CXL can be adopted as a GB MRL; no health effects are expected.	2025
Group of mammalian fats (except milk fats)	All mammals - fat† (1011020 1012020 1013020 1014020 1015020 1017020)	0.05	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required	2025
Group of milk fats	N/A	0.05	GB MRLs are not currently set on milk fats. Hexythiazox is fat soluble.	2025
Group of milks	Milk (1020000)	0.05	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025

Group of muscle (from mammals other than marine mammals)	All mammals-muscle† (1011010 1012010 1013010 1014010 1015010 1017010)	0.05*	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025
Hops, dried	Hops (0700000)	20	The CXL adopted in 2025 is equivalent to the current GB MRL. Therefore, no further consideration is required.	2025

† The CXL would apply to GB MRLs for swine, bovine, sheep, goat, equine and other farmed terrestrial animals.

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

The following residue definitions are applicable for the CXLs:

Table 0.5 Residue definitions

Commodity	Residue definition type	JMPR	GB	Are the residue definitions comparable
Plants	Enforcement	Hexythiazox	Hexythiazox	Yes
	Risk assessment	Sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox.	Hexythiazox	No
Livestock	Enforcement	Sum of hexythiazox	Hexythiazox	No

Commodity	Residue definition type	JMPR	GB	Are the residue definitions comparable
		and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox.		
	Risk assessment	Sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox.	Not assessed	No

The residue definition for risk assessment for plants in GB is not equivalent to the JMPR residue definition but data provided in residue trials to support the setting of CXLs is sufficient to cover hexythiazox and thus all the components of the residue definition applicable in GB. The JMPR residue definition is a common moiety approach whereas the GB residue definition is for hexythiazox only.

The residue definitions for livestock for enforcement and risk assessment are not comparable between the JMPR and GB. A residue definition for risk assessment for livestock has not been established in GB. The JMPR residue definition for enforcement and risk assessment is a common moiety approach. However, the JMPR has estimated residues <LOQ (0.05 mg/kg) in products of animal origin, therefore the CXLs based on the more comprehensive residue definition are unlikely to lead to a significant overestimation of residues. The STMR derived by the JMPR has therefore been used in the consumer

risk assessment. However, the residue definition for risk assessment for livestock in GB may need to be reconsidered in the future, e.g. as part of an application to specifically set GB MRLs in products of animal origin.

Conversion factors have not been calculated for the CXLs.

As outlined in Section 7.1, current GB MRLs lead to exposures exceeding the ADI. The main contributors to chronic exposures were citrus fruits, apples and pears. Therefore, the lowering of GB MRLs to CXLs for citrus fruits, apples and pears has been considered.

There are no GB authorisations for citrus fruit. There is an authorised use of hexythiazox on apple and pear in GB (use assessed under HSE reference COP 2019/00595). Residue trial data from the approval of hexythiazox was relied upon to support this authorised use (EFSA, 2010) and an STMR of 0.05 mg/kg was calculated. The MRL calculated to support this use was 0.15 mg/kg therefore the CXL of 0.4 mg/kg is sufficient to cover the authorised GB use.

As the current GB MRLs for other commodities in the pome fruit group do not contribute significantly to chronic exposures, they do not need to be lowered to the CXL at this time.

Additionally, the CXLs for strawberries, tea, eggs and cane fruits have been considered as they are higher than the current GB MRLs.

For cane fruits, the CXL of 4 mg/kg was adopted at the 48th Session of the Codex Alimentarius Commission, November 2025. The CXL for ‘cane fruits’ were set on the basis of residues trials data on raspberries which were submitted in the scope of this import tolerance application (see Section 3.2).

Residues in products of plant origin in line with the GB residue definition for risk assessment and residue definition for enforcement based on the available JMPR data are reported below.

Table 0.6 Residue data for products of plant origin based on CXLs

Commodity	**Residues of hexythiazox (RD-RA = RD-Enf) (mg/kg)**	**STMR (mg/kg)**
Strawberry	0.13, 0.17, 0.29, 0.30, 0.54, 0.62, 0.65, 1.8, 4.1	0.54
Tea	3.2, 3.7, 4.1, 4.5, 4.6, 4.8, 4.9, 5.2	4.55

Citrus fruit (pulp)	3 x < 0.05, 0.05, 3 x 0.06, 0.1, 2 x 0.11, 0.12, 0.15, 0.16, 0.18, 2 x 0.2, 0.29	0.110 (whole fruit) 0.077 (pulp†)
Pome fruit	2 x 0.05, 2 x 0.08, 3 x 0.09, 2 x 0.11, 0.12, 0.15, 0.16, 0.2, 2 x 0.21	0.11

†Proposed based on a ratio of 0.7 between the residues in whole fruits and citrus pulp.

The above STMR values have been included in the risk assessments performed in Section 7.1 (scenario 2). For citrus fruit, apples, pears, strawberry, tea, and cane fruit, the CXLs are acceptable; they do not contribute significantly to chronic exposures and no health effects are expected. Therefore, HSE recommends that the CXLs for citrus fruit, apples, pears, strawberry, tea, and cane fruit can be adopted in GB.

For eggs, the JMPR estimated an STMR value of 0.002 mg/kg which has been used in the consumer risk assessment (scenario 2, see Section 7.1). As the CXL for eggs does not contribute significantly to the chronic exposure assessment and therefore no health effects are expected, it is recommended that the higher CXL is adopted as a GB MRL.

Assessment

1 Methods of analysis

1.1 Methods for enforcement and monitoring of residues in food of plant origin

Analytical methods for the determination of hexythiazox in products of plant origin, in line with the residue definition for enforcement, were assessed for the approval of the active substance (EFSA, 2012).

The multi-residue DFG S19 method (extended revision) with GC-ECD detection and single residue method using HPLC-UV, are validated for the high water (apples, tomatoes), high acid (oranges, grapes) and high oil (cotton seed) commodity groups with an LOQ of 0.05 mg/kg. Acceptable ILV data were provided.

The applicant has submitted alternative enforcement methods for high acid commodities to cover the proposed uses on raspberries and blackberries. This alternative method has a lower LOQ of 0.01 mg/kg. The new data uses a QuEChERs method that is validated for dry (high starch), high acid and high water commodities with an LOQ of 0.01 mg/kg. A detailed assessment is conducted in confirmatory data for approval of the active (FI, 2014). Acceptable ILV data were provided from high water (apple) and high acid (grape) commodities and is summarised in Appendix C.1.1.2. Extraction efficiency is considered to have been sufficiently addressed (see Appendix C.1.1.3).

The plant commodities under consideration in the import tolerance application: raspberries and blackberries (high acid commodities), are covered by the analytical methods available.

All components in the enforcement residue definition (hexythiazox) are covered by the analytical methods.

1.2 Methods for enforcement and monitoring of residues in food of animal origin

Not required as the import tolerance application does not require the setting or amendment of MRLs in products of animal origin.

2 Mammalian toxicology

The toxicological end points established for the approval of the active substance are summarised in Table 2.1.

Table 2.1 Overview of the toxicological reference values for hexythiazox

TRVs	Source	Year	Value	Study relied upon	Safety factor
ADI	EFSA	2010	0.03 mg/kg bw/d	2 year rat	100
ARfD	EFSA	2010	Not allocated	No ARfD necessary	Not applicable

3 Residues in plants

3.1 Nature of residues in primary crops

Metabolism in primary crops was investigated following treatment in fruit (grape, citrus, pear and apple) and a leafy crop (tea) for the approval of hexythiazox (EFSA, 2010).

Table 3.1 Summary of the primary plant metabolism studies

Crop groups	Crop(s)	Applications	DAT [(a)] (days)
Fruit	Grape	Fruit, greenhouse, 1 x 210 g a.s./ha	Fruits: 0, 14, 21, 42 Leaves: 0, 14, 28, 42, 56
		Foliar, outdoor, 2 x 100 g a.s./ha	21
	Pear	Micro-pipette, greenhouse, 1 x 5 g a.s./hL	0, 5, 10, 20, 30, 60
	Citrus	Micro-pipette, greenhouse, 1 x 5.3 g a.s./hL	0, 7, 14, 30, 60, 91
	Apple	Micro-pipette, greenhouse, 1 x 5 g a.s./hL	10, 20, 30 and 59
Miscellaneous	Tea	Foliar, greenhouse, 1 x 200 g a.s./ha	0, 7, 14, 21

(a) DAT where identification/characterisation of the residues has been investigated

A summary of the available primary crop metabolism data is presented below (EFSA, 2012):

"Metabolism of hexythiazox in plants has been investigated in fruit crops (grape, citrus, pear and apple) and on a leafy crop (tea) using foliar applications of 14C-hexythiazox labelled on the thiazolidine moiety. Parent hexythiazox was by far the most predominant component of the radioactive residues, accounting for more than 60% of the TRR 60 days after the last application. Therefore, the residue definitions for enforcement and risk assessment were limited to hexythiazox only. The current residue definition set in Regulation (EC) No 396/2005 is identical with the enforcement residue definition derived during the peer review."

As acceptable metabolism data was presented for at least three crops belonging to the fruit crop group, uses within this group are supported. Therefore, the authorised uses of hexythiazox for raspberries and blackberries are supported by the available data.

An authorised GAP on raspberries and blackberries in the USA is notified in Appendix A. The application type in the studies included foliar spray applications, which is the same as the application type for the proposed use. On this basis the authorised uses in USA are supported by the available metabolism data.

The residue definition for risk assessment (RD-RA) in plants has been agreed as:

- Hexythiazox

The residue definition for enforcement (RD-Enf) in plants has been agreed as:

- Hexythiazox

In the exporting country (USA), tolerances are established for residues of hexythiazox according to the definition:

- Hexythiazox and its metabolites containing the (4-chlorophenyl)-4-methyl-2-oxo-3-thiazolidine moiety, calculated as the stoichiometric equivalent of hexythiazox.

The residue definition in GB is not equivalent to the residue definition in the USA but data provided in residue trials is sufficient to cover hexythiazox and thus all the components of the residue definition applicable in GB.

Hexythiazox was approved as a racemic mixture (equal mixture of the R and S isomers). The possible conversion of hexythiazox R-isomer to the S-isomer and vice versa has not been investigated. As well as the two enantiomers of the active substance, potentially two other diastereoisomers could be formed on metabolism/degradation. For the approval the following active substance confirmatory data requirement was set:

the possible impact of the preferential degradation and/or conversion of the mixture of isomers on the worker risk assessment, the consumer risk assessment and the environment.

HSE has concluded that the ADI is applicable to both the R and S isomers. A further consideration of the impact of the preferential degradation and/or conversion will be considered separately as part of the assessment of the active confirmatory data.

3.2 Magnitude of residues in primary crops

The uses notified in the MRL application are outlined in Appendix A.

Residue trials for import tolerance request

0153010 Blackberries

0153030 Raspberries (red and yellow)

The authorised critical outdoor GAP on blackberries and raspberries in the USA is 1 x 267 g a.s./ha with a PHI of three days for an oil-in-water emulsion (EW) formulation, and 1 x 210 g a.s./ha, with a PHI of three days for a water dispersible granules (WG) formulation.

The residue trials consisted of five trial locations where separate plots were treated either using an EW or WG formulation. Several nominal dose rates were also considered at the separate plots. In order to support the cGAP all residue trial data has been evaluated. A full analysis of the trials can be found in Appendix C.3.1.2. As more than one trial design has been performed at the same location (several nominal dose rates and formulation types), the highest residues from each trial location considering all application rates and formulation types have been selected for calculation of the STMR, HR and MRL.

The application rate of the two GAPs are within 25% of each other however the different formulation types (EW and WG), could influence the residue level. The Mann-Whitney U test was performed and concluded there was no significant differences in residues resulting from using the EW and WG formulations at either application rate and thus each trial pair is comparable.

In summary, five outdoor trials on raspberries were undertaken in USA using an EW and WG formulation. The trials were conducted at 261.5 – 296.9 g a.s./ha, PHI three days, BBCH 75 - 89. The trials are within 25% of the authorised GAP on raspberries and blackberries using the EW formulation, which is the authorised cGAP in relation to application rate.

The five trials meet the minimum number required for minor crops. The trials on raspberries can be extrapolated to support an MRL for blackberries as application is made after formation of the edible part.

The cGAP on raspberries and blackberries (PHI 3 days), is application after forming of the edible part, therefore half of the trials should be decline trials. For raspberries none of the available trials were decline trials, therefore the applicant was asked to clarify the lack of decline data. The applicant referenced decline trials considered under an MRL review for strawberries (Finland, 2012) as a permissible extrapolation to cane berries. This data indicated residues in strawberry declined over time (PHI 0 – 7 days). For the approval of

the active substance (Finland, 2005), decline trials were available for orange, mandarin, pear and apple and data showed a general decline of residues of hexythiazox over time (PHI 0 – 29 days). Though decline data for cane fruit would be beneficial, as decline data is available for other fruit which indicate a decline of residues of hexythiazox over time, the lack of decline trials for cane fruit can be considered a minor deficiency.

As raspberries and blackberries are tall crops, residues may be driven by spray concentration due to direct application to the plant and the fact that the spray is often applied to run off. The spray concentration used in the trials was 28.4 – 59.5 g a.s./hL. The maximum spray concentration in the GAP is 577 g a.s./hL (water volume: 46.8 L/ha), which is significantly higher than in the trials. From the trials data it is not possible to determine whether the application rate or spray concentration is predominantly driving the residue. However, considering the application is made close to harvest of a crop with a high foliage density, in practice larger water volumes are likely to be used and therefore the trials are considered to be representative of the actual in-use spray concentrations.

In the trials a non-ionic surfactant is used in the formulation at 0.25% v/v. Adjuvant use is not recommended on the US authorised labels, but the use of an adjuvant is considered to represent common agricultural practice in the exporting country.

Storage stability

Sufficient storage stability for hexythiazox in high acid commodities is available from the approval of the active substance (including the addendum to the DAR (FI, 2014)) for high acid commodities (strawberry, citrus, grape), to support the maximum storage period of 63 days in the trials on raspberries.

Analytical methods

Analysis for residues of hexythiazox was performed using LC-MS/MS method included in study report TCI-18-597 (see Appendix C.1.3 for validation data). The analytical method was considered sufficiently validated for the purposes of the regulatory process. The method determines hexythiazox residues as the metabolite PT-1-3, therefore a molecular weight calculation is required to convert residues into hexythiazox. The LOQ of the method is 0.02 mg/kg (residues expressed as hexythiazox).

Extraction efficiency was not investigated in the report. The method uses methanol and water for the extraction of residues from the fruit. The radiolabelled metabolism studies for the approval of the active generally used a combination of aqueous methanol and chloroform as the extraction solvents. Aqueous methanol-based extractions are shown to be adequate based on the metabolism studies for approval of the active substance where hexythiazox accounted for > 60% TRR, but extraction efficiency has not been fully addressed since the method included in study TCI-18-597 has not used chloroform. Extraction with chloroform released between 0.06 – 4.41% TRR in grapes (high acid commodity), 7.8 – 42.3% TRR in citrus (high acid commodity), 4.8– 27.7% TRR in pears

(high water commodity) and 2.6 – 18.6% TRR in apples (high water commodity), highlighting the significance of this solvent to extract radioactivity from plant matrices. The lack of specific data to address the extraction efficiency is unlikely to impact the MRL calculated or the outcome of the consumer risk assessment. Therefore, no further data are required at this time.

Calculated MRL

The current GB MRL for hexythiazox in or on raspberries and blackberries is 0.5 mg/kg. The residue trials support an MRL of 4.0 mg/kg when considering both formulation types and application rates. There is currently a MRL of 3.0 mg/kg set for hexythiazox in or on raspberries and blackberries in USA – see Appendix E for details.

The reason for the difference between the MRL of the exporting country and the MRL calculated by HSE is due to different trial selection. In the exporting country evaluation, only data from the EW formulation trials conducted at a nominal rate of 280 g a.s./ha have been selected which has led to a MRL of 3 mg/kg (unrounded 3.095 mg/kg).

The residues data submitted supports an MRL of 4 mg/kg and there is a CXL adopted in 2025 of 4 mg/kg for cane fruit, therefore HSE recommends that an MRL of 4 mg/kg is set in line with the CXL.

Table 3.2-1 Overview of the available residue trials data for import tolerance request

Commodity	Region/ Indoor (a)	Residue levels (mg/kg) observed in the trials representative for the intended GAPs (b)	Recommendations/ comments (OECD calculations)	MRL proposals (mg/kg)	HR (mg/kg) (c)	STMR (mg/kg) (d)
RD-RA: **Hexythiazox** **RD-Enf:** **Hexythiazox**						
Raspberries → blackberries (1 x ~ 270 g a.s./ha; 3 day PHI)	USA / outdoor	Based on highest residue data in each trial from all formulations and application rates: 0.631, 1.005, 1.035, 1.090, 1.655	MRL_{OECD}: 3.250 / 4 mg/kg An MRL of 4 mg/kg is calculated based on highest residue data in each trial from all formulations and application rates. This MRL is in line with the CXL adopted in 2025. Raspberries are a permissible extrapolation to blackberries.	**4**	1.655	1.035

(a) GB or the country for an import tolerance and whether the GAP is for an outdoor use or an indoor/protected/glasshouse use.

(b) Residue levels in trials conducted according to GAPs reported in ascending order. When residue definitions for enforcement and risk assessment differ, **Enf/RA** differentiate data expressed according to the residue definition for **Enf**orcement and **R**isk **A**ssessment.

(c) **HR**: Highest residue, according to the residue for risk assessment, (within brackets when expressed according to the residue definition for enforcement: HR_{Enf})

(d) **STMR**: Supervised Trials Median Residue according to the residue definition risk assessment (within brackets when expressed according to the residue definition for enforcement: $STMR_{Enf}$

Residue trials supporting existing GB use and consideration of CXLs

0130010 Apples

0130020 Pears

There is an authorised use of hexythiazox on apple and pear in GB (use assessed under HSE reference COP 2019/00595). Residue trial data from the approval of hexythiazox was relied upon to support this authorised use (EFSA, 2010). Eight outdoor trials on apples and two outdoor trials on pears were conducted in NEU using a WP formulation containing 100 g/kg hexythiazox. The trials were conducted at an application rate of 94 – 106 g a.s./ha with a PHI of 27 – 29 days, BBCH 74 - 81. The trials are within 25% of the authorised GAP on apples and pears (1 x 100 g a.s./ha, BBCH 51 – 79, PHI 28 days).

The MRL calculated to support this use was 0.15 mg/kg therefore the CXL of 0.4 mg/kg is sufficient to cover the authorised GB use.

Table 3.2-2 Overview of the available residue trials data for existing GB use and consideration of CXLs

Commodity	Region/ Indoor (a)	Residue levels (mg/kg) observed in the trials representative for the intended GAPs (b)	Recommendations/ comments (OECD calculations)	MRL proposal (mg/kg)	HR (mg/kg) (c)	STMR (mg/kg) (d)
RD-RA: Hexythiazox **RD-Enf: Hexythiazox**						
Pome fruits (apples and pears) (1 x ~100 g a.s./ha; 28 day PHI)	NEU / outdoor	<0.01, 7 x <0.05, 0.06, 0.08	MRL_{OECD}: 0.118 / 0.15 mg/kg	0.15	0.08	0.05

(a) GB or the country for an import tolerance and whether the GAP is for an outdoor use or an indoor/protected/glasshouse use.

(b) Residue levels in trials conducted according to GAPs reported in ascending order. When residue definitions for enforcement and risk assessment differ, **Enf/RA** differentiate data expressed according to the residue definition for **Enf**orcement and **R**isk **A**ssessment.

(c) **HR**: Highest residue, according to the residue for risk assessment, (within brackets when expressed according to the residue definition for enforcement: HR_{Enf})

(d) **STMR**: Supervised Trials Median Residue according to the residue definition risk assessment (within brackets when expressed according to the residue definition for enforcement: $STMR_{Enf}$

3.3 Conversion factors for risk assessment for products of plant origin

As the GB residue definitions for enforcement (RD-Enf) and risk assessment (RD-RA) are equivalent, conversion factors (CFs) for enforcement to risk assessment are not required.

3.4 Effect of industrial processing and/or household preparation

As the residues in the RAC are above 0.1 mg/kg, consideration of residues in processed commodities is required.

3.4.1 Nature of the residues in processed commodities

Hydrolysis of hexythiazox under representative conditions of pasteurisation, baking, brewing, boiling and sterilisation was investigated for the approval of hexythiazox (EFSA, 2010).

Hexythiazox was found to be stable across the standard conditions of pasteurisation and baking, boiling and brewing. The formation of the PT-1-3 metabolite was noted; however this was shown to be not significant under pasteurisation and baking/boiling. Under sterilisation conditions, hexythiazox is significantly degraded to PT-1-3 (48% TRR).

A summary of the available hydrolysis data is presented in Table 3.4.1, (EFSA 2010 and current assessment):

Table 3.4.1 Overview of the available hydrolysis studies

% applied radioactivity	**EFSA, 2010**		**Current assessment (see Appendix C.3.2.1)**	
Conditions	**Hexythiazox**	**PT-1-3**	**Hexythiazox**	**Cyclohexylamine**
Pasteurisation 20 min, 90°C, pH 4	79.8%	1.9%	98.9%	<LOQ
Baking and boiling 60 min, 100°C, pH 5	86.8%	2.3%	98.4%	0.5%
Sterilisation 20 min, 120°C, pH 6	48.7%	48.3%	54.4%	43.5%

The newly submitted hydrolysis studies and hydrolysis studies presented in EFSA, 2010, indicate that hexythiazox is stable under pasteurisation and baking, brewing and boiling conditions. However, hexythiazox is not stable under sterilisation conditions, degrading to cyclohexylamine or PT-1-3 dependent on the position of the radiolabel, ([thiazolidine-5-14C]-hexythiazox label vs [cyclohexyl-U-^{14}C]-hexythiazox label).

PT-1-3

In the EFSA RO, 2012 the following was discussed regarding the breakdown of hexythiazox to PT-1-3 during sterilisation:

"No final conclusions could be made on the nature of the residues in processed commodities in the course of the peer review, as no sufficient data on metabolite PT-1-3 were provided in the processing studies conducted on grape and citrus. Moreover, as PT-1-3 is more acutely toxic than the parent (LD50 = 341 mg/kg bw vs. >5000 mg/kg bw for hexythiazox), EFSA is of the opinion that additional toxicological information and additional data on the transfer of PT-1-3 are required before to conclude on a residue definition in processed commodities and before to propose transfer factors for hexythiazox."

PT-1-3 is not considered a concern for mutagenicity as toxicity of the metabolite was considered well addressed in confirmatory data for the approval of the active substance (FI, 2014). However, it was noted that occurrence of PT-1-3 in uses outside of those considered for approval needs to be considered. PT-1-3 is not predicted to occur in processed commodities of blackberries and raspberries as sterilisation to cane fruit which have a low pH (<4.5), is not routinely required. Processes intended to remove bacteria are normally limited to pasteurisation as heat tolerant bacteria such as *Clostridium botulinum* are less relevant at pH <4.5 (EFSA, 2018). Additionally, processing data on sterilised fruit products is not required according to SANCO 7035/VI/95 rev.5.

The available processing studies show that PT-1-3 is not present above LOQ in canned fruit and jam (see Section 3.4.2 and Appendix C.3.2.2). Therefore, for the crops under consideration in this application, the residue definition for primary crops can be considered applicable to processed crops and PT-1-3 is unlikely to be present in significant amounts in processed commodities of raspberries and blackberries.

Cyclohexylamine

The applicant has submitted a new hydrolysis study on hexythiazox. This study used a [cyclohexyl-U-^{14}C]-hexythiazox label in comparison to the [thiazolidine-5-14C]-hexythiazox label used in the studies considered for approval of the active substance. The new study shows that hexythiazox is stable across the standard conditions of pasteurisation (98.9% TRR); baking, boiling and brewing (98.4%); and that degradation of hexythiazox occurs under sterilisation conditions (54.4% TRR). This data shows similar results to the data presented in the studies for the approval of the active substance. However, the new study

shows significant degradation to cyclohexylamine (43.5% TRR) rather than the metabolite PT-1-3 due to the radiolabelling position.

Cyclohexylamine is not predicted to occur in processed commodities of blackberries and raspberries as due to their acidic properties these are not sterilised during industrial processing, (given pH is <4.5, pasteurisation would take place rather than sterilisation). Furthermore, new processing studies demonstrate that, after treatment at a comparable application rate to the authorised GAPs, processed fruit do not contain residues of cyclohexylamine above LOQ (see Section 3.4.2). Therefore, significant residues of cyclohexylamine occurring in processed raspberries and blackberries are not expected. The need for further consideration of the toxicity of cyclohexylamine and of a processing study simulating sterilisation conditions, would be required for commodities which are likely to undergo sterilisation.

3.4.2 Magnitude of the residues in processed commodities

Consideration of the magnitude of residues in processed commodities is required as residues are >0.1 mg/kg in the raw agricultural commodity. A summary of the available processing studies for hexythiazox applicable to the proposed uses are presented in Table 3.4.2 (EFSA, 2010).

The applicant has also submitted new data on strawberry to support raspberries and blackberries. Raspberry and blackberry RAC and processed products exhibit the same acidic properties as strawberries, therefore strawberry is a permissible extrapolation. A full evaluation of this data is presented in Appendix C.3.2.2. The relevant Pfs (parent only) derived for the approval of the active substance, in the new study evaluated, and extrapolations to the proposed uses are given in Table 3.4.2.

The newly evaluated data considered processing of strawberry RAC to canned strawberry and strawberry jam. Residues were analysed for: (4R, 5R)-hexythiazox and (4S, 5S)-hexythiazox, metabolites (4R, 5R)-PT-1-3 and (4S, 5S)-PT-1-3 and cyclohexylamine. Residues of PT-1-3 and cyclohexylamine were <LOQ (0.005 and 0.01 mg/kg respectively). The sum of (4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox residues has been presented as this would be most representative of the residue definition of hexythiazox. The preferential degradation of the enantiomers of hexythiazox was not significant in this study (difference in amount of isomer formed did not exceed > 10% for hexythiazox). Therefore, it is not necessary in the scope of this application to investigate preferential isomeric degradation and isomeric composition.

