AZOCYCLOTIN (129)

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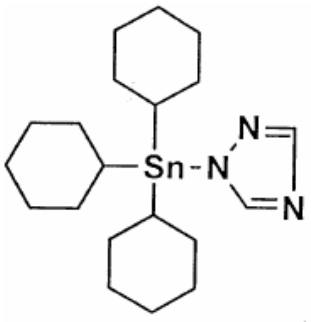
EXPLANATION

Azocyclotin is an organotin contact acaricide effective against phytophagous mites. The compound was evaluated by the JMPR a number of times between 1979 and 1994. At its 33rd Session, the CCPR decided to withdraw all azocyclotin CXLs and MRLs, with the exception of citrus fruits, grapes, meat (from mammals other than marine mammals), milk products and milks, as the manufacturer had indicated that these commodities would be supported. The compound was listed in the Periodic Re-Evaluation Programme at the 36th Session of the CCPR for periodic review by the 2005 JMPR. The present meeting received and evaluated information on azocyclotin identity, physical chemical properties, metabolism on cow and apple, environmental fate in water, methods of residue analysis, national use pattern and supervised residue trials on apples.

IDENTITY

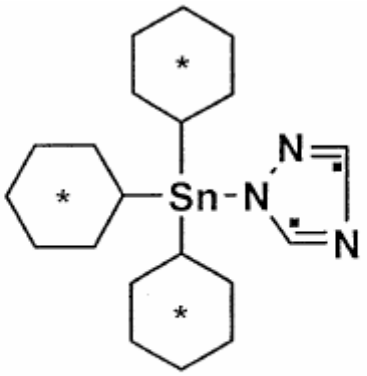
ISO common name:	Azocyclotin
Chemical names	
IUPAC	Tri(cyclohexyl)-1H-1,2,4-triazole-1-yltin
CAS	1-(tricyclohexylstannyl)-1H-1,2,4-triazole
CAS Number:	[41083-11-8]
CIPAC No.:	404
Structural formula	
Molecular formula:	C20H35N3Sn
Molecular weight:	436.2

Physical and chemical properties

Pure active ingredient

Appearance:	White powder
Melting point:	decomposes before melting
Boiling point:	Not applicable
Va pour pressure :	2 x 10^{-8} mPa at 20ºC
Hydrolysis:	pH = 4,7 or 9 $DT_{90} \leq 10$ min (Scholz, 1998)
Relative density:	1.335 g/cm^3

Radiolabeled compounds used in metabolism studies and in environmental fate in water.



(■: indicates triazole-3,5-^{14}C labelling position)
(∗: indicates cyclohexyl UL-^{14}C labelling position)

METABOLISM AND ENVIRONMENTAL FATE

Animal metabolism

In one metabolism study conducted in 1983, a single dairy cow was dosed for 5 consecutive days with [cyclohexyl-UL-^{14}C]azocyclotin at a rate of 0.5 mg/kg and slaughtered one hour after the last dosing (Strankowski and Murphy, 1983). Tissue samples were homogenized with acetonitrile:hydrochloric acid (99:1), filtered and the filtrate partitioned with acetone:chloroform (1:2). More than 98% of the applied radioactivity was extracted in tissues, mostly in the organic phase (from 71% in fat to 97% in heart tissue). Total ^{14}C residues were found primarily in liver and kidney extracts (Table 1). Radioactivity in milk, directly measured in the liquid scintillation counting, reached a maximum after 4 days.

Table 1. Residues of total ^{14}C in cow milk and tissues extracts, expressed in mg/kg azocyclotin equivalents.

Tissues, 5 days	mg/kg	Milk, Day and time	mg/kg
liver	0.34	1 pm	0.008
kidney	0.25	2 am	0.005
heart	0.12	2 pm	0.013
brain	0.04	3 am	0.007
renal fat	0.04	3 pm	0.014
omental fat	0.03	4 am	0.017
back fat	0.03	4 pm	0.017
loin muscle	0.03	5 am	0.015
shoulder muscle	0.03		
round muscle	0.03		

Organic tissue extracts were subject to thin layer chromatography (TLC) and milk extracts to gas chromatography analysis. Radioactive azocyclotin, non-radioactive dicyclohexyl tin oxide (DCTO), and cyclohexyl stannoic acid (MCTA) were chromatographed with the extracts. The distribution of the applied radioactivity is shown on Table 2. The results are expressed as azocyclotin and or/cyhexatin as no distinction could be made between the two compounds. Cyhexatin standard was not used in the experiment.

Table 2. Distribution of radioactivity in cow tissue and milk, as percent extracted [a].

Sample	Azocyclotin and or cyhexatin	DCTO	MCTA
Liver	55	18	23
Kidney	56	17	24
Heart	89	8	0
Fat	43	23	33
Loin muscle	84	15	0
Milk	92	4	4

a. Tissues were analyzed by TLC and milk by GC

Plant metabolism

One metabolism study in apple (Red Delicious) conducted in the United States in 1981 was submitted (Minor, 1983). A WP formulation of [cyclohexyl-UL- ^{14}C]azocyclotin was applied at a rate of 0.030 kg ai/hL as small droplets to the surface of individual apples. Each apple received 8 µCi of ^{14}C azocyclotin. Five apples were collected at 0, 7, 14, and 21 days post treatment.

Apple samples were washed in acetone, following drying the apples were peeled, with the peel and pulp fractions pulverized in dry ice, combusted to $^{14}CO_2$ and radioactivity trapped in an alkaline solution. Acetone extracts were radioassayed and mixed with decyl alcohol 1% v/v in chloroform.

The organic fraction was derivatized with phenylmagnesium bromide and submitted to TLC analysis (Table 3). The percent of applied radioactivity in the organosoluble fraction of the acetone wash dropped from 96% on samples collected on day 0 to 29% on day 21. Mass spectral data showed that radioactivity found on the origin did not contain the organotin moiety.

Table 3. Percent of applied radioactivity found in the acetone wash of apples treated with 14C azocyclotin.

Days	Organosoluble fraction	Azocyclotin / cyhexatin	DCTO	MCTA	Origin
0	96	88	3	1	3
7	66	49	7	2	7
14	30	21	4	<1	4
21	29	22	3	1	3

On day 21, 11% of the applied radioactivity was recovered in the peel and less than 1% in the pulp. Of the radioactivity found in the peel on day 21, 70% was identified, 11% stayed at the TLC origin and 17% remained in the aqueous phase. Radioactivity found in the aqueous fractions did not partition into hexane after derivatization with phenylmagnesium bromide, indicating the absence of the organotin moiety. Approximately 9% of the recovered radioactivity in the 21 days apple peel sample was reported as azocyclotin/cyhexatin, and 27% as DCTO and MCTA. It was not clear from the report whether cyhexatin standard was applied to the TLC, although it stated that the system could not resolve the two compounds.

Environmental fate in water

The hydrolysis of azocyclotin was studied in 0.01 M buffer solutions at pH 4, 7 and 9 and in drinking water (Scholz, 1998). The study was conducted with [triazole-3,5- ^{14}C]azocyclotin and [cyclohexyl-UL- ^{14}C]azocyclotin, at a concentration of about 30 µg ai/L.

The azocyclotin aqueous buffer solutions were incubated for 10, 30, and 60 minutes under sterile conditions and the azocyclotin drinking water solution for 10 minutes in the dark at 20 °C. Under the experimental conditions, azocyclotin was completely hydrolysed within 10 minutes ($DT_{90} \leq$ 10 minutes). Two hydrolysis products were observed: tricyclohexyltin hydroxide (cyhexatin) and 1,2, 4 triazole.

Figure 1 below shows the proposed metabolism of azocyclotin in animals, plants and water.

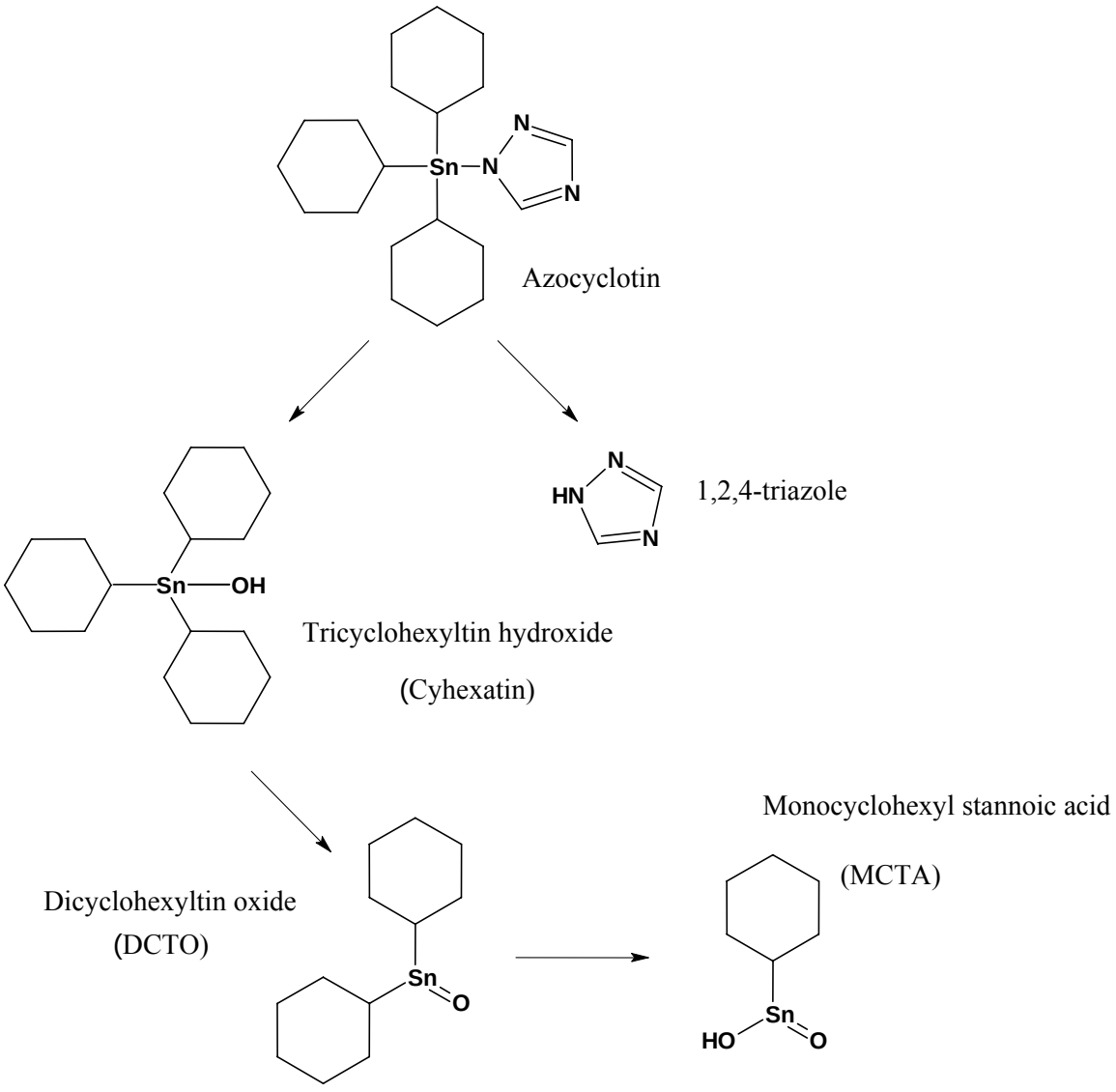


Figure 1. Proposed metabolic pathway of azocyclotin/cyhexatin in plants, animals and water.

METHODS OF RESIDUE ANALYSIS

Considering the very rapid hydrolysis of azocyclotin into cyhexatin shown in the water hydrolysis study, only cyhexatin residues are retrieved on crops treated with azocyclotin. Analytical methods to analyse cyhexatin and other metabolites coming from the use of azocyclotin or cyhexatin are treated within the cyhexatin evaluation of this Monograph.

USE PATTERN

Registered labels (not translated) of azocyclotin from Belgium, Spain, Portugal, Israel and Brazil were submitted. The products is registered for use on apples in Brazil as a SC (500 g/L) or WP (25 %) formulations, with an application rate of 0.025 and 0.02 kg ai./hL, respectively. A maximum of 2 applications per season were specified for the SC formulation. In both cases, the recommended volume is 1000 L/ha, with a 30 day PHI.

RESIDUES RESULTING FROM SUPERVISED TRIALS

Supervised field trials were conducted with azocyclotin on apples in Brazil, Chile and Israel (Table 4). Residues are reported as azocyclotin + cyhexatin, expressed as cyhexatin. DCTO was only analyzed in the Brazilian trial. The product has no registered use in Chile. Although registered in Israel, the trials conducted in this country could not be evaluated as a translated label was not submitted.

Table 4. Residues on apple fruit after treatment with a WP formulation of azocyclotin.

Country, Year (variety)	Application				PHI, Days	Cyhexatin, mg/kg	DCTO, mg/kg	Total, as cyhexatin, mg/kg	Study No.
	kg ai/ha	kg ai/hL	water, l/ha	no.					
Brazil, 1989 (fuji)	0.3	0.03	1000	2	0 7 15 30 45	0.35 0.40 0.17 <u>0.16</u> 0.14	<0.05 <0.05 0.07 <0.05 <0.05	0.35 0.40 0.24 <u>0.16</u> 0.14	0566-89
Chile, 1982 (golden delicious)	0.375-0.775	0.025	1500-3100	7	22	0.07			7515-81
Israel, 1978 (galia)	0.312		1250	2	0 6 13 29	0.2 0.15 <0.05 <0.05			7308a/78
	0.3125		1250	2	0 6 13 29	0.25 0.05 0.05 <0.05			7308b/78
	0.312		1250	2	0 6 13 29	0.15 0.05 0.05 <0.05			7308c/78
	0.312		1250	1	0 6 13 29	0.3 0.15 <0.05 <0.05			7310a/78
	0.312		1250	1	0 6 13 29	0.2 0.1 <0.05 <0.05			7310b/78
	0.312		1250	1	0 6 13 29	0.2 0.1 <0.05 <0.05			7310c/78

FATE OF RESIDUES IN STORAGE AND PROCESSING

Data on processing were submitted for cyhexatin

APPRAISAL

See the monograph on cyhexatin.

