HEXYTHIAZOX (176)

The first draft was prepared by Mr C Sieke of the Federal Institute for Risk Assessment, Berlin, Germany

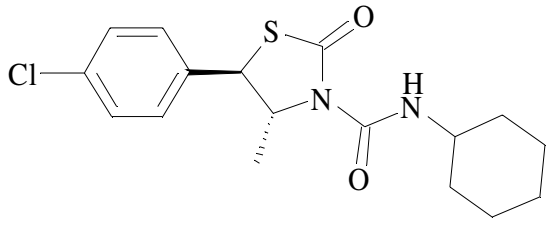
EXPLANATION

Hexythiazox is a non-systemic insecticide and miticide first evaluated by the 1991 JMPR and a number of times subsequently. It was recently reviewed for toxicology by the 2008 JMPR within the periodic review program of the CCPR. An ADI of 0–0.03 mg/kg bw was established. An ARfD was not considered necessary by the Meeting. In the 2009 JMPR hexythiazox was scheduled for periodic review for residues.

CCPR, at its 40th Session in 2008, noted that one manufacturer would submit residue data to JMPR for consideration by the 2009 JMPR. Information on GAPs was also provided by the Netherlands.

IDENTITY

ISO common name	Hexythiazox
Chemical name	
IUPAC	(4RS,5RS)-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-1,3-thiazolid ine-3-carboxamide
CA	trans-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidine- carboxamide
CIPAC No.	
CAS No.	78587-05-0
FAO Specification	none
Structural formula	



Molecular formula	$C_{17}H_{21}ClN_2O_2S$
Molecular mass	352.88 g/mol

Physical and chemical properties

Table 1 Physical and chemical properties

Property	Results	Method (test material)	Reference
Melting point	105.4 °C (378.6 K)	OECD 102 (pure active substance)	(Unemoto, T Hexyt_003)

Property	Results	Method (test material)	Reference
Relative density	1.2829 g/cm^3 (1282.9 kg/m^3) at 20 °C	OECD 109 (pure active substance)	(Tanaka, T Hexyt_006)
Vapour pressure	Vapour pressure at 25 °C: 1.3 x 10^{-9} kPa (measured: 1 × 10^{-8} mm HG)	OECD 104 (pure active substance)	(Teeter, D. Hexyt_002)
Physical state and colour	Pure active substance: white granular	(pure active substance)	(Higasida, S. Hexyt_001)
Odour	Pure active substance: scentless	(pure active substance)	(Higasida, S. Hexyt_001)
Solubility in water including effect of pH	Solubility in water at 25 °C Deionized water: 0.12 mg/L	OECD 105 (pure active substance)	(Teeter, D. Hexyt_002)
Solubility in organic solvents	n-Hexane 4.64 g/L n-Heptane 4.63 g/L Dichloromethane 619 g/L Acetone 159 g/L Toluene 233 g/L Xylene 230 g/L Methanol 17.6 g/L Ethanol 22.1 g/L Acetonitrile 34.5 g/L Ethylacetate 148 g/L	(pure active substance)	(Higashida, S Hexyt_005)
Partition coefficient n-octanol / water	log $P_{ow:}$ 2.75	EPA Guideline (1982) (pure active substance)	(Soeda, Y Hexyt_004)
Hydrolysis rate	pH 5 stable (DT_{50} > 194 d for 22 °C, 50 °C and 70 °C) pH 7 stable (DT_{50} > 194 d at 22 °C and 50 °C, DT50 12 d at 70 °C) pH 9.0 unstable (DT_{50} < 370 d at 22°C, DT_{50} 3.3 d at 50 °C, DT_{50} 0.2 d at 70 °C)	BBA Merkblatt Nr. 55 (pure active substance)	(Anonymous Hexyt_007)
Photochemical degradation	Testing conditions: 25 °C, pH 6 (sterile destilled water) and pH 8.1 (sterile natural water) Sterile distilled water: DT_{50} = 168 d (eq. of 1206 d natural sunlight) DT_{90} = 556 d (eq. of 3993 d natural sunlight) Sterile natural water: DT_{50} = 147 d (eq. of 1056 d natural sunlight) DT_{90} = 487 d (eq. of 3497 d natural sunlight)	(pure active substance)	(Saito, H Hexyt_008)
Dissociation constant	Titration method: not applicable Conductometric method: not applicable Spectrophotometric method: no dissociation detectable	OECD 112 (pure active substance)	(Higashida, S Hexyt_009)

Hydrolysis of hexythiazox

The behaviour of hexythiazox under hydrolytic conditions was investigated by van der Gaauw, A. (2002, Hexyt_043). [^{14}C]hexythiazox radiolabelled in the 5 position of the thiazolidine ring was used to fortify duplicate samples of buffer solutions at pH 4, 5 and 6 with a concentration of 0.4 mg/L each. These solutions were incubated for 90 °C to 120 °C to simulate hydrolytic conditions representative for pasteurisation, baking/boiling and sterilisation.

All samples were analysed before and after the incubation. TRR levels were measured by LSC, which the identification of metabolites was achieved by TLC analyses in comparison to reference compounds.

At pH 4 (90 °C for 20 minutes) and pH 5 (100 °C for 60 minutes) about 1 to 10% of the initial concentration degraded. At pH 6 (120 °C for 20 min) about half of the parent substance was hydrolysed. The only relevant product was identified as PT-1-3, found in amounts of 48.4% of the initial concentration (see Table 2).

Table 2 Recovery and distribution of metabolites after hydrolysis of [^{14}C]hexythiazox

Compound	pH4, 90 °C, 20 min		pH 5, 100 °C, 60 min		pH 6, 120 °C, 20 min	
	0 min	20 min	0 min	60 min	0 min	20 min
hexythiazox	89.7, 91.4 (89.7)	79.2, 80.5 (79.8)	87.5, 88.0 (87.8)	90.8, 82.9 (86.8)	88.4, 93.9 (91.2)	54.0, 43.3 (48.7)
Unknown 1	5.5, 5.6 (5.6)	5.6, 2.1 (3.8)	5.7, 5.7 (5.7)	3.6, 8.2 (5.9)	3.4, 3.6 (3.5)	3.6, 4.9 (4.3)
Unknown 2	2.3, 2.3 (2.3)	5.2, 6.6 (5.9)	3.3, 3.3 (3.3)	4.1, 3.2 (3.7)	0.8, 0.8 (0.8)	1.3, 1.6 (1.5)
PT-1-3	-	2.2, 1.7 (2.0)	-	1.9, 2.7 (2.3)	1.5, 1.6 (1.5)	43.8, 52.9 (48.4)
PT-1-2	1.6, 1.6 (1.6)	3.8, 4.6 (4.2)	3.2, 3.2 (3.2)	2.4, 3.2 (2.8)	2.9, 3.1 (3.0)	-
Unknown 3	-	-	-	ND, 2.0 (2.0)	-	ND, 0.9 (0.9)
Unknown 4	-	-	-	-	-	ND, 1.0 (1.0)
Unknown 5	-	-	-	-	-	ND, 0.8 (0.8)

ND not detectable

Formulations

Currently registered formulations containing hexythiazox are shown in Table 1.

Table 3 Registered formulations

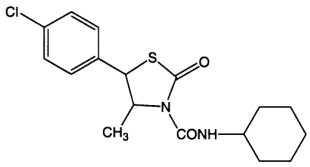
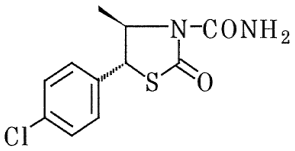
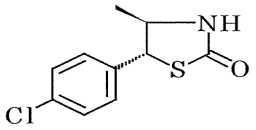
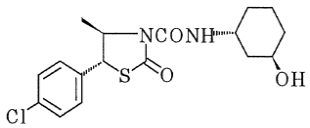
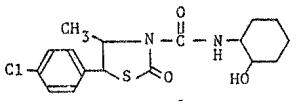
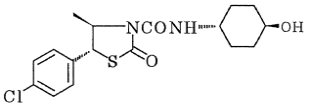
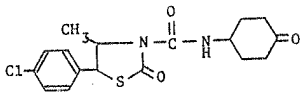
Formulation	ai/Formulation Type/Composition
Hexygon 50DF	500 g/kg, dry-flowable formulation
Hexygon Ovicide Miticide 50WP	500 g/kg, WP
Onager 1E	118 g/kg, EC
Onager 2E	242 g/kg, EC
Savey 50DF	500 g/kg, WG
Savey Ovicide Miticide 50WP	500 g/kg, WP

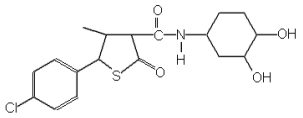
EC -emulsion concentrate; WG -wettable granule; WP -wettable powder

METABOLISM AND ENVIROMENTAL FATE

Chemical names, structures and code names of metabolites and degradation products of hexythiazox are shown below.

Table 4 Known metabolites of hexythiazox

Code Number	Description/Denomination (IUPAC Name)	Study metabolite identified in	Structure
NA-73 / parent	Hexythiazox (trans-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidine-carboxamide)	Apple, citrus, goat, grapes, hens, pear, rat, soil	
PT-1-2	(tran-5-(4-chlorphenyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Apple, Citrus, pear, rat, soil	
PT-1-3	(trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine)	Apple, grapes, rat, soil	
PT-1-4 (cis)	(trans-5-(4-chlorophenyl)-N-(*cis*-3-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Citrus, goat, rat	
PT-1-4 (trans)	(trans-5-(4-chlorophenyl)-N-(*trans*-3-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Goat	
PT-1-6 (trans)		Citrus	
PT-1-8 (cis)	(trans-5-(4-chlorophenyl)-N-(*cis*-4-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Apple, citrus ,goat, hens, pear, rat	
PT-1-8 (cis)-conjugate		Apple	
PT-1-8 (trans)	(trans-5-(4-chlorophenyl)-N-(*trans*-4-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Apple, citrus , goat, hens, pear, rat	
PT-1-8 (trans)-conjugate		Apple	
PT-1-9	(trans-5-(4-chlorophenyl)-4-methyl-N-(4-oxocyclohexyl)-2-oxothiazolidine-3-carboxamide)	Rat, soil	

Code Number	Description/Denomination (IUPAC Name)	Study metabolite identified in	Structure
PT-1-10	(trans-5-(4-chlorophenyl)-N-(3,4-dihydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide)	Goat, Hens	

Animal metabolism

The Meeting received animal metabolism studies with hexythiazox in rats, goats and laying hens. The studies on the metabolism of hexythiazox in animals using radioactive material were conducted with hexythiazox labelled with ^{14}C in the 5-position of the thiazolidine ring. The studies on rats were evaluated by the WHO Core Assessment Group, but briefly summarised within this document.

Rats

The metabolism of hexythiazox in rats is described in the toxicological evaluation of the JMPR Report 2008. In summary the absorption, distribution and excretion of [^{14}C]hexythiazox in rats was rapid at 10 mg/kg bw, but much slower at 880 mg/kg bw. The extent of absorption at 10 mg/kg bw was approximately 30% on the basis of the level of urinary excretion, but significantly lower at 880 mg/kg bw. Most (about 60–90%, depending on the administered dose) of the radiolabel was excreted in the faeces within 3 days. About 10–20% of the administered dose was excreted as intact hexythiazox at the lower dose and 65–70% at the higher dose. The highest concentrations of tissue residues were found in fat, adrenals, liver and ovaries; the main component in fat was hexythiazox. Metabolism was extensive, but most of the radioactive material was not attributed to specific metabolites. The main metabolic reactions identified were hydroxylation of the cyclohexane ring and cleavage of the amide bond to the cyclohexane ring.

Lactating goats

The metabolism of hexythiazox in goats was investigated by Koeppe (1986, Hexyt_040). One lactating goat was dosed twice daily for seven consecutive days with 46 mg per day (corresponding to approximately 26 ppm in the feed or 1.16 mg/kg bw) with [^{14}C]hexythiazox labelled in the 5 position of the thiazolidine ring. The compound was administered in two doses per day via capsule. Milk, urine and faeces were collected throughout the dosing period and samples of meat, fat, liver and kidney were taken at sacrifice.

The samples were analysed by LSC for total radioactivity. Milk samples were mixed with acetone to precipitate proteins, cooled overnight and centrifuged. The protein pellets were extracted two additional times using acetone/water. The remaining aqueous layer was partitioned with n-hexane, followed by three additional extractions using methylene chloride. Tissue samples were initially extracted with n-hexane, followed by a partitioning with methylene chloride or methanol to remove lipids in the extracts. All layers were analysed for radioactivity by LSC. For the identification of the radioactivity, the different layers were analysed by LC against reference compounds. The identification of metabolites found was confirmed by TLC and by mass spectroscopy.

In average most of the radioactivity administered was excreted via the faeces of the animal (56.2% of the administered dose). Urine contained about 18.1 % of the administered dose while in milk 0.3% of the radioactivity recovered was found (corresponding to approx. 0.1 mg/kg). The TRRs for the tissues are presented in Table 5.

Table 5 TRR found in tissues of one lactating goats dosed with 46 mg per day [^{14}C]hexythiazox

Tissue	TRR in mg/kg parent equivalents
Liver	2.2
Kidney	0.44
Flank muscle	0.09
Leg muscle	0.11
Loin muscle	0.1
Renal fat	0.55
Omental fat	0.52
Peripheral fat	0.24
Back fat	0.29

In milk and fat unchanged hexythiazox was the dominant residue, found in amounts of 31% (0.04 mg/kg) and 61% of the TRR (0.26 mg/kg), respectively.

In other tissues, the metabolites PT-1-4 (cis and trans), PT-1-8 and PT-1-10 were found at comparable levels. Hexythiazox was present, but its amounts were all at or below 10% of the TRR. An overview of the composition of radioactivity is presented in Table 6.

Table 6 Composition of radioactivity found in one lactating goat dosed with [^{14}C]hexythiazox

Compound	Milk		Liver		Kidney		Fat		Muscle	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
hexythiazox	0.04	31	0.17	8	0.004	1	0.26	61	0.01	10
PT-1-4 (trans)	0.01	11	0.06	3	0.007	2	0.005	1	0.01	5
PT-1-4 (cis)	0.01	5	0.32	15	0.06	14	0.09	22	0.02	23
PT-1-8	0.01	6	0.12	6	0.02	5	0.03	7	0.01	9
PT-1-10	0.01	7	0.69	31	0.11	26	0.02	5	0.02	16
Unidentified radioactivity	0.01	13	0.33	15	0.16	36	0.01	3	0.03	23
Polars	0.02	17								
Other	< 0.01	1	0.22	10	0.05	12	0.003	<1	0.01	12
Protein (after extraction)	0.01	10								
Not extractable			0.28	13	0.02	4	0.002	<1	0.01	3
Total	0.12	101	2.2	101	0.44	100	0.42	100	0.1	101

Laying hens

Four groups of laying hens (five animals each) were dosed with [^{14}C]hexythiazox, labelled in the 5-position of the thiazolidine ring, at a rate of 0.6 mg per day for 6 consecutive days by Chrzanowski (1985, Hexyt_041). One additional group was doses at 10× rate (6.0 mg per day). Eggs and excreta were collected throughout the dosing period and samples of meat, liver and fat were taken at sacrifice.

In all samples the TRR was measured by combustion with LSC detection. For the identification of the radioactivity, the samples were first ultrasonically extracted using methanol three times. Subsequently the extracts were partitioned with acetonitrile and n-hexane. The combined and concentrated extracts were used for TLC in comparison to reference substances. Unextracted residues were released as far as possible with 1N NaOH.

In the samples obtained eggs gave the highest radioactivity (0.5 to 2.1 mg/kg), followed by liver (0.14 to 1.6 mg/kg). In fat, kidney and muscle tissues the TRR was relatively low ranging from 0.01 to 0.07 mg/kg in the low dose group and 0.08 to 0.5 mg/kg in the high dose group (see Table 7).

Table 7 TRR found in eggs and tissues of laying hens dosed with 0.6 or 6 mg [^{14}C]hexythiazox per day

Tissue	TRR in mg/kg parent equivalents	
	Low dose (0.6 mg per day)	High dose (6 mg per day)
Eggs	0.5	2.1
Liver	0.14	1.6
Fat	0.07	0.5
Kidney	0.06	0.5
Breast muscle	0.01	0.08

For the identification of the radioactivity only the samples obtained from the high dose group were used. For eggs and liver only half of the total radioactivity could be extracted and identified. The parent substance was found in eggs at amounts of 4.4% of the TRR. Most of the radioactivity was found as PT-1-5, PT-1-8 (cis and trans) and PT-1-10, each at levels of 3.7% to 14% of the TRR. According to the study report the composition of radioactivity in muscle and kidney was comparable to liver.

In fat tissues unchanged parent was the dominating residue at a level of 48% of the TRR. The only other metabolite found was PT-1-8 cis and trans (20% and 26% of the TRR).

Table 8 Composition of radioactivity found in laying hens dosed with [^{14}C]hexythiazox at 6 mg/kg

Compound	Eggs		Liver [b]		Fat	
	mg/kg [a]	% TRR	mg/kg [a]	% TRR	mg/kg [a]	% TRR
hexythiazox	0.09	4.4	< 0.01	< 0.01	0.24	48
PT-1-8 (cis)	0.08	3.7	0.10	6.0	0.1	20
PT-1-8 (trans)	0.10	4.7	0.08	4.8	0.13	26
PT-1-10	0.29	14	0.22	14	< 0.01	< 0.01
Unidentified radioactivity	0.14	6.9	0.13	8.4	< 0.01	< 0.01
Protein bound	0.11	5.0	0.07	5.0	< 0.01	< 0.01
Unextracted	1.11	53	0.8	50	0.03	6
Total	1.93	92	1.41	88	0.5	100

[a] calculated by the author

[b] according to the study report comparable to muscle and kidney

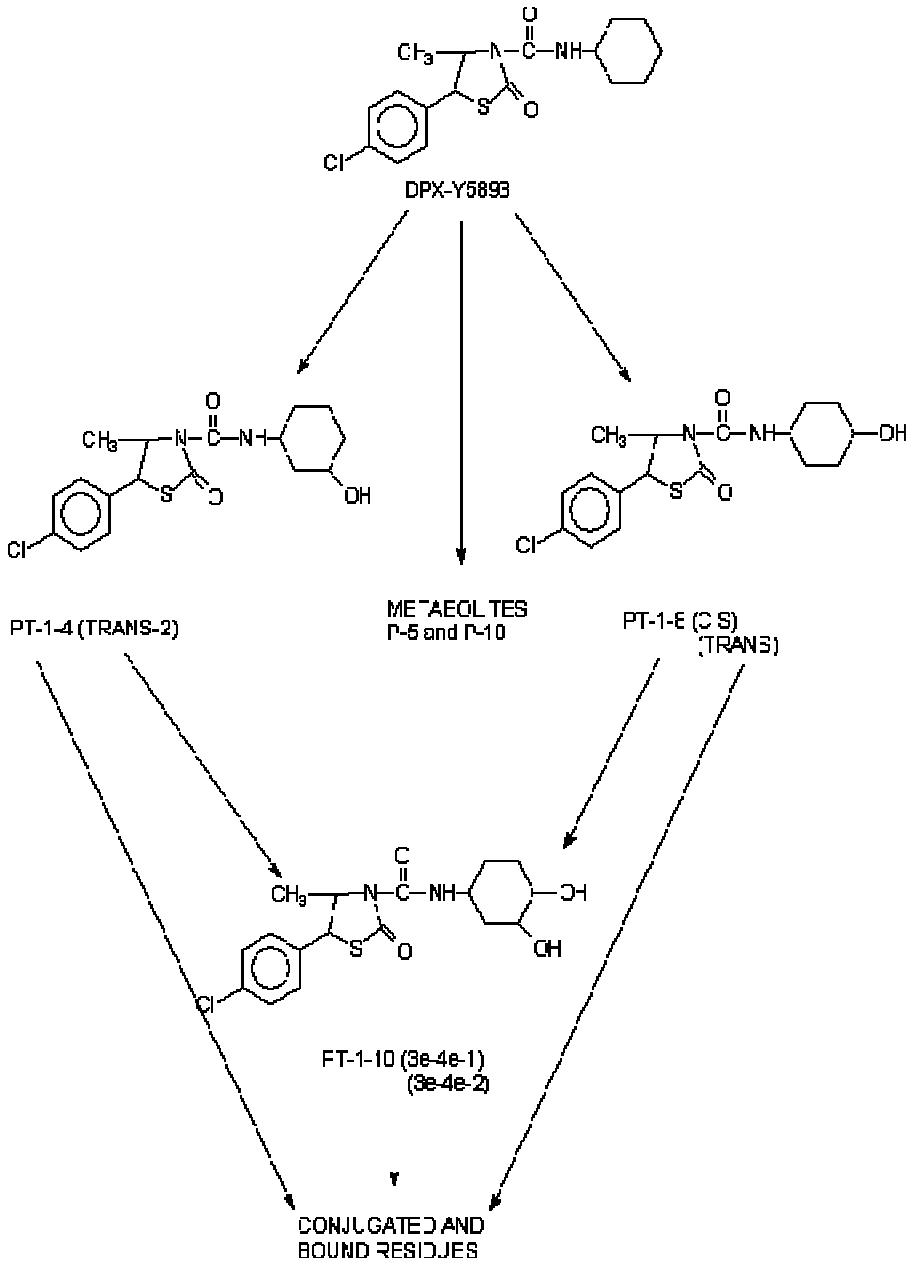


Figure 1 Proposed metabolic pathway in laying hens

Plant metabolism

The metabolism of hexythiazox following foliar application was investigated in the crop group of fruits on apples, citrus, grapes and pears. In addition one study on tea was submitted, which is representative of leafy crops. In all studies [^{14}C]hexythiazox labelled in the 5 position of the thiazolidine ring was used as test substance.

Apples

In this study on an apple fruit conducted by Soeda (1983, Hexyt_010) plant cultivated in greenhouse were treated with [^{14}C]hexythiazox labelled in the 5 position of the thiazolidine ring. The test substance was applied via micropipette at a rate of 1.2 mL per four leaves or 1 mL per apple using a test solution with 5 mg [^{14}C]hexythiazox per 100ml (corresponding to 5 g ai per hL).

Samples of treated and untreated leaves were taken 0, 10, 21, 30, 60 and 91 days after the application. In the first step, the surface of the leaves was washed using methyl alcohol (10 mL/leaf). The washed leaves were homogenized with 80% aqueous methanol, centrifuged and filtered. The fibrous residue was re-extracted in the same manner a further two times. The homogenate extracts were combined and adjusted to 50% aqueous methanol with distilled water. The 50% methanol solution was extracted twice with chloroform. Characterisation of the radioactivity was achieved by TLC. For the measurement of the total radioactivity LSC was used.

The recovery of the radioactivity in leaves decreased from 103.3% down to 95.1% after 91 days. Most of the radioactivity was found in the treated leaves. A very small amount of translocated radioactivity was found, less than 0.2% of the applied dose, during the experimental period. The radioactivity in the homogenate gradually increased and reached 23.7% of the applied dose at 91 days (see Table 9).

In the extracts most of the radioactivity was identified as unchanged parent compound. The surface wash contained metabolite PT-1-2 in amounts of 0.9–1.2% of the TRR. No further metabolites were identified in the surface wash. In the leaf extracts hexythiazox was also present in amounts of 3.1–6.6% of the TRR. Additional metabolites were identified at rates of 0.4–0.7% of TRR for PT-1-2, 0.5–2.5% TRR for cis PT-1-8 (including conjugates) and 1.8–6.8% TRR for trans-PT-1-8 (including conjugates) (see Table 10).

Table 9 Recovery and distribution of radioactivity in apple leaves after foliar treatment of [^{14}C]hexythiazox

Plant part and fraction	Days after treatment (% applied dose)					
	0	10	21	30	60	91
Treated leaf						
Methanol surface wash	103.3	94.3	92.1	85.2	81.9	69.6
Methanol/Cholorform extract		6.8	9.1	11.5	14.7	18.6
50% methanol extract		0.7	1.2	1.4	2.8	5.1
Fibrous residue		0.5	0.6	0.8	1.0	1.7
Subtotal	103.3	102.3	103.0	98.9	100.4	95.0
Untreated leaves						
Upper branch part than treated leaves		0.01	0.02	0.06	0.03	0.05
Lower branch part than treated leaves		n.d.	0.01	0.06	0.05	0.08
Subtotal		0.01	0.03	0.12	0.08	0.13
Total	103.3	102.3	103.0	99.0	100.5	95.1

n.d. not detected

Table 10 Balance of organo-soluble ^{14}C-compounds in apple leaves treated with [^{14}C]hexythiazox

Fraction	Compound	Days after treatment (% applied dose)				
		10	21	30	60	91
Surface wash	hexythiazox	91.5	89.4	82.5	79.2	67.3
	PT-1-2	1.2	1.1	1.3	1.2	0.9
	others	1.6	1.6	1.4	1.5	1.4
	subtotal	94.3	92.1	85.2	81.9	69.6
Flesh extract	hexythiazox	3.4	3.1	3.9	5.5	6.6
	PT-1-2	0.4	0.5	0.7	0.7	0.6
	PT-1-8 (cis)	< 0.1	0.1	0.1	0.2	0.4

Fraction	Compound	Days after treatment (% applied dose)				
		10	21	30	60	91
	PT-1-8 (cis)-conjugate	0.5	0.9	1.4	1.4	2.1
	PT-1-8 (trans)	0.2	0.3	0.4	0.7	0.8
	PT-1-8 (trans)-conjugate	1.6	3.2	3.9	4.9	6.0
	others	0.7	1.0	1.1	1.3	2.1
	subtotal	6.8	9.1	11.5	14.7	18.6
Total	hexythiazox	94.9	92.5	86.4	84.6	73.7
	PT-1-2	1.6	1.6	2.0	1.9	1.5
	PT-1-8 (cis)	< 0.1	0.1	0.1	0.2	0.4
	PT-1-8 (cis)-conjugate	0.5	0.9	1.4	1.4	2.1
	PT-1-8 (trans)	0.2	0.3	0.4	0.7	0.8
	PT-1-8 (trans)-conjugate	1.6	3.2	3.9	4.9	6.0
	others	2.3	2.6	2.5	2.8	3.5
	subtotal	101.1	101.2	96.7	96.6	88.2

For apple fruits single units were collected after 10, 20, 30 and 59 days. After washing the surface, the fruit was peeled and sectioned into flesh and core. Analysis was conducted according to the procedure described for leaves. In addition the fibrous residue of day 59 samples was extracted with acetone twice. For the measurement of the total radioactivity LSC was used (see Table 11).

