TRIFORINE (116)

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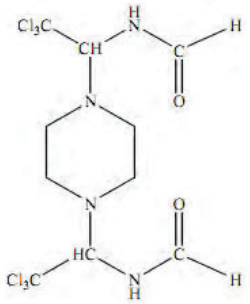
EXPLANATION

Triforine is a systemic fungicide for control of blackspot, powdery mildew and rust. It was first evaluated by JMPR in 1978 (T, R) and the latest toxic review was in 1997 (T). The ADI for Triforine was established as 0–0.02 mg/kg bw and no ARfD was set up in previous JMPR. Triforine was scheduled at the 45th session of the CCPR (2013) for the periodic re-evaluation of toxicity and residues by the 2014 JMPR.

The residue data was submitted by the manufacturer and would support the following commodities: apples, blueberries, Brussels sprouts, cereal grains, cherries, common beans, apricots, currants (black, red white), fruiting vegetables, cucurbits, gooseberries, peaches, plums (including prunes), strawberries and tomatoes.

IDENTITY

Common name	Triforine
Chemical name	
IUPAC:	*N,N'*-{piperazine-1,4-diylbis[(trichloromethyl)methylene]}diformamide
CAS:	*N,N'*-[1,4-piperazinediylbis(2,2,2-trichloroethylidene)]bis[formamide]
CAS Registry No:	26644-46-2
CIPAC No:	360
Synonyms:	W 524, CME 102, SAG 102, Cela W524
Structural formula:	
Molecular formula:	$C_{10}H_{14}Cl_6N_4O_2$
Molecular weight:	434.96

PHYSICAL AND CHEMICAL PROPERTIES

Technical material

Property	Results	Reference
Appearance (colour/ physical state/ odour)	Cream coloured/ solid, crystalline powder/ slightly like garlic (purity: not specified)	Jungblut, 1989 TF-302-006
Vapour pressure	8.0 × 10–2 Pa at 25 °C (98.1% purity)	Cardinaals, 1988 TF-306-004
Melting point	151.3–154.1 °C (98.1% purity) The colour turned from white into light brown at 148.6 °C.	Van Klooster-Cornelissen, 1988 TF-303-001
Octanol/water partition coefficient	log P_{ow} = 2.2 at 20 °C (98.1% purity)	Van Klooster-Cornelissen, 1988

Property	Results		Reference
			TF-315-002
Solubility in water	11.3 × 10–3 g/L in buffer solution, pH 5.0 9.0 × 10–3 g/L in buffer solution, pH 7.0 8.7 × 10–3 g/L in buffer solution, pH 9.0 at 20 °C (98.1% purity)		Van Helvoirt, 1988 TF-311-007
Solubility in organic solvents (98.1% purity)	Methanol (flask method)	46.9 g/L at 19.5 °C	Van Klooster-Cornelissen, 1989 TF-312-004
	Toluene (flask method)	0.11 g/L at 19.5 °C	
	Tetrahydrofuran (flask method)	168 g/L at 19.5 °C	
	Hexane (flask method)	< 4.7 × 10–3 g/L at 19.5 °C	
	Hexane (column method)	2.6 × 10–3 g/L at 19.5 °C	
Relative density	1.55 g/cm3 at 20.0–20.6 °C (98.1% purity)		Van Klooster-Cornelissen, 1988 TF-308-002
Henry's law constant	2.5 Pa × m3 × mol–1 (calculation) (98.1% purity)		Cardinaals, 1988 TF-306-006
Dissociation constant	pKa = 10.6 at 20 °C (98.1% purity)		Van Klooster-Cornelissen, 1989 TF-311-008

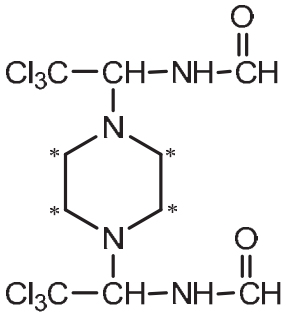
Radioactive substance

Property	Results	Reference
Hydrolysis	The calculated DT_{50} (24–25 °C) 3.5 days at pH 5 3.4 days at pH 7 3.5 days at pH 9	Obrist, 1989 TF-322-017
	The calculated DT_{50} (25 °C) 2.6 days at pH 5, 2.8 days at pH 7, 2.6 days at pH 9 for the ring labelled 2.9 days at pH 5, 3.1 days at pH 7, 3.1 days at pH 9 for the side chain labelled The hydrolysis products counting for > 10% of the initial dose: WOS 2379 and W2379	Bass, 1993 TF-322-018
Photolysis	Initial DT_{50} under simulated sunlight (12 h on/ 12 h off) = 1.5 days at pH 7 (25 °C) (equivalent to 2.1 days of Florida summer sunlight)	Waring, 1993 TF-324-009

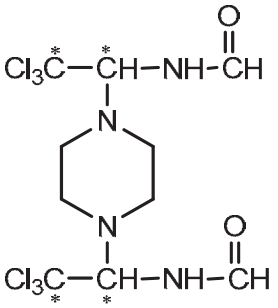
Formulations: Emulsifiable concentrate (EC)

METABOLISM AND ENVIRONMENTAL FATE

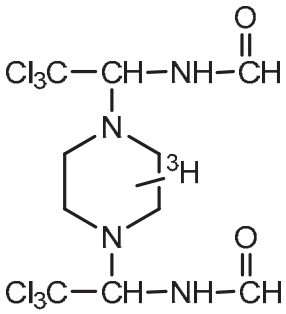
The metabolism, distribution of triforine has been investigated in animals and plants. The fate and behaviour of triforine in animals, plants and the environment was investigated using the [^{14}C]-labelled test materials shown in Figures 1.



[piperazine-^{14}C]-triforine



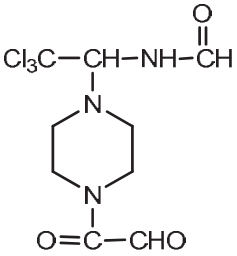
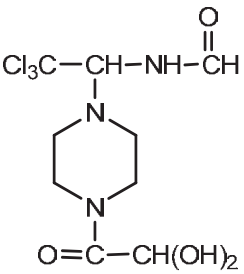
[side chain-^{14}C]-triforine

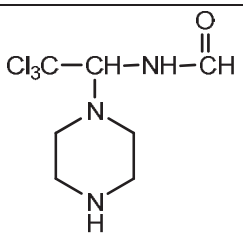
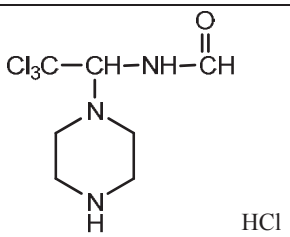
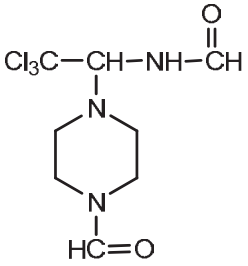
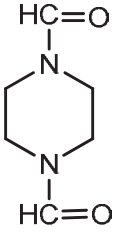
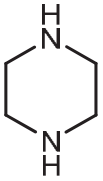
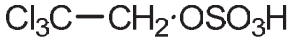
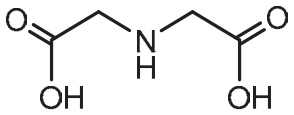
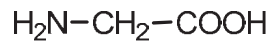


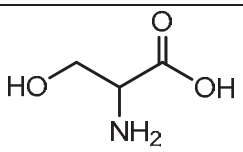
[piperazine-^{3}H]-triforine

Figure 1 [^{14}C] and [^{3}H]-Labelled test materials used in animals, plants metabolism studies, and the environmental fate studies

The chemical structures of the major degradation compounds from the metabolism of triforine are provided below.

Compound name		Structure	Found in metabolism studies
WOS 2379	*N*-{2,2,2-trichloro-1-[4-(2-oxoacetyl)piperazin-1-yl] ethyl}formamide		Livestock, Soil
W 2379	Hydrate of *N*-(2,2,2-thrichloro-1-[4-(2,2-dihydroxyacetyl)piperazin-1-yl]ethyl}formamide		Livestock

Compound name		Structure	Found in metabolism studies
W 1084	*N*-(2,2,2-trichloro-1-piperazin-1-yl-ethyl)formamide		Rat, Livestock, Plants
W 1069	*N*-(2,2,2-trichloro-1-piperazin-1-yl-ethyl)formamide hydrochloride		Livestock, Plants, Soil
W 625	*N*-[2,2,2-trichloro-1-(4-formyl piparazin-1-yl)ethyl]formamide		Plants, Soil
WOS 613	piperazine-1,4-dicarbaldehyde		Plants
Piperazine			Plants, Soil
Trichloroethanol	2,2,2-trichloroethanol		Rat, Livestock
Trichloroethanol sulphate			Livestock
Iminodiacetic acid			Plants
Glycine			Plants

Compound name		Structure	Found in metabolism studies
Serine			Plants

Animal metabolism

The Meeting received animal metabolism studies of triforine in rats, lactating goats and laying hens. The study on rats was evaluated by the WHO Core Assessment Group of the 2014 JMPR. A summary of the rat metabolism is given in this section.

Rats

Triforine is rapidly metabolized and excreted in rats. Highest residues were found in liver followed by kidney. Residues were lower in muscle and fat. The glucoronide of *N*-[2,2,2-trichloro-1-(piperazin-1-yl) ethyl]-formamide (W 1084), which was formed by the cleavage of a side chain, and the side-chain metabolites trichloroethanol including its glucuronide and *N*-acetylcysteine conjugate of 2,2,2-trichloroethylamine was detected in urine. W 1084 and triforine was detected in the faeces (Darda, 1974, Hawkins *et al.,* 1992).

Lactating goat

Study 1

The metabolism study for the lactating goats was performed with [piperazine-^{14}C]-triforine (Ellgehausen, 1981: TF-440-013). Three lactating goats weighing approximately 20 kg were individually housed in cages and allowed free access to feed and water during the whole study. The test item was given as suspension in 0.5% CMC (Carboxymethyl Cellulose) in distilled water. It was administered by stomach tube to the three goats, one receiving 25 mg/kg bw and the other two receiving 100 mg/kg bw. Non-labeled triforine was given once daily for 7 days, thereafter on Day 8, 9 and 10, [^{14}C]-labelled triforine was administered once daily.

Samples of milk were taken prior to the first treatment of [^{14}C]triforine, during the dosing period twice daily, at 8 hours and 24 hours after treatment, and thereafter every 24 hours. Collection of urine and faeces was performed daily. The animals were sacrificed 6 days after the last treatment and the fat, muscle, heart, liver, mammary glands, kidneys, brain and blood removed for analysis. One goat (Goat C) was sacrificed 4 hours after the last treatment.

Goat	Average dose (mg/kg bw/day)	ppm in feed Based on feed consumption of 2 kg/day	Time between last treatment and sacrifice
A	24.41	250	6 days
B	97.98	1000	6 days
C	96.65	1000	4 hours

The radioactivity administered to the goats was rapidly eliminated. A total of 46.6% and 71.5% of the applied radioactivity were eliminated in urine and faeces in 24 hours by Goats A and B, respectively. In the following 5 days, a further 15.9 and 14.0% were excreted by Goats A and B, respectively. The radioactivity found at sacrifice in tissues, blood, and milk of Goats A and B amounted to an average of 1.6%, 0.3% and 0.3% of the applied radioactivity. Goat C sacrificed 4 hours after the last treatment showed higher values in tissues and blood, i.e. 6.1% and 0.8% respectively. Total recoveries of radioactivity from Goats A and B were 65.5% and 89.1%.of the applied radioactivity, respectively.

The radioactivity in the milk was determined by combustion of 1 g aliquots. The radioactivity in urine was determined by direct liquid scintillation counting (LSC). The faecal samples were lyophilised, homogenized and removed for combustion followed by LSC of the radioactivity of carbon dioxide collected in scintillation cocktail. The radioactivity in blood was determined by combustion of 1 g samples. Tissues were solubilized overnight at 55 °C and radioassayed by LSC. The tissues, blood and milk samples were stored at -20 °C.

Table 1 Radioactivity in selected tissues from lactating goats (mg triforine equivalent/kg)

Goat	Tissues							
	Blood	Heart	Liver	Kidney	Muscle	Mammary	Brain	Fat
A	2.07	3.54	11.8	7.93	2.35	3.47	1.42	0.03
B	5.23	12.1	32.7	23.1	8.14	12.0	6.65	1.27
C	20.8	35.9	201	101	24.9	39.0	26.1	20.1

Table 2 Radioactivity in milk from lactating goat (mg triforine equivalent/kg)

Goat	Timing of sampling (hours after the first treatment of labelled triforine											
	0–8	8–24	24–32	32–48	48–52	48–56	56–72	72–96	96–120	120–144	144–168	168–192
	T a		T a		T a							
A	5.23	4.93	8.84	9.65	–	11.6	12.3	4.82	1.99	1.19	0.69	0.59
B	17.9	17.1	38.4	26.6	–	70.9	43.0	9.00	3.98	2.66	2.23	1.54
C	18.8	17.4	32.1	24.9	34.4	–	–	–	–	–	–	–

[a] Treatment with [^{14}C]-labelled triforine

Up to six metabolite fractions were isolated from urine and faeces extracts. The amount of triforine in urine and faeces ranged from 0.4% to 2.6% of the applied radioactivity. The major metabolite in urine was shown by co-chromatography to be W 1084. It amounted to 7.1% (Goat A) and 12.6% (goat B) of the applied radioactivity in urine and less than 1% in faeces.

The study was performed to determine the extractability of residues in liver, kidney and muscles of the goats and to determine the nature of the extractable radioactivity (Ellgehausen, 1982: TF-440-014). Until analysis the tissues were stored at -20 °C. Tissue samples (50 g) were extracted with acetone (100 mL) followed by methanol/water (8:2, 100 mL). Proteins of milk (100 g) were precipitated with acetone (200 mL) by centrifugation and removed. The protein precipitate was then extracted with acetone and methanol/water (8:2) as done with tissues. The organic solvent was evaporated and the remaining aqueous phase was partitioned with chloroform. The amount of extractables and non-extractables were determined by combustion and thin layer chromatography (TLC).

The residual radioactivity in the liver of Goat C, sacrificed 4 hours after the last administration of [^{14}C]triforine was found to be extractable up to 68.4% TRR. This extractable radioactivity consisted of at least five metabolite fractions. M1 and M2 represented unknown polar metabolite fractions whereas WOS 2379 and W 1084 were characterized. The residual radioactivity in the liver of Goat B, sacrificed 6 days after the last treatment, was extractable up to 14.1% TRR. The metabolite pattern found was similar to that found in the extractables of the liver of Goat C. The predominant metabolite fraction was M1 representing 10.2% TRR. Triforine, WOS 2379 and W 1084 accounted only for 1.3%, 1.6% and 1.0% TRR, respectively.

The residual radioactivity in the kidneys of Goat B and C was extractable up to 17.9% and 78.2% TRR, respectively. These figures corresponded to 4.13 and 78.2 mg equiv/kg. The metabolite pattern of the extractables was similar to that found in the extractable of the liver. The predominant extractable fractions found in Goat C was polar unknown metabolite fraction M1 accounting for 31.1% TRR. Triforine, WOS 2379 and W1084 represented at the same time 19.3%, 8.4% and 18.5% TRR, respectively. Characteristization of the extractable radioactivity of the kidneys of Goat B showed a similar metabolite pattern with regard to the relative amounts in the extracts. The

predominant extractable fraction was M1 accounting for 10.7% TRR. Triforine represented 3.6% TRR only.

Due to the low radioactivity concentration in muscle of Goat B and the low specific radioactivity, only muscles of Goat C were analyzed. The residual radioactivity accounted for 19.6 mg equiv/kg (78.7% TRR) was found to be extractable. Analysis by TLC showed that the predominant radioactive fraction was triforine with 40.6% TRR. The other metabolites accounted for 9.5% (W 1084), 13.0% (WOS 2379), 0.70% (M2) and 15.1% TRR (M1).

The radioactivity in the pooled milk fractions of Goat B sampled within 24 hours after the last administration of [^{14}C]triforine accounted for 49.6 mg equiv/kg.

Table 3 Extraction and characterization of residues in liver, kidney and muscle of Goat B sacrificed 6 days after the last treatment at 1000 ppm and Goat C sacrificed 4 hours after the last treatment at 1000 ppm

	Goat B			Goat C		
	% applied	% TRR	TRR(mg/kg)[a]	% applied	% TRR	TRR(mg/kg)[a]
Liver						
Extract	0.043	14.1	4.61	1.25	68.4	137
Triforine	0.004	1.3	0.43	0.278	15.2	30.6
M1-polar unknowns	0.031	10.2	3.33	0.331	18.1	36.4
M2-unknown (Rf=0.32)	< 0.001	< 0.03	< 0.1	0.144	7.9	15.8
WOS 2379	0.005	1.6	0.54	0.268	14.7	29.5
W 1084	0.003	1.0	0.32	0.229	12.5	25.2
Unextracted	0.262	85.9	28.1	0.578	31.6	63.5
Total in liver	0.305	100	32.7	1.83	100	201
kidney						
Extract	0.005	17.9	4.13	0.093	78.2	79.3
Triforine	0.001	3.6	0.83	0.023	19.3	19.6
M1-polar unknowns	0.003	10.7	2.48	0.037	31.1	31.6
M2-unknown (Rf=0.32)	< 0.001	< 0.1	< 0.01	0.001	0.8	0.85
WOS 2379	0.001	3.6	0.83	0.010	8.4	8.53
W1084	< 0.001	< 0.1	< 0.01	0.022	18.5	18.8
Unextracted	0.023	82.1	19.0	0.026	21.8	22.2
Total in kidney	0.028	100	23.1	0.119	100	101
muscle						
Extract	NA[b]	NA	NA	2.63	78.7	19.6
Triforine	NA	NA	NA	1.35	40.6	10.1
M1-polar unknowns	NA	NA	NA	0.505	15.1	3.76
M2-unknown (Rf=0.32)	NA	NA	NA	0.023	0.70	0.17
WOS 2379	NA	NA	NA	0.435	13.0	3.24
W1084	NA	NA	NA	0.318	9.5	2.37
Unextracted	NA	NA	NA	0.713	21.3	5.31
Total in kidney	NA	NA	NA	3.35	100	24.9
milk						
Extract		62.3	30.9	NA	NA	NA
Triforine	< 0.001	–	< 0.1	NA	NA	NA
M1-polar unknowns	0.146	62.3	30.9	NA	NA	NA
M2-unknown (Rf=0.32)	< 0.001	–	< 0.1	NA	NA	NA
WOS 2379	< 0.001	–	< 0.1	NA	NA	NA
W1084	< 0.001	–	< 0.1	NA	NA	NA
Unextracted	0.088	37.7	18.7	NA	NA	NA
Total in milk	0.234	100	49.6	NA	NA	NA

[a] mg triforine equivalent/kg tissue
[b] Not analyzed

The study was further performed for the investigation of the polar metabolite fractions and unextracted fraction (Schlüter, 1984: TF-440-015). The polar metabolite fraction M1 from Liver B, Liver C and milk was investigated. In all cases, thin layer chromatography showed that M1 consisted of a number of components that could not be well separated. Incubation with β-glucuronidase/aryl

sulphatase did not produce any difference in chromatographic profile indicating that M1 was not an easily hydrolyzed sulphate or glucuronide conjugate. When M1 was heated with strong acid piperazine was the only cleavage product. All the components in fraction M1 disappeared from the TLC plate and piperazine was formed.

Study 2

The adsorption, distribution, metabolism and excretion of radioactivity have been studied following repeated oral administration of [piperazine-^{14}C]triforine to the dairy goat at a mean dose level of 67 mg/day (Richardson, 1994: TF-440-019). This was equivalent to a dietary inclusion of approximately 49 ppm (based on the food consumption of the goat during the study). One goat received five daily oral doses of [^{14}C]triforine. The goat was given the dose in the morning before feeding but after milk and excreta collections. At study termination (*ca.* 6 h after the final dose) selected tissues were removed or sampled. The radiolabelled triforine derived material excreted was characterized using chromatographic procedures.

The overall recovery of the administered radioactivity was 72.3%, the majority of which was present in the urine (39.8%) and faeces (19.2%). Most of the remainder was associated with the contents of the gastro-intestinal tract (9.54%). Negligible radioactivity was recovered in cage washings/ debris (1.21%), milk (0.87%), tissues (0.82%) and residual carcass (0.88%).

From day 1, concentrations of radioactivity in whole milk were in the range 0.314 to 0.501 mg equiv/kg. Fractionation of 72–96 h whole milk showed that 32% of the radioactivity was found in cream and 76% was found in skim. Further fractionation showed that 7% of the radioactivity in the skimmed milk was found in the curds and 64% in whey. At *ca.* 6 h after the final dose, highest tissue residue levels were found in the liver (2.60 mg equiv/kg) and kidney (1.46 mg equiv/kg), with lower concentrations of 0.271 and 0.016 mg equiv/kg present in muscle and fat respectively.

Table 4 Extraction of radioactive residues from tissues and milk

	Liver		Kidney		Muscle		Fat		Milk (96–102 h)	
	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg
Extracted	53	1.39	55	0.787	60	0.179	53	0.012	72	0.366
Organic	5	0.131	7	0.100	5	0.013	–	–	4.5	0.023
Aqueous	37	0.973	38	0.543	26	0.078	–	–	48	0.240
Others							17	0.004	15	0.075
Unextracted	46	1.21	47	0.672	31	0.092	17	0.004	34	0.170
Total	99	2.60	102	1.46	91	0.271	70	0.016	106	0.536

Chromatography of the extracted radioactivity revealed metabolites with a wide range of polarity. TLC analysis proved to be the most efficient in terms of resolution of components. However given the very polar nature of some of the metabolites and low relative concentrations, the quality and hence the reproducibility of the chromatography in some solvent systems was poor. Comparison of the extracted radioactivity indicated that there were some similarities in the metabolite profiles for liver, kidney, muscle and urine; however, the metabolites in milk were very polar and more difficult to compare. The radioactivity which partitioned into organic solvent from liver extracts, kidney extracts, muscle extracts and urine all contained the same metabolites. The radioactivity which partitioned into the aqueous phase was more difficult to compare due to the polarity of the metabolites however there were some similarities in profiles for liver, kidney and muscle.

Piperazine was identified in liver extracts (5% TRR), in kidney extracts (6% TRR) and in urine (14% of the 96–102 h urine). W 1069 was identified as a minor metabolite in urine (8%).

The proportion of piperazine in tissue extracts, milk and urine was increased by acid treatment of the samples. These results when compared with the result of acid treatment of triforine hydrolysis products (which showed that the ring system was stable to this process) indicated that the increased proportion of piperazine arose from the cleavage of metabolites which featured remnants of one or both of the triforine side chains but without modification of the piperazine ring.

Unextracted residues in all tissues and milk were solubilized by 6 M acid treatment. Piperazine was identified in samples derived from the acid treatment of unextracted residues from liver but not in other samples (kidney and milk residues).

Laying hens

Study 1

The metabolism study for the laying hens was performed with [piperazine-^{14}C]-triforine (Ellgehausen, 1981: TF-440-012). Six-month old laying hens (white leghorn hybrids) were housed individually in metabolism cages. They were allowed free access to food and water during the study. The test item was given as suspension in 0.5% CMC (Carboxymethyl Cellulose) in distilled water. It was administered once daily into the crop by intubation to three groups of hens. One group (Group A) received 25 mg/kg bw/day; the other two groups (Groups B and C) received 100 mg/kg bw/day. Non-labelled triforine was given daily for 7 days at the same rates thereafter on day 8, 9 and day 10, [^{14}C]triforine was administered. Based on an assumed food consumption of 100 g diet per day and a hen body weight of 2 kg the 100 and 25 mg/kg dose were equivalent to 2000 ppm and 500 ppm dietary concentration, respectively.

Hen group	Average dose (mg/kg bw/day)	ppm in feed	Time between last treatment and sacrifice
A	23.40	500	7 days
B	96.79	2000	7 days
C	96.94	2000	4 hours

During the dosing period eggs were collected twice daily 8 hours and 24 hours after the treatment, thereafter every 24 hours. Collection of excreta was performed accordingly. The animals were sacrificed either 4 hours (Group C) or 7 days (Groups A and B) after the last treatment and the liver, heart, muscle, fat, and blood were sampled for analysis.

The eggs were divided into egg yolk/white and shells per group for each interval and pooled samples were homogenized. The subsamples were removed for combustion and radioactivity determination by liquid scintillation counting (LSC). The excreta samples per group for each interval were pooled, lyophilized, homogenized and subsamples were removed for combustion and radioactivity determination by LSC. Tissues and blood were solubilized overnight at 55 °C and direct radio-assayed by LSC. The tissues, blood and egg samples were stored until analysis at -20 °C.

The excreta samples during the experiment were pooled for intervals from day 8 to 8 hours after the last treatment and then thereafter to the end of experiment. The pools were homogenized and an aliquot of 50 g was taken for extraction. Each aliquot was extracted with acetone (3 × 200 mL) by strong agitation for 30 and finally 60 min. Thereafter the excreta samples were continuously extracted overnight in a Soxhlet apparatus. The radioactivity in the extracts was measured by LSC. TLC was used pre-coated silica gel 60 F 254 plates with various solvent systems. Three different solvent systems gave good separation of triforine and the available reference compound (W 1084).

The radioactivity administered to the hens was rapidly eliminated by the animals of all groups (53.7–83.6% in 56 hours after the first dose). In the following 7 days a further 10.2–14.8% of the administered radioactivity was excreted by the remaining groups giving 75.7% excreted from Group A and 93.8% from Group B.

At the lower dose level (Group A) the TRR ranged from < 0.05 mg/kg in fat to 1.80 mg/kg for liver. The corresponding figures at the higher dose level (Group B) were four times higher, clearly showing the direct correlation between dose level and tissue/organ residue. The animals of Group C, which received the same amount of triforine as Group B but which were killed 4 hours after the last treatment showed higher residual radioactivity in tissues and organs.

Table 5 Total radioactive residues in tissues of laying hens

	TRR (mg triforine equivalent/kg)

	Blood	Heart	Liver	Muscle	Muscle forestomach	Fat
Group A	1.25	1.22	1.80	0.58	0.74	< 0.05
Group B	4.30	4.37	5.89	1.86	3.10	0.25
Group C	23.5	28.7	140	14.1	21.4	2.26

The egg residues in Group A were on the average three times lower than in Group B or C. The highest values in eggs were found about 4 to 5 days after the first treatment with [^{14}C]triforine. No influence of the compound during the whole study on egg production was observed although the hens were dosed up to 100 mg/kg over a period of 10 days.

Table 6 Total radioactive residues in selected eggs of laying hens

Hours after the first dose	TRR (mg triforine equivalent/kg)		
	7 days after the last treatment (500 ppm)	7 days after the last treatment (2000 ppm)	4 hours after the last treatment (2000 ppm)
0–8 T	0.04	0.17	0.02
8–24	–	1.02	–
24–32 T	0.54	1.52	2.71
32–48	0.91	–	–
48–52 T	NS	NS	6.39
48–56	1.88	5.87	–
56–72	–	–	–
72–96	3.11	4.28	–
96–120	3.41	8.53	–
120–144	2.07	6.09	–
144–168	–	–	–
168–192	2.47	4.34	–
192–216	0.84	3.99	–

NS: no egg sampling
T: Treatment with [^{14}C]triforine

Metabolites were characterized by extraction of excreta followed by TLC. Analysis of the pooled 0–56 and 56–216 hours excreta from high and low dose application showed in general the same pattern of metabolites in the extractables. The major metabolite fraction characterized by TLC was W 1084.