RECOMMENDATIONS

Residue for compliance with MRLs and estimation of dietary intake in plant and animal commodities: cyhexatin

Table 5. Residue for estimation of dietary intake in plant and animal commodities: cyhexatin.

CCN	Commodity	Recommended MRL, mg/kg		STMR, mg/kg	HR, mg/kg
		New	Previous		
FP 0226	Apple	0.2	2[2/]	0.02	0.11
JF 226	Apple juice			0.008	
FP 0230	Pear	0.2	2[2/]	0.02	0.11
FC 004	Oranges	0.2	2[1/]	0.035	0.049
JF 04	Orange juice			0.002	
FB0269	Grapes	0.3	0.2[1/]	0.085	0.19
DF 0269	Grapes, dried (= currants, raisins and sultanas)			0.076	
JF 269	Grape juice			0.068	
FB 1236	Wine grape			0.060	
FB 21	Currants, red, black, white	0.1		0.05	
MM 0095	Meat (from mammals other than marine mammals)[3/]	W	0.2[1/]		
AO3 0001	Milk products[3]	W	0.05*[1/]		
ML 0106	Milks[3/]	W	0.05*[1/]		

[1]/ azocyclotin and cyhexatin; [2]/ cyhexatin; [3]/ The MRL accommodates external animal treatment.

DIETARY RISK ASSESSMENT

Long-term intake

The 2005 JMPR established a group ADI of 0–0.003 mg/kg bw for cyhexatin and azocyclotin. The IEDIs were calculated for the five GEMS/Food regional diets from the STMR and STMR-P values for fruits and processed products as estimated by the present Meeting (Annex 3). The group ADI for cyhexatin and azocyclotin is 0.003 mg/kg bw, and the calculated IEDIs ranged from 0 to 5% of the ADI. The results are shown in Annex 3 of the 2005 JMPR Report.

The Meeting concluded that these uses of cyhexatin and/or that of azocyclotin resulting in long-term intake of residues of cyhexatin, as considered by the JMPR, are unlikely to present a public health concern.

Short-term intake

The 2005 JMPR established a group ARfD of 0.02 mg/kg bw for women of childbearing age for cyhexatin and azocyclotin. The IESTI was calculated based on consumption data generated for the general population as no consumption data is available for this group of the population. The IESTI ranged from 3 to 20% ARfD. The results are shown in Annex 4 of the 2005 JMPR Report.

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CYHEXATIN (67)

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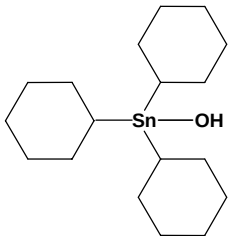
EXPLANATION

Cyhexatin is an organotin miticide used on fruit and vegetable crops. The compound has been reviewed a number of times by the JMPR since 1970, the most recent being for toxicology in 1994. Pending information on which commodities would be supported by the sponsor, at the 33rd Session of the CCPR, it was recommended that all CXLs, except those for apple, citrus fruits, grapes, meat (from mammals other than marine mammals), milk products, milks, and pear be withdrawn. The compound was listed in the Periodic Re-Evaluation Program at the 36th Session of the CCPR for periodic review by 2005 JMPR. The meeting received and evaluated information on metabolism, environmental fate, methods of residue analysis, freezer storage stability, national registered use patterns, supervised residue trials and processing.

IDENTITY

ISO common name:	Cyhexatin
Chemical names	
IUPAC:	tricyclohexyltin hydroxide
CAS:	tricyclohexylhydroxystannane
CAS number:	[13121-70-5]
Structural formula	
Molecular formula:	$C_{18}H_{34}OSn$
Molecular weight:	385.2 g/Mol

Physical and Chemical Properties

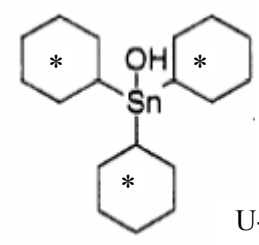
Pure active ingredient

Appearance:	White powder
Melting point:	Decomposed above 160ºC
Boiling point:	Not applicable
Vapour pressure :	1.17 x 10^{-7} Pa at 25°C
Relative density:	1.378 g/cm^3 at 20°C
Solubility in water at 20 ± 0.9°C	pH 4: 0.67 mg/L pH 7: ≤ 0.040 mg/L pH 10: ≤ 0.006 mg/L
Partition coefficient n-octanol /water	pH 4: log Pow > 4.6 at 20.3 ± 0.5 °C pH 7: log Pow ≥ 6.1 at 20.0 ± 1.2 °C pH 10: log Pow ≥ 6.9 at 20.0 ± 1.2 °C
Hydrolysis rate, sterile conditions, in the dark	pH 4: DT_{50} 299 days pH 7: DT_{50} 118 days

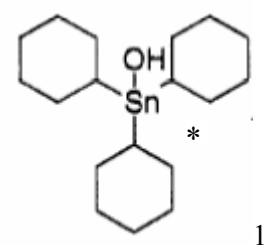
pH 10: DT_{50} 260-days.

METABOLISM AND ENVIRONMENTAL FATE

Radiolabeled compounds used in metabolism studies



U-^{14}C - cyhexatin



119Sn- cyhexatin

Metabolites found in the studies

DCTO: dicyclohexyltin oxide
MCTA: monocyclohexyl stannoic acid or cyclohexyl stannoic acid

Animal metabolism

Two lactating goats were dosed with ^{119}Sn-cyhexatin for four days at a rate of 100 ppm in the feed (Report No. GH-C 1875). Total collection of milk, urine and faeces were made during the dose period. The animals were slaughtered 5 to 7 hours after the final dose, and samples of gastrointestinal (GI) tract, muscle, fat, liver and kidney were taken. Tissue samples were extracted with chloroform:HCl (10:1) and body fat with dichloromethane. Milk samples were acidified with H_2SO_4 and extracted with diethyl ether.

On average, 68.5% of the ^{119}Sn activity was recovered from the animals, mostly in the faeces and in the GI tract (Table 1). The highest tissue residues were found in the liver, while the lowest were found in fat and milk. Radioactivity in milk was only detected days 2 and 3 in one goat and at day 2 in the other.

Table 1. Distribution of recovered ^{119}Sn activity, in goat body tissues.

	Total ^{119}Sn residue in mg/kg cyhexatin equivalents (percent of applied dose)	
Sample	**Goat 071**	**Goat 076**
Faeces	na. (40.7)	na. (47.3)
Urine	na. (0.1)	na. (< 0.1)
GI Tract	na. (31.7)	na. (16.4)
Milk (day 2/3)	0.01 / 0.02 (< 0.1)	0.02 / not detected (< 0.1)
Liver	1.83 (0.2)	0.45 (0.1)
Kidney	0.91 (< 0.1)	0.21 (< 0.1)
Muscle[a]	0.13 (< 0.1)	0.04 (< 0.1)
Fat[b]	0.07 (< 0.1)	0.03 (< 0.1)
Total	(72.7)	(63.7)

[a] Assumes 16% of bodyweight is muscle; [b] Assumes 20% of bodyweight is fat

The largest proportion of recovered radioactivity, 90% (muscle) to 100% (fat), was found in the organosoluble fraction of the tissue and milk extracts. HPLC and TLC analysis of the tissue extracts found that cyhexatin was the major residue (from 70 to 84% of the total radioactivity of the extract), with small amounts (< 10%) of dicyclohexyltin oxide (DCTO) and monocyclohexyl-stannoic acid (MCTA). Milk extracts showed 87% of the radioactivity as unchanged cyhexatin.

Two groups of six laying hens were dosed with 119Sn-cyhexatin for five days at 100 ppm in the feed (Report No. GH-C 1877). Eggs and faeces were collected daily during the experiment. The animals were slaughtered 6 hours after the final dose, and samples of GI tract, muscle, fat, skin, liver and kidney were taken. Tissue samples were extracted with chloroform:HCl (10:1) and body fat with dichloromethane.

On average, 66.3% of the applied ^{119}Sn activity was recovered in the collected samples; with the largest proportions found in droppings and the GI tract (Table 2). The highest tissue residue was found in liver and kidney. Residues in eggs increased during the dose period, up to a mean of 3.6 mg/kg cyhexatin equivalents in the egg yolk, representing < 0.2% of the applied radioactivity (Table 3).

Table 2. Residues of total ^{119}Sn and percentage of ^{119}Sn recovered in hen body tissues.

Sample	Total ^{119}Sn residue, in mg/kg cyhexatin equivalents (% of the applied dose)	
	Group 1	Group 2
Droppings	na. (64.3)	na. (62.8)
GI Tract	na. (2.6)	na. (1.1)
Liver	2.80 (0.2)	3.26 (0.2)
Kidney	2.52 (< 0.1)	3.18 (0.1)
Skin[a]	0.16 (0.1)	0.20 (0.1)
Breast muscle[a]	0.15 (0.1)	0.17 (0.1)
Thigh muscle[a]	0.24 (0.1)	0.27 (0.1)
Fat	0.29 (0.1)	0.44 (0.2)

[a] assumes the tissue is 15% of bodyweight.

Table 3. Residues of total ^{119}Sn and percentage of ^{119}Sn recovered in hen eggs.

Day	Total ^{119}Sn residue, in mg/kg cyhexatin equivalents (percent of the applied dose)			
	Group 1		Group 2	
	Yolk	white	Yolk	white
1	0.0	0.0	0.0	0.0
2	0.1 (< 0.01)	0.02 (< 0.01)	0.30 (0.01)	0.09 (< 0.01)
3	0.83 (0.02)	0.18 (0.01)	0.74 (0.01)	0.20 (0.01)
4	2.25 (0.06)	0.18 (0.01)	1.65 (0.04)	0.15 (0.01)
5	3.95 (0.10)	0.22 (0.01)	3.22 (0.09)	0.22 (0.01)

More than 90% of the tissue and egg radioactivity were extracted with organic solvents. HPLC and TLC analyses of the tissue extracts showed the presence of cyhexatin (approximately 20 to 50% of the extract radioactivity), of DCTO (9 – 30%) and MCTA (7 to 16%) and several unidentified polar metabolites. Egg white extract showed similar patterns, except that little cyhexatin was present (< 10% of the extracted radioactivity). In contrast, the yolk contained only cyhexatin.

Plant metabolism

A Dwarf Golden Delicious tree with apples approaching maturity was treated by foliar spraying with ^{119}Sn-Cyhexatin, formulated as a WP, at the rate of 3.8 kg ai/ha (Report No. GH-C 1902). Before spraying, the tree was encased in a plastic envelop open at the top, moreover one small branch with 5 apples was totally encased in double plastic bags to provide a measure of translocation.

Fourteen days after application apples were sampled for analysis of total ^{119}Sn residue and residue identification. Control samples were taken from unsprayed trees of the same variety. The apples were weighed, quartered, blended in a food blender and frozen. The control sample and two of the treated batches were peeled before blending and examined separately. The radioactivity was removed after successive extractions (shaking and/or overnight standing) with water, HCL and

organic solvent, until the radioactivity in the extract was very low. The apples that had been shielded from the spray application contained barely detectable amounts of ^{119}Sn residue.

The total ^{119}Sn-residue found in the 10.7 kg of treated apples collected was 1.37 mg/kg cyhexatin equivalent, equivalent to 3.1% of applied activity. Most of the recovered radioactivity was found in the peel (96%). Juice obtained from centrifugation of the whole fruit homogenate contained 4% of TRR. About 60% TRR was found in the acid extracts of hexane, methylene chloride or chloroform.

Combination of data from peel, double extraction with hexane and ether and HPLC analyses of methylated derivative showed that cyhexatin (approximately 45%), and inorganic tin (approximately 25%) were the main residues, with minor amounts of MCTA (approximately 14%) and DCTO (approximately 12%) present. Insoluble ^{119}Sn activity was estimated to be 4%. The residues were confirmed by gas chromatography-mass spectrometry (GC-MS).

A single grape vine (defined as one-half of the lateral portions of two separate adjacent vines), received one foliar application of WP U-^{14}C - cyhexatin, during the growing season at a rate of 0.3 kg ai/ha (Report No. KP-2002-38). At 10 and 28 days after application, the grape bunches and grape leaves were taken for analysis of total ^{14}C residue and residue identification. Control samples were taken from adjacent untreated plot. The majority of the TRR were found in the grape surface rinses (methanol with 2% acetic acid). Grape homogenate (methanol with 5% acetic acid) accounted for up to 17.4% of TRR (Table 4).

Table 4. Summary of radioactivity residues in/on grapes treated with ^{14}C cyhexatin

Days after Treatment (DAT)	**Surface rinse**		**Grape homogenate**	
	% TRR	**mg/kg cyhexatin eq.**	**% TRR**	**mg/kg cyhexatin eq.**
10	89.4	0.185	10.6	0.022
28	82.6	0.121	17.4	0.023

Cyhexatin accounted for the majority of the residue in the surface rinse, which also contained the metabolite DCTO (Table 5). Only the parent compound was detected in the grape homogenate. Polar residues were composed of at least two components present at or slightly less than 0.01 mg/kg cyhexatin eq.

Table 5. Summary of Residues In/On Grape Samples*.