Identification of the TRR reveals mostly unchanged parent hexythiazox on the surface as well as in the flesh and core. Traces of PT-1-2 and PT-1-8 (trans) were found in levels of less than 1.2% of the TRR (see Table 12).

Table 11 Recovery and distribution of radioactivity in apple fruits treated with [^{14}C]hexythiazox

Fraction	Days after treatment (% applied dose)			
	10	20	30	59
Surface wash	92.2	92.6	83.0	78.7
Peel				
80% Methanol				
Chloroform extract	2.6	4.4	8.7	10.5
50 % Methanol extract	0.2	0.3	0.4	0.8
Fibrous residue	0.3	0.7	1.6	1.1
Subtotal	3.1	5.4	10.7	12.4
Flesh	0.3	0.6	0.9	1.1
Core	0.1	0.1	0.1	0.1
Peduncle	< 0.01	< 0.01	< 0.01	< 0.01
Total	95.7	98.7	94.7	92.3
Fruit weight (g)	46.1	81.4	99.5	224.0
Concentration hexythiazox in mg/kg	1.01	0.54	0.44	0.20

Table 12 Balance of organo soluble ^{14}C-compounds in apple fruits treated with [^{14}C]hexythiazox

Fraction	Compound	Days after treatment (% applied dose)			
		10	20	30	59
Surface wash	hexythiazox	89.2	89.4	80.2	75.0
	PT-1-2	0.9	0.8	0.7	0.9
	PT-1-8 (trans)	0.5	0.6	0.5	0.8
	others	1.6	1.8	1.6	2.0
	subtotal	92.2	92.6	83.0	78.7
Peel extract	hexythiazox	2.1	3.6	7.4	8.5
	PT-1-2	0.2	0.3	0.4	0.3
	PT-1-8 (trans)	< 0.1	< 0.1	0.2	0.2
	others	0.4	0.5	0.7	1.5
	subtotal	2.7	4.4	8.7	10.5
Total	hexythiazox	91.3	93.0	87.6	83.5
	PT-1-2	1.1	1.1	1.1	1.2
	PT-1-8 (trans)	0.5	0.6	0.7	1.0
	others	2.0	2.3	2.3	3.5
	subtotal	94.9	97.0	91.7	89.2

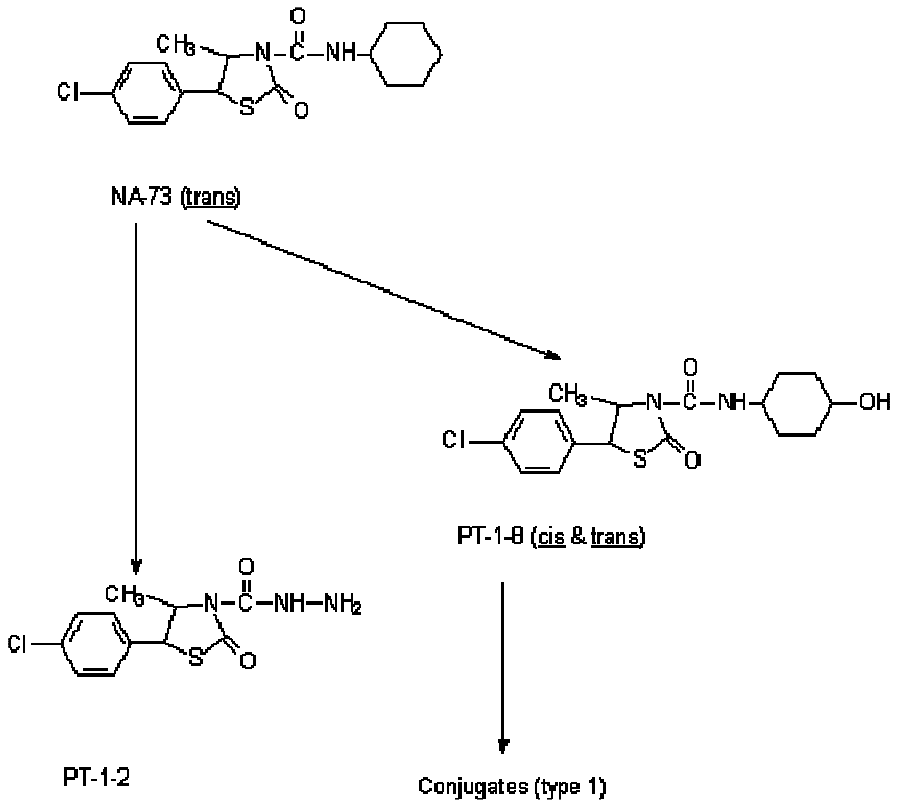


Figure 2 Proposed metabolic pathway of hexythiazox in apples

Citrus

For citrus fruit the metabolism of hexythiazox was investigated by Soeda (1983, Hexyt_011) on five year old citrus trees (*Citrus unshiu*, var. Sugiyamaunshiu). The citrus plants were treated on the leaf or fruit with [^{14}C]hexythiazox labelled in the 5-position of the thiazolidine ring and cultivated in a greenhouse. The test substance was applied via micropipette at a rate of 0.8 mL per four leaves or

0.4 mL per fruit using a test solution with 5.3 mg [^{14}C]hexythiazox per 100 mL (corresponding to 5 g ai per hL).

Samples of treated and untreated citrus leaves were taken at 7, 14, 30, 62 and 90 days after the application. Additionally untreated fruits from the treated branches were collected. In the first step the surface of the samples was washed using methyl alcohol (10 mL/leaf). The washed leaves were homogenized with 80% aqueous methanol, centrifuged and filtered. The fibrous residue was re-extracted in the same manner further two times. The homogenate extracts were combined and adjusted to 50% aqueous methanol with distilled water. The 50% methanol solution was extracted twice with dichloromethane. In addition, the remnants of the samples after 30. 62 and 90 days were treated with pectinase to release additional radioactivity. A final clean-up was achieved using a C18-SPE-cartrige and an elution with methanol. Characterisation of the radioactivity was achieved by TLC (see Table 13).

For citrus fruits, two units were collected after 7, 14, 30, 60 and 91 days. After washing the surface, the fruit was peeled and sectioned into flesh and peel. Analysis was conducted according to the procedure described for leaves, except chloroform was used instead of dichloromethane and that the aqueous layer was not analysed. For the measurement of the total radioactivity LSC was used (see Table 14)

Table 13 Recovery and distribution of radioactivity in citrus leaves and fruits after foliar treatment of [^{14}C]hexythiazox

Plant part and fraction	Days after treatment (% applied dose)				
	7	14	30	62	90
Treated leaf					
Methanol surface wash	92.5	87.0	74.5	63.0	58.0
80 % methanol extract	0.6	1.1	4.1	7.1	8.5
Chloroform extract	3.8	4.1	7.9	5.7	5.4
Fibrous residue	0.4	0.3	1.6	1.4	1.4
Subtotal	97.3	92.5	88.1	77.2	73.3
Untreated leaves	< 0.1	< 0.1	0.2	0.2	< 0.1
Stem	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Untreated fruit from the same branch					
Peel	0.1	0.2	0.2	0.4	0.3
Flesh	< 0.1	0.2	0.2	0.4	0.1
Total	97.4	92.9	88.7	78.2	73.7

Table 14 Recovery and distribution of radioactivity in citrus fruits treated with [^{14}C]hexythiazox

Fractions	Days after treatment (% applied dose)					
	0	7	14	30	60	91
Surface wash	99.2	91.4	76.4	65.5	35.4	24.4
Peel						
80% Methanol						
Chloroform extract	-	7.8	13.1	19.8	39.5	42.3
50 % Methanol	-	0.5	1.1	2.4	6.1	5.7
Fibrous residue	-	0.4	0.7	1.4	3.3	4.7
subtotal	-	8.7	14.9	23.6	48.9	52.7
Flesh	-	< 0.1	< 0.1	< 0.1	0.1	0.1
Total	99.2	100.1	91.3	89.1	84.4	77.2
Fruit weight						
Peel	14.0	11.4	12.8	17.5	20.7	29.3

Fractions	Days after treatment (% applied dose)					
	0	7	14	30	60	91
Flesh	33.9	36.9	40.4	69.0	78.8	106.9
Total	47.9	48.3	53.2	86.5	99.5	136.2
Concentration of hexythiazox						
Peel	1.52	1.90	1.52	1.09	0.89	0.57
Flesh	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

In the citrus leaves the share of unchanged parent compound decreased over the study time of 90 days from 93.5% to 52.5% of the applied radioactivity. Most of the residue was located on the surface of the leaves (> 90%). Organo-soluble metabolites were detected in amounts of less than 3% of the applied dose each. Expect of PT-1-2, which accounted 2.3% of the TRR after 90 days, all other structures identified were present at less than 1% of the TRR (see Table 15). In the aqueous layer higher amounts of PT-1-6 (trans-2) and PT-1-8 (trans) in concentrations of up to 1.3% and 3.0% of the TRR were identified (see Table 16).

Table 15 Balance of organo-soluble ^{14}C-compounds in citrus tree leaves treated with [^{14}C]hexythiazox

Plant part and fraction	Compound	Days after treatment (% applied dose)				
		7	14	30	62	90
Surface wash	hexythiazox	90.4	84.2	69.3	56.5	50.8
	PT-1-2	0.6	0.9	1.4	1.3	1.7
	others	1.5	1.9	3.8	5.2	5.5
	subtotal	92.5	87.0	74.5	63.0	58.0
Flesh extract	hexythiazox	3.1	3.0	4.5	2.5	1.7
	PT-1-2	0.2	0.3	0.6	0.6	0.6
	PT-1-4 (trans-2) conjugates	Not determined	Not determined	0.2	0.1	0.1
	PT-1-6 (trans-2) conjugates	Not determined	Not determined	0.5	0.3	0.4
	PT-1-8 (cis) conjugates	Not determined	Not determined	0.1	0.2	0.2
	PT-1-8 (trans) its conjugates	Not determined	Not determined	0.2 0.5	0.2 0.6	0.2 0.5
	others	0.5	0.8	1.3	1.2	1.7
	subtotal	3.8	4.1	7.9	5.7	5.4
Total	hexythiazox	93.5	87.2	73.8	59.0	52.5
	PT-1-2	0.8	1.2	2.0	1.9	2.3
	PT-1-4 (trans-2) conjugates	Not determined	Not determined	0.2	0.1	0.1
	PT-1-6 (trans-2) conjugates	Not determined	Not determined	0.5	0.3	0.4
	PT-1-8 (cis) conjugates	Not determined	Not determined	0.2	0.2	0.2
	PT-1-8 (trans) conjugates	Not determined	Not determined	0.5	0.6	0.5
	others	2.0	2.7	5.1	6.4	7.2
	total	96.3	91.1	82.4	68.7	63.4

Table 16 Balance of water-soluble ^{14}C-compound in citrus leaves treated with [^{14}C]hexythiazox

Fraction	Aglycone of conjugates	Days after treatment (% applied dose)		
		30	62	90
Chloroform extract after pectinase treatment	hexythiazox	1.3	0.7	1.1
	PT-1-4 (trans-2)	0.2	0.3	0.5
	PT-1-6 (trans-2)	0.5	1.0	1.3
	PT-1-8 (cis)	0.3	1.0	0.7
	PT-1-8 (trans)	0.8	2.4	3.0
	others	0.6	1.1	1.0
	subtotal	3.7	6.5	7.6
Aqueous layer	others	0.4	0.6	0.9
Total		4.1	7.1	8.5

In citrus fruits all radioactivity was found on the surface or the peel of the fruits. In the flesh no radioactivity above 0.001 mg/kg could be detected. In the surface wash and the peel extract the concentration of hexythiazox decreased from 98.1% down to 30.5% of the applied dose after 91 days. The only metabolite identified in the surface wash was PT-1-2 (up to 1.0% TRR), which was also found in the peel extract at higher amounts (up to 3.3% TRR). In the peel extract free and conjugated PT-1-4 (trans-2), PT-1-6 (trans-2), PT-1-8 (cis) and PT-1-8 (trans) were found. The conjugated form was always present in at least 2-fold higher amounts. In total PT-1-4 (trans-2), PT-1-6 (trans-2), PT-1-8 (cis) and PT-1-8 (trans) including conjugates were found in concentrations of up to 1.5%, 7.0%, 4.3% and 13.7% of the TRR, respectively (see Table 17).

Table 17 Balance of organo-soluble ^{14}C-compounds in citrus fruit treated with [^{14}C]hexythiazox

Fraction	Compound	Days after treatment (% applied dose)					
		0	7	14	30	60	91
Surface wash	hexythiazox	98.1	88.0	72.8	62.0	31.8	21.8
	PT-1-2	0.4	0.9	1.0	0.9	0.9	0.7
	others	0.7	2.5	2.6	2.6	2.7	1.9
	subtotal	99.2	91.4	76.4	65.5	35.4	24.4
Peel extract	hexythiazox	-	5.0	6.5	7.6	10.8	8.7
	PT-1-2	-	0.3	0.6	1.3	2.9	3.3
	PT-1-4 (trans-2) its conjugates	-	- 0.1	- 0.5	0.1 0.8	0.2 1.2	0.1 1.4
	PT-1-6 (trans-2) its conjugates	-	0.2 0.7	0.5 1.6	0.9 3.0	1.5 5.0	2.0 5.0
	PT-1-8 (cis) its conjugates	-	< 0.1 0.2	< 0.1 0.4	0.1 0.6	0.4 2.9	0.4 3.9
	PT-1-8 (trans) its conjugates	-	0.2 0.7	0.5 1.7	0.9 3.0	2.4 9.6	2.9 10.8
	others	-	0.4	0.8	1.5	2.6	3.8
	total	-	7.8	13.1	19.8	39.5	42.3
Total	hexythiazox	98.1	93.0	79.3	69.6	42.6	30.5
	PT-1-2	0.4	1.2	1.6	2.2	3.8	4.0
	PT-1-4 (trans-2) incl. conjugates	-	0.1	0.5	0.9	1.4	1.5
	PT-1-6 (trans-2) incl. conjugates	-	0.9	2.1	3.9	6.5	7.0
	PT-1-8 (cis)	-	0.2	0.4	0.7	3.3	4.3

Fraction	Compound	Days after treatment (% applied dose)					
		0	7	14	30	60	91
	incl. conjugates						
	PT-1-8 (trans) incl conjugates	-	0.9	2.2	3.9	12.0	13.7
	others	0.7	2.9	3.4	4.1	5.3	5.7
	total	99.2	99.2	89.5	85.3	74.9	66.7

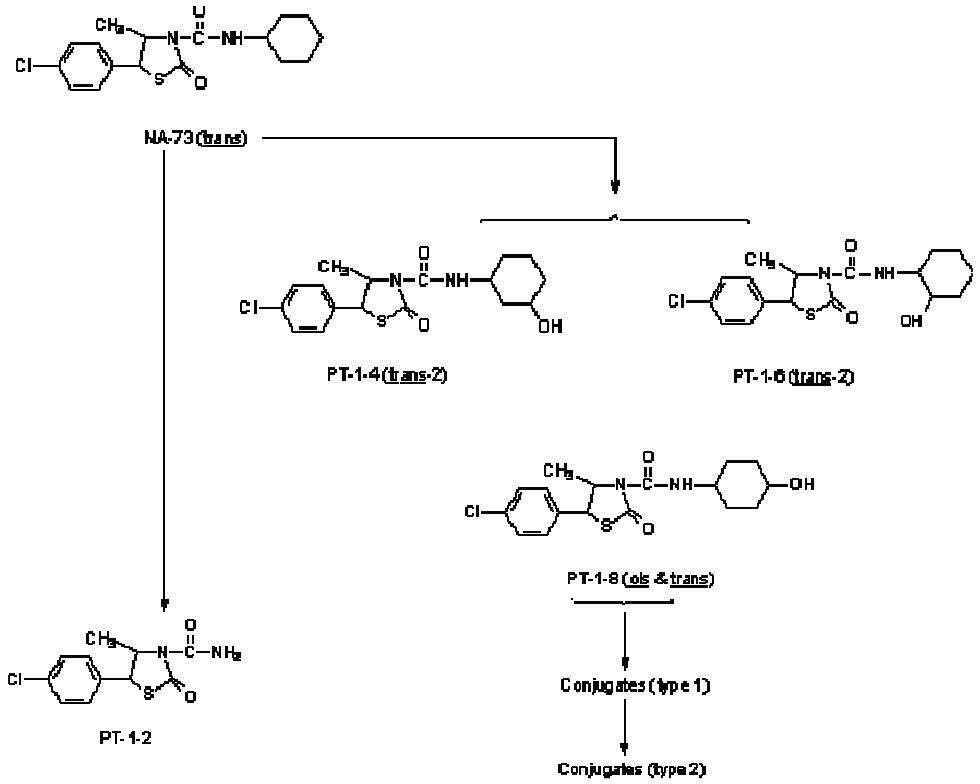


Figure 3 Proposed metabolic pathway of hexythiazox in citrus

Grapes

In a study conducted by Knight (2008, Hexyt_012) mature grape vines (variety: Thompson seedless) were grown under conditions typical of commercial production and treated with a 10% WP formulation of [^{14}C]hexythiazox. The active substance was labelled in the 5-position of the thiazolidine-ring. The plants received two treatments of 0.1 kg ai/ha each diluted in 1000 L water/ha. Samples of protected and unprotected fruits were collected 21 days after the final application. Leaves samples were collected in parallel, but no analysis was performed.

The samples of fruit were surface washed with methanol on the day of sampling. The washed fruit were extracted with methanol:water (80:20, v:v). This extract was added water to 50% water, then partitioned using chloroform. A subsample of these organosoluble extracts was treated hydrolytically over night at 37 °C with 1M hydrochloric acid and 0.2M sodium hydroxide. Residues remaining after extraction were combusted. The sum of the radioactivity recovered in the washes, extracts and in the solids was used to calculate the total radioactive residue (TRR, see Table 18). In the whole fruits TRR of 0.233 mg/kg were found. About 2/3 of the radioactivity was located on the surface of the fruits. Only a minor share of the residue measured could not be extracted (5.7% of the TRR).

An identification of the radioactivity found was achieved by liquid chromatography using LSC and UV detection against the retention times of standard substances. In total 4 different HPLC-gradient systems were used to reach a better resolution of the peaks. Mass sensitive methods for an identification of the radioactive residues were not used.

Table 18 Total radioactive residues in grapes after treatment with [^{14}C]hexythiazox

Fraction	Treated fruit		Protected fruits	
	% TRR	mg/kg	% TRR	mg/kg
Surface wash	62.9	0.147	46.9	0.005
Total extractable residue				
Organic extract	24.2	0.056	Not partitioned	Not partitioned
Aqueous extract	7.2	0.017	Not partitioned	Not partitioned
Subtotal	31.4	0.073	40.2	0.004
Unextracted residue	5.7	0.013	13.0	0.001
Total	100	0.233	100	0.010

The identification of the radioactivity in grape fruits revealed a large share of the TRR on the surface to be unchanged parent compound (62.5% of the TRR, 0.146 mg/kg). PT-1-3 was the only reference compound coeluating with a peak detected in NaOH treated organic extract (11.2% of the TRR, 0.026 mg/kg). Additional peaks were identified in all extracts/washes, but no identification of the radioactivity against reference compound and/or by mass spectrometric methods was achieved or conducted (see Table 19).

Table 19 Proportions of radioactive compounds in grapes treated with [^{14}C]hexythiazox

Identified component	Retention time (min)	Fruit surface wash %TRR (mg/kg parent eq.)	Organic fruit extract – initial partition %TRR (mg/kg parent eq.)	Organic fruit extract – repeat partition %TRR (mg/kg parent eq.)	NaOH treated organic fruit extract %TRR (mg/kg parent eq.)
	3 - 5	0.4 (0.001)	3.3 (0.008)	4.7 (0.011)	4.1 (0.010)
	5 - 12	-	12.1 (0.028)	11.1 (0.026)	0.8 (0.002)
PT-1-3	15 - 17	-	-	-	11.2 (0.026)
	17 - 20	-	-	-	2.2 (0.005)
	43 - 45	-	1.3 (0.003)	0.2 (0.001)	-
Hexythiazox	45 - 47	62.5 (0.146)	5.0 (0.012)	6.3 (0.015)	5.2 (0.012)
Others	-	-	2.5 (0.006)	2.1 (0.005)	0.9 (0.002)
Total	-	62.9 (0.147)	24.2 (0.057)	24.4 (0.058)	24.4 (0.057)

Pears

For pears the metabolism of hexythiazox was investigated by Soeda (1983, Hexyt_013). Four-year old pear trees (*Prunus serotinus, var. Chojuro*) were grown in pots, which were maintained in greenhouse. The plants were treated by application of a test solution containing 5 mg [^{14}C]hexythiazox per 100 mL (corresponding to 5 g ai per hL). Leaves and fruits of the pear trees received one application via micro-pipette of 2mL and 1 mL, respectively.

Two branches with four treated and 3-8 untreated leaves were harvested 0 (immediately after treatment), 5, 10, 20, 30, 60 and 90 days after treatment. The branch was sectioned into the treated leaves, untreated leaves and fruit. After measuring their fresh weights, the surface of the treated leaves was washed with methanol (15 mL per leaf). The washed leaves were homogenised with 80% aqueous methanol. The homogenate was centrifuged and then filtered. The fibrous residue was re-

extracted in the same manner two times. The homogenate extracts were combined and adjusted to 50% aqueous methanol with distilled water. The 50% methanol solution was extracted three times with equal volume of chloroform. The remaining aqueous solution was concentrated. The resulting aqueous solution was extracted with a half volume of n-butanol. Characterisation of the radioactivity was achieved by TLC. For the measurement of the total radioactivity LSC was used (see Table 20).

Table 20 Recovery and distribution of radioactivity in pear leaves after treatment with [^{14}C]hexythiazox

Fraction	Days after treatment (% applied dose)						
	0	5	10	20	30	60	90
Treated leaves	98.6	90.3	83.8	75.6	71.2	65.9	49.8
Methanol surface wash							
Methanol extract							
Chloroform extract	0.2	9.5	11.6	18.4	18.7	20.9	27.7
50% Methanol extract		0.8	1.2	3.0	2.9	5.0	8.0
Fibrous residue	-	0.4	0.8	1.2	1.5	2.2	4.8
Subtotal	98.8	101.0	97.4	98.2	94.3	94.0	90.3
Untreated leaves	-	0.01	0.03	0.06	0.11	0.13	0.29
Untreated fruit	-	0.01	0.01	0.03	0.03	0.15	0.27
Total	98.8	101.0	97.5	98.3	94.4	94.3	90.9

In the surface wash of the leaves the percentage of unchanged parent compound decreased from 93.1% down to 44.6% of the TRR of the whole leave. Metabolites were found in concentrations of less than 1% of the TRR in the surface wash, namely PT-1-2, PT-1-8 (cis) and PT-1-8 (trans).

In the leaf flesh the radioactivity increased during the timeframe of the study. Unchanged hexythiazox was present in all samples in concentrations of 3.8–7.8% of the TRR. The metabolite PT-1-2 was found in low levels of 1.7% of the TRR at maximum. Most of the radioactivity found was identified as PT-1-8 (cis) and PT-1-8 (trans) in their conjugated forms at amounts of up to 4.3% and 9.2% of the TRR, respectively (see Table 21).

Table 21 Balance of organo-soluble ^{14}C-compounds in pear leaves treated with [^{14}C]hexythiazox

Fraction	Compound	Days after treatment (% applied dose)						
		0	5	10	20	30	60	90
Surface wash	hexythiazox	93.1	86.0	79.8	70.5	67.1	61.8	44.6
	PT-1-2	0.8	0.4	0.4	0.5	0.4	0.4	0.4
	PT-1-8 (cis)	0.3	0.3	0.2	0.2	0.2	0.2	0.4
	PT-1-8 (trans)	0.3	0.2	0.3	0.3	0.3	0.3	0.6
	others	4.1	3.4	3.1	4.1	3.2	3.2	3.8
	subtotal	98.6	90.3	83.8	75.6	71.2	65.9	49.8
Flesh extract	hexythiazox	-	5.6	4.6	3.9	3.8	4.1	7.8
	PT-1-2	-	0.5	0.6	1.2	0.9	0.6	0.8
	PT-1-4 (trans-2)	-	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	PT-1-8 (cis) its conjugates	-	0.1 0.7	0.2 1.6	0.1 4.3	0.1 4.3	0.1 4.3	0.3 4.0
	PT-1-8 (trans) its conjugates	-	0.1 1.4	0.1 2.8	0.1 6.2	0.1 6.6	0.2 7.9	0.7 9.2
	others	-	1.1	1.7	2.6	2.9	3.7	4.9
	subtotal	-	9.5	11.6	18.4	18.7	20.9	27.7

Fraction	Compound	Days after treatment (% applied dose)						
		0	5	10	20	30	60	90
Total (surface and flesh)	hexythiazox	93.1	91.6	84.4	74.4	70.9	65.9	52.4
	PT-1-2	0.8	0.9	1.0	1.7	1.3	1.0	1.2
	PT-1-4 (trans-2)	-	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	PT-1-8 (cis) its conjugates	0.3 -	0.4 0.7	0.4 1.6	0.3 4.3	0.3 4.3	0.3 4.3	0.7 4.0
	PT-1-8 (trans) its conjugates	0.3. -	0.3 1.4	0.4 2.8	0.4 6.2	0.4 6.6	0.5 7.9	1.3 9.2
	others	4.1	4.5	4.8	6.7	6.1	6.9	8.7
	total	98.6	99.8	95.4	94.0	89.9	86.8	77.5

For the fruits two pears were harvested at 0, 5, 10, 20, 30 and 60 days after treatment. After washing the surface with methanol, the fruit was peeled and sectioned into flesh and core. The extraction and analysis of radioactive residues was performed according to the procedure described for pear leaves. In the fruits the TRR measure decreased from 0.82 mg/kg parent equivalents directly after treatment down to 0.11 mg/kg parent equivalents after 60 days. The percentage of radioactivity located on the surface also decreased from 99.4% of the TRR down to 67.6% of the TRR. A minor share of the residue (up to 19.5% of the TRR) was translocated into the flesh of the pears (see Table 22).