The processed fractions which are relevant to the proposed MRLs for raspberries and blackberries are:

- Preparation of fruit juice (category 1)
- Preparation of canned fruit (category 2)

- Preparation of other fruit products (includes production of jam, jelly, category 2)

Table 3.4.2 Overview of the available processing studies

Crop (RAC)/processed product	Number of trials	Processing Factor (Pf)		Extrapolations	Reference
		Individual values	Median Pf		
Orange and Mandarin/Juice (pasteurised)	6	-	0.25	Juice – raspberries, blackberries	EFSA, 2010
Orange/Canned fruit	6	-	0.14	Canned fruit – raspberries, blackberries	EFSA, 2010
Orange/marmalade	6	-	0.21	Jam/jelly – raspberries, blackberries	EFSA, 2010
Grape/Juice	4	-	0.25	Juice – raspberries, blackberries	EFSA, 2010
Strawberry/Canned fruit	2	0.393, 0.550	0.472	Canned fruit – raspberries, blackberries	Appendix C.3.2.2
Strawberry/Jam	2	0.283, 0.323	0.303	Jam/jelly – raspberries, blackberries	Appendix C.3.2.2

Pf factors are calculated as following:

$$\textbf{Pf} = \frac{\text{Residue level in processed fraction (expressed according to RD-Enf and RD-RA)}}{\text{Residue in RAC (expressed according to RD-Enf and RD-RA)}}$$

The available processing data are sufficient to support the authorised use on raspberries and blackberries. Based on the Pfs (parent only), no concentration of residues is expected in any of the processed fractions relevant to the proposed uses on raspberries and blackberries.

3.5 Rotational crops

No consideration of rotational crops was made as the impact of residues in rotational crops on the import tolerances was not required.

4 Residues in livestock

No consideration of residues in products of animal origin is required as raspberries and blackberries are not used as animal feedstuffs.

5 Residues in honey

Residues in honey are not applicable to import tolerances where no MRLs for the import of honey have been requested.

6 MRLs for products not covered in Sections 3 and 4

No MRL extrapolations are recommended on the basis of this assessment.

7 Consumer risk assessment

7.1 Dietary exposure

Dietary exposures have been estimated using the UK chronic model and the EFSA PRIMo.

Consideration of acute dietary exposure is not required as the active substance is not acutely toxic and an ARfD has not been allocated.

Scenario 1 – consideration of chronic risk related to proposed MRLs for raspberries and blackberries, and current GB MRLs for all other commodities

Chronic dietary exposures have been estimated based on the uses of hexythiazox considered in this application, the uses considered in previous assessments supporting existing GB MRLs (EFSA 2012, 2010) and, for the remaining commodities, the existing MRLs established in the GB MRL Statutory Register.

UK NEDIs

The UK NEDIs for the active substance and commodities listed in Table 7.1-1 have been calculated for ten consumer groups using the UK chronic model (version 1.1) as detailed in Regulatory Update 21/2005. The following assumptions have been made:

- For the NEDIs, the 'Rees-Day' approach is taken which sums the two highest 97.5th percentile intakes and the mean intakes for all remaining commodities.
- All produce eaten which may have been treated has been treated and contains residues at the levels given in Table 7.1-1.
- There is no loss of residue during transport, storage or processing of foods prior to consumption.

The input values for the UK consumer risk assessment are given in Table 7.1-1.

Table 7.1-1 Input values for the UK consumer risk assessment

Commodity	Chronic risk assessment	
	Input (mg/kg)	Comment
RD-RA:	**Hexythiazox**	
Raspberries	1.035	STMR (current assessment)
Blackberries	1.035	STMR (current assessment)

Commodity	Chronic risk assessment	
	Input (mg/kg)	Comment
RD-RA:	**Hexythiazox**	
Dates	0.26	STMR CXL (JMPR, 2009)
Tea (dried leaves)	1.28	STMR (EFSA, 2012)
Poultry	0.01	STMR CXL for poultry meat (JMPR, 2009)
Meat fat	0.01	STMR CXL (JMPR, 2009)
Meat excl. poultry & offal	0.01	STMR CXL (JMPR, 2009)
Other types of offal	0.01	STMR CXL based on edible offal (JMPR, 2009)
Milk	0.01	STMR CXL (JMPR, 2009)
All other commodities	MRL	GB MRL Statutory Register and Commission Regulation (EU) 2012/592

* indicates residues at the LOQ

In bold uses proposed as part of the current assessment.

Model outputs for the UK chronic model (version 1.1) are presented in Appendix B.

PRIMo

The PRIMo IEDIs for the active substance and commodities listed in Table 7.1-2 have been calculated using PRIMo revision 3.1 – Pesticide Residues Intake Model.

The following assumptions have been made:

- All produce eaten which may have been treated, has been treated and contains residues at the levels as given in Table 7.1-2.
- There is no loss of residue during transport, storage or processing of foods prior to consumption.

The input values for the PRIMo risk assessment are given in Table 7.1-2.

Table 7.1-2 Input values for the PRIMo consumer risk assessment

Commodity	**Chronic risk assessment**	
	Input (mg/kg)	**Comment**
RD-RA:	**Hexythiazox**	
Raspberries	**1.035**	**STMR (current assessment)**
Blackberries	**1.035**	**STMR (current assessment)**
Dates	0.26	STMR CXL (JMPR, 2009)
Tea (dried leaves)	1.28	STMR CXL (EFSA, 2012)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: muscle/meat	0.01	STMR CXL (JMPR, 2009)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: fat	0.01	STMR CXL (JMPR, 2009)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: edible offals (other than liver and kidney)	0.01	STMR CXL (JMPR, 2009)
Poultry: muscle/meat	0.01	STMR CXL (JMPR, 2009)
Poultry: edible offals (other than liver and kidney)	0.01	STMR CXL (JMPR, 2009)
Milk: cattle, sheep, goat, horse, others	0.01	STMR CXL (JMPR, 2009)
All other commodities	MRL	GB MRL Statutory Register and Commission Regulation (EU) 2012/592)

* indicates residues at the LOQ

In bold uses proposed as part of the current assessment.

Model outputs for EFSA PRIMo revision 3.1 are presented in Appendix B.

Conclusions

The highest UK NEDI was 136% of the ADI (toddler). The highest PRIMo IEDI was 127% of the ADI (NL toddler). Therefore, a chronic intake concern has been identified from exposure to hexythiazox from all dietary sources.

For the UK NEDI, two diets had exceedances of the ADI (toddler (136%) and infant (107%)). For the PRIMo IEDI, one diet showed an exceedance of the ADI (NL toddler (127%)).

For the toddler diet in the UK NEDI, raspberries and blackberries contribute up to 15% of the ADI. For the NL toddler diet in the PRIMo IEDI calculation, raspberries contribute 0.7% of the ADI and blackberries contribute 0.1% of the ADI. As a result, the proposed uses considered under the import tolerance request are not the main contributors to the exceedances of the ADI and further refinements to the consumer risk assessment can be made.

For the UK NEDI in scenario 1, the highest contributor to the ADI for toddlers is oranges (55% of the ADI) with the whole of the citrus fruit commodity group contributing 76% of the ADI. For the PRIMo IEDI in scenario 1, the highest contributor to the ADI for NL toddler is apples (36%). CXLs which are lower than the current GB MRLs are available for citrus fruit, apples and pears (see Section 'Consideration of CXLs'). Therefore in scenario 2, the chronic risk assessment has been recalculated with the STMR values available that support the CXLs.

Scenario 2 - Chronic risk assessment for proposed MRLs for raspberries and blackberries and available CXLs

In this scenario the following has been considered for the chronic risk assessment:

- Additional CXLs recommended for adoption as GB MRLs
    - Lowering of GB MRLs to CXLs for citrus fruits, apples and pears
    - Consideration of the CXLs which are higher than the current GB MRLs for strawberries, tea, eggs and cane fruit
- Raspberries and blackberries input based on the import tolerance request
- Currently established GB MRLs for all other commodities

As citrus fruits, apples and pears are the highest contributors to the %ADI in scenario 1, the adoption of CXLs which are lower than current GB MRLs has been considered.

The CXLs for strawberries, tea and eggs are higher than the current GB MRLs for these commodities, therefore assessment of their impact on the consumer risk assessment has

been made to determine whether adoption of the CXLs for these commodities in GB can be recommended.

The CXL adopted in November 2025 for cane fruits is higher than the current GB MRL for these commodities and the import tolerance request (see Appendix E). Therefore, assessment of the impact on the consumer risk assessment has been made to determine whether adoption of the CXL for these commodities in GB can be recommended. As the STMR derived from the residue trials submitted in the scope of the import tolerance request for raspberries and blackberries is higher than the STMR derived by the JMPR for cane fruit, this has been used in preference to the JMPR STMR for raspberries and blackberries only.

UK NEDI

The input values for the UK consumer risk assessment are those given in table in Table 7.1.-3.

Table 7.1-3 Input values for the UK consumer risk assessment under scenario 2

Commodity	**Chronic risk assessment**	
	Input (mg/kg)	**Comment**
RD-RA:	**Hexythiazox**	
Raspberries	**1.035**	**STMR (current assessment)**
Blackberries	**1.035**	**STMR (current assessment)**
Citrus fruit	**0.077**	**STMR-pulp CXL (JMPR, 2009)**
Apple	**0.11**	**STMR CXL (JMPR, 2009)**
Pear	**0.11**	**STMR CXL (JMPR, 2009)**
Strawberries	**0.54**	**STMR CXL (JMPR, 2011)**
Loganberries	**1.0**	**STMR CXL (JMPR, 2024)**
Tea (dried leaves)	**4.55**	**STMR CXL (JMPR, 2011)**

Commodity	Chronic risk assessment	
	Input (mg/kg)	Comment
RD-RA:	**Hexythiazox**	
Eggs	**0.002**	**STMR CXL (JMPR, 2009)**
Dates	0.26	STMR CXL (JMPR, 2009)
Poultry	0.01	STMR CXL for poultry meat (JMPR, 2009)
Meat fat	0.01	STMR CXL (JMPR, 2009)
Meat excl. poultry & offal	0.01	STMR CXL (JMPR, 2009)
Other types of offal	0.01	STMR CXL based on edible offal (JMPR, 2009)
Milk	0.01	STMR CXL (JMPR, 2009)
All other commodities	MRL	(GB MRL Statutory Register and Commission Regulation (EU) 2012/592

* indicates residues at the LOQ

In bold uses proposed or reviewed as part of the current assessment.

Model outputs for the UK chronic model (version 1.1) are presented in Appendix B.

PRIMo

The input values for the PRIMo risk assessment are those given in table in Table 7.1.-4.

Table 7.1-4 Input values for the PRIMo consumer risk assessment under scenario 2

Commodity	Chronic risk assessment	
	Input (mg/kg)	Comment
RD-RA:	**Hexythiazox**	
Raspberries	**1.035**	**STMR (current assessment)**

Commodity	Chronic risk assessment	
	Input (mg/kg)	Comment
RD-RA:	**Hexythiazox**	
Blackberries	**1.035**	**STMR (current assessment)**
Citrus fruit	**0.077**	**STMR-pulp CXL (JMPR, 2009)**
Apples	**0.11**	**STMR CXL (JMPR, 2009)**
Pears	**0.11**	**STMR CXL (JMPR, 2009)**
Strawberries	**0.54**	**STMR CXL (JMPR, 2011)**
Dewberries	**1.0**	**STMR CXL (JMPR, 2024)**
Other cane fruit	**1.0**	**STMR CXL (JMPR, 2024)**
Tea (dried leaves)	**4.55**	**STMR CXL (JMPR, 2011)**
Birds eggs	**0.002**	**STMR CXL (JMPR, 2009)**
Dates	0.26	STMR CXL (JMPR, 2009)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: muscle/meat	0.01	STMR CXL (JMPR, 2009)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: fat	0.01	STMR CXL (JMPR, 2009)
Swine, bovine, sheep, goat, equine, other farmed terrestrial animals: edible offals (other than liver and kidney)	0.01	STMR CXL (JMPR, 2009)
Poultry: muscle/meat	0.01	STMR CXL (JMPR, 2009)
Poultry: edible offals (other than liver and kidney)	0.01	STMR CXL (JMPR, 2009)
Milk: cattle, sheep, goat, horse, others	0.01	STMR CXL (JMPR, 2009)
All other commodities	MRL	(GB MRL Statutory Register and Commission Regulation (EU) 2012/592)

* indicates residues at the LOQ

In bold uses proposed or reviewed as part of the current assessment.

Model outputs for EFSA PRIMo revision 3.1 are presented in Appendix B.

Conclusions

The highest UK NEDI was 86% of the ADI (infant). The highest PRIMo IEDI was 73% of the ADI (NL toddler). Therefore, no health effects due to chronic exposure are expected.

7.2 Other routes of exposure

Not applicable

8 The conclusion of the competent authority

Sufficiently validated analytical methods for the determination of hexythiazox in products of plant origin, in line with the residue definition for enforcement, are available to support the uses under consideration in the import tolerance application.

Toxicological reference values were established for the approval of the active substance: an ADI of 0.03 mg/kg bw/day and no ARfD allocated or required.

The metabolism of hexythiazox in primary crops was investigated in fruits (grape, pear citrus, apple) and miscellaneous crops (tea) following foliar applications for the approval of the active substance (EFSA, 2010). The crops included in this import tolerance application belong to the fruit commodity group and are, therefore, covered by the metabolism studies available.

The residue definition for risk assessment (RD-RA) in plants has been agreed as:

- Hexythiazox

The residue definition for enforcement (RD-Enf) in plants has been agreed as:

- Hexythiazox

Five outdoor trials on raspberries conducted in the USA were submitted to support MRLs for raspberries and blackberries. The trials are supported by validated analytical methods and storage stability data.

Hydrolysis of hexythiazox under representative conditions of pasteurisation, baking, brewing, boiling and sterilisation was evaluated for the approval of the active substance. The hydrolysis data from the approval of the active substance (thiazolidine radiolabel), demonstrate that hexythiazox is stable under standard conditions of pasteurisation and baking, boiling and brewing with formation of the PT-1-3 metabolite shown to be not significant. Under sterilisation conditions, hexythiazox is degraded to PT-1-3 (48% TRR). New hydrolysis data (cyclohexyl radiolabel) demonstrates that hexythiazox is stable under standard conditions of pasteurisation and baking, boiling and brewing, whereas under sterilisation conditions, hexythiazox is degraded to cyclohexylamine (43.5% TRR). Specific residue definitions for processed commodities of raspberries and blackberries are not required as residues of PT-1-3 and cyclohexylamine were shown to be <LOQ in the relevant processed commodities and sterilisation is not routinely performed for cane fruit due to their low pH.

No consideration of rotational crops was made as the impact of residues in rotational crops on the import tolerances was not required.

Following estimations of dietary exposures related to the proposed MRLs for raspberries and blackberries, and current GB MRLs for all other commodities, HSE identified chronic intake concerns associated with current MRLs. The highest UK NEDI was 136% of the ADI (toddler). The highest PRIMo IEDI was 127% of the ADI (NL toddler). Therefore, a chronic intake concern has been identified from exposure to hexythiazox from all dietary sources. Consideration of acute exposure was not required as the active substance is not acutely toxic and an ARfD has not been allocated.

For the UK NEDI, two diets had exceedances of the ADI (toddler (136%) and infant (107%)). For the PRIMo IEDI, one diet showed an exceedance of the ADI (NL toddler (127%)). For the toddler diet in the UK NEDI and the NL toddler diet in the PRIMo IEDI calculation, raspberries and blackberries are not the main contributors to the exceedances of the ADI. The main contributors are citrus fruit, apples and pears (contribute up to 76%, 36% and 15% of the ADI respectively).

For citrus fruit, apples and pears, there are CXLs available which are lower than the current GB MRLs, and which contribute significantly less to chronic exposures. Additionally, the CXLs accommodate the authorised GB uses on apples and pears and there are no GB authorisations for citrus fruit. No health effects are expected. Therefore, HSE recommends that the GB MRLs for citrus fruit, apples and pears are lowered and the CXLs for these commodities adopted.

The CXLs for strawberries, teas and eggs are higher than the current GB MRLs. For cane fruits and eggs, new CXLs have been adopted in 2025 which are higher than the current GB MRLs. These CXLs are acceptable; they do not contribute significantly to chronic exposures and no health effects are expected. Therefore, HSE recommends that the CXLs for strawberry, tea, eggs and cane fruit can be adopted in GB.

Consideration of the chronic risk assessment was performed for the proposed MRLs for raspberries and blackberries, lowering of the GB MRLs for citrus fruit, apples and pears to the CXLs, adoption of the CXLs for strawberries, teas, eggs and other cane fruit, and all other current GB MRLs. The highest UK NEDI was 86% of the ADI (infant). The highest PRIMo IEDI was 73% of the ADI (NL toddler). Therefore, no health effects due to chronic exposure are expected from the consumption of commodities treated with hexythiazox.

HSE concludes that sufficient data has been provided to support the setting of new MRLs for raspberries and blackberries. HSE also recommends that the GB MRLs for citrus fruit, apples and pears are lowered to the CXLs, and that the CXLs for strawberries, tea, eggs and cane fruit are adopted. The MRLs considered will not result in consumer exposures exceeding the toxicological reference values and therefore these MRLs are unlikely to have harmful effects on human health..

HSE recommends that the MRLs outlined in Table 8.1 are amended in the GB MRL Statutory Register.

Table 8.1 MRLs proposed by HSE for hexythiazox

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0100000	**FRUITS, FRESH or FROZEN; TREE NUTS**			
0110000	Citrus fruits			
0110010	Grapefruits	1	**0.5**	2
0110020	Oranges	1	**0.5**	2
0110030	Lemons	1	**0.5**	2
0110040	Limes	1	**0.5**	2
0110050	Mandarins	1	**0.5**	2
0110990	Others - Citrus Fruit	1	**0.5**	2
0120000	Tree Nuts			
0120010	Almonds	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0120020	Brazil nuts	0.5	0.5	
0120030	Cashew nuts	0.5	0.5	
0120040	Chestnuts	0.5	0.5	
0120050	Coconuts	0.5	0.5	
0120060	Hazelnuts/cobnuts	0.5	0.5	
0120070	Macadamias	0.5	0.5	
0120080	Pecans	0.5	0.5	
0120090	Pine nut kernels	0.5	0.5	
0120100	Pistachios	0.5	0.5	
0120110	Walnuts	0.5	0.5	
0120990	Others - Tree nuts	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0130000	Pome fruits			
0130010	Apples	1	**0.4**	2
0130020	Pears	1	**0.4**	2
0130030	Quinces	0.5	0.5	
0130040	Medlars	0.5	0.5	
0130050	Loquats/Japanese medlars	0.5	0.5	
0130990	Others - Pome fruit	0.5	0.5	
0140000	Stone fruits			
0140010	Apricots	1	1	
0140020	Cherries (sweet)	1	1	
0140030	Peaches	1	1	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0140040	Plums	0.5	0.5	
0140990	Others - Stone fruit	0.5	0.5	
0150000	Berries and small fruits			
0151000	Grapes			
0151010	Table grapes	1	1	
0151020	Wine grapes	1	1	
0152000	Strawberries			
0152000	Strawberries	0.5	**6**	2
0153000	Cane fruits			
0153010	Blackberries	0.5	**4**	2
0153020	Dewberries	0.5	**4**	2