Study 2

The metabolism of triforine in laying hens was investigated after administration of [side chain-^{14}C]triforine for 10 consecutive days at a dose of 32 ppm in the feed (Mayo, 1994: TF-440-020). The dose was administered orally via a gelatine capsule at a rate of 3.5 mg/hen/day. Combined excreta from five treated hens and from two control hens were collected at 24-hour intervals from 24 hours prior to the first treatment up to the time of sacrifice. Any eggs laid were collected prior to administration of the next treatment, labelled and stored at 4 °C prior to further treatment. Hens were sacrificed *ca.* 6 hours after the last treatment and the tissues taken for analysis. There was no visible fat on the skin. All samples were stored at < -15 °C prior to analysis.

The combined extracts of the excreta collected at day 10 were analyzed directly by radio-TLC. Metabolites were scraped from TLC plates and extracted from the silica with methanol and further purified by HPLC. Liver, muscle and egg white and yolk samples were extracted sequentially with acetone (twice), methanol/water 8:2 (twice) and finally with water (twice). Samples of egg white and liver were homogenized and pre-incubated with protease in buffer solution for 12–18 hours at 37 °C before the same extraction process. The residue from the yolk extraction was re-extracted with the same solvent mixtures once more followed by a final water extraction. Skin was extracted by dissolving the sample in hexane and extracting the residue three times with methanol/acetone (9:1). The hexane phase was back extracted five times with acetonitrile. The extracts were radio-assayed separately and combined as appropriate for chromatographic analysis.

Radioactivity recovered in excreta during the 10 days accounted for about 85% of the total cumulative dose with 1.5% remaining in the gastrointestinal tract after sacrifice. Recovery of radioactivity in the faeces had increased from 76% on Day 1 to 90% between Day 6 and Day 9. A slight decrease to 85% observed at Day 10 may be attributed to sacrifice at 6 hours after the last treatment. Concentration of radioactivity in eggs increased steadily during the 10 days to a peak value of 1.6 mg equiv/kg (yolk) and 0.19 mg equiv/kg (white).

Table 7 The concentrations of radioactive components in tissues and eggs

	Fat		Liver		Liver (protease)[a]		Muscle	
	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR
Extract	0.09	94.6	0.84	48.9	1.6	94.6	0.21	87.7
Triforine	0.02	17.5	0.05	2.9	< 0.01	< 1.0	0.02	8.4
Fraction A	0.008	8.9	0.52	31.3	1.1	66.7	0.03	11.3
Fraction B	0.003	3.1	–	–	–	–	0.008	3.3
Component C/D (Trichloroethanol sulphate)	0.03	35.9	0.15	9.3	0.25	15.0	0.05	22.0
Fraction E	0.003	3.2	0.02	1.3	0.05	3.1	0.005	2.2
W 1069	–	–	0.04	2.1	–	–	0.05	21.5
Fraction H	0.008	8.9	–	–	–	–	–	–
Trichloroethanol	< 0.001	<1.0	< 0.01	<1.0	< 0.01	<1.0	< 0.01	<1.0
Fraction K	0.01	10.8	–	–	–	–	–	–
Others	0.003	2.8	–	–	0.04	2.3	0.02	8.4
Polar extracted	0.003	3.7	0.03	2.0	0.13	7.6	0.02	7.8
Unextracted	0.005	5.4	0.86	51.2	0.09	5.3	0.03	12.4
TRR	0.09	100	1.7	100	1.7	99.9	0.24	100
	Skin		Egg white[a,b]		Egg yolk[a,b]			
	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR		
Extract	0.18	75.6	0.12	72.6	0.86	85.5		
Triforine	0.01	5.4	0.02	13.2	0.02	2.1		
Fraction A	0.009	3.8	0.08	47.9	0.15	14.2		
Fraction B	0.004	1.6	–	–	0.07	6.3		
Component C/D (Trichloroethanol sulphate)	0.13	55.7	0.01	6.1	0.25	24.6		
Fraction E	0.004	1.5	–	–	–	–		
W 1069	0.004	1.7	–	–	0.10	10.2		
Fraction H	0.006	2.6	–	–	0.19	18.0		
Trichloroethanol	< 0.01	<1.0	–	–	–	–		
Fraction K	–	–	–	–	–	–		
Others	0.008	3.4	–	–	0.04	3.70		
Polar extracted	–	–	0.009	5.4	0.07	6.4		
Unextracted	0.06	24.4	0.04	27.4	0.15	14.6		
TRR	0.24	100	0.16	100	1.0	100		

[a] Extraction after protease treatment
[b] Representative pool from Day 7–9
Fraction A-K: Unidentified

Treatment of liver with protease reduced the unextracted radioactivity from 0.86 to 0.09 mg equiv/kg (51.2 to 5.3% TRR). Further quantities of the same radioactive components (mainly fraction A and component C/D) were extracted after the protease treatment. Identity of component C/D was confirmed by mass spectrometry as the sulphate conjugate of trichloroethanol. Protease treatment increased the amount of fraction A from 31.3% to 66.7% TRR. The fraction A in the protease-treated extract was separated into 5 separate components each of which accounted for 0.07–0.40 mg equiv/kg (4–24% TRR). The sulphate conjugate of trichloroethanol was present in liver accounting for 9% TRR. There appeared to be a small amount of triforine in liver (2.9% TRR, 0.05 mg/kg) before protease treatment but chromatography was poor. Treatment with β-glucuronidase/sulphatase or mild chemical hydrolytic treatment did not release any identifiable components. Strong acid/base hydrolysis generated some discrete less polar components.

The breast and thigh muscle was extracted separately and sub-samples were combined for chromatography. The main components were the trichloroethanol sulphate conjugate and W 1069 each accounting for about 22% TRR (0.05 mg equiv/kg). Triforine was present at 8.4% TRR (0.02 mg/kg).

Triforine accounted for 17.5% TRR (0.02 mg/kg) and the sulphate conjugate of trichloroethanol accounted for 35.9% TRR (0.03 mg equiv/kg) in fat. There were at least five other components but each was less than 0.01 mg equiv/kg.

Triforine was also found in skin at low levels (0.01 mg/kg). The main fraction corresponded to the retention time of the trichloroethanol sulphate (55.7% TRR, 0.13 mg/kg). There were at least five other components but each was less than 0.01 mg equiv/kg.

Treatment of egg white with protease reduced unextracted radioactivity from 0.09 to 0.04 mg equiv/kg (58.7 to 27.4% TRR). The major component was the Fraction A which accounted for 19% (0.03 mg/kg). It was further separated by TLC into two polar components. Triforine and the trichloroethanol sulphate conjugate were found in small amounts (0.01 and 0.02 mg/kg respectively). All other components were less than 0.01 mg/kg.

Treatment of egg yolk with protease reduced unextracted radioactivity from 0.30 to 0.15 mg equiv/kg (29.1 to 14.6% TRR). Hydrolytic treatment of the residue of protease treated egg yolk, after extraction, with acid separated this unextracted radioactivity into an acid treated extract and residue each accounting for either < 0.05 mg equiv/kg or < 10% egg yolk radioactivity. Increased amounts of the polar fraction A were extracted after the protease treatment. Fraction A was separated into two components each accounting for < 0.05 mg equiv/kg in egg yolk. The major component in egg yolk was the sulphate conjugate of trichloroethanol which accounted for 25% TRR. W 1069 was observed and accounted for a further 10% TRR. Component H (less polar than triforine) in egg yolk was not identified.

Summary of animal metabolism

The metabolism of ^{14}C labelled triforine has been studied in lactating goats and laying hens. Triforine is very rapidly degraded in the goat even at the high dose levels used in the metabolism studies. Oxidation and hydrolysis leading to removal of the side chains from the piperazine ring was the main route of degradation. Free piperazine was not a metabolite but piperazine was identified following the solubilization of the matrix components followed by strong acid hydrolysis. The main extracted product was triforine although there were higher amounts of a mixture of highly polar components which were not completely separated. They were not identified but appeared to yield mainly piperazine on reflux with hydrochloric acid.

As in the goat, one of the side chains was lost to form W 1069 and the carbon from the side chain was found mainly as trichloroethanol and its sulphate conjugate. The major portion of the residue even with a relatively short pre-slaughter interval was unextracted with a very thorough extraction sequence involving a range of solvent polarities and overnight contact with the matrix. It is possible that trichloroethanol was further metabolized into small fragments that were incorporated into the tissue and egg matrix components. It is assumed that W 1069 was further metabolized to piperazine containing compounds which would also be bound to matrix components.

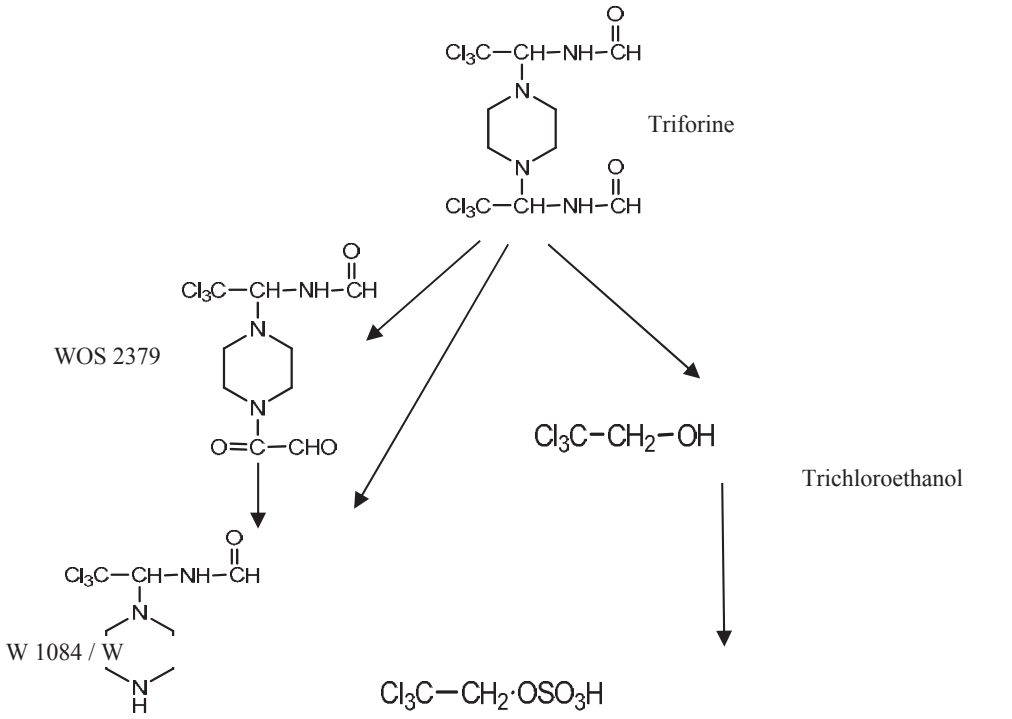


Figure 2 Metabolic Pathway of Triforine in livestocks

Plant metabolism

Plant metabolism studies were performed on apples, tomatoes and cucumber with triforine [^{14}C]-labelled in two carbons at the side chain, and on barley with triforine [^{3}H]-labeled at piperazine ring to track metabolites. Metabolites were identified using multiple chromatographic systems and authentic standards.

Apple

The metabolism of [^{14}C]triforine has been studied in apple fruits and leaves after five successive applications of a commercial formulation of 0.1% [side chain-^{14}C]-triforine at 8-day intervals (Hawkins *et al*, 1993: TF-640-037). Three 2–3 year old container grown apple trees (variety Lord Lambourne) on semi-dwarf root stock were placed outdoors in a netted enclosure. Samples of [^{14}C]triforine (*ca*. 6 mg) were mixed with 25°µL blank formulation (EC 190 g/L) giving *ca*. 31 mg of formulation. This formulation was diluted with water to give a final concentration of 1.2 g/L. Specific amounts of the formulated [^{14}C]triforine were applied to either apples (100 µL) or leaves (100 µL) using a syringe. The treatment was applied as a series of small droplets at random over the surface of the apple/leaf. Treated apple fruits were harvested 2 weeks after the last of five successive applications. Translocation from treated leaves into untreated apple fruits was also investigated. Some additional apple fruits and leaves were sampled about 2 hours after one application.

The recovery of radioactivity from selected apple fruits and leaves was measured about 2 hours after one application. The remaining apple fruits were taken, along with the leaves and untreated apples, 14 days after the fifth application of [^{14}C]triforine. Surface washes on all treated samples were initiated on the day of sample collection and samples were stored at < -15 °C overnight. The surface of each treated apple or leaf was washed by immersion in acetonitrile for 5 minutes during which time the container was placed in a sonic bath. The surface wash was then separated by decanting and the process repeated with two further acetonitrile washes. The volumes of the surface washes were measured and aliquots (approximately 100 µL) were removed for estimation of radioactivity by LSC. After the surface washes were completed the apple fruits were peeled and the

peel, flesh and leaves were separately homogenized with acetonitrile, sonicated and the samples were centrifuged. A further extraction was performed using acetonitrile: water (70:30).

Table 8 The distribution of radioactive residues in apple fruit and leaves

	2 hours after one application				2 weeks after five applications			
	Fruit		Leaf		Fruit		Leaf	
	%AR	%TRR	%AR	%TRR	%AR	%TRR	%AR	%TRR
Extract	95.4	99.4	57.8	96.6	27.4	84.7	20.4	92.1
Surface wash	94.8	98.8	54.9	91.8	23.8	73.2	14.7	66.7
Peel or leaf	0.4	0.4	2.9	4.8	1.4	4.5	5.7	25.4
Flesh	0.2	0.2	–	–	2.2	7.0	–	–
Unextracted	0.6	0.6	2.1	3.4	4.7	15.3	2.0	7.8
Total	95.8	100	59.9	100	32.2	100	22.3	99.9

After one application of [^{14}C]triforine three fruits and three leaves were taken for analysis. The radioactivity in the surface washes was 98.8% (fruit) and 91.8% (leaf) of TRR. Only small amount of radioactivity were in the remaining extracts of homogenized peel and flesh, 0.4 and 0.2% TRR respectively. Extracts of homogenized leaves contained 4.8% TRR. The mean concentrations in the treated fruits and leaves were 1.59 (fruit) and 92.4 (leaf) mg equiv/kg, respectively.

At harvest, after 5 successive applications of [^{14}C]triforine, 32.2% (fruit) and 22.3% (leaf) of the applied radioactivity was recovered. Acetonitrile surface washes of treated fruits at harvest contained 73.2% TRR. Extracts of peel and flesh homogenized with acetonitrile accounted for 4.5 and 7.0% TRR respectively. The mean concentration of 1.36 mg equiv/kg was recovered in the treated fruits.

At the time of harvest untreated fruits were taken from branches with treated leaves. The radioactivity in untreated fruits accounted for 0.0009 mg equiv/kg. Analysis of untreated fruits showed a very low degree of translocation during this period.

Samples of surface washes and extracts were pooled to give representative samples for both fruits and leaves, and analyzed directly by TLC or HPLC. Radiolabelled metabolites formed in the study were characterized by co-chromatographic comparison using two different systems.

Table 9 Proportion of radioactive components in apple fruits at harvest

	Surface wash		Peel		Flesh		Total	
	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2
	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)
Extract								
Triforine	68 (0.82)	74 (1.14)	2.3 (0.03)	2.5 (0.04)	3.0 (0.04)	2.8 (0.04)	73 (0.88)	79 (1.22)
W 1069	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.9 (0.01)	0.3 (0.005)	0.9 (0.01)	0.7 (0.01)	1.8 (0.02)	1.0 (0.02)
Unidentified A	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.3 (0.004)	0.1 (0.002)	0.3 (0.004)	0.2 (0.003)	0.6 (0.007)	0.3 (0.005)
Unidentified B	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.3 (0.004)	0.2 (0.003)	0.4 (0.005)	0.2 (0.003)	0.7 (0.008)	0.4 (0.006)
Unidentified C	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.5 (0.006)	0.3 (0.005)	1.3 (0.02)	0.8 (0.01)	1.8 (0.02)	1.1 (0.02)
WOS 613	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.5 (0.006)	0.2 (0.003)	1.1 (0.01)	0.6 (0.009)	1.6 (0.02)	0.8 (0.01)
W 625	< 0.7 (< 0.008)	< 0.8 (< 0.01)	0.5 (0.006)	0.3 (0.005)	0.9 (0.01)	0.6 (0.009)	1.4 (0.02)	0.9 (0.01)
Other	2 (0.02)	2 (0.03)	0.008 (0.0001)	< 0.04 (< 0.001)	< 0.08 (< 0.001)	< 0.06 (< 0.001)	2 (0.02)	2 (0.03)
Unextracted	–	–	14 (0.17)	12 (0.18)	2.4 (0.03)	1.8 (0.03)	16 (0.19)	14 (0.22)

Note: In order to provide material for duplicate chromatographic runs, surface washes and extracts containing most radioactive components were combined to obtain two pooled samples from different fruits and leaves.

The major component in surface washes and extracts of fruits was identified as triforine by co-chromatography with reference test substances using both normal phase TLC and reverse phase HPLC. Triforine accounted for 73–79% TRR at harvest. The final concentrations of triforine in the fruits at 2 weeks after the final application of triforine were 0.88–1.22 mg/kg.

Several minor components were observed in the extracts and each of these accounted for 1–2% TRR. Two of the identified metabolites, formed by degradation of the piperazine side chain, were the mono and di-formyl compounds W 625 and WOS 613. The third identified metabolite, formed by de-alkylation of one of the piperazine nitrogen, was the amine W 1069. A further three unidentified components A, B and C were also observed that did not co-chromatograph with the available reference compounds. All of these metabolites each accounted for 0.01–0.02 mg equiv/kg.

The nature of the radioactivity unextracted in the peel residue was investigated using some hydrolytic treatments. Apple peel was treated with pectinase enzyme, 0.6 M HCl at 37 °C for 18 hours and 6.0 M HCl at > 90 °C for 1 hour. After adjustment to pH 7 the aqueous layers were extracted with ethyl acetate. The treatments with pectinase and mild acid extracted only small amounts of radioactivity from peel (< 2%) but in these samples the unextracted residue amounted to > 10% recovered radioactivity. On hydrolysis with concentrated acid approximately 7% of the sample radioactivity was extractable. Attempts to chromatograph these extracts were unsuccessful due to the low levels of radioactivity. The radioactivity in the acid peel extract accounted for about 0.1 mg equiv/kg and in the unextracted residue accounted for about 0.09 mg equiv/kg.

Tomato

The metabolism of [^{14}C]triforine has been studied in tomatoes and leaves after four successive applications of a commercial formulation of 0.1% [side chain-^{14}C]-triforine at 8–10 days intervals (Hawkins *et al*, 1993: TF-640-038). Tomato plants (variety Moneymaker) were transplanted to 25 cm diameter plastic pots containing potting compost. The study was conducted in a controlled environment room with a daylength of 15 hours and day and night temperatures of 20.9 ± 1.1 °C. Samples of [^{14}C]triforine (approximately 12 mg) were mixed with 50 µL blank formulation (EC 190 g/L) giving *ca*. 62 mg of formulation. This formulation was diluted with water to give a final concentration of 1.2 g/L. Specific amounts of the formulated [^{14}C]triforine were applied to either tomatoes (100 µL) or leaves (200 µL) using a syringe. The treatment was applied as a series of small droplets at random over the surface of the tomato/leaf. The treated tomatoes were harvested at 2 hours and 3 days after the last of four successive applications. For comparison additional samples were taken 2 hours after the first application. Translocation from treated leaves into untreated tomatoes was also investigated.

The recovery of radioactivity from each treated tomato leaf was measured separately. Surface washes on all treated samples were collected on the day of sample collection and samples were stored at < –15 °C overnight. The surface of each treated tomato leaf was washed by immersion in acetonitrile for 5 minutes during which time the container was placed in a sonic bath. The surface wash was then separated by decanting, and the process repeated with two further acetonitrile washes. After the surface washes were completed the tomato fruit or leaf was homogenized with acetonitrile, sonicated and the sample centrifuged. The supernatant extract was removed and the process repeated (leaves at harvest were extracted a third time with acetonitrile: water (70:30 v/v)). The volumes of the surface washes and extracts were measured and aliquots (approximately 100 µL) were removed for estimation of radioactive content by LSC. The extracted residues were allowed to air-dry and the radioactive content determined by combustion of sub-samples. A similar extraction procedure was employed for the untreated tomatoes removed at harvest.

Table 10 The distribution of radioactive residues in tomatoes and leaves

	Tomatoes					
	2 hours after one application (n = 3)		2 hours after 4th application (n = 7)		3 days after 4th application (n = 8)	
	%AR	%TRR	%AR	%TRR	%AR	%TRR
Surface wash	93.6	95.6	97.2	91.9	85.1	90.9

	Tomatoes					
	2 hours after one application (n = 3)		2 hours after 4th application (n = 7)		3 days after 4th application (n = 8)	
	%AR	%TRR	%AR	%TRR	%AR	%TRR
Tomato extract	3.6	3.7	5.8	5.8	5.8	6.2
Unextracted	0.7	0.7	2.3	2.3	2.6	2.8
Total	97.9	100	100.2	100	93.5	99.9
	Leaves					
	2 hours after one application (n = 2)		3 days after 4th application (n = 8)			
	%AR	%TRR	%AR	%TRR		
Surface wash	93.0	95.1	79.2	86.1		
Leaf extract	1.9	1.9	9.4	10.2		
Unextracted	3.0	3.1	3.5	3.8		
Total	97.8	100.1	92.1	100.1		

Three tomatoes and two leaves were sampled for analysis 2 hours after the first application of [^{14}C]triforine. The radioactivity recovered in the surface washes was 95.6% (tomato) and 95.1% (leaf) TRR. Extracts of the homogenised tomato or leaf contained small amounts of radioactivity (3.7% TRR (tomato) and 1.9% TRR (leaf)). Radioactivity in the unextracted residues accounted for 0.7% TRR (tomato) and 3.1% TRR (leaf). The mean concentrations in whole tomato and leaf were 6.2 and 16.9 mg equiv/kg, respecively.

The initial surface washes of treated tomatoes at harvest contained 91.9% (harvest at 2 hours after the final application) and 90.9% (harvest at 3 days after the final application) of TRR. Acetonitrile extracts of homogenised tomatoes accounted for 5.8% TRR (2 hour harvest) and 6.2% TRR (3 day harvest). After this extraction, 2.3% TRR (2 hour harvest) and 2.8% TRR (3 day harvest) remained unextracted in the tomato residue. The TRR from the treated tomatoes accounted for mean concentrations of 15.6 (2 hour harvest) and 9.7 (3 day harvest) mg equiv/kg.

Leaves were only removed for analysis 3 days after the final application of [^{14}C]triforine. The TRR in these leaves accounted for a mean concentration of 89 mg equiv/kg.

At the time of harvest untreated tomatoes were taken from plants with treated leaves. The initial surface washes of the untreated tomatoes contained 18% TRR with 82% TRR in the remaining tomato flesh extract plus residue. The TRR in untreated tomatoes accounted for a mean concentration of 0.004 mg equiv/kg indicating a very low degree of translocation.

Samples of surface washes and extracts were pooled namely Pool 1 to 2 as in table below to give representative samples for both tomatoes and leaves and analyzed directly by TLC or HPLC. Radiolabelled metabolites formed in the study were characterized by co-chromatographic comparison using two different systems.

Table 11 Proportion of radioactive components in tomatoes at harvest

	2 hours after successive applications					
	Surface wash		Tomato extract		Total	
	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2
	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)
Extract						
Triforine	87.9 (11.6)	89.4 (18.2)	4.56 (0.60)	3.30 (0.67)	92.5 (12.2)	92.7 (18.9)
W 1069	< 0.9 (< 0.12)	< 0.9 (< 0.18)	0.23 (0.030)	0.90 (0.18)	0.23 (0.030)	0.90 (0.18)
Unidentified A	< 0.9 (< 0.12)	< 0.9 (< 0.18)	< 0.06 (< 0.008)	0.24 (0.049)	< 0.09 (< 0.12)	0.24 (0.049)
Unidentified B	< 0.9 (< 0.12)	< 0.9 (< 0.18)	0.17 (0.022)	0.24 (0.049)	0.17 (0.022)	0.24 (0.049)
Unidentified C	< 0.9 (< 0.12)	< 0.9 (< 0.18)	0.29 (0.038)	0.48 (0.098)	0.29 (0.038)	0.48 (0.098)
WOS 613	< 0.9	< 0.9	0.23	0.36	0.23	0.36

	2 hours after successive applications					
	Surface wash		Tomato extract		Total	
	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2
	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)
	(< 0.12)	(< 0.18)	(0.030)	(0.073)	(0.030)	(0.073)
W 625	< 0.9 (< 0.12)	< 0.9 (< 0.18)	0.17 (0.022)	0.24 (0.049)	0.17 (0.022)	0.24 (0.049)
Other	3.7 (0.49)	2.8 (0.57)	0.06 (0.008)	0.30 (0.061)	3.76 (0.50)	3.10 (0.63)
Unextracted	–	–	2.7 (0.36)	1.8 (0.37)	2.7 (0.36)	1.8 (0.37)
	3 days after a successive applications					
	Surface wash		Tomato extract		Total	
	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2
	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)
Extract						
Triforine	86.9 (10.3)	89.5 (7.3)	4.50 (0.53)	2.89 (0.24)	91.4 (10.8)	92.4 (7.58)
W 1069	< 0.9 (< 0.11)	< 0.9 (< 0.07)	1.05 (0.12)	0.78 (0.064)	1.05 (0.12)	0.78 (0.064)
Unidentified A	< 0.9 (< 0.11)	< 0.9 (< 0.07)	0.30 (0.035)	0.20 (0.016)	0.30 (0.035)	0.20 (0.016)
Unidentified B	< 0.9 (< 0.11)	< 0.9 (< 0.07)	0.38 (0.045)	0.20 (0.016)	0.38 (0.045)	0.20 (0.016)
Unidentified C	< 0.9 (< 0.11)	< 0.9 (< 0.07)	0.45 (0.053)	0.29 (0.024)	0.45 (0.053)	0.29 (0.024)
WOS 613	< 0.9 (< 0.11)	< 0.9 (< 0.07)	0.30 (0.035)	0.25 (0.021)	0.30 (0.035)	0.25 (0.021)
W 625	< 0.9 (< 0.11)	< 0.9 (< 0.07)	0.45 (0.053)	0.25 (0.021)	0.45 (0.053)	0.25 (0.021)
Other	2.7 (0.32)	2.8 (0.23)	0.15 (0.018)	0.05 (0.004)	2.85 (0.34)	2.85 (0.23)
Unextracted	–	–	2.8 (0.33)	2.8 (0.23)	2.8 (0.33)	2.8 (0.23)

Note: In order to provide material for duplicate chromatographic runs, surface washes and extracts containing most radioactivity were combined to obtain two pooled samples from different fruits and leaves.