Table 22 Recovery and distribution of radioactivity in pear fruits treated with [^{14}C]hexythiazox

Fraction	Days after treatment (% applied dose)					
	0	5	10	20	30	60
Surface wash	99.4	94.1	88.0	82.6	77.8	67.6
Peel						
Methanol extract						
Chloroform extract	0.1	4.8	8.7	6.6	5.0	6.0
50% Methanol extract		0.6	1.1	1.8	1.6	2.3
Ethylacetate & Chloroform	-	0.5	1.3	1.9	3.5	4.5
Fibrous residue	< 0.1	0.8	2.3	3.9	4.7	6.7
Subtotal	0.1	6.7	13.4	14.2	14.8	19.5
Flesh	-	0.3	1.2	1.7	2.0	3.2
Core	-	< 0.1	< 0.1	< 0.1	0.1	0.2
Total	99.5	101.1	102.6	98.5	94.7	90.5
Fruit weight	61.3 g	108.6 g	129.0 g	181.9 g	254.6 g	405.6 g
Concentration of hexythiazox	0.82 mg/kg	0.47 mg/kg	0.40 mg/kg	0.28 mg/kg	0.19 mg/kg	0.11 mg/kg

In the surface wash of pear fruits the unchanged parent compound was identified as the dominant residue amounting 95.0% of the TRR directly after application down to 57.8% of the TRR after 60 days. In addition the metabolites PT-1-2 and the cis and trans isomer of PT-1-8 were found in levels of up to 2.3%, 0.7% and 0.9% of the TRR, respectively. The peel extract revealed hexythiazox in levels up to 6.8% of the TRR after 60 days. Metabolites were found in relatively low levels of less than 1.7% of the TRR each. In the flesh of the pears no further analysis of the radioactivity was performed (see Table 23).

Table 23 Balance of organo-soluble ^{14}C-compound in pear fruits treated with [^{14}C]hexythiazox

Fraction	Compound	Days after treatment (% applied dose)					
		0	5	10	20	30	60
Surface wash	hexythiazox	95.0	90.5	84.1	78.1	71.2	57.8
	PT-1-2	0.8	0.6	0.5	0.6	1.2	2.3
	PT-1-8 (cis)	0.2	0.2	0.4	0.5	0.5	0.7
	PT-1-8 (trans)	0.2	0.3	0.5	0.7	0.7	0.9
	others	3.2	2.5	2.5	2.7	4.2	5.9
	subtotal	99.4	94.1	88.0	82.6	77.8	67.6
Peel extract	hexythiazox	-	3.1	5.6	4.3	5.2	6.8
	PT-1-2	-	0.3	0.4	0.4	0.4	0.5
	PT-1-4 (trans-2)	-	< 0.1	0.1	< 0.1	0.1	0.1
	PT-1-8 (cis) its conjugates	-	0.4 0.1	0.8 0.1	0.7 0.1	0.5 0.1	0.3 0.3
	PT-1-8 (trans) its conjugates	-	0.5 0.1	1.2 0.2	1.0 0.2	0.6 0.2	0.4 0.4
	others	-	0.8	1.6	1.8	1.4	1.7
	subtotal	-	5.3	10.0	8.5	8.5	10.5
Total (surface and peel)	hexythiazox	95.0	93.6	89.7	82.4	76.4	64.6
	PT-1-2	0.8	0.9	0.9	1.0	1.6	2.8
	PT-1-4 (trans-2)	-	< 0.1	0.1	< 0.1	0.1	0.1
	PT-1-8 (cis) its conjugates	0.2	0.6 0.1	1.2 0.1	1.2 0.1	1.0 0.1	1.0 0.3
	PT-1-8 (trans) its conjugates	0.2	0.8 0.1	1.7 0.2	1.7 0.2	1.3 0.2	1.3 0.4
	others	3.2	3.3	4.1	4.5	5.6	7.6
	total	99.4	99.4	98.0	91.1	86.3	78.1

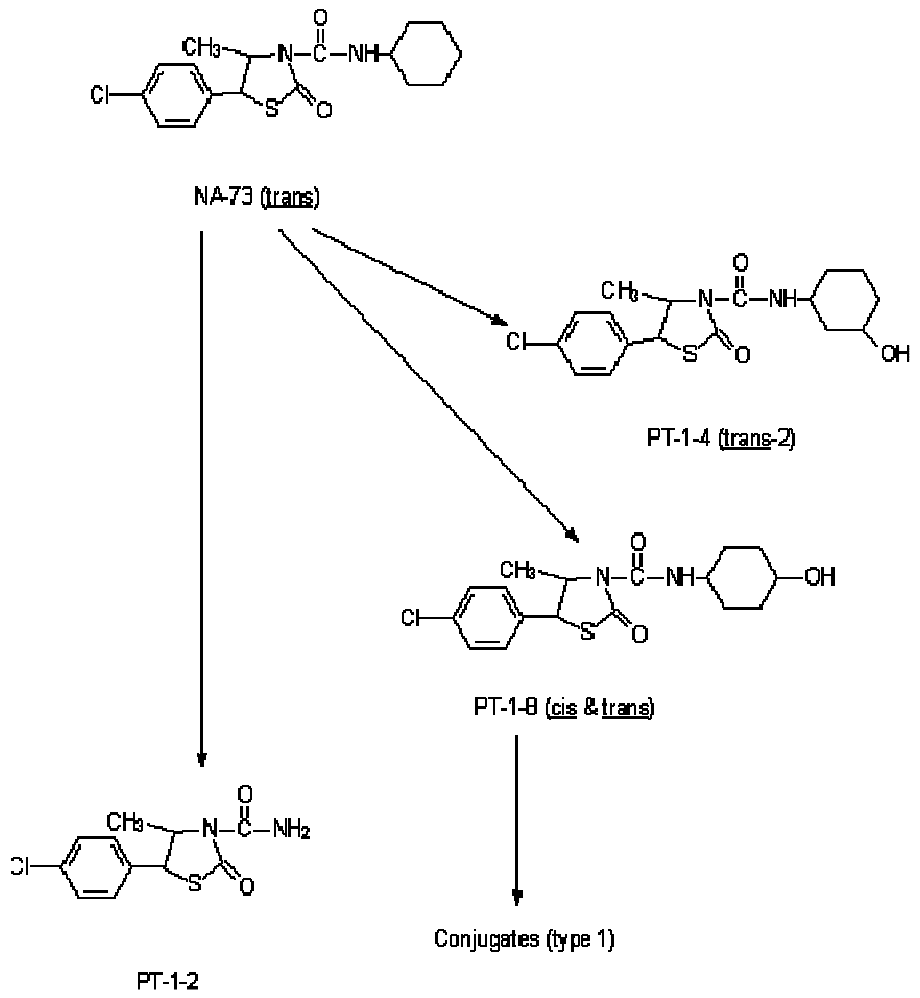


Figure 4 Proposed metabolic pathway of hexythiazox in pears

Tea

For tea the metabolism of hexythiazox was investigated by Saito (2004, Hexyt_042) using one spray application at a rate of 200 g ai/ha. Leaf specimens were collected 0, 7, 14 and 21 days after the treatment.

All samples of leaves were washed with methanol, cut to small pieces and homogenate-extracted with aqueous methanol. The extractable radioactivity was characterised by HPLC analyses. Further identification of radioactive residues was performed by LC-MS/MS and comparing the mass profiles with reference compounds. The TRR found in the samples was measured by LSC.

The TRR in the tea leaves did not change with increasing PHI. In all of the samples TRR levels of 8.17 to 9.03 mg/kg, calculated as parent equivalents, were found. In comparison to the PHI 0 days results more of the radioactivity was found in the extracts instead of the surface wash in the later samples (see Table 24).

Table 24 TRR found in tea leaves after treatment with 0.2 kg [^{14}C]hexythiazox per ha (results expressed as parent equivalents)

PHI	TRR (mg/kg)	Surface wash		Extract		Unextracted	
		% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
0	8.68	93.2	8.09	5.9	0.51	1.0	0.09
7	9.03	65.9	5.95	29.8	2.69	4.3	0.39

PHI	TRR (mg/kg)	Surface wash		Extract		Unextracted	
		% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
14	8.65	57.3	4.96	35.7	3.09	7.0	0.60
21	8.17	55.3	4.52	39.6	3.24	5.0	0.41

The identification of the radioactivity revealed a very limited degradation of the parent substance. In all samples hexythiazox was the dominant residue found in levels of at least 84.5% of the TRR. The only metabolites identified were PT-1-2 and PT-1-8 (trans), each at levels of less than 0.3% of the TRR. A summary of the results is presented in Table 25.

Table 25 Composition of residue in tea leaves treated with [^{14}C]hexythiazox

PHI	Hexythiazox		PT-1-2		PT-1-8 (trans)		Unknown		Total	
	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
0	97.9	8.50	-	-	-	-	1.1	0.10	99.0	8.60
7	93.3	8.42	0.1	0.01	0.1	0.01	2.2	0.20	95.7	8.64
14	86.2	7.45	0.2	0.01	0.2	0.02	6.5	0.56	93.0	8.05
21	84.5	6.90	0.3	0.02	0.2	0.02	10.0	0.82	95.0	7.76

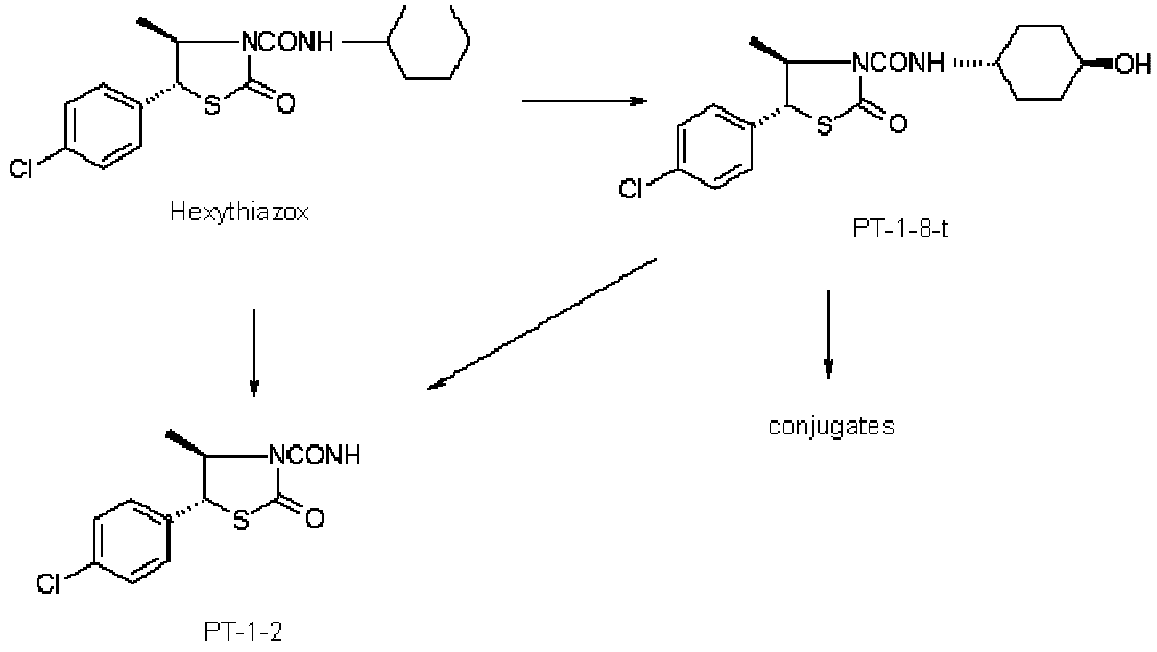


Figure 5 Proposed metabolic pathway of hexythiazox in tea leaves

Environmental fate in soil

The 2003 JMPR (JMPR, 2003) explained the data requirements for studies of environmental fate. The focus should be on those aspects that are most relevant to MRL setting. For hexythiazox, supervised residue trials data are available for foliar application only, which results in the normal requirements for hydrolysis and rotational crop studies. The 2003 report does not mention soil photolysis studies; however, such studies should be relevant for the same reasons as for aerobic soil degradation – nature and magnitude of residues in soil.

The Meeting received information on soil aerobic metabolism and hydrolysis in sterile buffer solutions only. No data concerning crop rotations was presented for hexythiazox.

Soil metabolism

Aerobic soil metabolism

The aerobic soil metabolism study is summarized below, showing the test conditions, the nature of the soils, estimated half-lives and the nature of identified soil metabolites. This is a laboratory soil incubation study with the ^{14}C labelled compound. Metabolism or degradation rates are influenced by the nature of the soil, temperature, moisture status of the soil and dose. Estimated aerobic soil metabolism half-lives for hexythiazox at 20 °C ranged from 32.1 to 35.2 days. After 153 days mineralisation and unextracted residues were in the range of 10–12.2% and 19.7–23% of the radioactivity, respectively.

The metabolite PT-1-9 was formed in the early stage of the study, reaching its maximum concentration of 10.1–14.4% of the applied radioactivity after 31 days. PT-1-2 and PT-1-3 were found in the later samples reaching a plateau after 90 days at individual amounts of 33.4–39.5% and 7.5–9.2% of the applied dose.

Ref: Shiotani, 2002, Hexyt_014
Test material: [^{14}C-5-thiazolidine]-hexythiazox
Duration: 153 days
Moisture: 26.8% (Cuckney), 37.5% (Wick)
pH: 6.7 (Cuckney), 6.2 (Wick)
Dose rate: 400 g ai/ha
Temp: 17–22 °C
Soil: sand (Cuckney) and sandy loam (Wick)
Organic carbon: 0.7% (Cuckney), 1.6% (Wick)
Half-life (parent): 35.2d (Cuckney), 32.1d (Wick)
^{14}C accountability: 91.2–100.2%
% hexythiazox remaining: 10.5% (Cuckney) and 8.6% (Wick) after 153 days
% mineralisation: 10% (Cuckney) and 12.2% (Wick) after 153 days
% unextracted: 19.7% (Cuckney) and 23% (Wick) after 153 days

Metabolites (Cuckney sand)	Max (% of dose)	Day
PT-1-9	14.4%	31
PT-1-2	39.5%	122
PT-1-3	7.5%	122

Metabolites (Wick sandy loam)	Max (% of dose)	Day
PT-1-9	10.1%	31
PT-1-2	34.2%	122
PT-1-3	9.2%	90

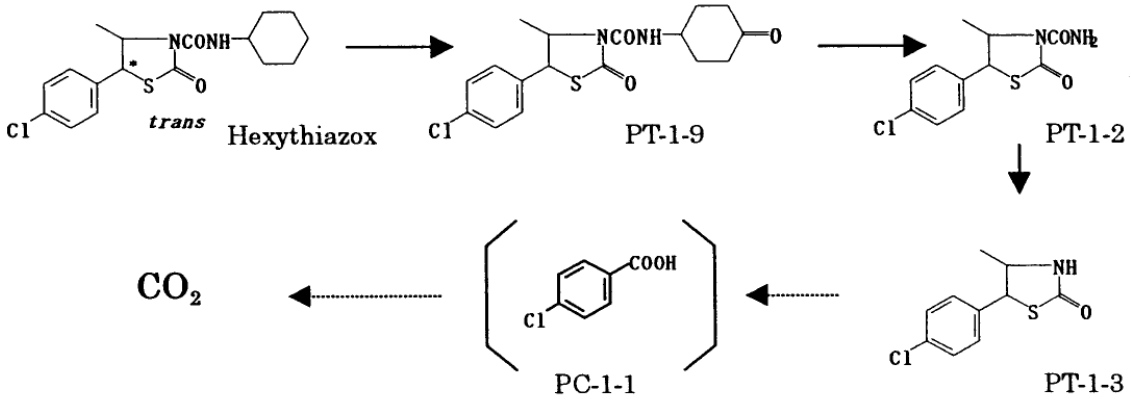


Figure 6 Proposed metabolic pathway of hexythiazox in soil under aerobic conditions

Rotational crops

The magnitude of residues of hexythiazox in rotational crops was investigated by Carringer (1998, Hexyt_063). In two field trials the parent substance was applied to bare soil at a rate of 0.21 kg ai/ha and incorporated into the soil before planting. After 30, 120 and 240/270 days lettuce, mustard, radish, sorghum and wheat were planted as follow crops.

For each crops and site duplicate samples were collected at the point of commercial harvest. All samples were analysed for the total residue after hydrolysis to PT-1-3 by HPLC-UV (225 nm). The residues found are summarised in Table 26.

Table 26 Hexythiazox residues (total residue determined as PT-1-3) in rotational crops after soil treatment at a rate of 0.21 kg ai/ha

Test Site	Plantback interval	Matrix	Residue in mg/kg parent equivalents
1 (CA)	30	Lettuce	< 0.01, < 0.01
	120	Lettuce	< 0.01, < 0.01
	30	Radish, roots	< 0.01, < 0.01
	30	Radish, tops	0.047, 0.038
	120	Radish, roots	< 0.01, < 0.01
	120	Radish, tops	< 0.01, < 0.01
	30	Sorghum, forage	< 0.01, < 0.01
	30	Sorghum, grain	< 0.01, < 0.01
	30	Sorghum, stover	0.012, 0.014
	120	Wheat, forage	< 0.01, < 0.01
	120	Wheat, grain	< 0.01, < 0.01
	120	Wheat, straw	< 0.01, < 0.01
	120	Wheat, hay	< 0.01, < 0.01
	240	Wheat, grain	< 0.01, < 0.01
	240	Wheat, hay	< 0.01, < 0.01
2 (NC)	30	Mustard	< 0.01, < 0.01
	120	Mustard	< 0.01, < 0.01
	30	Radish, roots	< 0.01, < 0.01
	30	Radish, tops	< 0.01, < 0.01
	120	Radish, roots	< 0.01, < 0.01
	120	Radish, tops	< 0.01, < 0.01
	30	Sorghum, forage	< 0.01, < 0.01
	30	Sorghum, grain	< 0.01, < 0.01
	30	Sorghum, stover	< 0.01, < 0.01
	120	Wheat, forage	< 0.01, < 0.01
	120	Wheat, grain	< 0.01, < 0.01
	120	Wheat, straw	< 0.01, < 0.01
	120	Wheat, hay	< 0.01, < 0.01
	270	Sorghum, grain	< 0.01, < 0.01

RESIDUE ANALYSIS

Analytical methods

The Meeting received information on analytical methods for the determination of residues of hexythiazox in target crops. For animal matrices no analytical methods or validation data was submitted.

Samples of plant origin

The analytical methods for samples of plant origin are summarised below, including the commodities, for which the methods were validated, analytes and their limit of quantitation (LOQ), determination technique and a brief description of the method. Recoveries are shown in Table 27.

An additional method for the determination of total hexythiazox residues after hydrolysis into PT-1-3 was submitted, but the study did not include validation data on fortified samples. Since this method was used in several field trials, a description of the method is presented.

Reference:	Perny, 2003, Hexyt_044
Commodities:	Tomatoes, strawberries (fruits, jam, canned fruits), grapes (fruits, juice, wine, raisins), melons (fruits, peel, pulp), cucumbers and peppers
Analytes:	hexythiazox
LOQ:	0.05 mg/kg
Determination:	HPLC-UV (225 nm)
Description:	Hexythiazox is extracted with methanol and then partitioned into n-hexane. After partition between n-hexane and acetonitrile, the acetonitrile layer is concentrated to dryness. The residue is cleaned-up by Florisil PR Column chromatography and a C18 solid phase extraction column. Hexythiazox is determined by HPLC-UV at 235 nm.

Reference:	Perny, 2003, Hexyt_045
Commodities:	Oranges (fruit, pulp, peel, juice, marmalade, preserve), mandarins (fruit, pulp, peel, juice, marmalade, preserve), apples, pears
Analytes:	hexythiazox
LOQ:	0.05 mg/kg
Determination:	HPLC-UV (225 nm)
Description:	Hexythiazox is extracted with methanol and the partitioned into n-hexane. After partition between n-hexane and acetonitrile, the acetonitrile layer is concentrated to dryness. The residue is cleaned-up by Florisil PR Column chromatography and a C18 solid phase extraction column. Hexythiazox is determined by HPLC-UV at 235 nm.

Reference:	Barber, 1987, Hexyt_038
(Method)	(AMR-985-87)
Commodities:	Apples, cabbage, grape, maize, peach, pear and sorghum
Analytes:	hexythiazox incl. metabolites, determined as PT-1-3
LOQ:	0.02 mg/kg
Determination:	HPLC-UV (225 nm)
Description:	The compounds are extracted simultaneously from the matrix by maceration in the presence of methanol. Following solvent concentration/conversion the parent compound and metabolites are converted by hydrolysis using 0.1N NaOH, to the more stable PT-1-3 metabolite. The samples are cleaned up by liquid-solid chromatography using small, disposable, silica gel columns, then

analysed by HPLC-UV. Some samples require an additional clean-up step in which the analyte is isolated from bulk interferences by gel permeation chromatography (GPC).

Table 27 Recoveries of hexythiazox in samples of plant origin

Reference (Author, Year)	Fortification levels (mg/kg)	Mean recovery (%)	Relative standard deviation (%)	No.	Range of recoveries (%)		Matrix/Analyte
					Low	High	
Hexyt_044	0.05	84	8.3	5	74	93	Tomato
Perny, 2003	0.5	92	8.4	5	87	105	
	0.05	97	6.4	3	90	102	Grapes, fruits
	0.5	83	1.8	3	82	85	
	0.05	81	3.8	3	78	84	Grapes, juice
	0.5	79	3.4	3	76	80	
	0.05	84	10.2	5	78	99	Wine
	0.5	75	4.6	5	71	79	
	0.05	100	9.5	5	86	109	Raisins
	0.5	80	12.8	5	71	98	
	0.05	87	6.5	3	80	91	Strawberries, fruits
	0.5	75	1.9	3	74	76	
	0.05	82	11.8	5	75	96	Strawberries, jam
	0.5	78	6.9	5	71	83	
	0.05	95	12.9	5	78	110	Strawberries, canned fruits
	0.5	73	6.7	5	67	80	
	0.05	82	10.8	3	72	88	Melons, fruits
	0.5	83	1.6	3	82	84	
	0.05	96	5.8	3	91	102	Melons, pulp
	0.5	86	18.1	3	76	104	
	0.05	77	8.6	3	73	85	Melons, peel
	0.5	76	2.9	3	74	77	
	0.05	76	6.6	3	72	81	Cucumbers
	0.5	73	3.9	3	70	76	
	0.05	73	3.2	3	71	75	Peppers
	0.5	72	1.2	3	71	72	
Hexyt_045	0.05	98	6.7	5	90	107	Oranges, fruit
Perny, 2003	0.5	74	2.9	5	70	76	
	0.05	79	2.2	5	77	80	Oranges, peel
	0.5	89	12.9	5	78	106	
	0.05	78	6.6	5	71	84	Oranges, pulp
	0.5	75	8.6	5	70	85	
	0.05	102	4.1	3	97	105	Oranges, juice
	0.5	96	12.8	3	88	110	
	0.05	82	7.5	3	76	88	Oranges,
	0.5	73	6.8	3	68	77	marmalade
	0.05	87	4.7	3	85	92	Oranges,
	0.5	87	4.2	3	83	90	preserve

Reference (Author, Year)	Fortification levels (mg/kg)	Mean recovery (%)	Relative standard deviation (%)	No.	Range of recoveries (%)		Matrix/Analyte
					Low	High	
	0.05	85	10.7	3	74	91	Mandarins, fruit
	0.5	79	13.3	3	71	91	
	0.05	81	5.9	3	75	84	Mandarins, peel
	0.5	100	5.7	3	96	106	
	0.05	103	6.0	3	97	109	Mandarins, pulp
	0.5	87	4.7	3	84	92	
	0.05	106	2.3	5	102	108	Mandarins, juice
	0.5	75	4.3	5	70	78	
	0.05	92	6.7	5	82	99	Mandarins, marmalade
	0.5	86	1.2	5	84	87	
	0.05	87	8.9	5	77	97	Mandarins, preserve
	0.5	76	1.1	5	75	77	
	0.05	95	4.9	3	92	100	Apples
	0.5	78	0.3	3	78	78	
	0.05	85	15.8	3	75	100	Pears
	0.5	84	5.5	3	79	87	

nr not reported

Samples of animal origin

No data on validated analytical methods were submitted to the Meeting. Again method AMR-985-87 is suitable for the analysis of hexythiazox including metabolites, determined as PT-1-3. Validation data using fortified samples is not available for this method.

Reference: Barber, 1987, Hexyt_038
(Method) (AMR-985-87)
Commodities: milk, eggs, animal tissues
Analytes: hexythiazox incl. metabolites, determined as PT-1-3
LOQ: 0.02 mg/kg
Determination: HPLC-UV (225 nm)
Description: The compounds are extracted simultaneously from the matrix by maceration in the presence of methanol. In the case of milk samples, the compounds are extracted using successive methanol partitions and centrifugation. Following solvent concentration/conversion the parent compound and metabolites are converted by hydrolysis using 0.1N NaOH, to the more stable PT-1-3 metabolite. The samples are cleaned up by liquid-solid chromatography using small, disposable, silica gel columns, then analysed by HPLC-UV. Some samples require an additional clean-up step in which the analyte is isolated from bulk interferences by gel permeation chromatography (GPC).

Reference: Tilting, 1999, Hexyt_064
(Method) (BASF 537/0)
Commodities: muscle (bovine & poultry), milk, eggs, bovine liver, bovine kidney, bovine fat
Analytes: hexythiazox incl. metabolites, determined as PT-1-3
LOQ: 0.05 mg/kg
Determination: HPLC-UV (225 nm)

Description: Hexythiazox was extracted from animal tissues and eggs with methanol but from milk and fat it was extracted with acetone. The extract was then liquid/liquid partitioned with dichloromethane. The dichloromethane extract was evaporated to dryness and the residue dissolved in iso-octane before a liquid/liquid extraction with acetonitrile. After evaporation of acetonitrile, the residue was hydrolysed with sodium hydroxide solution. In the hydrolysis, hexythiazox and all of its metabolites forming PT-1-3 are transformed to 5-(4-chlorophenyl)-4-methylthiazolidine-2-one (PT-1-3). After further dichloromethane partitioning steps (acidic and alkaline), the residue was dissolved in hexane/ acetone and cleaned up on a silica gel column. The eluate was then evaporated and the residue dissolved in acetonitrile/water. PT-1-3 was determined by reversed phase HPLC and UV detection at 225 nm (see Table 28).