DAT	**Residue Component**	**Surface Rinses**		**Homogenate**	
		% TRR	**mg/kg cyhexatin eq.**	**% TRR**	**mg/kg cyhexatin eq.**
10	Polar	3.0	0.0064	0.4	0.0009
	DCTO	7.7	0.0161	---	< 0.001
	Unknown	1.0	0.0020	---	< 0.001
	Cyhexatin	77.6	0.1608	4.7	0.0099
	Total Identified	85.3	0.1769	4.7	0.0099
	Other	4.0	0.0084	0.4	0.0009
28	Polar	7.2	0.0103	---	< 0.001
	DCTO	14.8	0.0220	---	< 0.001
	Unknown	0.8	0.0011	---	< 0.001
	Cyhexatin	59.1	0.0867	5.4	0.0072
	Total Identified	73.9	0.1087	5.4	0.0072
	Other	7.9	0.0114	---	Nd

A suggested metabolic pathway of cyhexatin in animal and plants is shown on Figure 1.

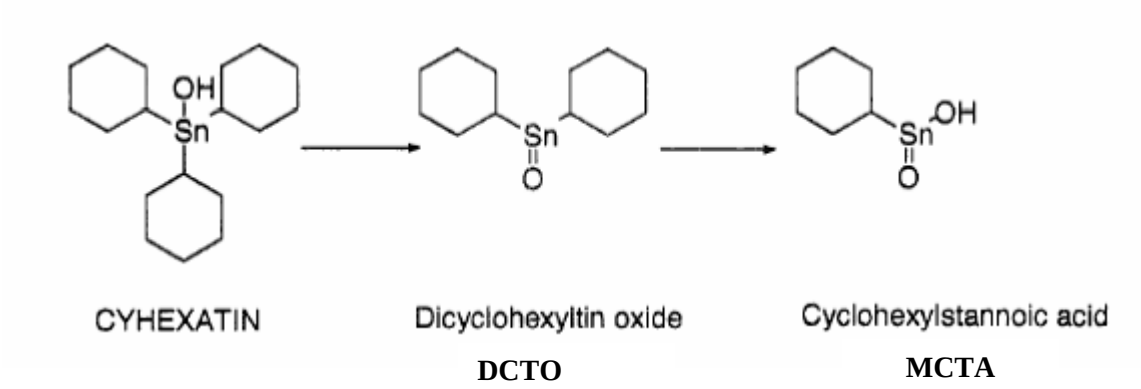


Figure 1. Proposed metabolic pathway of cyhexatin in plants and animals.

METHODS OF RESIDUE ANALYSIS

An analytical method was validated for cyhexatin and dicyclohexyldimethyltin (DCTO) in grapes (Report No. SIP 1303). The methodology involved extraction with a mixture of hexane and ethyl acetate in the presence of acetic acid and water. The extracted compounds were methylated with methyl magnesium chloride to form tricyclohexylmethyltin (TCMT) from cyhexatin and dicyclohexyldimethyltin (DCMT) from DCTO. The extracted derivatized compounds were cleaned with florisil, and quantitation was performed by gas chromatography with flame photometric detection (GC-FPD), in the sulphur mode. The results are shown on Table 6.

Table 6. Validation data for analytical method for the determination of residues of cyhexatin and the DCTO metabolite in grapes (n=4).

Compound	Fortification level (mg/kg)	Recovery rate (%)		Coefficient of variation (%)
		mean	range	
Cyhexatin	0.01	91.8	84.8-99.0	6.9
	0.10	94.2	91.5-96.9	2.4
DCTO	0.01	76.6	71.9-80.8	5.3
	0.10	70.9	70.6-71.6	0.7

The same method was also validated for grapes, employing different filters within the FPD, i.e., a tin filter (610 nm) for primary methodology and sulphur filter (393 nm) for confirmatory methodology. The results are shown on Table 7 (Report No. CTF 016/033702).

Table 7. Recovery rates (in percent) found in method validation residues of cyhexatin and DCTO in grapes (n=5).

Method	Fortification level (mg/kg)	Cyhexatin		DCTO	
		mean	range	mean	range
Primary (tin filter)	0.01	101	95 -107	75	71 - 79
	0.10	104	96 – 111	81	79 – 83
Confirmatory (sulfur filter)	0.01	97	90 - 103	66	61 - 71
	0.10	101	97 –105	75	73 – 79

The limits of detection on the primary and confirmatory systems were estimated to be 0.0012 mg/kg and 0.0008 mg/kg for cyhexatin, and 0.0018 mg/kg and 0.0007 mg/kg for DCTO, and the limit of quantification of 0.01 mg/kg for both components.

Matrix effects were tested on both primary and confirmatory systems by mixing a portion of control extract with a small volume of mixed calibration standard solution. For cyhexatin, on the

primary and confirmatory systems respectively, the concentrations determined were 100% and 99% compared with the theoretical concentration and for DCTO, they were 103% and 96%, respectively.

The reproducibility and degree of conversion of cyhexatin and DCTO to their respective derivatives TCMT and DCMT was assessed using standard solutions. The mean conversion efficiency of cyhexatin to TCMT was 110% with coefficient of variation of 5.4%. The mean conversion efficiency of DCTO to DCMT was 128% with a coefficient of variation of 9%. The derivatives were stable when stored at 4 ^{o}C in the dark after 7 days (mean of 106% remained).

The same analytical method was validated for orange and orange processed commodities (Report No. OXN 55/961360), using GC-FPD, in the tin mode (610 nm). The limits of quantification for cyhexatin and DCTO were 0.01 mg/kg for whole fruit, fresh juice, peel and molasses, 0.02 mg/kg for dry pulp and 0.10 mg/kg for peel oil and juice concentrate. The limits of detection were 0.0067, 0.0050, 0.0134, 0.0503 and 0.0670 mg/kg for cyhexatin in whole fruit, fresh juice and molasses, peel, dry pulp, peel oil and juice concentrate, 0.0064, 0.0048, 0.0127, 0.0477 and 0.0637 mg/kg for DCTO in the same matrices. The results are shown in Table 8.

Table 8. Validation recovery data (expressed as percentage) for analytical method for the determination of residues of cyhexatin and the DCTO metabolite in orange whole fruit and processed commodities.

Commodity	**Fortification level (mg/kg)**	**Cyhexatin**		**DCTO**	
		mean	**range**	**mean**	**range**
whole fruit **(n=2)**	0.01	111	106-116	112	108-115
	0.10	95	94-96	85	77-92
	1.00	91	91, 91	94	92-95
fresh juice **(n=2)**	0.01	100	96-104	105	100-109
	0.10	90	87-93	95	93-96
	1.00	89	86-91	89	85-93
juice concentrate **(n=1)**	0.10	77		90	
	0.25	87		101	
	1.00	80		80	
peel **(n=1)**	0.01	89		84	
	0.10	82		84	
	1.00	74		68	
dry pulp **(n=1)**	0.01	88		97	
	0.10	95		98	
	1.00	94		90	
molasses **(n=1)**	0.01	99		95	
	0.10	78		76	
	1.00	85		84	
peel oil **(n=1)**	0.10	89		103	
	0.25	96		99	
	1.00	98		94	

The analytical method was also validated for cyhexatin and dicyclohexyldimethyltin (DCTO) in apple and apple processed commodities (Report No. CTF 1B/942665), using GC/FPD in the sulphur mode (393 nm). The limit of quantitation of the method was 0.01 mg/kg, for both cyhexatin and DCTO in apple whole fruit, apple pomace (wet) and apple juice, and 0.05 mg/kg for both compounds in apple pomace (dry) whereas the limits of detection were 0.006 and 0.0057 for cyhexatin and DCTO respectively in all matrices.

The results are shown in Table 9.

Table 9. Validation recovery data (expressed as percentage) for analytical method for the determination of residues of cyhexatin and the DCTO metabolite in apple whole fruit and processed commodities.

Commodity	Fortification level (mg/kg)	Cyhexatin		DCTO	
		mean	range	mean	range
whole fruit **(n=2)**	0.01	102	102, 102	87	84, 90
	0.10	108	106, 111	102	102, 102
	1.00	112	109, 116	94	92-95
apple pomace (wet) **(n=1)**	0.01	112		80	
	0.10	111		71	
	1.00	103		82	
apple juice **(n=1)**	0.01	90		103	
	0.10	89		104	
	1.00	93		98	
apple pomace (dry) **(n=1)**	0.05	128		105	
	0.1	109		100	
	1.00	104		94	

Stability of residues in stored analytical samples

The storage stability of cyhexatin and its metabolite DCTO was studied in apples (Report No. CTF 6a/962496), grapes, wine and raisins (Report No. CTF 6b/962496). Samples, fortified at approximately 0.5 mg/kg level, were analysed after 0, 1, 3, 6 and 12 or 13 months storage at approximately –20°C in the dark (two samples at each level at each time). Method performance was tested by analysing two freshly fortified samples at each time interval. Recoveries were in the range of 80 to 100% in all cases, with exception of DCTO in some samples of grapes (6 and 13 months) wine and raisins (68–79%). The results are shown on Table 10.

Table 10. Stability of cyhexatin and DCTO in samples fortified at 0.5 mg/kg and stored at -20 ^{o}C (expressed in percentage remaining).

Time, months	Apples		Grapes		Wine		Raisins	
	Cyhexatin	DCTO	Cyhexatin	DCTO	Cyhexatin	DCTO	Cyhexatin	DCTO
0	106, 110	89, 87	105, 102	91, 93	99, 99	85, 89	96, 92	88, 87
1	87, 93	79[a], 72[a]	84, 71	74, 83	100, 89	81, 76	91, 86	82, 91
3	79, 81	77, 93	77, 76	85, 82	95, 93	79, 77	87, 93	84, 84
6	82, 81	83, 75	64, 64	70, 70	91, 89	75, 71	93, 109	86, 76
12	70, 70	64, 59	53, 48	54, 64	88, 94	76, 82	68, 51	61, 56

[a] corrected for the control residue at that interval

USE PATTERN

Cyhexatin is registered for use in many countries. The manufacturer submitted labels from a number of countries, but only information, relevant to this evaluation, is summarized in Table 11 below. Registered uses were also submitted by the Government of the Netherlands.

Table 11. Registered uses of cyhexatin.

Crop	Country	Form	Application				PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	Number	
Apple, Pear,	France	25%WP	Spraying	-	0.03	-	30
		600 g/L EC	Spraying	-	0.03	-	-
	Italy	20%WP	Spraying	Max 0.6/an	0.02-0.03	-	30
	Spain	25%WP	Spraying	-	0.025-0.037	-	28
		600 g/L EC	Spraying	-	0.03-0.036	-	28
Blackcurrant	France	600 g/L EC	Spraying	0.3		-	28

Crop	Country	Form	Application				PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hL	Number	
Citrus	Brazil	500g/L EC	Spraying	-	0.025	[1/]	30
	Spain	25%WP	Spraying	0.25-0.31	0.025-0.037	-	15
		600 g/L EC	Spraying	-	0.03	-	15
Grape, Grapevine	France	25% WP	Spraying	0.3		-	30
		600 g/L EC	Spraying	0.3		-	-
	Spain	25% WP	Spraying	0.25-0.31	0.025-0.037	-	30
		600 g/L EC	Spraying	-	0.03-0.036	-	30
Peach	France	25%WP	Spraying	-	0.03	-	30
Plum	France	25%WP	Spraying	-	0.03	-	30
		600g/L EC	Spraying	-	0.03	-	-.
	Spain	25%WP	Spraying	-	0.025-0.037	-	28
		600 g/L EC	Spraying	-	0.03-0.036	-	28

[1]/ the treatment can be repeated if necessary.

RESIDUES RESULTING FROM SUPERVISED TRIALS

Supervised field trials were conducted on pome fruit, stone fruit, grapes, blackcurrants, hops and citrus in Europe and Brazil (orange). A summary of the data received is summarized in Table 12.

Table 12. Supervised trials conducted with cyhexatin.

Table	Crop	Number of trials	Countries where trials were conducted
13	Orange and clementine	40	Brazil and Spain
14	Apple	53	France, Italy and the Netherlands
15	Pear	25	Italy
16	Grapes	45	France, Italy and Spain
17	Peach	16	France and Italy
18	Plum	6	France
19	Blackcurrant	3	France
20	Dried hops	19	Germany and United Kingdom

The studies were conducted according to GLP requirements and the data included details on method validation, dates of analysis, dates of sampling, sprayers used, their calibration, plot size, residue sample size and sampling method. All trials were conducted in the field using foliar applications. Data were not corrected for percent recovery of the method.

In the trials where both cyhexatin and DCTO were reported, the CG/FPD method, using either sulfur and/or tin filter, were used to analyse the samples. LOQ for both compounds in all cases was 0.01 mg/kg. For trials where only cyhexatin results are reported, the HPLC/UV analytical method used had LOQs of 0.05 or 0.1 mg/kg.

When residues were not detected they are shown as below the LOQ. Residue data were rounded to two significant figures or, for values near the LOQ, to one significant figure. Values underlined are within maximum GAP (± 30%) and were considered for the estimation of maximum residue levels, STMRs and HRs.

Citrus fruits

Thirty four supervised trials were conducted in oranges in Brazil from 1993 to 1995 (Study No. OXN 27/961612 and OXN 152/972905)). In each trial, six samples were analyzed and the mean residue reported. Where ever 2 applications were made, the first application was done 11 or 6 months before harvesting (Table 13).

Three trials were conducted in oranges and three in clementines in Spain in 1997 (Study No. SIP1063). In the Spanish trials, LOQ was 0.1 mg/kg (lowest recovery level in method validation) and limit of determination 0.002 mg/kg. Residues in parenthesis represented levels below the LOQ.

Table 13. Residues of cyhexatin in treated orange and clementine.