At 2 hours and 3 days after the final application only one major discrete component was observed in surface washes which accounted for 86.9–89.5% TRR. The major component in tomato extracts was also shown to co-chromatograph with triforine and accounted for 2.89–4.56% TRR. This major radioactive component was identified as triforine by co-chromatography with authentic test substance using both normal phase TLC and reverse phase HPLC. Triforine accounted for 91.4–92.7% TRR in in surface washes and extracts of tomatoes taken at 2 hours and 3 days after the final application of ^{14}C-triforine. In addition, W 1069, WOS 613 and W 625 were identified by co-chromatography with reference compounds in both normal phase TLC and reverse phase HPLC. Three further unidentified components A, B and C were observed that did not co-chromatograph with the available reference compounds. The major component present in the tomato at harvest was identified as triforine and accounted for means of 15.6 and 9.19 mg/kg in tomatoes taken 2 hours and 3 days after the final application of triforine respectively. The minor components W 1069, WOS 613, W 625 and each unidentified component (A-C) generally accounted for 0.02–0.1 mg equiv/kg. Radioactivity unextracted from the tomato accounted for 0.2–0.4 mg equiv/kg.

The unidentified radioactive components in the tomato extracts taken 3 days after the final application of [^{14}C]triforine were in the range of 0.02–0.05 mg equiv/kg. In order to provide further information to characterise these unidentified components, their partitioning behaviour was investigated (Hawkins *et al*, 1994: TF-640-040). Samples of the tomato extracts were diluted with water and extracted with ethyl acetate at both pH 2 and pH 9. In addition, further samples were incubated separately with β-glucuronidase/sulphatase and β-glucosidase. These incubates at pH 5

were also extracted with ethyl acetate. The radioactive components in these organic and aqueous layers were quantified by TLC and the partitioning behaviour of each component was calculated.

The unidentified metabolites A and B were shown to be polar water soluble components at pH 2 and 9 and were not hydrolysed with either β-glucuronidase/sulphatase or β-glucosidase. The metabolite C was partitioned between both the organic (*ca* 80%) and aqueous (*ca* 20%) layers at pH 2 and 9 but was entirely organo-soluble at pH 5 (after enzyme treatment). Component C was also not hydrolysed with the enzyme treatments.

Cucumber

The metabolism of [^{14}C]triforine has been studied in cucumbers and leaves after four successive applications of a commercial formulation of 0.1% [side chain-^{14}C]-triforine at 7-day intervals (Hawkins *et al*, 1993: TF-640-039). Cucumber plants (variety Brunex F1) were transplanted to 25 cm diameter plastic plant pots containing potting compost. The study was conducted in a controlled environment room with a daylength of 15 hours and day and night temperatures of 21.8 ± 0.5 °C. Samples of [^{14}C]triforine (*ca*. 6 mg) were mixed with 25 µL blank formulation (EC 190 g/L) giving *ca*. 31 mg of formulation. This formulation was diluted with water to give a final concentration of 1.2 g/L. Specific amounts of the formulated [^{14}C]triforine were applied to either cucumbers (200 µL first application, 300 µL remaining applications) or leaves (200 µL) using a syringe. The treatment was applied as a series of small droplets at random over the surface of the cucumber/leaf. The treated cucumbers were harvested 3 days after the last of four successive applications. For comparison additional samples were taken 2 hours after the first application.

The recovery of radioactivity from selected sample cucumbers and leaves was measured about 2 hours after the first application. The remaining cucumbers were taken, together with the leaves and untreated cucumbers, 3 days after the fourth application of [^{14}C]triforine. Surface washes on all treated samples were collected on the day of sample collection and samples were stored at < – 15 °C overnight. Each treated cucumber or leaf was surface washed by immersion in acetonitrile for 5 minutes during which time the container was placed in a sonic bath. The surface wash was then separated by decanting and the process repeated twice, once with acetonitrile and once with acetonitrile: water (70:30 v/v). After the surface washes were completed the cucumber was peeled and the peel or flesh was homogenized with acetonitrile, sonicated and the sample centrifuged. Leaves removed at harvest were also extracted using this procedure. The supernatant extract was removed and the process repeated once with acetonitrile and once with acetonitrile: water (70:30 v/v). The volumes of the surface washes and extracts were measured and aliquots (*ca*. 100 µL) removed for estimation of radioactive content by LSC. The extracted residues were allowed to air-dry and the radioactive content determined by combustion of sub-samples. A similar extraction procedure was employed for the untreated cucumbers removed at harvest.

Table 12 The distribution of radioactive residues in cucumbers and leaves

	2 hours after one application (n = 3)				3 days after 4 applications (n = 12)			
	Cucumber		Leaf		Cucumber		Leaf	
	%AR	%TRR	%AR	%TRR	%AR	%TRR	%AR	%TRR
Extract	91.1	98.9	96.6	99.7	76.1	93.4	90.7	99.0
Surface wash	88.2	95.8	95.9	99.0	68.9	84.5	85.5	93.4
Peel or leaf	1.6	1.7	0.7	0.7	6.1	7.5	5.2	5.6
Flesh	1.3	1.4	–	–	1.1	1.4	–	–
Unextracted	1.0	1.1	0.3	0.4	5.5	6.7	1.0	1.1
Total	92.0	100	96.8	100.1	81.6	100.1	91.6	100.1

Three cucumbers and three leaves were sampled for analysis 2 hours after the first application of [^{14}C]triforine. The mean amounts of radioactivity recovered in the surface washes was 95.8% TRR (cucumber) and 99.0% (leaf) TRR. Extracts of the homogenized cucumber peel and flesh contained small amounts of radioactivity (1.7% and 1.4% TRR) and radioactivity extracted from the leaf contained 0.7% TRR. Radioactivity in the unextracted residues accounted for 1.1% TRR

(cucumber) and 0.4% TRR (leaf). The mean concentrations in whole cucumber and leaf were 0.57 and 81.5 mg equiv/kg, respectively.

The initial surface washes of treated cucumbers at harvest accounted for 84.5% TRR. Extracts of homogenised cucumber peel and flesh accounted for 7.5% TRR (peel) and 1.4% TRR (flesh). After these extractions, 6.7% TRR remained unextracted in the residues. The TRR from the treated cucumbers accounted for a mean concentration of 2.17 mg equiv/kg.

The surface washes of treated leaves at harvest contained 93.4% TRR. Acetonitrile extracts of the homogenised leaves contained 5.6% TRR whilst 1.1% TRR remained unextracted in the leaf residue. The TRR in the leaf accounted for a mean concentration of 114 mg equiv/kg.

At the time of harvest untreated cucumbers were taken from plants with treated leaves. The initial surface washes of the untreated cucumbers contained 25% of TRR with 75% in the remaining cucumber flesh extract plus residue. The TRR in untreated cucumbers accounted for a mean concentration of 0.0044 mg equiv/kg indicating a very low degree of translocation.

Table 13 Proportion of radioactive components in cucumbers at harvest

	Surface wash		Peel		Flesh		Total	
	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2	Pool 1	Pool 2
	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)	%TRR (mg/kg)
Extract								
Triforine	84 (1.81)	81 (1.77)	3.3 (0.07)	5.6 (0.12)	0.24 (0.005)	0.34 (0.007)	87.5 (1.9)	86.9 (1.9)
W 1069	< 0.9 (< 0.02)	< 0.8 (< 0.02)	0.72 (0.02)	0.68 (0.01)	0.11 (0.002)	0.11 (0.002)	0.83 (0.02)	0.79 (0.02)
Unidentified A	< 0.9 (< 0.02)	< 0.8 (< 0.02)	1.6 (0.03)	1.6 (0.04)	0.13 (0.003)	0.08 (0.002)	1.73 (0.04)	1.68 (0.04)
Unidentified B	< 0.9 (< 0.02)	< 0.8 (< 0.02)	0.13 (0.003)	0.09 (0.002)	0.15 (0.003)	0.15 (0.003)	0.28 (0.006)	0.24 (0.005)
Unidentified C	< 0.9 (< 0.02)	< 0.8 (< 0.02)	0.20 (0.004)	0.26 (0.006)	0.15 (0.003)	0.10 (0.002)	0.35 (0.008)	0.36 (0.008)
WOS 613	< 0.9 (< 0.02)	< 0.8 (< 0.02)	0.13 (0.003)	< 0.09 (< 0.002)	0.21 (0.005)	0.27 (0.006)	0.34 (0.007)	0.27 (0.006)
W 625	< 0.9 (< 0.02)	< 0.8 (< 0.02)	0.26 (0.006)	0.26 (0.006)	0.20 (0.004)	0.18 (0.004)	0.46 (0.010)	0.44 (0.010)
Other	2.6 (0.06)	1.7 (0.04)	0.20 (0.004)	< 0.09 (< 0.002)	0.20 (0.004)	0.18 (0.004)	3.0 (0.06)	1.88 (0.04)
Unextracted	–	–	5.4 (0.12)	6.6 (0.14)	0.6 (0.01)	0.8 (0.02)	6.0 (0.13)	7.4 (0.16)

Note: In order to provide material for duplicate chromatographic runs, surface washes and extracts containing most radioactive components were combined to obtain two pooled samples from different fruits and leaves.

Three days after the final application only one major discrete component was observed in surface washes which accounted for 81–84% TRR. The major component in cucumber extracts was also shown to co-chromatograph with triforine and accounted for 3.3–5.6% TRR (peel) and 0.24–0.34% TRR (flesh). The major radioactive component was identified as triforine by co-chromatography with authentic test substance using both normal phase TLC and reverse phase HPLC. The total radioactivity associated with triforine in surface washes and extracts accounted for 86.9–87.5% TRR in cucumber taken 3 days after the final application of [^{14}C]triforine.

The extracts also contained several minor components each accounting for 0.3–2% TRR. Three of these were identified as the compounds W 1069, WOS 613 and W 625 by co-chromatography with reference compounds in both normal phase TLC and reverse phase HPLC. Three further unidentified components A, B and C were observed that did not co-chromatograph with the available reference compounds.

The major component present in the cucumber at harvest was identified as triforine and accounted for 1.9 mg/kg. The minor components W 1069, WOS 613, W 625 and unidentified

components A-C each accounted for 0.005–0.04 mg equiv/kg. Radioactivity unextracted from the cucumber accounted for 0.13–0.16 mg equiv/kg.

The unidentified radioactive components in the cucumber extracts taken 3 days after the final application of [^{14}C]triforine were in the range of 0.002–0.04 mg equiv/kg. In order to provide further information to characterise these unidentified components, their partitioning behaviour was investigated (Hawkins *et al*, 1994: TF-640-041). Samples of the cucumber extracts were diluted with water and extracted with ethyl acetate at both pH 2 and pH 9. In addition, further samples were incubated separately with β-glucuronidase/sulphatase and β-glucosidase. These incubates at pH 5 were also extracted with ethyl acetate. The radioactive components in these organic and aqueous layers were quantified by TLC and the partitioning behaviour of each component calculated.

The unidentified A and B were shown to be polar water-soluble components at pH 2 and 9 and were not hydrolysed with either β-glucuronidase/sulphatase or β-glucosidase. The unidentified C was partitioned between both the organic (40–80%) and aqueous (60–20%) layers at pH 2 and 9 but was entirely organo-soluble at pH 5 (after enzyme treatment).

Barley

Study 1

The metabolism of [^{3}H]triforine in barley plants has been studied (Rouchaud *et al,* 1977: TF-905-013). Barley plants (variety Hebe) were grown (33 plants/pot) in plastic pots (13 cm diameter), containing a mixture of sand and expanded perlite (1/1, v/v). Unlabelled triforine (30 mg/pot) and an equal weight of adjuvant powder were emulsified in water (30 mL/pot) and [^{3}H]triforine dissolved in methanol was added to the emulsion to give the preparation used for soil drenching. Three leaves were harvested at 15 and 30 days after treatment, immediately weighed and then homogenised (6 min, 4 °C) with ethanol. Each homogenate (3 mL) was filtered on glass filters, the solid residue washed on the filter with ethanol to remove any unbound label, dried under an infrared lamp and ^{3}H determined with a LSC.

The harvested leaves were frozen in plastic bags with an ethanol-solid CO_2 mixture and stored (-20 °C). The leaves (50 g), warmed up to room temperature, were homogenised with chloroform (300 mL). The supernatant was centrifuged and filtered, giving the primary chloroform extract and a solid residue. The primary chloroform extract was transferred to a separatory funnel and extracted with aqueous HCl, giving the secondary chloroform extract. The secondary chloroform extract was filtered through potassium carbonate and concentrated in a rotary vacuum evaporator. The hydrochloric acid extract was brought to pH 7 with aqueous 2.0 M and 0.1 M NaOH, and freeze-dried. The powder was put on a chromatographic column and eluted with the chloroform which had been used to rinse the dishes used in the freeze-drying. In some experiments, the hydrochloric acid extract was brought to pH 4 with aqueous 2.0 M and 0.1 M NaOH and freeze-dried. The identification of the radioactive TLC spots was made by comparison of their Rf values with those of standard compounds, using four TLC systems for each metabolite.

Each concentrate of the secondary chloroform and acid extracts was analysed by TLC using all four eluting solvents. The compositions of the two extracts, as shown by TLC, were different and no labelled compound was common to both. The secondary chloroform extract contained mostly triforine. In the hydrochloric acid extract, a metabolite was observed for which the chemical structure W 1084 was suggested. Another labelled compound in this extract was probably piperazine, the concentration of which increased with time after treatment. The amounts of piperazine observed were similar in freeze-dried pH 4 or pH 7 extracts. Triforine was found only in the secondary chloroform extract, and W 1084 and piperazine were present only in the 0.1 M HCl extract. None of these compounds was transformed into the others during the analytical process.

Table 14 Total percentage distribution of radioactivity in the leaves of barley plants treated with [^{3}H]triforine

	%TRR	
	15 days after treatment	30 days after treatment
Extract	76.9	61.8
Secondary chloroform extract	61.6	46.4
Triforine	57.5	43.2
Unidentified	4.1	3.2
0.1 M HCl extract	15.3	15.4
W 1084	12.9	8.4
Piperazine	0.3	4.0
Unidentified	2.1	3.0
Unextracted	23.1	38.2

Study 2

The leaves of barley plants root-treated with [^{3}H]-triforine (uniformly labelled in the piperazine ring) were analysed 30 days after treatment (Rouchaud *et al*, 1978: TF-640-008). The distribution of the methanol-soluble ^{3}H-constituents was similar to that of the chloroform soluble (Study 1): 45% triforine, 10% W 1084, 5% piperazine. Methanol extraction left a solid plant residue which contained 33% of the total ^{3}H which had been incorporated into the leaves. Methanol acidified with hydrochloric acid extracted a further 18% of the triforine-derived bound residues as W 1084 (8%) and piperazine (10%). In the plants, these compounds had thus been complexed to plant constituents.

Hot dimethyl sulphoxide (DMSO) extracted a further 13% of the total ^{3}H, leaving a solid residue (mainly cellulose) which contained 2% of ^{3}H, perhaps incorporated into the cellulose. Evaporation of the solvent from the DMSO extract gave a solid substance with the radioactivity (13%), which could not be extracted by methanol. A part (7%) of this radioactivity could be released by successive hydrolysis with aminoglucosidase and β-glucosidase, which generated a complex mixture of polar and water soluble unknown radioactive compounds not including piperazine. These latter compounds would be the products of extensive metabolism of triforine (and its metabolite piperazine) bound to, or incorporated into starch. Most (11%) of the radioactivity of this solid could be released by hydrochloric acid hydrolysis, which also generated a complex mixture of polar and water soluble unknown radioactive compounds not including piperazine; a part (4%) of them could have been associated with lignin in the plant.

Study 3

The metabolism of the [^{3}H]-triforine, uniformly labelled in the piperazine ring, has been studied in barley (Rouchaud *et al*, 1978: TF-640-010). Barley (variety Hebe) was sown and grown normally in an experimental field. At growth stage J (during the stem extension stage when the second node of the stem was formed and the next-to-last leaf was just visible), the aerial part of the plants was sprayed with an aqueous emulsion of a mixture of the commercial formulation of triforine and [^{3}H]-triforine. The total dose of 0.25 kg ai/ha was that of agronomic practice. Barley was harvested when ripe, and straw and grain were analysed separately.

The straw and grains were washed rapidly and successively with water and methanol, the washing liquids being discarded as they did not contain significant amount of radioactivity. Extraction with methanol was followed by centrifugation. The first extract was macerated for 72 hours at 20 ^{o}C (300 mL to 100 g straw/grains). Three sequential extractions (300 mL methanol) were performed and the methanol extracts were combined. The straw was chopped and the grain was ground for extraction. This process was repeated with a further four samples of grain (100 g each) to provide sufficient material for metabolite identification. The extracts were partitioned with chloroform against dilute HCl. The metabolites in both phases were separated by column chromatography and characterized by TLC. Metabolites were identified by cleaning up by a preparative TLC followed by derivatisation and confirmation by co-chromatography with derivatized reference compounds.

The total radioactivity concentration was 20 times higher in straw than in grain. In straw and grain respectively, 12 and 25% of the total incorporated radioactivity in each of these tissues were methanol soluble; this corresponded to the higher content of cellulosic and lignified tissues in straw than in grain, and the correspondingly higher solubilisation of the radioactive residues. The amount of methanol soluble radioactivity was 14 times higher in straw than in grain.

The methanol soluble radioactive residue contained the triforine and its metabolites which were free and unbound in barley straw and grain. No radioactive piperazine was observed, in spite of the high detection sensitivity for radioactivity. Triforine was identified and accounted for 0.034 mg/kg (18% TRR) in straw and 0.0018 mg/kg (13% TRR) in grain. W 1084 was identified at 0.009 mg/kg (7% TRR) in straw and 0.0006 mg/kg (7% TRR) in grain. Two other radiolabelled components were identified: Glycine was found at 0.043 mg/kg (33% TRR) in straw and 0.0033 mg/kg (34% TRR) in grain. Iminodiacetic acid was also identified at 0.021 mg/kg (17% TRR) in straw and 0.001 mg/kg (11% TRR) in grain.

Extraction of the grain with methanol left methanol-insoluble solids containing an amount of radioactivity (the bound residue) which represented 75% of the total radioactivity incorporated into the grain. Methanol acidified with hydrochloric acid extracted a further 7% TRR of the triforine-derived bound residues in the form of radioactive iminodiacetic acid (1.1% TRR), glycine (3.3% TRR), serine (0.9% TRR), ethanolamine (0.2% TRR) and unidentified compounds (1.5% TRR). Aqueous 0.03 M NaOH extracted a further 27% of the total tritium which had been incorporated by means of chemical bonds into the protein fraction; acid hydrolysis of the proteins yielded radioactive glycine (9.2% TRR), serine (3.9% TRR) and unidentified compounds (13.9% TRR) which could have been a mixture of a large number of other amino acids. The plant solids (which contained 41% of the total tritium) left after the alkaline aqueous extractions were processed and separated into tritiated cellulose (4% TRR) and starch (37% TRR) fractions. The starch was hydrolysed aand the resulting glucose was converted into the osazone (34% TRR). After being recrystallized several times, the osazone contained a constant specific radioactivity, indicating that [^{3}H]-glucose was present. No piperazine was observed in the bound residues in the grain. (Rouchaud *et al*, 1979: TF-905-020)

Extraction of the straw with methanol left methanol-insoluble solids containing an amount of radioactivity (the unextracted residue) which represented 88% of ^{3}H (as with all the subsequently referred % of ^{3}H relative to the total of ^{3}H incorporated into the straw). Methanol acidified with hydrochloric acid extracted a further 8% TRR of the triforine-derived bound residues as radioactive iminodiacetic acid (0.4% TRR), glycine (3.2% TRR), serine (2.0% TRR), ethanolamine (0.2% TRR) and unidentified compounds (2.2% TRR). A neutral detergent solution extracted a further 3% of the radioactive triforine-derived bound residues as unidentified compounds; three radioactive compounds, which were dissolved by the acidified methanol and by the neutral detergent solution, were thus in the straw complexed to straw constituents. An acid detergent solution extracted a further 58% of the total ^{3}H, which was really incorporated by means of chemical bonds into the hemicelluloses fraction; the acid hydrolysis of the hemicelluloses yielded a mixture of monosaccharides which were derivatised into a mixture of osazones (50% TRR). The plant solids (which contained 19% of the total ^{3}H), remained after the acid detergent extraction, were processed and separated into the ^{3}H containing cellulose (13% TRR) and lignin (6% TRR) fractions. No piperazine was observed in the bound residues in the grain. (Rouchaud *et al*, 1979: TF-640-014)

Summary of plant metabolism

Triforine was the major component present in the edible portion of the harvested crops. Only small amounts of metabolites were observed and those identified contained the intact piperazine ring. In barley metabolism was much more extensive with more than 90% of the terminal residue in grain and straw being present as natural products either extractable with neutral solvent (monomers) or incorporated into plant polymers and only extractable after acid hydrolysis or digestion of the plant constituents. Triforine, glycine and iminodiacetic acid were present in small amounts in the methanol extracts of grain and straw with triforine predominating in both grain and straw. Triforine and extractable metabolites were all less than 0.01 mg/kg in harvested grain following application at approximately 0.25 kg ai/ha.

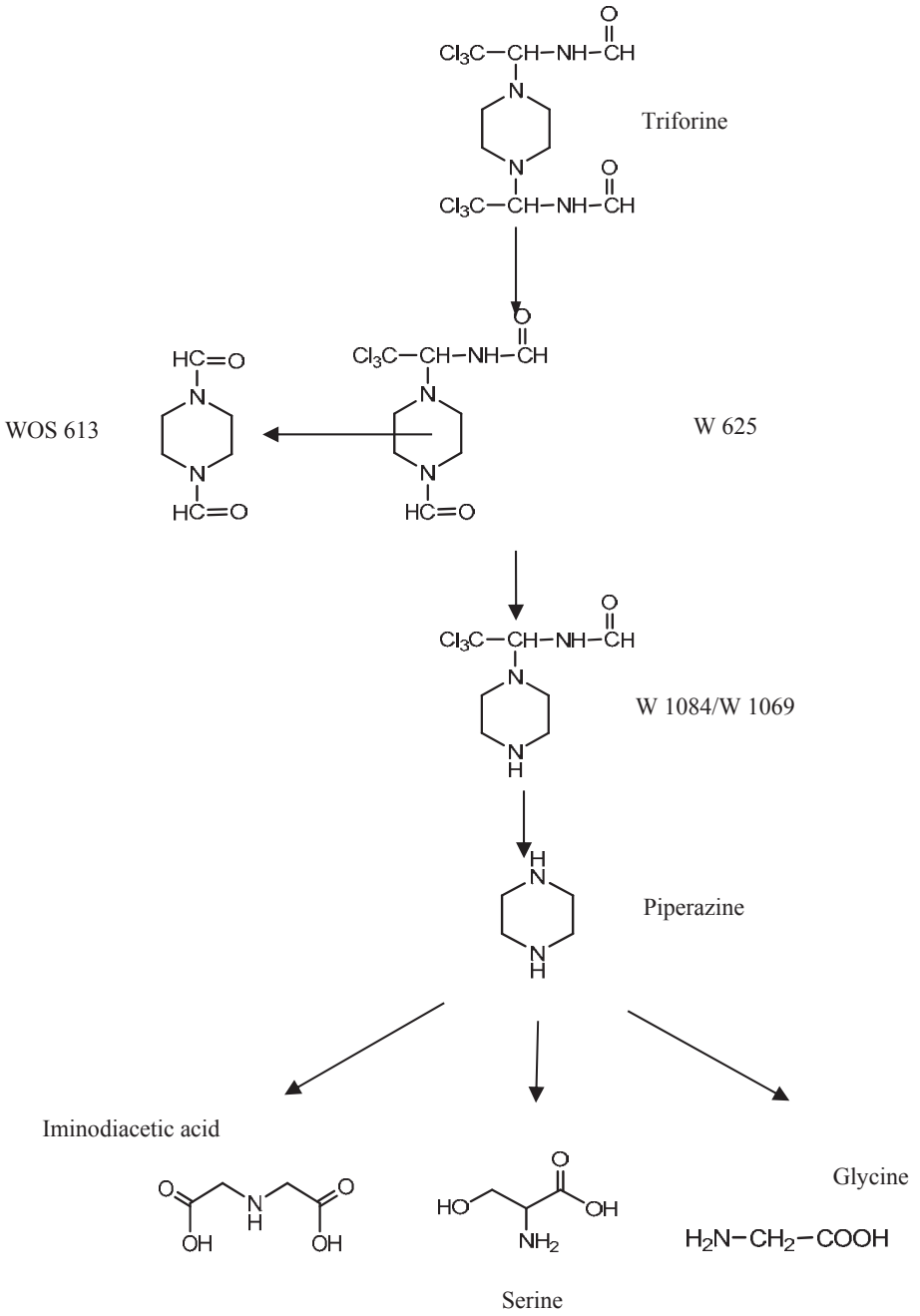


Figure 3 Metabolic pathway of triforine in plants

Environmental fate in soil

The Meeting received information on aerobic degradation in soil, photolysis on soil surface and hydrolytic degradation study. Because triforine is intend for use as foliar treatment, aerobic degradation, soil photolysis and hydrolytic degradation study relevant to the current evaluations are reported below (FAO Manual 2009).

The fate and behaviour of triforine in soils were investigated using [piperazine-^{14}C] and [side chain-^{14}C] labelled compounds.

Aerobic degradation

Study 1

The degradation of [piperazine-^{14}C]-triforine in a silty loam soil and a sandy loam soil when incubated at 20 °C under aerobic and anaerobic conditions has been studied over a period of 184 and 60 days respectively (Rainford, 1990: TF-620-005). Throughout the study evolved CO_2 and organic volatiles were collected from the flaks of soil and aliquots removed for analysis. The soil was extracted using acetone and other solvents, including caustic extracts. The extracts were analyzed for [^{14}C]triforine and its degradation products by TLC. The mean overall recoveries of applied radioactivity for the aerobic and anaerobic incubates containing the sandy loam soil were 88.2 $\pm$ 3.8% and 79.9 $\pm$ 5.7% respectively and for the silty loam soil were 93.7 $\pm$ 4.6% and 92.6 $\pm$ 5.9% respectively. No significant production of $^{14}CO_2$ occurred before 3 weeks. After 184 days approximately 24% of the applied radioactivity had evolved as $^{14}CO_2$ from both soils under aerobic conditions. The distribution of radioactivity recovered from the two soil types under aerobic varied slightly. The applied radioactivity in the acetone extracts declined more quickly from the silty loam soil (80% at 0 day, 13% at 28 days and 1% at 184 days) than the sandy loam soil (85% at 0 day, 54% at 28 days and 18% at 184 days). In both soil types an increase in the proportion of applied radioactivity in the caustic extracts occurred reaching a maximum of 36% at 28 days for the silty loam soil and 23% at 42 days for the sandy loam soil. The percentage of applied radioactivity present as bound residues were higher in the silty loam soil (47% at 60 days) compared to that in the sandy loam soil (12% at 42 days).