Table 28 Recoveries of hexythiazox (determined as PT-1-3) in samples of animal origin

Reference (Author, Year)	Fortification levels (mg/kg)	Mean recovery (%)	Relative standard deviation (%)	No.	Range of recoveries (%)		Matrix/Analyte
					Low	High	
Hexyt_064 Tilting 1999	0.05	84	8	5	76	92	Bovine muscle
	0.5	79	7	5	70	84	
	0.05	91	9	5	77	99	Bovine liver
	0.5	89	14	5	70	102	
	0.05	91	13	5	81	110	Bovine kidney
	0.5	76	11	5	67	85	
	0.05	108	3	5	103	110	Bovine fat
	0.5	95	9	5	81	101	
	0.05	78	9	5	70	83	Milk
	0.5	73	9	5	62	79	
	0.05	79	10	5	70	87	Eggs
	0.5	71	2	5	69	73	
	0.05	81	9	5	69	86	Poultry liver
	0.5	81	11	5	74	93	

Stability of pesticides in stored analytical samples

Reference: Gomyo, 1990, Hexyt_015

Commodities: Macerated: strawberry, cucumber, water melon, grape, green pepper, mandarin orange (peel, pulp and whole fruits), pears and apples
Chopped: cucumber, strawberry, tea, Chinese citron (peel and pulp) and mandarin orange (peel and pulp)

Analytes: hexythiazox

Material and Method: After macerisation an aliquot of 20-50g of all commodities was fortified with 20 or 25 µg of hexythiazox and stored in a freezer at –30 °C (see Table 29). In addition an experiment was conducted by using chopped fruits treated in field instead of fortified homogenate (see Table 30). Storage samples were extracted with methanol and partitioned against n-hexane. After washing the n-hexane with alkaline solution, the residue was transferred into acetonitrile. The anaylsis of the residues was performed by liquid chromatography (225 nm) at a limit of detection of 0.02 mg/kg (0.05 mg/kg for tea) and a LOQ of 0.05 mg/kg.

Table 29 Freezer storage stability of hexythiazox residues in plant commodities after fortification at 0.5 or 1.0 mg/kg

Reference (Author, Year)	Storage interval (months)	Fortification level (mg/kg)	Recovery (% fortification compared to nominal fortification level)	Matrix
Gomyo, 1990, Hexyt_015	1 3	0.5 0.5	92 74	Strawberry, homogenised
	1 3	0.5 0.5	87 86	Cucumber, homogenised
	1 3	0.5 0.5	82 73	Apple, homogenised
	1	0.5	93	Water melon, homogenised
	1	0.5	63	Grape, homogenised
	1	0.5	84	Green pepper, homogenised
	1 3 7 12	1.0 1.0 1.0 1.0	87 78 86 87	Mandarin orange pulp, homogenised
	1 3 7 12	1.0 1.0 1.0 1.0	82 81 93 87	Mandarin orange peel, homogenised
	1 3 7 12	1.0 1.0 1.0 1.0	88 84 91 88	Mandarin orange whole fruits, homogenized
	1 3 7 12	1.0 1.0 1.0 1.0	94 84 87 85	Apple, homogenised
	1 3 7 12	1.0 1.0 1.0 1.0	78 86 84 83	Pear, homogenised

Table 30 Freezer storage stability of hexythiazox residues in plant commodities after field treatment

Reference (Author, Year)	Commodity	Months after harvest	Residue found (mg/kg)	Percent remaining
Gomyo, 1990, Hexyt_015	Cucumber	0 1	0.06 0.06	- 100
	Strawberry	0 1	0.06 0.06	- 100
	Tea	0 2	67 61	- 92
	Tea	0 4	4.3 4.3	- 100
	Chinese citron peel	0 1 5	0.37 0.36 0.40	- 97 108
	Chinese citron pulp	0 1	0.02 0.02	- 100
	Mandarin orange peel	0 1	0.87 0.88	- 101

Reference (Author, Year)	Commodity	Months after harvest	Residue found (mg/kg)	Percent remaining
		13	0.88	101
	Mandarin orange peel	0 1 13	1.0 1.0 1.0	- 102 99
	Mandarin orange peel	0 2	0.4 0.38	- 95

USE PATTERN

Hexythiazox is an acaricide which has ovicidal, larvicidal and nymphicidal activity and can be applied at any stage of plant growth from budding to fruiting. There are several potential application timings that can be utilised in the protection of top fruit, e.g., the winter eggs controlled by an early spring treatment, other infestations in late spring, and re-infestation in summer and occasionally early autumn. In relation to this monograph only information on uses either directly before harvest or after formation of the edible part of the crops were submitted for evaluation.

Table 31 List of registered uses

Commodity	Country	Field (F), Indoor (I), Post-harvest (P)	Application	Formulation	kg ai/ha	kg ai/hl	No. of treatments	PHI (days)	Remarks
Apples	Netherlands	F	foliar	WP, 10%	0.06	0.004	1	28	
Cane berries	USA	n.s.	foliar	DF, 50%	0.21	Min. 0.45	1	3	120 d label restriction on rotational crops
Cane berries	USA	n.s.	foliar	WP, 50%	0.21	Min. 0.45	1	3	120 d label restriction on rotational crops
Chili peppers	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Chili peppers	Netherlands	I	foliar	Wp, 10%	0.08	0.005	1	3	
Citrus fruits	USA	n.s.	foliar	EC, 12%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Citrus fruits	USA	n.s.	foliar	EC, 24%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Citrus fruits	USA	n.s.	foliar	DF, 50%	0.21	Max. 0.11	1	28	120 d label restriction on rotational crops
Citrus fruits	USA	n.s.	foliar	WP, 50%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Corn	USA (CA only)	n.s.	foliar	EC, 12%	0.2	0.11 - 0.42	1	45	120 d label restriction on rotational crops
Cotton	USA (CA only)	n.s.	foliar	EC, 12%	0.17	Min. 0.88	1	35	120 d label restriction on rotational crops
Cotton	USA (CA only)	n.s.	foliar	EC, 24%	0.17	Min. 0.91	1	35	120 d label restriction on rotational crops
Cotton	USA (CA only)	n.s.	foliar	DF, 50%	0.17	Min. 0.37	1	35	120 d label restriction on rotational crops
Cotton	USA (CA only)	n.s.	foliar	WP, 50%	0.17	Min. 0.37	1	35	120 d label restriction on rotational crops
Cucumbers	Netherlands	F	foliar	EC, 25%	0.04	0.005	1	3	
Cucumbers	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Cucumbers	Netherlands	F	foliar	WP, 10%	0.04	0.005	1	3	

Commodity	Country	Field (F), Indoor (I), Post-harvest (P)	Application	Formulation	kg ai/ha	kg ai/hl	No. of treatments	PHI (days)	Remarks
Cucumbers	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Dates	USA	n.s.	foliar	DF, 50%	0.21	n.s.	1	90	120 d label restriction on rotational crops
Dates	USA	n.s.	foliar	WP, 50%	0.21	n.s.	1	90	120 d label restriction on rotational crops
Eggplants	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Eggplants	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Gherkins	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Gherkins	Netherlands	F	foliar	EC, 25%	0.04	0.005	1	3	
Gherkins	Netherlands	F	foliar	WP, 10%	0.04	0.005	1	3	
Gherkins	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Grapes	USA	n.s.	foliar	EC, 12%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Grapes	USA	n.s.	foliar	EC, 24%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Grapes	USA	n.s.	foliar	DF, 50%	0.21	Max. 0.11	1	28	120 d label restriction on rotational crops
Grapes	USA	n.s.	foliar	WP, 50%	0.21	Max. 0.11	1	28	120 d label restriction on rotational crops
Hops	USA	n.s.	foliar	DF, 50%	0.21	Min. 0.45	1	n.s.	treatment up to burr formation, 120 d label restriction on rotational crops
Hops	USA	n.s.	foliar	WP, 50%	0.21	Min. 0.45	1	n.s.	treatment up to burr formation, 120 d label restriction on rotational crops
Melons, except water melons	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Melons, except water melons	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Okra	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Okra	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Pear	Netherlands	F	foliar	WP, 10%	0.06	0.004	1	28	
Peppers	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Peppers	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Pome fruits	USA	n.s.	foliar	EC, 12%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Pome fruits	USA	n.s.	foliar	EC, 24%	0.2	Max. 0.11	1	28	120 d label restriction on rotational crops
Pome fruits	USA	n.s.	foliar	DF, 50%	0.21	Min. 0.45	1	28	120 d label restriction on rotational crops
Pome fruits	USA	n.s.	foliar	WP, 50%	0.21	Min. 0.45	1	28	120 d label restriction on rotational crops
Squash, summer	Netherlands	I	foliar	Ec, 25%	0.08	0.005	1	3	

Commodity	Country	Field (F), Indoor (I), Post-harvest (P)	Application	Formulation	kg ai/ha	kg ai/hl	No. of treatments	PHI (days)	Remarks
Squash, summer	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Squash, winter	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Squash, winter	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Stone fruits	USA	n.s.	foliar	EC, 12%	0.2	Min. 0.42	1	28	120 d label restriction on rotational crops
Stone fruits	USA	n.s.	foliar	EC, 24%	0.2	Min. 0.43	1	28	120 d label restriction on rotational crops
Stone fruits	USA	n.s.	foliar	DF, 50%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops
Stone fruits	USA	n.s.	foliar	WP, 50%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops
Strawberries	Netherlands	F	foliar	WP, 10%	0.05	0.005	1	3	
Strawberries	Netherlands	I	foliar	WP, 10%	0.06	0.005	1	3	
Strawberries	USA	n.s.	foliar	DF, 50%	0.21	Min. 0.45	1	3	120 d label restriction on rotational crops
Strawberries	USA	n.s.	foliar	WP, 50%	0.21	Min. 0.45	1	3	120 d label restriction on rotational crops
Tomatos	Netherlands	I	foliar	EC, 25%	0.08	0.005	1	3	
Tomatos	Netherlands	I	foliar	WP, 10%	0.08	0.005	1	3	
Tree nuts	USA	n.s.	foliar	EC, 12%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops
Tree nuts	USA	n.s.	foliar	EC, 24%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops
Tree nuts	USA	n.s.	foliar	DF, 50%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops
Tree nuts	USA	n.s.	foliar	WP, 50%	0.2	Min. 0.45	1	28	120 d label restriction on rotational crops

n.s. Not stated

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Trials were generally well documented with laboratory and field report. Laboratory reports included method validation with procedural recoveries from spiking at residues levels similar to those occurring in samples from supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the tables except where residues in control samples exceeded the LOQ. Residue data are recorded unadjusted for recovery.

In trials where duplicate field samples from an unreplicated plot were taken at each sampling time and analysed separately each figure is presented individually. When samples were analysed more than once all results are listed and the mean is presented in brackets.

When residues were not detected they are show as below the LOQ (e.g., < 0.01 mg/kg). Application rates and spray concentrations have generally been rounded to two significant figures. For residues above the LOQ results were rounded to two significant figures or one significant figure near the LOQ. Residue values from trials conducted according to maximum GAP have been used for the estimation of maximum residue levels. Those results included in the evaluation are underlined.

Conditions of the supervised residue trials were generally well reported in detailed field reports. Most trial designs used non-replicated plots. Most field reports provided data on the sprayers used, plot size, field sample size and sampling date.

Except specifically noted the residue data in the following tables represents the sum of hexythiazox and all metabolites hydrolysable to PT-1-3, expressed as hexythiazox.

Table 32 Hexythiazox - supervised residue trials

Commodity	Indoor/Outdoor	Treatment	Countries	Table
Grapefruit	Outdoor	Foliar	USA	Table 33
Lemons	Outdoor	Foliar	USA	Table 34
Mandarins	Outdoor	Foliar	Greece, Italy, Spain	Table 35
Oranges	Outdoor	Foliar	Greece, Italy, Spain, USA	Table 36
Almonds	Outdoor	Foliar	USA	Table 37
Pecans	Outdoor	Foliar	USA	Table 38
Apples	Outdoor	Foliar	USA	Table 39
Pears	Outdoor	Foliar	USA	Table 40
Cherries	Outdoor	Foliar	USA	Table 41
Nectarines	Outdoor	Foliar	USA	Table 42
Peaches	Outdoor	Foliar	USA	Table 43
Plums	Outdoor	Foliar	USA	Table 44
Blackberries	Outdoor	Foliar	USA	Table 45
Grapes	Outdoor	Foliar	Austria, France, Italy, Spain, USA	Table 46
Raspberries	Outdoor	Foliar	USA	Table 47
Strawberries	Outdoor	Foliar	USA	Table 48
Dates	Outdoor	Foliar	USA	Table 49
Tomatoes	Indoor	Foliar	France, Italy, The Netherlands	Table 50
Cucumber	Indoor	Foliar	Italy, The Netherlands, Spain	Table 51
Melons	Indoor	Foliar	France, The Netherlands, Spain	Table 52
Sweet corn	Outdoor	Foliar	USA	Table 53
Snap beans (fresh)	Outdoor	Foliar	USA	Table 54
Lima beans (succulent)	Outdoor	Foliar	USA	Table 55

Commodity	Indoor/Outdoor	Treatment	Countries	Table
Bean (pulses)	Outdoor	Foliar	USA	Table 56
Cotton seeds	Outdoor	Foliar	USA	Table 57
Hops	Outdoor	Foliar	USA	Table 58
Maize, grain	Outdoor	Foliar	USA	Table 59
Almonds hulls	Outdoor	Foliar	USA	Table 60
Sweet corn, forage	Outdoor	Foliar	USA	Table 61
Cotton, gin trash	Outdoor	Foliar	USA	Table 62
Maize, forage	Outdoor	Foliar	USA	Table 63
Maize, stover	Outdoor	Foliar	USA	Table 64

Table 33 Hexythiazox residues in grapefruit following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Willacy (TX) 2003 (Rio Red)	EC, 12	1	0.21	0.03	Whole fruits	< 0.05 < 0.05	28 28	TCI-03-084, TCI-03-084-03 Carringer, 2004, Hexyt_030
USA, Willacy (TX) 2003 (Rio Red)	WP, 50	1	0.21	0.03	Whole fruits	< 0.05 < 0.05	28 28	TCI-03-084, TCI-03-084-03 Carringer, 2004, Hexyt_030
USA, Tulare (CA) 2003 (Mellogold)	EC, 12	1	0.21	0.006	Whole fruits	0.16 0.14	28 28	TCI-03-084, TCI-03-084-04 Carringer, 2004, Hexyt_030
USA, Tulare (CA) 2003 (Mellogold)	WP, 50	1	0.21	0.006	Whole fruits	< 0.05 0.18	28 28	TCI-03-084, TCI-03-084-04 Carringer, 2004, Hexyt_030
USA, Tulare (CA) 2003 (Mellogold)	EC, 12	1	0.21	0.01	Whole fruits	0.06 < 0.05	28 28	TCI-03-084, TCI-03-084-05 Carringer, 2004, Hexyt_030
USA, Tulare (CA) 2003 (Mellogold)	WP, 50	1	0.21	0.01	Whole fruits	< 0.05 0.05	28 28	TCI-03-084, TCI-03-084-05 Carringer, 2004, Hexyt_030

Table 34 Hexythiazox residues in lemons following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Ventura (CA) 2002 (Eureka)	EC, 12	1	0.21	0.045	Whole fruits	0.20 0.12	28 28	TCI-02-069, TCI-02-069-03 Carringer, 2003, Hexyt_029
USA, Tulare (CA) 2002 (Pryor)	EC, 12	1	0.21	0.038	Whole fruits	0.07 0.1	28 28	TCI-02-069, TCI-02-069-04 Carringer, 2003, Hexyt_029
USA, Ventura (CA) 2002 (Monroe)	EC, 12	1	0.21	0.015	Whole fruits	0.15 0.14	28 28	TCI-02-069, TCI-02-069-05 Carringer, 2003, Hexyt_029
USA, Tulare (CA) 2002 (Lisbon)	EC, 12	1	0.21	0.041	Whole fruits	0.05 0.06	28 28	TCI-02-069, TCI-02-069-06 Carringer, 2003, Hexyt_029
USA, Kern (CA) 2002 (Lisbon)	EC, 12	1	0.21	0.008	Whole fruits	0.29 0.16	27 27	TCI-02-069, TCI-02-069-07 Carringer, 2003, Hexyt_029

Table 35 Hexythiazox residues in mandarins following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Italy, Tarante 2002 (Oroval)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 < 0.05, < 0.05 (< 0.05) 0.15 < 0.05	 14 14 14	RD-03124, A2059 IT2 Perny, 2003, Hexyt_051
Spain, Mesas del Guadalora 2002 (Hortenique)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp 	 0.13 0.09 0.07 < 0.05, 0.07 (0.06) 0.3 0.32 0.16 0.1 < 0.05 < 0.05 < 0.05 < 0.05	 0 3 7 14 0 3 7 14 0 3 7 14	RD-03124, A2059 PA1 Perny, 2003, Hexyt_051

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Spain, Homachuelos 2002 (Marisol)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 < 0.05, < 0.05 (< 0.05) 0.28 < 0.05	 14 14 14	RD-03124, A2059 PA2 Perny, 2003, Hexyt_051
Spain, Homachuelos 2002 (Marisol)	WP, 10	1	0.78	0.02	Hexythiazox: Whole fruit (RAC) canned fruit marmalade final juice PT-1-3: marmalade	 0.14 < 0.05 < 0.05 0.06 < 0.05	 14 14 14 14 14	RD-03124, A2059 PA2 Perny, 2003, Hexyt_051
Spain, Ulldecona 2002 (Oro Nules)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp 	 < 0.05 < 0.05 0.07 < 0.05, < 0.05 (< 0.05) 0.47 0.22 0.15 0.05 < 0.05 < 0.05 < 0.05 < 0.05	 0 3 8 14 0 3 8 14 0 3 8 14	RD-03124, A2059 ES1 Perny, 2003, Hexyt_051
Spain, Vinaros 2002 (Marisol)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 0.07, 0.08 (0.08) 0.14 < 0.05	 15 15 15	RD-03124, A2059 ES2 Perny, 2003, Hexyt_051
Spain, Vinaros 2002 (Marisol)	WP, 10	2	0.8	0.02	Hexythiazox: Whole fruit (RAC) peel peeled fruit canned fruit marmalade sieving waste raw juice wet pomace dry pomace pulp final juice PT-1-3: marmalade	 0.34 2.0 < 0.05 0.06 0.09 0.08 0.17 0.51 2.5 0.82 0.07 < 0.05	 15 15 15 15 15 15 15 15 15 15 15 15	RD-03124, A2059 ES2 Perny, 2003, Hexyt_051

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Greece, Igoumenitsa 2002 (Clementine)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 0.09, 0.09 (0.09) 0.2 < 0.05	 15 15 15	RD-03124, A2059 GR1 Perny, 2003, Hexyt_051
Greece, Igoumenitsa 2002 (Clementine)	WP, 10	2	0.8	0.02	Hexythiazox: Whole fruit (RAC) canned fruit marmelade final juice PT-1-3: marmalade	 0.77 < 0.05 0.1 0.09 < 0.05	 15 15 15 15 15	RD-03124, A2059 GR1 Perny, 2003, Hexyt_051

Table 36 Hexythiazox residues in oranges following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Kern (CA) 2002 (Olinda)	EC, 12	1	0.21	0.037	Whole fruits	< 0.05 < 0.05	28 28	TCI-02-069, TCI-02-069-01 Carringer, 2003, Hexyt_029
USA, Tulare (CA) 2002 (Atwood Navel)	EC, 12	1	0.21	0.012	Whole fruits	0.12 0.12	28 28	TCI-02-069, TCI-02-069-02 Carringer, 2003, Hexyt_029
USA, Tulare (CA) 2003 (Washington Navel)	EC, 12	1	0.21	0.036	Whole fruits	0.15 0.12 0.13 0.14 0.12 0.2 0.11 0.12	7 7 13 13 28 28 34 34	TCI-03-084, TCI-03-084-01 Carringer, 2004, Hexyt_030
USA, Tulare (CA) 2003 (Washington Navel)	WP, 50	1	0.21	0.036	Whole fruits	0.11 0.07	28 28	TCI-03-084, TCI-03-084-01 Carringer, 2004, Hexyt_030
USA, Willacy (TX) 2003 (Marrs)	EC, 12	1	0.21	0.009	Whole fruits	0.11 0.05	28 28	TCI-03-084, TCI-03-084-02 Carringer, 2004, Hexyt_030
USA, Willacy (TX) 2003 (Marrs)	WP, 50	1	0.21	0.009	Whole fruits	0.05 0.06	28 28	TCI-03-084, TCI-03-084-02 Carringer, 2004, Hexyt_030

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 2006 (Valencia)	EC, 12	1	1.05	0.056	Whole fruits Juice Pulp, dried Citrus oil	0.29 0.44 < 0.02 < 0.02 0.81, 0.75 (0.78) 1.0, 0.53 (0.76) 60 32	28 28 28 28 28 28 28 28	TCI-06-142, TCI-06-142-01 Carringer, 2006, Hexyt_031
Italy, Taranto 2002 (Navel 115)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 0.07, < 0.05 (0.06) 0.19 < 0.05	 14 14 14	RD-03122, A2058 IT2 Perny, 2003, Hexyt_050
Italy, Taranto 2002 (Navel 115)	WP, 10	2	0.8	0.02	Hexythiazox: Whole fruit (RAC) canned fruits marmalade final juice PT-1-3: marmalade	 0.67 0.05 0.18 0.15 < 0.05	 14 14 14 14 14	RD-03122, A2058 IT2 Perny, 2003, Hexyt_050
Spain, Mesas de Guadalora 2002 (Salustiana)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp 	 < 0.05 < 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) 0.07 0.14 0.11 0.08 < 0.05 < 0.05 < 0.05 < 0.05	 0 3 7 14 0 3 7 14 0 3 7 14	RD-03122, A2058 PA1 Perny, 2003, Hexyt_050
Spain, Palma del Rio 2002 (New Holl)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 < 0.05, < 0.05 (< 0.05) 0.2 < 0.05	 14 14 14	RD-03122, A2058 PA2 Perny, 2003, Hexyt_050

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Spain, Palma del Rio 2002 (New Holl)	WP, 10	2	0.8	0.02	Hexythiazox: Whole fruit (RAC) canned fruits marmalade final juice PT-1-3: marmalade	 0.44 < 0.05 0.06 0.13 < 0.05	 14 14 14 14 14	RD-03122, A2058 PA2 Perny, 2003, Hexyt_050
Spain, Alcanar 2002 (Salustiana)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp 	 0.07 0.06 < 0.05 < 0.05, < 0.05 (< 0.05) 0.14 0.17 0.09 0.2 < 0.05 < 0.05 < 0.05 < 0.05	 0 3 7 13 0 3 7 13 0 3 7 13	RD-03122, A2058 ES1 Perny, 2003, Hexyt_050
Spain, Calig 2002 (Navel New Gold)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 0.08, 0.06 (0.07) 0.18 < 0.05	 13 13 13	RD-03122, A2058 ES2 Perny, 2003, Hexyt_050
Spain, Calig 2002 (Navel New Gold)	WP, 10	2	0.8	0.02	Hexythiazox: Whole fruit (RAC) Peel peeled fruit canned fruits marmalade sieving waste raw juice wet pomace dry pomace pulp final juice PT-1-3: marmalade	 0.85 1.2 0.28 0.06 0.09 0.18 0.33 0.52 2.4 1.4 0.22 < 0.05	 13 13 13 13 13 13 13 13 13 13 13 13	RD-03122, A2058 ES2 Perny, 2003, Hexyt_050
Greece, Igoumenitsa 2002 (Navelina)	WP, 10	3	0.08	0.002	Hexythiazox: Whole fruit Peel Pulp	 < 0.05, < 0.05 (< 0.05) 0.19 < 0.05	 15 15 15	RD-03122, A2058 GR1 Perny, 2003, Hexyt_050

Table 37 Hexythiazox residues in almonds following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1995 (Carmel)	WP, 50	1	0.25	0.026	Nutmeat	< 0.02 < 0.02	28 28	AA950602, AA950602 CA1 Carringer, 1996, Hexyt_019 amended by Carringer, S. 1997, Hexyt_020
USA, Kern (CA) 1995 (Carmel)	WP, 50	1	0.25	0.026	Nutmeat	< 0.02 < 0.02	28 28	AA950602, AA950602 CA2 Carringer, 1996, Hexyt_019 amended by Carringer, 1997, Hexyt_020

Table 38 Hexythiazox residues in pecan following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Macon (AL) 1996 (Cape Fear)	WP, 50	1	0.41	0.029	Nutmeat	< 0.02 < 0.02	29 29	AA960608, AA960608 AL Carringer, 1997, Hexyt_021
USA, Irwin (GA) 1996 (Desirable)	WP, 50	1	0.42	0.029	Nutmeat	< 0.02 < 0.02	29 29	AA960608, AA960608 GA Carringer, 1997, Hexyt_021
USA, Rapides (LA) 1996 (Jackson/Cape Fear)	WP, 50	1	0.41	0.081	Nutmeat	< 0.02 < 0.02	29 29	AA960608, AA960608 LA Carringer, 1997, Hexyt_021
USA, Uvalde (TX) 1996 (Wichita)	WP, 50	1	0.42	0.063	Nutmeat	< 0.02 < 0.02	28 28	AA960608, AA960608 TX1 Carringer, 1997, Hexyt_021
USA, Lubbock (TX) 1996 (Western Schlox)	WP, 50	1	0.42	0.04	Nutmeat	< 0.02 < 0.02	28 28	AA960608, AA960608 TX2 Carringer, 1997, Hexyt_021