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0153030	Raspberries (red and yellow)	0.5	**4**	2
0153990	Others - Cane fruit	0.5	**4**	2
0154000	Other small fruits and berries			
0154010	Blueberries	0.5	0.5	
0154020	Cranberries	0.5	0.5	
0154030	Currants (black, red and white)	0.5	0.5	
0154040	Gooseberries (green, red and yellow)	0.5	0.5	
0154050	Rose hips	0.5	0.5	
0154060	Mulberries (black and white)	0.5	0.5	
0154070	Azaroles/Mediterranean medlars	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0154080	Elderberries	0.5	0.5	
0154990	Others - Other small fruit and berries	0.5	0.5	
0160000	Miscellaneous fruits with			
0161000	Edible peel			
0161010	Dates	2	2	
0161020	Figs	0.5	0.5	
0161030	Table olives	0.5	0.5	
0161040	Kumquats	0.5	0.5	
0161050	Carambolas	0.5	0.5	
0161060	Kaki/Japanese persimmons	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0161070	Jambuls/jambolans	0.5	0.5	
0161990	Others - Edible peel	0.5	0.5	
0162000	Inedible peel, small			
0162010	Kiwi fruits (green, red, yellow)	1	1	
0162020	Litchis/lychees	0.5	0.5	
0162030	Passionfruits/maracujas	0.5	0.5	
0162040	Prickly pears/cactus fruits	0.5	0.5	
0162050	Star apples/cainitos	0.5	0.5	
0162060	American persimmons/Virginia kaki	0.5	0.5	
0162990	Others - Inedible peel, small	0.5	0.5	
0163000	Inedible peel, large			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0163010	Avocados	0.5	0.5	
0163020	Bananas	0.5	0.5	
0163030	Mangoes	0.5	0.5	
0163040	Papayas	0.5	0.5	
0163050	Granate apples/pomegranates	0.5	0.5	
0163060	Cherimoyas	0.5	0.5	
0163070	Guavas	0.5	0.5	
0163080	Pineapples	0.5	0.5	
0163090	Breadfruits	0.5	0.5	
0163100	Durians	0.5	0.5	
0163110	Soursops/guanabanas	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0163990	Others - Inedible peel, large	0.5	0.5	
0200000	**VEGETABLES, FRESH or FROZEN**			
0210000	Root and tuber vegetables			
0211000	Potatoes			
0211000	Potatoes	0.05*	0.05*	
0212000	Tropical root and tuber vegetables			
0212010	Cassava roots/manioc	0.5	0.5	
0212020	Sweet potatoes	0.5	0.5	
0212030	Yams	0.5	0.5	
0212040	Arrowroots	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0212990	Others - Tropical root and tuber vegetables	0.5	0.5	
0213000	Other root and tuber vegetables except sugar beets			
0213010	Beetroots	0.5	0.5	
0213020	Carrots	0.5	0.5	
0213030	Celeriacs/turnip rooted celeries	0.5	0.5	
0213040	Horseradishes	0.5	0.5	
0213050	Jerusalem artichokes	0.5	0.5	
0213060	Parsnips	0.5	0.5	
0213070	Parsley roots/Hamburg roots parsley	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0213080	Radishes	0.5	0.5	
0213090	Salsifies	0.5	0.5	
0213100	Swedes/rutabagas	0.5	0.5	
0213110	Turnips	0.5	0.5	
0213990	Others - Other root and tuber vegetables except sugar beet	0.5	0.5	
0220000	Bulb vegetables			
0220010	Garlic	0.5	0.5	
0220020	Onions	0.5	0.5	
0220030	Shallots	0.5	0.5	
0220040	Spring onions/green onions and Welsh onions	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0220990	Others - bulb vegetables	0.5	0.5	
0230000	Fruiting vegetables			
0231000	Solanaceae and Malvaceae			
0231010	Tomatoes	0.5	0.5	
0231020	Sweet peppers/bell peppers	0.5	0.5	
0231030	Aubergines/eggplants	0.5	0.5	
0231040	Okra/lady's fingers	0.5	0.5	
0231990	Others - Solanacea	0.5	0.5	
0232000	Cucurbits with edible peel			
0232010	Cucumbers	0.5	0.5	
0232020	Gherkins	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0232030	Courgettes	0.5	0.5	
0232990	Others - Cucurbits-edible peel	0.5	0.5	
0233000	Cucurbits with inedible peel			
0233010	Melons	0.5	0.5	
0233020	Pumpkins	0.5	0.5	
0233030	Watermelons	0.5	0.5	
0233990	Others - Cucurbits - inedible peel	0.5	0.5	
0234000	Sweet corn			
0234000	Sweet corn	0.5	0.5	
0239000	Other fruiting vegetables			
0239000	Other fruiting vegetables	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0240000	Brassica vegetables (excluding brassica roots and brassica baby leaf crops)			
0241000	Flowering brassica			
0241010	Broccoli	0.5	0.5	
0241020	Cauliflowers	2	2	
0241990	Others - Flowering Brassicas	1	1	
0242000	Head brassica			
0242010	Brussels sprouts	5	5	
0242020	Head cabbages	2	2	
0242990	Others - Head Brassicas	3	3	
0243000	Leafy brassica			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0243010	Chinese cabbages/pe-tsai	0.5	0.5	
0243020	Kales	0.5	0.5	1
0243990	Others - Leafy Brassicas	1	1	
0244000	Kohlrabies			
0244000	Kohlrabies	1	1	
0250000	Leaf vegetables, herbs and edible flowers			
0251000	Lettuces and salad plants			
0251010	Lamb's lettuces/corn salads	0.5	0.5	
0251020	Lettuces	0.5	0.5	
0251030	Escaroles/broad-leaved endives	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0251040	Cresses and other sprouts and shoots	0.5	0.5	
0251050	Land cresses	0.5	0.5	
0251060	Roman rocket/rucola	0.5	0.5	
0251070	Red mustards	0.5	0.5	
0251080	Baby leaf crops (including brassica species)	0.5	0.5	
0251990	Others - Lettuce and other salad plants including brassica	0.5	0.5	
0252000	Spinaches and similar leaves			
0252010	Spinaches	0.5	0.5	
0252020	Purslanes	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0252030	Chards/beet leaves	0.5	0.5	
0252990	Others - Spinach and similar (leaves)	0.5	0.5	
0253000	Grape leaves and similar species			
0253000	Grape leaves and similar species	0.5	0.5	
0254000	Watercresses			
0254000	Watercresses	0.5	0.5	
0255000	Witloofs/Belgian endives			
0255000	Witloofs/Belgian endives	0.5	0.5	
0256000	Herbs and edible flowers			
0256010	Chervil	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0256020	Chives	0.5	0.5	
0256030	Celery leaves	0.5	0.5	
0256040	Parsley	0.5	0.5	
0256050	Sage	0.5	0.5	
0256060	Rosemary	0.5	0.5	
0256070	Thyme	0.5	0.5	
0256080	Basil and edible flowers	0.5	0.5	
0256090	Laurel/bay leaves	0.5	0.5	
0256100	Tarragon	0.5	0.5	
0256990	Others - Herbs	0.5	0.5	
0260000	Legume vegetables			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0260010	Beans (with pods)	0.5	0.5	
0260020	Beans (without pods)	0.5	0.5	
0260030	Peas (with pods)	0.5	0.5	
0260040	Peas (without pods)	0.5	0.5	
0260050	Lentils	0.5	0.5	
0260990	Others - Legume vegetables (fresh)	0.5	0.5	
0270000	Stem vegetables			
0270010	Asparagus	0.5	0.5	
0270020	Cardoons	0.5	0.5	
0270030	Celeries	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0270040	Florence fennels	0.5	0.5	
0270050	Globe artichokes	0.5	0.5	
0270060	Leeks	0.5	0.5	
0270070	Rhubarbs	0.5	0.5	
0270080	Bamboo shoots	0.5	0.5	
0270090	Palm hearts	0.5	0.5	
0270990	Others - Stem vegetables (fresh)	0.5	0.5	
0280000	Fungi, mosses and lichens			
0280010	Cultivated fungi	0.5	0.5	
0280020	Wild fungi	0.5	0.5	
0280990	Mosses and lichens	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0290000	Algae and prokaryotes organisms			
0290000	Algae and prokaryotes organisms	0.05*	0.05*	
0300000	**PULSES, DRY**			
0300010	Beans	0.5	0.5	
0300020	Lentils	0.2	0.2	
0300030	Peas	0.2	0.2	
0300040	Lupins/lupini beans	0.2	0.2	
0300990	Others - pulses	0.2	0.2	
0400000	**OILSEEDS AND OIL FRUITS**			
0401000	Oilseeds			
0401010	Linseeds	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0401020	Peanuts/groundnuts	0.5	0.5	
0401030	Poppy seeds	0.5	0.5	
0401040	Sesame seeds	0.5	0.5	
0401050	Sunflower seeds	0.5	0.5	
0401060	Rapeseeds/canola seeds	0.5	0.5	
0401070	Soyabeans	0.5	0.5	
0401080	Mustard seeds	0.5	0.5	
0401090	Cotton seeds	0.5	0.5	
0401100	Pumpkin seeds	0.5	0.5	
0401110	Safflower seeds	0.5	0.5	
0401120	Borage seeds	0.5	0.5	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0401130	Gold of pleasure seeds	0.5	0.5	
0401140	Hemp seeds	0.5	0.5	
0401150	Castor beans	0.5	0.5	
0401990	Others - Oilseeds	0.5	0.5	
0402000	Oil fruits			
0402010	Olives for oil production	0.5	0.5	
0402020	Oil palms kernels	0.05*	0.05*	
0402030	Oil palms fruits	0.05*	0.05*	
0402040	Kapok	0.05*	0.05*	
0402990	Others - Oilfruits	0.05*	0.05*	
0500000	**CEREALS**			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0500010	Barley	0.2	0.2	
0500020	Buckwheat and other pseudocereals	0.5	0.5	
0500030	Maize/corn	0.5	0.5	
0500040	Common millet/proso millet	0.5	0.5	
0500050	Oat	0.5	0.5	
0500060	Rice	0.5	0.5	
0500070	Rye	0.5	0.5	
0500080	Sorghum	0.5	0.5	
0500090	Wheat	0.5	0.5	
0500990	Others - cereals	0.05*	0.05*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0600000	**TEAS, COFFEE, HERBAL INFUSIONS, COCOA AND CAROBS**			
0610000	Teas			
0610000	Teas	4	**15**	2
0620000	Coffee beans			
0620000	Coffee beans	0.05*	0.05*	
0630000	Herbal infusions from Dried product			
0631000	Flowers			
0631010	Chamomile	0.05*	0.05*	
0631020	Hibiscus/roselle	0.05*	0.05*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0631030	Rose	0.05*	0.05*	
0631040	Jasmine	0.05*	0.05*	
0631050	Lime/linden	0.05*	0.05*	
0631990	Others - Flowers	0.05*	0.05*	
0632000	Leaves and herbs			
0632010	Strawberry	0.05*	0.05*	
0632020	Rooibos	0.05*	0.05*	
0632030	Mate	0.05*	0.05*	
0632990	Others - Herbal infusions (leaves and herbs)	0.05*	0.05*	
0633000	Roots			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0633010	Valerian	0.05*	0.05*	
0633020	Ginseng	0.05*	0.05*	
0633990	Others - Roots	0.05*	0.05*	
0639000	Other herbal Infusions - Parts of the plant other than flowers, leaves and herbs, and roots			
0639000	Any other parts of the plant	0.05*	0.05*	
0640000	Cocoa beans			
0640000	Cocoa beans	0.05*	0.05*	
0650000	Carobs/Saint John's breads			
0650000	Carobs/Saint John's breads	0.05*	0.05*	
0700000	**HOPS**			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0700000	Hops	20	20	
0800000	**SPICES**			
0810000	Seed spices			
0810010	Anise/aniseed	0.05*	0.05*	
0810020	Black caraway/black cumin	0.05*	0.05*	
0810030	Celery seed	0.05*	0.05*	
0810040	Coriander seed	0.05*	0.05*	
0810050	Cumin seed	0.05*	0.05*	
0810060	Dill seed	0.05*	0.05*	
0810070	Fennel seed	0.05*	0.05*	
0810080	Fenugreek	0.05*	0.05*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0810090	Nutmeg	0.05*	0.05*	
0810990	Others - Seeds	0.05*	0.05*	
0820000	Fruit spices			
0820010	Allspice/pimento	0.05*	0.05*	
0820020	Sichuan pepper	0.05*	0.05*	
0820030	Caraway	0.05*	0.05*	
0820040	Cardamom	0.05*	0.05*	
0820050	Juniper berry	0.05*	0.05*	
0820060	Peppercorn (black, green and white)	0.05*	0.05*	
0820070	Vanilla	0.05*	0.05*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0820080	Tamarind	0.05*	0.05*	
0820990	Others - Fruit spices	0.05*	0.05*	
0830000	Bark spices			
0830010	Cinnamon	0.05*	0.05*	
0830990	Others - Bark	0.05*	0.05*	
0840000	Root and rhizome spices			
0840010	Liquorice	0.05*	0.05*	
0840020	Ginger	0.05*	0.05*	3
0840030	Turmeric/curcuma	0.05*	0.05*	
0840040	Horseradish	0.05*	0.05*	4
0840990	Others - Roots or rhizome	0.05*	0.05*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0850000	Bud spices			
0850010	Cloves	0.05*	0.05*	
0850020	Capers	0.05*	0.05*	
0850990	Others - Buds	0.05*	0.05*	
0860000	Flower pistil spices			
0860010	Saffron	0.05*	0.05*	
0860990	Others - Flower pistil spices	0.05*	0.05*	
0870000	Aril spices			
0870010	Mace	0.05*	0.05*	
0870990	Others - Aril spices	0.05*	0.05*	
0900000	**SUGAR PLANTS**			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
0900010	Sugar beet roots	0.05*	0.05*	
0900020	Sugar canes	0.05*	0.05*	
0900030	Chicory roots	0.05*	0.05*	
0900990	Others - Sugar plants	0.05*	0.05*	
1000000	**PRODUCTS OF ANIMAL ORIGIN - TERRESTRIAL ANIMALS**			
1010000	Commodities from			
1011000	Swine			
1011010	Muscle - swine	0.05	0.05	
1011020	Fat - swine	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1011030	Liver - swine	0.05	0.05	
1011040	Kidney - swine	0.05	0.05	
1011050	Edible offals (other than liver and kidney) - swine	0.05	0.05	
1011990	Others - swine	0.05	0.05	
1012000	Bovine			
1012010	Muscle - bovine	0.05	0.05	
1012020	Fat - bovine	0.05	0.05	
1012030	Liver - bovine	0.05	0.05	
1012040	Kidney - bovine	0.05	0.05	
1012050	Edible offals (other than liver and kidney) - bovine	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1012990	Others - bovine	0.05	0.05	
1013000	Sheep			
1013010	Muscle - sheep	0.05	0.05	
1013020	Fat - sheep	0.05	0.05	
1013030	Liver - sheep	0.05	0.05	
1013040	Kidney - sheep	0.05	0.05	
1013050	Edible offals (other than liver and kidney) - sheep	0.05	0.05	
1013990	Others - sheep	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1014000	Goat			
1014010	Muscle - goat	0.05	0.05	
1014020	Fat - goat	0.05	0.05	
1014030	Liver - goat	0.05	0.05	
1014040	Kidney - goat	0.05	0.05	
1014050	Edible offals (other than liver and kidney) - goat	0.05	0.05	
1014990	Others - goat	0.05	0.05	
1015000	Equine			
1015010	Muscle - equine	0.05	0.05	
1015020	Fat - equine	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1015030	Liver - equine	0.05	0.05	
1015040	Kidney - equine	0.05	0.05	
1015050	Edible offals (other than liver and kidney) - equine	0.05	0.05	
1015990	Others - equine	0.05	0.05	
1016000	Poultry			
1016010	Muscle - poultry	0.05	0.05	
1016020	Fat - poultry	0.05	0.05	
1016030	Liver - poultry	0.05	0.05	
1016040	Kidney - poultry	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1016050	Edible offals (other than liver and kidney) - poultry	0.05	0.05	
1016990	Others - poultry	0.05	0.05	
1017000	Other farmed terrestrial animals			
1017010	Muscle - other farmed terrestrial animals	0.05	0.05	
1017020	Fat - other farmed terrestrial animals	0.05	0.05	
1017030	Liver - other farmed terrestrial animals	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1017040	Kidney - other farmed terrestrial animals	0.05	0.05	
1017050	Edible offals (other than liver and kidney) - other farmed terrestrial animals	0.05	0.05	
1017990	Others - Other farm animals	0.05	0.05	
1020000	Milk			
1020010	Cattle - milk	0.05	0.05	
1020020	Sheep - milk	0.05	0.05	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1020030	Goat - milk	0.05	0.05	
1020040	Horse - milk	0.05	0.05	
1020990	Others - Milk and cream	0.05	0.05	
1030000	Birds eggs			
1030010	Chicken - eggs	0.02*	**0.05**	2
1030020	Duck - eggs	0.02*	**0.05**	2
1030030	Geese - eggs	0.02*	**0.05**	2
1030040	Quail - eggs	0.02*	**0.05**	2
1030990	Others - Birds' eggs	0.02*	**0.05**	2
1040000	Honey and other apiculture products			

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes
1040000	Honey and other apiculture products	0.02*	0.02*	
1050000	Amphibians and reptiles			
1050000	Amphibians and reptiles	0.02*	0.02*	
1060000	Terrestrial invertebrate animals			
1060000	Terrestrial invertebrate animals	0.02*	0.02*	
1070000	Wild terrestrial vertebrate animals			
1070000	Wild terrestrial vertebrate animals	0.02*	0.02*	

GB Code No	Commodity to which the MRL applies	Current MRL in force (mg/kg)	Proposed MRL (mg/kg)	Footnotes

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

Part 1 of the GB MRL Statutory Register should be consulted for the full list of products of plant and animal origin to which the maximum residue levels of pesticides ('MRLs') apply

Footnotes

Kales

1) MRLs shall apply to radish leaves as from 1 January 2025.

MRL clarification

2) This MRL is a CXL adopted in 2026

Ginger

3) The applicable maximum residue level for ginger (Zingiber officinale) in the spice group (code 0840020) is the one set for ginger roots (Zingiber officinale) in the Part 1B of the Statutory Register (code 0213040-006, equal to the one of horseradish (Armoracia rusticana) code 0213040), taking into account changes in the levels by processing (drying), according to Art. 20 (1) of Assimilated Regulation 396/2005.

Horseradish

4) The applicable maximum residue level for horseradish (Armoracia rusticana) in the spice group (code 0840040) is the one set for horseradish (Armoracia rusticana) in the Vegetables category, root and tuber vegetables group (code 0213040), taking into account changes in the levels by processing (drying) according to Art. 20 (1) of Assimilated Regulation 396/2005.

References

Finland, 2005. Draft Assessment Report (DAR) on the active substance hexythiazox prepared by the rapporteur Member State Finland in the framework of Council Directive 91/414/EEC, October 2005

Finland, 2009. Draft Assessment Report (DAR) on the active substance hexythiazox prepared by the rapporteur Member State Finland in the framework of Council Directive 91/414/EEC, Additional report, October 2009

Finland, 2012. Review of the existing MRLs for hexythiazox, Prepared under Article 12.1 of Regulation (EC) No 396/2005, August 2012

Finland, 2014. Draft Assessment Report (DAR) on the active substance hexythiazox prepared by the rapporteur Member State Finland in the framework of Council Directive 91/414/EEC, Confirmatory Data, Revised February 2014

EFSA (European Food Safety Authority), 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance hexythiazox. EFSA Journal 2010; 8(10):1722.

EFSA (European Food Safety Authority), 2012. Modification of the existing MRL for hexythiazox in tea. EFSA Journal 2012; 10 (1):2514.

EFSA (European Food Safety Authority), 2018. Database of processing techniques and processing factors compatible with the EFSA food classification and description system Food Ex 2. EFSA Supporting publication 2018:EN-1508.

JMPR, 2009. Report by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) on Hexythiazox in 2009

JMPR, 2011. Report by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) on Hexythiazox in 2011

JMPR, 2024. Summary report of the 2024 Joint FAO/WHO Meeting on Pesticide Residues (JMPR).

Appendix A – GAPs notified in the MRL application

Crop and/or situation (a)	GB or Country For Import Tolerance	Product name	F, G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. a.s. (i)	method kind (f-h)	range of growth stages & season (j)	number min-max (k)	Interval between application (min)	kg a.s /hL min-max (l)	Water (L/ha) min-max	kg a.s./ha min-max (l)		
Raspberries, Blackberries	USA	Savey 50 DF	F	Two spotted Spider Mite, McDaniel Spider Mite, Yellow Spider Mite, Pacific Mite	WG	500 a.s. g/kg	Foliar, Broadcast	At infestation	1	N/A	0.299 – 0.449	Air application: min 46.8	0.140 – 0.210	3	Do not make more than one application per year.
Raspberries, Blackberries	USA	Onager EW Miticide	F	Two-spotted spider mite, McDaniel Spider Mite, Yellow Spider Mite, Pacific Mite	EW	119.3 a.s g/L	Foliar, Broadcast	At infestation	1	N/A	Air application: 0.214 – 0.577	Air application: Min 46.8	0.100 – 0.267	3	Do not make more than one application per year. Do not apply more than 32 ozs (0.907 kg a.i) of formulated product per acre per year.
Apple, Pear	UK	Nissorun SC	F	Spider mites (*Panonychus ulmi;* METTUL; *Tetranychus urticae;* TETRUR)	SC	250 g/L	High volume spraying	At infestation (BBCH 51-79)	1	-	-	500-1500	0.1	28	Max. 3 m crown height (32.5 g as/ha and per m crown height)

(a) For crops, the GB and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) State if the use is outdoor, field use (F) or glasshouse (G) or indoor use (I).
(c) *e.g.* biting and sucking insects, soil borne insects, foliar fungi, weeds

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluroxypyr). In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(j) 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 (k) Indicate the minimum and maximum number of applications possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

Appendix B – UK models and Pesticide Residues Intake Model (PRIMo)

Table B.1 Chronic risk assessment undertaken using UK model version 1.1 – scenario 1

Active substance: Hexythiazox **ADI:** 0.03 mg/kg bw/day **Source:** EFSA 2010

			TOTAL INTAKE based on 97.5th percentile									
			ADULT	INFANT	TODDLER	4-6 YEARS	7-10 YEARS	11-14 YEARS	15-18 YEARS	VEGETARIAN	ELDERLY (OWN HOME)	ELDERLY (RESIDENTIAL)
	mg/kg bw/day		0.01816	0.03204	0.04072	0.02960	0.02825	0.01810	0.01463	0.02012	0.01543	0.00928
	% of ADI		61%	*107%*	*136%*	99%	94%	60%	49%	67%	51%	31%
Commodity	**STMR (mg/kg)**	**P**	**COMMODITY INTAKES (mg/kg bw/day)**									
Grapefruit	1		0.00193	0.00160	0.00581	0.00528	0.01152	0.00210	0.00146	0.00234	0.00240	0.00194
Lemons	1		0.00013	0.00069	0.00032	0.00013	0.00009	0.00008	0.00014	0.00022	0.00033	0.00007
Limes	1		0.00028	L/C	0.00163	0.00022	0.00016	0.00016	0.00024	0.00028	0.00034	0.00053
Mandarins	1		0.00140	L/C	0.00639	0.00361	0.00294	0.00152	0.00167	0.00118	0.00157	0.00067
Oranges	1		0.00386	0.01074	0.01639	0.01121	0.00836	0.00798	0.00662	0.00457	0.00357	0.00273
Almonds	0.5		0.00005	0.00022	0.00010	0.00008	0.00006	0.00004	0.00005	0.00005	0.00005	0.00002
Brazil nuts	0.5		0.00007	L/C	0.00010	0.00008	0.00007	0.00003	0.00002	0.00006	0.00005	L/C
Cashew nuts	0.5		0.00008	L/C	0.00026	0.00009	0.00001	0.00003	0.00002	0.00009	0.00011	0.00001
Chestnuts	0.5		0.00007	L/C	L/C	L/C	L/C	L/C	0.00002	0.00013	0.00008	L/C

Coconuts	0.5		0.00007	0.00005	0.00016	0.00013	0.00009	0.00009	0.00007	0.00019	0.00005	0.00004
Hazelnuts	0.5		0.00005	L/C	0.00011	0.00005	0.00007	0.00003	0.00004	0.00003	0.00003	0.00001
Pecan nuts	0.5		0.00003	L/C	0.00002	L/C	0.00001	0.00004	L/C	0.00018	0.00005	L/C
Pistachios	0.5		0.00019	L/C	0.00017	L/C	0.00012	L/C	L/C	0.00006	L/C	L/C
Walnuts	0.5		0.00006	L/C	0.00021	0.00003	0.00004	0.00003	0.00005	0.00008	0.00009	0.00003
Peanuts	0.5		0.00020	0.00030	0.00054	0.00040	0.00029	0.00033	0.00016	0.00022	0.00020	0.00004
Apples	1		0.00268	0.00843	0.01487	0.00943	0.00752	0.00410	0.00357	0.00334	0.00219	0.00107
Pears	1		0.00140	0.00255	0.00653	0.00363	0.00221	0.00185	0.00145	0.00188	0.00228	0.00119
Apricots	1		0.00037	0.00134	0.00103	0.00062	0.00042	0.00037	0.00022	0.00076	0.00044	0.00037
Peaches	1		0.00136	0.00134	0.00314	0.00158	0.00117	0.00076	0.00045	0.00094	0.00093	0.00043
Plums	0.5		0.00046	0.00024	0.00108	0.00068	0.00039	0.00014	0.00012	0.00035	0.00033	0.00010
Cherries	1		0.00047	0.00143	0.00105	0.00151	0.00055	0.00071	0.00059	0.00052	0.00035	0.00008
Table grapes	1		0.00132	0.00166	0.00470	0.00216	0.00259	0.00110	0.00063	0.00204	0.00133	0.00046
Wine grapes	1		0.00984	0.00122	0.00089	0.00091	0.00032	0.00101	0.00353	0.00972	0.00665	0.00146
Strawberries	0.5		0.00030	0.00096	0.00100	0.00067	0.00045	0.00034	0.00025	0.00048	0.00051	0.00026
Blackberries	1.04		0.00012	L/C	0.00202	0.00007	0.00034	0.00026	0.00010	0.00032	0.00027	0.00004
Loganberries	0.5		0.00004	0.00030	0.00057	0.00008	0.00025	0.00013	0.00008	0.00011	0.00008	0.00005
Raspberries	1.04		0.00043	L/C	0.00247	0.00068	0.00105	0.00027	0.00007	0.00042	0.00087	0.00039
Gooseberries	0.5		0.00012	0.00026	0.00033	0.00012	0.00012	0.00012	0.00009	0.00036	0.00041	0.00012
Blackcurrants	0.5		0.00029	0.00059	0.00090	0.00090	0.00069	0.00051	0.00056	0.00018	0.00027	0.00014
Red currants	0.5		0.00004	L/C	0.00039	L/C	0.00003	0.00006	0.00002	0.00002	0.00017	L/C
White currants	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Avocados	0.5		0.00039	L/C	0.00063	L/C	L/C	L/C	0.00016	0.00034	0.00026	L/C
Bananas	0.5		0.00103	0.00348	0.00332	0.00224	0.00173	0.00103	0.00073	0.00107	0.00082	0.00091
Dates	0.26		0.00006	L/C	0.00010	0.00012	0.00004	0.00001	L/C	0.00012	0.00018	0.00006
Figs	0.5		0.00015	0.00019	0.00020	0.00006	0.00009	0.00002	0.00003	0.00033	0.00010	0.00003

Kiwi fruit	1		0.00070	L/C	0.00231	0.00201	0.00118	0.00093	0.00231	0.00122	0.00054	0.00015
Lychees	0.5		0.00017	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Mangoes	0.5		0.00034	L/C	0.00081	0.00070	0.00088	0.00029	0.00182	0.00027	0.00008	L/C
Olives	0.5		0.00013	L/C	0.00030	0.00030	L/C	0.00003	L/C	0.00010	0.00022	L/C
Passion fruit	0.5		0.00007	L/C	L/C	L/C	L/C	L/C	L/C	0.00011	L/C	L/C
Pineapples	0.5		0.00058	0.00259	0.00236	0.00338	0.00122	0.00073	0.00052	0.00058	0.00038	0.00031
Pomegranates	0.5		0.00060	0.00028	0.00041	0.00021	0.00025	0.00028	0.00001	0.00027	0.00031	0.00050
Beetroot	0.5		0.00019	L/C	0.00075	0.00020	0.00016	0.00017	0.00012	0.00024	0.00025	0.00009
Carrots	0.5		0.00035	0.00176	0.00123	0.00095	0.00061	0.00042	0.00049	0.00044	0.00048	0.00039
Celeriac	0.5		0.00019	L/C	L/C	0.00002	0.00003	L/C	L/C	L/C	L/C	L/C
Horseradish	0.5		0.00001	L/C	L/C	L/C	L/C	L/C	L/C	L/C	0.00001	L/C
Jerusalem artichokes	0.5		0.00008	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Parsnips	0.5		0.00016	0.00046	0.00059	0.00036	0.00025	0.00020	0.00013	0.00021	0.00031	0.00014
Radishes	0.5		0.00016	L/C	0.00049	L/C	0.00011	0.00006	0.00005	0.00015	0.00012	0.00005
Salsify	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Swedes	0.5		0.00024	0.00140	0.00086	0.00034	0.00039	0.00030	0.00023	0.00025	0.00033	0.00024
Turnips	0.5		0.00017	L/C	0.00049	0.00044	0.00028	0.00028	0.00017	0.00008	0.00031	0.00020
Yam	0.5		0.00146	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Garlic	0.5		0.00003	L/C	0.00003	0.00005	0.00007	0.00004	0.00006	0.00007	0.00007	L/C
Onions	0.5		0.00026	0.00056	0.00056	0.00046	0.00039	0.00037	0.00025	0.00036	0.00027	0.00015
Spring onions	0.5		0.00013	L/C	0.00008	0.00033	0.00009	0.00004	0.00005	0.00013	0.00013	0.00004
Tomatoes	0.5		0.00069	0.00091	0.00132	0.00096	0.00092	0.00054	0.00067	0.00088	0.00073	0.00067
Peppers	0.5		0.00018	L/C	0.00040	0.00020	0.00034	0.00016	0.00014	0.00030	0.00028	0.00009
Aubergines	0.5		0.00016	L/C	0.00077	0.00038	0.00013	0.00026	0.00019	0.00031	0.00020	L/C
Marrows	0.5		0.00025	L/C	0.00078	0.00020	0.00030	0.00032	0.00013	0.00026	0.00069	0.00032
Cucumbers	0.5		0.00020	0.00011	0.00121	0.00077	0.00052	0.00026	0.00023	0.00027	0.00024	0.00009

Gourd	0.5		0.00027	L/C	L/C	L/C	L/C	0.00013	L/C	0.00010	L/C	L/C
Courgettes	0.5		0.00021	0.00074	0.00119	0.00064	0.00039	0.00021	0.00019	0.00028	0.00026	0.00022
Melons	0.5		0.00124	0.00152	0.00262	0.00176	0.00152	0.00108	0.00138	0.00127	0.00149	0.00049
Sweet corn	0.5		0.00026	0.00051	0.00113	0.00054	0.00059	0.00025	0.00031	0.00028	0.00042	0.00017
Broccoli	0.5		0.00032	0.00057	0.00086	0.00061	0.00052	0.00036	0.00031	0.00034	0.00048	0.00017
Cauliflower	2		0.00174	0.00630	0.00434	0.00335	0.00171	0.00148	0.00171	0.00244	0.00227	0.00133
Brussels sprouts	5		0.00303	0.01167	0.00897	0.00729	0.00369	0.00463	0.00316	0.00397	0.00480	0.00231
Head cabbage	2		0.00109	0.00352	0.00341	0.00253	0.00150	0.00143	0.00106	0.00151	0.00232	0.00147
Chinese cabbage	0.5		0.00025	L/C	L/C	L/C	L/C	L/C	L/C	0.00025	0.00017	L/C
Kohl Rabi	1		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Cress	0.5		0.00002	L/C	0.00002	0.00003	0.00001	0.00002	0.00001	0.00004	0.00005	0.00002
Lettuce	0.5		0.00031	0.00018	0.00043	0.00034	0.00036	0.00020	0.00022	0.00035	0.00027	0.00014
Spinach	0.5		0.00026	0.00050	0.00078	0.00043	0.00044	0.00031	0.00017	0.00034	0.00028	0.00018
Watercress	0.5		0.00008	L/C	L/C	0.00003	0.00003	0.00009	L/C	0.00012	0.00015	L/C
Chicory	0.5		0.00004	L/C	L/C	L/C	L/C	L/C	L/C	0.00004	L/C	L/C
Parsley	0.5		0.00008	L/C	0.00006	L/C	0.00008	0.00002	0.00001	0.00009	0.00009	0.00018
Beans with pods	0.5		0.00026	0.00060	0.00096	0.00066	0.00033	0.00018	0.00035	0.00020	0.00036	0.00016
Runner Beans	0.5		0.00031	L/C	0.00074	0.00025	0.00037	0.00029	0.00025	0.00076	0.00049	0.00028
Beans without pods	0.5		0.00022	0.00029	0.00120	0.00019	0.00053	0.00019	0.00021	0.00032	0.00040	0.00026
Peas with pods	0.5		0.00014	L/C	0.00023	0.00063	0.00011	0.00014	0.00008	0.00013	0.00026	L/C
Peas without pods	0.5		0.00039	0.00120	0.00102	0.00070	0.00051	0.00037	0.00046	0.00044	0.00050	0.00036
Beansprouts	0.5		0.00020	L/C	0.00045	0.00028	0.00028	0.00018	0.00013	0.00019	0.00029	0.00012
Asparagus	0.5		0.00020	L/C	L/C	L/C	L/C	L/C	0.00011	0.00040	0.00022	L/C
Bamboo shoots	0.5		0.00008	L/C	0.00014	L/C	0.00003	0.00013	0.00003	0.00009	0.00005	L/C
Celery	0.5		0.00016	0.00021	0.00021	0.00014	0.00008	0.00013	0.00009	0.00023	0.00024	0.00006
Fennel	0.5		0.00019	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C