Degradation half-lives of 35.8 and 69.6 days were determined for triforine in the silty and sandy loam soils respectively under aerobic conditions. After 184 days, approximately 0.35% and 6% of the applied radioactivity remained as triforine in the two soils respectively. The decline in triforine concentrations was accompanied by an increase in bound radioactivity and a large number of very minor degradation products. No one component at any time represented more than 3% of applied radioactivity. Very tentative identification of four degradates was made: W 625, WOS 2379, piperazine and W 1069. Due to the very low levels present there was no possibility of further identification of any of these degradates from samples obtained from this study.

Under aerobic conditions, [^{14}C]triforine is degraded to at least 14 degradates in silty loam and eight degradates in sandy loam when incubated for up to 184 days at 20 °C. No major degrades were produced. The rate of degradation in the silty loam exceeded that in the sandy loam. In both soil types, degradation was accompanied by the evolution of $^{14}CO_2$, indicating that degradation involved cleavage of the ring structure and bound residues.

Study 2

The aerobic degradation and metabolism of [side chain-^{14}C]-triforine was investigated in a US soil (sandy loam) under laboratory conditions (20 $\pm$ 2 °C, in the dark) for 365 days (Wyss-Benz, 1993: TF-620-033). The test article was applied at a maximum recommended field rate of 0.38 kg ai/ha corresponding to 0.512 mg ai/kg dry soil in the top 5 cm or 0.051 mg ai/100 g soil sample. Duplicate soil samples were applied for 0, 7, 14, 28, 56, 84, 112, 147, 189, 238 and 365 days of incubation. Samples were submitted to several extractions with first acetonitrile, and then acetonitrile/water (1:1). Extracts of acetonitrile were combined, concentrated and submitted to TLC and HPLC analysis.

The mean recoveries from duplicate samples ranged from 91.0% to 106% of the radioactivity applied, with an average mean recovery from all samples of 97.1 $\pm$ 5.6%. The radioactivity extracted from the soil decreased from 101% of the radioactivity applied (0.519 mg equiv/kg dry soil) on day 0 to 13.2% (0.067 mg equiv/kg) on day 365. The non-extracted radioactivity increased from 4.6% (0.024 mg equiv/kg) on day 0 to 38.2% (0.196 mg equiv/kg) on day 238, and then decreased slightly until day 365 to 35.0% (0.179 mg equiv/kg). The non-extracted radioactivity bound to the organic matter fractions was compared between day 147 and day 365. On day 147, 58.0% of the non-extracted radioactivity was found to be associated with fulvic acid, 9.9% with humic acids and 24.7% with

humin fraction. On day 365, 10% of the radioactivity proved to be more strongly bound as 32.5% were found in the humin fraction and only 49.8% in the fulvic acid fraction.

Mineralization of triforine took place from the beginning of the study, i.e. on day 7 with 1.3% (0.006 mg equiv/kg) and increased to 44.7% (0.229 mg equiv/kg) on day 365. No volatile compounds other than $^{14}CO_2$ could be detected. The mineralization was still detectable at the end of the study. The biomass was low at the beginning of the study but increased during the study from 6.0 mg C/100 g dry soils to 18.6 mg C/100 g dry soil on day 365. Most of the radioactivity extracted from the soil was identified as parent. The rate of disappearance was calculated using sampling intervals from day 0 to day 84 only. Half-life (DT_{50}) was determined by the first order reaction kinetics model as 23.9 days with a DT_{90} value of 79.3 days

Many minor degradation products were detected in the extracts during the study. Attempts were made to isolate degradates, however it was very difficult to identify them. One fraction was characterized as reference compound—the hydrochloride salt (W 1069), however the levels were small at a maximum of 0.08 mg/kg on day 56, decreasing until the end of the study to 0.026 mg/kg.

It can be concluded from this study that triforine was rapidly degraded and readily mineralized in the sandy loam soil under the chosen experimental conditions and that many minor degradation products representing < 0.01 mg equiv/kg were formed.

Study 3

The decomposition of triforine in five soils (Speyer 2.2, Riverside, Sion Hill, Middlefield and Silt loam) was studied in laboratory tests (Jones, 1989: TF-620-011). Treated soils were incubated aerobically at 20 $\pm$ 3 °C in the dark. The concentration of triforine in each soil was determined at intervals of 0, 2, 8, 16, 32, 64, 100, 147 and 164 days after treatment.

Soil samples were extracted into acetone/chloroform (3:7). The extract was cleaned up by solid phase extraction chromatography using C_{18} bond elute columns. The final extract was then quantified by reverse phase HPLC using a variable wavelength UV absorbance detector. The limit of detection of the HPLC system was 0.1 mg/L of triforine. The microbial biomass was determined by monitoring the $^{14}CO_2$ evolution from duplicate samples of known masses of test soils fortified with [^{14}C]glucose.

The mean percent nominal recoveries of triforine from the fortified control soil samples ranged between 77 and 85% respectively. There was a significant reduction in the measured concentration of triforine. The DT_{50} values for the five soils ranged between 1 and 7 days.

Table 15 The DT_{50} and DT_{90} values for the five soils

Soil type	50% Degradation time	90% Degradation time
Speyer 2.2 (loamy sand)	7 days	116 days
Riverside (clay loam)	7 days	69 days
Sion Hill (sandy loam)	7 days	78 days
Middlefield (silty clay)	1 day	3 days
Silt loam (silt loam)	4 days	55 days

Soil photolysis

The artificial sunlight photodegradation of [piperazine-^{14}C]triforine was studied on sandy loam soil. The artificial sunlight source was a xenon lamp that had a special energy distribution similar to that of natural sunlight (Saxena, 1990: TF-620-008). Soil samples in petri dishes were prepared and fortified with [^{14}C]triforine at concentration of 10 mg ai/kg. Soils samples were placed in a xenon lamp chamber and irradiated continuously (24 hours/day) at a temperature of 22.4 to 27.2 °C. Dark control samples were placed in a glass chamber and maintained in the dark at 25 °C. Traps for volatile components were connected to the irradiation and dark control chambers. In addition, a charcoal trap was connected to the irradiation chamber. Two soil samples were analyzed at hour 0, and then duplicated irradiated soil samples were removed for analysis after 1, 2, 4, 8, 10, 24, 30 and 48 hours

of irradiation. Samples were extracted with methanol: water (9:1). The extracts as well as the extracted soil (oxidized by combustion) were analyzed by liquid scintillation counting. The distribution of radioactivity in the methanol: water extract was determined by thin layer chromatography (TLC). The TLC plates were analyzed using a linear analyzer.

The recovery of applied radioactivity for the irradiated and dark control soil samples ranged from 92.2% to 104% and from 91.0% to 104%, respectively. The applied radioactivity remaining in the methanol: water extracts ranged from 97.9% to 72.1% for the irradiated samples and from 101.2% to 83.4% for the dark control samples. The applied radioactivity remaining in the methanol: water extracted soil ranged from a mean of 25.2% to 1.9% at all study intervals for the irradiated samples and from a mean of 1.9% to 18% for the dark control samples. The cumulative radioactivity in the traps was 0.5% or less at all study intervals for both test conditions.

Analysis of the methanol: water extracts of the study samples using TLC system showed that the [^{14}C]triforine degraded rapidly on soil when irradiated with a xenon lamp. The degradation was biphasic. The calculated degradation half-life of [^{14}C]triforine was 11.4 hours of artificial sunlight, equivalent to 0.5 natural sunlight days for phase 1 (hours 0 to 8). For phase 2 (hours 8 to 48), the half-life was 70.9 hours of artificial sunlight equivalent to 3.16 natural sunlight days. Radiolabelled triforine degraded under dark conditions, with a half-life of 76.5 hours. For the irradiated samples, **[**^{14}C]triforine was observed at all intervals by TLC analysis. Several peaks were observed: one had similar Rf value to that of non-radiolabelled standard W 1069. The maximum was 9.9% at hour 48. For the dark control samples, [^{14}C]triforine was observed at all intervals by TLC analysis. Several peaks were observed, the maximum was 10.3% at hour 24.

RESIDUE ANALYSIS

Analytical methods

Descriptions of analytical methods together with validation data for residues of triforine in plant and animal matrices were submitted to the Meeting. The methods rely on an initial extraction, usually with acetone. After solvent partition, the triforine and metabolites residues are degraded by heating with sulphuric acid. The residues of triforine and metabolites containing piperazine ring can be measured by the analysis of degradate (chloral hydrate) with GC-ECD, typically to an LOQ of 0.01 mg/kg.

Detailed descriptions of all these analytical methods are presented below.

Plant matrices

Cereals (green plants, straw, grain), fruit, vegetables, meat, milk, soil, water (102FX-522-009, TF-240-002)

Analyte:	Triforine	GC-ECD	RU 3,26/12/10
LOD:	0.005–0.01 mg/kg		
Description	The samples are blended with acetone. After removal of the acetone by distillation the triforine in the remaining aqueous phase is partitioned into toluene. The toluene is evaporated and the active substance was degraded by heating with dilute sulphuric acid. Chloral hydrate thus formed is distilled, extracted with ethyl formate and determined by gas chromatography with an electron capture detector.		

Plant and animal products (102AA-522-008, TF-244-006)

Analyte:	W 1084	GC-ECD
LOD:	0.01 mg/kg	
Description	The samples are blended with acetone. After removal of the acetone by distillation the triforine is partitioned into toluene. The remaining aqueous phase contains W 1084, which is the main metabolite of triforine especially in animals. The aqueous solution is heated with dilute sulphuric acid. Chloral hydrate formed is distilled, extracted with ethyl formate and determined by gas chromatography with an electron capture detector.	

Chicory, carrot, red beet, Brussels sprout, white cabbage (102AX-522-015, TF-244-010)

Analyte:	Triforine	GC-ECD
LOQ:	0.01 mg/kg	
Description	The samples are extracted with acetone. After filtration and evaporation of acetone, triforine is partitioned from the remaining aqueous solution into dichloromethane. The solvent is evaporated and the active substance degraded by heating with dilute sulphuric acid. Chloroform that is formed is determined by head-space gas chromatography with an electron capture detector.	

Cherry, peach, plum, prune (TF-244-011)

Analyte:	Triforine, W 1084, 2,2,2-trichloroethanol, WOS 2379, W 625	GC-ECD	FAMS 041-01
LOQ:	0.01 mg/kg		
Description	The homogenised samples are diluted with water and sulfuric acid is added. Triforine, W 1084, WOS 2379 and W 625 are degraded by heating. Chloral hydrate and 2,2,2-trichloroethanol are separated by distillation, extracted with ethyl formate and determined by capillary gas chromatography with an electron capture detector.		

Green peppers, tomatoes, eggplant, Japanese persimmon (SAI No.135)

Analyte:	Triforine	LC-MS
LOQ:	0.01 mg/kg	
Description:	The samples are homogenised with acetone. The sample solution is purified with a graphite carbon mini-column, a C_{18} mini-column and a silica gel mini-column. The elution is evaporated and dissolved with methanol. The residue is determined by LC-MS.	

Blueberry and tomato (2040W)

Analyte:	Triforine (m/z 435→390 for quantification, 435→215 for confirmation)	LC-MS/MS
LOQ:	0.01 mg/kg for blueberries and tomatoes, 0.05 mg/kg for tomato paste	
Description:	The samples are extracted with acetone. The extract is subjected to further clean-up involving three SPE cartridge (ENVI-Carb, C_{18} and Silica gel) clean-ups. The final samples are analysed by LC-MS/MS for quantitation of triforine.	

The recoveries from plant matrices obtained during method validation are summarized in Table 16.

Table 16 Summary of recovery data for triforine and its metabolites fortified into plant matrices

Commodity		Fortification mg/kg	N	Range Recovery (%)	Mean recovery (%)	% RSD	Reference Method
Cucumber	Triforine	0.20	3	83–119	100	18.3	102AX-522-014, TF-244-008
Apple	Triforine	0.02 0.20	3 8	77–91 71–117	82 89	9.5 17.0	102AX-522-013, TF-244-009
Cherry	Triforine W 1084 Trichloroethanol WOS 2379 W 625	0.01–0.1 0.02–0.1 0.01–0.1 0.01–0.1 0.01–0.1	4 3 8 4 4		91 76 73 92 103	6 2 10 12 13	FAMS 041-01, TF-244-011

Commodity		Fortification mg/kg	N	Range Recovery (%)	Mean recovery (%)	% RSD	Reference Method
Peach	Triforine	0.01–0.1	4		82	6	
	W 1084	0.01–0.1	4		93	13	
	Trichloroethanol	0.01–0.1	8		66	19	
	WOS 2379	0.01–0.1	4		86	21	
	W 625	0.01–0.1	4		89	15	
Plum	Triforine	0.01–0.1	4		82	16	
	W 1084	0.01–0.1	5		92	11	
	Trichloroethanol	0.01–0.1	5		73	11	
	WOS 2379	0.01–0.1	4		108	7	
	W 625	0.01–0.1	4		92	7	
prune	Triforine	0.01–0.1	4		87	9	
	W 1084	0.01–0.1	4		92	12	
	Trichloroethanol	0.01–0.1	4		78	11	
	WOS 2379	0.01–0.1	4		85	21	
	W 625	0.01–0.1	4		81	9	
Cucumber	Triforine	0.01	2	78, 98	88		CFS 1994-105, TF-244-012
		0.10	2	80, 88	84		
		1.0	2	86, 95	91		
	W 1084	0.01	3	70–98	83	17.0	
		0.10	2	91, 93	92		
		1.0	2	76, 103	90		
	Trichloroethanol	0.01	2	65, 72	69		
		0.10	2	79, 88	84		
		1.0	2	97, 97	97		
	WOS 2379	0.01	2	103, 105	104		
		0.10	2	77, 78	78		
		1.0	4	64–71	68	4.5	
	W 625	0.01	2	87, 97	92		
		0.10	2	85, 89	87		
		1.0	2	71, 75	73		
Green pepper	Monitoring ion 391.7	0.01	3	101–113	107	5.6	SAI No.135
		1	3	92–97	95	2.8	
Japanese persimmon	Monitoring ion 391.7	0.01	3	96–105	101	4.5	
		1	3	91–96	94	2.8	
Eggplant	Monitoring ion 391.7	0.01	3	73–85	78	8.2	
		1	3	82 - 91	87	5.2	
Tomato	Monitoring ion 391.7	0.01	3	101–116	109	1.6	
		1	3	96–99	97	6.9	
Blueberry	Mass transition 435s tr	0.01	5	73–75	74	1	2040W
		0.10	5	71–88	76	9	
	Mass transition 435→215	0.01	5	68–74	71	3	
		0.10	5	68–85	75	9	
Tomato	Mass transition 435s tr	0.01	5	88–103	95	6	
		0.10	5	81–99	89	8	
	Mass transition 435→215	0.01	5	58–92	74	19	
		0.10	5	82–97	90	7	
Tomato paste	Mass transition 435s tr	0.05	5	71–94	79	11	
		0.10	5	69–77	74	4	
	Mass transition 435→215	0.05	5	72–91	79	9	
		0.10	5	72–83	77	5	

Animal matrices

Animal product (102FX-523-001, TF-245-001)

Analyte: Triforine, W 1084, W 2379 GC-ECD

LOD: 0.001 mg/kg for milk and 0.003 mg/kg for the other materials (muscle, liver, kidney and fat)

Description The samples are blended with acetone. The organic solvent is removed by distillation. Triforine and possible metabolites containing the Cl_3C-CH group (W 1084, W 2379) are degraded by heating with dilute sulphuric acid. Chloral hydrate formed is distilled, extracted with ethyl formate and determined by gas chromatography with an ECD.

Milk (TF-245-002)

Analyte: Triforine, W 1084, Trichloroethanol GC-ECD FAMS 037-01

LOQ: 0.001 mg/kg for triforine and trichloroethanol, 0.002 mg/kg for W 1084

Description The sample is diluted with water and sulphuric acid is added. Triforine and W 1084 are degraded by heating. Chloral hydrate formed and 2,2,2-trichloroethanol are separated by distillation, extracted with ethyl formate and determined by capillary gas chromatography with an ECD.

Bovine tissue (kidney, liver, muscle), fat and cream (TF-245-003)

Analyte: Triforine, W 1084, Trichloroethanol GC-ECD FAMS 038-01

LOQ: 0.01 mg/kg

Description The homogenised samples are diluted with water and sulphuric acid is added. Triforine and W 1084 are degraded by heating. Chloral hydrate formed and 2,2,2-trichloroethanol are separated by distillation, extracted with ethyl formate and determined by capillary gas chromatography with an ECD.

Egg (TF-245-005)

Analyte: Triforine, W 1084, Trichloroethanol GC-ECD FAMS 084-01

LOQ: 0.01 mg/kg

Description The homogenised samples are diluted with water and sulphuric acid is added. Triforine and W 1084 are cleaved upon heating. Chloral hydrate formed and 2,2,2-trichloroethanol are separated by distillation, extracted with ethyl formate and determined by capillary gas chromatography with an ECD.

The recoveries from animal matrices obtained during method validation are summarized in Table 17.

Table 17 Summary of recovery data for triforine and its metabolites fortified into animal matrices

Commodity		Fortification mg/kg	N	Range of Recovery (%)	Mean recovery (%)	% RSD	Reference
Milk	Triforine	0.001–0.1	5		75	15	FAMS 037-01
	W 1084	0.002–0.1	4		63	4	TF-245-002
	Trichloroethanol	0.001–0.1	10		86	8	
Bovine kidney	Triforine	0.01–0.1	4		68	4	FAMS 038-01
	W 1084	0.01–0.1	4		70	5	TF-245-003
	Trichloroethanol	0.01–0.1	4		89	6	
Bovine liver	Triforine	0.01–0.1	4		68	8	
	W 1084	0.01–0.1	4		68	5	
	Trichloroethanol	0.01–0.1	4		95	10	
Bovine muscle	Triforine	0.01–0.1	4		70	3	
	W 1084	0.01–0.1	5		81	10	
	Trichloroethanol	0.01–0.1	4		92	4	
Peritoneal fat	Triforine	0.01–0.1	4		78	3	
	W 1084	0.01–0.1	4		91	9	
	Trichloroethanol	0.01–0.1	4		90	3	
Subcutaneous fat	Triforine	0.01–0.1	4		76	4	
	W 1084	0.01–0.1	4		75	78	
	Trichloroethanol	0.01–0.1	4		88	7	

Commodity		Fortification mg/kg	N	Range of Recovery (%)	Mean recovery (%)	% RSD	Reference
Cream	Triforine W 1084 Trichloroethanol	0.01–0.1 0.01–0.1 0.01–0.1	4 4 4		73 88 88	12 7 4	
Egg	Triforine W 1084 Trichloroethanol	0.01–0.1 0.01–0.1 0.01–0.1	8 8 8		90 93 88	6 8 6	FAMS 084-01 TF-245-005
Egg	Triforine	0.01 0.10	3 3	71–76 75–78	73 76	4.0 2.0	FAMS 084-01 TF-245-004
	W 1084	0.01 0.10	3 3	83–89 95–101	86 98	3.5 3.1	
	Trichloroethanol	0.01 0.10	3 3	90–95 94–98	92 95	2.9 2.4	
Milk	Triforine	0.001 0.01	3 3	92–101 97–103	96 100	4.9 3.0	FAMS 037-01 TF-245-006
	W 1084	0.002 0.02	3 3	102–116 106–115	111 111	6.8 4.1	
	Trichloroethanol	0.001 0.01	3 3	97–107 89–92	103 91	5.0 1.7	
Liver	Triforine	0.01 0.1	3 3	100–116 93–114	107 106	7.8 10.9	FAMS 038-01 TF-245-006
	W 1084	0.01 0.1	3 3	66–77 97–117	70 107	9.1 9.3	
	Trichloroethanol	0.01 0.1	3 3	69–77 65–66	74 66	5.9 0.88	
Kidney	Triforine	0.01 0.1	3 3	77–82 78–94	80 84	3.2 10.4	
	W 1084	0.01 0.1	3 3	88–96 117–127	93 121	4.9 4.6	
	Trichloroethanol	0.01 0.1	3 3	86–97 77–83	90 80	6.8 3.8	
Muscle	Triforine	0.01 0.1	3 3	80–85 72–107	83 88	3.2 20.3	
	W 1084	0.01 0.1	3 3	108–135 107–111	123 109	11.1 1.8	
	Trichloroethanol	0.01 0.1	3 3	82–88 74–78	85 76	3.6 2.8	
Fat	Triforine	0.01 0.1	3 3	118–123 85–101	121 93	2.1 8.6	
	W 1084	0.01 0.1	3 3	113–134 100–104	121 102	9.4 2.0	
	Trichloroethanol	0.01 0.1	3 3	97–102 96–100	100 98	2.5 2.0	

Stability of pesticide residues in stored analytical samples

The Meeting received data on the stability of triforine residues in apples, cherries, plums, peaches, blueberries and hops (cones and processed fractions) samples stored frozen.

The freezer stability study of triforine was conducted on apples, cherries, peaches and blueberries (Eich, 1979: TF-326-010). Untreated samples of blueberries, cherries, apples and peaches were chopped and fortified with triforine at 0.1 or 1 mg/kg respectively. The homogenised samples were stored deep frozen (-20 °C) for different time periods up to 12 months. Samples were analyzed after storage using GC-ECD method RU 3, 26/12/10.

Table 18 Recovery of triforine from stored fortified samples

Storage interval	Residue (mg/kg)	
	0.1 mg/kg fortification	1.0 mg/kg fortification
Apples		
0 month	0.10	0.92

Storage interval	Residue (mg/kg)	
	0.1 mg/kg fortification	1.0 mg/kg fortification
2 months	0.09	0.88
4 months	0.09	0.88
12 months	0.10	0.83
Cherries		
0 month	0.10	0.93
2 months	0.11	0.97
4 months	0.11	0.95
12 months	0.11	0.95
Peaches		
0 month	0.09	1.04
2 months	0.09	0.91
4 months	0.10	0.99
12 months	0.12	1.06
Blueberries		
0 month	0.09	0.84
2 months	0.08	0.83
4 months	0.10	0.78
12 months	0.11	0.92

Means values of two replicates, corrected by procedural recovery.

The storage stability of triforine was investigated under frozen conditions (Weeren, 1994: TF-326-025). Samples of hops and the processed fractions were fortified with triforine at a level of up to 100 mg/kg. Samples were stored in a freezer at -18 °C and analyzed using analytical method RU 3, 26/12/10 after 1, 15, 30, 59, 96, and 180 days of storage.

Table 19 Recovery (%) of triforine from stored fortified samples of hops and processed fractions

Storage interval	Green cones						
	0.5 mg/kg fortification		5 mg/kg fortification			50 mg/kg fortification	
	% remaining	Mean	Procedural	% remaining	Mean	% remaining	Mean
1 day	79, 82	81	90, 93	81, 84	83	96, 97	97
93 days	72, 77	75	86, 89	70, 71	71	76, 80	78
175 days	67, 74	71	73, 88	66, 67	67	67, 75	71
Storage interval	Dried cones						
	10 mg/kg fortification				100 mg/kg fortification		
	Procedural	% remaining		Mean	% remaining		Mean
1 day	90, 91	82, 95		89	76, 85		81
96 days	70, 82	68, 73		71	66, 74		70
181 days	78, 82	68, 70		69	68, 71		70
Storage interval	Spent hops [0.5 mg/kg fortification]						
	Procedural		% remaining		Mean		
1 day	85, 88		79, 79		79		
15 days	77, 83		80, 83		82		
30 days	82, 86		75, 78		77		
59 days	92, 93		73, 74		74		
Storage interval	Beer [0.5 mg/kg fortification]						
	Procedural		% remaining		Mean		
1 day	97, 99		81, 86		84		
15 days	79, 88		75, 77		76		
28 days	81, 95		83, 92		88		
Storage interval	Yeast [0.5 mg/kg fortification]						
	Procedural		% remaining		Mean		
1 day	84, 93		77, 88		83		
15 days	93, 102		64, 66		65		
28 days	77, 80		62, 65		64		

The storage stability of triforine was tested on plum samples under deep-frozen conditions (Schulz, 1993: TF-712-089). The samples were stored at -20 °C in the dark and fortified with triforine at 1 mg/kg. Samples were analyzed using analytical method RU 3, 26/12/10.

Table 20 Recovery of triforine from stored fortified samples of plums

Storage interval	Pitted fruits [1.0 mg/kg fortification]		
	Procedural	% remaining	Mean
8 months	82	75, 81, 87	81

USE PATTERN

Triforine is registered in many countries for the control of various fungal diseases on fruits, fruiting vegetables, legumes, tree nuts, etc. The Meeting received labels in the countries of North and South America, Africa, Asia and Oceania. The information available to Meeting on registered uses of triforine is summarized in Table 21 below.