Table 39 Hexythiazox residues in apples following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Ottawa (MI) (Golden Delicious)	WP, 50	1	0.14	0.025	Fruits	0.12 0.18	28 28	AA970610, AA970610-MI Carringer, 1998, Hexyt_034
USA, Grant (WA) (Red Delicious Classic)	WP, 50	1	0.14	0.007	Fruits	0.06 0.04	28 28	AA970610, AA970610-WA1 Carringer, 1998, Hexyt_034
USA, Grant (WA) (Red Delicious)	WP, 50	1	0.14	0.008	Fruits	0.05 0.04	28 28	AA970610, AA970610-WA2 Carringer, 1998, Hexyt_034
USA, Benton (WA) (Rome)	WP, 50	1	0.14	0.006	Fruits	0.04 0.04	28 28	AA970610, AA970610-WA3 Carringer, 1998, Hexyt_034
USA, Franklin (WA) (Fuji)	WP, 50	1	0.14	0.004	Fruits	0.03 0.02	28 28	AA970610, AA970610-WA4 Carringer, 1998, Hexyt_034
USA, Wayne (NY) (Granny Smith)	EC, 24	1	0.22	0.023	Fruits	0.09 0.15 0.2 0.19 0.16	28 28 28 28 28	TCI-03-083, TCI-03-083-01 Carringer, 2004, Hexyt_035
USA, Wayne (NY) (Granny Smith)	WP, 50	1	0.21	0.022	Fruits	0.06 0.04 0.04 0.04 0.05	28 28 28 28 28	TCI-03-083, TCI-03-083-01 Carringer, 2004, Hexyt_035
USA, Ottawa (MI) (Ida Red)	EC, 24	1	0.21	0.023	Fruits	0.14, 0.15 (0.15) 0.2, 0.21 (<u>0.21</u>) 0.1, 0.11 (0.11) 0.11, 0.12 (0.12) 0.14, 0.14 (0.14)	28 28 28 28 28	TCI-03-083, TCI-03-083-02 Carringer, 2004, Hexyt_035
USA, Ottawa (MI) (Ida Red)	WP, 50	1	0.21	0.023	Fruits	0.09, 0.1 (0.1) 0.05, 0.07 (0.06) 0.08, 0.09 (0.09) 0.04, 0.06 (0.05) 0.1, 0.09 (0.1)	28 28 28 28 28	TCI-03-083, TCI-03-083-02 Carringer, S., 2004, Hexyt_035
USA, Ephrata (WA) (Braeburn)	EC, 24	1	0.21	0.022	Fruits	0.12 0.11 0.2 0.13 0.21	28 28 28 28 28	TCI-03-083, TCI-03-083-03 Carringer, 2004, Hexyt_035

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Ephrata (WA) (Braeburn)	WP, 50	1	0.21	0.023	Fruits	0.11 0.12 0.1 0.13 0.08	28 28 28 28 28	TCI-03-083, TCI-03-083-03 Carringer, 2004, Hexyt_035
USA, Wayne (NY) 2005 (Twenty Ounce)	EC, 12	1	0.22	0.038	Fruits	0.08 0.11	28 28	TCI-05-124, TCI-05-124-01 Carringer, 2006, Hexyt_036
USA, Wayne (NY) 2005 (Rome)	EC, 12	1	0.21	0.011	Fruits	0.05 0.09	28 28	TCI-05-124, TCI-05-124-02 Carringer, 2006, Hexyt_036
USA, Wayne (NY) 2005 (Rome)	EC, 12	1	0.21	0.035	Fruits	0.05 0.05	28 28	TCI-05-124, TCI-05-124-02 Carringer, 2006, Hexyt_036
USA, Albermarle (VA) 2005 (Rome)	EC, 12	1	0.21	0.009	Fruits	0.14 0.16	28 28	TCI-05-124, TCI-05-124-03 Carringer, 2006, Hexyt_036
USA, Albermarle (VA) 2005 (Rome)	EC, 12	1	0.21	0.033	Fruits	0.09 0.06	28 28	TCI-05-124, TCI-05-124-03 Carringer, 2006, Hexyt_036
USA, Ottawa (MI) 2005 (Golden Delicious)	EC, 12	1	0.21	0.037	Fruits	0.07 0.08	28 28	TCI-05-124, TCI-05-124-04 Carringer, 2006, Hexyt_036
USA, Cache (UT) 2005 (McIntosh)	EC, 12	1	0.21	0.012	Fruits	0.12 0.09	27 27	TCI-05-124, TCI-05-124-05 Carringer, 2006, Hexyt_036
USA, Cache (UT) 2005 (McIntosh)	EC, 12	1	0.21	0.033	Fruits	0.1 0.11	27 27	TCI-05-124, TCI-05-124-05 Carringer, 2006, Hexyt_036
USA, Tulare (CA) 2005 (Granny Smith)	EC, 12	1	0.21	0.036	Fruits	0.05 0.02	28 28	TCI-05-124, TCI-05-124-06 Carringer, 2006, Hexyt_036
USA, Grant (WA) 2005 (Red Delicious)	EC, 12	1	0.21	0.035	Fruits	0.14 0.15	28 28	TCI-05-124, TCI-05-124-07 Carringer, 2006, Hexyt_036

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Grant (WA) 2005 (Red Delicious)	EC, 12	1	0.21	0.012	Fruits	0.06 0.08	28 28	TCI-05-124, TCI-05-124-08 Carringer, 2006, Hexyt_036
USA, Washington (ID) 2005 (Granny Smith)	EC, 12	1	0.21	0.032	Fruits	0.09 0.09	28 28	TCI-05-124, TCI-05-124-09 Carringer, 2006, Hexyt_036

Table 40 Hexythiazox residues in pears following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Wayne (NY) 2005 (Clapp´s Favorite)	EC, 12	1	0.21	0.015	Fruits	0.1 0.11	28 28	TCI-05-124, TCI-05-124-10 Carringer, 2006, Hexyt_036
USA, Tulare (CA) 2005 (Bosc)	EC, 12	1	0.21	0.038	Fruits	0.09 0.1	28 28	TCI-05-124, TCI-05-124-11 Carringer, 2006, Hexyt_036
USA, Tulare (CA) 2005 (Olympic)	EC, 12	1	0.21	0.007	Fruits	0.06 0.04	27 27	TCI-05-124, TCI-05-124-12 Carringer, 2006, Hexyt_036
USA, Grant (WA) 2005 (Concord)	EC, 12	1	0.21	0.037	Fruits	0.12 0.12	28 28	TCI-05-124, TCI-05-124-13 Carringer, 2006, Hexyt_036
USA, Grant (WA) 2005 (Bartlett)	EC, 12	1	0.21	0.011	Fruits	0.06 0.06	27 27	TCI-05-124, TCI-05-124-14 Carringer, 2006, Hexyt_036
USA, Payette (ID) 2005 (Bartlett)	EC, 12	1	0.21	0.032	Fruits	0.16 0.12	28 28	TCI-05-124, TCI-05-124-15 Carringer, 2006, Hexyt_036

Table 41 Hexythiazox residues in cherries following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1995 (Bart)	WP, 50	1	0.21	0.012	Whole fruits	0.1 <u>0.12</u>	24 24	AA950603, AA950603 CA1 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Tulare (CA) 1995 (Lanon)	WP, 50	1	0.21	0.011	Whole fruits	0.02 <u>0.04</u>	28 28	AA950603, AA950603 CA2 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Hood River (OR) 1995 (Van)	WP, 50	1	0.21	0.012	Whole fruits	0.03 <u>0.06</u>	28 28	AA950603, AA950603 OR1 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Grant (WA) 1995 (Bung)	WP, 50	1	0.21	0.016	Whole fruits	0.07 <u>0.08</u>	28 28	AA950603, AA950603 WA Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Conklin (MI) 2008 (Napoleon)	EC, 12	1	0.21	0.012	Whole fruits	0.51 0.45	7 7	TCI-08-192, TCI-08-192-01 Wyatt, 2009, Hexyt_049
USA, Conklin (MI) 2008 (Montmorency)	EC, 12	1	0.21	0.033	Whole fruits	0.67 0.43	7 7	TCI-08-192, TCI-08-192-02 Wyatt, 2009, Hexyt_049
USA, Marengo (IL) 2008 (North Star)	EC, 12	1	0.21	0.033	Whole fruits	0.75 0.45	7 7	TCI-08-192, TCI-08-192-03 Wyatt, 2009, Hexyt_049
USA, Plainview (CA) 2008 (Tulare)	EC, 12	1	0.21	0.011	Whole fruits	0.22 0.46	7 7	TCI-08-192, TCI-08-192-04 Wyatt, 2009, Hexyt_049

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Royal City (WA) 2008 (Bing)	EC, 12	1	0.21	0.033	Whole fruits	0.47 0.3	7 7	TCI-08-192, TCI-08-192-05 Wyatt, 2009, Hexyt_049
USA, Weiser (ID) 2008 (Montmorency)	EC, 12	1	0.22	0.011	Whole fruits	0.52 0.9	7 7	TCI-08-192, TCI-08-192-06 Wyatt, 2009, Hexyt_049

Table 42 Hexythiazox residues in nectarines following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1995 (Fairlane)	WP, 50	1	0.21	0.047	Whole fruits	0.05 0.05	28 28	AA950603, AA950603 CA4 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Hood River (OR) 1995 (Fantasia)	WP, 50	1	0.21	0.014	Whole fruits	0.07 0.09	28 28	AA950603, AA950603 OR2 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Saluda (SC) 1995 (Southern Beauty)	WP, 50	1	0.21	0.022	Whole fruits	0.05 0.04	27 27	AA950603, AA950603 SC Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017

Table 43 Hexythiazox residues in peaches following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1995 (Starnes)	WP, 50	1	0.22	0.041	Whole fruits	0.18 0.15	28 28	AA950603, AA950603 CA3 Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Ottawa (MI) 1995 (Bellaire)	WP, 50	1	0.21	0.032	Whole fruits	0.09 0.08	28 28	AA950603, AA950603 MI Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Medina (TX) 1995 (Redskin)	WP, 50	1	0.21	0.027	Whole fruits	0.09 0.09	30 30	AA950603, AA950603 TX Carringer, 1996, Hexyt_016 amended by Carringer, 1997, Hexyt_017
USA, Alton (NY) 2008 (Red Haven)	EC, 12	1	0.21	0.038	Whole fruits	0.06 0.09	7 7	TCI-08-192, TCI-08-192-07 Wyatt, 2009, Hexyt_049
USA, Monetta (SC) 2008 (Contender)	EC, 12	1	0.21	0.016	Whole fruits	0.07 0.15	7 7	TCI-08-192, TCI-08-192-08 Wyatt, 2009, Hexyt_049
USA, Chula (GA) 2008 (Hawthorne)	EC, 12	1	0.20	0.04	Whole fruits	0.36 0.15	7 7	TCI-08-192, TCI-08-192-09 Wyatt, 2009, Hexyt_049
USA, Montezuma (GA) 2008 (Scarlet Prince)	EC, 12	1	0.21	0.011	Whole fruits	0.11 0.07	7 7	TCI-08-192, TCI-08-192-10 Wyatt, 2009, Hexyt_049
USA, Conklin (MI) 2008 (Bellaire)	EC, 12	1	0.21	0.033	Whole fruits	0.12 0.24	7 7	TCI-08-192, TCI-08-192-11 Wyatt, 2009, Hexyt_049

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, D'Hanis (TX) 2008 (La Feliciana)	EC, 12	1	0.21	0.014	Whole fruits	0.37 0.58	7 7	TCI-08-192, TCI-08-192-12 Wyatt, 2009, Hexyt_049
USA, Porterville (CA) 2008 (Elberta)	EC, 12	1	0.21	0.033	Whole fruits	0.05 0.07	7 7	TCI-08-192, TCI-08-192-13 Wyatt, 2009, Hexyt_049
USA, Kingsburg (CA) 2008 (Klamt Cling)	EC, 12	1	0.21	0.01	Whole fruits	0.19 0.24	7 7	TCI-08-192, TCI-08-192-14 Wyatt, 2009, Hexyt_049
USA, Sanger (CA) 2008 (Ryan Sun)	EC, 12	1	0.21	0.035	Whole fruits	0.15 0.12	7 7	TCI-08-192, TCI-08-192-15 Wyatt, 2009, Hexyt_049

Table 44 Hexythiazox residues in plums following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Stanislaus (CA) 1996 (French)	WP, 50	1	0.42	0.045	Plums Prunes	0.03, 0.03 (0.03) 0.03, 0.03 (0.03) 0.14 0.14	7 7 7 7	AA960607, AA960607 CA Carringer, 1997, Hexyt_018
USA, Conklin (MI) 2008 (Stanley)	EC, 12	1	0.21	0.036	Whole fruits	0.36 0.36	7 7	TCI-08-192, TCI-08-192-16 Wyatt, 2009, Hexyt_049
USA, Dinuba (CA) 2008 (Fryer´s)	EC, 12	1	0.20	0.011	Whole fruits	0.03 0.03	7 7	TCI-08-192, TCI-08-192-17 Wyatt, 2009, Hexyt_049
USA, Exeter (CA) 2008 (Flavour Fall)	EC, 12	1	0.21	0.033	Whole fruits	0.06 0.06	7 7	TCI-08-192, TCI-08-192-18 Wyatt, 2009, Hexyt_049
USA, Ducor (CA) 2008 (Black Cat)	EC, 12	1	0.22	0.01	Whole fruits	0.03 < 0.02	7 7	TCI-08-192, TCI-08-192-19 Wyatt, 2009, Hexyt_049

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Hickman (CA) 2008 (Grand Rosa)	EC, 12	1	0.21	0.037	Whole fruits	0.1 0.06	7 7	TCI-08-192, TCI-08-192-20 Wyatt, 2009, Hexyt_049
USA, Monmouth (OR) 2008 (Moyer)	EC, 12	1	0.21	0.014	Whole fruits	0.06 0.07	7 7	TCI-08-192, TCI-08-192-21 Wyatt, 2009, Hexyt_049

Table 45 Hexythiazox residues in blackberries following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, unknown 1998 (unknown)	WP, 50	1	0.42		Fruits	0.91 0.84	21 21	PR. No.: 03238, 03238.98-OR18 Samoil, 1998, Hexyt_039

Table 46 Hexythiazox residues in grapes following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Yates (NY) 2002 (Concord)	EC, 12	1	0.21	0.045	Fruits	0.12 <u>0.19</u>	28 28	TCI-02-070, TCI-02-070-01 Carringer, 2003, Hexyt_032
USA, Tulare (CA) 2002 (Crimson)	EC, 12	1	0.21	0.035	Fruits	<u>0.04</u> 0.03	28 28	TCI-02-070, TCI-02-070-02 Carringer, 2003, Hexyt_032
USA, Kern (CA) 2002 (Red Globe)	EC, 12	1	0.21	0.022	Fruits	0.05 <u>0.13</u>	28 28	TCI-02-070, TCI-02-070-03 Carringer, 2003, Hexyt_032
USA, Tulare (CA) 2002 (Ruby Red)	EC, 12	1	0.21	0.022	Fruits	0.13 <u>0.13</u>	28 28	TCI-02-070, TCI-02-070-04 Carringer, 2003, Hexyt_032

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 2002 (Thompson Seedless)	EC, 12	1	0.21	0.037	Fruits	0.05 0.04	28 28	TCI-02-070, TCI-02-070-05 Carringer, 2003, Hexyt_032
USA, Tulare (CA) 2002 (Emperor)	EC, 12	1	0.22	0.011	Fruits	0.24 0.15	28 28	TCI-02-070, TCI-02-070-06 Carringer, 2003, Hexyt_032
USA, Grant (WA) 2002 (White Reisling)	EC, 12	1	0.21	0.032	Fruits	0.25 0.31	28 28	TCI-02-070, TCI-02-070-07 Carringer, 2003, Hexyt_032
USA, Grant (WA) 2002 (Cabernet Sauvignon)	EC, 12	1	0.21	0.012	Fruits	0.29 0.31	28 28	TCI-02-070, TCI-02-070-08 Carringer, 2003, Hexyt_032
USA, Dundee (NY) 2004 (DeChaunac)	EC, 12	1	0.21	0.022	Fruits	0.35 0.48	28 28	TCI-04-087, TCI-04-087-01 Carringer, 2005, Hexyt_033
USA, Dundee (NY) 2004 (DeChaunac)	WP, 50	1	0.21	0.022	Fruits	0.31 0.3	28 28	TCI-04-087, TCI-04-087-01 Carringer, 2005, Hexyt_033
USA, Kingsburg (CA) 2004 (Crimson)	EC, 12	1	0.21	0.034	Fruits	0.21 0.16	28 28	TCI-04-087, TCI-04-087-02 Carringer, 2005, Hexyt_033
USA, Kingsburg (CA) 2004 (Crimson)	WP, 50	1	0.21	0.034	Fruits	0.14 0.14	28 28	TCI-04-087, TCI-04-087-02 Carringer, 2005, Hexyt_033
USA, Richgrove (CA) 2004 (Ruby Seedless)	EC, 12	1	0.21	0.033	Fruits	0.16 0.13	28 28	TCI-04-087, TCI-04-087-03 Carringer, 2005, Hexyt_033
USA, Richgrove (CA) 2004 (Ruby Seedless)	WP, 50	1	0.21	0.033	Fruits	0.12 0.22	28 28	TCI-04-087, TCI-04-087-03 Carringer, 2005, Hexyt_033

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Polar (CA) 2004 (Thompson Seedless)	EC, 12	1	0.21	0.012	Fruits	0.06 0.03 0.04 0.03 0.03 < 0.02 0.03 0.03	21 21 28 28 35 35 42 42	TCI-04-087, TCI-04-087-04 Carringer, 2005, Hexyt_033
USA, Polar (CA) 2004 (Thompson Seedless)	WP, 50	1	0.21	0.012	Fruits	0.04 0.04	28 28	TCI-04-087, TCI-04-087-04 Carringer, 2005, Hexyt_033
USA, East Williamson (NY) 2008 (Cayuga White)	EC, 12	1	0.21	0.038	Fruits	0.2 0.17	7 7	TCI-08-193, TCI-08-193-01 Wyatt, 2009, Hexyt_052
USA, Dundee (NY) 2008 (DeChaunac)	EC, 12	1	0.21	0.015	Fruits	0.5 0.42	7 7	TCI-08-193, TCI-08-193-02 Wyatt, 2009, Hexyt_052
USA, Dinuba (CA) 2008 (Alicante)	EC, 12	1	0.21	0.035	Fruits	0.1 0.04	7 7	TCI-08-193, TCI-08-193-03 Wyatt, 2009, Hexyt_052
USA, Plainview (CA) 2008 (Crimson)	EC, 12	1	0.21	0.009	Fruits	0.37 0.44	7 7	TCI-08-193, TCI-08-193-04 Wyatt, 2009, Hexyt_052
USA, Lindsay (CA) 2008 (Red Globe)	EC, 12	1	0.21	0.034	Fruits	< 0.02 0.12	7 7	TCI-08-193, TCI-08-193-05 Wyatt, 2009, Hexyt_052
USA, Poplar (CA) 2008 (Flame)	EC, 12	1	0.21	0.012	Fruits	0.08 0.08	7 7	TCI-08-193, TCI-08-193-06 Wyatt, 2009, Hexyt_052
USA, Porterville (CA) 2008 (Thompson)	EC, 12	1	0.21	0.03	Fruits	0.05 0.08	7 7	TCI-08-193, TCI-08-193-07 Wyatt, 2009, Hexyt_052

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Delano (CA) 2008 (Alicante)	EC, 12	1	0.21	0.012	Fruits	0.17 0.15	7 7	TCI-08-193, TCI-08-193-08 Wyatt, 2009, Hexyt_052
USA, Hickman (CA) 2008 (Chardonnay)	EC, 12	1	0.21	0.032	Fruits	0.5 0.47	7 7	TCI-08-193, TCI-08-193-09 Wyatt, 2009, Hexyt_052
USA, Paso Robles (CA) 2008 (Chardonnay)	EC, 12	1	0.21	0.011	Fruits	0.12 0.2	7 7	TCI-08-193, TCI-08-193-10 Wyatt, 2009, Hexyt_052
USA, Ephrata (WA) 2008 (White Riesling)	EC, 12	1	0.21	0.038	Fruits	0.32 0.3	7 7	TCI-08-193, TCI-08-193-11 Wyatt, 2009, Hexyt_052
USA, George (WA) 2008 (Cabernet Sauvignon)	EC, 12	1	0.21	0.014	Fruits	0.72 0.59	7 7	TCI-08-193, TCI-08-193-12 Wyatt, 2009, Hexyt_052
Italy, Mornico 2002 (Chardonnay)	WP, 10	2	0.083 0.084	0.008 0.008	Fruits	0.19 0.11 0.17 0.09 0.08	0 7 14 20 20	RD-03120, A2066 IT1 Perny, 2003, Hexyt_053
Italy, Monleale 2002 (Dolcetto)	WP, 10	2	0.083 0.077	0.008 0.009	Fruits	0.09 0.06	20 20	RD-03120, A2066 IT2 Perny, 2003, Hexyt_053
Italy, Monleale 2002 (Dolcetto)	WP, 10	2	0.80 0.83	0.08 0.083	Grapes (RAC) wine, red juice, red raisins	2.4 < 0.05 0.19 1.3	20 20 20 20	RD-03120, A2066 IT2 Perny, 2003, Hexyt_053
France (South), Duras 2002 (Merlot)	WP, 10	2	0.077 0.078	0.008 0.008	Fruits	0.24 0.16 0.15 0.12 0.14	0 7 14 20 20	RD-03120, A2066 DR1 Perny, 2003, Hexyt_053
France (South), Fronton 2002 (Negrette)	WP, 10	2	0.08 0.083	0.008 0.008	Fruits	0.1 0.06	21 21	RD-03120, A2066 TL1 Perny, 2003, Hexyt_053

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
France (South), Fronton 2002 (Negrette)	WP, 10	2	0.81 0.82	0.08 0.08	Grapes (RAC) must, red lees, red wet pomace, red dry pomace, red AF wine, red MLF wine, red wine, red lees, juice wet pomace, juice juice, red raisins	0.51 0.2 0.16 8.5 12 < 0.05 < 0.05 < 0.05 9.6 7.0 0.38 1.7	21 21 21 21 21 21 21 21 21 21 21 21	RD-03120, A2066 TL1 Perny, 2003, Hexyt_053
Spain, Los Palacios 2002 (Macebeo)	WP, 10	2	0.079 0.082	0.008 0.008	Fruits	0.08 0.06 0.05 < 0.05 < 0.05	0 7 14 21 21	RD-03120, A2066 PA1 Perny, 2003, Hexyt_053
Spain, Calonge 2002 (Malvasia)	WP, 10	2	0.078 0.079	0.008 0.008	Fruits	< 0.05 < 0.05	22 22	RD-03120, A2066 ES1 Perny, 2003, Hexyt_053
France (North), Bischoffsheim 2002 (Chardonnay)	WP, 10	2	0.082 0.087	0.008 0.008	Fruits	0.13 0.1 0.1 0.09 0.09	0 6 14 20 20	RD-03120, A2066 AN1 Perny, 2003, Hexyt_053
France (North) Furdenheim 2002 (Pinot Noir)	WP, 10	2	0.082 0.081	0.008 0.008	Fruits	0.19 0.15	21 21	RD-03120, A2066 AN2 Perny, 2003, Hexyt_053
France (North) Furdenheim 2002 (Pinot Noir)	WP, 10	2	0.78 0.81	0.08 0.08	Grapes (RAC) wine, white juice, white raisins	2.7 < 0.05 < 0.05 4.6	21 21 21 21	RD-03120, A2066 AN2 Perny, 2003, Hexyt_053
France (North) Méhers 2002 (Sauvignon)	WP, 10	2	0.082 0.084	0.008 0.008	Fruits	< 0.05 0.06 < 0.05 0.06 < 0.05	0 7 14 21 21	RD-03120, A2066 CT1 Perny, 2003, Hexyt_053
France (North) Martigne-Briand 2002 (Chenin)	WP, 10	2	0.082 0.083	0.008 0.008	Fruits	< 0.05 0.06	19 19	RD-03120, A2066 BM1 Perny, 2003, Hexyt_053

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
France (North) Martigne-Briand 2002 (Chenin)	WP, 10	2	0.80 0.83	0.08 0.083	Grapes (RAC) must, white lees, white wet pomace, white dry pomace, white AF wine, white wine, white lees, juice wet pomace, juice juice, white raisins	0.57 0.07 0.57 2.0 5.6 < 0.05 < 0.05 2.1 2.7 0.08 0.8	19 19 19 19 19 19 19 19 19 19 19	RD-03120, A2066 BM1 Perny, 2003, Hexyt_053
Austria Eisenstadt 2002 (Gruener Veltiner)	WP, 10	2	0.08	0.008	Fruits	0.28 0.2 0.13 0.16 0.14	0 7 14 21 21	RD-03120, A2066 AU1 Perny, 2003, Hexyt_053
Austria Bad Voeslau 2002 (Zierfandler)	WP, 10	2	0.08	0.008	Fruits	0.15 0.18	21 21	RD-03120, A2066 AU2 Perny, 2003, Hexyt_053

AF wine: wine after alcoholic fermentation

MLF wine: wine after malolactic fermentation

Table 47 Hexythiazox residues in raspberries following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, unknown 1998 (unknown)	WP, 50	1	0.42	0.22	Fruits	0.3 0.41	21 21	PR. No.: 03238, 03238.98-MI23 Samoil, 1998, Hexyt_039
USA, unknown 1998 (unknown)	WP, 50	1	0.42	0.22	Fruits	0.35 0.29	21 21	PR. No.: 03238, 03238.98-WA39 Samoil, 1998, Hexyt_039
USA, unknown 1998 (unknown)	WP, 50	1	0.42	0.22	Fruits	0.66 0.54	21 21	PR. No.: 03238, 03238.98-OR17 Samoil, 1998, Hexyt_039

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, unknown 1998 (unknown)	WP, 50	1	0.42	0.22	Fruits	0.78 0.92	21 21	PR. No.: 03238, 03238.98-PA01 Samoil, 1998, Hexyt_039

Table 48 Hexythiazox residues in strawberries following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Yates (NY) 2001 (Honeoye)	WP, 50	1	0.21	0.08	Fruits	0.13 0.11	3 3	TCI-01-001, TCI-01-001-01 Carringer, 2001, Hexyt_028
USA, Tulare (CA) 2001 (Seascape)	WP, 50	1	0.21	0.06	Fruits	0.28 0.3 0.25 0.22 0.1 0.16 0.03 0.04 < 0.02 < 0.02	3 3 7 7 14 14 21 21 28 28	TCI-01-001, TCI-01-001-02 Carringer, 2001, Hexyt_028
USA, Washington (OR) 2001 (Puget Reliance)	WP, 50	1	0.21	0.11	Fruits	0.17 0.16	3 3	TCI-01-001, TCI-01-001-03 Carringer, 2001, Hexyt_028

Table 49 Hexythiazox residues in dates following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Coachella (CA) 1999 (Deglet Noor)	WP, 50	1	0.21	0.02	Fruits	0.07 0.26	91 91	IR-4 No. 06957, CA82 Samoil, 2001, Hexyt_027
USA, Coachella (CA) 1999 (Deglet Noor)	WP, 50	1	0.21	0.02	Fruits	0.09 0.11	91 91	IR-4 No. 06957, CA83 Samoil, 2001, Hexyt_027

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Coachella (CA) 1999 (Deglet Noor)	WP, 50	1	0.21	0.02	Fruits	0.3 0.63	91 91	IR-4 No. 06957, CA84 Samoil, 2001, Hexyt_027