Globe artichokes	0.5		0.00016	L/C	L/C	L/C	L/C	L/C	L/C	0.00010	L/C	L/C
Leeks	0.5		0.00025	L/C	0.00032	0.00018	0.00015	0.00018	0.00011	0.00024	0.00029	0.00018
Rhubarb	0.5		0.00020	0.00036	0.00055	0.00012	0.00025	0.00007	0.00008	0.00017	0.00034	0.00020
Cultivated mushrooms	0.5		0.00020	0.00025	0.00053	0.00025	0.00020	0.00015	0.00021	0.00033	0.00021	0.00015
Beans	0.5		0.00078	0.00295	0.00236	0.00168	0.00143	0.00105	0.00106	0.00088	0.00070	0.00049
Lentils	0.5		0.00036	0.00072	0.00092	0.00098	0.00032	0.00062	0.00025	0.00035	0.00025	0.00012
dried Peas	0.5		0.00034	L/C	0.00087	0.00023	0.00037	0.00060	0.00032	0.00029	0.00053	0.00036
Oilseeds	0.5		0.00159	0.00315	0.00362	0.00358	0.00280	0.00202	0.00176	0.00234	0.00160	0.00193
Potatoes	0.05		0.00016	0.00056	0.00046	0.00041	0.00035	0.00027	0.00023	0.00018	0.00016	0.00016
Tea (dried leaves)	1.28		0.00027	0.00091	0.00034	0.00021	0.00015	0.00014	0.00017	0.00029	0.00027	0.00029
Hops (dried 0.25% of beer)	20		0.00124	L/C	L/C	L/C	L/C	0.00013	0.00110	0.00105	0.00124	0.00094
Oats	0.5		0.00018	0.00110	0.00061	0.00038	0.00023	0.00018	0.00032	0.00032	0.00026	0.00028
Barley	0.2		0.00005	L/C	0.00007	0.00007	0.00016	0.00004	0.00005	0.00005	0.00005	0.00003
Millet	0.5		L/C	L/C	0.00014	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Buckwheat	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Maize	0.5		0.00003	0.00229	0.00036	0.00025	0.00009	0.00008	0.00009	0.00016	0.00007	0.00004
Wheat	0.5		0.00180	0.00140	0.00425	0.00444	0.00337	0.00249	0.00202	0.00213	0.00163	0.00173
Rice	0.5		0.00113	0.00140	0.00237	0.00186	0.00254	0.00196	0.00133	0.00100	0.00060	0.00024
Rye	0.5		0.00026	0.00068	0.00019	0.00022	0.00024	0.00013	0.00006	0.00030	0.00022	0.00008
Poultry	0.01		0.00002	0.00002	0.00003	0.00003	0.00002	0.00002	0.00002	0.00002	0.00002	0.00001
Meat fat	0.01		0.00000	0.00000	0.00001	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
Meat excl. poultry & offal	0.01		0.00002	0.00004	0.00004	0.00003	0.00003	0.00002	0.00002	0.00000	0.00002	0.00002
All types of kidney	0.05		0.00001	0.00002	0.00007	0.00002	0.00001	0.00001	0.00002	L/C	0.00002	0.00002
All types of Liver	0.05		0.00002	0.00011	0.00012	0.00002	0.00002	0.00003	0.00001	L/C	0.00003	0.00002
Other types of offal	0.01		0.00001	0.00002	0.00002	0.00001	0.00001	0.00001	0.00000	0.00000	0.00001	0.00001
Eggs	0.02		0.00002	0.00009	0.00007	0.00005	0.00003	0.00003	0.00002	0.00002	0.00002	0.00003

Milk	0.01		0.00008	0.00098	0.00056	0.00029	0.00018	0.00012	0.00009	0.00010	0.00009	0.00012
Sugar beet	0.05		0.00070	0.00167	0.00279	0.00168	0.00157	0.00100	0.00096	0.00060	0.00053	0.00076

* 0.00000 corresponds to <0.000005 mg/kg bw/day (any value ≥0.000005 is rounded to 0.00001

L/C Low consumption (<0.1 g/day) or low number of consumers (<4)

Table B.2 Chronic risk assessment undertaken using PRIMo revision 3.1 - scenario 1

Chronic risk assessment: JMPR methodology (IEDI/TMDI)												
				No of diets exceeding the ADI :		1				Exposure resulting from	
	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	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food	126.5%	NL toddler	37.96	35.9%	Apples	14.5%	Pears	11.7%	Maize/corn	1.8%	
	95.5%	DE child	28.66	41.6%	Apples	13.4%	Oranges	7.0%	Wheat	0.6%	
	64.5%	NL child	19.35	19.3%	Apples	6.9%	Wheat	4.7%	Oranges	2.2%	
	56.4%	GEMS/Food G06	16.91	12.1%	Wheat	6.0%	Tomatoes	3.5%	Table grapes	0.9%	
	53.3%	IE adult	16.00	5.9%	Sweet potatoes	4.2%	Wine grapes	3.8%	Wheat	0.4%	
	46.7%	GEMS/Food G11	14.01	6.2%	Soyabeans	6.0%	Wheat	5.2%	Apples	1.2%	
	46.5%	GEMS/Food G15	13.95	7.6%	Wheat	5.5%	Head cabbages	3.6%	Apples	0.9%	
	46.4%	FR child 3 15 yr	13.91	11.4%	Oranges	7.7%	Wheat	5.6%	Apples	1.0%	
	46.2%	GEMS/Food G08	13.85	6.8%	Wheat	4.0%	Apples	3.5%	Wine grapes	1.0%	
	45.7%	RO general	13.71	9.6%	Head cabbages	8.4%	Wheat	5.6%	Wine grapes	0.9%	
	45.2%	GEMS/Food G10	13.55	6.5%	Wheat	5.4%	Soyabeans	3.8%	Oranges	0.8%	
	45.1%	GEMS/Food G07	13.53	7.0%	Wheat	4.9%	Wine grapes	4.6%	Oranges	1.0%	
	42.1%	DK child	12.64	9.2%	Rye	7.7%	Apples	7.4%	Wheat	0.5%	
	40.1%	FR toddler 2 3 yr	12.02	10.6%	Apples	5.1%	Wheat	4.8%	Oranges	0.8%	
	36.7%	DE women 14-50 yr	11.02	8.6%	Apples	6.4%	Oranges	3.6%	Wheat	1.1%	
	36.4%	SE general	10.92	5.3%	Wheat	4.2%	Head cabbages	3.5%	Apples	0.8%	
	35.8%	UK infant	10.75	5.2%	Apples	4.4%	Wheat	4.3%	Oranges	0.9%	
	35.6%	PT general	10.69	8.3%	Wine grapes	6.5%	Wheat	3.5%	Apples	0.9%	

	35.4%	UK toddler	10.61	6.6%	Oranges	6.5%	Wheat	5.7%	Apples	1.2%	
	34.4%	DE general	10.33	8.1%	Apples	5.2%	Oranges	3.1%	Wheat	1.0%	
	33.7%	ES child	10.11	7.4%	Wheat	7.2%	Oranges	3.8%	Apples	0.4%	
	29.1%	NL general	8.73	4.9%	Apples	3.4%	Oranges	3.2%	Wheat	1.0%	
	28.4%	IT toddler	8.51	11.1%	Wheat	3.0%	Apples	2.4%	Tomatoes	0.4%	
	26.5%	FR adult	7.96	7.7%	Wine grapes	3.7%	Wheat	2.6%	Apples	0.4%	
	24.9%	FI 3 yr	7.47	3.1%	Apples	2.2%	Bananas	2.0%	Wheat	0.8%	
	24.3%	ES adult	7.29	4.3%	Oranges	3.9%	Wheat	2.6%	Apples	0.2%	
	22.5%	IT adult	6.75	6.9%	Wheat	2.6%	Apples	1.9%	Tomatoes	0.2%	
	21.3%	UK vegetarian	6.39	3.4%	Wheat	2.9%	Oranges	2.7%	Wine grapes	0.3%	
	19.5%	FR infant	5.85	5.6%	Apples	1.9%	Carrots	1.8%	Cauliflowers	0.6%	
	18.8%	FI 6 yr	5.65	1.9%	Apples	1.6%	Wheat	1.3%	Bananas	0.7%	
	18.4%	DK adult	5.53	3.2%	Apples	3.2%	Wine grapes	1.9%	Wheat	0.2%	
	18.2%	PL general	5.47	6.8%	Apples	2.4%	Head cabbages	1.5%	Tomatoes	0.6%	
	18.0%	LT adult	5.40	6.2%	Apples	2.7%	Head cabbages	1.8%	Rye	0.6%	
	17.6%	UK adult	5.29	3.6%	Wine grapes	2.8%	Wheat	1.9%	Oranges	0.3%	
	14.2%	FI adult	4.26	1.9%	Apples	1.4%	Oranges	1.2%	Rye	1.1%	
	6.4%	IE child	1.92	1.9%	Wheat	1.1%	Apples	0.5%	Rice	0.1%	
	Conclusion: The estimated TMDI/NEDI/IEDI was in the range of 0 % to 126.5 % of the ADI. For 1 diet(s) the ADI is exceeded.										

Table B.3 Chronic risk assessment undertaken using UK model version 1.1 – scenario 2

Active substance: Hexythiazox **ADI:** 0.03 mg/kg bw/day **Source:** EFSA 2010

	TOTAL INTAKE based on 97.5th percentile									
	ADULT	**INFANT**	**TODDLER**	**4-6 YEARS**	**7-10 YEARS**	**11-14 YEARS**	**15-18 YEARS**	**VEGETARIAN**	**ELDERLY (OWN HOME)**	**ELDERLY (RESIDENTIAL)**
mg/kg bw/day	0.01689	0.02572	0.02261	0.01842	0.01226	0.01078	0.01098	0.01889	0.01478	0.00775
% of ADI	56%	86%	75%	61%	41%	36%	37%	63%	49%	26%

Commodity	**STMR (mg/kg)**	**P**	**COMMODITY INTAKES (mg/kg bw/day)**									
Grapefruit	0.077		0.00015	0.00012	0.00045	0.00041	0.00089	0.00016	0.00011	0.00018	0.00019	0.00015
Lemons	0.077		0.00001	0.00005	0.00002	0.00001	0.00001	0.00001	0.00001	0.00002	0.00003	0.00001
Limes	0.077		0.00002	L/C	0.00013	0.00002	0.00001	0.00001	0.00002	0.00002	0.00003	0.00004
Mandarins	0.077		0.00011	L/C	0.00049	0.00028	0.00023	0.00012	0.00013	0.00009	0.00012	0.00005
Oranges	0.077		0.00030	0.00083	0.00126	0.00086	0.00064	0.00061	0.00051	0.00035	0.00028	0.00021
Almonds	0.5		0.00005	0.00022	0.00010	0.00008	0.00006	0.00004	0.00005	0.00005	0.00005	0.00002
Brazil nuts	0.5		0.00007	L/C	0.00010	0.00008	0.00007	0.00003	0.00002	0.00006	0.00005	L/C
Cashew nuts	0.5		0.00008	L/C	0.00026	0.00009	0.00001	0.00003	0.00002	0.00009	0.00011	0.00001
Chestnuts	0.5		0.00007	L/C	L/C	L/C	L/C	L/C	0.00002	0.00013	0.00008	L/C
Coconuts	0.5		0.00007	0.00005	0.00016	0.00013	0.00009	0.00009	0.00007	0.00019	0.00005	0.00004
Hazelnuts	0.5		0.00005	L/C	0.00011	0.00005	0.00007	0.00003	0.00004	0.00003	0.00003	0.00001
Pecan nuts	0.5		0.00003	L/C	0.00002	L/C	0.00001	0.00004	L/C	0.00018	0.00005	L/C
Pistachios	0.5		0.00019	L/C	0.00017	L/C	0.00012	L/C	L/C	0.00006	L/C	L/C
Walnuts	0.5		0.00006	L/C	0.00021	0.00003	0.00004	0.00003	0.00005	0.00008	0.00009	0.00003
Peanuts	0.5		0.00020	0.00030	0.00054	0.00040	0.00029	0.00033	0.00016	0.00022	0.00020	0.00004

Apples	0.11		0.00029	0.00093	0.00164	0.00104	0.00083	0.00045	0.00039	0.00037	0.00024	0.00012
Pears	0.11		0.00015	0.00028	0.00072	0.00040	0.00024	0.00020	0.00016	0.00021	0.00025	0.00013
Apricots	1		0.00037	0.00134	0.00103	0.00062	0.00042	0.00037	0.00022	0.00076	0.00044	0.00037
Peaches	1		0.00136	0.00134	0.00314	0.00158	0.00117	0.00076	0.00045	0.00094	0.00093	0.00043
Plums	0.5		0.00046	0.00024	0.00108	0.00068	0.00039	0.00014	0.00012	0.00035	0.00033	0.00010
Cherries	1		0.00047	0.00143	0.00105	0.00151	0.00055	0.00071	0.00059	0.00052	0.00035	0.00008
Table grapes	1		0.00132	0.00166	0.00470	0.00216	0.00259	0.00110	0.00063	0.00204	0.00133	0.00046
Wine grapes	1		0.00984	0.00122	0.00089	0.00091	0.00032	0.00101	0.00353	0.00972	0.00665	0.00146
Strawberries	0.54		0.00032	0.00104	0.00108	0.00073	0.00048	0.00037	0.00027	0.00052	0.00055	0.00028
Blackberries	1.04		0.00012	L/C	0.00202	0.00007	0.00034	0.00026	0.00010	0.00032	0.00027	0.00004
Loganberries	1		0.00008	0.00060	0.00113	0.00017	0.00050	0.00025	0.00016	0.00022	0.00016	0.00010
Raspberries	1.04		0.00043	L/C	0.00247	0.00068	0.00105	0.00027	0.00007	0.00042	0.00087	0.00039
Gooseberries	0.5		0.00012	0.00026	0.00033	0.00012	0.00012	0.00012	0.00009	0.00036	0.00041	0.00012
Blackcurrants	0.5		0.00029	0.00059	0.00090	0.00090	0.00069	0.00051	0.00056	0.00018	0.00027	0.00014
Red currants	0.5		0.00004	L/C	0.00039	L/C	0.00003	0.00006	0.00002	0.00002	0.00017	L/C
White currants	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Avocados	0.5		0.00039	L/C	0.00063	L/C	L/C	L/C	0.00016	0.00034	0.00026	L/C
Bananas	0.5		0.00103	0.00348	0.00332	0.00224	0.00173	0.00103	0.00073	0.00107	0.00082	0.00091
Dates	0.26		0.00006	L/C	0.00010	0.00012	0.00004	0.00001	L/C	0.00012	0.00018	0.00006
Figs	0.5		0.00015	0.00019	0.00020	0.00006	0.00009	0.00002	0.00003	0.00033	0.00010	0.00003
Kiwi fruit	1		0.00070	L/C	0.00231	0.00201	0.00118	0.00093	0.00231	0.00122	0.00054	0.00015
Lychees	0.5		0.00017	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Mangoes	0.5		0.00034	L/C	0.00081	0.00070	0.00088	0.00029	0.00182	0.00027	0.00008	L/C
Olives	0.5		0.00013	L/C	0.00030	0.00030	L/C	0.00003	L/C	0.00010	0.00022	L/C
Passion fruit	0.5		0.00007	L/C	L/C	L/C	L/C	L/C	L/C	0.00011	L/C	L/C
Pineapples	0.5		0.00058	0.00259	0.00236	0.00338	0.00122	0.00073	0.00052	0.00058	0.00038	0.00031

Pomegranates	0.5		0.00060	0.00028	0.00041	0.00021	0.00025	0.00028	0.00001	0.00027	0.00031	0.00050
Beetroot	0.5		0.00019	L/C	0.00075	0.00020	0.00016	0.00017	0.00012	0.00024	0.00025	0.00009
Carrots	0.5		0.00035	0.00176	0.00123	0.00095	0.00061	0.00042	0.00049	0.00044	0.00048	0.00039
Celeriac	0.5		0.00019	L/C	L/C	0.00002	0.00003	L/C	L/C	L/C	L/C	L/C
Horseradish	0.5		0.00001	L/C	L/C	L/C	L/C	L/C	L/C	L/C	0.00001	L/C
Jerusalem artichokes	0.5		0.00008	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Parsnips	0.5		0.00016	0.00046	0.00059	0.00036	0.00025	0.00020	0.00013	0.00021	0.00031	0.00014
Radishes	0.5		0.00016	L/C	0.00049	L/C	0.00011	0.00006	0.00005	0.00015	0.00012	0.00005
Salsify	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Swedes	0.5		0.00024	0.00140	0.00086	0.00034	0.00039	0.00030	0.00023	0.00025	0.00033	0.00024
Turnips	0.5		0.00017	L/C	0.00049	0.00044	0.00028	0.00028	0.00017	0.00008	0.00031	0.00020
Yam	0.5		0.00146	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Garlic	0.5		0.00003	L/C	0.00003	0.00005	0.00007	0.00004	0.00006	0.00007	0.00007	L/C
Onions	0.5		0.00026	0.00056	0.00056	0.00046	0.00039	0.00037	0.00025	0.00036	0.00027	0.00015
Spring onions	0.5		0.00013	L/C	0.00008	0.00033	0.00009	0.00004	0.00005	0.00013	0.00013	0.00004
Tomatoes	0.5		0.00069	0.00091	0.00132	0.00096	0.00092	0.00054	0.00067	0.00088	0.00073	0.00067
Peppers	0.5		0.00018	L/C	0.00040	0.00020	0.00034	0.00016	0.00014	0.00030	0.00028	0.00009
Aubergines	0.5		0.00016	L/C	0.00077	0.00038	0.00013	0.00026	0.00019	0.00031	0.00020	L/C
Marrows	0.5		0.00025	L/C	0.00078	0.00020	0.00030	0.00032	0.00013	0.00026	0.00069	0.00032
Cucumbers	0.5		0.00020	0.00011	0.00121	0.00077	0.00052	0.00026	0.00023	0.00027	0.00024	0.00009
Gourd	0.5		0.00027	L/C	L/C	L/C	L/C	0.00013	L/C	0.00010	L/C	L/C
Courgettes	0.5		0.00021	0.00074	0.00119	0.00064	0.00039	0.00021	0.00019	0.00028	0.00026	0.00022
Melons	0.5		0.00124	0.00152	0.00262	0.00176	0.00152	0.00108	0.00138	0.00127	0.00149	0.00049
Sweet corn	0.5		0.00026	0.00051	0.00113	0.00054	0.00059	0.00025	0.00031	0.00028	0.00042	0.00017
Broccoli	0.5		0.00032	0.00057	0.00086	0.00061	0.00052	0.00036	0.00031	0.00034	0.00048	0.00017
Cauliflower	2		0.00174	0.00630	0.00434	0.00335	0.00171	0.00148	0.00171	0.00244	0.00227	0.00133

Brussels sprouts	5		0.00303	0.01167	0.00897	0.00729	0.00369	0.00463	0.00316	0.00397	0.00480	0.00231
Head cabbage	2		0.00109	0.00352	0.00341	0.00253	0.00150	0.00143	0.00106	0.00151	0.00232	0.00147
Chinese cabbage	0.5		0.00025	L/C	L/C	L/C	L/C	L/C	L/C	0.00025	0.00017	L/C
Kohl Rabi	1		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Cress	0.5		0.00002	L/C	0.00002	0.00003	0.00001	0.00002	0.00001	0.00004	0.00005	0.00002
Lettuce	0.5		0.00031	0.00018	0.00043	0.00034	0.00036	0.00020	0.00022	0.00035	0.00027	0.00014
Spinach	0.5		0.00026	0.00050	0.00078	0.00043	0.00044	0.00031	0.00017	0.00034	0.00028	0.00018
Watercress	0.5		0.00008	L/C	L/C	0.00003	0.00003	0.00009	L/C	0.00012	0.00015	L/C
Chicory	0.5		0.00004	L/C	L/C	L/C	L/C	L/C	L/C	0.00004	L/C	L/C
Parsley	0.5		0.00008	L/C	0.00006	L/C	0.00008	0.00002	0.00001	0.00009	0.00009	0.00018
Beans with pods	0.5		0.00026	0.00060	0.00096	0.00066	0.00033	0.00018	0.00035	0.00020	0.00036	0.00016
Runner Beans	0.5		0.00031	L/C	0.00074	0.00025	0.00037	0.00029	0.00025	0.00076	0.00049	0.00028
Beans without pods	0.5		0.00022	0.00029	0.00120	0.00019	0.00053	0.00019	0.00021	0.00032	0.00040	0.00026
Peas with pods	0.5		0.00014	L/C	0.00023	0.00063	0.00011	0.00014	0.00008	0.00013	0.00026	L/C
Peas without pods	0.5		0.00039	0.00120	0.00102	0.00070	0.00051	0.00037	0.00046	0.00044	0.00050	0.00036
Beansprouts	0.5		0.00020	L/C	0.00045	0.00028	0.00028	0.00018	0.00013	0.00019	0.00029	0.00012
Asparagus	0.5		0.00020	L/C	L/C	L/C	L/C	L/C	0.00011	0.00040	0.00022	L/C
Bamboo shoots	0.5		0.00008	L/C	0.00014	L/C	0.00003	0.00013	0.00003	0.00009	0.00005	L/C
Celery	0.5		0.00016	0.00021	0.00021	0.00014	0.00008	0.00013	0.00009	0.00023	0.00024	0.00006
Fennel	0.5		0.00019	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Globe artichokes	0.5		0.00016	L/C	L/C	L/C	L/C	L/C	L/C	0.00010	L/C	L/C
Leeks	0.5		0.00025	L/C	0.00032	0.00018	0.00015	0.00018	0.00011	0.00024	0.00029	0.00018
Rhubarb	0.5		0.00020	0.00036	0.00055	0.00012	0.00025	0.00007	0.00008	0.00017	0.00034	0.00020
Cultivated mushrooms	0.5		0.00020	0.00025	0.00053	0.00025	0.00020	0.00015	0.00021	0.00033	0.00021	0.00015
Beans	0.5		0.00078	0.00295	0.00236	0.00168	0.00143	0.00105	0.00106	0.00088	0.00070	0.00049
Lentils	0.5		0.00036	0.00072	0.00092	0.00098	0.00032	0.00062	0.00025	0.00035	0.00025	0.00012

dried Peas	0.5		0.00034	L/C	0.00087	0.00023	0.00037	0.00060	0.00032	0.00029	0.00053	0.00036
Oilseeds	0.5		0.00159	0.00315	0.00362	0.00358	0.00280	0.00202	0.00176	0.00234	0.00160	0.00193
Potatoes	0.05		0.00016	0.00056	0.00046	0.00041	0.00035	0.00027	0.00023	0.00018	0.00016	0.00016
Tea (dried leaves)	4.55		0.00097	0.00324	0.00119	0.00073	0.00054	0.00050	0.00062	0.00102	0.00095	0.00104
Hops (dried 0.25% of beer)	20		0.00124	L/C	L/C	L/C	L/C	0.00013	0.00110	0.00105	0.00124	0.00094
Oats	0.5		0.00018	0.00110	0.00061	0.00038	0.00023	0.00018	0.00032	0.00032	0.00026	0.00028
Barley	0.2		0.00005	L/C	0.00007	0.00007	0.00016	0.00004	0.00005	0.00005	0.00005	0.00003
Millet	0.5		L/C	L/C	0.00014	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Buckwheat	0.5		L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C	L/C
Maize	0.5		0.00003	0.00229	0.00036	0.00025	0.00009	0.00008	0.00009	0.00016	0.00007	0.00004
Wheat	0.5		0.00180	0.00140	0.00425	0.00444	0.00337	0.00249	0.00202	0.00213	0.00163	0.00173
Rice	0.5		0.00113	0.00140	0.00237	0.00186	0.00254	0.00196	0.00133	0.00100	0.00060	0.00024
Rye	0.5		0.00026	0.00068	0.00019	0.00022	0.00024	0.00013	0.00006	0.00030	0.00022	0.00008
Poultry	0.01		0.00002	0.00002	0.00003	0.00003	0.00002	0.00002	0.00002	0.00002	0.00002	0.00001
Meat fat	0.01		0.00000	0.00000	0.00001	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
Meat excl. poultry & offal	0.01		0.00002	0.00004	0.00004	0.00003	0.00003	0.00002	0.00002	0.00000	0.00002	0.00002
All types of kidney	0.05		0.00001	0.00002	0.00007	0.00002	0.00001	0.00001	0.00002	L/C	0.00002	0.00002
All types of Liver	0.05		0.00002	0.00011	0.00012	0.00002	0.00002	0.00003	0.00001	L/C	0.00003	0.00002
Other types of offal	0.01		0.00001	0.00002	0.00002	0.00001	0.00001	0.00001	0.00000	0.00000	0.00001	0.00001
Eggs	0.002		0.00000	0.00001	0.00001	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
Milk	0.01		0.00008	0.00098	0.00056	0.00029	0.00018	0.00012	0.00009	0.00010	0.00009	0.00012
Sugar beet	0.05		0.00070	0.00167	0.00279	0.00168	0.00157	0.00100	0.00096	0.00060	0.00053	0.00076

Table B.4 Chronic risk assessment undertaken using PRIMo revision 3.1 - scenario 2

Chronic risk assessment: JMPR methodology (IEDI/TMDI)												
				No of diets exceeding the ADI :	-- -						Exposure resulting from	
	Calculated exposure (% of ADI)	MS Diet	Exposure (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		MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	73.1%	NL toddler	21.94	11.7%	Maize/corn	9.0%	Bananas	6.6%	Wheat		1.8%	
	48.9%	GEMS/Food G06	14.66	12.1%	Wheat	6.0%	Tomatoes	3.5%	Table grapes		0.9%	
	44.4%	IE adult	13.33	5.9%	Sweet potatoes	4.2%	Wine grapes	3.8%	Wheat		0.4%	
	42.0%	DE child	12.59	7.0%	Wheat	4.6%	Apples	4.6%	Table grapes		0.5%	
	40.2%	GEMS/Food G15	12.06	7.6%	Wheat	5.5%	Head cabbages	3.4%	Wine grapes		0.9%	
	39.8%	RO general	11.94	9.6%	Head cabbages	8.4%	Wheat	5.6%	Wine grapes		0.8%	
	39.3%	GEMS/Food G08	11.80	6.8%	Wheat	3.5%	Wine grapes	3.3%	Soyabeans		1.0%	
	38.2%	GEMS/Food G10	11.47	6.5%	Wheat	5.4%	Soyabeans	2.8%	Head cabbages		0.8%	
	37.2%	GEMS/Food G11	11.15	6.2%	Soyabeans	6.0%	Wheat	3.4%	Wine grapes		1.2%	
	36.8%	NL child	11.03	6.9%	Wheat	3.4%	Table grapes	3.2%	Bananas		2.1%	
	36.6%	GEMS/Food G07	10.99	7.0%	Wheat	4.9%	Wine grapes	3.0%	Soyabeans		1.0%	
	32.3%	DK child	9.70	9.2%	Rye	7.4%	Wheat	2.7%	Cucumbers		0.4%	
	29.8%	FR child 3 15 yr	8.94	7.7%	Wheat	1.4%	Tomatoes	1.4%	Cauliflowers		0.9%	
	29.2%	PT general	8.75	8.3%	Wine grapes	6.5%	Wheat	1.5%	Tomatoes		0.9%	
	28.1%	SE general	8.44	5.3%	Wheat	4.2%	Head cabbages	3.0%	Bananas		0.7%	