Table 21 Registered uses of triforine on crops

Crop	Country	For G	Formulation		Application				Application rate per treatment			PHI, days
			Type	Conc. of ai g/L	Method	Max number	Timing	Interval	Max spray conc g ai/hL	Water volume L/ha	Max rate g ai/ha	
Pome fruits												
Apple	Algeria	F	EC	190	Foliar spray	NS [a]	NS	NS	28.5	–	–	7
Apple	Argentina	F	EC	190	Foliar spray	3	1st: Pink button 2nd:3/4 of the petals drop, 3rd: 15 to 20 days after the second application	NS	23.8	–	–	14
Apple	Australia	F	EC	190	Foliar spray	4	NS	10–14 days	22.8	–	–	1
Apple	Brazil	F	EC	190	Foliar spray	3	1st: First sign of infection	7–10 days	23.7	1000–1500	–	5
Apple	Canada	F	EC	190	Foliar spray	5	1st: Tight cluster 5th: petal fall stages [b]	NA	–	–	475	–
Apple	Chile	F	EC	190	Foliar spray	3	1st: Green tip	7 days	15.2 [d]	–	285 [d]	7
Apple	Kasakhstan	F	EC	190	Foliar spray	NS	1st: First sign of infection	NS	–	200–400	380	20
Apple	Kenya	F	EC	190	Foliar spray	NS	1st: First sign of infection	7–10 days	–	400–600	380	–
Apple	Mexico	F	EC	190	Foliar spray	NS	NS	7 days	23.8	–	–	14
Apple	New Zealand	F	EC	190	Foliar spray	3 [c]	1st: Green tip 3rd:full bloom	7–10 days (to full bloom) 10–14 days(from full bloom)	19	2500 (at least)	–	35
Pear	Israel	F	EC	190	Foliar spray	NS	NS	NS	9.5	1000–2000	190	14
Persimmon	Japan	F	EC	180	Foliar spray	4	NS	NS	18	2000–7000	–	14
Stone fruits												

Crop	Country	For G	Formulation		Application				Application rate per treatment			PHI, days
			Type	Conc. of ai g/L	Method	Max number	Timing	Interval	Max spray conc g ai/hL	Water volume L/ha	Max rate g ai/ha	
Stone fruits excluding plums (Brownrot)	New Zealand	F	EC	190	Foliar spray	3	1st: Pink fall 3rd:shuck fall	7–10 days	19	2000 (at least)	–	1
	New Zealand	–	EC	190	Dip fruit for 30 seconds.	NS	Post-harvest	NS	19	–	–	1
Stone fruits excluding plums (Rust)	New Zealand	F	EC	190	Foliar spray	3	1st: First sign of infection	10–14 day	19	–	–	1
Peach, nectarine, apricot, plum, prune	Australia	F	EC	190	Foliar spray	3	3rd: 1 week before harvest	14 days	19	–	–	7
	Australia	–	EC	190	Dip for 30 seconds. Renew the dip after 48 hours.	NS	Post-harvest	NS	19	–	–	–
Peach, Cherry, Plum, Prune	Canada	F	EC	190	Foliar spray	3	1st: Early bloom stage 3rd: full bloom stage	NS	14 –	– –	– 475	–
Cherry, Nectarine, Peach, Plum	Chile	F	EC	190	Foliar spray	3	1st: Balloon 3rd: 100% bloom	NS	19	–	285	14
Apricot	Israel	F	EC	190	Foliar spray	NS	NS	NS	19	1000–2000	380	14
Cherry	Australia	–	EC	190	Dip for 30 seconds. Renew the dip after 48 hours.	4	Post-harvest	NS	14.3	–	–	–
Nectarine	South Africa	F	EC	190	Foliar spray	NS	NS	NS	19	2500–3500	665	3
Peach	Argentina	F	EC	190	Foliar spray	2	1st: Appearance of the flowers 2nd: fruits with 1 cm in diameter	NS	23.7	–	–	14
Peach	Brazil	F	EC	190	Foliar spray	3	1st: First sign of infection	7–10 days	23.7	(400–1000) [e]	(237)	3
Peach	Japan	F	EC	180	Foliar spray	5	NS	NS	18	2000–7000	–	1
Peach	Mexico	F	EC	190	Foliar spray	NS	NS	7 days	28.5	100	–	14
Peach	South Africa	F	EC	190	Foliar spray	2	NS	13–15 days	19	2500–3500	665	3
Plum	Mexico	F	EC	190	Foliar spray	NS	NS	7 days	28.5	100	–	14
Plum and Prune	South Africa	F	EC	190	Foliar spray	2	3 days before harvest	7 days	24.7	2500–3500	865	3
Berries												
Blueberry	Canada (except Eastern Canada)	F	EC	190	Foliar spray	4	1st: Bud break 4th: 10–14 days after early bloom	10–14 days	–	1000	570	60

Crop	Country	For G	Formulation		Application				Application rate per treatment			PHI, days
			Type	Conc. of ai g/L	Method	Max number	Timing	Interval	Max spray conc g ai/hL	Water volume L/ha	Max rate g ai/ha	
	Canada (Eastern Canada only)	F	EC	190	Foliar spray	3	1st: leaf-bud break 3rd: pink-bud bloom	10–14 days	–	1000	570	60
Cranberry	Canada (B.C. only)	F	EC	190	Foliar spray	3	1st: Bud break	10–14 days		1000–1500	570	60
Currants (Red and black)	New Zealand	F	EC	190	Foliar spray	3	1st: Green tip 3rd:10% flowering	10–14 days	38	2000–4000	–	14
Grape	Argentina	F	EC	190	Foliar spray	3	1st: 15 to 20 cm long, 2nd: in bloom 3rd: 30 days after the second application	NS	23.8	–	–	14
Grape	Chile	F	EC	190	Foliar spray	3	1st: First sign of infection	NS	11.4	–	–	14
Grape	Kasakhstan	F	EC	190	Foliar spray	NS	1st: First sign of infection	NS	–	200–400	285	30
Grape	Kenya	F	EC	190	Foliar spray	NS	NS	NS	–	400–600	285	–
Grape	New Zealand	F	EC	190	Foliar spray	4	1st: Bud burst	2–3 weeks	19	2000	380 (at least)	14
Grape	Tunisia	F	EC	190	Foliar spray	NS	NS	NS	23.8	–	–	–
Raspberry	Chile	F	EC	190	Foliar spray	3	1st: Bud break 3rd: flowering	14 days	–	–	285	14
Strawberry	Brazil	F	EC	190	Foliar spray	4	NS	7 days	28.5	800	–	2
Strawberry	Chile	F	EC	190	Foliar spray	3	1st: First sign of infection	NS	–	–	285	1
Strawberry	Japan	F	EC	180	Foliar spray	5	NS	NS	9	1000–3000	–	1
Strawberry	Mexico	F	EC	190	Foliar spray	4	NS	4, 7 or 10 days	–	–	190	14
Strawberry	New Zealand	F	EC	190	Foliar spray	NS	NS	7–10 days	38	2000 (at least)	–	14
Strawberry	South Korea	F	EC	190	Foliar spray	3	1st: First sign of infection	7 days	19	–	–	5
Fruiting vegetable, cucurbits												
Cucurbits (cucumber, marrow, melons etc.)	Kenya	F	EC	190	Foliar spray	NS	1st: First sign of infection	7–10 days	–	400–600	285	7
Cucurbits	New Zealand	F	EC	190	Foliar spray	2	1st: First sign of infection	10 days	28.5	1500 (at least)	–	3
Cucurbits	South Africa	F	EC	190	Foliar spray	NS	1st: First sign of infection	7–10 day	19–28.5	–	190 (at least)	1
Cucumber Melon Squash	Israel	F	EC	190	Foliar spray	NS	NS	NS		250–500	152	3

Crop	Country	For G	Formulation		Application				Application rate per treatment			PHI, days
			Type	Conc. of ai g/L	Method	Max number	Timing	Interval	Max spray conc g ai/hL	Water volume L/ha	Max rate g ai/ha	
Cucumber/melons/watermelons	Mexico	F	EC	190	Foliar spray	3	NS	7 days	–	–	285	7
Cucumber	Algeria	F	EC	190	Foliar spray	NS	NS	NS	28.5	–	–	7
Cucumber	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection	NS	–	–	285	5
Cucumber	Japan	F	EC	180	Foliar spray	5	NS	NS	18	1000–3000	–	1
Cucumber	Kasakhstan	F	EC	190	Foliar spray	NS	1st: First sign of infection	NS	–	200–400	190	20
Cucumber	South Korea	F	EC	190	Foliar spray	2	1st: First sign of infection	10 days	19	–	–	2
Melon	Brazil	F	EC	190	Friar spray	3	1st: Early symptoms appearance	7–10 days	23.7	400–1000	–	5
Melon	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection	NS	–	–	285	2
Melon	Japan	F	EC	180	Foliar spray	6	NS	NS	9	1000–3000	–	1
Pumpkin	Argentina	F	EC	190	Foliar spray	NS	1st: First sign of infection	1–2 weeks	28.5	–	–	14
Pumpkin	Mexico	F	EC	190	Foliar spray	3	NS	7 days	–	–	285	7
Squash	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection		–	–	285	8
Watermelon	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection		–	–	285	–
Fruiting vegetable other than cucurbits												
Eggplant	Israel	F	EC	190	Foliar spray	NS	NS	NS	–	250–500	190	3
Eggplant	Japan	F	EC	180	Foliar spray	5	NS	NS	18	1000–3000	–	1
Eggplant	Kenya	F	EC	190	Foliar spray	NS	NS	NS	–	400–600	285	14
Eggplant	Mexico	F	EC	190	Foliar spray	3	NS	5 or 8 days	–	–	285	15
Pepper	Israel	F	EC	190	Foliar spray	NS	NS	NS	–	250–500	190	3
Pepper	Japan	F	EC	180	Foliar spray	3	NS	NS	18	1000–3000	–	14
Pepper	Kenya	F	EC	190	Foliar spray	NS	NS	NS	–	400–600	285	14
Pepper	Mexico	F	EC	190	Foliar spray	3	NS	7 days	–	–	285	14
Red Pepper (including bell pepper)	South Korea	F	EC	190	Foliar spray	2	1st: First sign of infection	10 days	19	–	–	7
Tomato	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection	NS	–	–	285	3
		F	EC	190	Foliar spray (under plastic)	4	1st: First sign of infection	15 days	28.5	–	–	3
Tomato	Israel	F	EC	190	Foliar spray	NS	NS	NS	–	250–500	190	3
Tomato	Japan	F	EC	180	Foliar spray	3	NS	NS	18	1000–3000	–	1

Crop	Country	For G	Formulation		Application				Application rate per treatment			PHI, days
			Type	Conc. of ai g/L	Method	Max number	Timing	Interval	Max spray conc g ai/hL	Water volume L/ha	Max rate g ai/ha	
Tomato	Kenya	F	EC	190	Foliar spray	NS	NS	NS	–	400–600	285	2
Tomato	Mexico	F	EC	190	Foliar spray	4	1st: First sign of infection	7 days	–	–	380	3
Tomato	New Zealand	F	EC	190	Foliar spray	NS	NS	10–14 days	28.5	at least 1500	–	3
Legume vegetables												
Beans	Argentina	F	EC	190	Foliar spray	2	2nd: 60 days after planting	15–30 days	38	–	–	8
Beans French bean	Brazil	F	EC	190	Foliar spray	3	1st: Early symptoms	7–10 days	28.7	400–1000	290	10
Beans	Chile	F	EC	190	Foliar spray	4	1st: First sign of infection	NS	–	–	285	10
Beans, green	South Africa	F	EC	190	Foliar spray	NS	1st: First sign of infection	7–10 day	28.5	1000	–	3
Lupin	South Africa	F	EC	190	Foliar spray	NS	1st: First sign of infection	2–3 weeks	28.5	500	143	7
		F	EC	190	Aerial spray	NS	NS	NS	–	–	143	7
Peas, shelled	Japan	F	EC	180	Foliar spray	3	NS	NS	12.7	1000–3000	–	1
Peas	South Africa	F	EC	190	Foliar spray	NS	NS	7–10 day	28.5	1000	285	4
		F	EC	190	Aerial spray	NS	NS	NS	–	40 (at least)	285	4
Cereals												
Cereals	Tunisia	F	–	190	Foliar spray	NS	NS	NS	19	–	–	–

[a] NS: not shown
[b] May be applied 2 weeks after petal fall (mid-summer) if necessary.
[c] Apply maximum six times in seasons of extreme disease pressure.
[d] Use the indicated doses in mL/100 L of water to dilute applications (Python). In concentrated sprays, doses are per hectare should be used. Using lower doses under normal pressure conditions. In case of severe attacks or extreme conditions, using a high dose and smaller range.
[e] Apply the sufficient to wet the plant with the mixture until it drops.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The Meeting received information on triforine supervised field trials for the following crops.

Group	Commodity	Table
Pome fruits	Apple	Table 22–25
	Pear	Table 26
Stone fruits	Cherry	Table 27, 28
	Plum (including Prune)	Table 29–31
	Apricot	Table 32, 33
	Nectarine	Table 34
	Peach	Table 35–39
Berries and other small fruits	Raspberry	Table 40
	Blueberry	Table 41
	Black currant	Table 42
	Grape	Table 43–45

Group	Commodity	Table
	Cranberry	Table 46
	Strawberry	Table 47–49
Fruiting vegetables, Cucurbits	Cucumber	Table 50, 51
	Squash	Table 52, 53
	Melon	Table 54–56
Fruiting vegetables, other than cucurbits	Peppers	Table 57–59
	Egg plant	Table 60, 61
	Tomato	Table 62–64
Legume vegetables	Common Bean	Table 65, 66
Cereal grains	Barley	Table 67
	Wheat	Table 68, 69
Straw, fodder and forage of cereals	Barley straw and forage	Table 70
	Wheat straw and forage	Table 71

Triforine formulation was applied for foliar treatment. Each of the field trial sites generally consisted of untreated control plot and treated plot. Application rates and spray concentrations have generally been rounded to two significant figures.

Residue values from the trials, which have been used for the estimation of maximum residue levels, STMRs and HRs, are underlined.

Laboratory reports included method validation with procedural recoveries from spiking at residue levels similar to those occurring in samples from the supervised trials. Date of analyses and duration of residue sample storage were also provided. Although trials included control plots, no control data are recorded in the tables except when residues were found in samples from control plots. Residue data are not corrected for percent recovery.

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

Pome fruits

Apple

Three residue trials in apples were conducted in the USA. Triforine was quantified by GC-ECD with a LOQ of 0.004 mg/kg.

Three residue trials in apples were conducted in the USA. Method RU3, 26/12/10 was used to analyze apple fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.006 mg/kg.

One residue trial in apples was conducted in Canada. Triforine was quantified by GC-ECD with a LOQ of 0.005 mg/kg.

Three residue trials in apples were conducted in Australia. Method RU3, 26/12/10 was used to analyze apple fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.05 mg/kg.

One residue trial in apples was conducted in Germany. Method RU3, 26/12/10 was used to analyze apple fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Seven residue trials in apples were conducted in France. Method RU3, 26/12/10 was used to analyze apple fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Two residue trials in apples were conducted in Brazil. Method RU3, 26/12/10 was used to analyze apple fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.02 mg/kg.

Table 22 Triforine residues on apples from supervised trials in the USA and Canada

Apple, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Canada	EC 190	–	–	0.475	5	–		Timing: 1st:tight cluster 5th: petal fall stages
USA, 1978 Highland/NY (Rome, Cortland, Golden Delicious, McIntosh, Delicious)	EC 200	0.009	–	–	11	0 [c]	0.37 0.47 0.63 0.39 0.59	102FX-532-2010 [a, b] TF-711-010 Sampling to analysis: 202 days
USA, 1978 Kingston/RI (Red Delicious, McIntosh, Golden Delicious)	EC 200	0.009	–	–	7	0 [c]	0.016 0.047 0.083	102FX-532-2011 [a, b] TF-711-011 Sampling to analysis: 333 days
USA, 1980 Fabius/NY (McIntosh, IDA Red, Golden Delicious)	EC 200	0.009	–	–	4	21 [d]	0.030, 0.009 0.010, 0.013 0.035, 0.016	102FX-532-2012 [a, b] TF-711-012 Sampling to analysis: 145–161 days
						37	0.008	
					10	105 [d]	< 0.005, < 0.006 < 0.005, < 0.006 < 0.005, < 0.006	
						121	< 0.006	
Canada, 1984 Trenton/Ontario (McIntosh)	EC 190	0.015	–	–	5	87	0.019	102FX-532-2018 [a, b] TF-711-016 Only information on the date of the last application (7th June) is available. Sampling to analysis: 38 days
		–	–	0.40	4	103	0.041	
USA, 1977 Kingston/RI (Mixed Varieties)	EC 200	0.015	–	0.56	6	0 7 14 21	0.09 0.09 0.03 0.04	102FX-532-2019 [a] TF-711-017 Sampling to analysis: 272–368 days
USA, 1977 Jackson Springs/NC (Golden Delicious)	EC 200	0.015	–	0.56	5	0 7 14 21	0.41 0.34 0.19 0.14	
USA, 1977 Franklin/MI (Red Delicious)	EC 200	0.015	–	0.56	5	14 28	0.41 0.10	

Analytical portion: fruit

[a] The detail of in-field study was not shown in the study report.

[b] The detail of analytical method was not shown in the study report.

[c] Each residue data for each variety was provided.

[d] Duplicate residue data for each variety were provided.

Table 23 Triforine residues on apples from supervised trials in Australia

Apple, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, Australia	EC 190	0.023	–	–		4	1		Interval: 10–14 days
Australia, 1975 Gladysdale (Granny Smith)	EC 190	–	–	–		control		0.06	TF-711-039 [a] Sampling to analysis: 285–399 days
		–	–	0.188	Semi mature	10	107	0.08	
		–	–	0.250	Semi mature	10	107	0.10, 0.13 mean 0.12	
Australia, 1975 Moorooduc (Jonathan)	EC 190	–	–	–		control		0.05	
		–	–	0.125	Semi mature	8	80	< 0.05, < 0.05, 0.05 mean 0.05	
		–	–	0.188	Semi mature	8	80	0.13	
		–	–	0.250	Semi mature	8	80	0.06, 0.10, 0.16 mean 0.11	
Australia, 1975 Merrindale (Jonathan)	EC 190	–	–	0.125	Semi mature	1	0 3 7 14	0.18, 0.30 mean 0.24 0.16, 0.19 mean 0.18 0.38, 0.53 mean 0.46 c: 0.17 0.12, 0.23 mean 0.18 c: 0.06	
		–	–	0.250	Semi mature	1	0 3 7 14	0.33, 0.40 mean 0.37 0.32, 0.33 mean 0.33 < 0.05, 0.22 mean 0.14 c: 0.17 < 0.05, 0.11 mean 0.08 c: 0.06	
		–	–	0.500	Semi mature	1	0 3 7 14	0.90, 1.0 mean 0.95 0.76, 0.79 mean 0.78 < 0.05, 0.22 mean 0.14 c: 0.17 0.25, 0.36 mean 0.31 c: 0.06	

Analytical portion: fruit

[a] The detail of the in-field study was not shown in the study report.

Table 24 Triforine residues on apples from supervised trials in Germany and France

Apple, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
Germany, 1987 – (Golden Delicious)	EC 200	0.025	2500	0.625	–	4	105	0.02	102FX-532-2037 [a] TF-711-035 Sampling to analysis: - days Mean recovery 66.6%

Apple, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
France, 1990 Rhone (Golden Delicious)	EC 190	0.040	950	0.380	From stage F to J (3.5 to 6 cm)	9	0 1 2 4 6 8 10 11	0.27 0.19 0.10 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	BETR.91.012 [b] TF-711-040 Sampling to analysis: 387–465 days
France, 1990 Les Valentous (Golden Delicious)	EC 190	0.100	380	0.380	From first stage in the formulation of the fruit to 6.5 cm	12	0 1 2 4 6 8 10	0.26 0.17 0.08 < 0.01 < 0.01 < 0.01 < 0.01	
France, 1992 Saint Epain (Smoothee)	EC 190	0.086	330	0.285	–	1	2	0.12	BETR.93.009[2)] TF-711-041 Sampling to analysis: 82–93 days
	EC 190	0.086	330	0.285	–	2	2	0.10	
France, 1995 Fargues st Hilaire (Golden smoothe)	EC 190	–	500	0.333	Maturity	1	3 7 15 29 59 122 175	0.09 0.07 0.09 0.06 0.04 0.04 0.06	CFS 1995-039 TF-711-042 Sampling to analysis: 7–119 days
France, 1995 Brissac-Quince, (Jonagold)	EC 190	–	300	0.333	Maturity	1	3 10 17 34 63 125 182	0.02 < 0.01 0.03 0.02 0.02 0.01 0.02	
France, 1995 Brissac-Quince, (Golden Delicious)	EC 190	–	333	0.333	Maturity	1	3 10 18 34 63 129 186	0.14 0.07 0.06 0.03 0.03 0.08 0.06	
France, 1995 LesChiclets, Molleges (Granny Smith)	EC 190	–	1200	0.333	Maturity	1	3 10 18 32 63 116 183	0.25 0.27 0.17 0.19 0.12 0.11 0.14	

Analytical portion: fruit

[a] The detail of in-field study was not shown in the study report.

[b] The detail of analytical method was not shown in the study report.

Table 25 Triforine residues on apples from supervised trials in Brazil

Apple, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Brazil	EC 190	0.024	–	–	3	5		Timing: 1st First sign infection Interval: 7–10 days
Brazil 1995 SanJose (Fuji)	EC 190	0.024	–	–	3	5	< 0.02	BASF 1995/306189 Sampling to analysis—days
		0.048	–	–	3	5	0.02	
Brazil 1995 Vermelha (Fuji)	EC 190	0.024	–	–	3	5	< 0.02	BASF 1995/306190 Sampling to analysis—days
		0.048	–	–	3	5	< 0.02	

Analytical portion: fruit

Pear

One residue trial in pears was conducted in Australia. Method RU3, 26/12/10 was used to analyze pear fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.05 mg/kg.

Table 26 Triforine residues on pears from supervised trials in Australia

Pear, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
Australia, 1975 Merrindale (William bon chretien)	EC 190	–	–	–		control		0.05	TF-711-039 a Sampling to analysis: 285–399 days
		–	–	0.125	Semi mature	1	0 3 7 14	0.75 0.42 0.47 0.40	
		–	–	0.250	Semi mature	1	0 3 7 14	0.13 0.78 0.73 0.31	
		–	–	0.500	Semi mature	1	0 3 7 14	0.68 1.85 1.63 0.70	

Analytical portion: fruit

[a] The details of in-field study were not shown in the study report.

Stone fruits

Cherry

Three residue trials in cherries were conducted in Canada. Method RU3, 26/12/10 was used to analyze cherry fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.007 mg/kg.

Seven residue trials in cherries were conducted in the USA. Method RU3, 26/12/10 was used to analyze cherry fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.001–0.01 mg/kg.

Ten residue trials in cherries were conducted in Germany. Method RU3, 26/12/10 was used to analyze cherry fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 27 Triforine residues on cherries from supervised trials in USA and Canada

Cherry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Canada	EC 190	0.014 –	– –	– 0.475	3 3	– –		Timing: 1st : Early bloom stage 3rd : full bloom stage
USA, 1980 Alton/NY (Montmorency)	EC 200	0.013	500–1000	–	5	0 7	0.99 1.1	102FX-532-2210 [a, b] TF-712-010 Sampling to analysis: 138–145 days Recovery = 60 % (n = 1; 1.0 ppm)
		0.018	500–1000	–	5	0 7 9	1.0 0.38 0.09	
USA, 1978 Corvallis/OR (Montmorency, Black Rep., Corum, Royal Ann)	EC 200	0.018	–	–	3 5	83 6 8	0.007 1.2, 1.2 mean 1.2 1.8	102FX-532-2211 [a] TF-712-011 Sampling to analysis: 269–290 days
	WP 500	0.030	–	–	3 5	83 6 8	0.017 1.9, 1.9 mean 1.9 2.4	
	F 800	0.030	–	–	3 5	83 6 8	0.005 5.5, 3.5 mean 4.5 3.4	
USA, 1980 Linden/CA (Sweet)	EC 182	0.018	–	–	2	4	1.5, 1.5 mean 1.5	102FX-532-2212 [b] TF-712-012 Sampling to analysis: 147 days
	EC 182 + WP 500	0.018 + 0.030 Post-harvest	–	–	1 + 1	(4)+0	1.8, 1.7 mean 1.8	
Canada, 1981 Osoyoos/British Columbia (Lambert)	EC 190	–	1000	0.475	4	1 3 7	1.1, 1.5 mean 1.3 1.8, 1.4 mean 1.6 1.2, 0.95 mean 1.1	102FX-532-2213 [a, b] TF-712-013 Sampling to analysis: 307–313 days
Canada, 1981 Cedar Springs/ Ontario (Hedelfingen, Windsor, Van, Stella)	EC 190	–	1000	0.475	5	3	0.71	
USA, 1977 Davis, CA (Bing)	EC 190	0.018	–	–	3	0 3 7 14	1.9 1.1 1.1 0.88	102FX-532-2215 TF-712-015 Sampling to analysis: 307–343 days
USA, 1977 Corvallis/OR (Montmorency, Royal Ann)		0.018	–	–	1	0 3 7 14 0 3	1.6 0.59 0.41, 1.5 mean 0.96 0.15, 0.29 mean 0.22 1.3 0.85	
USA, 1977 Alton, Sodius, Wayne, NY (Montmorency)		0.018	–	–	6 7 7 7	1 3 7 15	2.1 1.5 1.2 0.78	
USA, 1977 East Lansing/MI		0.018	–	–	5	0 3 7	0.94 0.66 0.54	

Cherry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
(Montmorency)						14	0.15	
Canada, 1983 Osoyoos, British Columbia (Van)	EC 190	–	–	0.235	3	1 3 7	1.3 1.2 1.0	10212-532-2217 [a] TF-712-017 Sampling to analysis: 307–343 days
		–	–	0.475	3	1 3 7	3.3 2.6 1.3	
		–	–	0.950	3	1 3 7	3.9 4.0 2.4	

Analytical portion: fruit Analytical portion: fruit
[a] The detail of the in-field study was not shown in the study report
[b] The detail of analytical method was not shown in the study report

Table 28 Triforine residues on cherries from supervised trials in Germany

Cherry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Germany, 1989 Ingelheim (Schattenmorelle)	EC 190	–	1500	0.428	5	0 3 7 10 14	0.79 0.36 0.18 0.084 0.12	10249-532-2222 [a] TF-712-070 Sampling to analysis: 143–157 days
Germany, 1989 Öhringen (Schattenmorelle)	EC 190	–	1500	0.428	5	0 3 7 10 14	1.7, 2.2 mean 2.0 0.56, 0.57 mean 0.57 0.23, 0.26 mean 0.25 0.053, 0.079 mean 0.066 0.046, 0.058 mean 0.052 c: 0.01–0.113	10249-532-2223, 2226 [a] TF-712-071, 074 Sampling to analysis: 325–345 days
Germany, 1989 Altenhain/Taunus (Schattenmorelle)	EC 190	–	1500	0.428	5	0 3 7 10 14	0.787 1.230 0.746 0.913 0.135	10249-532-2224 [a] TF-712-072 Sampling to analysis: 318–332 days
Germany, 1989 Ingelheim (Schattenmorelle)	EC 190	–	1500	0.428	5	0 3 7 10 14	0.636 0.357 0.165 0.072 0.060	10249-532-2225 [a] TF-712-073 Sampling to analysis: 318–339 days
Germany, 1990 Ffm (Schattenmorelle)	EC 190	–	1500	0.428	7	0 3 7 10 14	0.92 0.88 0.42 0.43 0.11	10249-532-2228 [a] TF-712-075 Sampling to analysis: 21–35 days
Germany, 1990 Maintal (Schattenmorelle)	EC 190	–	1500	0.428	7	0 3 7 10 14	0.90 0.53 0.19 0.10 0.09	10249-532-2229 [a] TF-712-076 Sampling to analysis: 216–230 days

Cherry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
					7	0 3 7 10 14	1.2 1.2 0.42 0.39 0.24 c: 0.07–0.44	10249-532-2230 [a] TF-712-077 Sampling to analysis: 216–230 days
Germany, 1989 Altenhain (Schattenmorelle)	EC 190	–	1500	0.428	7	0 3 7 10 14	1.2 0.47 0.39 0.49 < 0.005	10249-532-2231 [a] TF-712-078 Sampling to analysis: 17–30 days
Germany, 1990 Ingelheim (Schattenmorelle)	EC 190	–	1500	0.428	7	0 3 7 10 14	0.68 0.60 0.30 0.17 0.14	10249-532-2232 [a] TF-712-079 Sampling to analysis: 25–39 days
Germany, 1990 Öhringen (Schattenmorelle)	EC 190	–	1500	0.428	5	0 3 7 10 14	0.54 0.42 0.13 0.27 0.07 c: 0.39–1.16	10249-532-2233 [a] TF-712-080 Sampling to analysis: 223–237 days
Germany, 1992 – (Schattenmorelle)	EC 190	0.015	1500	0.225	5	0 3 7 10 14 0 3 7 10 14	0.63, 0.68, 0.53 mean 0.61 0.47, 0.60, 0.42 mean 0.50 0.39, 0.30, 0.13 mean 0.27 0.49, 0.17, 0.26 mean 0.31 < 0.01, 0.14, 0.07 mean 0.07 0.75, 0.81, 0.64 mean 0.73 0.55, 0.71, 0.50 mean 0.59 0.46, 0.36, 0.15 mean 0.32 0.58, 0.21, 0.31 mean 0.37 < 0.01, 0.17, 0.08 mean 0.09	10249-532-2234 [a] TF-712-090 Sampling to analysis: 33–47 days

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

Plum

Three residue trials in plums were conducted in Canada. Method RU3, 26/12/10 was used to analyze plum fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.07 mg/kg.