Table 50 Hexythiazox residues in protected tomatoes following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Italy, Palagiano 2002 (Naxome)	WP, 10	1	0.1	0.007	Hexythiazox: Fruits	< 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05	0 1 3 7	RD-03083, A2064 IT1 Perny, 2003, Hexyt_056
Italy, Rivalta Bormida 2002 (Cuore di Bue)	WP, 10	1	0.11	0.007	Hexythiazox: Fruits	< 0.05, < 0.05 (< 0.05)	3	RD-03083, A2064 IT2 Perny, 2003, Hexyt_056
Italy, Santena 2002 (Jama)	WP, 10	1	0.099	0.007	Hexythiazox: Fruits	< 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05	0 1 3 7	RD-03083, A2064 IT3 Perny, 2003, Hexyt_056
France (South) Cambes 2002 (Lerika)	WP, 10	1	0.097	0.007	Hexythiazox: Fruits	< 0.05 < 0.05, < 0.05 (< 0.05)	1 3	RD-03083, A2064 DR1 Perny, 2003, Hexyt_056
The Netherlands, Melderslo 2002 (Cedrico)	WP, 10	1	0.099	0.007	Hexythiazox: Fruits	0.08 0.07 0.05, 0.05 (0.05) < 0.05	0 1 3 6	RD-03083, A2064 NL1 Perny, 2003, Hexyt_056
France (North), Oberschaeffolsheim 2002 (Grapella)	WP, 10	1	0.1	0.007	Hexythiazox: Fruits	< 0.05, < 0.05 (< 0.05)	3	RD-03083, A2064 AN1 Perny, 2003, Hexyt_056
Italy, Castel d'Azzano 2001 (Ulisse)	WP, 10	1	0.097	0.007	Hexythiazox: Fruits	0.05 < 0.05	3 7	RD-II02307, HE1/I/09PO Perny, 2002, Hexyt_057
Italy, Ognissanti 2001 (Concara)	WP, 10	1	0.1	0.007	Hexythiazox: Fruits	< 0.05 < 0.05 < 0.05 < 0.05	0 1 3 7	RD-II02307, HE1/I/10PO Perny, 2002, Hexyt_057

Table 51 Hexythiazox residues in protected cucumbers following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
Italy, Motta di Costigliole 2002 (Hiyield PS)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	0.06 < 0.05 < 0.05 < 0.05	0 1 3 7	RD-03119, A2067 IT1 Perny, 2003, Hexyt_058
Italy, Piana di Bra 2002 (Edona)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	< 0.05	3	RD-03119, A2067 IT2 Perny, 2003, Hexyt_058
Spain, Penaflor 2002 (Edona)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	< 0.05 < 0.05 < 0.05 < 0.05	0 1 3 7	RD-03119, A2067 PA1 Perny, 2003, Hexyt_058
Spain, Vilassar de Mar 2002 (Sol verde)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	< 0.05 < 0.05	1 3	RD-03119, A2067 ES1 Perny, 2003, Hexyt_058
The Netherlands, Melderslo 2002 (Sabrina)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	< 0.05 < 0.05 < 0.05 < 0.05	0 1 3 6	RD-03119, A2067 NL1 Perny, 2003, Hexyt_058
The Netherlands, America 2002 (Sabrina)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	< 0.05	3	RD-03119, A2067 NL2 Perny, 2003, Hexyt_058
Italy, Motta di Costigiole 2003 (Hiyield PS)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	0.08 < 0.05 < 0.05 < 0.05	0 1 3 7	RD-03239, A3005 IT1 Perny, 2004, Hexyt_059
Italy, Bra 2003 (Edona)	WP, 10	1	0.08	0.005	Hexythiazox: Fruits	0.07 < 0.05	1 3	RD-03239, A3005 IT2 Perny, 2004, Hexyt_059

Table 52 Hexythiazox residues in protected melons following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
France (South), Mours Saint-Eusébe 2002 (Eliobelle)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh	 < 0.05 < 0.05, < 0.05 (< 0.05) 0.06 < 0.05 < 0.05 < 0.05	 1 3 1 3 1 3	RD-03118, A2068 BD1 Perny, 2003, Hexyt_060
France (South), Roumagne 2002 (Impact)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh	 < 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05 0.18 0.06 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05	 0 1 3 7 0 1 3 7 0 1 3 7	RD-03118, A2068 DR1 Perny, 2003, Hexyt_060
Spain, Fuente Palmera 2002 (Sancho)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh	 < 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05 < 0.05 < 0.05 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05	 0 1 3 7 0 1 3 7 0 1 3 7	RD-03118, A2068 PA1 Perny, 2003, Hexyt_060
Spain, Los Palacious y Villafrance 2002 (Albino)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh	 < 0.05 < 0.05, < 0.05 (< 0.05) 0.11 0.27 < 0.05 < 0.05	 1 3 1 3 1 3	RD-03118, A2068 PA2 Perny, 2003, Hexyt_060

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
The Netherlands, Ridderkerk 2002 (Haon)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh 	 < 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05	 0 1 3 7 0 1 3 7 0 1 3 7	RD-03118, A2068 NL1 Perny, 2003, Hexyt_060
The Netherlands, Oostvoorne 2002 (Haon)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh 	 < 0.05, < 0.05 (< 0.05) < 0.05 < 0.05 < 0.05 < 0.05	 3 1 3 1 3	RD-03118, A2068 NL2 Perny, 2003, Hexyt_060
France (South), Roumagne 2003 (Escrito)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh 	 < 0.05 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05	 0 1 3 7 0 1 3 7 0 1 3 7	RD-03226, A3007 DR1 Perny, 2004, Hexyt_061
France (South), Mours Saint-Eusébe 2003 (Héliobelle)	WP, 10	1	0.08	0.008	Hexythiazox: whole fruit peel flesh 	 < 0.05 < 0.05, < 0.05 (< 0.05) < 0.05 < 0.05 < 0.05 < 0.05	 1 3 1 3 1 3	RD-03226, A3007 BD1 Perny, 2004, Hexyt_061

Table 53 Hexythiazox residues in sweet corn cobs and ears following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Porterville (CA) 2007 (Bodacious)	EC, 12	1	0.21	0.11	Sweet corn ear	< 0.02, 0.05 (0.03) < 0.02, < 0.02 (< 0.02) 0.03, 0.07 (0.05) < 0.02, < 0.02 (< 0.02	21 28 35 42	TCI-07-179, TCI-07-179-01 Wyatt, 2009, Hexyt_055
USA, Corvallis (OR) 2007 (Suregold)	EC, 12	1	0.21	0.11	Sweet corn ear	0.024, < 0.02 (0.022)	28	TCI-07-179, TCI-07-179-02 Wyatt, 2009, Hexyt_055
USA, Ephrata (WA) 2008 (Basin Super Sweet)	EC, 12	1	0.21	0.11	Sweet corn ear	< 0.02, < 0.02 (< 0.02)	28	TCI-07-179, TCI-07-179-03 Wyatt, 2009, Hexyt_055

Table 54 Hexythiazox residues in snap beans (green beans) following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Porterville (CA) 2008 (Blue Lake 274)	EC, 12	1	0.21	0.11	Fresh beans	0.15, 0.12 (0.14)	14	TCI-07-178, TCI-07-178-10 Wyatt, 2009, Hexyt_062
USA, Madras (OR) 2007 (Snap 91G)	EC, 12	1	0.21	0.11	Fresh beans	0.04, 0.03 (0.04)	14	TCI-07-178, TCI-07-178-11 Wyatt, 2009, Hexyt_062

Table 55 Hexythiazox residues in succulent lima beans following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Porterville (CA) 2007 (Lee)	EC, 12	1	0.21	0.11	Succulent seed without pod	< 0.02, < 0.02 (< 0.02)	14	TCI-07-178, TCI-07-178-07 Wyatt, 2009, Hexyt_062
USA, Porterville (CA) 2008 (Henderson)	EC, 12	1	0.21	0.11	Succulent seed with pod Succulent seed without pod	0.06, 0.04 (0.05) 0.35, 0.37 (0.36)	14 14	TCI-07-178, TCI-07-178-08 Wyatt, 2009, Hexyt_062

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Ephrata (WA) 2008 (Fordhook Bush Lima)	EC, 12	1	0.21	0.11	Succulent seed with pod Succulent seed without pod	< 0.02, < 0.02 (< 0.02) 0.32, 0.21 (0.27)	14 14	TCI-07-178, TCI-07-178-09 Wyatt, 2009, Hexyt_062

Table 56 Hexythiazox residues in dry beans (pulses) following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Norwich (ND) 2007 (Maverick)	EC, 12	1	0.21	0.11	Seed without pod	< 0.02, < 0.02 (< 0.02) 0.03, < 0.02 (0.03) < 0.02, < 0.02 (< 0.02) < 0.02, < 0.02 (< 0.02)	7 14 21 28	TCI-07-178, TCI-07-178-01 Wyatt, 2009, Hexyt_062
USA, Grand Island (NE) 2008 (Chase)	EC, 12	1	0.21	0.11	Seed without pod	< 0.02, < 0.02 (< 0.02)	14	TCI-07-178, TCI-07-178-02 Wyatt, 2009, Hexyt_062
USA, Larned (KS) 2007 (Field Bean)	EC, 12	1	0.21	0.11	Seed without pod	0.3, 0.32 (0.31)	14	TCI-07-178, TCI-07-178-03 Wyatt, 2009, Hexyt_062
USA, Jerome (ID) 2008 (Othello)	EC, 12	1	0.21	0.11	Seed without pod	0.03, 0.03 (0.03)	14	TCI-07-178, TCI-07-178-04 Wyatt, 2009, Hexyt_062
USA, San Ardo (CA) 2007 (Lee)	EC, 12	1	0.21	0.11	Seed without pod	< 0.02, < 0.02 (< 0.02)	14	TCI-07-178, TCI-07-178-05 Wyatt, 2009, Hexyt_062
USA, Jerome (ID) 2007 (Othello)	EC, 12	1	0.21	0.12	Seed without pod	< 0.02, < 0.02 (< 0.02)	14	TCI-07-178, TCI-07-178-06 Wyatt, 2009, Hexyt_062

Table 57 Hexythiazox residues in cottonseeds following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1996 (Maxxa)	WP, 50	2	0.17	0.09	Ginned seed	0.05 <u>0.07</u>	32 32	AA960603, AA960603 CA1 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Maxxa)	EC, 5	2	0.2 0.17	0.1 0.09	Ginned seed	0.06 0.05	32 32	AA960603, AA960603 CA1 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, King (CA) 1996 (Maxxa)	WP, 50	2	0.18 0.17	0.091 0.087	Ginned seed	<u>0.1</u> 0.05	35 35	AA960603, AA960603 CA2 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, King (CA) 1996 (Maxxa)	EC, 5	2	0.20 0.18	0.1 0.09	Ginned seed	0.06 0.04	35 35	AA960603, AA960603 CA2 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Acala Maxxa)	WP, 50	2	0.18	0.09	Ginned seed	0.09 <u>0.1</u>	28 28	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Acala Maxxa)	EC, 5	2	0.21 0.18	0.11 0.09	Ginned seed	0.07 0.04	28 28	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1996 (Acala Maxxa)	WP, 50	2 1.05	1.05 1.05	0.54 0.54	Cottonseed Hulls Meal Refined oil	1.1, 1.2 (1.2) 0.85 0.23 0.23 0.01 < 0.01 0.16 0.15	14 14 14 14 14 14 14 14	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Acala Maxxa)	EC, 5	2 1.19 1.05	0.61 0.54	Cottonseed Hulls Meal Refined oil	1.1 1.5 0.22 0.16 0.02 < 0.01 0.13 0.16	14 14 14 14 14 14 14 14	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023	

Table 58 Hexythiazox residues in hops following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Canyon (ID) 1995 (Galena)	WP, 50	1	0.29	0.03	Cones, dry	0.34 0.36	45 45	AA950601, AA950601 ID Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025
USA, Canyon (ID) 1995 (Galena)	WP, 50	1	0.29	0.031	Cones, dry	0.1 < 0.1	59 59	AA950601, AA950601 ID Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025
USA, Manon (OR) 1995 (Nugget)	WP, 50	1	0.29	0.037	Cones, dry	1.3 0.99	44 44	AA950601, AA950601 OR Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Manon (OR) 1995 (Nugget)	WP, 50	1	0.27	0.039	Cones, dry	0.21 0.2	59 59	AA950601, AA950601 OR Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025
USA, Benton (WA) 1995 (Galena)	WP, 50	1	0.28	0.02	Cones, dry	3.6 3.4, 4.0 (3.7)	45 45	AA950601, AA950601 WA Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025
USA, Benton (WA) 1995 (Galena)	WP, 50	1	0.25	0.018	Cones, dry	1.2 1.9	60 60	AA950601, AA950601 WA Carringer, 1996, Hexyt_024 amended by Carringer, 1996, Hexyt_025

Table 59 Hexythiazox residues in maize grain following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Kingman (KS) 2003 (Pioneer)	EC, 12	1	0.21	0.11	Grain	< 0.02, < 0.02 (< 0.02)	96	TCI-03-078, TCI-03-078-01 Carringer, 2005, Hexyt_037
USA, Hockley (TX) 2003 (F3175)	EC, 12	1	0.21	0.11	Grain	< 0.02, < 0.02 (< 0.02) < 0.02, < 0.02 (< 0.02) < 0.02, < 0.02 (< 0.02) < 0.02, < 0.02 (< 0.02)	89 96 103 110	TCI-03-078, TCI-03-078-02 Carringer, 2005, Hexyt_037
USA, Hockley (TX) 2004 (Pioneer)	EC, 12	1	0.22	0.11	Grain	< 0.02, < 0.02 (< 0.02)	110	TCI-03-078, TCI-03-078-03 Carringer, 2005, Hexyt_037
USA, Hockley (TX) 2004 (Pioneer)	EC, 12	1	1.07	0.56	Grain	< 0.02, < 0.02 (< 0.02)	110	TCI-03-078, TCI-03-078-03 Carringer, 2005, Hexyt_037

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Hinton (OK) 2008 (DKC51-45 RR2)	EC, 12	1	0.21	0.11	Grain	< 0.02, < 0.02 (< 0.02)	79	TCI-08-228, TCI-08-228-01 Wyatt, 2009, Hexyt_054
USA, York (NE) 2008 (A1005005)	EC, 12	1	0.21	0.11	Grain	< 0.02, < 0.02 (< 0.02)	105	TCI-08-228, TCI-08-228-02 Wyatt, 2009, Hexyt_054
USA, York (NE) 2008 (A1005005)	EC, 12	1	1.05	0.56	Grain	< 0.02, < 0.02 (< 0.02)	105	TCI-08-228, TCI-08-228-02 Wyatt, 2009, Hexyt_054

Table 60 Hexythiazox residues in almond hulls following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1995 (Carmel)	WP, 50	1	0.25	0.026	Hulls	1.4 0.9	28 28	AA950602, AA950602 CA1 Carringer, 1996, Hexyt_019 amended by Carringer, 1997, Hexyt_020
USA, Kern (CA) 1995 (Carmel)	WP, 50	1	0.25	0.026	Hulls	1.1 1.2	28 28	AA950602, AA950602 CA2 Carringer, 1996, Hexyt_019 amended by Carringer, 1997, Hexyt_020

Table 61 Hexythiazox residues in sweet corn forage following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Porterville (CA) 2007 (Bodacious)	EC, 12	1	0.21	0.011	Forage	2.4, 2.1 (2.3) 2.4, 1.4 (1.9) 1.0, 2.1 (1.6) 0.89, 1.7 (1.3)	21 28 35 42	TCI-07-179, TCI-07-179-01 Wyatt, 2009, Hexyt_055

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Corvallis (OR) 2007 (Suregold)	EC, 12	1	0.21	0.011	Forage	0.42, 0.49 (0.46)	28	TCI-07-179, TCI-07-179-02 Wyatt, 2009, Hexyt_055
USA, Ephrata (WA) 2008 (Basin Super Sweet)	EC, 12	1	0.21	0.011	Forage	0.66, 0.56 (0.61)	28	TCI-07-179, TCI-07-179-03 Wyatt, 2009, Hexyt_055

Table 62 Hexythiazox residues in cotton gin trash following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1996 (Maxxa)	WP, 50	2	0.17 0.17	0.22 0.22	Gin trash	1.1 1.6	32 32	AA960603, AA960603 CA1 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Maxxa)	EC, 5	2	0.2 0.17	0.21 0.09	Gin trash	1.1 1.6	32 32	AA960603, AA960603 CA1 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, King (CA) 1996 (Maxxa)	WP, 50	2	0.18 0.17	0,091 0,087	Gin trash	0.43 0.26	35 35	AA960603, AA960603 CA2 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, King (CA) 1996 (Maxxa)	EC, 5	2	0.20 0.18	0.1 0.09	Gin trash	0.88 2.3	35 35	AA960603, AA960603 CA2 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Tulare (CA) 1996 (Acala Maxxa)	WP, 50	2	0.18 0.18	0.091 0.09	Gin trash	0.75 0.68	28 28	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023
USA, Tulare (CA) 1996 (Acala Maxxa)	EC, 5	2	0.21 0.18	0.11 0.09	Gin trash	1.5 1.1	28 28	AA960603, AA960603 CA3 Carringer, 1997, Hexyt_022 amended by Willard, 1998, Hexyt_023

Table 63 Hexythiazox residues in maize forage following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Cunningham (KS) 2003 (Pioneer)	EC, 12	1	0.21	0.11	Forage	0.13 0.05	44 44	TCI-03-078, TCI-03-078-01 Carringer, 2005, Hexyt_037
USA, Levelland (TX) 2003 (F3175)	EC, 12	1	0.21	0.11	Forage	0.79 0.82 0.7 1.4 1.1 0.59 0.54 1.7	39 39 46 46 53 53 60 60	TCI-03-078, TCI-03-078-02 Carringer, 2005, Hexyt_037
USA, Levelland (TX) 2004 (Pioneer)	EC, 12	1	0.22	0.11	Forage	0.88 0.52 0.91 0.26	30 30 44 44	TCI-03-078, TCI-03-078-03 Carringer, 2005, Hexyt_037
USA, Hinton (OK) 2008 (DKC51-45 RR2)	EC, 12	1	0.21	0.11	Forage	0.99, 1.1 (1.1)	49	TCI-08-228, TCI-08-228-01 Wyatt, 2009, Hexyt_054
USA, York (NE) 2008 (A1005005)	EC, 12	1	0.21	0.11	Forage	0.65, 0.51 (0.58)	42	TCI-08-228, TCI-08-228-02 Wyatt, 2009, Hexyt_054

Table 64 Hexythiazox residues in maize stover following foliar application

Location, Year (variety)	Form, % ai	Application data			Residues data			Reference (Report ,Trial No., Author)
		No.	kg ai/ha	kg ai/hL	Sample	Residues [mg/kg]	PHI [days]	
USA, Cunningham (KS) 2003 (Pioneer)	EC, 12	1	0.21	0.11	Stover	0.25 0.24	96 96	TCI-03-078, TCI-03-078-01 Carringer, 2005, Hexyt_037
USA, Levelland (TX) 2003 (F3175)	EC, 12	1	0.21	0.11	Stover	0.63 0.83 0.44 0.58 0.68 0.77 0.44 0.83	89 89 96 96 103 103 110 110	TCI-03-078, TCI-03-078-02 Carringer, 2005, Hexyt_037
USA, Levelland (TX) 2004 (Pioneer)	EC, 12	1	0.22	0.11	Stover	0.07 0.13	110 110	TCI-03-078, TCI-03-078-03 Carringer, 2005, Hexyt_037
USA, Hinton (OK) 2008 (DKC51-45 RR2)	EC, 12	1	0.21	0.11	Stover	1.2, 1.4 (1.3)	79	TCI-08-228, TCI-08-228-01 Wyatt, 2009, Hexyt_054
USA, York (NE) 2008 (A1005005)	EC, 12	1	0.21	0.11	Stover	0.7, 0.48 (0.59)	105	TCI-08-228, TCI-08-228-02 Wyatt, 2009, Hexyt_054

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

The Meeting received information on the fate of hexythiazox residues during processing of oranges, plums and cotton. Information on the behaviour during hydrolysis was available from the physical-chemical properties part conducted in sterile buffer solutions at 50 °C or 70 °C. It was shown, that hexythiazox is stable under these conditions at a pH of 7 or less. At a pH of 9 DT_{50} values of 78h at 50 °C and 4.6h at 70 °C were estimated.

In addition a study on the hydrolysis under simulated processing conditions was described in the section of the physical-chemical properties. It was shown that hexythiazox was stable under condition of pasteurisation (90 °C, pH4, 20min) and cooking (100 °C, pH5, 60min), but half of the initial concentration was transformed into PT-1-3 after sterilisation (120 °C, pH6, 20min).

Processing factors have been calculated for hexythiazox residues and are presented in Table 65.

In a field trial conducted by Carringer (2006, Hexyt_031) on oranges the trees were treated once with an application rate of 1.05 kg ai/ha (0.056 kg ai/hl). Samples of oranges were collected 28 days after the treatment and processed into orange juice, dried pulp and citrus oil. In a first step the

fruits were washed and the peel was removed for the oil recovery. This step was performed by an abrasion peeler breaking the oil sacs. A mist of cold water was sprayed into the peeler to trap the volatile citrus oil. The oil emulsion was treated with pectinase, separated from the solids, centrifuged and the crude citrus oil finally dried over anhydrous sodium sulfate. For the orange juice the fruits were passed through a juice extractor. The juice obtained from the procedure was pasteurised and stored in sealed jars. The dry pulp contained all remainings and was dried at 59–76 °C for 8–14h, until a dry matter content of about 90% was reached.

In an additional studies involving three field trials by Perny (2003, Hexyt_050) oranges were treated twice with application rates of 0.8 kg ai/ha each. Samples of orange fruits were collected 14 days after the last treatment and processed into canned fruits, marmalade, juice, dry pomace and wet pomace. In the first step the fruits were peeled. For canning syrup was added and the fruits were pasteurised at 95 °C for 3 minutes. Marmalade was made of peeled oranges cooked for 40 minutes. After the adding of sugar the jars were sterilised at 120 °C for 10 minutes. For orange juice half fruits were pressed and the juice obtained was pasteurised at 95°C for 1min. The leftovers (dry and wet pulp) not treated any further except drying.

The corresponding residue trial data is presented in Table 36. The resulting processing factors are presented in Table 65.

For grapes the processing was investigated by Perny (2003, Hexyt_053) in four supervised field trials conducted in Europe 2002. The vines were treated with two application of approx. 0.8 kg ai/ha each. Samples were collected after 19–21 days and processed into red wine (two trails), white wine (two trials), pomace, juice and raisins. Winemaking was conducted according to the normal procedures. For red juice the grapes were crushed to obtain the must, which was heated at 70 °C for 20 minutes for colour extraction. After separation of the pomace the clear juice was sulphured and pasteurised at 75 °C for 20min. White juice was received by pressing the grapes and pasteurising the juice obtained at 75 °C for 20min. Raisins were produced by first dipping the grape berries in an alkaline solution of potassium carbonate and ethyl oleate. Subsequently the berries were dried on trays at 40 °C until the remaining humidity was 16%.

The corresponding residue trial data is presented in Table 46. The resulting processing factors are presented in Table 65.

The processing of plums into prunes was investigated in one field trial by Carringer (1997, Hexyt_018). The plum trees were treated once with an application rate of 0.42 kg ai/ha (0.045 kg ai/hL). Fruits were sampled 7 days after the application. The fruits were dried without washing in a dehydrator at 75–86 °C for 19h. The corresponding residue trial data is presented in Table 44. The resulting processing factors are presented in Table 65.

For cottonseed two supervised field trials were conducted by Carringer (1997, Hexyt_022). The cotton plants were treated once at exaggerated rates in comparison to the labels of 1.05 kg ai/ha. Samples of the seeds were picked 14 days after the application. The seeds were mechanically delinted and hulled, producing kernels and hulls. The kernel material was dried in a oven at 54–71 °C. Subsequently the kernels were heated at 77–87 °C and extruded to gain the collets for crude oil extraction. The extraction was achieved by using hot hexane three times. After the refining of the crude oil the hexane was removed in a vacuum evaporator. The corresponding residue trial data is presented in Table 57. The resulting processing factors are presented in Table 65.

Table 65 Summary of processing factors for hexythiazox in plant commodities

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Median or best estimate
Oranges	Juice	< 0.05, < 0.07, 0.22, 0.26, 0.3	0.22
	Marmalade	0.11, 0.14, 0.27	0.14
	Canned fruits	0.07, 0.07, < 0.11	0.07
	Pulp, dry	1.8, 2.7	2.3

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Median or best estimate
	Citrus oil	72, 210	141
	Wet pomace	0.61	0.61
	Dry pomace	2.9	2.9
Grapes	Wine, red	< 0.02, < 0.1	< 0.06
	Wine, white	< 0.02, < 0.09	< 0.06
	Juice, red	0.08, 0.75	0.42
	Juice, white	< 0.02, 0.14	0.08
	Raisins	0.52, 1.4, 1.7, 3.3	1.6
	Must, red	0.39	0.39
	Must, white	0.12	0.12
	Wet pomace	3.4, 16.6	10
	Dry pomace	9.8, 23.2	16.5
Plums	Prunes	4.8, 5	4.9
Cotton	Hulls	0.15, 0.22	0.19
	Meal	< 0.01, 0.01	0.01
	Refined oil	0.11, 0.15	0.13

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

For residues in farm animals studies on lactating cows and laying hens were submitted.

Cattle feeding studies

In the first study two lactating cows were doses over a period of 14 consecutive days with hexythiazox at rates of 12 mg or 120 mg per animal and day (Kido, 1985, Hexyt_046). Milk was collected over the whole study period. After the dosage period the animals were kept 8 days for withdrawal before being sacrificed. Samples of fat, muscle, kidney and liver were taken for analysis.

All samples were first extracted using acetone, followed by partitioning with dichloromethane, hexane and acetonitrile. After evaporation of the solvent the residue was hydroxylated in methanol and 0.01N NaOH for 20min. After a final cleanup (again partitioning with dichloromethane, hexane and acetonitrile) residues were analysed and determined by HPLC-UV (235 nm) against reference standards. This method measured the sum of hexythiazox and its metabolites, determined as PT-1-3.

In none of the samples residues above the limit of quantification of 0.05 mg/kg were found.