	27.0%	UK infant	8.09	4.4%	Wheat	3.1%	Brussels sprouts	2.4%	Bananas	0.8%	
	23.1%	FR adult	6.94	7.7%	Wine grapes	3.7%	Wheat	2.1%	Tea (dried leaves of Camellia sinensis)	0.3%	
	23.1%	UK toddler	6.92	6.5%	Wheat	1.8%	Bananas	1.3%	Beans	1.1%	
	22.7%	FR toddler 2 3 yr	6.80	5.1%	Wheat	1.6%	Cauliflowers	1.3%	Beans (with pods)	0.8%	
	22.5%	IT toddler	6.74	11.1%	Wheat	2.4%	Tomatoes	1.2%	Peaches	0.4%	
	21.9%	DE women 14-50 yr	6.56	3.6%	Wheat	2.8%	Wine grapes	1.2%	Tomatoes	1.0%	
	21.8%	ES child	6.53	7.4%	Wheat	1.7%	Bananas	1.6%	Tomatoes	0.3%	
	21.2%	DE general	6.37	3.1%	Wheat	2.8%	Wine grapes	1.1%	Tomatoes	1.0%	
	20.7%	NL general	6.22	3.2%	Wheat	2.0%	Wine grapes	1.3%	Cauliflowers	1.0%	
	20.0%	FI 3 yr	6.00	2.2%	Bananas	2.0%	Wheat	1.7%	Cucumbers	0.8%	
	17.7%	IT adult	5.30	6.9%	Wheat	1.9%	Tomatoes	1.3%	Peaches	0.2%	
	16.7%	UK vegetarian	5.02	3.4%	Wheat	2.7%	Wine grapes	1.0%	Tomatoes	0.3%	
	16.6%	ES adult	4.97	3.9%	Wheat	1.4%	Wine grapes	1.3%	Tomatoes	0.2%	
	15.1%	FI 6 yr	4.54	1.6%	Wheat	1.3%	Bananas	1.2%	Cucumbers	0.7%	
	14.7%	UK adult	4.42	3.6%	Wine grapes	2.8%	Wheat	0.8%	Tea (dried leaves of Camellia sinensis)	0.3%	
	13.9%	DK adult	4.16	3.2%	Wine grapes	1.9%	Wheat	0.9%	Rye	0.2%	
	12.7%	FR infant	3.81	1.9%	Carrots	1.8%	Cauliflowers	1.3%	Wheat	0.5%	
	11.7%	LT adult	3.51	2.7%	Head cabbages	1.8%	Rye	1.8%	Wheat	0.5%	
	11.0%	PL general	3.29	2.4%	Head cabbages	1.5%	Tomatoes	1.1%	Table grapes	0.6%	
	10.6%	FI adult	3.19	1.2%	Rye	1.0%	Wine grapes	0.9%	Coffee beans	1.1%	
	5.2%	IE child	1.55	1.9%	Wheat	0.5%	Rice	0.3%	Bananas	0.1%	

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

Appendix C - Detailed evaluation of the additional studies relied on

C.1 Methods of analysis

C.1.1 Methods for enforcement and monitoring of residues in food and feed of plant origin

C.1.1.1 Method validation

No new studies evaluated in this application.

C.1.1.2 Independent laboratory validation of Method B1310/B1308

Reference: Independent Laboratory Validation of the Analytical Method for the Determination of Residues of Hexythiazox in Foodstuffs of Plant origin, [redacted] 2015, Study No S15-0261

GLP: Yes

Acceptability of the method: Acceptable

Principle of the method

No significant deviations to the method principles in methods B1310/B1308 was noted. Samples of apple (fruit) and grape (bunches) were analysed. Differences in chromatographic parameters were related to different manufacturers for the HPLC-MS/MS system and column. These differences do not impact the acceptability of the ILV.

Method B1310/B1308 has been previously evaluated in the confirmatory data for approval of the active substance (FI, 2014). A summary of this method is provided below:

10 g of blended sample were weighed into a 50 mL centrifuge tube and spiked if necessary. 10 mL of Acetonitrile / 0.1 % acetic acid was added and shaken. 4 g magnesium sulphate and 1 g NaCl were added and the whole sample was shaken and centrifuged. After complete separation of the phases, the supernatant was filtered and 1.0

mL was transferred into a vial containing 40 µL of the triphenyl phosphate 2.5 µg/mL + 2.5% formic acid solution. The vial was homogenised prior to LC-MS/MS analysis.

The analysis was performed using the following LC-MS/MS conditions:

Table C.1.1.2-1 Analytical conditions of method

HPLC-MS/MS System	Method B1310/B1308: WATERS XEVO-TQMS LC/MS/MS (orange matrices) or WATERS Quattro-Premier (grape matrices) ILV: Agilent 1290 Infinity Binary LC System		
Column	Waters BEH C18, 50 mm x 2.1 mm, 1.7 µm particle size		
Column temperature	40 °C		
Sample temperature	15 °C		
Injection volume	10 µL		
Mobile phase	A: Water + 0.1% formic acid B: Methanol + 0.1% formic acid		
Gradient	Time (min)	Mobile phase A (%)	Mobile phase B (%)
	0.00	90	10
	2.00	0	100
	3.20	0	100
	3.25	90	10
	4.00	90	10
Flow rate	0.4 mL/min		
Retention time	Hexythiazox approx. 2.5 min PT-1-3 approx. 2.0 min. TPP approx. 2.3 min		

Ionisation mode	ESI
Source polarity	Turbo Ion Spray, positive
Acquisition mode	MS/MS
Curtain gas	30 units
Collision energy	15 - 27 units
Dwell time	20 ms
Ions monitored	m/z 353.1→228.0 (quantification for hexythiazox) m/z 353.1→168.0 (confirmation for hexythiazox) m/z 228.0→168.0 (quantification for PT-1-3) m/z 228.0→115.0 (confirmation for PT-1-3) m/z 228.0→151.0 (confirmation for PT-1-3) m/z 327.0→215.0 (quantification for TPP)

Results and discussion

Table C.1.1.2-2 ILV recovery results for hexythiazox and PT-1-3 in apple and grape

Analyte	**Matrix**	**Ion transition**	**Fortification level (mg/kg)**	**No samples per level**	**Range of recoveries (%) (mean)**	**RSD (%)**
Hexythiazox	Apple	353 → 228 Quantification	0.01	5	97 – 109 (105)	4.6
			0.1	5	100 – 108 (105)	3.2
		353 → 168	0.01	5	97 – 107 (101)	4.0

Analyte	Matrix	Ion transition	Fortification level (mg/kg)	No samples per level	Range of recoveries (%) (mean)	RSD (%)
		Qualification	0.1	5	98 – 113 (104)	5.8
	Grape	353 → 228	0.01	5	87 – 104 (93)	7.0
		Quantification	0.1	5	88 – 97 (92)	3.7
		353 → 168	0.01	5	86 – 98 (89)	5.9
		Qualification	0.1	5	83 – 91 (86)	3.6
PT-1-3	Apple	228 → 116	0.01	5	80 – 88 (84)	3.6
		Quantification	0.1	5	81 – 89 (86)	3.6
		228 → 115	0.01	5	81 – 86 (84)	3.1
		Qualification	0.1	5	79 – 91 (87)	5.3
	Grape	228 → 116	0.01	5	98 – 103 (100)	2.7
		Quantification	0.1	5	93 – 98 (95)	1.9
		228 → 115	0.01	5	97 – 108 (103)	4.8
		Qualification	0.1	5	93 – 98 (95)	2.0

The analytical recovery of the method was determined by comparing analysed and nominal concentrations from the recovery experiments.

The spike concentrations were in the range 0.01 to 0.1 mg/kg (LOQ and 10 x LOQ). Five samples were prepared at each fortification level. Mean recovery levels were within the range 84 - 105% and are acceptable. The % RSD at each fortification level was < 20%.

Table C.1.1.2-3 Characteristics of ILV of the analytical method B1310/B1308 for the quantitation of hexythiazox residues in apple and grape

	Hexythiazox
Chromatographic method	HPLC-MS/MS
Specificity demonstrated (yes/no, by…)	Yes - Specificity was demonstrated by retention time match with a control sample. Two ions were monitored with a m/z ratio greater than 100. The method is highly specific therefore no confirmatory technique required

	Hexythiazox
Linearity demonstrated (yes/no)	Yes <u>Apple</u> Hexythiazox: Quantifier mass transition: y = 0.0139x – 0.0062, r ≥ 0.9997 Qualifier mass transition: y = 0.0077x – 0.0037, r ≥ 0.9996 PT-1-3: Quantifier mass transition: y = 0.0234x – 0.0187, r ≥ 0.9994 Qualifier mass transition: y = 0.0053x – 0.0015, r ≥ 0.9993 <u>Grape</u> Hexythiazox: Quantifier mass transition: y = 0.0198x – 0.0021, r ≥ 0.9998 Qualifier mass transition: y = 0.0114x + 0.0003, r ≥ 0.9997 PT-1-3: Quantifier mass transition: y = 0.0232x – 0.0057, r ≥ 0.9991 Qualifier mass transition: y = 0.0052x + 0.00, r ≥ 0.9997
Accepted calibration range in concentration units (e.g. in µg/ml or ng/µl)	3.0 – 120 µg/L, equivalent to 0.003 – 0.12 mg/kg hexythiazox in apple and grape samples

	Hexythiazox
Calibration consist of at least 3 levels (duplicated points) or 5 levels (single points)? (yes/no)	Yes – seven single points
Matrix effects	Matrix effects for hexythiazox were significant (> 20%). Therefore, matrix-matched standards were used for the quantification of hexythiazox in apple and grape. Matrix effects for PT-1-3 were found to be insignificant. However, matrix-matched standards were used.
Absence of interference >30% of LOQ in blank sample is demonstrated (yes/no)	Analysis of a reagent blank and unfortified control samples demonstrated no significant interference (> 30% of the sample fortified at the LOQ), at the retention time of interest.
Chromatogram of sample spiked at LOQ demonstrates sufficient S/N ration? (yes/no)	Yes
LOQ (mg/kg)	0.01

Conclusion

No deviation to the original method described in the confirmatory data for approval of the active substance (FI, 2014) is shown. The ILV for methods B1310/B1308 for analysis of hexythiazox and PT-1-3 in high water (apple) and high acid (grape) matrices using HPLC-MS/MS fulfils the requirements with regard to linearity, specificity, repeatability, limit of quantification and recoveries. The ILV is satisfactorily validated in accordance with SANTE 2020/12830 rev.1.

C.1.1.3 Extraction efficiency of the monitoring method B1310/B1308

Reference:	Hexythiazox: Cross Validation of Analytical Methods for the Determination of Hexythiazox in incurred Crop Commodities [Apple, Strawberry and Grape], [redacted] 2021, Study No: UP/19/003
GLP:	Yes
Acceptability of the method:	Acceptable

Method

As the solvent used in the metabolism studies (aqueous methanol followed by chloroform), was different to the one used in the monitoring methods validated in reports B1310 and B1308 (acetonitrile/acetic acid, 99.9/0.1), a cross-validation was performed. The solvent systems compared in this study were acetonitrile/acetic acid 99.9:0.1% and methanol/water (80/20).

The cross-validation study compared the amount of hexythiazox (mg/kg) found following extraction using the metabolism method for the approval of the active, to the amount of hexythiazox found using enforcement methods B1310 and B1308, to extract grape, strawberry and apple samples containing incurred residues. Three incurred samples per matrix, taken from field studies where the test item Hexythiazox 250 SC was previously applied at exaggerated application rate, were extracted using both methodologies.

Samples were extracted using a solvent mixture representative for the crop metabolism studies (methanol/water 80/20) and the solvents from the proposed monitoring methods (acetonitrile/acetic acid, 99.9/0.1). Residues of hexythiazox were determined by HPLC-MS/MS in high acid matrices (grapes and strawberry) and high water matrices (apples).

A non-GLP analysis of PT-1-3 was generated alongside this study.

For the residue monitoring method, hexythiazox was extracted from each matrix by shaking in acetonitrile/acetic acid 99.9:0.1% solution. 4g of magnesium sulphate and 1g of NaCl was added to the extract and shaken. Following the separation of the phases, the supernatant was filtered and transferred into a vial containing triphenyl phosphate (2.5 µg/mL) + 2.5% formic acid, for final determination by liquid chromatography with tandem mass spectrometry (LC-MS/MS), monitoring two ion mass transitions.

For the plant metabolism method, hexythiazox was extracted from each matrix by shaking in methanol/water (80/20) solution. The phases were separated through centrifugation. Following the separation of the phases, the supernatant was filtered and transferred into a

vial containing triphenyl phosphate (2.5 µg/mL) + 2.5% formic acid, for final determination by liquid chromatography with tandem mass spectrometry (LC-MS/MS), monitoring two ion mass transitions.

Results and discussions

In the crop metabolism studies presented for approval, the %TRR recovered after 56 – 60 days from treatment was > 90 %TRR in apples, grapes, pears, and 84% TRR for citrus fruit. A comparison between the amount of hexythiazox found when extracted using a solvent mixture representative for the crop metabolism studies, (methanol/water 80/20) or solvents from the monitoring methods, (acetonitrile/acetic acid 99.9/0.1), is presented in the table below. The data shows that extraction efficiency was at least 76.7% across high acid and high water commodity groups. As the residue results for extraction efficiency is demonstrated to be above 70% and hence do not differ by > 30%, the extraction efficiency of the monitoring method has been sufficiently addressed.

Table C.1.1.3-1 Comparison of extraction efficiency between the metabolism method for approval of the active and the monitoring method B1310/B1308

Matrix	**Metabolism method**	**Monitoring method B1310/B1308**	**Extraction efficiency[(a)]**
	Residues (mg/kg) (mean)	**Residues (mg/kg) (mean)**	
Grape	2.69, 1.79, 2.68 (2.39)	2.41, 2.15, 2.25 (2.27)	95.0
Strawberry	0.235, 0.694, 0.656 (0.528)	0.219, 0.491, 0.506 (0.405)	76.7
Apple	0.468, 0.410, 0.373 (0.417)	0.462, 0.498. 0.482 (0.481)	115

[(a)] Extraction efficiency calculated based on the ratio of mean residues from monitoring method / mean residues from metabolism method.

Conclusion

It can be concluded that methods B1310/B1308 effectively extract hexythiazox from grape and orange (high acid commodities). Extraction efficiency has been sufficiently addressed in accordance with SANTE/2017/10632 rev.3.

C.1.2 Methods for enforcement and monitoring of residues in food and feed of animal origin

No additional studies submitted.

C.1.3 Methods for risk assessment for residues in food and feed of plant origin

C.1.3.1 Method used in study report TCI-18-597 (raspberry residue trials)

Reference:	Magnitude of the Residue of Hexythiazox in or on Raspberry Raw Agricultural Commodities Following One Foliar Application of Onager Optek™ Miticide or Savey® 50 DF Ovicide/Miticide (2018), [redacted] 2018, Study No: TCI-18-597, GPL Study No: 180776
GLP:	Yes
Acceptability of the method:	Acceptable

Principle of the method

Approximately 3 g of homogenous raspberry sample were weighed into 250 mL bottles. Samples were extracted by adding 36 mL of water and letting the samples soak for 30 minutes. After soaking, 84 mL of methanol was added to each sample, and the samples were blended. Samples were centrifuged and filtered by vacuum. The remaining solids were re-extracted with 80 mL of methanol/water (70:30, v/v) and shaken by hand to break up the matrix. The entire sample was filtered and the solids were added to the filter cake.

The combined extract was brought to a final volume of 200 mL using methanol and mixed. Samples were evaporated to remove the methanol with nitrogen in a water bath set to 35 ºC. The sample was reconstituted to 3.5 mL with water and 3.5 mL of 0.5 N sodium hydroxide (aq.) was added to each sample. The samples were placed in a water bath set at 60 °C and incubated for 30 minutes, converting the hexythiazox residues to PT-1-3 residues (a more stable metabolite). The samples were allowed to cool to an ambient temperature.

Once cooled, 3.2 mL of 0.5 N hydrochloric acid (aq.) was added to each sample, and the pH was adjusted to pH 6 using 0.5 N hydrochloric acid (aq.). The sample was loaded onto a SPE column (C18 3 mL, 200 mg). The column was washed with 9 mL of water then drained using vacuum.

Residues of PT-1-3 were eluted from the SPE column with 2 mL of acetonitrile. High vacuum was applied to collect the remainder of the liquid. The eluate was brought to a final volume of 9 mL with water. The cleaned extracts were vialed for analysis by LC-MS/MS for the determination of PT-1-3 residues. All values were reported are given as hexythiazox molar equivalents (determined by molecular weight of hexythiazox / PT-1-3 to give conversion factor of 1.55).

Samples requiring further dilutions were diluted with acetonitrile/water (25:75, v/v) so that the concentration fell within the range of the calibration curve.

The analysis was performed using the following LC-MS/MS conditions:

Table C.1.3.1-1 Analytical conditions of method

HPLC-MS/MS System	Sciex API5000 LC/MS/MS		
Column	Phenomenex Luna Phenyl-Hexyl, 150 mm x 4.6 mm, 3.0 µm particle size		
Column temperature	40 °C		
Injection volume	10 µL		
Mobile phase	A: Acetonitrile B: 10 mM ammonium formate in water		
Gradient	Time (min)	Mobile phase A (%)	Mobile phase B (%)
	0.00	25	75
	6.00	95	5
	9.00	95	5
	9.10	25	75
	10.50	25	75
Flow rate	600 µL/min		
Retention time	PT-1-3 approx. 7.33 min		
Interface and source polarity	Turbo Ion Spray, positive		

Acquisition mode	MRM
Curtain gas	30 units
Collision gas	5 units
Ion spray voltage	4500 V
GS1	40 units
GS2	40 units
Ions monitored	m/z 228→168 (quantification)

Results and discussion

Table C.1.3.1-2 Recovery Results in raspberries

Matrix	**Fortification level (mg/kg)**	**No samples per level**	**Range of recoveries (%)**	**Mean recovery (%)**	**RSD (%)**
Raspberry	0.02	3	86 - 87	86	0.67
	1.0	3	88 - 93	91	2.7

The analytical recovery of the method was determined by comparing analysed and nominal concentrations from the recovery experiments.

The spike concentrations were in the range 0.02 to 1.0 mg/kg. Three samples were prepared at each fortification level which does not meet the minimum required samples in accordance with SANTE/2020/12830 rev.1. The individual recovery values and the mean recovery levels were within the range 86 - 93 % and the % RSD at each fortification level was < 20%.

Procedural recoveries were performed for this method through concurrent analysis of freshly fortified control samples along with field samples in study report TCI-18-597. This shows that the method demonstrated acceptable recoveries during the residue study. The additional procedural recoveries and %RSD data provide further confidence in the method

validation and confirms the method is fit for purpose. A summary of the procedural recovery data is shown below:

Table C.1.3.1-3 Concurrent recovery results in raspberries

Matrix	Fortification level (mg/kg)	No samples per level	Range of recoveries (%)	Mean recovery (%)	RSD (%)
Raspberry	0.02	3	90 - 99	95	4.9
	1.0	1	87	87	N/A
	2.0	2	85 - 89	87	6.2

Table C.1.3.1-4 Characteristics of the analytical method for the quantitation of hexythiazox residues in raspberries

	Hexythiazox
Chromatographic method	HPLC-MS/MS
Specificity demonstrated (yes/no, by…)	Yes - Specificity was demonstrated by retention time match with a raspberry fortified control sample. Only one ion transition was monitored with a m/z ratio greater than 100. However, confirmation is not a requirement for methods for risk assessment for residues.
Linearity demonstrated (yes/no)	Yes demonstrated across the range 0.125 – 5.00 ng/mL y = 19300x – 200, r ≥ 0.9998
Accepted calibration range in concentration units (e.g. in µg/ml or ng/µl)	0.125 – 5.00 ng/mL (equivalent to 0.001 – 0.388 mg/kg hexythiazox. If necessary samples can be diluted further with acetonitrile/water (25:75, v/v) so that the concentration falls within the range of the calibration curve)

	Hexythiazox
Calibration consist of at least 3 levels (duplicated points) or 5 levels (single points)? (yes/no)	Yes – six single points
Matrix effects	Not investigated At least one untreated control sample was analysed with each batch of samples analysed to demonstrate that there is no significant interference from the sample matrix or analytical reagents.
Absence of interference >30% of LOQ in blank sample is demonstrated (yes/no)	Analysis of unfortified control samples demonstrated no significant interference (> 30% of the sample fortified at the LOQ), at the retention time of interest.
Chromatogram of sample spiked at LOQ demonstrates sufficient S/N ration? (yes/no)	Yes
LOQ (mg/kg)	0.02 for hexythiazox (quantified as the PT-1-3 metabolite)

Extraction efficiency: The radiolabelled metabolism studies for the approval of the active generally used aqueous methanol and chloroform as extraction solvents. As only methanol or aqueous methanol was utilised in this method as an extraction solvent and not an aqueous methanol : chloroform solvent mixture, it cannot be concluded that extraction efficiency has been fully addressed. The lack of specific data to address the extraction efficiency is unlikely to impact the MRL calculated or the outcome of the consumer risk assessment. Therefore, no further data are required at this time.

Conclusion

The method included in Study ID 180776 (modification of method ‘Meth-220’) for analysis of hexythiazox determined as PT-1-3, fulfils the requirements with regards to linearity, specificity, matrix effects and limit of quantification. The limit of quantification is 0.02 mg/kg. With regards to recovery and repeatability, three samples were prepared at each fortification level which does not meet the minimum required samples in accordance with

SANTE/2020/12830 rev.1. However, additional acceptable procedural recovery data from study report TCI-18-597 confirms the method can be considered fit for purpose.

Therefore, the method included in Study ID 180776 was considered sufficiently validated for the purposes of the regulatory process in accordance with SANTE/2020/12830 Rev. 1.

C.1.3.2 Method used in study report R C0012 (raspberry processing study) and method used in study report RD-12169 and RD-12079 (cyclohexylamine storage stability studies)

Reference:	Validation of an Analytical Method for the Determination of Hexythiazox and Metabolites in Strawberry and Jam, [redacted] 2021, Study No: UP/20/002 Freezer Storage Stability of Hexythiazox and its Metabolites in Crop Matrices, [redacted] 2022, Study No. UP19004, Report No. RD-12169 Method validation and freezer storage stability testing of Hexythiazox and metabolites in oily matrix under frozen conditions (≤ -18 °C), [redacted] 2024, Study No. IF21-05915983, Report No. RD-12079
GLP:	Yes
Acceptability of the method:	Acceptable

Method UP/20/002 was used to determine residues of hexythiazox, PT-1-3 and cyclohexylamine in study report R C0012 for strawberry RAC (high acid commodity) and strawberry jam (high water commodity). A similar method (UP19001) was used in study report RD-12169 and study report RD-12079. Method UP19001 was used to determine residues of cyclohexylamine in spinach (high water commodity), dry haricot beans (high protein commodity), barley grain (high starch commodity), grape (high acid commodity) and sunflower seeds (high oil commodity). Study report UP19001 has not been submitted in the scope of this application but method validation is presented in report No RD-12169 and RD-12079 for dry haricot beans and sunflower seeds respectively. Due to the similarities in analytical methodologies, all method validation data to support studies R C0012, RD-12169 and RD-12079 has been summarised here.

Principle of the method

Strawberry RAC and Jam – low sugar

Approximately 10 g of homogenised sample was weighed in a 50 mL tube. 0.1% acetic acid in acetonitrile (15 mL) was added and the sample was shaken and centrifuged. The supernatant was decanted into a clean tube. The extraction was repeated with 0.1% acetic acid in acetonitrile: water (50:50 v/v, 7.5 mL) and water (7.5 mL). Supernatants were combined. The samples were made up to 40 mL using water and centrifuged. An aliquot of

the sample was filtered and 100 µL of the filtered sample was transferred into a HPLC vial containing 900 µL of water and shaken.

The sample concentration for hexythiazox is 0.125 ng/mL (0.005 mg/kg).

Jam – high sugar

Approximately 5 g of homogenised sample was weighed in a 50 mL centrifuge tube. 0.1% acetic acid in acetonitrile (7.5 mL) was added and the sample was shaken and centrifuged. The supernatant was decanted into a clean centrifuge tube. The extraction was repeated with 0.1% acetic acid in acetonitrile: water (50:50 v/v) (5.0 mL) and water (10.0 mL). Supernatants were combined. The samples were made up to 25 mL using water and centrifuged. An aliquot of the sample was filtered and 100 µL of the filtered sample was transferred into a HPLC vial containing 900 µL of water and shaken.

The sample concentration for hexythiazox is 0.1 ng/mL (0.005 mg/kg).

Dry haricot beans

Approximately 10 g of homogenised sample was weighed in a 50 mL tube. 0.1% acetic acid in acetonitrile (15 mL) was added and the sample was shaken and centrifuged. The supernatant was decanted into a clean tube. The extraction was repeated with 0.1% acetic acid in acetonitrile: water (50:50 v/v, 15 mL) and water (15 mL). Supernatants were combined. The samples were made up to 40 mL using water and centrifuged. An aliquot of the sample was filtered and 100 µL of the filtered sample was transferred into a HPLC vial containing 900 µL of water and shaken.