Country, Year (site)	Application				PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	no.				
Orange								
Brazil, 1993- 1994 (Bebedouro)	WP	1.0	0.025	2	28	0.01	< 0.01	OXN/27/B/ 1B/0[a]
	EC	1.1	0.025	2	28	< 0.01	< 0.01	
	WP	2.0	0.05	2	28	0.03	0.02	
	EC	2.2	0.050	2	28	0.05	0.05	
	WP	1.0	0.025	2	28	0.02	0.01	
	EC	1.1	0.025	2	28	0.01	0.01	
(Limeira)	WP	1.1	0.025	2	28	0.03	0.02	OXN/27/L/ 2B/0[a]
	EC	1.1	0.025	2	28	0.03	0.04	
	WP	2.1	0.05	2	28	0.11	0.06	
	EC	2.2	0.05	2	28	0.06	0.06	
Brazil, 1995 (Bebedouro)	WP	0.94	0.025	2	25	0.06	0.03	OXN/152/B/ 1B/0[a,b]
	EC	0.93	0.025	2	25 w	0.05	0.03	
	WP	1.7	0.05	2	25 w	0.15	0.04	
	EC	1.88	0.05	2	25 w	0.18	0.08	
(Araraquara)	WP	0.81	0.025	2	27 w	0.05	0.02	OXN/152/A /2B/O[a]
	EC	0.78	0.025	2	27 w	0.04	0.03	
	WP	1.54	0.05	2	27 w	0.13	0.05	
	EC	1.55	0.05	2	27	0.14	0.08	
(Araraquara)	WP	0.76	0.025	1	27	0.06	0.03	OXN/152/A /2B/O[a]
	EC	0.79	0.025	1	27	0.05	0.03	
	WP	1.56	0.05	1	27	0.16	0.05	
	EC	1.56	0.05	1	27	0.18	0.10	
(Descalvado)	WP	0.94	0.025	2	0	0.54	0.02	OXN152/D/3B/0[a]
					1	0.64	0.04	
					3	0.50	0.04	
					7	0.43	0.07	
					25	0.07	0.03	
	EC	0.93	0.025	2	0	0.60	0.04	
					1	0.87	0.06	
					3	0.59	0.07	
					7	0.36	0.08	
					25	0.07	0.04	
	WP	1.8	0.05	2	0	1.2	0.04	
					1	1.4	0.07	
					3	1.4	0.09	
					7	0.85	0.09	
					25	0.13	0.05	
	EC	1.8	0.05	2	0	1.5	0.08	
					1	2.0	0.13	
					3	1.7	0.13	
					7	0.73	0.19	
					25	0.17	0.09	
	WP	1.9	0.05	1	0	1.5	0.05	
					1	1.0	0.07	
					3	1.5	0.08	
					7	1.1	0.11	
					25	0.15	0.06	
	EC	1.9	0.05	1	0	0.88	0.03	
					1	1.6	0.06	
					3	0.92	0.10	
					7	0.56	0.09	
					25	0.11	0.06	

Country, Year (site)	Application				PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	no.				
(Limeira)	WP	0.64	0.025	2	0 1 3 7 25	0.43 0.38 0.70 0.21 0.05	0.04 0.03 0.05 0.07 0.03	OXN/152/L/ 4B/0[a]
	EC	0.65	0.025	2	0 1 3 7 25	0.43 0.43 0.41 0.27 0.04	0.04 0.05 0.06 0.08 0.03	
	WP	1.3	0.05	2	0 1 3 7 25	0.72 0.85 0.78 0.38 0.12	0.07 0.05 0.08 0.09 0.05	
	EC	1.3	0.05	2	0 1 3 7 25	0.88 0.83 0.78 0.54 0.13	0.06 0.06 0.10 0.15 0.07	
	WP	1.2	0.05	1	0 1 3 7 25	1.1 0.99 1.0 0.46 0.11	0.04 0.03 0.08 0.09 0.04	
	EC	1.3	0.05	1	0 1 3 7 25	1.0 1.0 1.3 0.59 0.17	0.05 0.05 0.13 0.11 0.09	
Spain, 1997 (Valencia)	EC	0.36	-	1	0 15 30 45	< 0.1 (0.09) < 0.1 (0.05) < 0.1 (0.04) < 0.1 (0.03)	-	SIP1063 R9522/2
	EC	0.36	-	1	80	< 0.1 (0.02)	-	R9415
	EC	0.36	-	1	60	< 0.1 (< 0.002)	-	R9414/2
Clementine								
Spain, 1997 (Castellón)	EC	0.36	-	1	60	< 0.1 (< 0.002)		R9414/1
	EC	0.36	-	1	0 15 30 45	0.16 < 0.1 (0.07) < 0.1 (0.02) < 0.1 (< 0.002)		R9522/1
(Alicante)	EC	0.36	-	1	0 15 30 45	0.13 < 0.1 (0.02) < 0.1 (0.02) < 0.1 (0.02)		R9522/3

[a]. mean of six orange samples; [b]. pooled peel

Pome fruits

Fifty three residue trials were conducted in apples in Europe between 1991 and 2001 (Table 14) and 25 trials were conducted in pears in Italy in 1993 and 1994 (Table 15). In the Italian trials, conducted in 1990 (trials AC01 to AC08), recoveries on method validation at the LOQ ranged from 52.1-74.5% for pears and from 40.2 to 72.1% for apples. Only a summary of the method validation was presented.

Table 14. Residues of cyhexatin in treated apples.

Country, Year (variety) location	Application					PHI, Days	Cyhexatin, mg/kg	DCTO, mg/kg	Ref...
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
France, 1991, (golden delicious)	WP	0.125	0.03	415	1	10 21 30	0.17 0.10 0.03	-	E5435
France, 1992, (starkingson)	-	0.39	0.08	500	2	0 7 14 21 29	0.54 0.29 0.14 < 0.05 < 0.05	-	7378
France, 1992, (Granny smith)	-	0.24	0.06	400	2	0 control 7 14 21 30 control	0.42 0.20 0.19 0.16 0.27 0.12 0.10	-	7380
France, 1992, (golden delicious)	-	0.27	0.09 0.06	288 414	2	0 control 7 14 21 30 control	0.49 0.19 0.26 0.41 0.13 0.14 0.11	-	7382
France, 1993, (Oregon)	-	0.39	0.03	500	1	60	< 0.05	-	8288
(Granny smith)	-	0.30	0.06	500	1	32	< 0.05	-	8290
(starking)	-	0.41	0.09	420	1	89 control	0.08 0.08	-	8292
France, 1993 Domaine d'Auroux	WP	0.3	0.03	1000	2	30	0.03	0.01	CTF/1/2F/A
	EC	0.3	0.03	1000	2	30	0.04	< 0.01	
	EC	0.6	0.06	1000	2	30	0.09	0.02	
France, 1993 Route de Mercey	WP	0.3	0.03	1000	2	30	0.06	< 0.01	CTF/1/1F/A
	EC	0.3	0.03	1000	2	30	0.08	< 0.01	
France, 1994 Domaine D'Auroux	WP	0.3	0.03	1000	2	31	0.03	0.01	CTF2/1F/A[a]
	EC	0.3	0.03	1000	2	31	0.04	0.01	
	EC	0.6	0.06	1000	2	31	0.12	0.02	
France, 1994 Route de Mercey	WP	0.3	0.03	1000	2	0 3 7 14 21 28 34	0.19 0.15 0.13 0.12 0.10 0.06 0.05	< 0.01 0.01 0.02 0.02 0.01 0.01 < 0.01	CTF2/2F/A[a]
France, 2000, (golden delicious)	WP	0.3	-	1000	1	29	0.04	< 0.01	003602-01
	WP	0.6	-	1000	1	29	0.05	0.01	
	WP	0.3	-	1000	1	0 3 10 15 30	0.35 0.26 0.10 0.08 0.06	0.01 0.01 0.01 0.01 < 0.01	003602-03
	WP	0.6	-	1000	1	0 3 10 14 30	0.93 0.38 0.25 0.25 0.10	0.03 0.02 0.02 0.02 < 0.01	
France, 2001, (braeburn)	WP	0.3	-	1000	1	0 3 7 14 30	0.29 0.22 0.20 0.16 0.11	< 0.01 < 0.01 0.01 0.01 0.01	013602-01

Country, Year (variety) location	Application					PHI, Days	Cyhexatin, mg/kg	DCTO, mg/kg	Ref...
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
	WP	0.6	-	1000	1	0 3 7 14 30	0.55 0.55 0.52 0.29 0.20	< 0.01 0.02 0.02 0.02 0.03	
France, 2001, (pink lady)	WP	0.3	-	1000	1	30	0.04	< 0.01	013602-02
	WP	0.3	-	1000	1	30	0.08	0.02	
Italy, 1990, (stark red)	EC	0.54	0.03	1800	1	7 14 21 28 35	0.27 0.20 < 0.1 < 0.1 < 0.1	-	AC01-CD
	EC	1.0	0.06	1800	1	7 14 21 28 35	0.58 0.19 0.25 0.25 0.14	-	
Italy, 1990 (cooper)	EC	0.54	0.03	1700	1	0 7 14 21 28 35	0.26 0.18 0.12 < 0.1 < 0.1 < 0.1	-	AC02-CD
	EC	1.0	0.06	1700	1	0 7 14 21 28 35	0.53 0.39 < 0.1 < 0.1 < 0.1 < 0.1	-	
Italy, 1990 (stark red)	EC	0.54	0.03	1800	3	30 35 42	< 0.1 < 0.1 < 0.1	-	AC03-CD
	EC	1	0.06	1800	3	30 35 42	0.15 < 0.1 < 0.1	-	
Italy, 1990 (cooper)	EC	0.52	0.03	1750	3	30 35 42	< 0.1 < 0.1 < 0.1	-	AC04-R1
	EC	1.0	0.06	1750	3	30 35 42	< 0.1 < 0.1 < 0.1	-	
Italy, 1993 Palu	WP	0.3	0.03	1000	2	30	0.02	< 0.01	CTF/1/5I/A
	EC	0.3	0.03	1000	2	30	0.02	< 0.01	
	EC	0.6	0.06	1000	2	30	0.04	0.01	
Italy, 1993 Martino Buon	WP	0.3	0.03	1000	2	30	0.02	< 0.01	CTF/1/6I/A
	EC	0.3	0.03	1000	2	30	0.02	< 0.01	
	EC	0.6	0.06	1000	2	30	0.04	< 0.01	
Italy, 1994 (golden delicious)	WP	0.3	0.03	1000	2	30	0.03	< 0.01	CTF/2/5I/A[a]
	EC	0.3	0.03	1000	2	30	0.02	< 0.01	
	EC	0.6	0.06	1000	2	30	0.02	< 0.01	
Italy, 1994 Palu	WP	0.3	0.03	1000	2	0 3 7 14 21 30	0.14 0.07 0.06 0.06 0.02 0.03	< 0.01 0.02 0.01 0.02 < 0.01 < 0.01	CTF/2/6I/A[a]
	EC	0.3	0.03	1000	2	0 3 7 14 21 30	0.26 0.12 0.09 0.05 0.02 0.02	< 0.01 0.02 0.02 0.01 < 0.01 < 0.01	

Country, Year (variety) location	Application					PHI, Days	Cyhexatin, mg/kg	DCTO, mg/kg	Ref...
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
	EC	0.6	0.06	1000	1	0 3 7 14 21 30	0.64 0.24 0.30 0.10 0.06 0.03	0.01 0.03 0.03 0.02 0.02 0.01	
	EC	1.2	0.12	1000	1	0 3 7 14 21 30	0.53 0.44 0.18 0.18 0.15 0.06	0.01 0.04 0.04 0.04 0.03 0.02	
Netherlands, 1993, (elstar)	EC	0.37	0.04	1000	2	28	0.02	< 0.01	F93223001
	WP	0.37	0.04	1000	2	28	0.02	< 0.01	
	EC	0.25	0.03	1000	2	28	0.03	< 0.01	F93223002
	WP	0.25	0.03	1000	2	28	0.02	< 0.01	
Netherlands, 2000, (jonagold)	WP	0.3	0.03	1000	1	30	0.02	< 0.01	003602
	WP	0.6	0.06	1000	1	30	0.05	< 0.01	
Netherlands, 2001, (elstar)	WP	0.3	0.03	1000	1	0 3 7 14 30	0.16 0.08 0.05 0.03 0.02	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	013602
	WP	0.6	0.06	1000	1	0 3 7 14 30	0.24 0.15 0.14 0.08 0.05	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	

[a] Each residue value represents the average of three analytical samples.

Table 15. Residues of cyhexatin in treated pear.