Six residue trials in plums were conducted in USA. Method RU3, 26/12/10 was used to analyze plum fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Six residue trials in plums were conducted in Germany. Methods RCC Prj. No275793 and RU3, 26/12/10 were used to analyze plum fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

One residue trial was conducted in France. Triforine was quantified by GC-ECD with a LOQ of 0.005 mg/kg.

One residue trial was conducted in South Africa. Triforine was quantified by GC-ECD with a LOQ of 0.1 mg/kg.

Table 29 Triforine residues on plums from supervised trials in USA and Canada

Plum, country, year (variety)	Application						Commodity	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.				
GAP, Canada	EC 190	0.014 –	– –	– 0.475	– –	3 3	Fruit	–		Timing: 1st : Early bloom stage 3rd : full bloom stage
USA, 1977 Parlier/CA (Casselman)	EC 200	0.018	–	–	–	3	Fruit	0 5 11	0.43 0.29 < 0.01	TF-712-061 [a] Sampling to analysis: 282–307 days
USA, 1977 Weatherford/TX (Ozark Premier)		0.018	–	–	–	2	Fruit	0 0 0	0.58 0.46 0.49 mean 0.51	
USA, 1977 Davis/CA (French)	EC 200	0.018	–	–	–	3	Fruit Dried (Prune)	0 10	2.0 0.91	102FX-538-002[a] TF-712-066 Sampling to analysis: 239–262 days
USA, 1977 Corvallis/OR (Early Italian)	EC 200	0.018	–	–	–	1	Fruit	0 3 7 14	0.34 0.39 0.17 0.15	
USA, 1977 Alton, sodus, Wayne/NY (Fehlenburg)	EC 200	0.018	–	–	–	10	Fruit	0 3 8 14	1.6 1.3 1.2 1.2	
USA, 1980 Parlier /CA (Casselman)	EC 200	0.018	–	–	–	2	Fruit	4	0.75, 1.7 mean 1.2	102FX-532-2212 [a, b] TF-712-012 Sampling to analysis: 77 days
	EC 200 + WP 500	0.018 + 0.033 Post-harvest	–	–	–	2 + 1	Fruit	(4)+0	1.2, 1.3 mean 1.3	
Canada, 1981 Osoyoos/British Columbia (Santa Rosa)	EC 190	–	1000	0.475	–	4	Fruit	1 3 7	1.3, 1.0 mean 1.2 0.63, 0.64 mean 0.64 0.71, 0.42 mean 0.57	102FX-532-2213 [a, b] TF-712-013 Sampling to analysis: 307–313 days
Canada, 1981 Cedar Springs/Ontario (Early Italian)	EC 190	–	1000	0.475	–	4	Prune	1 3 7	1.1, 0.93 mean 1.0 0.99, 1.1 mean 1.0 0.50, 0.57 mean 0.54	
Canada, 1983 Osoyoos, British Columbia (–)	EC 190	–	–	0.235	–	3	Fruit	1 3 7	0.45 0.40 0.43	10212-532-2217[a] TF-712-017 Sampling to analysis: 307–343 days
		–	–	0.475	–	3	Fruit	1 3 7	0.71 0.60 0.39	
		–	–	0.235	–	1–2	Prune	1 3 7	0.53 0.40 0.45	
		–	–	0.475	–	1–2	Prune	1 3 7	0.26 0.96 0.61	

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

[b] The details of the analytical method were not shown in the study report.

Table 30 Triforine residues on plums from supervised trials in Germany and France

Plum, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
France, 1981 Toulouse (–)	Vereor Multi Triforine +Carbdenazime 100	0.021	1000	0.210	3	1	0.38	10288-532-2301 [a, b] TF-712-060 Sampling to analysis: 223 days
Germany, 1990 Kriftzen (Ortenauer)	EC 190	0.028	1500	0.427	4	0 3 7 10 14	0.41 0.35 0.22 0.27 0.13	TF-712-091 [a, b] TF -712-081 to 84 (4 reports) Sampling to analysis: 24–54 days
Germany, 1990 Ingelheim (Chridimer)	EC 190	0.028	1500	0.427	3	0 3 7 10 14	0.57 0.32 0.18 0.21 0.17	
Germany, 1990 Veitshöchheim (Chridimer)	EC 190	0.028	1500	0.427	3	0 3 7 10 14	0.47 0.29, 0.11, 0.26 0.10	
Germany, 1990 Öhringen (Hauszwetsche)	EC 190	0.028	1500	0.427	3	0 3 7 10 14	4.09 0.47 c: 0.02 0.64 c: 0.03 0.79 0.53	
Germany, 1992 – (–)	EC 200	–	–	0.428	3	0 7	0.2 0.15	SHTR.93.004 TF-712-088 Sampling to analysis: 225–255 days
Germany, 1991 – (–)	–	–	–	–	–	0 3 7 10 14	0.63 0.50 0.54 0.35 0.19	10249-532-2312 [a] TF -712-089 R-9141-01,02,03,04 Sampling to analysis: - days
						0 4 7 11	0.83 0.39 0.41 0.56	
						0 3 7 10 14	0.058 0.056 0.048 0.031 0.013	
						0 3 7 11 14	0.14 0.090 0.083 0.045 0.027	

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

[b] The details of the analytical method were not shown in the study report.

Table 31 Triforine residues on plums from supervised trials in South Africa

Plum, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, South Africa	EC 190	0.025	2500–3500	0.865	2	3		Interval: 7 days
South Africa, 1979 Stellenbosch (Santa Rosa, Beauty)	Denarin 200	0.030	1000–1100	0.300	2	0 4 17	0.75 0.43 0.38	311/8978/S39 a, b TF -712-065 LOQ: < 0.1
		0.030	900	0.300	2	0 4	0.75 0.35	

Analytical portion: fruit
[a] The detail of the in-field study were not shown in the study report.
[b] The detail of analytical method was not shown in the study report.

Apricot

Two residue trials in apricots were conducted in the USA. Triforine was quantified by GC-ECD with a LOQ of 0.007–0.01 mg/kg.

A total of five residue trials in apricots were conducted in France, Greece and Italy. Methods FAMS 041-01 and AGR010 were used to analyze apricot fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 32 Triforine residues on apricots from supervised trials in the USA

Apricot, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
USA, 1977 Brentwood/CA (Blenheim)	EC 190	0.018	–	–	Blossom	3	3 7 13	2.0 1.6 0.81	102FX -532 –2502 TF-712-068 Sampling to analysis: 289–298days
USA, 1980 Brentwood /CA (–)	EC 200	0.018	–	–	–	1	4	0.49	102FX-532-2212[a] TF-712-012 Recovery = 58.8% (n = 1; 0.51 ppm) Sampling to analysis: 125–126 days
						2	4	0.76	
	EC 200 + WP 500	0.018 + 0.030 Post-harvest				1 + 1	(4)+0	2.5, 2.6	

Analytical portion: fruit
[a] The details of the analytical method were not shown in the study report.

Table 33 Triforine residues on apricots from supervised trials in France, Greece and Italy

Plum, country, year (variety)	Application						Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS (BBCH)	no.				
France, 1998 Quartier La Garenne/Mezoargues (Hargrand /Myroboland)	DC 190	0.038	981–1020	0.373–0.388	77–81	3	Whole fruit	–0 +0 3 7 10 13	0.37 0.78 1.1 0.74 0.44 0.40	CFS 1999-065 TF-712-093 Sampling to analysis: 234 days
							Flesh	–0 +0 3 7 10 13	0.39 0.83 1.1 0.78 0.44 0.42	

Plum, country, year (variety)	Application						Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS (BBCH)	no.				
France, 1998 Rognonas/Beaucaire (Precoce de Thyrinthe /Myroboland)	DC 190	0.038	1025–1054	0.390–0.401	81	3	Whole fruit	3 7 13	0.53 0.41 0.29	CFS 1999-064 TF-712-095 Sampling to analysis: 247 days
							Flesh	3 7 13	0.56 0.44 0.30	
Greece, 1999 Portaria-Halkidiki (Tirinthos)	DC 190	0.038	1490	0.566	85	3	Whole fruit	7	0.18	TF-HE-99-21 TF-712-096 Sampling to analysis: 70 days
Italy, 1999 Bentivoglio (Caldese)	DC 190	0.038	597–643	0.227–0.244	77	3	Whole fruit	–0 +0 3 7 10 14	0.13 0.52 0.31 0.14 0.069 0.070	TF-IT-1999-1 TF-712-097 Sampling to analysis: 153 days
Italy, 1999 Imola (Portici)	DC 190	0.038	670–789	0.254–0.300	81	3	Whole fruit	7	0.066	TF-IT-1999-2 TF-712-098 Sampling to analysis: 146 days

Nectarine

Four residue trials in nectarine were conducted in USA. Triforine was quantified by GC-ECD with a LOQ of 0.001–0.007 mg/kg.

Table 34 Triforine residues on nectarine from supervised trials in the USA

Nectarine, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
USA, 1978 Parlier/CA (Le Grand)	EC 190	0.018	–	–	4	0 6	0.59 0.19	102FX-532-2211 TF-712-011 Sampling to analysis: 259–265 days
	WP 500	0.03	–	–	4	0 6	2.8 1.8	
	F 800	0.015	–	–	4	0 6	3.6 2.4	
USA, 1980 Parlier/CA (Le Grand)	EC 190	0.018	–	–	1 2	10	0.32 0.32	102FX-532-2212 [2] TF-712-012 Sampling to analysis: 88 days Recovery 55.13% (0.48 mg/kg)
	EC 190 + WP 500	0.018 + 0.03 Post-harvest	–	–	2 + 1	(10) 0	0.11 0.93	
USA, 1981 Sultana (–)	EC 182	0.018	–	–	3	2	0.036, 0.043 mean 0.040	102FX-532-2418[2] TF-712-037 Sampling to analysis: 175 days
USA, 1977 Parlier/CA (–, Le Grand, Red Bud)	EC 190	0.018	–	–	3	0 1 3 7	0.54 0.21 0.11 0.08	102FX-532-2419[1] TF-712-038 Sampling to analysis: 245–322 days
						0 5 11	0.50 0.47 0.28	

Nectarine, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
						0 1 3 7	0.73 0.64 0.53 0.34	

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Peach

Nineteen residue trials in peaches were conducted in USA. Method RU3, 26/12/10 was used to analyze peach fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.001–0.01 mg/kg.

One residue trails in peaches was conducted in Canada. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Total three residue trials in peaches were conducted in France and Greece. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Two residue trials in peaches were conducted in Japan. Triforine was quantified by LC-MS with a LOQ of 0.01 mg/kg.

Two residue trials in peaches were conducted in Brazil. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Two residue trials in peaches were conducted in South Africa. Triforine was quantified by GC-ECD with a LOQ of 0.1 mg/kg.

Table 35 Triforine residues on peaches from supervised trials in the USA and Canada

Peach, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Canada	EC 190	0.014 –	– –	– 0.475	3 3	– –		Timing: 1st : Early bloom stage 3rd : full bloom stage
USA, 1978 Lockford/CA (Loadel)	EC 190	0.018	–	–	2	133	0.006	102FX-532-2211 TF -712-011 Sampling to analysis: 189–235 days
					4	0 5	3.5 2.0	
USA, 1978 Parlier/CA (Fay Elberta)	EC 190	0.018	–	–	4	0 7	4.3 3.3	
USA, 1978 Corvallie /OR (Elberta)	EC 190	0.018	–	–	3	160	0.015	
					5	7	0.12	
USA, 1978 Lockford/CA (Loadel)	WP 500	0.030	–	–	2	133	0.012	
					4	0 5	4.6 5.2	
USA, 1978 Davis/CA (Halloween)	WP 500	0.030	–	–	1 Po	0	8.8 5.1	
USA, 1978 Parlier/CA (Fay Elberta)	WP 500	0.030	–	–	4	0 7	11 4.3	
USA, 1978 Corvallie /OR (Elberta)	WP 500	0.030	–	–	3	160	0.004	
					5	7	3.5	
USA, 1978	F	0.015	–	–	2	133	0.022	

Peach, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Lockford/CA (Loadel)	800				4	0 5	6.8 7.4	
USA, 1978 Parlier/CA (Fay Elberta)	F 800	0.015	–	–	4	0 7	5.7 4.5	
USA, 1978 Corvallie /OR (Elberta)	F 800	0.015	–	–	3	160	0.02	
					5	7	0.07	
USA, 1980 Parlier/CA (Fay Elberta)	EC 190	0.018	–	–	2	10	0.34 0.96	102FX-532-2212 [b] TF-712-012 Recovery 56.22% (0.48 mg/kg) Sampling to analysis: 88 days
	EC 190 + WP 500 (Post-harvest)	0.03	–	–	2 + 1	(10) 0	1.0 1.8	
USA, 1983 /CA (–)	EC 182 Aerial	–	–	0.504	4	0 1 3 7	0.32 0.36 0.70 0.62 0.21, 0.084 0.031 0.043	102FX-532-2414 [a, b] TF-712-033 Sampling to analysis: 176–183 days
		–	–	0.672	4	0 1 3 7	0.80, 0.71 0.50, 0.23, 0.15, 0.14, 0.21, 0.35	
Canada, 1981 British Colombia (Red Fairhaven)	EC 190	–	–	0.235	3	1 3 7	0.60 0.61 0.37	10212-532-2217 [a, b] TF-712-017
		–	–	0.475	3	1 3 7	1.5 1.2 0.67	
USA, 1981 Sultana	EC 190	0.018	–	–	3	0	0.58, 0.014	102FX-532-2418 [a, b] TF-712-037 Sampling to analysis: 175 days
USA, 1977 Kingston/RI (mixed)	EC 190	–	–	0.672	4	0 1 3	1.9 0.6 0.41	102FX-532-2420 TF-712-039 Sampling to analysis: 218–253 days
USA, 1977 Linden /CA (Dixon)		–	–	0.672	3	0 7 15	4.3 3.5 2.4	
		–	–	0.448	3	0 7 15	3.6 1.5 0.66	
USA, 1977 Parlier/CA (Fay Elberta)		–	–	0.672	3	0 5 11	1.2 0.97 0.49	
USA, 1977 Corvallis /OR (Elberta)		–	–	0.672	3	0 3 7 14	1.1, 0.99 0.9 0.34 0.16	
USA, 1977 Blacksburg /VA (Elberta)		–	–	0.448	2	0 3 7 14	1.0 0.26 0.23 0.98	
USA, 1977 Weatherford /TX (Red Globe)		–	–	0.448	2	0	0.55 0.72	

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Table 36 Triforine residues on peach from supervised trials in France and Greece

Peach, country, year (variety)	Application						Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.				
France, 1990 Cabannes (Elegant Lady)	EC 190	0.054 – 0.076	500–700	0.380	G to J stage	8	Whole fruit	0 3 7 14 28 42	0.14 0.07 0.05 0.03 < 0.01 < 0.01	BETR.91.016 TF-712-087 Sampling to analysis: 434–463 days
Greece, 1999 Skidra Pelis (Andross / GF 677)	DC 190	0.038	996–999	0.379	BBCH 85	3	Flesh	3 7 14	1.1 0.82 0.68	CFS 1999-041 TF-712-92 Sampling to analysis: 189–207 days
							Whole fruit	3 7 14	0.99 0.75 0.62	
		0.024	1504	0.361		1	Flesh	3 7 14	0.59 0.61 0.27	
							Whole fruit	3 7 14	0.54 0.56 0.25	
France, 1999 Barbentane (Gracia)	EC 190	0.038	1000	0.380	BBCH 77–85	3	Whole fruit	3 7 14	0.52 0.42 0.23	TF-FR-99-F01 TF-712-100 Sampling to analysis: 113–123 days

Table 37 Triforine residues on peaches from supervised trials in Japan

Peach, country, year (variety)	Application					Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.				
GAP, Japan	EC 180	0.015 – 0.018	2000–7000	–	5	Fruit	1		
Japan, 2009–2010 Ezohara Yamanashi (Hikawa-Hakuhou)	EC 180	0.023	3548	0.798	5	Pulp	1 3 7 14	0.03 0.07 0.04 < 0.01	Sampling to analysis: 60–91 days
						Whole fruit	1 3 7 14	0.77 0.84 0.69 0.15	
Japan, 2009–2010 Kishigawacho /Wakayama (Hakuhou)	EC 180	0.023	4000	0.900	5	Pulp	1 3 7 14	0.08 0.05 0.04 < 0.01	
						Whole fruit	1 3 7 14	1.4 0.62 0.32 0.10	

Table 38 Triforine residues on peaches from supervised trials in Brazil

Peach, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Brazil	EC 190	0.024	(400–1000)	0.237	3	3		Timing: 1st : First sign of infection Interval: 7–10 days
Brazil, 1985/86 Cascata (Magno)	Saprol EC	0.015	–	–	3	3 7	1.5 0.95	TF-712-036 a, b
		0.030	–	–	3	3 7	9.4 4.2	
Brazil, 1996 Charqueadas (Sinuelo)	Saprol EC	0.024	–	–	3	4	< 0.01	BASF 1986/306182
		0.048	–	–	3	4	< 0.01	

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Table 39 Triforine residues on peaches from supervised trials in South Africa

Peach, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, South Africa	EC 190	0.019	2500–3500	0.665	2	3		Interval: 13–15 days
South Africa, 1977 Ganskraal (Woltemade)	Denarin 200	0.025	3000	0.750	2	0 4 8	1.1,1.4 mean 1.2 1.0,1.0 mean 1.0 0.69,0.70 mean 0.70	0311/8994/P131 TF-712-049 a, b)
South Africa, 1977 Lourensford (Woltemade)	Denarin 200	0.025	3000	0.750	2	0 2 7	1.3,1.7 mean 1.5 1.6,1.6 mean 1.6 1.0,1.0 mean 1.0	

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Berries and other small fruits

Cane berries

Raspberries, Red, black

One residue trial in raspberries was conducted in France. The 190 g/L DC formulation was applied five times at a rate equivalent to 0.33–3.8 kg ai/ha. Method FAMS 041-01 was used to analyze raspberry fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 40 Triforine residues on raspberries from supervised trials in France

Raspberries, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
France, 1993 Machy/Chasselay (Meeker)	DC 190	–	–	0.332	5,10,30 and 40 cm shoot length, end of flowering	5	16	0.24	CFS1994-024 TF-713-046 Sampling to analysis: 128–141 days
				0.760		5	16	0.56	
				3.8		5	16	2.4	

Analytical portion: fruit

Bush berries

Blueberries

Five residue trials in blueberries were conducted in Canada. Triforine was quantified by LC-MS/MS with a LOQ of 0.01 mg/kg.

Table 41 Triforine residues on blueberries from supervised trials in Canada

Blueberries, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, Canada (except Eastern Canada)	EC 190	–	1000	0.570	1st: bud-break 4th: 10–14 days after early bloom*	4	60		Interval: 10–14 days
GAP, Eastern Canada only	EC 190	–	1000	0.570	1st: leaf-bud break 3rd: pink-bud stage	3	60		Interval: 10–14 days
Canada, 2010 Mount Stewart/ Prince Edward Island (Wild Low Bush) [Eastern Canada]	Saprol 190 DC	0.059	964–1022	0.564–0.598	1st: leaf-bud break 3rd: pink bud stage	3	78	< 0.01	875.2100-10-543-24A-13~20 Sampling to analysis: 63–109 days
		0.059	991–1015	0.579–0.594			78	< 0.01	
Canada, 2010 Mount Vernon/ Prince Edward Island (Wild Low Bush) [Eastern Canada]	Saprol 190 DC	0.058	981–999	0.574–0.584	1st: leaf-bud break 3rd: pink bud stage	3	85	< 0.01	
Canada, 2010 Burford/Ontario (Patriot/Blue Crop) [Eastern Canada]	Saprol 190 DC	0.058	1059–1079	0.577–0.586	1st: leaf-bud break 3rd: pink bud stage	3	45 49	< 0.01 < 0.01	
		0.060	1050–1071	0.583–0.602			56 60	< 0.01 < 0.01	
		0.059	1054–1068	0.559–0.593			60	< 0.01	
Canada, 2010 Abbotsford/British Columbia (Reka/Patriot) [Canada except Eastern Canada]	Saprol 190 DC	0.058	998–1010	0.582–0.589	1st: leaf-bud break 4th: 10–14 days after early bloom	4	60	0.018 0.011 Mean: 0.015	875.2100-10-543-24A-13~20 Sampling to analysis: 63–109 days
Canada, 2010 Delta/British Columbia (Reka/Patriot) [Canada except	Saprol 190 DC	0.059	985–1016	0.574–0.592	1st: leaf-bud break 4th: 10–14 days after early bloom	4	61	< 0.01	

Blueberries, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
Eastern Canada]									

Analytical portion: fruit

Currant, Black

Total four residue trials in black currants were conducted in Germany and UK. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 42 Triforine residues on black currants from supervised trials in Germany and the UK

Berries, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Germany, 1975 Hamburg	DC 190	0.015	–	–	5	0 7 14 21	5.6 3.2 1.1 0.89	102FX-532-3205 TF-713-025 Sampling to analysis: 181–202 days
UK, 1976 Charlsfield (Baldwin/Wellington)	EC 190	–	–	0.492	4	7 14 7	1.0 0.61 c: 0.015 0.75 c: 0.009	102FX-532-3212 TF-713-032 Sampling to analysis: 82–92 days Recovery 66–72%
UK, 1976 Matley (Baldwin)		–	–	0.280	5 6	16 7	0.17 0.71 c: 0.038	
UK, 1976 Risby (Wellington)		–	–	0.560	4	14	1.2 c: 0.014	

Analytical portion: fruit

Small fruit vine climbing

Grapes

Seven residue trials in grapes were conducted in Germany. Method RU 3, 26/12/10 was used to analyze grape fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01–0.05 mg/kg.

Two residue trials in grapes were conducted in Mexico. Triforine was quantified by GC-ECD with a LOQ of 0.002–0.003 mg/kg.

One residue trial in grapes was conducted in New Zealand. Triforine was quantified by GC-ECD with a LOQ of 0.1 mg/kg.

Table 43 Triforine residues on grapes from supervised trials in Germany

Grapes, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Germany, 1983 Schwabenheim (Müller-Thurgau)	EC 190	0.029	200	0.570	3	0 21 28 35	5.5 1.9 1.6 1.4	10238-532-3003 [a] TF -713-003 Sampling to analysis: 67–112 days

Grapes, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Germany, 1983 Bockenheim (Müller-Thurgau)	EC 190	0.029	200	0.570	3	0 21 28 35 44	1.7 0.55 0.39 0.38 0.25	10238-532-3004 TF-713-004 Sampling to analysis: 51–103 days
Germany, 1983 Kippenhausen (Müller-Thurgau)	EC 190	0.029	150	0.427	3	0 21 28 35 42 49	1.6 0.25 0.13 0.11 0.08 0.08	10238-532-3005 TF-713-005 Sampling to analysis: 64–119 days
Germany, 1978 Impflingen (Reichensteiner)	EC 190	0.014	2000	0.285	3	0 14 21 28 35	0.64 0.72 0.55 0.50 0.51	102FX-532-3009 TF-713-009 Sampling to analysis: 107–142 days
Germany, 1977 Schwabenheim (Müller-Thurgau)	EC 190	0.029	1160	0.331	3	0 14 21 28 35	1.93 0.38 0.22 0.17 0.18	10238-532-3010 TF -713-010 Sampling to analysis: 89–124 days
Germany, 1977 Haugnau/Bodensee (Müller-Thurgau)	EC 190	0.019	1200	0.228	3	0 21 28 35 42	2.76 0.88 0.52 0.38 0.40	10238-532-3011 TF -713-011 Sampling to analysis: 64–106 days
Germany, 1984 Schwabenheim (Kerner)	EC 190	0.057	887	0.505	1	0 3 7 10 14 21	1.1 0.96 0.95 0.79 0.6 0.65	10238-532-3012 TF -713-012 Sampling to analysis: 73–101 days

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

Table 44 Triforine residues on grapes from supervised trials in Mexico

Grapes, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Mexico, 1983 Caborca (Thompson seedless)	EC 190	–	–	0.273	1	0 3 7 14 21	0.21, 0.22, 0.26, 0.25, 0.31 0.46, 0.69, 0.02, 0.21, 0.12 0.79, 0.37, 0.37, 0.74, 0.12 < 0.002(2), 0.40, 0.19, 0.34 0.22, 0.33, 0.26, 0.46, 0.16	102FX-532-3007 a, b TF -713-007 Sampling to analysis: 204–224 days
Mexico, 1983 San Juan Del Rio, Torreon (Carignan)	EC 190	–	–	0.285	1	0 3 7 14 21	0.93, 0.61, 1.17, 3.38, 1.88 1.55, 0.30, 0.041, 3.93, 0.72 0.79, 1.53, 0.076, 2.91, 0.36 2.43, 0.19, 0.026, 4.81, 1.12 0.18, 0.24, 0.18, 0.39, 1.89	102FX-532-3008 b TF -713-008 Sampling to analysis: 814–834 days

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

[b] The details of the analytical method were not shown in the study report.

Table 45 Triforine residues on grapes from supervised trials in New Zealand

Grapes, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, New Zealand	EC 190	0.019	–	0.380 (at least)	1st: bud burst	4	14		Interval: 2–3 weeks
New Zealand, 1978 Blenheim (Cabernet Sauvignon)	EC 200	0.02	8970	0.18	Bud burst, blossom.	8	1 7 14 21	< 0.1 < 0.1 < 0.1 < 0.1	102FX-532-3013 TF -713-013 Sampling to analysis: 108–129 days

Analytical portion: fruit

Low growing berries

Cranberry

Two residue trials in cranberry were conducted in the USA. Method RU 3, 26/12/10 was used to analyze cranberry fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.004–0.01 mg/kg.

Table 46 Triforine residues on cranberries from supervised trials in the USA

Cranberry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Canada	EC 190	–	1000–1500	0.570	3	60		Timing: 1st: bud break Interval: 10–14 days
USA, 1977 Long Beach, Grayland Bog/WA (–)	EC 190	–	–	0.336	1	84 91 114 125 143	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	102FX-532-3402 [a] TF-713-038 Sampling to analysis: 196–237 days
USA, 1983 Plymouth/MA (–)	EC 190	–	–	1.05	1	64	0.022, 0.020, 0.016, 0.016 mean 0.019	102FX-532-3401 TF-713-041 Sampling to analysis: 248 days
		–	–	2.10	1	64	0.022, 0.038, 0.029, 0.026 mean 0.029	

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

Strawberry

Two residue trials in strawberries were conducted in Mexico. Triforine was quantified by GC-ECD.

Two residue trials in strawberries were conducted in Brazil. Triforine was quantified by GC with a LOQ of 0.02 mg/kg.