Sunflower seeds

Approximately 2 g of homogenised sample was weighed in a 50 mL tube. 0.1% acetic acid in acetonitrile (15 mL) was added and the sample was shaken and centrifuged. The supernatant was decanted into a clean tube. The extraction was repeated with 0.1% acetic acid in acetonitrile: water (50:50 v/v, 15 mL) and water (10 mL). Supernatants were combined. The samples were made up to 40 mL using water and centrifuged. An aliquot of the sample was filtered and 500 µL of the filtered sample was transferred into a HPLC vial containing 500 µL of water and shaken.

Final determination of the samples was performed by LC-MS/MS using the following conditions.

Table C.1.3.2-1 Analytical conditions of method for hexythiazox and PT-1-3

HPLC-MS/MS System	Agilent 1290 Infinity HPLC with AB Sciex QTrap 6500 AB Sciex QTRAP 5500 mass spectrometer and Shimadzu Exion LC AD UHPLC

Column	Chiralpak AS-RH, 150 mm x 4.6 mm, 5.0 µm particle size		
Column temperature	20 °C		
Injection volume	100 µL		
Mobile phase	A: Water B: 0.1% acetic acid in acetonitrile		
Gradient	Time (min)	Mobile phase A (%)	Mobile phase B (%)
	0.00	85	15
	2.00	70	30
	12.0	50	50
	17.0	20	80
	21.5	20	80
	21.6	85	15
	23.0	85	15
Flow rate	0.6 mL/min		
Retention time	(4S, 5S)-Hexythiazox approx. 20.50 min (4R, 5R)-Hexythiazox approx. 20.90 min (4S, 5S)-PT-1-3 approx. 18.90 min (4R, 5R)-PT-1-3 approx. 18.10 min		
Ionisation mode	ESI		
Interface and source polarity	Turbo Ion Spray, positive		
Scan type	MRM		
Curtain gas	20 units		

Collision gas	-2.00 units
Ion spray voltage	4000 V
GS1	50 units
GS2	60 units
Ions monitored	m/z 353→228 (quantification for hexythiazox) m/z 353→168 (confirmation for hexythiazox) m/z 228→168 (quantification for PT-1-3) m/z 228→116 (confirmation for PT-1-3)

Table C.1.3.2-2 Analytical conditions of method for cyclohexylamine

HPLC-MS/MS System	Agilent 1290 Infinity HPLC with AB Sciex Qtrap 6500 AB Sciex QTRAP 5500 mass spectrometer and Shimadzu Exion LC AD UHPLC		
Column	Phenomenex, Kinetex PFP 100A, 75 mm x 4.6 mm, 2.6 µm particle size		
Column temperature	40 °C		
Injection volume	20 µL		
Mobile phase	A: Water B: 0.1% acetic acid in acetonitrile		
Gradient	Time (min)	Mobile phase A (%)	Mobile phase B (%)
	0.00	70	30
	3.00	50	50
	5.00	50	50
	8.00	70	30
Flow rate†	0.7 mL/min		

Retention time	Cyclohexylamine approx. 3.55 min

† For analysis of sunflower seeds (high oil commodity), a flow rate of 1.5 mL/min was used

MS conditions for strawberry, jam-low sugar, jam – high sugar and dry haricot beans:

Ionisation mode	ESI
Interface and source polarity	Turbo Ion Spray, positive
Scan type	MRM
Curtain gas	20 units
Collision gas	-2.00 units
Ion spray voltage	4000 V
GS1	50 units
GS2	50 units
Ions monitored	m/z 100→83 (quantification for cyclohexylamine) m/z 100→55 (confirmation for cyclohexylamine)

MS conditions for sunflower seeds

Ionisation mode	ESI
Interface and source polarity	Turbo Ion Spray, positive
Scan type	MRM
Curtain gas	45 psig
Collision gas	9 psig
Ion spray voltage	5500 V
Ions monitored	m/z 100→83 (quantification for cyclohexylamine) m/z 100→55 (confirmation for cyclohexylamine)

Results and discussion

Table C.1.3.1-3 Recovery Results for hexythiazox, PT-1-3 and cyclohexylamine in strawberry commodities (study No: UP/20/002)

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Analyte	Recovery range (%) (mean)	%RSD
Strawberry RAC	353 → 228 Quantification	0.005	3	(4R, 5R)-Hexythiazox	92.8 – 111 (100)	9.7
	353 → 168 Qualification		3		95.2 – 114 (102)	10.9
	353 → 228 Quantification		3	(4S, 5S)-Hexythiazox	99.2 – 113 (103)	8.7
	353 → 168 Qualification		3		96.8 – 115 (104)	9.3
	228 → 168 Quantification		3	(4R, 5R)-PT-1-3	97.6 – 111 (102)	7.5
	228 → 116 Qualification		3		96.8 – 110 (102)	7.1
	228 → 168 Quantification		3	(4S, 5S)-PT-1-3	97.6 – 108 (102)	5.3
	228 → 116 Qualification		3		96.8 – 105 (101)	4.0
	353 → 228 Quantification	0.05	3	(4R, 5R)-Hexythiazox	87.2 – 103 (93.9)	8.9
	353 → 168 Qualification		3		85.6 – 102 (92.5)	8.9
	353 → 228 Quantification		3	(4S, 5S)-Hexythiazox	88.0 – 103 (94.1)	8.5
	353 → 168 Qualification		3		88.0 – 102 (93.6)	8.2
	228 → 168 Quantification		3	(4R, 5R)-PT-1-3	94.4 – 104 (98.7)	5.0
	228 → 116 Qualification		3		94.4 – 106 (99.2)	5.8

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Analyte	Recovery range (%) (mean)	%RSD
	228 → 168 Quantification		3	(4S, 5S)-PT-1-3	92.0 – 101 (95.7)	4.8
	228 → 116 Qualification		3		92.0 – 99.2 (95.5)	3.8
	100 → 83 Quantification	0.01	3	Cyclohexylamine	80.8 – 86.4 (82.9)	3.7
	100 → 55 Qualification		3		80.4 – 84.0 (82.3)	2.2
	100 → 83 Quantification	0.1	3		109 – 110 (109)	0.8
	100 → 55 Qualification		3		110 – 111 (110)	0.6
Jam (low sugar)	353 → 228 Quantification	0.005	3	(4R, 5R)-Hexythiazox	83.9 – 85.2 (84.6)	0.8
	353 → 168 Qualification		3		81.2 – 87.2 (83.8)	3.7
	353 → 228 Quantification		3	(4S, 5S)-Hexythiazox	90.4 – 104 (95.7)	7.6
	353 → 168 Qualification		3		92.8 – 105 (97.3)	6.7
	228 → 168 Quantification		3	(4R, 5R)-PT-1-3	184.0 – 100 (89.9)	9.8
	228 → 116 Qualification		3		84.0 – 106 (91.4)	13.9
	228 → 168 Quantification		3	(4S, 5S)-PT-1-3	78.2 – 101 (86.5)	14.3
	228 → 116 Qualification		3		72.7 – 96.8 (80.8)	17.1
	353 → 228 Quantification	0.05	3	(4R, 5R)-Hexythiazox	74.1 – 88.0 (79.5)	9.3

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Analyte	Recovery range (%) (mean)	%RSD
	353 → 168 Qualification		3		74.4 – 88.6 (79.6)	9.8
	353 → 228 Quantification		3	(4S, 5S)-Hexythiazox	88.0 – 105 (93.9)	10.1
	353 → 168 Qualification		3		90.4 – 107 (96.3)	9.8
	228 → 168 Quantification		3	(4R, 5R)-PT-1-3	82.7 – 96.8 (91.7)	8.5
	228 → 116 Qualification		3		86.7 – 97.5 (93.5)	6.3
	228 → 168 Quantification		3	(4S, 5S)-PT-1-3	83.2 – 96.8 (92.2)	8.5
	228 → 116 Qualification		3		79.1 – 96.4 (88.9)	10.0
	100 → 83 Quantification	0.01	3	Cyclohexylamine	74.8 – 79.2 (76.9)	2.9
	100 → 55 Qualification		3		79.2 – 86.0 (83.5)	4.5
	100 → 83 Quantification	0.1	3		87.6 – 94.8 (92.0)	4.2
	100 → 55 Qualification		3		89.6 – 95.6 (92.8)	3.3
Jam (high sugar)	353 → 228 Quantification	0.005	6	(4R, 5R)-Hexythiazox	99.4 – 107 (103)	3.0
	353 → 168 Qualification		6		92.5 – 104 (99.7)	4.4
	353 → 228 Quantification		6	(4S, 5S)-Hexythiazox	98.5 – 107 (102)	3.3
	353 → 168 Qualification		6		95.7 – 103 (100)	3.6

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Analyte	Recovery range (%) (mean)	%RSD
	228 → 168 Quantification		6	(4R, 5R)-PT-1-3	92.1 – 110 (99.5)	6.6
	228 → 116 Qualification		6		105 – 113 (109)	2.4
	228 → 168 Quantification		6	(4S, 5S)-PT-1-3	96.3 – 110 (107)	6.0
	228 → 116 Qualification		6		102 – 117 (107)	6.1
	353 → 228 Quantification	0.05	6	(4R, 5R)-Hexythiazox	97.6 – 105 (101)	3.2
	353 → 168 Qualification		6		96.4 – 103 (99.8)	2.6
	353 → 228 Quantification		6	(4S, 5S)-Hexythiazox	93.8 – 103 (98.4)	3.4
	353 → 168 Qualification		6		95.7 – 103 (99.3)	2.6
	228 → 168 Quantification		6	(4R, 5R)-PT-1-3	101 – 106 (103)	2.2
	228 → 116 Qualification		6		103 – 107 (104)	1.2
	228 → 168 Quantification		6	(4S, 5S)-PT-1-3	101 – 110 (105)	3.1
	228 → 116 Qualification		6		89.3 – 103 (97.4)	5.0
	100 → 83 Quantification	0.01	6	Cyclohexylamine	83.0 – 92.0 (86.8)	4.0
	100 → 55 Qualification		6		65.5 – 86.0 (73.9)	10.0
	100 → 83 Quantification	0.1	6		85.5 – 99.0 (92.3)	4.8

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Analyte	Recovery range (%) (mean)	%RSD
	100 → 55 Qualification		6		86.5 – 99.5 (92.8)	4.9

The analytical recovery of the method was determined by comparing analysed and nominal concentrations from the recovery experiments.

The spike concentrations were in the range 0.005 to 0.1 mg/kg. In the RAC and jam (low sugar), three samples were prepared at the LOQ and a higher level for both transitions and in jam (high sugar), at least six samples were prepared at LOQ and a higher level for both transitions for (4R, 5R)-Hexythiazox and (4S, 5S)-Hexythiazox, (4R, 5R)-PT-1-3, (4S, 5S)-PT-1-3, and cyclohexylamine. As at least six samples were prepared for each fortification level overall for all analytes, the minimum required samples in accordance with SANTE/2020/12830 rev.1 have been tested.

Acceptable mean recoveries in the range of 73.9 – 110% are presented for each fortification level in the RAC, jam (low sugar) and jam (high sugar) and the % RSD at each fortification level was < 20%.

Table C.1.3.1-4 Recovery Results for cyclohexylamine in dry haricot beans and sunflower seeds (report No. RD-12169 and RD-12079)

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Recovery range (%) (mean)	%RSD
Dry haricot beans	100 → 83 Quantification	0.01	6	64.9 – 75.3 (70.0)	5.1
	100 → 55 Qualification		6	66.5 – 76.2 (70.7)	5.0
	100 → 83 Quantification	0.1	6	75.1 – 77.2 (76.5)	1.2
	100 → 55 Qualification		6	75.2 – 77.4 (76.5)	1.1

Matrix	Transition	Fortification level (mg/kg)	No samples per level	Recovery range (%) (mean)	%RSD
Sunflower seeds	100 → 83 Quantification	0.01	6	83.0 – 90.1 (87.0)	3.1
	100 → 55 Qualification		6	81.6 – 91.9 (87.3)	4.9
	100 → 83 Quantification	0.1	6	84.0 – 88.3 (86.9)	2.3
	100 → 55 Qualification		6	84.2 – 90.0 (87.9)	2.5

The spike concentrations were in the range 0.01 to 0.1 mg/kg (LOQ – 10xLOQ). Six samples were prepared for each fortification level. Acceptable mean recoveries in the range of 70.0 – 87.9% are presented for each fortification level in dry haricot beans and sunflower seeds and the % RSD at each fortification level was < 20%.

Table C.1.3.1-5 Characteristics of the analytical method for the quantitation of hexythiazox, PT-1-3 and cyclohexylamine residues in strawberry RAC and processed commodities

	Hexythiazox
Chromatographic method	HPLC-MS/MS
Specificity demonstrated (yes/no, by…)	Yes – Specificity was demonstrated by retention time match of samples with calibration standards for each analyte. Two ion transitions were monitored for each analyte with a m/z ratio ≥ 100.

	Hexythiazox
Linearity demonstrated (yes/no)	**(4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3:** Yes – demonstrated across the range 0.03 – 2.0 ng/mL. Responses were linear. Samples prepared that deviated from the target concentration to be prepared by > 20% were discounted from the calibration curve (outliers). However, an acceptable number of levels were available. In strawberry RAC, jam (low sugar) and jam (higher (sugar), r ≥ 0.9953 which is acceptable. **Cyclohexylamine:** Yes demonstrated across the range 0.06 – 4.0 ng/mL. Responses were linear. Samples prepared that deviated from the target concentration to be prepared by > 20% were discounted from the calibration curve (outliers). However, an acceptable number of levels were available. In strawberry RAC, jam (low sugar) and jam (higher (sugar), r ≥ 0.9992 which is acceptable.
Accepted calibration range in concentration units (e.g. in µg/ml or ng/µl)	**(4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3:** 0.03 – 2.0 ng/mL – equivalent to 0.0012 – 0.08 mg/kg in RAC and jam (low sugar) and equivalent to 0.0015 – 0.10 mg/kg in jam (high sugar). **Cyclohexylamine:** 0.06 – 4.0 ng/mL – equivalent to 0.0024 – 0.16 mg/kg in RAC and jam (low sugar and equivalent to 0.003 – 0.20 mg/kg in jam (high sugar).

	Hexythiazox
Calibration consist of at least 3 levels (duplicated points) or 5 levels (single points)? (yes/no)	Yes – eight single points.
Matrix effects	Matrix matched calibration solutions were used.
Absence of interference >30% of LOQ in blank sample is demonstrated (yes/no)	Analysis of reagent blank and control samples demonstrated no significant interference (> 30% of the sample fortified at the LOQ), at the retention time of interest for (4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3 and cyclohexylamine.
Chromatogram of sample spiked at LOQ demonstrates sufficient S/N ration? (yes/no)	Yes
LOQ (mg/kg)	**0.005** mg/kg for (4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3 **0.01** mg/kg for Cyclohexylamine

Table C.1.3.1-6 Characteristics of the analytical method for the quantitation of cyclohexylamine residues in dry haricot beans and sunflower seeds

	Cyclohexylamine
Chromatographic method	HPLC-MS/MS
Specificity demonstrated (yes/no, by…)	Yes – Specificity was demonstrated by retention time match of samples with calibration standards for each analyte. Two ion transitions were monitored for each analyte with a m/z ratio ≥ 100.

	Cyclohexylamine
Linearity demonstrated (yes/no)	Yes demonstrated across the range 0.0375 – 1.50 ng/mL for dry haricot beans and 0.076 – 4.0 ng/mL for sunflower seeds. Responses were linear. In dry haricot beans, r ≥ 0.9990 which is acceptable. In sunflower seeds, r ≥ 0.9998 which is acceptable.
Accepted calibration range in concentration units (e.g. in µg/ml or ng/µl)	0.0375 – 1.50 ng/mL – equivalent to 0.003 – 0.15 mg/kg in dry haricot beans. 0.076 – 4.0 ng/mL – equivalent to 0.003 – 0.16 mg/kg in sunflower seeds.
Calibration consist of at least 3 levels (duplicated points) or 5 levels (single points)? (yes/no)	Yes – eight single points for dry haricot beans and seven single points for sunflower seeds.
Matrix effects	Matrix matched calibration solutions were used.
Absence of interference >30% of LOQ in blank sample is demonstrated (yes/no)	Analysis of reagent blank and control samples demonstrated no significant interference (> 30% of the sample fortified at the LOQ), at the retention time of interest for cyclohexylamine.
Chromatogram of sample spiked at LOQ demonstrates sufficient S/N ration? (yes/no)	Yes
LOQ (mg/kg)	**0.01** mg/kg for Cyclohexylamine

Extraction efficiency: Method UP/20/002 and UP19001 uses acetonitrile/acetic acid (99.9/0.1) for the extraction of residues. The radiolabelled metabolism studies for the approval of the active generally used a combination of aqueous methanol and chloroform as the extraction solvents. The applicant has provided a cross-validation study to assess the extraction efficiency of acetonitrile/acetic acid solvent systems and an evaluation of this data can be found in Appendix C.1.1.1.2. Extraction efficiency was confirmed to be

acceptable for the monitoring method B1310/B1308 as it is above 70% and does not differ by > 30%. Therefore the solvent system of acetonitrile/ acetic acid (99.9/0.1) has been demonstrated as efficient for the extraction of residues for high acid commodities. For other crop commodity groups extraction efficiency has not been addressed but as extraction efficiency was not demonstrated for the approval of the active, further consideration is not required in the scope of this application.

Conclusion

The method included in study No. UP/20/002 for analysis of (4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3 and cyclohexylamine, using HPLC-MS/MS for final determination, fulfils the requirements with regard to linearity, specificity, repeatability, limit of quantification and recoveries. The limit of quantification is 0.005 mg/kg for (4S, 5S)-Hexythiazox, (4R, 5R)-Hexythiazox, (4S, 5S)-PT-1-3, (4R, 5R)-PT-1-3, and 0.01 mg/kg for cyclohexylamine. Therefore, the method is satisfactorily validated in accordance with SANTE 2020/12830 rev.1 for strawberry (high acid commodity) and strawberry jam (high water commodity).

For the method included in report No. RD-12169 and RD-12079, method validation data for detection of cyclohexylamine is only submitted to support the use on dry haricot beans (high protein commodity) and sunflower seeds (high oil commodity). However the principle of the method is similar for all commodities considered within report No.RD-12169 and similar to the method UP/20/002. The method for analysis of cyclohexylamine using HPLC-MS/MS for final determination, fulfils the requirements with regard to linearity, specificity, repeatability, limit of quantification and recoveries. The limit of quantification is 0.01 mg/kg for cyclohexylamine. Therefore, the method is satisfactorily validated in accordance with SANTE 2020/12830 rev.1 dry haricot beans (high protein commodity) and sunflower seeds (high oil commodity).

C.1.4 Methods for risk assessment for residues in food and feed of animal origin

No additional studies submitted.

C.1.5 Methods for risk assessment for toxicological studies

No additional studies submitted.

C.2 Mammalian toxicology

No additional studies submitted

C.3 Residue data

C.3.1 Nature and magnitude of residues in primary crops

C.3.1.1 Nature of residues

No additional studies submitted.

C.3.1.2 Magnitude of residues

C.3.1.2.1 Raspberry

Reference:	Magnitude of the Residue of Hexythiazox in or on Raspberry Raw Agricultural Commodities Following One Foliar Application of Onager Optek™ Miticide or Savey® 50 DF Ovicide/Miticide (2018), [redacted] 2018, Study No: TCI-18-597
Guideline(s):	Yes Residue Chemistry Test Guidelines, OPPTS 860.1000 Background Residue Chemistry Test Guidelines, OPPTS 860.1500, Crop Field Trials
Deviations:	No significant deviations
GLP:	Yes
Validity of the study:	Acceptable

Materials and methods

Five trials on raspberries were conducted in the USA in the 2018 growing season. At each trial site there were four treated plots that were treated with either 'Onager Optek Miticide', an oil-in-water emulsion (EW) formulation containing 119.3 a.s. g/L hexythiazox, or 'Savey 50DF Ovicide/Miticide', a water dispersible granules (WG) formulation containing 500 a.s. g/kg hexythiazox. The application rates tested at each plot were either 262 g a.s./ha or 280 g a.s./ha. The plot details and the nomenclature reported in this evaluation is shown in the table below:

Table C.3.1.2.1-1 Details on plots used in residue trials

Plot number	Product	Formulation type	Target application rate (g a.s/ha)
Plot 1	N/A – control plot	N/A	N/A
Plot 2	Onager Optek Miticide	EW	262
Plot 3	Onager Optek Miticide	EW	280
Plot 4	Savey 50DF Ovicide/Miticide	WG	262
Plot 5	Savey 50DF Ovicide/Miticide	WG	280

‘Onager Optek Miticide’ or ‘Savey 50DF Ovicide/Miticide’ was applied as a foliar spray at a rate of 261.5 – 296.9 g a.s./ha in 468 – 926 L/ha of water. One application was made three days before harvest, BBCH 75 – 89. With regards to application rate ‘Onager Optek Miticide’ is the authorised cGAP in USA. Bridging trials were performed using ‘Savey 50 DF Ovicide/Miticide’. The application rates in the authorised GAPs for the USA are within 25% of each other. However, the formulation type may affect how long the residue remains on the crop, therefore the Mann-Whitney U test was performed and concluded there was no significant differences in residues resulting from using ‘Onager Optek Miticide’ or ‘Savey 50DF Ovicide/Miticide’ at either application rate and thus each trial pair is comparable. Data was therefore selected from all trials.

Weather data were reported for the trials and no exceptional events were noted. The trials were at harvest trials. Samples of raspberry whole fruit were taken at three days after last application. Samples containing at least 1 kg were collected from both treated and control plots. Samples were frozen within 4 hours and stored at ≤-10 ºC until analysis. Freezer temperatures ranged from -29 °C to -4 °C throughout the sample storage period. Temperatures briefly exceeded -10 °C due to equipment malfunction however, the samples remained frozen and therefore there is no impact on the study. The maximum storage interval between harvest and analysis was 63 days. The stability of hexythiazox and has been demonstrated for this period of time when stored at ≤-18 °C in high acid crops (strawberry, citrus, grape) for the approval of the active and in the addendum (FI, 2014).

Analysis of the samples was performed within 5 days of extraction. Analysis at later dates were due to the concentration of samples not falling within the range of the calibration curve, hence samples were diluted and analysed on a later date. Samples were stored frozen prior to homogenisation and then returned to frozen storage following homogenisation. Procedural recoveries were performed on low spikes (0.02 mg/kg) and high spikes (1.0 – 2.0 mg/kg) on each date of analysis. However, there is no data to support extract stability nor procedural recovery data for analysis of samples after 24 hours. Residue data has been presented as an average of the residue data collected from analysis of samples that were diluted and analysed up to 5 days after extraction. The applicant was asked to clarify how samples were stored between extraction and analysis and confirm whether samples were stored under the same conditions as the spikes. The applicant supplied confirmation that all samples and procedural recoveries were stored under the same frozen conditions and samples were stored frozen between extraction and analysis.

Analysis was performed using LC-MS/MS method included in study report TCI-18-597 (Study ID: 180776, modification of method 'Meth-220'). Full details and validation data for this method can be found in Appendix C.1.3. The analytical method was considered sufficiently validated for the purposes of the regulatory process. The method determines hexythiazox residues as the metabolite PT-1-3, therefore a molecular weight (MW) calculation is required to convert residues into hexythiazox (MW hexythiazox/MW PT-1-3 = conversion factor of 1.55). The LOQ of the method is 0.02 mg/kg (residues expressed as hexythiazox). Acceptable procedural recovery data for hexythiazox (fortified samples at 0.02, 1.0 and 2.0 mg/kg), using an appropriate number of samples were presented and were in the acceptable range of 70 and 110%. Extraction efficiency was not investigated in the report.

Results and discussions

Five trials conducted in the USA are available on raspberries which is acceptable and meets the minimum number required for minor crops.

All treated plots are within ± 25% of the authorised cGAP for 'Onager Optek Miticide' which is the authorised cGAP in relation to application rate. As more than one trial design has been performed at the same location (several nominal dose rates), the highest residue for each trial has been selected (GB extrapolations guidance, 2024).

No residues were detected in control samples for all trials.

A summary of the residues trials is given in Table C.3.1.2.1-2.

Residues of hexythiazox in raspberries at three days after last application were between 0.486-1.66 mg/kg.

Table C.3.1.2.1-2 Residue trials on raspberries

Reference:	Magnitude of the Residue of Hexythiazox in or on Raspberry Raw Agricultural Commodities Following One Foliar Application of Onager Optek™ Miticide or Savey® 50 DF Ovicide/Miticide (2018), [redacted] 2018, Study No: TCI-18-597		
GLP:	Yes	Sample storage conditions:	Max 63 days at -29 °C to -4 °C
Crop/crop group:	Raspberries / fruit	Analytical method:	Method included in report TCI-18-597. Validated
Indoor/outdoor:	Outdoor	Limit of Quantification (mg/kg):	0.02
Formulation:	EW (Onager Optek Miticide) or WG (Savey 50DF Ovicide/Miticide)	Residues calculated as:	Hexythiazox
Content of active substance:	119.3 g/L (Onager Optek Miticide) or 500 g/kg (Savey 50 DF Ovicide/Miticide)		

Trial No Location Year	Commodity Variety	Date of 1.Sowing or planting 2.Flowering 3.Harvest	Formulation type	Application rate per treatment			Dates of treatment or number and last date	Interval between applications (days)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
				g a.s./ ha	Water (L/ha)	g a.s./ hL					Hexythiazox		

Trial No Location Year	Commodity Variety	Date of 1.Sowing or planting 2.Flowering 3.Harvest	Formulation type	Application rate per treatment			Dates of treatment or number and last date	Interval between applications (days)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
TCI-18-597-01 New Tripoli, Pennsylvania 2018	Raspberry / Boyne	1. 2003 2. N/A 3. 05 Jul 2018	Plot 2: EW Plot 3: EW Plot 4: WG Plot 5: WG	270.2 290.0 279.2 296.9	673 664 701 673	40.1 43.7 39.8 44.1	02 Jul 2018	BBCH 85	Fruit Fruit Fruit Fruit	0.8305 0.8925 <u>1.005</u> 0.9460	3 3 3 3		Each trial consisted of five plots: Plot 1: untreated Plot 2: EW formulation Onager Optek™ Miticide at a nominal rate of 262 g a.s/ha
TCI-18-597-02 Sparta, Michigan 2018	Raspberry / Killarney	1. 25 Apr 2002 2. N/A 3. 06 Jul 2018	Plot 2: EW Plot 3: EW Plot 4: WG Plot 5: WG	261.6 282.9 266.3 283.4	701 711 711 711	37.3 39.8 37.5 39.9	03 Jul 2018	BBCH 75 – 85	Fruit Fruit Fruit Fruit	1.430 <u>1.655</u> 1.435 1.495	3 3 3 3		Plot 3: EW formulation Onager Optek™ Miticide at a nominal rate of 280 g a.s/ha).