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
Italy, 1990, (decana del comizio)	EC	0.54	0.03	1800	1	0 6 14 28 35	0.28 < 0.05 < 0.05 < 0.05 < 0.05	-		AC05-CD
	EC	1.1	0.06	1800	1	0 6 14 28 35	0.67 0.49 0.14 < 0.05 < 0.05	-		
Italy, 1990, (abate fetel)	EC	0.54	0.03	1800	1	7 14 21 28 35 42	0.16 < 0.05 < 0.05 < 0.05 < 0.05 < 0.05	-		AC06-CD
	EC	1.1	0.06	1800	1	7 14 21 28 35 42	0.38 0.18 0.07 0.05 < 0.05 < 0.05	-		
Italy, 1990, (decana del comizio)	EC	0.6	0.03	1800	3	30 35 42	0.16 < 0.05 < 0.05	-		AC07-R1

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
Italy, 1990 (abate fetel)	EC	1.1	0.06	1800	3	30 35 42	0.12 < 0.05 < 0.05	-		AC08-R1
	EC	0.6	0.03	1800	3	30 35 42	0.07 < 0.05 < 0.05	-		
Italy, 1993 (kaise allexander) Iesolo	WP	0.3	0.03	1000	2	32	< 0.01	< 0.01	< 0.01	CTF/1/7I/P[a]
	EC	0.3	0.03	1000	2	32	< 0.01	< 0.01	< 0.01	
	EC	0.6	0.06	1000	2	32	0.02	< 0.01	0.02	
Italy, 1993 (decana) B. di Terrazzo	WP	0.3	0.03	1000	2	30	< 0.01	< 0.01	< 0.01	CTF/1/8I/P[a]
	EC	0.3	0.03	1000	2	30	0.01	< 0.01	0.01	
	EC	0.6	0.06	1000	2	30	0.01	< 0.01	0.01	
Italy, 1994 (decana)	WP	0.3	0.03	1000	2	28	0.02	< 0.01	0.02	CTF/2/7I/P[a]
	EC	0.3	0.03	1000	2	28	0.02	< 0.01	0.02	
	EC	0.6	0.06	1000	2	28	0.04	0.01	0.05	
Italy, 1994, (abate fetel)	WP	0.3	0.03	1000	2	0 3 7 14 21 30	0.20 0.11 0.07 0.02 < 0.01 0.02	< 0.01 0.02 0.02 < 0.01 < 0.01 < 0.01	0.20 0.13 0.09 0.02 < 0.01 0.02	CTF/2/8I/P[a]
	EC	0.3	0.03	1000	2	0 3 8 14 21 31	0.23 0.16 0.06 0.02 0.03 < 0.01	0.01 0.02 0.01 < 0.01 < 0.01 < 0.01	0.24 0.18 0.07 0.02 0.03 < 0.01	
	EC	0.6	0.06	1000	1	0 3 7 14 21 30	0.42 0.32 0.15 0.04 0.06 0.03	0.01 0.03 0.03 0.01 0.02 < 0.01	0.43 0.35 0.18 0.05 0.08 0.03	
	EC	1.2	0.12	1000	1	0 3 7 14 21 30	0.90 0.55 0.26 0.16 0.14 0.07	0.02 0.04 0.03 0.04 0.04 < 0.01	0.92 0.58 0.29 0.20 0.18 0.07	
Italy, 1994, (conference)	WP	0.3	0.03	1000	2	30	< 0.01	< 0.01	< 0.01	CTF/2/9I/P[a]
	EC	0.3	0.03	1000	2	30	0.01	< 0.01	0.01	
Italy, 1994 (decana del comizio)	WP	0.3	0.03	1000	2	30	< 0.01	< 0.01	< 0.01	CTF/2/10I/P[a]
	EC	0.3	0.03	1000	2	30	< 0.01	< 0.01	< 0.01	

[a] Each residue value represents the average of three analytical samples.

Grapes

Forty nine trials were conducted in France (31), Italy (11) and Spain (7) on grapes from 1990 to 2002 (Table 16). In the French trials conducted in 1990, the HPLC/UV method was used (LOQ of 0.1 mg/kg) and only cyhexatin was analyzed. In all the other trials, both cyhexatin and DCTO were analyzed, using CG/FPD method (LOQ of 0.01 mg/kg). In all reports, a total or partial method validation was presented.

Table 16. Residues of cyhexatin and dicyclohexyltin oxide (DCTO) in grapes treated with cyhexatin.

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Total, as Cyhexatin, mg/kg	Ref...
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
France, 1990 (grenache)	EC	0.75	0.03	250	1	0 16 23 29	< 0.1 < 0.1 < 0.1 < 0.1			5509
	EC	0.75	0.03	250	1	33	< 0.1			
France, 1990 (riesling)	EC	0.75	0.03	250	1	0 8 15 22	< 0.1 < 0.1 < 0.1 < 0.1			5511
	EC	0.75	0.03	250	1	22	< 0.1			
France, 1990 (carbernet)	EC	0.75	0.03	250	1	0 7 14 21	1.2 0.74 0.20 0.38			5513
	EC	0.75	0.03	250	1	21	1.1			
France, 1993, (chardonnay)	WP	0.3		500	2	30	0.19	0.03	0.22	CTF1943275[a] Site 3F/V
	EC	0.3		500	2	30	0.15	0.02	0.17	
	EC	0.6		500	2	30	0.23	0.03	0.26	
France, 1993, (merlot)	WP	0.3		500	2	30	0.11	0.03	0.14	CTF1943275 Site 4F/V
	EC	0.3		500	2	30	0.12	0.02	0.14	
France, 1994, (chardonnay)	WP	0.3		500	2	30	0.08	0.01	0.09	CTF2C/951652[a] Site 3F/V
	EC	0.3		500	2	30	0.09	0.01	0.10	
	EC	0.6		500	2	30	0.26	0.03	0.29	
France, 1994, (merlot)	WP	0.3		500	2	30	0.06	0.02	0.08	CTF2C/951652 Site 4F/V
	EC	0.3		500	2	30	0.10	0.02	0.12	
France, 1994, (gamay)	WP	0.3		500	2	0 3 7 14 21 27	0.15 0.11 0.08 0.06 0.06 0.06	0.01 0.01 0.02 0.01 0.02 0.02	0.16 0.12 0.10 0.07 0.08 0.08	CTF2C/951652 Site 14F/V
	EC	0.3		500	2	0 3 7 14 21 27	0.25 0.18 0.18 0.16 0.08 0.07	0.02 0.02 0.02 0.02 0.01 0.01	0.27 0.20 0.20 0.18 0.09 0.08	
France, 2000 (chenin)	WP	0.3		500	1	0 3 7 14 30	0.20 0.20 0.17 0.16 0.04	< 0.01 < 0.01 0.01 0.01 0.01	0.20 0.20 0.18 0.17 0.05	003601-01
France, 2000 (cabernet franc)	WP	0.3		500	1	0 3 7 14 29	0.25 0.18 0.19 0.07 0.05	< 0.01 < 0.01 0.01 < 0.01 < 0.01	0.25 0.18 0.20 0.07 0.05	003601-02
France, 2000 (chenin)	WP	0.3		500	1	29	0.17	0.02	0.19	003601-03
France, 2001 (cot)	WP	0.3		500	1	0 3 7 14 28	0.50 0.35 0.30 0.22 0.17	0.01 0.01 0.02 0.02 0.01	0.51 0.36 0.32 0.24 0.18	013601-01
France, 2001 (cabernet franc)	WP	0.3		500	1	29	0.09	< 0.01	0.09	013601-02
France, 2001 (chardonnay)	WP	0.3		500	1	30	0.11	0.01	0.12	013601-03

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO, mg/kg	Total, as Cyhexatin, mg/kg	Ref...
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
France, 2003 (cabernet franc)	WP	0.3		300	1	0 3 7 14 28	1.1 0.55 0.35 0.16 0.15	0.02 0.06 0.04 0.04 0.03	1.1 0.61 0.39 0.20 0.18	033601-01
France, 2003 (chenin)	WP	0.3		300	1	0 3 7 15 28	0.67 0.47 0.33 0.22 0.12	0.02 0.02 0.03 0.03 0.02	0.69 0.49 0.36 0.25 0.14	033601-02
France, 2003 (pinot meunier)	WP	0.3		300	1	29	0.02	< 0.01	0.02	033601-03
Italy, 1993 (merlot)	WP	0.3		500	2	30	0.07	0.03	0.10	CTF1943275[a] Site 9I/V
	EC	0.3		500	2	30	0.09	0.02	0.11	
	EC	0.6		500	2	30	0.25	0.06	0.31	
Italy, 1993 (verduzzo)	WP	0.3		500	2	30	0.04	0.02	0.06	CTF1943275 Site 10I/V
	EC	0.3		500	2	30	0.07	0.02	0.09	
Italy, 1994 (merlot)	WP	0.3		500	2	0 3 7 14 21 29	0.18 0.16 0.12 0.03 0.03 0.02	< 0.01 0.01 0.03 0.01 0.01 < 0.01	0.18 0.17 0.15 0.04 0.04 0.02	CTF2C/951652 Site 11I/V
	EC	0.3		500	2	0 3 7 14 21 29	0.21 0.18 0.11 0.06 0.03 0.02	< 0.01 0.02 0.02 0.02 0.01 < 0.01	0.21 0.20 0.13 0.08 0.04 0.02	
	EC	0.6		500	2	0 3 7 14 21 29	0.54 0.39 0.33 0.12 0.09 0.07	0.02 0.03 0.05 0.03 0.03 0.03	0.56 0.42 0.38 0.15 0.12 0.10	
Italy, 1994 (verduzzo)	WP	0.3		500	2	29	0.07	0.02	0.09	CTF2C/951652 Site 12I/V
	EC	0.3		500	2	29	0.09	0.02	0.11	
Italy, 2002	WP	0.3		800	1	30	0.11	0.02	0.13	SIP 1307
Spain, 1993 (bobal)	WP	0.3		500	2	30	0.05	0.01	0.06	CTF1943275[a] Site 11I/V
	EC	0.3		500	2	30	0.08	0.02	0.10	
	EC	0.3		500	1	30	0.02	< 0.01	0.02	
Spain, 1994 (bobal)	WP	0.3		500	2	30	0.14	0.03	0.17	CTF2C/951652 Site 13S/V
	EC	0.3		500	2	30	0.06	0.02	0.08	
	EC	0.3		500	2	62	0.02	< 0.01	0.02	
Spain, 2001 (moecatel romana)	WP	0.3		800	1	0 3 7 14 30	0.60 0.34 0.23 0.20 0.12	0.02 0.02 0.02 0.02 < 0.01	0.62 0.36 0.25 0.22 0.12	SIP1307

[a] residues are the mean of 2 analytical samples

Stone fruits

Studies were conducted on peaches (Table 17) and plums (Table 18) in France and in Italy. In the Italian trials conducted on peach, the HPLC/UV method was used (LOQ of 0.1 mg/kg) and analyzed only for cyhexatin. Recovery test was not reported but LOQ was stated as being 0.05 mg/kg. In all French trials, analysis for both cyhexatin and DCTO was done using the CG/FPD method (LOQ of 0.01 mg/kg); a total or partial method validation was presented.

Table 17. Residues of cyhexatin and dicyclohexyltin oxide (DCTO) in peaches treated with cyhexatin.

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
France, 1994 (red haven)	EC 1	0.45	0.075	600	1	0 14 28	1.1 0.34 0.08	0.04 0.05 0.01	1.2 0.39 0.09	SIC 7a 9257
	EC 2	0.45	0.075	600	1	0 14 28	1.3 0.29 0.04	0.03 0.04 < 0.01	1.3 0.33 0.04	
France, 1994 (flavour crest)	EC 1	0.45	0.075	600	1	0 14 28	0.96 0.18 0.04	0.03 0.02 < 0.01	0.99 0.20 0.04	SIC 7a 9259
	EC 2	0.45	0.075	600	1	0 14 28	0.99 0.17 0.12	0.03 0.02 0.02	0.12 0.19 0.14	
France, 1994 (red wing)	EC 1	0.45	0.075	600	1	0 14 28	0.38 0.04 0.03	< 0.01 < 0.01 < 0.01	0.38 0.04 0.03	SIC 7a 9260
	EC 2	0.45	0.075	600	1	0 14 28	0.40 0.03 0.04	0.01 0.01 < 0.01	0.40 0.04 0.04	
France, 1994 (dolores)	EC 1	0.45	0.075	600	1	0 14 28	1.1 0.19 0.12	0.05 0.05 0.01	1.6 0.24 0.13	SIC 7a 9261
	EC 2	0.45	0.075	600	1	0 14 28	0.76 0.23 0.08	0.05 0.03 0.02	0.81 0.25 0.10	
France, 1994, (spring crest)	EC 1	0.45	0.075	600	1	0 14 28	1.38 0.21 0.10	0.03 0.04 0.02	1.4 0.25 0.12	SIC 7a 9262
	EC 2	0.45	0.075	600	1	0 14 28	1.2 0.25 0.08	0.03 0.04 0.02	1.2 0.29 0.10	
Italy, 1990, (july lady)	EC	0.57	0.03	1900	1	0 7 14 27 34	1.1 0.82 0.19 <u>0.09</u> 0.10			AC15-CD
	EC	1.14	0.06	1900	1	0 7 14 27 34	1.4 0.96 0.44 0.24 0.16			
Italy, 1990, (july lady)	EC	0.57	0.03	1900	1	14 27 34	0.17 <u>0.21</u> 0.13			AC16-R1
	EC	1.14	0.06	1900	1	14 27 34	0.36 0.36 0.19			
Italy, 1990, (july lady)	EC	0.6	0.03	2000	1	14 27 34	0.38 <u>0.41</u> 0.42			AC17-R2
	EC	1.2	0.06	2000	1	14 27 34	0.87 0.40 1.0			

EC 1 =600g ai/L; EC 2 = 400 g ai/L

Table 18. Residues of cyhexatin and dicyclohexyltin oxide (DCTO) in plums treated with cyhexatin.

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
France, 1994, (prune d'ente)	EC 1	0.45	0.09	500	1	0 14 28	0.41 0.12 0.05	0.01 0.02 0.01	0.42 0.14 0.06	SIC 7b 9251
	EC 2	0.45	0.09	500	1	0 14 28	0.21 0.18 0.04	0.01 0.03 < 0.01	0.22 0.21 0.04	
	EC 1	0.45	0.09	500	1	0 14 28	0.12 0.06 0.01	0.01 0.01 < 0.01	0.13 0.07 0.0	SIC 7b 9253
	EC 2	0.45	0.09	500	1	0 14 28	0.08 0.02 0.01	< 0.01 < 0.01 < 0.01	0.08 0.02 0.01	
	EC 1	0.45	0.09	500	1	0 14 28	0.72 0.39 0.11	0.02 0.07 0.03	0.74 0.46 0.14	SIC 7b 9255
	EC 2	0.45	0.09	500	1	0 14 28	0.86 0.26 0.12	0.03 0.04 0.02	0.89 0.30 0.14	

EC 1 =600g ai/L; EC 2 = 400 g ai/L

Blackcurrant

Three trials were conducted in France in 1995/96 (Table 19). Residues of cyhexatin were determined by either GC/S-FPD or GC/MS. Method validation was presented in separate reports (Reports R6139 and RF 5108).