Four residue trials in strawberries were conducted in Japan. Triforine was quantified by GC with a LOQ of 0.005 mg/kg.

Table 47 Triforine residues on strawberries from supervised trials in Mexico

Strawberry, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, Mexico	EC 190	–	–	0.190	–	4	14		Interval: 4, 7 or 10 days
Mexico, 1978 Irapuato/Gto (Tioga)	EC 190	0.019	1010	0.190	–	4	0 3 7 14 22	1.4 1.3 1.2 0.57 0.14	102FX-532-3108 TF-701-004 Sampling to analysis: 344–366 days
Mexico, 1979 Irapuato/Gto (Fresno)	EC 190	–	1010	0.190	Flowering and production	4	0 1 3	1.4 1.0 0.78	102FX-532-3109 TF-713-019 Sampling to analysis: 49–52 days

Analytical portion: fruit

Table 48 Triforine residues on strawberries from supervised trials in Brazil

Strawberry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Brazil	EC 190	0.029	800	0.228	4	2		Interval: 7 days
Brazil, 1985 Botucatu (Campinas)	EC 190	–	–	0.370	4	2 4 7	0.9 0.3 0.2	102FX-532-3101 [a, b] TF-713-014
		–	–	0.741		2 4 7	2.0 1.2 0.5	
Brazil, 1985 Botucatu (Campinas)	EC 190	–	–	0.428	4	2 4 7	1.2 0.4 0.2	102FX-532-3102 [a, b] TF-713-015
		–	–	0.855		2 4 7	3.2 1.0 0.7	

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

[b] The details of the analytical method were not shown in the study report.

Table 49 Triforine residues on strawberries from supervised trials in Japan

Strawberry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Japan	EC 180	0.009	1000–3000	–	5	1		
Japan, 1982 Greenhouse Hanyu-shi/Saitama (Reikou)	EC 150	0.007–0.010	2000	0.142–0.190	5	1 3 7	0.78 0.41 0.26	Sampling to analysis: 57–184 days
Japan, 1982 Greenhouse Toriya-cho/Nara (Houkou-Wase)	EC 150	0.010–0.013	1500	0.142–0.190	5	1 3 7	0.48 0.45 0.23	
Japan, 1985 Greenhouse Honjo/Tochigi (Reikou)	EC 150	0.008	1500	0.113	5	1 3	0.20 0.12	Sampling to analysis: 58–153 days

Strawberry, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Japan, 1985 Greenhouse Toyota-machi/Shizouka (Houkou-Wase)	EC 150	0.008	1500	0.113	5	1 3	0.39 0.25	

Analytical portion: fruit

Fruiting vegetables, Cucurbits

Cucumber

Four residue trials in cucumber were conducted in the USA. Triforine was quantified by GC-ECD with a LOQ of 0.004 mg/kg.

One residue trial in cucumber was conducted in Canada. Method RU 3, 26/12/10 was used to analyze cucumber fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD.

One residue trial in cucumber was conducted in Mexico. Method RU 3, 26/12/10 was used to analyze cucumber fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD.

Total three residue trials in cucumber were conducted in Hungary, France and Germany. Triforine was quantified by GC with a LOQ of 0.02 mg/kg.

Table 50 Triforine residues on cucumbers from supervised trials in USA, Canada and Mexico

Cucumber, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, Mexico	EC 190	–	–	0.285		3	7		Interval: 7 days
Mexico, 1978 Culiacan, Sin (Poinsett)	EC 190	–	320	0.285	Mature	3	0 3 7 14 22	0.065 0.17 0.066 0.008 0.009	102FX-532-3108 TF-701-004 Sampling to analysis: 359–379 days
Canada, 1984 – (–)	EC 190	–	–	0.285	–	1	1	0.13 0.14 0.14 mean: 0.14	102FX-532-4503 TF-723-012 Sampling to analysis: 352 days
USA, 1984 Homestead/ FL (–)	EC 190	–	–	0.285	–	4	3	0.014, 0.041 0.047, 0.024 mean: 0.032	102FX-532-4504 TF-723-013 Sampling to analysis: 98 days
				0.570			3	0.050, 0.053 0.056, 0.037 mean: 0.049	
USA, 1986 Lafayette/IN (–)	EC 190	–	–	0.285	–	4	2	0.031, 0.013 0.033, 0.030 mean: 0.027	10238-532-4516 TF-723-024 Sampling to analysis: 224 days (Control< 0.004–0.015)
				0.570			2	0.013, 0.035 0.064, 0.027 mean: 0.035	
USA, 1986 Weslaco/TX (–)	EC 190	–	–	0.285	–	4	2	0.14, 0.11, 0.20, 0.22 mean: 0.17	10238-532-4522 TF-723-030 Sampling to analysis: 285 days
				0.570			2	0.39, 0.30, 0.19, 0.36 mean: 0.31	
USA, 1987 Columbus/OH (–)	EC 190	–	–	0.285	–	5	1	0.14, 0.16, 0.098, 0.16 mean: 0.14	10238-532-4523 TF-723-031

Cucumber, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
				0.570			1	0.052, 0.099 0.034, 0.079 mean: 0.066	Sampling to analysis: 105 days

Analytical portion: fruit

Table 51 Triforine residues on cucumber from supervised trials in Hungary, France and Germany

Cucumber, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
Hungary, 1985 Nograd cucumber (–)	EC 190	0.057	500	0.285	–	1	0 1 5 10 14 21	2.0, 2.6, 3.0 Mean: 2.5 1.2, 2.9, 3.2 Mean: 2.4 0.29, 0.55, 0.62 Mean:0.49 0.065, 0.10, 0.13 Mean: 0.10 0.010, 0.040 0.097 Mean: 0.049 < 0.001(3)	10238-532-4515 TF-723-023 [a] Sampling to analysis: 37–65 days Recovery 61%
Germany, 1989 Bonn Cucumber (Sporu)	EC 190	0.029–0.228	1200–1500	0.342	–	8	0 1 2 3 4	0.22 0.025 0.097 0.11 0.022	10249-532-4526 TF-723-048 [a] Sampling to analysis: 257–274 days
France, 1993 Tassin Cucumber (Girola)	EC 190	0.024	1201	0.285	Flowering –mature	3	3	0.17	CFS1994-095 TF-723-057 Sampling to analysis: 235–239 days

Analytical portion: fruit

[a] The details of the in-field study were not shown in the study report.

Squash

Total three residue trials in courgettes were conducted in France and Germany. Method RU 3, 26/12/10 was used to analyze courgette fruits samples for the residues of Triforine. Triforine was quantified by GC with a LOQ of 0.02 mg/kg.

Five residue trials in winter and summer squash were conducted in USA. Triforine was quantified by GC-ECD with a LOQ of 0.003–0.005 mg/kg.

Table 52 Triforine residues on summer squash from supervised trials in France and Germany

Squash, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
France, 1979 – Courgettes (–)	EC 100 + Carbendazim	0.020	2000	0.400	–	5	7	0.05	10238-532-4701 TF-723-040 [a] Sampling to analysis: 123 days

Squash, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
France, 1979 – Courgettes (–)	EC 190	0.015	2000	0.570	–	5	7	0.02	10238-532-4702 TF-723-041 [a] Sampling to analysis: 123 days
Germany, 1989 Frankfurt Courgettes (Chinese Schlange)	EC 190	0.029	600	0.171	–	9	0 1 2 3 4	0.097 c: 0.014 0.10 0.023 0.090 c: 0.013 0.084	10249-532-4525 TF-723-047 [a] Sampling to analysis: 268–285 days

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.

Table 53 Triforine residues on summer and winter squash from supervised trials in the USA

Squash, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
USA, 1987 Lafayette/IN Squash (–)	EC 190	–	–	0.285	5	1	0.097, 0.097, 0.111, 0.005 mean: 0.078	TF-723-044 [a, b] Sampling to analysis: 222 days
				0.456		1	0.18, 0.22 0.23, 0.26 mean: 0.22	
USA, 1987 Brulington/VT Summer Squash (–)	EC 190	–	–	0.228	5	1	0.026, 0.036 0.044, 0.044 mean: 0.038	102FX-532-4706 [a, b] TF-723-045 Sampling to analysis: 329 days
				0.456		1	0.054, 0.059 mean: 0.057	
USA, 1987 Salisbury/MD Pumpkins (–)	EC 190	–	–	0.228	1	1	0.031, 0.032 0.061, 0.074 mean: 0.038	102FX-532-4707 [a, b] TF-723-046 Sampling to analysis: 361 days Control: < 0.004–0.085
				0.456		1	0.12, 0.13, 0.14, 0.21 mean: 0.22	
USA, 1987 Davis/CA Squash (–)	EC 190	–	–	0.228	5	1	0.076, 0.13, 0.21, 0.32 mean: 0.17	TF-723-053 [a, b] Sampling to analysis: 317 days Control: < 0.003–0.007
				0.456		1	0.23, 0.23, 0.24, 0.28 mean: 0.25	
USA, 1987 Lafayette/IN Pumpkins (–)	EC 190	–	–	0.228	5	1	0.018, 0.028, 0.028, 0.029 mean: 0.026	102FX-532-4704 [b] TF-723-043 Sampling to analysis: 142 days
				0.456		1	0.027, 0.029, 0.030, 0.031 mean: 0.029	

Analytical portion: fruit
[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Melon

Three residue trials in melon were conducted in USA. Triforine was quantified by GC-ECD with a LOQ of 0.003–0.004 mg/kg.

One residue trial in melon was conducted in Mexico. Triforine was quantified by GC-ECD with a LOQ of 0.004 mg/kg.

Two trials were conducted in Italy and France on melon. Triforine was quantified by GC-ECD.

Two trials in melon were conducted in Japan. Triforine was quantified by GC-ECD with a LOD of 0.005 mg/kg.

Table 54 Triforine residues on melons from supervised trials in USA and Mexico

Melon, country, year (variety)	Application						DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	GS	no.			
GAP, Mexico	EC 190	–	–	0.285		3	7		Interval: 7 days
Mexico, 1979 Apatsingan/Mich Cantaloupe (Top Mark)	EC 190	–	400	0.285	Fully grown 45 days after sowing	3	0 1 3 7 14 21	0.35 0.18 0.090 0.039 0.017 0.006	102FX-532-4604 [a] TF-723-036 Sampling to analysis: 76–97 days
USA, 1985 Weslaco/TX Cantaloupes	EC 190	–	–	0.228	–	1	3	0.023, 0.027, 0.032, 0.039 mean: 0.030	102FX-532-4603 TF-723-035 Sampling to analysis: 96 days
				0.456		1	3	0.048, 0.081 0.089, 0.108 mean: 0.082	
USA, 1986 Lafayette,/IN Muskmelons	EC 190	–	–	0.228	–	5	1	0.036, 0.078, 0.091 mean: 0.068	102FX-532-4607 TF-723-039 Sampling to analysis: 317 days
				0.456		5	1	0.22, 0.23 0.34 mean: 0.26	
USA, 1987 Davis/CA Cantaloupes	EC 190	–	–	0.228	–	5	1	0.009, 0.015 0.018, 0.029 mean: 0.018	TF-723-053 Sampling to analysis: 433 days (Control< 0.004–0.015)
				0.456		5	1	< 0.004, 0.011 0.024, 0.028 mean: 0.017	

Analytical portion: whole fruit

[a] The details of the analytical method were not shown in the study report.

Table 55 Triforine residues on melons from supervised trials in France and Italy

Melons, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
France, 1981 Toulouse Melons (Orlinabel)	Vereor Multi (100 g ai/L) + Carbendazim	0.02	1000	0.20	4	1	0.059	10288-532-4602 [a] TF-723-034
Italy, 1977 Melons	EC 190	0.029	1000	0.285	1	0 3 7 10	0.72 0.43 0.11 0.15	102FX-532-4606 [a] TF-723-038

Analytical portion: whole fruit

[a] The details of the analytical method were not shown in the study report.

Table 56 Triforine residues on melons from supervised trials in Japan

Melons, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Japan	EC 180	0.009	1000–3000	–	6	1		
Japan, 1978 Greenhouse Hamamatsu, Shizuoka, Muskmelon (Earl's-Favorite)	EC 150	0.015 – 0.019	3000	0.450–0.563	6	1 3 5 7	< 0.005 < 0.005 < 0.005 < 0.005	Sampling to analysis: 61–212 days
Japan, 1978 Greenhouse Tateyama, Chiba Muskmelon (Earl's-Favorite)	EC 150	0.015	2500	0.375	6	1 3 5 7	0.006 0.007 < 0.005 < 0.005	

Analytical portion: whole fruit

Fruiting vegetables, other than Cucurbits

Peppers

Two residue trials in peppers were conducted in Mexico. Method RU 3, 26/12/10 was used to analyze pepper fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.003–0.004 mg/kg.

Four residue trials in peppers were conducted in Japan. Triforine was quantified by GC-ECD with a LOD of 0.005 mg/kg or LC-MS with a LOQ of 0.01 mg/kg.

One trial in chilli peppers was conducted in Korea. Triforine was quantified by GC-ECD with a LOQ of 0.05 mg/kg.

Table 57 Triforine residues on peppers from supervised trials in Mexico

Peppers, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Mexico	EC 190	–	–	0.285	3	14		Interval: 7 days
Mexico, 1978 Culiacan,Sin Pepper (chilli) (Wonder 300)	EC 190	–	160	0.285	3	7 16 23	0.24 0.12 0.14	102FX-532-3108 TF-701-004 Sampling to analysis: 352–368 days
Mexico, 1979 Culiacan, Sin Pepper (Yolo Wonder)	EC 190	–	160	0.285	3	0 1 3	2.6 0.95 0.45	102FX-532-4401 TF-723-007 Sampling to analysis: 96–99 days

Analytical portion: fruit

Table 58 Triforine residues on peppers from supervised trials in Japan

Peppers, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Japan	EC 180	0.018	1000–3000	–	3	14		
Japan, 1983 Ushiku, Ibaraki Pepper (Green) (Ace) Greenhouse	EC 150	0.015	1500	0.23	3	1 3	0.79 0.54	Sampling to analysis: 60 days
		0.008	1500	0.11		1	0.41	
Japan, 1983 Miyazaki, Miyazaki, Pepper (Green) (Tosa-Kotobuki) Greenhouse	EC 150	0.015	2000	0.30	3	1 3	1.2 1.2	
		0.008	2000	0.15		1	0.63	
Japan, 1983 Konan, Kochi Pepper (Green) (Tosahime R) Greenhouse	EC 150	0.015	2500	0.38	3	1 3 14	1.2 1.0 0.22	
		0.010	2500	0.25	1	1 3 14	0.52 0.44 0.08	
Japan, 1983 Miyazaki, Miyazaki, Pepper (Green) (Kyosuzu) Greenhouse	EC 150	0.015	3000	0.45	3	1 3 14	0.59 0.56 0.06	
		0.010	3000	0.30	1	1 3 14	0.36 0.28 0.06	

Analytical portion: fruit

Table 59 Triforine residues on pepper from supervised trials in South Korea

Peppers, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, South Korea	EC 190	0.019	–	–	2	7		Timing: First sign of infection Interval: 10 days
S.Korea, 2009 Chungcheongnam-do Peppers (chilli) (Nokkwang) Greenhouse	DC 190	0.019 –	2000	0.380	1	1 3 5 7	0.62, 0.61, 0.64, mean 0.62 0.51, 0.53, 0.53 mean 0.52 0.42, 0.47, 0.52 mean 0.47 0.33, 0.35, 0.37 mean 0.35	Sampling to analysis: 22–28 days
					2	1 3 5 7	1.04, 1.08, 1.02 mean 1.05 0.83, 0.80, 0.78 mean 0.80 0.76, 0.91, 0.84 mean 0.84 0.33, 0.35, 0.37 mean 0.35	

Analytical portion: fruit

Eggplant

Two residue trials in eggplants were conducted in Mexico. Method RU 3, 26/12/10 was used to analyze eggplant fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD.

Five residue trials in eggplants were conducted in Japan. Triforine was quantified by GC-ECD with a LOD of 0.005 mg/kg or LC-MS with a LOQ of 0.01 mg/kg.

Table 60 Triforine residues on eggplants from supervised trials in Mexico

Eggplant, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Mexico	EC 190	–	–	0.285	3	15		Interval: 5 or 8 days
Mexico, 1976 Sinaloa	EC 190	–	–	0.285	3	0 2 4 6	0.37 0.30 0.69 0.28	102FX-532-4403 [a, b] TF-723-009
Mexico, 1979 Culiacan, Sin (Black Beauty)	EC 190	–	160	0.285	3	0 3 7 14 21	0.19 0.058 0.032 0.066 0.017	102FX-532-3108 TF-701-004 Sampling to analysis: 355–376 days

Analytical portion: whole fruit

[a] The details of the in-field study were not shown in the study report.

[b] The details of the analytical method were not shown in the study report.

Table 61 Triforine residues on eggplants from supervised trials in Japan

Eggplant, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Japan	EC 180	0.018	1000–3000	–	5	1		
Japan, 2008 Kohnan, Kochi (Ryoma)	EC 150	0.015	3000	0.450	5	1 3 7 14	0.28 0.24 0.06 < 0.01	Sampling to analysis: 100 days
Japan, 2008 Miyazaki, Miyazaki (Kokuyou)	EC 150	0.015	3000	0.450	5	1 3 7 14	0.38 0.25 0.12 0.02	
Japan, 1986 Sousa-shi, Chiba (Senryo)	EC 150	0.015	3000	0.450	5	1	0.39	Sampling to analysis: 30–92days
Japan, 1986 Shakudo, Osaka (Senryo-2)	EC 150	0.015	2500	0.375	5	1	0.29	
Japan, 1986 Noichi-cho, Kochi (Hayabusa)	EC 150	0.015	2600	0.390	5	1	0.25	

Analytical portion: fruit

Tomato

Twelve residue trials in tomatoes were conducted in USA. Triforine was quantified by GC-ECD with a LOQ of 0.003 mg/kg and LC-MS/MS with a LOQ of 0.01 mg/kg.

Six residue trials in tomatoes were conducted in Mexico. Triforine was quantified by LC-MS/MS with a LOQ of 0.01 mg/kg and GC-ECD with a LOD of 0.005 mg/kg.

One trial in tomatoes was conducted in Denmark Method RU 3, 26/12/10 was used to analyze eggplant fruits samples for the residues of Triforine. Triforine was quantified by GC-ECD.

Five trials in tomatoes were conducted in Japan. Triforine was quantified by GC-ECD with a LOD of 0.005 mg/kg and LC-MS with a LOQ of 0.01 mg/kg.

Table 62 Triforine residues on tomatoes from supervised trials in the USA and Mexico

Tomato, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no			
GAP, Mexico	EC 190	–	–	0.380	4	3		Timing: 1st: first sign of infection Interval: 7 days
USA, 1985 Orlando/FL (–)	EC 190	–	–	0.192	5	0 (12h)	0.032, 0.032, 0.143 mean: 0.069	102FX-532-4303[1)] TF-723-003 Sampling to analysis: 31–155 days
USA, 1985 Winterville/GA (–)		–	–	0.192	5	0	0.68, 0.54, 0.27 mean: 0.49 c: 0.006, 0.028	
USA, 1985 Elko/SC (–)		–	–	0.192	5	0	0.067, 0.079, 0.065 mean: 0.070	
USA, 1985 Geneseo/IL (–)		–	–	0.179	5	0	0.052, 0.11, 0.091 mean: 0.085	
USA, 1985 Fremont/OH (–)		–	–	0.192	5	0 (4h)	0.025, 0.063, 0.093 mean: 0.060	
USA, 1985 Tudor/CA (–)		–	–	0.192	5	0	0.26, 0.18, 0.25 mean: 0.23	
USA, 1985 Uvalde/TX (–)		–	–	0.192	5	0	0.19, 0.063, 0.098 mean: 0.12	
USA, 1985 Fresno/CA (–)	EC 190	–	–	0.183	5	0 3 7 14 21	0.039, 0.027, 0.013 mean: 0.026 0.022, 0.023 mean: 0.023 0.021, 0.022 mean: 0.022 0.010, 0.011 mean: 0.011 0.011, 0.013 mean: 0.012	102FX-532-4303[1)] TF-723-003 Sampling to analysis: 174–218 days
USA, 1985 Phelps/NY (–)		–	–	0.192	5	0 3 7 14 21	0.085, 0.038, 0.079 mean: 0.067 0.038, 0.030 mean: 0.034 0.029, 0.021 mean: 0.025 0.011, 0.009 mean: 0.010 0.008, 0.009 mean: 0.009	
Mexico, 2010 Chaves Talamanda /Sinaloa (Toro/Brigade/ UG194-06)	DC 190	–	494–510	0.386–0.398	4	3	0.085,0.081 mean 0.083	810.1500-10-479-15B-01-22 Sampling to analysis: 30–68 days
Mexico, 2010 Costencia /Sinaloa (Toro/Brigade/ UG194-06)	DC 190	–	495–518	0.386–0.404	4	3	0.076, 0.12 mean 0.096	
Mexico, 2010 Guasave/Sinaloa (Toro/Brigade/	DC 190	–	496–518	0.386–0.405	4	3	0.11, 0.15 mean 0.13	

Tomato, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no			
UG194-06)								
Mexico, 2010 Meneadero /Baja California (Alto May 0142/Torres)	DC 190	–	504–517	0.394–0.403	4	3	0.28, 0.26 mean 0.27	
Mexico, 2010 Colnett/Baja California (Alto May 0142/Torres)	DC 190		500–515	0.390–0.401	4	3	0.39, 0.40 mean 0.40	
			490–505	0.383–0.394	4	3	0.28, 0.21 mean 0.25	
			482–509	0.375–0.397	4	3	0.21, 0.21 mean 0.21	
USA, 2010 Yuma/AZ (Camelia/Yaqui/ Giante Verde)	DC 190	–	455–480	0.381–0.402	4	3	0.087, 0.11 mean 0.096	
			465–477	0.390–0.398	4	3	0.059, 0.060 mean 0.059	
			410–476	0.343–0.400	4	3	0.21, 0.36 mean 0.28	
USA, 2010 Thermal/CA (Yaqui)	DC 190		467–488	0.386–0.410	4	3	0.16, 0.18 mean 0.17	
USA, 2010 Yuma/AZ (Mountain Fresh)	DC 190	–	453–480	0.379–0.403	4	3 5 7 8 12	0.091, 0.052 mean 0.071 0.019, 0.038 mean 0.028 0.039, 0.049 mean 0.042 0.039, 0.045 mean 0.042 0.014, 0.025 mean 0.020	
Mexico, 1978 Culiacan, Sin (Walter)	DC 190	–	160	0.285	3	0 3 7 14	0.13 0.066 0.030 0.034	102FX-532-3108 TF-701-004 Sampling to analysis: 352–373 days

Analytical portion: whole fruit

[a] The details of the analytical method were not shown in the study report.

Table 63 Triforine residues on tomatoes from supervised trials in Denmark

Tomato, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Denmark, 1988 – (–)	EC 190	–	5000	0.950	1	1 3 5 7	0.39 0.48 0.30 0.23	102FX-532-4306 TF-723-006 Sampling to analysis: 435–442 days

Analytical portion: fruit

Table 64 Triforine residues on tomatoes from supervised trials in Japan

Tomato, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
GAP, Japan	EC 180	0.018	1000–3000	–	3	1		
Japan, 2008 Ushiku/Ibaraki (Momotaro T93) Greenhouse	EC 150	0.015	3000	0.450	1	1 3 7 14	0.09 0.09 0.11 0.10	Sampling to analysis: 30–68 days
					3	1 3 7 14	0.26 0.30 0.30 0.17	
Japan, 2008 Miyazaki/Miyazaki (House Taro) Greenhouse	EC 150	0.015	3000	0.450	1	1 3 7 14	0.16 0.16 0.18 0.14	
					3	1 3 7 14	0.56 0.67 0.42 0.29	
Japan, 1986 Mito/Ibaraki (First memory) Greenhouse	EC 150	0.015	3000	0.450	3	1	0.17	Sampling to analysis: 62–123 days
Japan, 1986 Habikino/Osaka (Momotaro) Greenhouse	EC 150	0.015	3000	0.450	3	1	0.28	
Japan, 1986 Yatsushiro/Kumamoto (First) Greenhouse	EC 150	0.015	3000	0.450	3	1	0.14 c: 0.007	

Analytical portion: fruit

Legume vegetables

Common bean

Four residue trials in beans were conducted in Brazil. Triforine in pods and seeds was quantified by GC-ECD with a LOQ of 0.01–0.02 mg/kg.

One trial in beans was conducted in South Africa. Triforine in pods was quantified by GC with a LOQ of 0.01 mg/kg.

Table 65 Triforine residues on beans from supervised trials in Brazil

Bean, country, year (variety)	Application					Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.				
GAP, Brazil	EC 190	–	400–1000	0.285	3	–	10		Timing: 1st: early symptoms Interval: 7–10 days
Brazil, 1985 Cambui String beans (–)	EC 190	–	–	0.285	5	Pods	1 3 4 5 6	1.9 0.4 0.6 0.2 0.2	TF-720-001 [b] Sampling to analysis: 18–23 days
				0.570			1 3 4 5	4.0 0.9 0.9 0.7	

Bean, country, year (variety)	Application					Analytical portion	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.				
							6	0.4	
Brazil, 1984 Prudente (–)	EC 190	–	–	0.285	3	Seeds	21	< 0.01	102FX-532-4003 [a] TF-720-003 Sampling to analysis: 213 days
Brazil, 1985 Guaira (Carioca)	EC 190	–	–	0.285	4	Seeds	28	< 0.01	TF-720-004 Sampling to analysis: 134 days
				0.570			28	< 0.01	
Brazil, 1996 Tupaciguar (–)	EC 190	–	–	0.285	3	Seeds	10	< 0.01	BASF 1996/306188
				0.570			10	< 0.01	

[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Table 66 Triforine residues on beans from supervised trials in South Africa

Bean, country, year (variety)	Application					Commodity	DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.				
GAP, South Africa	EC 190	28.5	1000	0.285	NS	–	3		Timing: 1st: first sign of infection Interval: 7–10 days
South Africa, 1976 Transvaal (Gelatin)	EC 190	–	–	0.285	4	Pods	0 3 5 7 10	1.2 0.44 0.44 0.34 0.01	TF-720-005 [a, b] Sampling to analysis: 121–131 days

[a] The details of the in-field study were not shown in the study report.
[b] The details of the analytical method were not shown in the study report.

Cereal grains

Barley

Two residue trials in barley were conducted in France. Method RU 3, 26/12/10 was used to analyze barley grain samples for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 67 Triforine residues on barley from supervised trials in France

Barley, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
France, 1979 - (Lely)	Vereor Multi (100 g ai/L)	0.05	500	0.250	1	64	< 0.01	10283-532-0102 [a] TF-730-024 Sampling to analysis: 146 days
France, 1979 (Astrix) (Six-row)	Vereor Multi (100 g ai/L)	0.05	500	0.250	1	50	< 0.01	10283-532-0103 TF-730-025 Sampling to analysis: 174 days

Analytical portion: grains
[a] The details of the in-field study were not shown in the study report.