Trial No Location Year	Commodity Variety	Date of 1.Sowing or planting 2.Flowering 3.Harvest	Formulation type	Application rate per treatment			Dates of treatment or number and last date	Interval between applications (days)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
TCI-18-597-03 Roseburg, Oregon 2018	Raspberry / Tulameen	1. 10 Mar 2016 2. N/A 3. 14 Jun 2018	Plot 2: EW Plot 3: EW Plot 4: WG Plot 5: WG	265.0 283.9 263.2 283.6	468 477 468 477	56.6 59.5 56.2 59.5	11 Jun 2018	BBCH 87	Fruit Fruit Fruit Fruit	1.050 <u>1.090</u> 0.732 1.055	3 3 3 3		Plot 4: WG formulation Savey® 50 DF Ovicide/Miticide at a nominal rate of 262 g a.s/ha)
TCI-18-597-04 Corvallis, Oregon 2018	Raspberry / Squamish	1. 01 Apr 2016 2. N/A 3.18 Jun 2018	Plot 2: EW Plot 3: EW Plot 4: WG Plot 5: WG	263.0 280.4 263.4 280.8	926 926 926 926	28.4 30.3 28.4 30.3	15 Jun 2018	BBCH 88	Fruit Fruit Fruit Fruit	0.5605 <u>1.035</u> 0.574 0.8300	3 3 3 3		Plot 5: WG formulation Savey® 50 DF Ovicide/Miticide at a nominal rate of 280 g a.s/ha)

Trial No Location Year	Commodity Variety	Date of 1.Sowing or planting 2.Flowering 3.Harvest	Formulation type	Application rate per treatment			Dates of treatment or number and last date	Interval between applications (days)	Growth stage at last treatment	Portion analysed	Residues (mg/kg)	PHI (days)	Remarks
TCI-18-597-05 Sherwood, Oregon 2018	Raspberry / Cascade Delight	1. 11 Mar 2015 2.N/A 3. 25 Jun 2018	Plot 2: EW Plot 3: EW Plot 4: WG Plot 5: WG	261.5 284.1 269.7 280.9	533 542 552 533	49.1 52.4 48.9 52.7	22 Jun 2018	BBCH 78 – 89	Fruit Fruit Fruit Fruit	0.5395 0.4855 0.631 0.6205	3 3 3 3		

(a) Hexythiazox determined as molar equivalent of PT-1-3 (MW hexythiazox/MW PT-1-3 to give conversion factor of 1.55)

C.3.2 Nature and magnitude of residues in processed commodities

C.3.2.1 Nature of residues (Standard hydrolysis study)

Reference: Hexythiazox – High Temperature Hydrolysis of [cyclohexyl-U-14C]- Hexythiazox in Sterile Buffer, [redacted] 2020. Study No: 814685

Guideline(s): Yes

OECD Guideline 507, Nature of the Pesticide Residues in Processed Commodities – High Temperature Hydrolysis, October 2007

Deviations: No

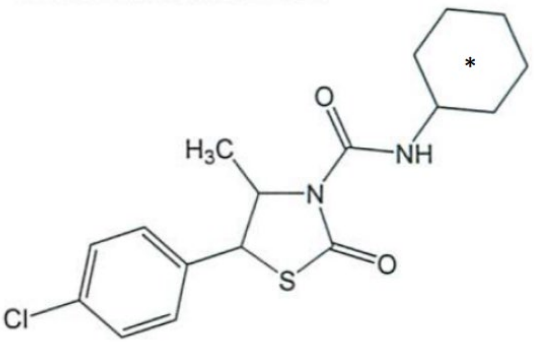
GLP: Yes

Validity of the study: Acceptable

Materials and methods

A study investigating the hydrolytic stability of hexythiazox under conditions representative of pasteurisation, baking, brewing, boiling and sterilisation was carried out using hexythiazox labelled in the cyclohexyl ring.

Table C.3.2.1-1 Details on test material

Test item:	C-label Hexythiazox
Description:	[cyclohexyl-U-^{14}C]-Hexythiazox
Specific activity:	5.92 MBq/mg
Radiochemical purity:	100%
Chemical structure	 * indicates label position

Radiolabelled stock solutions were prepared by dilution of an aliquot (5 µL) of [cyclohexyl-U-^{14}C]-hexythiazox using acetonitrile (1 mL). Triplicate aliquots (10 µL) of stock solution were obtained and analysed by LSC prior to all main test treatment occasions. Concentrations of stock solutions 1, 2 and 3 from initial aliquots taken for LSC after preparation were 30.8, 31.3 and 27.7 mg/L.

The pH 4 treated buffer solution was prepared by adding an aliquot of stock solution 2 (32.6 mg/L) to an autoclaved 250 mL amber jar containing 70 mL of sterilised pH 4 buffer solution. Triplicate aliquots (100 µL) were obtained for LSC analysis prior to treatment to confirm concentration and homogeneity.

The pH 5 treated buffer solution was prepared by adding an aliquot of stock solution 2 (34.8 mg/L) to an autoclaved 100 mL glass duran containing 75 mL of sterilised pH 5 buffer solution. Triplicate aliquots (100 µL) were obtained for LSC analysis prior to treatment to confirm concentration and homogeneity. Initial aliquots were repeated after ultrasonication to try increase dissolution of the test item.

The pH 6 treated buffer solution was prepared by adding an aliquot of stock solution 3 (29.7 mg/L) to an autoclaved 125 mL amber jar containing 75 mL of sterilised pH 6 buffer solution. Initial triplicate aliquots were repeated after ultrasonication as initial results from LSC were shown to be inhomogeneous.

After preparation of treated buffer solutions, sub-samples of each treated buffer solution were obtained for sterility checking and pH measurement. Solubility and the potential for adsorption to test vessels were investigated at each pH prior to conducting main tests.

The radiochemical purity of [cyclohexyl-U-^{14}C]-hexythiazox was determined on the day of each test. An aliquot of stock solution and treatment solution was analysed by reversed phase HPLC with radio detection. Non-radiolabelled test item was mixed with stock solution to confirm the retention time of hexythiazox.

To determine the test item applied, triplicate aliquots (100 µL) of each treated buffer solution were weighed into liquid scintillation vials and counted by LSC prior to treatment of vessels. The weight of treated buffer solution added to each vessel was then used to calculate the test item applied.

The nominal concentration for each test was 0.1 mg/L with < 1% acetonitrile co-solvent.

Incubations were performed in triplicate in the dark to minimise any photolytic effects. The conditions used are reported in Table C.3.2.1-2.

Table C.3.2.1-2 Nominal hydrolytic conditions and simulated processes studied

Temperature (°C)	pH	Time (min)	Process represented

90 ± 1.7	4 ± 0.1	20	Pasteurisation
100 ± 3.9	5 ± 0.1	60	Baking, boiling, brewing
120 ± 0.5	6 ± 0.1	20	Sterilisation

Triplicate weighed aliquots (100 µL) were obtained from each incubate for LSC analysis. All incubates and extracts were stored frozen at – 20 °C. All main test LSC and chromatographic analysis was performed on the day of incubation and sampling, therefore no further consideration of storage stability is required.

Incubate samples from each pH test were analysed by HPLC to quantify the test item and degradation products formed during incubation. LC-MS analysis was used to confirm the identity of [cyclohexyl-U-14C]-hexythiazox and to identify the only major degradant as cyclohexylamine.

The identification of cyclohexylamine using LC-MS/MS analysis was only done for the pH 6 replicate 3 incubate. Assignment of cyclohexylamine in all other samples was based on retention time only. Overall, it is considered that sufficient identification has been achieved.

All replicates in the initial pH 4 test had low material balance. Recovered radioactivity for all samples in the initial pH 4 test was ≤ 90% AR (applied radioactivity), with a mean of 81.1% AR. The vessel type was changed for the main test to account for possible volatile degradants. The main test vessels were replaced with MonoTrap™ vessels with highly porous disk in headspace to capture any potential volatile components which may have resulted in the loss of radioactivity.

Investigation of possible volatile components:

To investigate the possibility of a loss of volatile components during the drying phase of fraction collection, analysis of a solution of the pH4 treated buffer solution and non-radiolabelled hexythiazox was performed by reverse-phase HPLC and LSC. Analysis using liquid fraction collection and LSC determined [cyclohexyl-U-^{14}C]-hexythiazox as the only major component (100.0 %TRR). It can therefore be concluded that significant volatile components were not lost during this test and [cyclohexyl-U-^{14}C]-hexythiazox is the only major component in pH 4 sample incubate.

The remaining pH 6 test analysis was performed using fraction collection with LSC to avoid loss of any potential volatile components under different incubation conditions. As acceptable mass balance results were available for pH 5 test, no further investigations for pH 5 incubation conditions were performed.

Results and discussion

Sterile buffer solutions were shown to have a pH ± 0.1 of nominal target value immediately prior to preparation of treatment solutions. Measurements of treatment solutions after application and in incubate samples after sampling showed no significant change to pH. All treatment solutions and incubate samples were determined to have no turbidity and were therefore confirmed as sterile.

The mean radioactivity (of three replicate aliquots) recovered in pH 4, 5 and 6 sterilised buffer samples was 98.7, 93.9 and 96.6% AR respectively. This confirms there was no significant loss of radioactivity during the reactions. The majority of radioactivity was recovered in the sample incubates with a mean of 98.0, 91.9 and 93.9% AR during pH 4, 5 and 6 incubations respectively. The remaining radioactivity was recovered from the extraction of traps suspended in the headspace of sample vessels and accounted for a mean of 0.7, 2.0 and 2.7% AR in pH 4, 5 and 6 incubates respectively.

The mean concentration of [cyclohexyl-U-14C]-hexythiazox in sample incubates was 0.080, 0.060 and 0.036 mg/L for pH 4, 5 and 6 respectively. This equates to a mean recovery of 98.9, 98.4 and 54.4% of the applied radioactivity for pH 4, 5 and 6 sample incubates respectively.

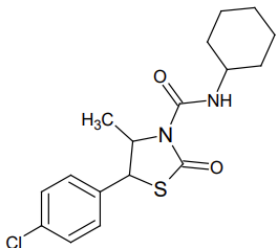
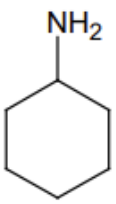
Cyclohexylamine was only detected in pH 5 and 6 sample incubates. In pH 5 incubates, levels of cyclohexylamine were ≤0.9% of the applied TRR (≤0.001 mg/L). In pH 6 incubates, cyclohexylamine was present at a mean concentration of 43.5% AR (0.029 mg/L).

Table C.3.2.1-2 Standard hydrolysis study for hexythiazox

Processes represented (conditions)	**Parent**	**Recoveries**							
	Initial conc. (mg/L)	**Hexythiazox (mean)**		**Cyclohexylamine (Mean)**		**Sum of minor components (Mean)**		**Total**	
		% AR	**mg/L**	**% AR**	**mg/L**	**% AR**	**mg/L**	**% AR**	**mg/L**

Pasteurisation (pH 4, 20 min, 90 °C)	0.082	98.3 – 100.0 (98.9)	0.078 – 0.081 (0.080)	<0.55	<0.001	<0.55 – 1.7 (1.1)	<0.001 – 0.001 (0.001)	100.0	0.079 – 0.081 (0.080)
Baking, boiling, brewing (pH 5, 60 min, 100 °C)	0.068	98.0 – 99.0 (98.4)	0.059 – 0.061 (0.060)	<0.55 – 0.9 (0.5)	<0.001 – 0.001 (<0.001)	1.0 – 1.1 (1.1)	0.001	100.0	0.061 – 0.062 (0.061)
Sterilisation (pH 6, 20 min, 120 °C)	0.072	51.1 – 56.7 (54.4)	0.032 – 0.039 (0.036)	41.0 – 46.6 (43.5)	0.029	< 0.55 – 3.6 (2.1)	<0.001 – 0.002 (0.001)	99.6 - 100.0 (100.0)	0.062 – 0.070 (0.066)

Table C.3.2.1-3 Compounds identified in the standard hydrolysis study

Common name	Chemical name	Chemical structure	Toxicological information available	Included in residue definition (Y/N)
Hexythiazox	(4RS,5RS)-5-(4-chlorophenyl)-N-cyclohexyl-4- methyl-2-oxo-1,3-thiazolidine-3-carboxamide		Yes	Y
Cyclohexylamine	Cyclohexylamine		No	N

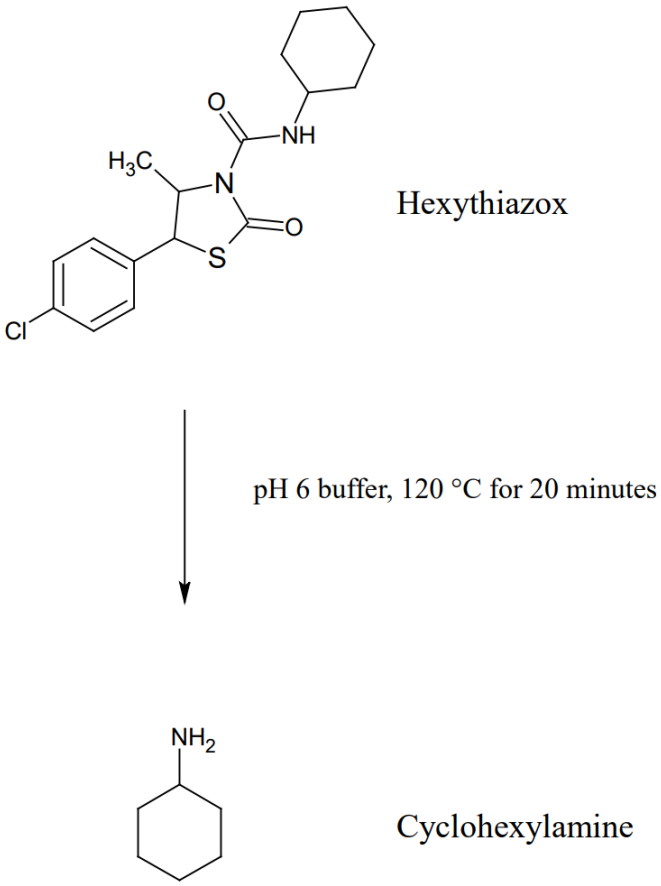


Figure C.3.2.1-1 Proposed degradation pathway of hexythiazox under sterilisation conditions (pH 6, 20 min, 120 °C)

Conclusions

Hexythiazox was found to be hydrolytically stable in buffer solutions, with [cyclohexyl-U-^{14}C]-Hexythiazox representing ≥98.0 % TRR, under conditions representative of pasteurisation (pH 4, 90 °C, 20 min) and baking, boiling, brewing (pH 5, 100 °C, 60 min). Hexythiazox was degraded under conditions simulating sterilisation (pH 6, 120 °C, 20 min) with [cyclohexyl-U-^{14}C]-Hexythiazox representing ≥51.1 % TRR and major degradant cyclohexylamine representing ≥41.0 % TRR

C.3.2.2 Magnitude of residues (Processing studies)

C.3.2.2.1 Processing study on strawberry

Reference:	Determination of Residues of Hexythiazox and its Metabolites in Strawberry RAC and Processed Fractions Following treatment with Hexythiazox 250 SC under Field Conditions in Northern and Southern Europe in 2020, [redacted] 2021, Report No: R C0012
Guideline(s):	Yes OECD Guideline 508, Magnitude of the Pesticide Residues in Processed Commodities, October 2008
Deviations:	Yes – see below. No significant impact on the study.
GLP:	Yes
Validity of the study:	Acceptable

Materials and methods

A processing study for strawberries (varieties Sonata and Albion), was conducted at two trial locations in France and Spain in the 2020 growing season using 'Hexythiazox 250 SC', a suspension concentrate (SC) formulation containing 250 g/L hexythiazox. In the trials, one foliar application of 'Hexythiazox 250 SC' was made to each of the treated plots at a rate of 469.3 – 504.4 g a.s./ha in 469 - 504 L/ha water (spray concentration approximately 100 g a.s./hL). The application was made at BBCH 67 – 85 with a three day PHI. Each field trial included one treated plot and one untreated control plot. Samples were taken when fruit was ripe (between BBCH 67 – 89). A minimum of 1 kg of ripe fruits were randomly collected from each plot. Weather data were reported for the trials and no exceptional events were noted.

In trial C0012 MA1, hexythiazox was applied in the field one year before the trial. The study report argues that no trial site without hexythiazox application during last year was available. Hexythiazox and its metabolites have DT_{90} values which exceed 100 days and therefore are persistent (hexythiazox up to 248 days, metabolite PT-1-2 up to 877 days and metabolite PT-1-3 up to 180 days, EFSA, 2010). As residues observed in the untreated plots are < LOQ (< 0.005 mg/kg), it can be concluded that the application of hexythiazox in the past year has not impacted the residue levels present in the RAC.

<u>Processing of canned fruits</u>

Approximately 2 kg of unwashed raw agricultural commodity (RAC) fruits were prepared with the stems and crowns removed. After preparation, the fruits were put into glass jars and covered with approximately 500 g syrup (water + sugar). 0.3 g of citric acid was added and samples were pasteurised at 90 - 95°C for 10 minutes. After pasteurisation, the samples were cooled and stored frozen until analysis.

Processing of strawberry jam

Approximately 2 kg of unwashed RAC fruits were prepared with stems and crowns removed. After preparation, fruits were crushed and 100 – 1500g sugar was added. The mixture was cooked under vacuum at 60°C until obtaining a sugar content of 62%. After cooking and cooling down, 4.21 – 6.1 g citric acid was added and the jam was canned and pasteurised for 10 min at 90-95 °C. The pH of the jam was 2.5 – 3.0.

Storage stability

The RAC samples were stored frozen at ≤-18 ˚C within 6 hours of harvest. Samples for processing were stored refrigerated prior to processing (for up to 2 days) and then frozen at ≤-18 ˚C immediately afterwards. RAC and processed samples were stored frozen for up to 228 days.

Sufficient storage stability is available to support the storage of samples in this study. For hexythiazox and PT-1-3 residues, sufficient storage stability is available to support the storage length of the RAC and canned strawberry (high acid commodity) from the approval of the active substance (FI, 2014) for at least 365 days at ≤-18 ˚C (data available for strawberry, citrus, grape). Sufficient storage stability is also available to support the storage length of the strawberry jam (high water commodity) from the active approval as hexythiazox and PT-1-3 residues were considered to be stable across the high water crop group for at least 365 days at ≤-18 ˚C (data available for apple, marmalade and apple processed commodities). For cyclohexylamine, newly submitted storage stability studies demonstrate that cyclohexylamine is stable in all commodity groups for up to 14 months at ≤-18 ˚C (see Appendix C.3.6.1).

The applicant has submitted a new storage stability study for PT-1-3 in strawberry jam. Evaluation of this study is not necessary as data from the approval of the active substance is sufficient. The study has only been checked to ensure no adverse data is reported.

The interval between extraction and analysis for the RAC and processed commodities was a maximum of 8 days at ≤-18ºC. Extract stability was demonstrated in report UP/20/002 for at least 40 days for all analytes in strawberry RAC and jam (low and high sugar).

Analytical method

Analysis was performed using LC-MS/MS method detailed in study report UP/20/002. Full details and validation data for this method can be found in Appendix C.1.3.2. The analytical method was satisfactorily validated in accordance with SANTE/2020/12830 rev. 1 for high acid (strawberry fruit) and high water commodities (jam). The method can quantify the isomeric forms of hexythiazox and PT-1-3 separately. The LOQ of the method for (4S, 5S)-Hexythiazox, (4R, 5R)- Hexythiazox, (4S, 5S)-PT-1-3 and (4R, 5R)-PT-1-3 is 0.005 mg/kg and for cyclohexylamine the LOQ is 0.01 mg/kg.

Acceptable procedural recovery data using the appropriate number of samples for the hexythiazox isomers, PT-1-3 isomers and cyclohexylamine in RAC and jam (fortified samples at 0.005, 0.05 and 2.5 mg/kg), with mean recoveries in the range of 75 - 106% were recorded (see Table C.3.2.2-1). This confirms the method is acceptable for the analysis of these residues in the RAC and jam and the number of samples at each level is considered sufficient given that the analytical method is fully validated on high acid and high water commodities.

Canned strawberries are a high acid commodity, therefore could be covered by the validation data for strawberry RAC, provided acceptable reduced procedural recovery data is provided. The suitability of the method has not been demonstrated for canned fruit as concurrent recoveries should be demonstrated with a minimum of three recoveries at LOQ and three recoveries at higher level for each analyte. Only 1-2 procedural recoveries have been provided for each analyte and the procedural recoveries for the hexythiazox isomers at LOQ for canned strawberry are outside of the acceptable range (123 – 133%). However, this can be considered a minor deficiency as procedural recoveries data at the fortification levels closest to levels in canned strawberries (0.05 mg/kg) are within the acceptable limits which suggests the method is functional at the levels found in the processing study.

Table C.3.2.2-1 Procedural Recovery Results in strawberry commodities

Analyte	**Level (mg/kg)**	**Strawberry RAC**		**Canned Strawberry**		**Strawberry jam**	
		Recovery (%) (mean)	**%RSD**	**Recovery (%) (mean)**	**%RSD**	**Recovery (%) (mean)**	**%RSD**
(4R, 5R)-Hexythiazox	0.005	87, 96, 101 (95)	7.3	133	-	110	-
	0.05	106, 106, 107 (106)	0.8	110	-	87	-
	2.5	75, 106 (91)	-	90	-	89, 100 (94)	-

Analyte	Level (mg/kg)	Strawberry RAC		Canned Strawberry		Strawberry jam	
		Recovery (%) (mean)	%RSD	Recovery (%) (mean)	%RSD	Recovery (%) (mean)	%RSD
(4S, 5S)-Hexythiazox	0.005	97, 102, 106 (101)	4.3	123	-	93, 106 (100)	-
	0.05	105, 106 (106)	1.1	104	-	85, 110 (98)	-
	2.5	75	-	89	-	85, 103 (94)	-
(4R, 5R)-PT-1-3	0.005	115	-	105	-	90	-
	0.05	102	-	86	-	101	-
	2.5	108	-	94	-	90	-
(4S, 5S)-PT-1-3	0.005	111	-	93, 102 (98)	-	91	-
	0.05	102	-	84, 96 (90)	-	101	-
	2.5	108	-	94, 94 (94)	-	100	-
Cyclohexyl amine	0.01	74, 114 (94)	-	106	-	79	-
	0.1	101, 108 (104)	-	105	-	97	-

Results and discussions

No residues above LOQ were detected for metabolites (4R, 5R)-PT-1-3, (4S, 5S)-PT-1-3 (<0.005 mg/kg) or cyclohexylamine (<0.01 mg/kg) in the RAC or processed commodities, therefore processing factors for these metabolites cannot be calculated.

The residue definition for enforcement and risk assessment is hexythiazox. Therefore, the sum of (4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox residues has been taken. The preferential degradation of the enantiomers of hexythiazox was not significant in this study

(difference in amount of isomer formed did not exceed > 10% for hexythiazox). Therefore, it is not necessary in the scope of this application to investigate preferential isomeric degradation and isomeric composition.

The processing of hexythiazox in RAC to processed commodities was determined in two trials, therefore the mean value in the processed commodities was used to calculate the processing factor (the residue in the processed product divided by the residue in the RAC). As replicates were performed in each trial the mean residues of the two replicates has been reported.

Table C.3.2.2-2 Processing study on strawberry with hexythiazox

Commodity	Trial No.	Residues (mg/kg) RD-Enf = RD-RA			Pf[(a)] based on mean sum of 4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox residues	Pf[(a)] mean of two trials	Comments/ Reference
		(4S, 5S)-Hexythiazox (mean)	(4R, 5R)-Hexythiazox (mean)	Sum of (4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox			
RAC	C0012 ES1	0.296, 0.304 (0.300)	0.244, 0.246 (0.245)	0.540, 0.550 (0.545)	-	**-**	RAC sample replicates are taken from the same bulk sample as the processed fractions.
	C0012 MA1	0.109, 0.151 (0.130)	0.0908, 0.151 (0.121)	0.200, 0.302 (0.251)	-	**-**	
Canned strawberry	C0012 ES1	0.106	0.108	0.214	0.393	**0.472**	Mean processing factor based on sum of (4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox residues.