In a second study by Prince (1985, Hexyt_047) twelve lactating Holstein cows were divided into 4 groups receiving doses of 0, 5, 15 or 50 ppm hexythiazox for a period of 28 consecutive days. One animal from each dose group was kept for an additional withdrawal period of 7 days. Throughout the study period samples of milk were collected. After the withdrawal period the animals were sacrificed and samples of fat, liver, kidney and muscle were taken.

All samples were extracted using acetone, followed by partitioning with methylene chloride. The aqueous layer was discarded and the methylene chloride layer washed with 0.1N NaOH. After

evaporation of the solvent the residue was hydroxylated in iso-propanol and 0.01N NaOH. The final cleanup was achieved by partitioning with hexane and methanol, followed by a solid phase column with alumina. HPLC-UV (225 nm) was used for the determination of the residues. This method measured the sum of hexythiazox and its metabolites, determined as PT-1-3.

In the groups receiving doses of 0, 5 or 15 ppm per day, no residues above the LOQ of 0.01 mg/kg were found in any sample expect liver. For the dose group 50 ppm residues in milk were slightly above the LOQ. The separation into skim milk and cream revealed most of the residue in the fat fraction. No residues above the LOQ were found in skim milk, while in cream levels ranging from < 0.01 to 0.1 mg/kg were found. Highest residues were found in the liver, going up to 0.186 mg/kg in the 50 ppm dose group. A summary of the data obtained from the dose groups 5, 15 and 50 ppm are presented in Table 66 and Table 67.

Table 66 Residues in the milk of lactating cows dosed with hexythiazox for 28 consecutive days (total residue determined as PT-1-3)

Days	Group 5 ppm	Group 15 ppm	Group 50 ppm
	mg/kg per animal (group mean)	mg/kg per animal (group mean)	mg/kg per animal (group mean)
1	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)
14	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	0.02, 0.03, 0.02 (0.02)
21	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	0.01, 0.02, < 0.01 (0.01)
28	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	0.01, 0.01, 0.01 (0.01)

Table 67 Residues in the tissues of lactating cows dosed with hexythiazox for 28 consecutive days (total residue determined as PT-1-3)

Tissue	Group 5 ppm	Group 15 ppm	Group 50 ppm
	mg/kg per animal (group mean)	mg/kg per animal (group mean)	mg/kg per animal (group mean)
Liver	< 0.01, < 0.01, < 0.01 (< 0.01)	0.08, 0.09, < 0.01 (0.06)	0.186, 0.141, 0.03 (0.119)
Kidney	< 0.01, 0.02, < 0.01 (0.01)	0.02, < 0.01, < 0.01 (0.01)	0.022, 0.025, < 0.01 (0.019)
Renal fat	< 0.01, < 0.01, < 0.01 (< 0.01)	0.01, < 0.01, < 0.01 (0.01)	0.03, 0.022, < 0.01 (0.021)
Omental fat	< 0.01, < 0.01, < 0.01 (< 0.01)	0.01, < 0.01, < 0.01 (0.01)	0.03, 0.025, < 0.01 (0.022)
Subcutaneous fat	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)
Muscle	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)

Laying hens

For laying hens a livestock feeding study was conducted by Hughes (1985, Hexyt_048). The animals were separated into 4 groups receiving doses of 0, 5, 15 or 50 ppm hexythiazox for 28 consecutive days. Each group consisted of 4 subgroups with 5 animals each. From each dose group one subgroup was kept 7 additional days for withdrawal. For the duration of the study eggs were collected. At the end of the dose period the animals were sacrificed and samples of fat, muscle, liver and kidney were taken.

All samples were extracted using acetone, followed by partitioning with methylene chloride. The aqueous layer was discarded and the methylene chloride layer washed with 0.1N NaOH. After evaporation of the solvent the residue was hydroxylated in iso-propanol and 0.01N NaOH. The final cleanup was achieved by partitioning with hexane and methanol, followed by a solid phase column with alumina. HPLC-UV (235 nm) was used for the determination of the residues. This method measured the sum of hexythiazox and its metabolites, determined as PT-1-3.

In eggs residues were found in all dose groups ranging from < 0.01 to 0.058 mg/kg for the 5 ppm group up to 0.03 to 0.36 mg/kg for the 50 ppm group. A separate analysis of egg white and egg yolk on day 20 reveals higher residues in the yolk by a factor of 1.7 to 2.5. In muscle no residues above the LOQ of 0.01 mg/kg could be detected. Highest residues in the tissues were found in liver and fat. A summary of the results is presented in Table 68 to Table 70.

Table 68 Residues in the eggs of laying hens dosed with hexythiazox for 28 consecutive days (total residue determined as PT-1-3)

Days	Group 5 ppm	Group 15 ppm	Group 50 ppm
	mg/kg per subgroup (group mean)	mg/kg per subgroup (group mean)	mg/kg per subgroup (group mean)
1	0.02, 0.02, 0.01 (0.02)	0.02, 0.02, 0.06, 0.06 (0.04)	0.22, 0.16, 0.11, 0.03 (0.13)
2	0.02, < 0.01, 0.02, 0.02 (0.02)	0.06, 0.09, 0.05, 0.05 (0.06)	0.15, 0.15, 0.15, 0.06 (0.13)
4	0.02, 0.02, 0.02, 0.01 (0.02)	0.07, 0.08, 0.12, 0.05 (0.08)	0.19, 0.15, 0.17, 0.17 (0.17)
7	0.04, 0.04, 0.06, 0.06 (0.05)	0.11, 0.08, 0.08, 0.05 (0.08)	0.22, 0.2, 0.29, 0.29 (0.25)
14	0.03, 0.04, 0.04, 0.05 (0.04)	0.13, 0.16, 0.13, 0.09 (0.13)	0.31, 0.32, 0.27, 0.29 (0.3)
21	0.02, 0.03, 0.03, 0.03 (0.03)	0.09, 0.13, 0.11, 0.09 (0.11)	0.29, 0.24, 0.22, 0.19 (0.24)
28	0.02, 0.03, 0.02, 0.03 (0.03)	0.09, 0.11, 0.15, 0.09 (0.11)	0.3, 0.36, 0.16, 0.28 (0.28)

Table 69 Residues in the egg white and egg yolk of laying hens dosed with hexythiazox for 28 consecutive days (total residue determined as PT-1-3)

Dose group	Egg white	Egg yolk
	mg/kg per subgroup (group mean)	mg/kg per subgroup (group mean)
5 ppm	0.03	0.05
15 ppm	0.11	0.19
50 ppm	0.17	0.42

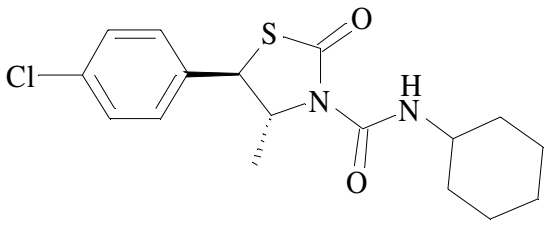
Table 70 Residues in the tissues of laying hens dosed with hexythiazox for 28 consecutive days (total residue determined as PT-1-3)

Tissue	Group 5 ppm	Group 15 ppm	Group 50 ppm
	mg/kg per subgroup (group mean)	mg/kg per subgroup (group mean)	mg/kg per subgroup (group mean)
Fat	0.05, 0.05, 0.05 (0.05)	0.08, 0.06, 0.08 (0.07)	0.16, 0.17, 0.15 (0.16)
Liver	0.02, 0.03, 0.02 (0.02)	0.07, 0.05, 0.03 (0.05)	0.1, 0.12, 0.1 (0.11)
Muscle	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)	< 0.01, < 0.01, < 0.01 (< 0.01)
Kidney	< 0.01, < 0.01, < 0.01 (< 0.01)	0.02, 0.01, 0.01 (0.01)	0.02, 0.04, 0.02 (0.03)

APPRAISAL

Hexythiazox is a non-systemic insecticide and miticide first evaluated by the 1991 JMPR and a number of times subsequently. It was recently reviewed for toxicology by the 2008 JMPR within the periodic review program of the CCPR. An ADI of 0–0.03 mg/kg bw was established. An ARfD was not considered necessary by the Meeting. In the 2009 JMPR hexythiazox is scheduled for periodic review for the residue section.

The 40th Session of the CCPR scheduled this compound for periodic evaluation by the 2009 JMPR (ALINORM 08/40/24, Appendix X). Information on GAPs was also provided by the Netherlands.



The following abbreviations are used for the metabolites discussed below:

hexythiazox	trans-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidine-carboxamide
PT-1-2	tran-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-3-carboxamide
PT-1-3	trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine
PT-1-4	trans-5-(4-chlorophenyl)-N-(cis/trans-3-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide
PT-1-8	rans-5-(4-chlorophenyl)-N-(cis/trans-4-hydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide
PT-1-10	trans-5-(4-chlorophenyl)-N-(3,4-dihydroxycyclohexyl)-4-methyl-2-oxothiazolidine-3-carboxamide

Animal metabolism

The Meeting received animal metabolism studies with ^{14}C-hexythiazox in rats, lactating goats and laying hens. Parent substance labelled in the 5-position of the thiazolidine ring was used in all of these studies. In general the metabolism of hexythiazox in animals is relatively limited. In all species the hydroxylation of the cyclohexane ring was the dominating biotransformation, resulting in the metabolites PT-1-4, PT-1-8 and PT-1-10. The cleavage of the amide bond was observed in rats only.

In the 2008 Evaluation for toxicology it was reported that in rats most of the administered radioactivity (60–90%) was excreted via the faeces. Depending on the dose level 10–20% (at 10 mg/kg bw dose) up to 65–70% (880 mg/kg bw dose) of the radioactivity was identified as unchanged parent substance. The highest concentrations of tissue residues were found in fat, adrenals, liver and ovaries; the main component in fat was hexythiazox. Metabolism of the absorbed dose was extensive, but most of the radioactive material was not attributed to specific metabolites. The main metabolic reactions identified were hydroxylation of the cyclohexane ring and cleavage of the amide bond to the cyclohexane ring. The main identified metabolite was PT-1-8 (cis) representing approximately 10% of the administered radioactivity.

For lactating goats one animal was dosed with 46 mg per day (approx. 26 ppm or 1.16 mg/kg bw) for seven consecutive days. Most of the excretion of radioactivity was observed via faeces (56.2%) and urine (18.1%). In milk 0.3% of the administered dose (corresponding to approximately 0.1 mg/kg) was found. For the tissues liver was found with the highest TRR levels of 2.2 mg/kg. Kidney and fat contained 0.44 and 0.55 mg/kg, respectively. In muscle the lowest TRR levels of 0.11 mg/kg at maximum were measured. Identification of the radioactivity revealed unchanged parent hexythiazox as dominant residue in fat tissue and milk (61% TRR and 31% TRR, respectively). In liver, muscle and kidney hexythiazox was found at levels of 10% of the TRR or less. Most of the TRR was identified as PT-1-4 (cis) or PT-1-10 at levels up to 23% TRR and 36% TRR, respectively.

The metabolism of hexythiazox in laying hens was investigated using doses of 0.6 or 6 mg per animal per day for 6 consecutive days. In this case the highest residues were found in the eggs of the animals at levels of 0.5 mg/kg for the low dose group and 2.1 mg/kg for the high dosed animals. The highest residues in all tissues were detected in the liver, ranging from 0.14 mg/kg (low dose) up to 1.6 mg/kg (high dose). Kidney and fat tissues were in the same range of 0.06–0.07 mg/kg for the low dose group and 0.5 mg/kg for the high dose group. In muscle very low residues of 0.01 to 0.08 mg/kg were found. Identification of the radioactivity was conducted for eggs, liver and fat only. Eggs and liver gave very high unextracted residues in the range of 50% of the TRR. In the extracts the results were comparable to rats and lactating goats. In fat tissue most of the residue consisted of unchanged hexythiazox (48% of the TRR while in eggs and liver mainly hydroxylated metabolites (PT-1-8 and PT-1-10) were identified.

Plant metabolism

The Meeting received plant metabolism studies with [^{14}C]hexythiazox in apples, citrus, grapes, pears and tea. Parent substance labelled in the 5-position of the thiazolidine ring was used in all of these studies.

In general the biotransformation of hexythiazox is relatively slow. In most of the studies unchanged hexythiazox was the dominating residue found mainly on the surface. Following a period of three week a minor translocation into the plants of PT-1-2 and PT-1-3, the remaining cleavage products after removal of the cyclohexane ring, can be observed whereas parent hexythiazox remained nearly immobile.

In the study on apples, leaves and fruits were treated by micro pipette at a rate equivalent to a concentration of 5 g ai/hL. Leaf samples were taken 0, 10, 21, 30, 60 and 91 days after the application and single fruit samples 10, 20, 30 and 59 days after the application. In the surface wash as well as in the extracts of the samples unchanged parent compound was the dominant residue accounting for 73.7–94.9% of the TRR. The leaf extracts contained additional metabolites at rates of 0.4–0.7% of TRR for PT-1-2, 0.5–2.5% TRR for cis-PT-1-8 (including conjugates) and 1.8–6.8% TRR for trans-PT-1-8 (including conjugates). In apple fruits traces of PT-1-2 and PT-1-8 (trans) were found in levels of less than 1.2% of the TRR.

For citrus fruits a similar methodology as for apples was used. The application rate was at a comparable concentration of 5.3 g ai/hL. Samples of treated and untreated citrus leaves and fruits were taken 7, 14, 30, 60 or 62 and 90 or 91 days after the application. In the surface wash and the peel extract the concentration of hexythiazox decreased from 98.1% down to 30.5% of the applied dose after 91 days. The only metabolite identified in the surface wash was PT-1-2 (up to 1.0% TRR), which was also found in the peel extract at higher amounts (up to 3.3% TRR). In the peel extract free and conjugated PT-1-4 (trans-2), PT-1-6 (trans-2), PT-1-8 (cis) and PT-1-8 (trans) were found. The conjugated form was always present in at least 2-fold higher amounts. In total PT-1-4 (trans-2), PT-1-6 (trans-2), PT-1-8 (cis) and PT-1-8 (trans) including conjugates were found in concentrations of up to 7.0%, 4.3% and 13.7% of the TRR, respectively.

Grapes were treated twice with an amount of 0.1 kg ai/ha of labelled hexythiazox each. Sampling of the leaves and fruits was conducted 21 days after the final application, but only the fruits were analysed for radioactive residues. In the fruits TRR of 0.233 mg/kg could be found. 62.9% of the TRR was located in the surface of the fruits and was released with the surface wash. Nearly all of the radioactivity coeluated with the parent reference compound. The fruit extract contained about 31.4% of the TRR in total. Hexythiazox was detected in all phases (5.0–6.3% TRR), but unidentified peaks were present in higher concentrations (up to 12.1% of the TRR). In the remainings, hydrolysed using NaOH 11.2%, the TRR were identified as PT-1-3. In this study no confirmation of the identity of metabolites via mass spectrometric methods was conducted.

In pears the leaves and fruits of the trees were also treated by micro pipette at a rate equivalent to a concentration of 5 g ai/hL. Leaf samples were taken 0, 5, 10, 20, 30, 60 and 90 days after the application and fruit samples 0, 5, 10, 20, 30 and 60 days after the application. In the surface

wash as well as in the peel extract of the fruits hexythiazox was identified as the dominant residue amounting 64.6–95.0% of the TRR. The metabolites PT-1-2, PT-1-4 (trans-2) and the cis and trans isomers of PT-1-8 were identified in the fruits, but none at levels of more than 2.3% of the TRR.

In the leaves a comparable distribution of the radioactive residues was observed. Unchanged hexythiazox was dominant in the surface extract (93.1–44.6% of the TRR). In leaf tissue higher amounts of metabolites were found in comparison to the fruits. The metabolite PT-1-2 was found at low levels of 1.2% of the TRR. Most of the radioactivity found was identified as PT-1-8 (cis) and PT-1-8 (trans) in their conjugated forms at amounts of up to 4.3% and 9.2% of the TRR, respectively.

For tea the plants were treated once at a rate of 0.2 kg ai/ha. Leaf specimens were collected at 0, 7, 14 and 21 days after the treatment. The TRR in the tea leaves did not change with increasing PHI. In all of the samples TRR levels of 8.17 to 9.03 mg/kg, calculated as parent equivalents, were found. In comparison to the 0 day PHI results, more of the radioactivity was found in the extracts rather than the surface wash in the later samples (93.2% surface wash at PHI 0 down to 55.3% at PHI 21). The identification of the radioactivity revealed very limited degradation of the parent substance. In all samples hexythiazox was the dominant residue found at levels of at least 84.5% of the TRR. The only metabolites identified were PT-1-2 and PT-1-8 (trans), each at levels of less than 0.3% of the TRR.

Environmental fate in soil

Hexythiazox is degraded in soil quite rapidly with half-life rates of about one month. The main metabolites found in soil consisted of cleavage products of the parent molecule (PT-1-3 and PT-1-2). Under consideration of a rotational crop study using unlabelled material a significant uptake by follow crops is not expected.

For the environmental fate of hexythiazox in soil one study on the aerobic metabolism is available. Estimated aerobic soil metabolism half-lives for hexythiazox at 20 °C ranged from 32.1 to 35.2 days. After 153 days mineralisation and unextracted residues were in the range of 10–12.2% and 19.7–23% of the radioactivity, respectively.

The metabolite PT-1-9 was formed in the early stage of the study, reaching its maximum concentration of 10.1–14.4% of the applied radioactivity after 31 days. PT-1-2 and PT-1-3 were found in the later samples reaching a plateau after 90 days at individual amounts of 34.2–39.5% and 7.5–9.2% of the applied dose.

In addition to soil metabolism a field rotational crop study was submitted to the Meeting. Bare soil was treated at rates of 0.21 kg ai/ha and incorporated into the soil before planting. After 30, 120 and 240 days lettuce, mustard, radish, sorghum and wheat were planted as follow crops. Except for one sample each of radish tops (0.046 mg/kg) and sorghum stover (0.014 mg/kg) no hexythiazox residues above the LOQ of 0.01 mg/kg were found (sum of hexythiazox and all metabolites hydrolysable to PT-1-3, expressed as hexythiazox).

No confined study on rotational crops was submitted to the Meeting. Given that cleavage of the molecule is the only significant transformation step observed in soil metabolism studies and the results of the analysis of all residues hydrolysable to PT-1-3 in the unlabelled study, the Meeting considered the residue situation in rotational crops to have been investigated sufficiently.

Methods of residue analysis

The Meeting received information on analytical methods for the determination of hexythiazox in plant and animal matrices.

In the methods hexythiazox is extracted with methanol and the partitioned into n-hexane. After partition between n-hexane and acetonitrile, the acetonitrile layer is concentrated to dryness. The residue is cleaned-up by Florisil PR Column chromatography and a C18 solid phase extraction column. Hexythiazox is determined by HPLC-UV at 225 nm. The LOQ was 0.05 mg/kg for all plant matrices. Analytical recovery data were satisfactory for hexythiazox in plant commodities. Residue

methods were tested by independent laboratories unfamiliar with the analysis and were found to have satisfactory recoveries and no background interferences.

In supervised field trials an additional method was described measuring the total residue of hexythiazox including metabolites after hydrolysis with 0.1N NaOH into PT-1-3. The separation and detection of PT-1-3 is achieved via HPLC-UV. This method is applicable to plant and animal matrices, but no studies including validation data for animal material were submitted. In the corresponding field trials LOQs of 0.02 mg/kg were achieved.

For animal matrices the samples are extracted with methanol (muscle, kidney, liver and eggs) or acetone (milk and fat). The extract was then liquid/liquid partitioned, evaporated to dryness and hydrolysed with sodium hydroxide solution. After further cleaned up on a silica gel column PT-1-3 was determined by reversed phase HPLC and UV detection at 225 nm. The LOQ achieved in the validations was 0.05 mg/kg for all matrices.

Although no data on analytical multi-residue method for plant commodities were submitted to Meeting it is noted that hexythiazox parent substance is validated within the QuEChERS-Multimethod.

Stability of residues in stored analytical samples

Information was received on the freezer storage stability of hexythiazox residues in plant commodities.

The storage stability of hexythiazox was investigated in one study including homogenated samples with a fortification level of 0.5 or 1.0 mg/kg (strawberry, cucumber, water melon, grape, green pepper, mandarin orange pulp and whole fruits, pears and apples) as well as treated field samples, which were chopped instead of macerated (cucumber, strawberry, tea, Chinese citron peel and pulp and mandarin orange peel and pulp). All samples were stored at –30 °C for a period of one month up to 13 months, analysed for hexythiazox and compared to the nominal level of fortification. Expect for homogenised grapes (63% recovery) all samples were stable and gave recoveries of at least 70% of the initial dose.

For the storage stability of hexythiazox in animal commodities no data on the storage stability was submitted to the Meeting. Under consideration of a residue definition for hexythiazox involving all metabolites containing the PT-1-3-moiety, it was concluded by the Meeting that theoretical breakdown products of hexythiazox are also measured by the analytical method. In view of this estimation of the "total residue" further data on the storage stability of hexythiazox residues is not considered necessary.

Definition of the residue

The residue following use of hexythiazox on crops is predominantly unchanged hexythiazox. After 30 days at least 70% of the radioactivity was identified as parent substance mainly located on the plant surface. At higher PHI of 60 to 90 days 30% to 60% of the radioactivity was still present as hexythiazox. Metabolites identified were mainly hydroxylated at the cyclohexane ring (PT-1-4, PT-1-8 and PT-1-10), followed by cleavage and removal of the cyclohexane-ring forming PT-1-2 in amounts of less than 4% of the TRR after up to 90 days. The combined quantities of PT-1-4, PT-1-8 and PT-1-10 were at levels of less than 10% of the hexythiazox levels in all samples analysed. In summary at all sampling dates most of the residue was identified as unchanged hexythiazox parent located on the surface.

The hydroxyl-metabolites (PT-1-4 and PT-1-8) are not mutagenic in bacteria and are of low acute toxicity (oral LD_{50} > 5000 mg/kg bw). These metabolites, together with PT-1-10 are formed in rats. Although there are no repeat dose toxicity studies on these compounds, it is considered realistic to assume them to have similar toxicity to hexythiazox.

In soil, degradation of hexythiazox is dominated by a cleavage resulting mainly in PT-1-2. The uptake from the soil observed in field rotation studies is very limited, showing most residues

below 0.01 mg/kg (measured as PT-1-3 after hydrolytic extraction). Only in radish tops (0.046 mg/kg) and sorghum stover (0.012 mg/kg) total hexythiazox residues, determined as PT-1-3 for analysis, were found above the LOQ of 0.01 mg/kg after 30 days.

Metabolite PT-1-3 is of greater acute toxicity than hexythiazox, while it is not mutagenic in bacteria there are no data on its toxicity after repeat dosing.

Following normal solvent extraction no PT-1-3 was identified in metabolism studies.

The Meeting was aware that according to the hydrolysis study, using aqueous buffer solutions parent hexythiazox in sterilised food commodities might be subject to a transformation into PT-1-3 to a certain extent. Quantitative data representing realistic processing conditions are not available, since all information is based on residues converted to PT-1-3 for analysis. In general the Meeting expects the contribution to dietary intake to be small in comparison to the overall intake.

The Meeting concluded parent hexythiazox is a representative marker for hexythiazox residues in all plant commodities and decided to set the residue definition for enforcement purposes in plant commodities to be parent hexythiazox only.

For dietary intake assessment the toxicological significant metabolites PT-1-4, PT-1-8 and PT-1-10, also identified in the rat, amounted in sum less than 10% of the TRR according to the results of metabolism studies using radiolabelled material. No data on the ratio between hexythiazox and all residues converted to PT-1-3 under field conditions were submitted. The plant specific metabolite PT-1-3 was not identified in any sample in plant metabolism studies and the Meeting considered it to be an analytical artefact. Although the low share of PT-1-4, PT-1-8 and PT-1-10 would not suggest an inclusion into the residue definition for risk assessment purposes of plant commodities normally, the Meeting acknowledged that no data besides metabolism studies are available to confirm this assumption. Taking into account a possible deviations in the rate of metabolisation under field conditions, the Meeting agreed to define the residue definition for intake purposes as "sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox" to cover all of the residue of toxicological concern.

In animals hexythiazox is also hydroxylated at various positions of the cyclohexane ring. A cleavage into PT-1-3 was not observed. In fatty tissues, milk and eggs hexythiazox was the dominant residue. Watery matrices like liver, kidney and muscle mainly contained a mixture of hydroxylated metabolites. Residues found in fatty tissues of goats and laying hens were by a factor of 5 to 8 times higher in comparison to muscle. For milk (skim milk ↔ cream) and eggs (egg white ↔ egg yolk) higher residues of total PT-1-3 were found in the fat, based on the livestock feeding studies submitted. Due to overall low residues a ratio could not be estimated.

For animal matrices the metabolism results in a higher percentage of hydrolysed metabolites with hexythiazox being found at very low levels or even below the LOQ. In addition, no analytical methods for the parent substance alone are available, as well as livestock feeding studies analysed for single substances instead of the total residues determined as PT-1-3. In view of these factors the Meeting concluded that the residue definition (for risk assessment and enforcement) for hexythiazox in animal matrices is sum of hexythiazox including all metabolites hydrolysable to PT-1-3, expressed as hexythiazox. The residue is considered as fat soluble.

Definition of the residue (for compliance with MRLs) for plant commodities: *hexythiazox*

Definition of the residue (for estimation of dietary intake) for plant commodities: sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox

Definition of the residue (for compliance with MRLs and for estimation of dietary intake) for animal commodities: sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox

The residue is fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised residue trials data for hexythiazox on citrus (grapefruit, lemons, mandarins and oranges), almonds, pecan, apples, pears, stone fruit (cherries, nectarines, peaches and plums), blackberries, grapes, raspberries, strawberries, dates, tomatoes, cucumbers, melons, sweet corn, fresh beans, succulent beans, dry beans, cotton, hops and corn.

In trials where duplicate field samples from replicated or unreplicated plots were taken at each sampling time and analysed separately, the sample with higher residues was taken as the best estimate of the residue from the plot. Supervised field trials conducted with different formulations at identical varieties, locations and dates were not considered as independent. The highest result according to the corresponding GAP was selected in these cases.

Labels (or translation of labels) were available from the Netherlands and USA describing the registered uses of hexythiazox.

The NAFTA calculator was used as a tool in the estimation of the maximum residue level from the selected residue data set obtained from trials conducted according to GAP. As a first step, the Meeting reviewed all relevant factors related to each data set in arriving at a best estimate of the maximum residue level using expert judgement. Then, the NAFTA calculator was employed. If the statistical calculation spreadsheet suggested a different value from that recommended by the JMPR, a brief explanation of the deviation was supplied. Some common factors that may lead to rejection of the statistical estimate include when the number of data points in a data set is < 15 or when there are a large number of values < LOQ.