Table 19. Residues of cyhexatin in blackcurrant in France.

Application					PHI, days	Cyhexatin, mg/kg	Ref.
Form	kg ai/ha	kg ai/hL	water, L/ha	no.			
EC	0.3		600	1	21 28	< 0.05 < 0.05	RCASS195/77
EC	0.3		600	1	0 7 14 21 30	0.94 0.17 0.11 0.08 < 0.05	RCASS196/11
EC	0.3		600	1	30	0.05	RCASS196/12

Hops

Supervised trials were conducted in hops in the United Kingdom. The samples were harvested and placed in a hop kiln for 16 hours before analysis by the CG/FPD method for cyhexatin and DCTO residues (Table 20).

Table 20. Residues of cyhexatin and DCTO in dried hops.

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
United kingdom, 1994 (RH40)	WP	0.6	0.03	2000	3	0 7 14 28	20 10 6.0 2.6	2.5 2.2 1.6 1.5	23 12 7.6 4.1	PWT113 136 HOP/1
	EC	0.6	0.03	2000	3	0 7 14 28	29 8.4 3.1 3.2	4.3 1.8 0.8 1.7	31 10 3.9 4.9	
United kingdom, 1994 (Target)	WP	0.6	0.03	2000	3	0 7 14 28	24 19 8.2 3.5	2.8 2.5 2.0 1.8	27 22 10 5.3	PWT113 136/HOP/2
	EC	0.6	0.03	2000	3	0 7 14 28	34 19 14 6.2	5.1 4.0 2.9 3.4	39 23 17 9.6	
United kingdom, 1994 (Target)	WP	0.6	0.03	2000	3	0 7 14 28	16 7.6 4.2 1.7	2.6 1.4 1.1 0.96	19 9.0 5.3 8.7	PWT113 136/HOP/3
	EC	0.6	0.03	2000	3	0 7 14 28	16 14 6.3 2.2	2.6 2.3 1.7 1.3	19 17 9.0 4.5	
United kingdom, 1994 (Challenger)	WP	0.6	0.03	2000	3	0 7 14 28	18 12 6.1 1.7	1.5 2.2 1.9 1.2	20 14 8.0 2.9	PWT113 136/HOP/4
	EC	0.6	0.03	2000	3	0 7 14 28	31 19 9.8 2.0	2.6 2.6 2.4 1.3	34 22 12 3.3	
Germany, 1985, (northern brewer)	EC	0.72-1.08	0.036	2000-3000	4	7 12 15	41 24 20	22 17 13	63 41 33	GHE-P1691, RT159(A)
Germany, 1985, (huller)	EC	0.72-1.08	0.036	2000-3000	4	7 12 15	17 7.2 2.8	4.3 2.4 1.3	21 9.6 4.1	GHE-P1691, RT160(A)
Germany, 1985, (perle)	EC	0.96	0.024	4000	4	7 10 14	12 16 17	6.4 7.3 11	18 23 28	GHE-P1691, RT178(C)
Germany, 1985, (hallertauer mittelfraue)	EC	0.96	0.024	4000	4	7 10 14	34 28 22	8.7 9.7 7.6	43 38 30	GHE-P1691, RT178(A)
Germany, 1985, (perle)	EC	0.96	0.024	4000	2	7 10 14	20 26 23	8.7 11 11	29 37 34	GHE-P1691, RT178(B)
Germany, 1985, (northern brewer)	WG	0.72-1.08	0.036	2000-3000	4	7 12 15	36.7 28.8 28.7	16 18 44	53 47 73	GHE-P1692, RT159(B)
Germany, 1985, (huller)	WG	0.72-1.08	0.036	2000-3000	4	7 12 15	40.4 15.4 12.6	12 4.7 6.0	52 20 19	GHE-P1692, RT160(B)
Germany, 1985, (tettnanger fruhhopfer)	WG	0.6-0.96	0.024	2500-4000	4	7 10 14	30.2 24.2 34.1	12 7.7 7.9	42 31 42	GHE-P1692, RT192
Germany, 1985, (hallertauer mittelfraue)	WG	0.96	0.024	4000	4	7 10 14	67.2 63.5 48.3	21 16 15	88 80 63	GHE-P1692, RT178(E)

Country, Year (variety)	Application					PHI, days	Cyhexatin, mg/kg	DCTO mg/kg	Total, as cyhexatin, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.					
Germany, 1985, (perle)	WG	0.96	0.024	4000	4	7 10 14	68.1 69.5 35.4	13 25 25	81 95 60	GHE-P1692, RT178(F)
Germany, 1985, (perle)	WG	0.96	0.024	4000	2	7 10 14	58.2 51.5 32.4	14 19 17	72 71 49	GHE-P1692, RT178(D)

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

Citrus

Nineteen processing studies were conducted in oranges treated with cyhexatin (0.025 or 0.50 kg ai/ha). The samples were washed and processed, according to commercial practice, to juice (fresh, pasteurized and concentrated), peel, peel oil, dry pulp and molasses.

No residues of cyhexatin or DCTO were found in any of fresh or pasteurized juice samples (< 0.01 mg/kg). Residues in the concentrated juice were all < 0.1 mg/kg.

No residues of DCTO were found in the peel (< 0.01 mg/kg) and residues of cyhexatin in the peel were always lower than in the whole fruit (PF from < 0.3 to 0.4). In four trials, analysis of molasses was undertaken. Residues of cyhexatin were at or below the LOQ (PF of < 0.5 to 0.2), and no residues of DCTO were detected. Residues of cyhexatin concentrated in dried pulp and in peel oil. Details of the trials are shown on Table 21.

Table 21. Residues in orange and processing products (Report No OXN 152/972905 and OXN 27/961612.

Orange, RAC		Peel		Dried pulp				peel oil			
Cy, mg/kg	DCTO, mg/kg	Cy, mg/kg	PF	Cy, mg/kg	PF	DCTO, mg/kg	PF	Cy, mg/kg	PF	DCTO, mg/kg	PF
0.03	0.01	0.01	0.3	0.04	1.3	< 0.02	<2.0	2.9	97	0.33	33
0.05	0.03	0.01	0.2	0.07	1.4	< 0.02	< 0.7	3.7	74	0.59	20
0.17	0.05	0.03	0.2	0.1	0.6	0.02	0.4	9.1	54	1.6	32
0.16	0.07	0.03	0.2	0.16	1.0	0.05	0.7	13.8	86	3.1	44
0.04	0.01	< 0.01	< 0.3	0.04	1.0	< 0.02	<2.0	4.1	102	0.24	24
0.03	0.01	< 0.01	< 0.3	0.21	7.0	0.03	3.0	2.6	86	0.22	22
0.07	0.02	0.02	0.3	0.08	1.1	< 0.02	<1.0	6.3	90	0.83	42
0.1	0.03	0.03	0.3	0.09	0.9	0.02	0.7	7.7	77	2.5	83
0.13	0.03	0.05	0.4	0.04	0.3	< 0.02	< 0.7	17.8	137	2.8	93
0.23	0.08	0.08	0.3	0.26	1.1	0.05	0.6	33	144	7.7	96
0.15	0.04	0.04	0.3	0.19	1.3	0.03	0.8	18.5	123	3.6	90
0.12	0.05	0.04	0.3	0.18	1.5	0.03	0.6	13.9	116	3.1	62
0.02	0.01	< 0.01	< 0.5	0.05	2.5	< 0.02	<2.0	2.1	107	0.59	59
0.09	0.04	0.03	0.3	0.1	1.1	0.02	0.5	8.4	93	1.6	41
0.11	0.07	0.03	0.3	0.13	1.2	0.03	0.4	9.6	87	2.7	38
0.02	< 0.01	< 0.01	-	0.03	1.5	< 0.02	-	2.9	148	0.6	>60

Orange, RAC		Peel		Dried pulp				peel oil			
Cy, mg/kg	DCTO, mg/kg	Cy, mg/kg	PF	Cy, mg/kg	PF	DCTO, mg/kg	PF	Cy, mg/kg	PF	DCTO, mg/kg	PF
0.02	0.02	< 0.01	0.5	0.04	2	< 0.02	1.0	2.4	119	0.71	36
0.05	0.02	< 0.01	0.2	0.08	1.6	< 0.02	1.0	5.0	100	1.2	60
0.06	0.04	< 0.01	0.2	0.08	1.3	0.03	0.8	6.3	104	2.1	53

Apples

Twenty three processing studies were conducted in apples (Reports CTF 1E/942670 and CTF/2B/951488). Treated samples were crushed with an electric crusher and then pressed to produce juice and wet pomace, which was oven dried to provide dried pomace. Pectolytic enzymes (0.04%) were added to the apple juice and the juice was left to settle for at least 12 hours, decanted, filtered and heated to approximately 88–90 ^{o}C.

None of the juice samples analysed had detectable residues of cyhexatin or DCTO. The residues in the treated apple (RAC), wet pomace and dry pomace and the respective calculated processing factor (PF) are shown on Table 22. Residues of cyhexatin and DCTO concentrated in wet pomace but decreased in the dry pomace in the majority of samples analysed.

Table 22. Apple juice processing residues.

Apple, RAC		Wet pomace				Dry pomace			
Cy, mg/kg	DCTO, mg/kg	Cy, mg/kg	PF	DCTO, mg/kg	PF	Cy, mg/kg	PF	DCTO, mg/kg	PF
0.03	< 0.01	0.08	2.7	0.03	>3	0.04	1.3	< 0.01	-
0.06	< 0.01	0.08	1.3	0.02	>2	0.02	0.3	< 0.01	-
0.09	0.02	0.15	1.7	0.04	2.0	0.13	1.4	0.01	0.5
0.06	< 0.01	0.1	1.7	< 0.01	-	0.03	0.5	< 0.01	-
0.1	< 0.01	0.16	1.6	< 0.01	-	0.03	0.3	< 0.01	-
< 0.01	< 0.01	0.05	>5	0.02	>2	0.03	>3	< 0.01	-
0.02	< 0.01	0.05	2.5	0.02	>2	0.04	2.0	< 0.01	-
0.03	0.01	0.1	3.3	0.02	2.0	0.12	4.0	0.02	2.0
0.02	< 0.01	0.05	2.5	0.02	>2	< 0.01	< 0.05	< 0.01	-
0.03	< 0.01	0.05	1.7	0.02	>2	< 0.01	< 0.03	< 0.01	-
0.05	0.01	0.11	2.2	0.03	3.0	0.01	0.2	< 0.01	<1
0.03	0.01	0.05	1.7	0.03	3.0				
0.04	0.01	0.05	1.3	0.03	3.0				
0.12	0.02	0.16	1.3	0.07	3.5				
0.05	< 0.01	0.11	2.2	0.01	>1				
0.12	< 0.01	0.22	1.8	0.02	>2				
0.03	< 0.01	0.04	1.3	0.02	>2				
0.03	< 0.01	0.06	2.0	0.02	>2				
0.02	< 0.01	0.14	7.0	0.05	>5				
0.03	< 0.01	0.03	1.0	0.01	>1				
0.02	< 0.01	0.03	1.5	0.01	>1				
0.03	0.01	0.05	1.7	0.02	2.0				
0.06	0.02	0.09	1.5	0.03	1.5				

Grapes

Twenty eight processing trials were conducted in grapes (Reports CTF1F/943275 and CTF 2C/951652). The treated samples (0.3 kg ai/ha, 30 days PHI) were pressed with a manual hydraulic press and a sample of wet pomace was taken to be oven dried to provide dried pomace. The must was decanted for at least 12 hours with the addition of pectolytic enzymes and potassium metabisulphite. The clear must was then fermented to produce wine, simulating commercial practice. For the production of grape juice, the treated grapes were manually crushed. To obtain raisins, the treated grapes were placed in an oven and allowed to dry for at least 3 days at 60 ^{o}C. Samples of treated grapes, must, wet and dry pomace, juice, wine and raisins were analyzed for cyhexatin. Residues of cyhexatin were found to concentrate in all samples of wet and dry pomace, and in some samples of raisins. Residues decreased in juice and wine (Table 23).

Hops

Dried hops samples from 3 trials conducted in 1994 in the United Kingdom (0.6 kg ai/ha, 7 days PHI) were processed to beer and residues analyzed for cyhexatin and DCTO. No details of the brewing process were given in the report. Residues of cyhexatin in dried hops were 7.9, 13.5 and 18.2 mg/kg and for DCTO they were 1.9, 2.3 and 3.7 mg/kg. No residue of any compound was found in the beer.

Table 23. Residues of cyhexatin in grapes and processed products and processing factors (PF).