Commodity	Trial No.	Residues (mg/kg) RD-Enf = RD-RA			Pf[(a)] based on mean sum of	Pf[(a)] mean of two trials	Comments/ Reference
	C0012 MA1	0.0768	0.0612	0.138	0.550		
Strawberry jam	C0012 ES1	0.0783	0.0975	0.176	0.323	**0.303**	Mean processing factor based on sum of (4S, 5S)-Hexythiazox and (4R, 5R)-Hexythiazox residues.
	C0012 MA1	0.041	0.03	0.071	0.283		

(a) Processing factor

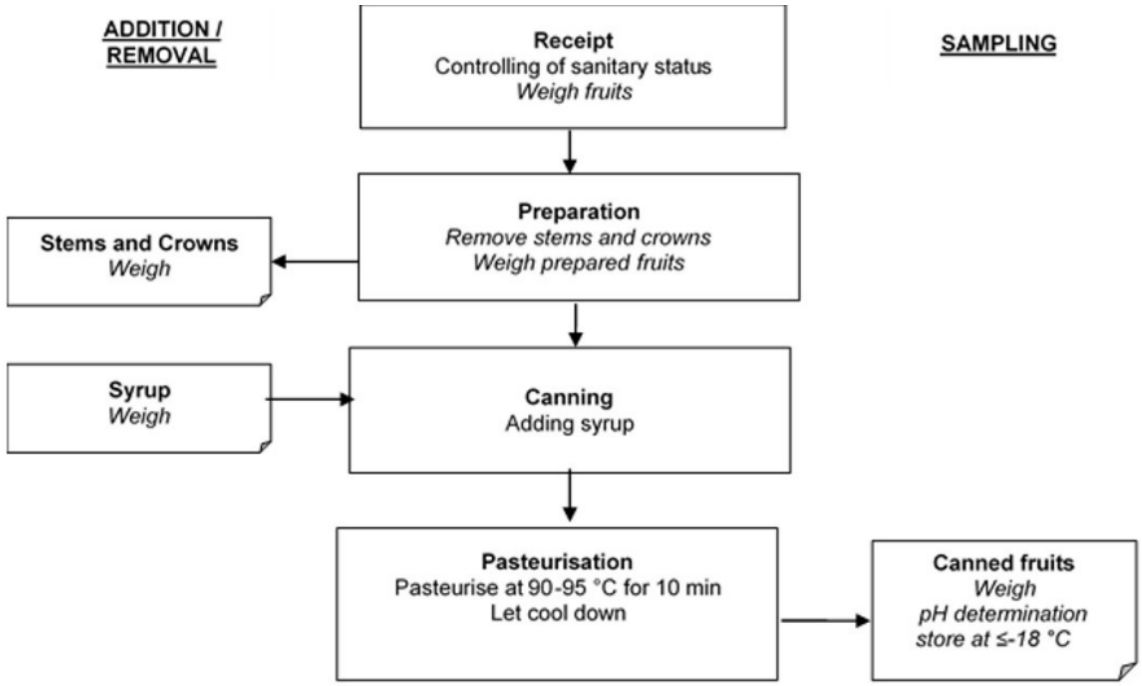


Figure C.3.2.2-1 Processing flowchart for canned fruits

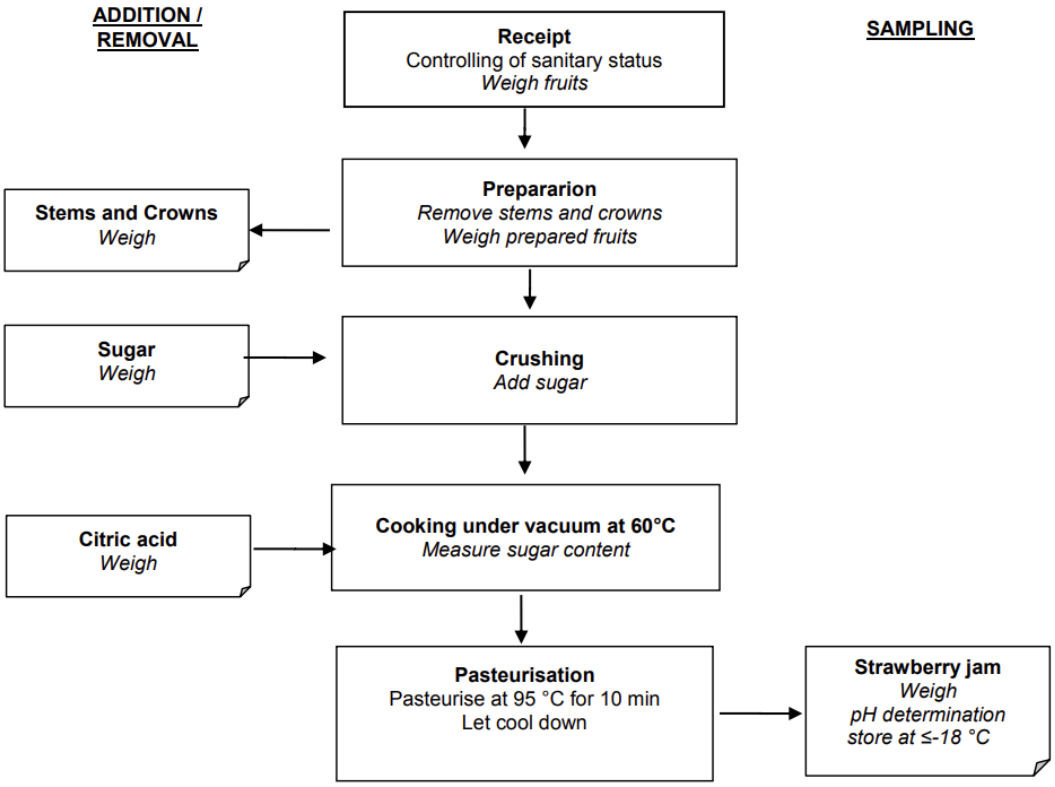


Figure C.3.2.2-2 Processing flowchart for strawberry jam

Conclusion

For hexythiazox, a processing factor below one was obtained for canned strawberry and strawberry jam (mean Pf: 0.472 and 0.303 respectively), indicating there is a dilution of residues upon processing.

Processing factors for PT-1-3 and cyclohexylamine could not be calculated due to residues in the RAC and processed commodities being <LOQ.

C.3.3 Nature and magnitude of residues in rotational crops

C.3.3.1 Nature of residue

No additional studies submitted

C.3.3.2 Magnitude of residues (field rotational crop studies)

No additional studies submitted

C.3.4 Nature and magnitude of residues in livestock

No additional studies submitted.

C.3.5 Residues in honey

No additional studies submitted.

C.3.6 Storage stability

C.3.6.1 Storage stability of residues in plant products

Stability of cyclohexylamine in high water, high protein, high starch and high acid commodities

Reference:	Freezer Storage Stability of Hexythiazox and its Metabolites in Crop Matrices, [redacted] 2022, Study No. UP19004, Report No. RD-12169
Guideline(s):	OECD 506, Guideline for the Testing of Chemicals, Stability of Pesticide Residues in Stored Commodities, October 2007
Deviations:	None which impact the integrity of the study
GLP:	Yes
Validity of the study:	Acceptable

In the above study storage stability data for (4S,5S)-Hexythiazox and (4R,5R)-Hexythiazox and its metabolites (4S,5S)-PT-1-2, (4R,5R)-PT-1-2, (4S,5S)-PT-1-3, (4R,5R)-PT-1-3, PC-1-1 (4-chlorobenzoic acid), and cyclohexylamine, is presented. As residues are not analysed for PT-1-2 or PC-1-1 in residue trials or processing studies, further consideration of storage stability for these metabolites is not required. Sufficient storage stability in high acid and high water commodities (relevant to the RAC and processed forms), is available from the approval of the active substance and its addendum for hexythiazox and PT-1-3 to support the use on raspberries and blackberries. As a result, additional storage stability data for hexythiazox and PT-1-3 is not required to support the proposed uses on raspberries and blackberries. The study has been checked for adverse data. It is noted some instability is demonstrated for PT-1-3 in barley grain (high starch commodity) and dry haricot beans (high protein commodity). However, as these commodity groups are not relevant to the proposed uses on raspberries, blackberries and their processed forms, further consideration is not required here.

The study has been evaluated to consider storage stability for cyclohexylamine only.

Materials and methods

The frozen storage of cyclohexylamine was studied in barley grain (high starch commodity), spinach (high water commodity), grapes (high acid commodity), and dry haricot beans (high protein commodity) for 14 months.

Untreated homogenate crop sample matrices (10 g) were individually fortified at concentrations of 0.1 mg/kg (10x LOQ). Six samples per commodity matrix were kept at ≤-18°C for up to 14 months. Samples for day 0 analysis were initially fortified with all analytes and immediately analysed. Three fortified samples (two stability samples to be analysed and a third back up sample), and three unfortified samples (one untreated control sample and two procedural recovery samples fortified on the day of analysis), were stored frozen.

After time intervals of approximately 3, 6, 12 and 14 months, samples were removed from storage and were analysed for cyclohexylamine. For the 3-, 6- and 12-month timepoints, two stored stability samples were analysed alongside one control and two procedural recovery samples. For the 14 month timepoint, all three stored stability samples were analysed concurrently. Procedural (fresh) recoveries were undertaken concurrently on samples fortified at 0.1 mg/kg for cyclohexylamine.

Residues of cyclohexylamine were determined according to the LC-MS/MS method UP19001. The analytical method for dry haricot beans was re-validated within the scope of the storage stability study. Full details and validation data for this method can be found in Appendix C.1.3.2. The LOQ for cyclohexylamine is 0.01 mg/kg. The analytical methodology was satisfactorily validated in accordance with SANTE/2020/12830 rev. 1 for strawberry (high acid commodity), strawberry jam (high water commodity), dry haricot beans (high protein commodity) and sunflower seeds (high oil commodity). For storage stability studies, the group of dry matrices is split into high protein content and high starch content matrices. However, since their properties during sample preparation are similar, both matrices are combined into one matrix group for analytical purposes. Therefore, the method is validated for all commodity groups. Additional commodities belonging to the same commodity groups do not require a separate validation. Procedural recoveries were taken for two freshly spiked samples at 0.1 mg/kg at each sampling time point (total of at least eight samples per commodity matrix). Overall mean procedural recoveries per commodity matrix were within the acceptable range 70-110%.

Results and discussions

At each storage interval, residues of cyclohexylamine in the control samples were below 30% of the LOQ. Stored sample and concurrent recoveries were not corrected for interferences in corresponding controls.

The recoveries of compound from crop matrices after the various storage periods are summarised below in Table C.3.6.1-1.

Table C.3.6.1-1 Stability of cyclohexylamine residues following storage at -18°C

Commodity	Level (mg/kg)	Storage interval months (days)	Fresh recovery (mean, %)	Residues after storage (mg/kg)		Recovery (% of nominal fortification level)
				Individual values	Mean	
Spinach	0.1	0	88.8, 89.6 (89.2)	-	-	-
		3 (91)	71.6, 72.4 (72.0)	0.224, 0.228	0.226	226
		6 (185)	52.8, 58.0 (55.4)	0.103, 0.117, 0.122	0.114	114
		12 (369)	94.8, 97.2 (96.0)	0.106, 0.113	0.109	109
		14 (433)	91.2, 94.0 (92.6)	0.0904, 0.0916, 0.108	0.0967	96.7
Dry haricot beans	0.1	0	102, 104 (103)	-	-	
		3 (89)	62.0, 65.2 (63.6)	0.0548, 0.0552	0.0550	55.0
		14 (439)	96.0, 205†	0.0860, 0.103, 0.117	0.102	102
Barley grain	0.1	0	102, 102 (102)	-	-	-
		3 (87)	82.4, 84.4 (83.4)	0.0744, 0.0748	0.0746	74.6

Commodity	Level (mg/kg)	Storage interval months (days)	Fresh recovery (mean, %)	Residues after storage (mg/kg)		Recovery (% of nominal fortification level)
				Individual values	Mean	
		6 (196)	78.4, 83.2 (80.8)	0.0628, 0.0636	0.0632	63.2
		14 (440)	90.0, 93.2 (91.6)	0.0740, 0.0748, 0.0772	0.0753	75.3
Grape	0.1	0	110, 110 (110)	-	-	-
		3 (88)	102, 114 (107)	0.0816, 0.0816	0.0816	81.6
		6 (173)	93.2, 104 (98.8)	0.0800, 0.0820	0.0810	81.0
		14 (438)	93.6, 98.8 (96.2)	0.0796, 0.0816	0.0809	80.9

† Procedural recovery omitted due potential fortification error (see further discussion below)

The majority of the mean procedural recoveries at each sampling time point (freshly spiked control samples 0.1 mg/kg) were within the range 70 – 120 % demonstrating the effectiveness of the method at each time interval, with the exception of:

- The mean recovery of cyclohexylamine (55.4% and 63.6%) at the storage interval of 6 months for spinach and 3 months for dry haricot beans respectively.
- In dry haricot beans at the 14-month time point, one high individual recovery (205%) was obtained.

No specific explanation for the low mean procedural recovery results of 55.4% and 63.6% was given. It is noted that at the 3 month time point for dry haricot beans, the residues after storage showed significant variation (55% recovery of the nominal fortification level). For spinach and dry haricot beans all other mean procedural recoveries including the 14 month timepoint are within the acceptance criteria and significant degradation was not observed at the 14 month timepoint (< 30% amount of cyclohexylamine degraded). As significant decline in residues is not observed in the samples at the 14 month time point and the mean recoveries at later time points are acceptable, it is considered unlikely that

significant breakdown has occurred. As such the poor recoveries might be due to experimental variation and do not affect the final timepoint.

In dry haricot beans at the 14 month time point an individual procedural recovery of 205% was obtained for cyclohexylamine. The other individual procedural recovery was 96.0% and the mean stored recovery was 102%. Therefore, it was suggested that the extraction was conducted correctly, and an error was made in the fortification or extraction of this one procedural recovery. This result was omitted and the residues after storage data accepted based on the one acceptable procedural recovery and the comparable stored recovery results at the 14 month time point.

At some time points a significant difference (greater than 20%), was observed between the residue results after storage for the duplicate samples from the same time point. Therefore, additional analysis of further samples was performed.

Spinach

Residues after storage for cyclohexylamine were 226% of the nominal fortification level at the 3 month time point. However, residues declined between the 6 to 14 month time point but no significant degradation was observed (recovery of nominal fortification level between 96.7 – 114 %).

Residues of cyclohexylamine were stable in spinach (high water commodity) for up to 14 months.

Dry haricot beans

Residues after storage for cyclohexylamine at the 3 month time point were 55.0% of the nominal fortification level. However, results at the 14 month time for cyclohexylamine were 102%, indicating no significant degradation had occurred.

Residues of cyclohexylamine were stable in dry haricot beans (high protein commodity) for up to 14 months.

Barley grain

Residues at the 6 month time point for cyclohexylamine were 63.2% of the nominal fortification level and indicate significant degradation has occurred. However, procedural recovery at this time point had decreased and results at the 14 month time for cyclohexylamine were 75.3%, indicating no significant degradation had occurred and that there is not a decline on storage.

Residues of cyclohexylamine were stable in barley grain (high starch commodity) for up to 14 months.

Grape

The data shows no significant degradation over the time period analysed. Residues of cyclohexylamine were stable in grape (high acid commodity) for up to 14 months.

Conclusion

Cyclohexylamine has been demonstrated to be stable in spinach (high water commodity), dry haricot beans (high protein commodity), barley grain (high starch commodity) and grape (high acid commodity) for at least 14 months when stored at ≤-18°C.

High oil commodities

Reference:	Method validation and freezer storage stability testing of Hexythiazox and metabolites in oily matrix under frozen conditions (≤ -18 °C), [redacted] 2024, Study No. IF21-05915983, Report No. RD-12079
Guideline(s):	OECD 506, Guideline for the Testing of Chemicals, Stability of Pesticide Residues in Stored Commodities, October 2007
Deviations:	No
GLP:	Yes
Validity of the study:	Acceptable

In the above study, storage stability data for (4S,5S)-Hexythiazox and (4R,5R)-Hexythiazox and its metabolites (4S,5S)-PT-1-2, (4R,5R)-PT-1-2, (4S,5S)-PT-1-3, (4R,5R)-PT-1-3, PC-1-1 (4-chlorobenzoic acid), and cyclohexylamine is presented.

The study has been evaluated to consider storage stability for cyclohexylamine only. As high oil commodities are not relevant to the proposed uses on raspberries, blackberries and their processed forms no further consideration is required here for (4S,5S)-Hexythiazox and (4R,5R)-Hexythiazox and its metabolites (4S,5S)-PT-1-2, (4R,5R)-PT-1-2, (4S,5S)-PT-1-3, (4R,5R)-PT-1-3 and PC-1-1 (4-chlorobenzoic acid). The study has been checked for adverse data. It is noted some instability is demonstrated for hexythiazox and PT-1-3 in sunflower seed (high oil commodity). However, as this commodity group is not relevant to the proposed uses on raspberries, blackberries and their processed forms, further consideration is not required here.

In accordance with OECD 506, as only one diverse commodity has been analysed in the report No. RD-12169 for high acid and high water commodity groups, further demonstration of storage stability of cyclohexylamine is needed to support the proposed uses. Extrapolation from each of the five commodity groups can be made where residues in the proposed uses would be assumed to be stable for the same duration of time under the same storage conditions.

Materials and methods

The frozen storage of cyclohexylamine was studied in sunflower seeds (high oil commodity) for 18 months.

Untreated homogenate crop sample matrices (2 g) were individually fortified at concentrations of 0.1 mg/kg (10xLOQ). Samples were kept at ≤-18°C in the dark for up to 545 days in centrifuge tubes. Three fortified samples and three unfortified samples (one untreated control sample and two procedural recovery samples fortified on the day of analysis), were stored frozen.

After time intervals of approximately 0, 3, 6, 14 and 18 months, samples were removed from storage and were analysed for cyclohexylamine. Procedural (fresh) recoveries were undertaken concurrently on samples fortified at 0.1 mg/kg for cyclohexylamine.

Residues of cyclohexylamine were determined according to the method principles of LC-MS/MS method UP19001. Full details and validation data for this method can be found in Appendix C.1.3.2. The LOQ for cyclohexylamine is 0.01 mg/kg. The analytical methodology was satisfactorily validated in accordance with SANTE/2020/12830 rev. 1 for sunflower seeds (high oil commodity). Additional commodities belonging to the same commodity groups do not require a separate validation. Procedural recoveries were taken for two freshly spiked samples at 0.1 mg/kg at each sampling time point (total of ten samples for sunflower seeds). Mean procedural recoveries at each sampling time point were within the acceptable range 70-110%.

Results and discussions

At each storage interval, residues of cyclohexylamine in the control samples were below 30% of the LOQ. Stored sample and concurrent recoveries were not corrected for interferences in corresponding controls.

The recoveries of cyclohexylamine from sunflower seeds after the various storage periods are summarised below in Table C.3.6.1-2.

Table C.3.6.1-2 Stability of cyclohexylamine residues following storage at -18°C

Commodity	Level (mg/kg)	Storage interval months (days)	Fresh recovery (mean, %)	Residues after storage (mg/kg)		Recovery (% of nominal fortification level)
				Individual values	Mean	
Sunflower seeds	0.1	0	76.0, 85.6 (80.8)	0.0792, 0.0799, 0.0812	0.0801	80.6
		3 (94)	90.0, 96.9 (93.4)	0.0978, 0.0984, 0.102	0.0994	99.9

Commodity	Level (mg/kg)	Storage interval months (days)	Fresh recovery (mean, %)	Residues after storage (mg/kg)		Recovery (% of nominal fortification level)
				Individual values	Mean	
		6 (181)	98.5, 100.0 (99.3)	0.0927, 0.0929, 0.0951	0.0936	93.4
		14 (423)	98.0, 107.1 (102.6)	0.0793, 0.0876, 0.0883	0.851	85.3
		18 (545)	108.5, 109.8 (109.1)	0.0912, 0.0926, 0.0948	0.0929	92.7

The mean procedural recoveries (freshly spiked control samples at 0.1 mg/kg) were in the range 80.8 – 109.1% demonstrating the effectiveness of the method at each time interval.

The data show no significant degradation over the time period analysed (< 30% amount of cyclohexylamine degraded).

Conclusion

Cyclohexylamine has been demonstrated to be stable in sunflower seeds (high oil commodity) for at least 18 months when stored at ≤-18°C.

The storage stability study RD-12079 confirms the stability of cyclohexylamine in one additional commodity category (high oil commodity) for up to 18 months. The studies RD-12169 and RD-12079 support the stability of cyclohexylamine in the RAC and processed products of magnitude processing study R C0012.

C.3.6.2 Storage stability of residues in animal products

No additional studies submitted.

C.3.6.3 Storage stability in honey

No additional studies submitted.

Appendix D – List of endpoints

The endpoints outlined in Table D.1 have been derived as a result of this assessment. All other endpoints remained unchanged. The full list of endpoints is outlined in EFSA, 2010.

Table D.1 Nature of the residue on processing

Conditions	Stability		Comment
	EFSA, 2010	**Current assessment**	
Pasteurisation (20 min, 90°C, pH 4)	Hexythiazox: 79.8% AR PT-1-3: 1.9% AR	Hexythiazox: 98.9% AR Cyclohexylamine: <LOQ	
Baking, brewing and boiling (60 min, 100°C, pH 5)	Hexythiazox: 86.8% AR PT-1-3: 2.3%	Hexythiazox: 98.4% AR Cyclohexylamine: 0.5% AR	
Sterilisation (20 min, 120°C, pH 6)	Hexythiazox: 48.7% AR PT-1-3: 48.3% AR	Hexythiazox: 54.4% AR Cyclohexylamine: 43.5% AR	Hexythiazox is not stable under sterilisation conditions.
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). Sterilisation not relevant to the proposed MRLs on raspberries and blackberries.		

Appendix E – Import Tolerances

Sufficient information was provided to confirm that the GAPs outlined in Appendix A have been authorised in USA.

A copy of the current national legislation in the exporting country related to the MRLs under consideration was provided. The MRLs in force in the exporting country are tabulated in Table E.1.

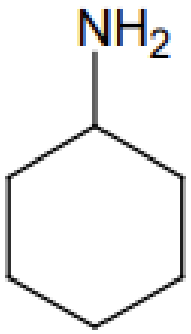
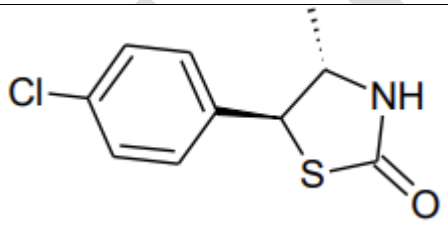
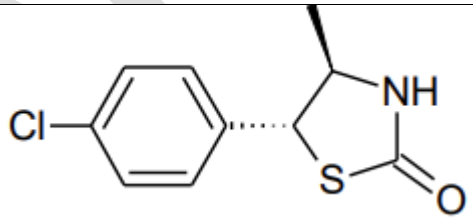
Table E.1 MRLs in force in the exporting country

Commodity	**MRL in force in the exporting country (mg/kg)**
Enforcement residue definition	**for products of plant origin: Hexythiazox**
Raspberries	3.0
Blackberries	3.0

For the import tolerance request on raspberries and blackberries, whilst considering the residue trials on all formulation types and applications, an MRL of 4 mg/kg is derived. However, there is currently an MRL of 3 mg/kg set for hexythiazox in or on raspberries and blackberries in the exporting country due to the extrapolation from one formulation type and one application rate only. HSE recommends that an MRL of 4 mg/kg is set in line with the CXL.

Appendix F – Compound codes

Table F.1 List of metabolites identified in new studies

Code/Trivial name	Chemical name	Structural formula
Cyclohexylamine	Cyclohexylamine	
PT-1-3	(4S,5S)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one	
	(4R,5R)-5-(4-chlorophenyl)-4-methyl-1,3-thiazolidin-2-one	

Appendix G – Abbreviations

ADI	Acceptable daily intake
ADME	Absorption, distribution, metabolism and excretion
Animal model 2017	EFSA model used to calculate the dietary burden of livestock using the OECD feeding tables
ARfD	Acute reference dose
a.s.	Active substance
BBCH	Growth stages of mono- and dicotyledonous plants
bw	Body weight
CF	Conversion factor
cGAP	Critical GAP
CXL	Codex maximum residue limit
DAR	Draft assessment report
DAT	Days after treatment
DT_{90}	Period required for 90% dissipation (define method of estimation)
DT_{50}	Period required for 50% dissipation (define method of estimation)
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
GAP	Good Agricultural Practice
GB	Great Britain
GC-MS	Gas chromatography with mass spectrometry

GLP	Good laboratory practice
HPLC-MS/MS (LC-MS/MS)	High-performance liquid chromatography with tandem mass spectrometry
HR	Highest residue
HSE	Health and Safety Executive
IEDI	International estimate of daily intake
IESTI	International estimate of short-term intake
ILV	Independent laboratory validation
ISO	International Organisation for Standardization
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LC_{50}	Lethal concentration, median
LD_{50}	Lethal dose, median
LOAEL	Lowest observed adverse effect level
LOD	Limit of detection or limit of determination (should be defined)
LoEP	List of endpoints
LOQ	Limit of quantification **NB** the limit of quantification and limit of determination are the same. Assimilated Regulation 396/2005 refers to the limit of determination Assimilated Regulation 1107/2009 refers to the limit of quantification MRLs marked with an asterisk (e.g. 0.01* mg/kg) are MRLs set at the limit of determination/quantification
MRL	Maximum residue level
NEDI	National estimate of dietary intake
NESTI	National estimate of short-term intake

NOAEL	No observed adverse effect level
NRL	National reference laboratory
OECD	Organisation for Economic Co-operation and Development
PBI	Plant-back interval
PES	Post-extraction solids
Pf	Processing factor
PHI	Preharvest interval
PRIMo	(EFSA) Pesticide Residue Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA	Risk assessment
RD	Residue definition
RD-Enf	Residue definition for enforcement (also referred to as RD-Mo i.e. residue definition for monitoring)
RD-RA	Residue definition for risk assessment
RTI	Re-treatment interval
STMR	Supervised trials median residue
TRR	Total radioactive residue
TTC	Threshold of toxicological concern
WG	Water dispersible granule
WHO	World Health Organization

Additional studies relied upon

Author(s)	Year	Title/Testing Facility/Report No/GLP or GEP Status/Published or not	Submitter
[redacted]	2012	Validation of the analytical method for the determination of Hexythiazox and its metabolite PT-1-3 in orange whole fruit, flesh, skin and processed fractions (marmalade, juice and canned fruits), Study No: B1310 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2012	Validation of the analytical method for the determination of Hexythiazox and its metabolite PT-1-3 in grapes RAC and processed fractions (juice, wine, wet pomace and raisins), Study No: B1308 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2021	Hexythiazox: Cross Validation of Analytical Methods for the Determination of Hexythiazox in incurred Crop Commodities [Apple, Strawberry and Grape] Study No: UP/19/003 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2015	Independent Laboratory Validation of the Analytical Method for the Determination of Residues of Hexythiazox in Foodstuffs of Plant origin, Study No S15-0261 GLP Unpublished	Gowan Crop Protection Limited

Author(s)	Year	Title/Testing Facility/Report No/GLP or GEP Status/Published or not	Submitter
[redacted]	2021	Validation of an Analytical Method for the Determination of Hexythiazox and Metabolites in Strawberry and Jam Study No: UP/20/002 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2018	Magnitude of the Residue of Hexythiazox in or on Raspberry Raw Agricultural Commodities Following One Foliar Application of Onager Optek™ Miticide or Savey® 50 DF Ovicide/Miticide (2018), Study No: TCI-18-597 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2020	Hexythiazox - High Temperature Hydrolysis of [cyclohexyl-U-14C]- Hexythiazox in Sterile Buffer. Study No: 814685 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2021	Determination of Residues of Hexythiazox and its Metabolites in Strawberry RAC and Processed Fractions Following treatment with Hexythiazox 250 SC under Field Conditions in Northern and Southern Europe in 2020 Report No: R C0012 GLP Unpublished	Gowan Crop Protection Limited
[redacted]	2022	Freezer Storage Stability of Hexythiazox and its Metabolites in Crop Matrices Study No. UP19004 Report No. RD-12169 GLP Unpublished	Gowan Crop Protection Limited

Author(s)	Year	Title/Testing Facility/Report No/GLP or GEP Status/Published or not	Submitter
[redacted]	2024	Method validation and freezer storage stability testing of Hexythiazox and metabolites in oily matrix under frozen conditions (≤ -18 °C) Study No. IF21-05915983 Report No. RD-12079 GLP Unpublished	Gowan Crop Protection Limited