Citrus fruits

Hexythiazox is registered in the USA for use on citrus fruits at a rate of 1 × 0.2 kg ai/ha with a PHI of 28 days. Supervised residue trials conducted in the US on grapefruits, lemons and oranges according to this GAP were submitted.

For whole grapefruits residues were (n = 6): < 0.05, < 0.05, 0.05, 0.06, 0.16 and 0.18 mg/kg. The distribution between pulp and whole fruits was not measured.

In whole lemons fruits residues were (n = 5): 0.06, 0.1, 0.15, 0.2 and 0.29 mg/kg. The distribution between pulp and whole fruits was not measured.

For whole oranges residues were (n = 6): < 0.05, 0.06, 0.11, 0.11, 0.12 and 0.2 mg/kg. The distribution between pulp and whole fruits was not measured.

For mandarins and oranges additional field trials conducted in Southern Europe were submitted, but no corresponding GAP is available. Since these trials contained analytical results for whole fruits and pulp, the data from day 14 is used to estimate the residue ratio between both matrices. Individual ratios were (n = 5) < 0.56, < 0.63, < 0.71, < 0.83 and < 0.83. Additional trials are available, but no residues above the LOQ were found in whole fruits as well as in citrus pulp. The Meeting estimated a factor of 0.7 for the ratio of residues between whole citrus fruits and citrus pulp.

The Kruskal-Wallis-Test for grapefruits, lemons and oranges (residues below the LOQ were treated as residues at the LOQ) indicated that the residue populations were not significantly different and may be combined.

The Meeting decided to combine the US data for grapefruits, lemons and oranges for the whole group of citrus fruits, resulting in residues of < 0.05(3), 0.05, 0.06(3), 0.1, 0.11, 0.11, 0.12, 0.15, 0.16, 0.18, 0.2, 0.2 and 0.29 mg/kg for the whole fruits (n = 17). Under consideration of the ratio of 0.7 between the residues in whole fruits and citrus pulp an STMR value of 0.077 mg/kg was estimated by the Meeting.

The Meeting confirmed the previous recommendation on a maximum residue level for hexythiazox in citrus fruits of 0.5 mg/kg (whole fruit) and estimated an STMR value for hexythiazox in citrus fruit of 0.077 mg/kg (pulp).

The value derived from use of the NAFTA calculator of 0.45 mg/kg (95/99 95th percentile) was in good agreement with the estimate of 0.5 mg/kg made by the Meeting (after rounding up to one significant figure).

Pome fruit

For pome fruit hexythiazox is registered in the USA at rates of 1 × 0.2 kg ai/ha with a PHI of 28 days. Supervised residue trials conducted in the US on apples and pears according to this GAP were submitted.

For apples residues were (n = 15): 0.05, 0.05, 0.08, 0.08, 0.09(3), 0.11, 0.11, 0.12, 0.15, 0.16, 0.2, 0.21 and 0.21 mg/kg.

In pears residues were (n = 6): 0.06, 0.06, 0.1, 0.11 and 0.16 mg/kg.

Based on the results for apples the Meeting estimated a maximum residue level and an STMR value for hexythiazox in pome fruits of 0.4 and 0.11 mg/kg, respectively.

The value derived from use of the NAFTA calculator of 0.35 mg/kg was in good agreement with the estimate of 0.4 mg/kg made by the Meeting (after rounding up to one figure (NAFTA 95/99 95th percentile)).

The Meeting withdraws its previous recommendations of maximum residue levels of 0.5 mg/kg for hexythiazox in apples and pears.

Stone fruit

Hexythiazox is registered on stone fruit in the USA with an application rate of 1 × 0.2 kg ai/ha with a PHI of 28 days. Supervised residue trials conducted in the US on cherries, nectarines and peaches according to this GAP were submitted.

For cherries residues were (n = 4): 0.04, 0.06, 0.08 and 0.12 mg/kg.

For nectarines residues were (n = 3): 0.05, 0.05 and 0.09 mg/kg.

For peaches residues were (n = 3): 0.09, 0.09 and 0.18 mg/kg.

Additional trials on plums and other stone fruit were submitted, but the PHI of 7 days was below the registered GAP in the US.

The Meeting decided to combine the data for nectarines and peaches treated according to US GAP , resulting in residues of 0.05, 0.05, 0.09(3) and 0.18 mg/kg (n = 6).

Considering the supportive data for cherries the Meeting estimated a maximum residue level and an STMR value for hexythiazox in stone fruits of 0.3 and 0.09 mg/kg, respectively.

The value derived from use of the NAFTA calculator was 0.3 mg/kg, which agreed with the maximum residue level of 0.3 mg/kg estimated by the current Meeting.

The Meeting withdraws its previous recommendations of maximum residue levels for hexythiazox of 1 mg/kg in cherries, 1 mg/kg in peaches and 0.2 mg/kg in plums (including prunes).

Currants (red, white)

Hexythiazox is registered in the USA on currants at a rate of 0.21 kg ai/ha with a PHI of 3 days. Supervised residue trials submitted on blackberries and raspberries were conducted with an application rate of 0.42 kg ai/ha with a PHI of 21 days.

The Meeting noted that the data from USA does not match GAP and can not be used for a maximum residue level estimation. The Meeting withdraws its previous recommendations for currants (red, white) of 0.2 mg/kg.

Grapes

For grapes hexythiazox is registered in the USA at a rate of 1 × 0.2 kg ai/ha with a PHI of 28 days. Corresponding supervised residues trials were conducted according to the maximum GAP with two formulations in the US.

For grapes residues were (n = 12): 0.04, 0.04, 0.05, 0.13, 0.13, 0.19, 0.21, 0.22, 0.24, 0.31, 0.31 and 0.48 mg/kg.

Additional supervised field trials were submitted for Europe, but no corresponding GAPs are available.

The Meeting confirms its previous recommendation of a maximum residue level of 1 mg/kg and estimated an STMR value for hexythiazox in grapes of 0.2 mg/kg.

An estimate of 1 mg/kg, derived from the use of the NAFTA calculator, was in agreement with the maximum residue level estimated by the current Meeting.

Strawberries

Hexythiazox is registered in the USA on strawberries at a rate of 0.21 kg ai/ha with a PHI of 3 days. Corresponding supervised residues trials were conducted according to the maximum GAP with two formulations in the US. Residues found in strawberries were (n = 3): 0.13, 0.17 and 0.3 mg/kg.

The Meeting noted that the data from USA for strawberries, representing a major crop, were not sufficient for a maximum residue level estimation. The Meeting withdraws its previous recommendation for strawberries of 0.5 mg/kg.

Dates

In dates hexythiazox is used according to US GAP with an application rate of 0.21 kg ai/ha and a PHI of 90 days. Corresponding supervised residues trials were conducted according to the maximum GAP in the US. Residues found in dates were (n = 3): 0.11, 0.26 and 0.63 mg/kg.

The Meeting estimated a maximum residue level and an STMR value for hexythiazox in dates of 2 and 0.26 mg/kg, respectively.

An estimate of 2 mg/kg, derived from the use of the NAFTA calculator, was in agreement with the maximum residue level estimated by the current Meeting.

Tomatoes

For protected tomatoes hexythiazox is registered in the Netherlands with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. Supervised residue trials on protected tomatoes corresponding to the maximum GAP are available from France and Italy. Residues found in the fruits were (n = 8): < 0.05(6), 0.05 and 0.05 mg/kg.

The Meeting confirmed the maximum residue level for hexythiazox in tomatoes of 0.1 mg/kg and estimated an STMR value of 0.05 mg/kg.

Statistical calculations were not conducted, as the majority of reported residue levels were below the LOQ.

Egg plant

Hexythiazox is registered in the Netherlands for protected eggplants with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. No supervised residue trials on eggplants were submitted to the Meeting.

The Meeting decided that tomatoes can be extrapolated to eggplants. Based on the residue data for tomatoes the Meeting estimated a maximum residue level and an STMR value for hexythiazox in eggplants of 0.1 and 0.05 mg/kg, respectively.

Sweet corn

For sweet corn supervised residue trials were submitted to the Meeting although no corresponding GAP is available.

The Meeting concluded that maximum residue levels on sweet corn could not be estimated without a corresponding GAP.

Fruiting vegetables, Cucurbits (except watermelon)

For cucumbers hexythiazox is registered in the Netherlands for field and glasshouse use with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. Supervised residue trials on protected cucumbers corresponding to the maximum GAP are available from Italy, Spain and the Netherlands. Residues found in the fruits were (n = 8): < 0.05(8) mg/kg.

Hexythiazox is registered in the Netherlands for protected melons (except water melons) with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. Supervised residue trials on protected melons corresponding to the maximum GAP are available from France, Spain and the Netherlands.

Residues found in melon whole fruits were (n = 8): < 0.05(8) mg/kg.

Residues found in melon pulp were (n = 8): < 0.05(8) mg/kg.

Hexythiazox is registered in the Netherlands for protected summer squash with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. No supervised residue trials on squashes were submitted to the Meeting.

Hexythiazox is registered in the Netherlands for protected winter squash with an application rate of 1 × 0.08 kg ai/ha (0.005 kg ai/hL) with a PHI of 3 days. No supervised residue trials on squashes were submitted to the Meeting.

The Meeting decided that data for cucumbers can be extrapolated to summer squash and data for melons to winter squash. Based on the identical residue data for protected cucumbers and melons the Meeting estimated a maximum residue level and an STMR value for hexythiazox in fruiting vegetables, cucurbits expect water melons of 0.05 and 0.05 mg/kg, respectively.

Statistical calculations were not possible, since all reported residue levels were below the LOQ.

The Meeting withdraws its previous recommendation of maximum residue levels of 0.1 mg/kg for hexythiazox in cucumbers.

Common beans (pods and/or immature seeds)

For common beans (pods and/or immature seeds) supervised residue trials were submitted to the Meeting although no corresponding GAP is available.

The Meeting withdraws its previous recommendation of maximum residue levels of 0.5 mg/kg for hexythiazox in common beans (pods and/or immature seeds).

Pulses

For pulses supervised residue trials were submitted to the Meeting although no corresponding GAP is available.

The Meeting concluded that maximum residue levels on pulses could not be estimated without corresponding GAP.

Maize

Hexythiazox is registered in maize in the USA with an application rate of 1 × 0.2 kg ai/ha with a PHI of 45 days. Supervised residue trials conducted in the US were available using one application at rates of 0.21 or 1.1 kg ai/ha and PHIs of 79 up to 110 days, which did not match the US GAP.

The Meeting noted that the data from USA did not match GAP for maize and could not be used to estimate a maximum residue level.

Tree nuts

In tree nuts hexythiazox is registered in the USA at a rate of 1 × 0.2 kg ai/ha with a PHI of 28 days. Supervised field trials were conducted in the US at rates of 0.25 kg ai/ha up to 0.42 kg ai/ha on almonds and pecan with a PHI of 28 and 29 days. For almonds residues were (n = 2): < 0.02 and < 0.02 mg/kg. In pecans residues of < 0.02(5) mg/kg were found.

The Meeting estimated a maximum residue level based on the LOQ of the analytical method for hexythiazox parent of 0.05(*) mg/kg. Under consideration of the non-systemic properties the Meeting estimated an STMR value of 0 mg/kg for hexythiazox in tree nuts.

Statistical calculations were not possible, as all reported residue levels were below the LOQ.

Cotton

For cotton hexythiazox is registered in the USA (California only) at a rate 1 × 0.17 kg ai/ha with a PHI of 35 days. Supervised field trials from the US were submitted involving two applications in an 2–3 months interval with 0.17 to 0.21 kg ai/ha each and a PHI of 28–35 days. Residues found in the ginned seeds were (n = 3): 0.07, 0.1 and 0.1 mg/kg.

The Meeting noted that the data from USA for cotton were not sufficient for a maximum residue level estimation.

Hops

Hexythiazox is registered in the USA for hops with an application rate of 1 × 0.21 kg ai/ha without a specified PHI. In one supervised field trials according to GAP residues in hops were (n = 1): 1.9 mg/kg

The Meeting noted that the data for hops from USA was insufficient for a maximum residue level estimation and withdraws its previous recommendation of 2 mg/kg for hexythiazox in dry hops.

Almond hulls

In almonds hexythiazox is registered in the USA at a rate of 1 × 0.2 kg ai/ha with a PHI of 28 days. Supervised field trials were conducted in the US at rates of 0.25 kg ai/ha on almonds with a PHI of 28 days. For almond hulls residues were (n = 2): 1.2 and 1.4 mg/kg.

The Meeting noted that the data for almond hulls from USA was insufficient for a maximum residue level estimation.

Cotton gin trash

For cotton hexythiazox is registered in the USA at a rate 1 × 0.17 kg ai/ha with a PHI of 35 days. Supervised field trials from the US were submitted involving two applications in an 2–3 months

interval with 0.17 to 0.21 kg ai/ha each and a PHI of 28 days. Residues found in gin trash were (n = 3): 1.5, 1.6 and 2.3 mg/kg.

The Meeting noted that the data from USA for cotton gin trash was insufficient to give any recommendation.

Maize forage

Hexythiazox is registered for use in maize in the USA with an application rate of 1 × 0.2 kg ai/ha and a PHI of 45 days. Supervised residue trials conducted in the US were available using one application at a rate of 0.21 kg ai/ha with a PHI of 44 to 49 days. Residues found in maize forage were (n = 5): 0.13, 0.58, 0.91, 1.1 and 1.7 mg/kg.

The Meeting estimated an STMR value and a highest residue value for hexythiazox in maize forage of 0.91 and 1.7 mg/kg, respectively.

Maize stover

For maize stover, hexythiazox is registered in the USA with an application rate of 1 × 0.2 kg ai/ha with a PHI of 45 days. Supervised residue trials conducted in the US, using one application at rates of 0.21 kg ai/ha with a PHI of 79 up to 110 days, did not match the US GAP.

The Meeting noted that as the data from the USA did not match GAP for maize it could not be used for a recommendation.

Fate of residues during processing

The Meeting received information on the fate of hexythiazox residues during processing of oranges, grapes, plums and cotton seeds. Also information was provided on hydrolysis studies with hexythiazox to assist with identification of the nature of the residue during processing. Processing factors presented below have been calculated for hexythiazox for all commodities relevant to trade and/or the dietary intake estimation. Further data on processed commodities are presented in the evaluation for this active substance.

Hexythiazox was stable at pH4, 80 °C for 20 minutes and pH5, 100 °C for 60 minutes, simulating pasteurisation and cooking of commodities.

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors	Median or best estimate [a]
Oranges	Juice	< 0.05, < 0.07, 0.22, 0.26, 0.3	0.22
	Marmalade	0.11, 0.14, 0.27	0.14
	Pulp, dry	1.8, 2.7	2.3
Grapes	Wine, red	< 0.02, < 0.1	< 0.06
	Wine, white	< 0.02, < 0.09	< 0.06
	Juice, red	0.08, 0.75	0.42
	Juice, white	< 0.02, 0.14	0.08
	Raisins	0.52, 1.4, 1.7, 3.3	1.6
	Pomace, wet	3.4, 16.6	10
Plums	Prunes, dried	4.8, 5	4.9

Under simulated sterilisation conditions (pH6, 120 °C for 20 minutes) hexythiazox degraded into PT-1-3, leaving only half of the initial concentration in the test solutions.

[a] processing factors presented are based on the total residue hydrolysable to PT1-3

Oranges were processed into juice, marmalade and dry pulp. Processing factors were 0.22, 0.14 and 2.3, respectively. Based on the median residue of 0.11 mg/kg for whole citrus fruits, STMR-P values for hexythiazox residues were 0.024 mg/kg in orange juice, 0.015 mg/kg in marmalade and 0.25 mg/kg in dry pulp.

Grapes were processed into red and white wine, red and white juice, raisins and wet pomace. Processing factors were < 0.06 for wine (red and white combined), 0.42 for juice (based on red juice), 1.6 for raisins and 10 for wet grape pomace. Based on the STMR value of 0.2 mg/kg for grapes STMR-P values for hexythiazox were 0.01 mg/kg for wine (red and white), 0.084 mg/kg for grape juice, 0.32 mg/kg for raisins and 2 mg/kg for wet pomace.

Based on the average dry-matter content of grape pomace, wet of 15% the Meeting estimated a maximum residue level of 15 mg/kg for grape pomace, dry.

Plums were processed into prunes, resulting in a processing factor of 4.9. Based on the STMR of 0.09 mg/kg for stone fruit a STMR-P value of 0.44 mg/kg for dried prunes was estimated.

Based on the highest residue of 0.18 mg/kg for stone fruit and the processing factor of 4.9 for dried prunes, the Meeting estimated a maximum residue level of 1 mg/kg and an STMR-P value of 0.44 mg/kg for hexythiazox in dried prunes.

Residues in animal commodities

Livestock dietary burden

The Meeting received lactating dairy cow and laying hens feeding studies which provided information on likely residues resulting in animal commodities, milk and eggs from hexythiazox residues in the animal diet.

Lactating dairy cows

In a study two lactating cows were dosed over a period of 14 consecutive days with hexythiazox at rates of 12 mg or 120 mg per animal and day. Milk was collected over the whole study period. After the dosage period the animals were kept 8 days for withdrawal before being sacrificed. Samples of fat, muscle, kidney and liver were taken for analysis. All samples were analysed for the sum of hexythiazox and its metabolites, determined as PT-1-3. In none of the samples residues above the limit of quantification of 0.05 mg/kg were found.

In a second study twelve lactating Holstein cows were divided into four groups receiving doses of 0, 5, 15 or 50 ppm hexythiazox for a period of 28 consecutive days. One animal of each dose group was kept for an additional withdrawal period of 7 days. During the whole period of time samples of milk were collected. After the withdrawal period the animals were sacrificed and samples of fat, liver, kidney and muscle were taken. All samples were analysed for the sum of hexythiazox and its metabolites, determined as PT-1-3. In the groups receiving doses of 0, 5 or 15 ppm per day, no residues above the LOQ of 0.01 mg/kg were found in any sample expect liver (0.06 mg/kg), kidney (0.01 mg/kg) and renal/omental fat (0.01 mg/kg). For the dose group 50 ppm residues in milk were slightly above the LOQ (< 0.01–0.02 mg/kg). The separation into skim milk and cream revealed that most of the residue is found in the fat fraction. No residues above the LOQ of 0.01 mg/kg were found in skim milk, while in cream levels ranging from 0.02 to 0.1 mg/kg were found. Highest residues were found in the liver, going up to 0.186 mg/kg in the 50 ppm dose group.

Laying hens

For laying hens the animals were separated into four groups receiving doses of 0, 5, 15 or 50 ppm hexythiazox for 28 consecutive days. Each group consisted of four subgroups with four animals each. For each dose group one subgroup was kept 7 additional days for withdrawal. During the whole period of time eggs were collected. At the end of the dose period the animals were sacrificed and samples of fat, muscle, liver and kidney were taken. All samples were analysed for the sum of hexythiazox and its metabolites, determined as PT-1-3. In eggs residues were found in all dose groups ranging from < 0.01 to 0.058 mg/kg for the 5 ppm group up to 0.03 to 0.36 mg/kg for the 50 ppm group. A separate analysis of egg white and egg yolk on day 20 reveals higher residues in the yolk by a factor of 1.7 to 2.5. In muscle no residues above the LOQ of 0.01 mg/kg could be detected. Highest

residues in the tissues were found in liver and fat. Residues were 0.03 mg/kg and 0.05 mg/kg for the 5ppm group, 0.07 mg/kg and 0.08 mg/kg for the 15ppm group and 0.12 mg/kg and 0.17 mg/kg for the 50 ppm group, respectively.

Estimated maximum and mean dietary burdens of livestock

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6 of the 2009 JMPR Report. The calculations were made according to the livestock diets from US-Canada, EU and Australia in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Livestock dietary burden, hexythiazox, ppm of dry matter diet					
	US-Canada		EU		Australia	
	max.	mean	max.	mean	max.	mean
Beef cattle	1.7	0.9	3.5	1.9	6.1[a]	4.5[b]
Dairy cattle	2.2	1.2	3.0	1.4	6.1	4.5
Poultry—broiler	0	0	0	0	0	0
Poultry—layer	0	0	0.4[c]	0.2[d]	0	0

[a] Highest maximum beef or dairy cattle burden suitable for MRL estimates for mammalian meat and milk

[b] Highest mean beef or dairy cattle burden suitable for STMR estimates for mammalian meat and milk

[c] Highest maximum broiler or layer poultry burden suitable for MRL estimates for poultry meat and eggs

[d] Highest mean broiler or layer poultry burden suitable for MRL estimates for poultry meat and eggs

Animal commodities, MRL estimation

In the table below, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding studies are shown in square brackets [] and estimated concentrations related to the dietary burden are shown without brackets.

Dietary burden (ppm) Feeding level [ppm]	Milk/Eggs	Muscle	Liver	Kidney	Fat
HR	mean	highest	highest	highest	highest
HR beef or dairy cattle (6.1) [5, 15]	Milk 0.01 [< 0.01, < 0.01]	0 [< 0.01, < 0.01]	0.03 [< 0.01, 0.09]	0.02 [0.02, 0.02]	0.01 [< 0.01, 0.01]
HR laying hens (0.4) [5]	Eggs 0.004 [0.05]	0 [< 0.01]	0.002 [0.03]	0.01 [< 0.01]	0.004 [0.05]
STMR	mean	mean	mean	mean	mean
STMR beef or dairy cattle (4.5) [5, 15]	Milk 0.01 [< 0.01, < 0.01]	0 [< 0.01, < 0.01]	0.01 [< 0.01, 0.06]	0.01 [0.01, 0.01]	0.01 [< 0.01, 0.01]
STMR laying hens (0.2) [5]	Eggs 0.002 [0.05]	0 [< 0.01]	0.001 [0.02]	0.01 [< 0.01]	0.002 [0.05]

In lactating cows as well as in laying hens no residues above the LOQ of 0.05 mg/kg for the analytical method for enforcement purposes were estimated. The Meeting estimated maximum residue levels for mammalian meat (fat), eggs, milk, milk fat, edible offal (mammalian) and poultry edible offal of 0.05 mg/kg. For poultry meat (fat) the Meeting estimated a maximum residue level of 0.05(*) mg/kg.

The Meeting estimated an STMR value for hexythiazox in whole milk of 0.01 mg/kg. The separation of skim milk and cream was conducted for the 50ppm dose group revealing residues up to 0.1 mg/kg in the fat. Under consideration of the maximum dietary burden of 5.7 ppm the Meeting also estimated an STMR value of 0.01 mg/kg for hexythiazox in milk fat.

The residue arising from a dietary burden of 5.7 ppm was 0.01 mg/kg in the fat. Since the target tissue for hexythiazox residues in animal tissues is fat, the Meeting estimated an STMR value of 0.01 mg/kg for mammalian meat (fat basis). For mammalian meat (muscle) the Meeting estimated an STMR value of 0 mg/kg.

In kidney and liver the Meeting estimated STMR values 0.01 mg/kg, respectively.

For eggs the Meeting estimated an STMR value of 0.002 mg/kg. In poultry tissues STMR values were estimated at levels of 0.01 mg/kg for poultry edible offal of, 0.002 mg/kg for poultry meat (fat) and 0 mg/kg for poultry meat (muscle).

RECOMMENDATIONS

The Meeting estimated the STMR and MRL values shown below.

Definition of the residue (for compliance with MRL) for plant commodities: *hexythiazox*

Definition of the residue (for estimation of dietary intake) for plant commodities: *sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox*

Definition of the residue (for compliance with MRL and for estimation of dietary intake) for animal commodities: *sum of hexythiazox and all metabolites containing the trans-5-(4-chlorophenyl)-4-methyl-2-oxothiazolidine-moiety (PT-1-3), expressed as hexythiazox*

The residue is fat-soluble.

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	HR, mg/kg
CCN	Name	New	Previous		
FP 0226	Apple	W [a]	0.5		
FS 0013	Cherries	W [a]	1		
FC 0001	Citrus fruits	0.5	0.5	0.077 (pulp)	
VP 0526	Common beans (pods and/or immature seeds)	W	0.5		
VC 0424	Cucumbers	W	0.1		
FB 0279	Currants (red, white)	W	0.2		
FT 0295	Date	2		0.26	
DF 0269	Dried grapes			0.32	
MO 0105	Edible offal (mammalian)	0.05		0.01	
VO 0440	Egg plant	0.1		0.05	
PE 0112	Eggs	0.05		0.002	
VC 0045	Fruiting vegetables, cucurbits except watermelons	0.05		0.05	
JF 0269	Grape juice			0.084	
AB 0269	Grape pomace, dry	15 (dry)			
-	Grape pomace, wet			2.0	
FB 0269	Grapes	1	1	0.2	
DH 1100	Hops, dry	W	2		
AF 0645	Maize forage			0.91	1.7 (highest residue)
MM 0095	Meat (from mammals other than marine mammals)	0.05		0.01 (fat) 0 (muscle)	
FM 0183	Milk fats	0.05		0.01	
ML 0106	Milks	0.05		0.01	

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	HR, mg/kg
CCN	Name	New	Previous		
JF 0004	Orange juice			0.024	
AB 0001	Orange, dry pulp			0.25	
FS 0247	Peach	W [a]	1		
FP 0230	Pear	W [a]	0.5		
FS 0014	Plums (including prunes)	W [a]	0.2		
FP 0009	Pome fruit	0.4		0.11	
PM 0110	Poultry meat	0.05* (fat)		0.002 (fat) 0 (muscle)	
PO 0111	Poultry, edible offal of	0.05		0.01	
DF 0014	Prunes [b]	1		0.41	
FS 0012	Stone fruit	0.3		0.09	
FB 0275	Strawberry	W	0.5		
VO 0448	Tomato	0.1	0.1	0.05	
TN 0085	Tree nuts	0.05*		0	
-	Wine			0.01	

[a] replaced by a group maximum residue level

[b] dried fruits

DIETARY RISK ASSESSMENT

Long-term intake

The evaluation of hexythiazox resulted in recommendations for MRLs and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 13 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3 of the 2009 JMPR Report.

The IEDIs in the thirteen Cluster Diets, based on the estimated STMRs were 0–2% of the maximum ADI (0.03 mg/kg bw). The Meeting concluded that the long-term intake of residues of hexythiazox from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The 2008 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of hexythiazox residues is unlikely to present a public health concern.

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