Grapes,	Wet pomace		dry pomace		Raisin		Juice		Wine	
mg/kg	mg/kg	PF	mg/kg	PF	mg/kg	PF	mg/kg	PF	mg/kg	PF
0.19	0.24	1.3	0.31	1.6	0.13	0.7	0.14	0.7	0.07	0.3
0.15	0.29	1.9	0.37	2.5	0.13	0.9	-	-	0.18	1.0
0.22	0.50	2.3	0.73	3.3	0.35	1.6	0.29	1.3	0.29	1.3
0.11	0.25	2.3	0.43	3.9	0.09	0.8	0.09	0.8	0.09	0.7
0.12	0.36	3.0	0.48	4.0	0.11	0.9	0.01	0.1	0.12	0.5
0.07	0.15	2.1	0.41	5.9	0.06	0.9	0.05	0.7	0.07	0.7
0.09	0.20	2.2	0.42	4.7	0.06	0.7	0.07	0.8	0.1	1.0
0.25	0.68	2.7	1.96	7.8	0.17	0.7	0.27	1.1	0.19	0.7
0.04	0.10	2.5	0.33	8.3	0.07	1.8	0.04	1.0	0.04	0.5
0.07	0.11	1.6	0.31	4.4	0.10	1.4	0.05	0.7	0.04	0.5
0.05	0.17	3.4	0.29	5.8	0.04	0.8	0.04	0.8	0.06	1.0
0.02	0.05	2.5	0.06	3.0	0.02	1.0	0.07	0.9	0.04	0.5
0.08	0.14	1.8	0.40	5.0	0.11	1.4	0.02	1.0	0.01	-
0.08	0.26	3.3	0.49	6.1	0.02	0.3	< 0.01	< 0.1	< 0.01	< 0.1
0.10	0.16	1.6	0.58	5.8	0.20	2.0	< 0.01	< 0.0	< 0.01	< 0.0
0.26	0.39	1.5	1.17	4.5	0.43	1.7	< 0.01	< 0.2	< 0.01	< 0.2
0.06	0.35	5.8	0.46	7.7	0.08	1.3	< 0.01	< 0.1	< 0.01	< 0.1
0.10	0.39	3.9	0.57	5.7	0.07	0.7	< 0.01	< 0.5	< 0.01	< 0.5
0.02	0.02	1.0	0.05	2.5	0.01	0.5	< 0.01	< 0.5	< 0.01	< 0.5
0.02	0.02	1.0	0.06	3.0	0.01	0.5	< 0.01	< 0.1	< 0.01	< 0.1
0.08	0.10	1.3	0.10	1.3	0.02	0.3	< 0.01	< 0.1	< 0.01	< 0.1
0.07	0.24	3.4	0.18	2.6	0.06	0.9	< 0.01	< 0.1	< 0.01	< 0.1
0.09	0.32	3.6	0.53	5.9	0.10	1.1	< 0.01	< 0.1	< 0.01	< 0.1

Grapes,	Wet pomace		dry pomace		Raisin		Juice		Wine	
mg/kg	mg/kg	PF	mg/kg	PF	mg/kg	PF	mg/kg	PF	mg/kg	PF
0.14	0.42	3.0	0.53	3.8	0.07	0.5	< 0.01	< 0.5	< 0.01	< 0.5
0.02	0.08	4.0	0.14	7.0	0.02	1.0	< 0.01	< 0.2	< 0.01	< 0.2
0.06	0.23	3.8	0.39	6.5	0.06	1.0	< 0.01	< 0.2	< 0.01	< 0.2
0.06	0.18	3.0	0.31	5.2	0.06	1.0	< 0.01	< 0.1	< 0.01	< 0.1
0.07	0.32	4.6	0.53	7.6	0.12	1.7	< 0.01	< 0.1	< 0.01	< 0.1

APPRAISAL

Azocyclotin and cyhexatin are organotin acaricides effective against phytophagous mites. The compounds have been reviewed by the JMPR many times since 1970, the last residue evaluation of azoccyclotin being in 1991 and of cyhexatin in 1992. In 2005, the Meeting established a group ADI of 0–0.003 mg/kg bw and a group ARfD of 0.02 for women of child-bearing age for cyhexatin and azocyclotin.

At the 22nd Session of CCPR, the Committee decided to harmonize the residue definition of azocyclotin and cyhexatin as the sum of both compounds, expressed as cyhexatin. The Committee also decided to have two separate but identical lists of CXLs. At the 33rd Session of CCPR, all CXLs were withdrawn, with the exception of apple, citrus fruits, grapes, meat (from mammals other than marine mammals), milk products, milks and pear for cyhexatin, and citrus fruits, grapes, meat (from mammals other than marine mammals), milk products and milks for azocyclotin. The compounds were listed in the Periodic Re-Evaluation Programme at the 36th Session of CCPR for periodic review by the 2005 JMPR.

The present meeting received and evaluated information on the identity and physical chemical properties of the compounds, metabolism in farm animals and plants, methods of residue analysis and freezer storage stability for cyhexatin, national use patterns, supervised residue trials and processing studies.

Animal metabolism

Three metabolism studies conducted in farm animals were submitted. One study was conducted in dairy cows dosed with cyclohexyl UL-^{14}C-azocyclotin (gelatin capsule with β lactose) for 5 consecutive days at a rate of 0.5 mg/kg bw. Kidney, liver, heart, brain, muscle, omental, renal and back fat samples were excised and analysed. More than 98% of the radioactivity present in the tissues was extracted. Liver, kidney and heart contained the greatest radioactive residues (0.34, 0.25 and 0.12 mg/kg azocyclotin equivalents (eq.), respectively). Muscle, fat and brain contained 0.09, 0.10 and 0.04 mg/kg azocyclotin eq, respectively. Milk collected once or twice a day during the dosing period, reached a maximum residue level at day 4 (0.02 mg/kg azocyclotin eq). Most of the extracted radioactivity (43% TRR in fat, 84% in muscle, and 92% in milk) was assigned as azocyclotin/cyhexatin, as it was stated that no distinction could be made between the compounds in the TLC plate. No cyhexatin standard was, however, applied to the TLC. Dicyclohexyl tin oxide (DCTO) was responsible for up to 23% TRR in fat and up to 15% in loin muscle. From 4% TRR (milk) to 33% (fat) was identified as cyclohexyl stannoic acid (MCTA), which was not detected in heart or muscle.

One study conducted in two lactating goats dosed with ^{119}Sn-cyhexatin for 4 days at 100 ppm in the feed was submitted. On average, 68.5% of the administered radioactivity was recovered from the animals, from which 44% was found in the faeces, 24% in the gastrointestinal (GI) tract and 0.15% in the liver (mean of 1.1 mg/kg cyhexatin eq). Less than 0.1% was found in the other tissues and milk, corresponding, on average, to 0.56 mg/kg cyhexatin eq. in kidney, 0.08 mg/kg cyhexatin eq

in muscle and up to 0.02 mg/kg eq in milk. Most of the radioactivity found in tissues was cyhexatin (from 70 to 84% TRR in the organic extract), with less than 10% of DCTO and MCTA. Only the parent compound was found in milk.

In one study conducted with laying hens (two groups of six) dosed with ^{119}Sn-cyhexatin for 5 days at 100 ppm in the feed, most of the administered radioactivity (mean of 66.3%) was found in the excreta (63.5%). Liver and kidney had the highest residues (mean of 3.0 and 2.8 mg/kg cyhexatin eq., respectively), followed by muscle (mean of 0.42 mg/kg cyhexatin eq.) and fat (0.36 mg/kg cyhexatin eq.). Residues in eggs increased during the dose period and were concentrated in the yolk. On day 2, mean residues in the yolk were 0.2 mg/kg cyhexatin eq. and in egg white, 0.055 mg/kg. On day 5, residues reached 3.6 and 0.22 mg/kg cyhexatin eq in yolk and white respectively. The organic tissue extracts showed mostly cyhexatin (up to 50% TRR), DCTO (up to 30% TRR) and MCTA (up to 16% TRR). Egg white contained less than 10% TRR of cyhexatin, while only the parent compound was found in the yolk.

Metabolism studies conducted in rats with cyhexatin and azocyclotin and evaluated by the present Meeting (Toxicological evaluation) showed a similar metabolic pathway described for farm animals.

Plant metabolism

Three studies conducted in plants were submitted. Apples, treated with cyclohexyl UL-^{14}C-azocyclotin applied at a rate of 0.03 kg ai/hL, had most of the applied radioactivity in the organic fraction of the acetone wash of the fruits (from 96% at day 0 to 29% at day 21). On average, 78% TRR was azocyclotin/cyhexatin, 9% DCTO and 2% MCTA. On day 21, 11% of the applied radioactivity was found in the peel and < 1% in the pulp. Only 70% TRR found in the peel was characterized, being approximately 9% azocyclotin/cyhexatin and 27% DCTO and MCTA (11% stayed at the TLC origin and 17% remained in the aqueous phase).

In one study conducted with ^{119}Sn cyhexatin on apples at 3.8 kg ai/ha rate, the applied radioactivity was recovered after successive extractions with water, HCl and organic solvents. Most of the radioactivity at 14 days PHI was found in the peel (96% TRR) and whole fruit contained 4% TRR. Peel organic extracts showed approximately 45% TRR as cyhexatin, 25% as inorganic tin, 14% as MCTA and 12% as DCTO.

In one study conducted in grapes treated with U-^{14}C-cyhexatin at 0.3 kg ai./ha, a mean of 86% TRR was found on the fruit surface and 14% in the grape homogenate (acid methanol extraction) at 10 or 28 days after application. Cyhexatin accounted for 77.6 and 59% TRR in the grape surface after 10 and 28 days, respectively, while DCTO accounted for 7.7 and 14.8%. In the fruit homogenate, only cyhexatin was detected (5% TRR).

In summary, the metabolism of azocyclotin and cyhexatin in animal and plants appears to be similar, and occurs through the loss of the triazole moiety (from azocyclotin) to produce cyhexatin, with subsequent hydrolysis of the cyclohexyl ring to yield DCTO and MCTA.

Environmental fate

One hydrolysis study was conducted in water with [triazole-3,5-^{14}C]azocyclotin and [cyclohexyl-UL-^{14}C]azocyclotin, at a concentration of about 30 µg ai./L in 0.01 M buffer solutions at pH 4, 7 and 9 and in drinking water. The buffer solutions were incubated for 10, 30, and 60 minutes under sterile conditions and the drinking water solution for 10 minutes in the dark at 20°C. Azocyclotin was completely hydrolysed within 10 minutes ($DT_{90} \leq 10$ minutes), and cyhexatin and 1,2, 4 triazole were the degradation products identified.

Degradation studies with cyhexatin in soil, field dissipation studies, adsorption/desorption studies in soil and degradation studies in water/sediment system were provided to the Meeting. However, these studies are not relevant to the present evaluation.

Method of analysis

As only cyhexatin and DCTO residues are detected in plants treated with azocyclotin, no analytical method to analyse azocyclotin was submitted.

Complete method validation studies to analyse residues of cyhexatin and DCTO in various crops were submitted. The methodology involves extraction with a mixture of hexane and ethyl acetate in the presence of acetic acid and water, followed by methylation with methyl magnesium chloride to form tricyclohexylmethyltin (TCMT) from cyhexatin and dicyclohexyldimethyltin (DCMT) from DCTO. The extract with the methylated compounds was cleaned-up with florisil, and quantification was performed by gas chromatography with flame photometric detection (GC-FPD) using a sulfur filter or using a tin filter as a primary methodology followed by confirmation using a sulfur filter. No matrix effects were found in the method, regardless of the filter used. The methylated compounds were found to be stable after 7 days stored in the dark at 4^{o}C.

For grapes, oranges, fresh orange juice, peel and molasses, apples, apple pomace (wet) and apple juice, the LOQ for both cyhexatin and DCTO was set at 0.01 mg/kg. The LOQ was 0.02 mg/kg for orange dry pulp, 0.05 mg/kg for apple pomace and 0.10 mg/kg for peel oil and juice concentrate. The limits of detection ranged from 0.005 to 0.013 mg/kg. Recovery at the LOQ level and at 0.1 mg/kg ranged from 71 to 128% for cyhexatin and from 61 to 83% for DCTO.

In some residue trials, a method to analyse only cyhexatin was used. The method involves extraction of the residues with chloroform, clean up with silica gel and quantification by reverse phase HPLC/UV at 215–225 nm. In this methodology, LOQs of 0.05 or 0.1 mg/kg were reported, and recoveries at these levels presented in the trial reports were normally within the 70 to 120% range.

Stability of pesticide residues in stored analytical samples

The stability of stored analytical samples fortified with cyhexatin and DCTO was studied in apples, grapes, raisins and wine. Samples fortified at 0.5 mg/kg were stored up to 12 months at -20^{o} C in the dark. In most cases, residues were stable for up to a year (≥ 70% remained), except for cyhexatin and DCTO in grapes and raisins (approximately 50% remained) and DCTO in apples (62% remained).

Definition of the residue

The hydrolysis study conducted with azocyclotin showed that 90% of this compound degrades to cyhexatin in less than 10 minutes. Therefore, no residues of azocyclotin are expected to be present in the application solution, and consequently, in treated plants. Metabolism studies conducted in animal and plants with azocyclotin and cyhehatin have shown that cyhexatin is the major residue to be found. Residues of the dicyclohexyltin oxide metabolite (DCTO) can be higher than 10% TRR in some cases, but this metabolite is not considered of toxicological concern.

The log P_{ow} of cyhexatin (6.1 at pH 7) suggests that the compound is fat soluble. However, metabolism studies conducted in cows, goats and hens indicated that cyhexatin does not concentrate in fat.

The Meeting agreed that the residue definition for azocyclotin and cyhexatin in plants and animal products for both enforcement and dietary intake assessment purposes is cyhexatin. The residue definition applies to residues coming from the use of azocyclotin and/or cyhexatin.

Results of supervised trials on crops

Orange and clementine

Thirty four trials were conducted with cyhexatin in oranges in Brazil from 1993 to 1995 using 1 or 2 applications at 0.025 or 0.05 kg ai/hL (GAP is 0.025 kg ai/hL). Residues found, of cyhexatin in whole fruit with a 30 day PHI, in 16 trials conducted according to Brazilian GAP were < 0.01, 0.01 (2), 0.02, 0.03 (2), 0.04 (2), 0.05 (4), 0.06 (2) and 0.07 (2) mg/kg. Residues from trials conducted at double rates reached a maximum of 0.18 mg/kg with a 30 day PHI.

In twenty nine trials (see processing studies), residues were also analysed in peel. On average, residues of cyhexatin in the peel at PHI represented 30% of the residues in the whole fruit.

Three trials were conducted in Spain in 1997 with oranges and three with clementines at 0.36 kg ai/ha (GAP is 0.25 to 0.31 kg ai/hL, 15 days PHI). Residues of cyhexatin from trials conducted according to GAP were < 0.1 mg/kg (0.05 mg/kg) in orange and < 0.1 mg/kg (0.02 and 0.07 mg/kg) in clementine. The LOQ was 0.1 mg/kg, but values below the limit of quantification were reported.

Residues of cyhexatin coming from 17 trials conducted according to GAP in Brazil and Spain in orange were < 0.01, 0.01 (2), 0.02, 0.03 (2), 0.04 (2), 0.05 (4), 0.06 (2) and 0.07 (2) and < 0.1 mg/kg. The Meeting estimated a maximum residue level of 0.2 mg/kg for azocyclotin and cyhexatin in oranges. Considering that 70% of cyhexatin residues in oranges are present in the pulp, and the supervised trial median and highest residue in whole fruit were 0.05 mg/kg and 0.07 mg/kg, respectively, the Meeting estimated an STMR of 0.035 mg/kg and an HR of 0.049 mg/kg in orange pulp.

The Meeting also recommends the withdrawal of the current MRL of 2 mg/kg for azocyclotin and cyhexatin in citrus fruit. The numbers of trials conducted in clementines, according to GAP, were not considered sufficient to make any recommendation for this commodity.

Apple and pears

Eight trials were conducted with azocyclotin in apples. In one trial conducted in Brazil (GAP of a maximum of 2 applications at 0.02 to 0.025 kg ai/hL, 30 day PHI) residues of cyhexatin at the 30 day PHI were 0.16 mg/kg. One trial was conducted in Chile (no GAP) and six in Israel. Although azocyclotin is registered in Israel, the trials conducted in this country could not be evaluated as a translated label was not submitted.

Fifty three trials were conducted with cyhexatin in apples in Europe from 1991 to 2001, of which 24 were in France, 21 in Italy and eight in the Netherlands. In 13 trials conducted in France at GAP (0.03 kg ai/hL), residues of cyhexatin at a 30 day PHI were 0.03 (3), 0.04 (4), 0.06 (3), 0.08 (2) and 0.11 mg/kg. In 12 trials conducted at the same GAP in Italy, residues at the 30 day PHI were < 0.1 (4), 0.02 (6) and 0.03 (2) mg/kg.

In six trials conducted in the Netherlands according to Italian and French GAP, residues at the 30 day PHI were 0.02 (5) and 0.03 mg/kg. Currently, there is no GAP for cyhexatin in apple in the Netherlands.

Twenty trials were conducted with cyhexatin in pears in Italy. In 16 trials conducted according to GAP (0.03 kg ai/hL), residues at 30 a day PHI were, < 0.01 (7), < 0.05 (2), 0.01 (2) and 0.02 (3) 0.07 and 0.16 mg/kg.

The Meeting agreed that residues of cyhexatin from the 48 trials conducted according to GAP (apple and pears conducted with cyhexatin in Europe and one trial conducted with azocyclotin in apples in Brazil) can be grouped together as reflecting the use of cyhexatin and azocyclotin. They were, in ranked order < 0.01 (7), 0.01 (2), 0.02 (14), 0.03 (6), 0.04 (4), < 0.05 (2), 0.06 (3), 0.07, 0.08 (2), < 0.1 (4), 0.11 and 0.16 (2) mg/kg.

The Meeting recommended a maximum residue level of 0.2 mg/kg for azocyclotin and cyhexatin in apples and pears. The Meeting also estimated an STMR of 0.025 mg/kg and an HR of 0.16 mg/kg.

The Meeting recommended withdrawal of the current MRLs of 2 mg/kg for cyhexatin in apples and pears.

Grapes

Forty nine trials were conducted with cyhexatin in France (31), Italy (11) and Spain (7) on grapes from 1990 to 2002. GAP rate in France and Spain is similar (0.3 kg ai/ha). In 19 trials conducted at 0.3 kg ai/ha in France, residues of cyhexatin within 30 days PHI were, in rank order, 0.02, 0.04, 0.05, 0.06 (2), 0.07, 0.08, 0.09 (2), 0.10, 0.11 (2), 0.12 (2), 0.15 (2), 0.17 (2) and 0.19, mg/kg. In Spain, residues in the 6 trials conducted according to GAP were 0.02, 0.05, 0.06, 0.08, 0.12 and 0.14 mg/kg.

Cyhexatin is not registered in Italy, but the trials conducted in this country were evaluated against the Spanish GAP. Eleven trials conducted at GAP gave residues at a 30 day PHI of 0.02 (2), 0.04, 0.05, 0.07 (3), 0.08, 0.09 (2) and 0.11 mg/kg

Residues of cyhexatin from 36 trials conducted in Europe according to GAP were grouped as 0.02 (4), 0.04 (2), 0.05 (3), 0.06 (3), 0.07 (4), 0.08 (3), 0.09 (4), 0.10, 0.11 (3), 0.12 (3), 0.14, 0.15 (2), 0.17 (2) and 0.19, mg/kg.

The Meeting recommended a maximum residue level of 0.3 mg/kg, an STMR of 0.085 mg/kg and an HR of 0.19 mg/kg for cyhexatin and azocyclotin in grapes.

The Meeting also recommended the withdrawal of the current MRLs of 0.2 mg/kg for cyhexatin and azocyclotin in grapes.

Stone fruit

Sixteen trials were conducted with cyhexatin in peaches in France and Italy and 6 trials were conducted in plums in France at rates of 0.03 to 0.09 kg ai/hL. GAP rate in France is 0.03 kg ai/hL (30 days PHI) and in Spain is 0.025–0.037 kg ai/hL. There is no registered use of cyhexatin on peaches in Italy. In three trials conducted at 0.03 kg ai/hL in peaches in Italy, residues of cyhexatin 27 days after application were 0.09, 0.21 and 0.41 mg/kg. In 10 French trials conducted at 0.075 kg ai/hL in peaches and at 0.09 kg ai/hL in plums, residues reached a maximum of 0.14 mg/kg at the 30 day PHI.

The number of trials conducted according to GAP was not considered sufficient to recommend maximum residue levels for cyhexatin and azocyclotin in peaches or plums.

Currants, red, black, white

Three trials were conducted with blackcurrants according to French GAP (0.3 kg ai/ha, 28 day PHI). Residues of cyhexatin found 30 days after application were < 0.05 (2) and 0.05 mg/kg. The Meeting recommended a maximum residue level of 0.1 mg/kg and an STMR of 0.05 mg/kg for cyhexatin and azocyclotin in currants, red, black, white.

Dried hops

Nineteen trials were conducted in hops in the United Kingdom and Germany at rates from 0.6 to 1.1 kg ai/ha. Residues of cyhexatin ranged from 63 mg/kg (0 days) to 2.9 (28 days). Cyhexatin has no registered use in UK or Germany, nor is this compound registered for dried hops in other countries in Europe. The Meeting made no recommendation for dried hops.

Fate of residues during processing

Nineteen processing studies were conducted in oranges treated with cyhexatin (0.025 or 0.50 kg ai/ha). Residues of cyhexatin in concentrated juice were all < 0.1 mg/kg. No residues were found in any of the fresh or pasteurized juice samples (< 0.01 mg/kg) produced from orange samples containing from 0.02 to 0.23 mg/kg cyhexatin. A processing factor (PF) of 0.04 (0.01/0.23) was applied to an STMR of 0.05 mg/kg in oranges and the Meeting recommended an STMR of 0.002 mg/kg in orange juice.

Residues of cyhexatin in the peel represented, on average, 30% of residues in the whole fruit. In four trials where molasses samples were analysed, residues of cyhexatin were at or below the LOQ.

Residues of cyhexatin concentrated in dried pulp and in peel oil had mean PFs of 1.6 and 102, respectively. Based on the estimates for oranges, the Meeting estimated a median residue of 0.08 mg/kg for citrus dried pulp.

Twenty three processing studies were conducted in apples. Residues in apples ranged from < 0.01 to 0.12 mg/kg, but none of the juice samples analysed had detectable residues of cyhexatin. A PF of 0.08 (0.01/0.12) was applied to an STMR of 0.025 mg/kg for apple, and the Meeting estimated an STMR of 0.002 mg/kg in apple juice.

Residues of cyhexatin concentrated in wet pomace, with PFs ranging from 1 to > 5 (median of 1.7). The Meeting estimated a median residue of 0.272 mg/kg for cyhexatin in wet pomace. The processing factor for dry pomace ranged from < 0.05 to 4.

Twenty eight processing trials were conducted in grapes. Residues decreased in juice and wine, and were not detected in most of the samples. Median PFs were 0.8 and 0.7 for juice and wine, respectively. These PFs were applied to the STMR on grapes of 0.085 mg/kg. The Meeting recommended STMRs of 0.068 mg/kg for juice and of 0.060 mg/kg for wine.

Processing factors for raisins ranged from 0.3 to 2 (median of 0.9). The Meeting recommended an STMR of 0.076 mg/kg for cyhexatin in grapes, dried (= currants, raisins and sultanas).

Residues of cyhexatin concentrated in all samples of wet and dry pomace with a mean PF of 2.6 and 4.8, respectively.

In three processing studies conducted in dried hops, residues of cyhexatin ranged from 1.9 to 18.2 mg/kg, but no residues of any compound were found in beer.

Farm animal dietary burden

The Meeting estimated the dietary burden of cyhexatin coming from the use of azocyclotin and cyhexatin, in cattle and poultry on the basis of the diets listed in Appendix IX of the *FAO Manual* and the highest and median residues estimated at this Meeting.

Table 24. Calculation of the dietary burden for maximum residue level and STMR estimation.

Commodity	Median residue	Group	% DM	Residues dw	*Diet content (%)*			Residue contribution, mg/kg		
					Beef cattle	*Dairy cows*	*Poultry*	Beef cattle	Dairy cows	Poultry
Apple wet pomace	0.04	AB	40	0.067	*40*	*20*	-	0.027		0
Citrus dried pulp	0.08	AB	91	0.08	*20*	*20*	-		0.016	0
				Total	***40***	***20***	**-**	**0.027**	**0.016**	**0**

Farm animal feeding studies

No animal feeding studies were provided to the Meeting. The calculated cyhexatin dietary burden was 0.027 ppm for mammals and 0 ppm for poultry. No registered direct use of azocyclotin or cyhexatin on animals was provided to the Meeting.

Metabolism studies in goats and hens were conducted at a dose of 100 ppm of ^{119}Sn cyhexatin, approximately 3700 times the calculated dietary burden in goats. In these studies, only total radioactivity was quantified in milk and tissues. Residues in goats were 0.02 mg/kg cyhexatin equivalents in milk, 0.13 mg/kg in muscle, 0.91 mg/kg in kidney and 1.83 mg/kg in liver. In the metabolism study conducted with hens, maximum total radioactivity in tissues and eggs was found in liver (3.0 mg/kg cyhexatin equivalents).

The Meeting concluded that no residues of cyhexatin are expected in animal commodities. No recommendations could be made as no analytical methods for animal commodities were submitted to the Meeting.

RECOMMENDATIONS

Residue for compliance with MRLs and estimation of dietary intake in plant and animal commodities: *cyhexatin.*

Table 25. Residue for estimation of dietary intake in plant and animal commodities: cyhexatin.

CCN	Commodity	Recommended MRL, mg/kg		STMR, mg/kg	HR, mg/kg
		New	Previous		
FP 0226	Apple	0.2	2[2/]	0.02	0.11
JF 226	Apple juice			0.008	
FP 0230	Pear	0.2	2[2/]	0.02	0.11
FC 004	Oranges	0.2	2[1/]	0.035	0.049
JF 04	Orange juice			0.002	
FB0269	Grapes	0.3	0.2[1/]	0.085	0.19
DF 0269	Grapes, dried (= currants, raisins and sultanas)			0.076	
JF 269	Grape juice			0.068	
FB 1236	Wine grape			0.060	
FB 21	Currants, red, black, white	0.1		0.05	
MM 0095	Meat (from mammals other than marine mammals)[3/]	W	0.2[1/]		
AO3 0001	Milk products[3]	W	0.05*[1/]		
ML 0106	Milks[3/]	W	0.05*[1/]		

[1]/ azocyclotin and cyhexatin; [2]/ cyhexatin; [3]/ The MRL accommodates external animal treatment.

DIETARY RISK ASSESSMENT

Long-term intake

The 2005 JMPR established a group ADI of 0–0.003 mg/kg bw for cyhexatin and azocyclotin. The IEDIs were calculated for the five GEMS/Food regional diets from the STMR and STMR-P values for fruits and processed products as estimated by the present Meeting (Annex 3). The group ADI for cyhexatin and azocyclotin is 0.003 mg/kg bw, and the calculated IEDIs ranged from 0 to 5% of the ADI. The results are shown in Annex 3 of the 2005 JMPR Report.

The Meeting concluded that these uses of cyhexatin and/or that of azocyclotin resulting in long-term intake of residues of cyhexatin as considered by the JMPR are unlikely to present a public health concern.

Short-term intake

The 2005 JMPR established a group ARfD of 0.02 mg/kg bw for women of childbearing age for cyhexatin and azocyclotin. The IESTI was calculated based on consumption data generated for the general population as no consumption data is available for this group of the population. The IESTI ranged from 3 to 20% ARfD. The results are shown in Annex 4 of the 2005 JMPR Report.

An ARfD for the rest of the population was considered unnecessary and no intake calculations were performed for the general population and for children.

The Meeting concluded that the short-term intake of residues of cyhexatin, from uses of cyhexatin and azocyclotin, on commodities that have been considered by the JMPR, is unlikely to present a public health concern.

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