Wheat

Total three residue trials in wheat were conducted in Austria, France and UK. Method RU 3, 26/12/10 was used to analyze wheat grain samples for the residues of Triforine. Triforine in grains was quantified by GC-ECD with a LOQ of 0.01–0.02 mg/kg.

Two residue trials in wheat were conducted in Brazil. Triforine in grains was quantified by GC-ECD with a LOQ of 0.01 mg/kg.

Table 68 Triforine residues on wheat from supervised trials in Austria, France and UK

Wheat, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Austria, 1980 – wheat (–)	Vereor Multi (100 g ai/L)	–	–	0.200	1	30	< 0.01	10288-532-0003 [a] TF-730-003 Sampling to analysis: 102 days
France, 1980 – (Lutin)	Vereor Multi (100 g ai/L)	0.05	500	0.250	2	61	< 0.01	10283-532-0004 [a] TF-730-004 Sampling to analysis: 150 days Analytical method: RU 3, 26/12/10
UK, 1977 Abbenes (Lely)	Funginex (200 g ai/L)	0.06	500	0.300	1	72	< 0.01 (4)	102FX-532-0014 [a] TF-730-013 Sampling to analysis: 150 days Analytical method: RU 3, 26/12/10

Analytical portion: grains

[a] The details of the in-field study were not shown in the study report.

Table 69 Triforine residues on wheat from supervised trials in Brazil

Wheat, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
Brazil, 1978 Municipio de Paicandu-Pr. (BH1146)	EC 190	–	200	0.285	3	–	< 0.01	102FX-532-0015[a] TF-730-014
Brazil, 1984 Guaira/SP (–)	EC 190	–	400	0.285–0.380	4	30	< 0.01	102FX-532-0016 TF-730-015 Sampling to analysis: 134 days Analytical method: RU 3, 26/12/10

Analytical portion: grains

[a] The details of the analytical method were not shown in the study report.

Straw, fodder and forage of cereals

Barley straw and forage

Two residue trials in barley straw and forage were conducted in France. Method RU 3, 26/12/10 was used to analyze barley straw and forage for the residues of Triforine. Triforine was quantified by GC-ECD with a LOQ of 0.04–0.07 mg/kg.

Table 70 Triforine residues on barley straw from supervised trials in France

Barley,	Application	DAT	Residues,	Ref

country, year (variety)	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.	Days	mg/kg	
France, 1979 – (Lely)	Vereor Multi (100 g ai/L)	0.05	500	0.250	1	64	0.07	10283-532-0102 [a] TF-730-024 Sampling to analysis: 146 days Analytical method: RU 3, 26/12/10
France, 1979 Astrix (Six-row)	Vereor Multi (100 g ai/L)	0.05	500	0.250	1	50	0.08	10283-532-0103 [a] TF-730-025 Sampling to analysis: 174 days Analytical method: RU 3, 26/12/10

Analytical portion: straw
[a] The details of the in-field study were not shown in the study report.

Wheat straw and forage

Total two residue trials in wheat straw and forage were conducted in France and UK. Method RU 3, 26/12/10 was used to analyze wheat straw and forage for the residues of Triforine. Triforine in grains was quantified by GC-ECD with a LOQ of 0.01–0.04 mg/kg.

Table 71 Triforine residues on wheat straw from supervised trials in France and UK

Wheat, country, year (variety)	Application					DAT Days	Residues, mg/kg	Ref
	Form, g ai/L	kg ai/hL	water, L/ha	kg ai/ha	no.			
France, 1980 - (Lutin)	Vereor Multi (100 g ai/L)	0.05	500	0.250	2	61	0.04	10283-532-0004 [a] TF-730-004 Sampling to analysis: 150 days
UK, 1977 Abbenes (Lely)	Funginex (200 g ai/L)	0.06	500	0.300	1	72	0.05,0.07, 0.06,0.07 Mean:0.06	102FX-532-0014 [a] TF-730-013 Sampling to analysis: 150 days

Analytical portion: straw
[a] The details of the in-field study were not shown in the study report.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In Processing

The Meeting received information on the fate of triforine residues during the processing of plums, grapes, tomatoes and hops.

The Meeting did not receive information on supervised field trials with hops. Therefore, the study on processing of hops is not summarized in this report.

Plum

The plum samples were treated with formulation containing triforine as active ingredient. The analytical material was shipped under deep-frozen conditions. The samples were stored in a deep-freeze compartment in the dark. The plum samples were heated to make processed commodities (compote, stewed and jam).

The samples were blended with acetone. After removal of the acetone by distillation, triforine in the remaining aqueous phase was partitioned into toluene. The toluene was evaporated and the

active substance degraded by heating with diluted sulfuric acid. Chloral hydrate thus formed was distilled and determined by GC-ECD (RU 3, 26/12/10).

Table 72 Triforine residues in processed commodities of plums

Country, year	Application				DAT Days	Commodity	Residues		Ref
	kg ai/hL	water, L/ha	kg ai/ha	no.			mg/kg	PF	
Germany, 1990	0.028	1500	0.427	4	7	Fruit Compote	0.22 0.06	 0.27	TF-712-091
				3	7	Fruit Compote Jam	0.11 0.10 0.10	 0.91 0.91	
Germany, 1992	–	–	0.428	2	7	Fruit Dried (prunes) Jam	0.15 0.12 0.02	 0.80 0.13	SHTR.93.004 TF-712-088
Germany, 1991	–	–	0.428	3–4	7	Fruit Stewed Dried plums	0.048 < 0.01 0.023	 < 0.21 0.48	10249-532-2312 TF -712-089

Grapes

The samples were blended with acetone. After removal of the acetone by distillation, triforine in the remaining aqueous phase was partitioned into toluene. The toluene was evaporated and the active substance degraded by heating with diluted sulfuric acid. Chloral hydrate thus formed was distilled and determined by GC-ECD (RU 3, 26/12/10). The LOQ was 0.01 mg/kg. Procedural recoveries were 90% for fruits, 111% for juice and 95% for wine, respectively.

Table 73 Triforine residues in processed commodities of grapes

Country, year	Application				DAT Days	Commodity	Residues		Ref
	kg ai/hL	water, L/ha	kg ai/ha	no.			mg/kg	PF	
Germany, 1984	0.057	887	0.505	1	21	Fruit Juice Wine	0.65 0.20 0.09	 0.31 0.14	10238-532-3012 TF -713-012

Tomato

Study 1

Fresh tomatoes were dipped in a spray wash of EC formulation solution diluted to 1.3% or 4%. After treatment the fruits were dried under room temperature for one day. Five kg of treated tomatoes were homogenized and the juice was separated by a suction filter. 300 g juice was concentrated by freeze drying to water content of 16% for purée, 28% for ketchup and 73% for dehydrated pulp.

Fifty grams of chopped tomatoes, 50 g juice or the whole quantity of each material were extracted with acetone. The solvent was removed and the residues partitioned into toluene. The organic phase was separated and evaporated. After addition of sulphuric acid, triforine was decomposed in the heat. Chloral hydrate formed was distilled and determined by GC-ECD.

Table 74 Triforine residues in processed commodities of tomatoes

Country, year	Application	Commodity	Residues		Ref.
			mg/kg	PF	
Germany, 1982	Dipped in 1.3% solution	tomatoes juice puree ketchup dehydrated pulp	3.4 2.6 8.9 15.6 36.3	 0.76 2.6 4.6 11	TF-790-019 Eichler, 1982

Country, year	Application	Commodity	Residues		Ref.
			mg/kg	PF	
	Dipped in 4% solution	tomatoes	8.8		
		juice	6.5	0.74	
		puree	20.6	2.3	
		ketchup	36.9	4.2	
		dehydrated pulp	96.4	11	

Study 2

At two locations (California and New York) processing tomatoes were treated at the normal application rate (0.183 kg ai/ha) and five times rate (0.964 kg ai/ha) and processed into tomato juice, wet pomace, dry pomace, paste or puree, and ketchup in order to determine possible residues in these commodities. Field samples were received in good condition frozen in dry ice and transferred to freezer at -20 °C.

The samples were washed and chopped in mechanical slicer. The tomato juice was preheated at 82.2 °C, sterilized at 126.6 °C and filled at 87.7 °C with 60 g salt tablet in can. Tomato juice was boiled in a vacuum kettle for 2.5 hours with constant stirring to prepare paste.

The residues were extracted using standard method via Chloral hydrate formation and analysis determined by GC-ECD.

Table 75 Triforine residues in processed commodities of tomatoes

country, year	Application		DALA Days	Commodity	Residues, mg/kg		Ref
	kg ai/ha	no.			mg/kg	PF	
USA, 1986 Fresno/CA	0.183	5	0	Tomatoes	0.039, 0.027, 0.013 mean: 0.026		102FX-532-4303 TF-723-003, TF-790-020 Beevers and McLellan, 1986
				Juice	< 0.003, < 0.003 mean < 0.003	< 0.12	
				Ketchup	< 0.003, < 0.003 mean < 0.003	< 0.12	
				Paste	< 0.003, < 0.003 mean < 0.003	< 0.12	
				Puree	< 0.003, < 0.003 mean < 0.003	< 0.12	
				Wet Pomace	< 0.003, < 0.003 mean < 0.003	< 0.12	
				Dry Pomace	0.033, 0.048 mean 0.041	1.6	
USA, 1985 Geneva/NY	0.964	5		Juice	0.047, 0.051, 0.053, 0.057		
				Ketchup	0.039, 0.040, 0.054, 0.068		
				Paste	0.15, 0.12, 0.095, 0.082		
				Puree	0.096, 0.092, 0.10, 0.095		
				Wet Pomace	6.2, 2.9		
				Dry Pomace	7.3, 7.5, 4.8, 3.7		

Study 3

The test substance, formulated as a dispersible concentrate (190 g triforine/L), was applied four times as a foliar treatment at an exaggerated (5×) application rate. The target application rate for each event was 1.95 kg ai/ha. Bulk tomato samples were shipped ambient to the processing facility, where tomato puree and paste were produced. Those samples were shipped frozen to the analytical laboratory and maintained in frozen storage until analysis. Following extraction and clean-up, triforine residues were separated and measured using HPLC-MS/MS. The LOQ was defined as 0.01 mg/kg. The overall mean procedural recovery was 77%, with a RSD of 8.8%.

Table 76 Triforine residues in processed commodities of tomatoes from supervised trials

Country, year (variety)	Application			DALA Days	Commodity	Residues		Ref.
	kg ai/ha	water, L/ha	no.			mg/kg	PF	
USA, 2010 Yuma/AZ (6366)	1.96 1.94 1.92 1.93	564 557 550 555	4	3	Tomato RAC Puree Paste	1.0, 1.3 mean 1.2 0.15, 0.19 mean 0.17 < 0.01, < 0.01	 0.14 < 0.008	47915A003 Hummel, 2011 Sampling to analysis: 71-125 days

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

The Meeting received a lactating goat feeding study.

Lactating goat

The study was designed to determine the residues of triforine found in milk and tissues following oral administration to lactating goats (Eichler, 1974: TF-440-016). Three groups of goats, each group containing three animals, were orally dosed with triforine for 30 days at dosages of approximately 5, 15 and 50 mg triforine per animal per day. This would be equivalent to total dietary residues of approximately 5, 15 and 50 ppm feed. Dose levels were based on a nominal feed intake of 1 kg (dry matter equivalent) per day for a goat. The concentrate mixture with flour containing triforine was used for administration.

Milking was done daily at morning and evening. The pooled samples of day 3, 5, 8, 11, 15, 22, 29 and of day 31 were stored deep frozen (-20 °C) until analysis. At the morning of day 31, all goats were sacrificed and the edible tissues (liver, kidney, muscle and fat) from each animal were collected. All samples were stored at -20 °C until they were analyzed. The storage period was between 1 day and 4 weeks.

The analytical procedures consider both triforine and those metabolites containing Cl_3C-CH group. The results were expressed as triforine equivalents and corrected with recoveries. The chopped samples were extracted with acetone and the extracts were concentrated by rotary evaporation. The remaining aqueous phase was mixed with sulphuric acid and distilled under nitrogen. To the aqueous solution of chloral hydrate formed, sodium chloride was added. The chloral hydrate was extracted with ethyl formate and quantified as chloral hydrate using gas chromatography with an electron capture detector. The LOQ of this method in milk and tissues was 0.001 mg/L and 0.003 mg/kg, respectively. Concurrent recoveries obtained from control samples spiked with the test item were reported to be 80 $\pm$ 10%.

No residues were detected in milk from the lowest dose level with the exception of two animals on day 29 (traces only considered as outliers). Residues in milk from group of 15 ppm feed were at the level of 0.001–0.003 mg/L on sampling days 8, 22 and 29. The milk collected on the other days did not contain detectable residues. At the high dose group (50 ppm feed), residue levels reached a plateau at the level of 0.002–0.010 mg/L after 3 days. One day after the last administration, no residues were detected in milk. The results indicate no increase of the residues during the treatment phase and a rapid decline in levels detected in milk during the last part of the withdrawal period.

Table 77 Residues of triforine and those metabolites containing Cl_3C-CH group in whole milk

Day	Residues, mg/L			
	Control	5 ppm feed	15 ppm feed	50 ppm feed
3	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)	0.006, 0.008, 0.010 mean 0.008
5	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)	0.002, 0.003, 0.005 mean 0.003
8	< 0.001 (3)	< 0.001 (3)	0.001, 0.002, 0.003	0.004, 0.004, 0.006

Day	Residues, mg/L			
	Control	5 ppm feed	15 ppm feed	50 ppm feed
			mean 0.002	mean 0.005
11	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)	0.004, 0.004, 0.004 mean 0.004
15	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)	0.003, 0.003, 0.003 mean 0.003
22	< 0.001 (3)	< 0.001 (3)	0.001, 0.001, 0.003 mean 0.002	0.005, 0.005, 0.007 mean 0.006
29	< 0.001 (3)	< 0.001, 0.002, 0.003 mean 0.002	0.001, 0.002, 0.002 mean 0.002	0.005, 0.005, 0.007 mean 0.006
31	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)	< 0.001 (3)

In tissues, no significant residues were detected in the fat, liver, kidney and muscle of 5 ppm and 15 ppm feed groups except several samples from 15 ppm feed animals exceeding slightly the LOQ. In the 50 ppm feed group, residues were detected in all of the analyzed tissues with the exception of muscle in an animal and fat of all animals. The maximum values in kidney and liver were 0.009 and 0.012 ppm, respectively.

Table 78 Residues of triforine and those metabolites containing Cl_3C-CH group in tissues

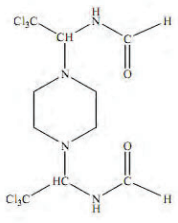
Group	Residues, mg/kg			
	Liver	Kidney	Muscle	Fat
Control	< 0.003 (3)	< 0.003, 0.007, 0.009 mean 0.006	< 0.003 (3)	< 0.003 (2), 0.011 mean 0.006
5 ppm feed	< 0.003 (3)	< 0.003 (3)	< 0.003 (3)	< 0.003 (3)
15 ppm feed	< 0.003 (2), 0.004 mean 0.003	< 0.003 (2), 0.006 mean 0.004	< 0.003, 0.003, 0.005 mean 0.004	< 0.003 (3)
50 ppm feed	0.004 (2), 0.012 mean 0.007	0.003, 0.005, 0.009 mean 0.006	< 0.003 (2), 0.005 mean 0.005	< 0.003 (3)

APPRAISAL

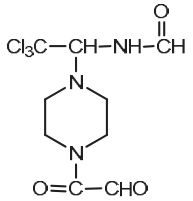
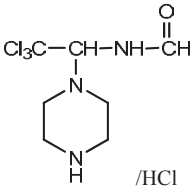
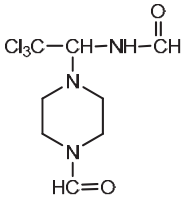
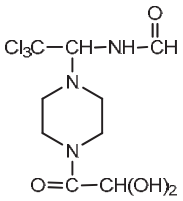
Triforine is a systemic fungicide for control of powdery mildews, rusts, scabs and rots. It was first evaluated by JMPR in 1977 (T), 1978 (T, R) and lastly in 1997 (T). The ADI for Triforine was 0–0.02 mg/kg bw and no ARfD was recommended by the previous JMPR. Triforine was scheduled at the Forty-fifth Session of the CCPR (2013) for the periodic re-evaluation of toxicity and residues by the 2014 JMPR.

The Meeting received information on identity, physical and chemical properties, animal and plant metabolism, environmental fate in soil, analytical methods, storage stability, use patterns, supervised trials, farm animal feeding studies and fates of residues in processing.

N,N'-{piperazine-1,4-diylbis[(trichloromethyl)methylene]}diformamide



In this appraisal, the following abbreviated names were used for metabolites.

WOS 2379	W 1084/W 1069	W 625	W 2379
			
N-{2,2,2-trichloro-1-[4-(2-oxoacetyl)piperazin-1-yl] ethyl}formamide	*N*-(2,2,2-trichloro-1-piperazin-1-yl-ethyl) formamide/ hydrochloride	*N*-[2,2,2-trichloro-1-(4-formyl piparazin-1-yl) ethyl]formamide	Hydrate of *N*-{2,2,2-trichloro-1-[4-(2-oxoacetyl)piperazin-1-yl] ethyl}formamide

Animal metabolism

The Meeting received animal metabolism studies with triforine in rats, lactating goat and laying hens. The metabolism and distribution of triforine in animals were investigated using the [^{14}C-piperazine] and [^{14}C-side chain]-labelled triforine.

Metabolism in rats was summarized and evaluated by the WHO panel of the JMPR in 2014.

Triforine is rapidly metabolized and excreted in rats. Highest residues were found in liver followed by kidney. Residues were lower in muscle and fat. Radioactive residues were identified in the excreta only. *N*-[2,2,2-trichloro-1-(piperazin-1-yl) ethyl]-formamide (W 1084), which is formed by the cleavage of a side chain, was the major component in urine of rats. It was excreted in urine as the glucuronide. The side-chain metabolites trichloroethanol including its glucuronide and *N*-acetylcysteine conjugate of 2,2,2-trichloroethylamine was detected in urine. W 1084 and triforine were detected in the faeces of rats.

Lactating goats were administered with [piperazine-^{14}C]-triforine as an oral dosage equivalent to a dietary level of 250 or 1000 ppm once daily for 3 consecutive days. The goats were sacrificed 4 hours or 6 days after the last treatment.

Radioactivity administered to the goats was rapidly eliminated in urine and faeces. A total of 47% and 72% of the applied radioactivity were eliminated in 24 hours, and a further 16 and 14% were excreted in the following 5 days by the 250 ppm and the 1000 ppm dose group goats, respectively.

Up to 68% of the residual radioactivity in the liver of goat sacrificed 4 hours after the last treatment was extracted. The extracted radioactivity consisted of at least five metabolite fractions. M1 and M2 represented unknown polar metabolite fractions whereas WOS 2379 and W 1084 were characterized. The fraction M1 represented 18% TRR. Triforine, WOS 2379 and W 1084 accounted for 15%, 15% and 13% TRR, respectively. Up to 14% of the residual radioactivity in the liver of goat sacrificed 6 days after the last treatment was extracted. This metabolite pattern was similar to that in the extracted radioactivity of the liver of goat sacrificed 4 hours after the last treatment.

Seventy-eight percent of the residual radioactivity in the kidneys of goats sacrificed 4 hours after the last treatment was extracted. The metabolite pattern of the extracted radioactivity was similar to that in the extracted radioactivity of the liver. The predominant fraction found in the extracted radioactivity of goat sacrificed 4 hours after the last treatment was metabolite fraction M1 (31% TRR). Triforine, WOS 2379 and W1084 represented 19%, 8.4% and 19% TRR, respectively. Analysis of the extracted radioactivity of the kidneys of a goat sacrificed 6 days after the last treatment showed a similar metabolite pattern in terms of their relative amounts in the extracts. The predominant fraction was M1 accounting for 11% TRR. Triforine represented 3.6% TRR.

Seventy-nine percent of the residual radioactivity in the muscle of goat sacrificed 4 hours after the last treatment was extracted. The predominant radioactive fraction was triforine at 41% TRR. The other metabolites accounted for 9.5% (W 1084), 13% (WOS 2379), 0.70% (M2) and 15% TRR (M1).

In one study, laying hens were orally administered with [piperazine-^{14}C]-triforine at the dietary dose equivalent to 500 or 2000 ppm in the feed once daily for 3 consecutive days. The hens were sacrificed 4 hours or 7 days after the last treatment.

The radioactivity administered to the hens was rapidly eliminated (54–84% in 56 hours after the first dose). In the following 7 days a further 10–15% of the administered radioactivity was excreted (76% excreted from 500 ppm dosed hens and 94% from 2000 ppm dosed hens).

The highest values in eggs were found about 4 to 5 days after the first treatment with [^{14}C] triforine.

In the other study, laying hens were administered with [side chain-^{14}C]-triforine for 10 consecutive days at a dose of 32 ppm in the feed. Radioactivity recovered in excreta during the 10 days accounted for about 85% of the total cumulative dose.

Total radioactivity in eggs increased steadily during the 10 days to a peak value of 1.6 mg equiv/kg (yolk) and 0.19 mg equiv/kg (white). The major components in egg white and egg yolk were the fraction A which accounted for 48% TRR (0.08 mg/kg) and the sulphate conjugate of trichloroethanol which accounted for 25% TRR (0.25 mg/kg), respectively. W 1069 was observed and accounted for 10% TRR (0.10 mg/kg) in egg yolk. Triforine accounted for 13% TRR(0.02 mg/kg) and 2.1% TRR(0.02 mg/kg) in egg white and egg yolk, respectively.

The fraction A in the protease-treated extract of liver was separated into five components each of which accounted for 0.07–0.40 mg equiv/kg (4–24% TRR). The sulphate conjugate of trichloroethanol was present in liver accounting for 9% TRR. There appeared to be a small amount of triforine in liver (2.9% TRR, 0.05 mg/kg).

The main components in muscle were the trichloroethanol sulphate conjugate and W 1069 each accounting for about 22% TRR (0.05 mg equiv/kg). Triforine was present at 8.4% TRR (0.02 mg/kg).

Triforine accounted for 18% TRR (0.02 mg/kg) and the sulphate conjugate of trichloroethanol accounted for 36% TRR (0.03 mg equiv/kg) in fat.

Triforine was also found in skin at low levels (0.01 mg/kg). The retention time of the main fraction corresponded to that of trichloroethanol sulphate (56% TRR, 0.13 mg/kg).

In animal metabolism studies, triforine, W 1084/W 1069, WOS 2379 and trichloroethanol sulphate were predominantly found in tissues of lactating goats and laying hens. The major component in milk and egg white was the polar fraction consisting of several components but they were not identified. Triforine was identified in egg white and egg yolk. Excretion, distribution and triforine and its metabolites found in excreta of lactating goats and laying hens were similar to those in rats.

Plant metabolism

The Meeting received plant metabolism studies performed on apples, tomatoes and cucumber with triforine ^{14}C-labelled in two carbons at the side chain, and on barley with triforine ^{3}H-labelled at piperazine ring ([side chain-^{14}C] and [piperazine-^{3}H]).

In an outdoor apple metabolism study, a number of fruits or leaves of apple were treated at random on the surface with [side chain-^{14}C]-triforine at a rate of 1.2 g ai/L in a series of small droplets. Treated apple fruits were harvested 2 weeks after the last of five successive applications with 8-day intervals. After five successive applications of [^{14}C] triforine, 32% (fruit) and 22% (leaf) of the applied radioactivity were recovered. On an average, 1.36 mg equiv/kg was recovered in the treated fruits.

The major component in the surface washes and extracts of fruits was identified as triforine accounted for 73–79% TRR (0.88–1.2 mg/kg) two weeks after the last application. Several minor components were observed in the extracts and each of them accounted for 1–2% TRR.

In an indoor tomato metabolism study, a number of fruits or leaves of tomato were treated at random on the surface with [side chain-^{14}C]-triforine at a rate of 1.2 g ai/L in a series of small droplets. The treated tomatoes were harvested at 2 hours and 3 days after the last of four successive applications with 8–10 days intervals. The initial surface washes of treated tomatoes at harvest contained, on an average, 92% (2 hours after the last application) and 91% (3 days after the last application) of TRR. Acetonitrile extracts of washed and homogenised tomatoes accounted for, on an average, 5.8% TRR (2 hours after the last application) and 6.2% TRR (3 days after the last application). The TRR from the treated tomatoes accounted for, on an average, 16 (2 hours after the last application) and 9.7 (3 day after the last application) mg equiv/kg.

Triforine in the surface washes and extracts accounted for 91–93% TRR (7.6–19 mg/kg) in tomatoes taken at 2 hours and 3 days after the final application of [^{14}C] triforine. The extracts also contained several minor components each accounting for, on an average, 0.05–1.1% TRR.

In an indoor cucumber metabolism study, a number of fruits or leaves of cucumber were treated at random on the surface with [side chain-^{14}C]-triforine at a rate of 1.2 g ai/L in a series of small droplets. The treated cucumbers were harvested 3 days after the last of four successive applications at 7-day intervals. The surface washes of treated cucumbers at harvest contained, on an average, 85% of TRR. Extracts of washed and homogenised cucumber peel and flesh accounted for, on an average, 7.5% TRR (peel) and 1.4% TRR (flesh). The TRR from the treated cucumbers accounted for, on an average, 2.2 mg equiv/kg.

The major radioactive component was identified as triforine in the surface washes and extracts accounted for 87–88% TRR (1.9 mg/kg) in cucumber taken 3 days after the final application of [^{14}C] triforine. The extracts also contained several minor components each accounting for means of 0.3–2% TRR.

In the first indoor barley metabolism study, [piperazine-^{3}H]-triforine was applied to barley plants grown in plastic pots as soil drenching. The leaves were harvested at 15 and 30 days after treatment.

Triforine was identified as a major component in the barley leaves, amounting to 58% TRR at 15 days after the treatment and 43% TRR at 30 days after the treatment. W 1084 was also observed in the 0.1M HCl extract (8.4–13% TRR).

In the second indoor barley metabolism study, the leaves of barley plants root-treated with [piperazine-^{3}H]-triforine were collected 30 days after treatment. The major component was identified as triforine, accounted for 45% TRR, and W 1084 and piperazine were also observed.

In the third outdoor barley metabolism study, the plants (during the stem extension stage when the second node of the stem was formed and the next-to-last leaf was just visible) were sprayed with an aqueous emulsion of a mixture of the commercial formulation of triforine and [piperazine-^{3}H]-triforine at a rate of 0.25 kg ai/ha. Barley was harvested when ripe, and straw and grain were analysed separately.

The methanol soluble radioactive residue contained triforine and its metabolites which were free in barley straw and grain. Triforine accounted for 0.034 mg/kg (18% TRR) in straw and 0.0018 mg/kg in grain (13% TRR). W 1084 was identified as a minor component. Two other radiolabelled components were identified in straw: glycine at 0.043 mg/kg (33% TRR) and iminodiacetic acid at 0.021 mg/kg (17% TRR), respectively.

In the plant metabolism studies, triforine was the major component of the residues found in all plants studied.

Environmental fate

The Meeting received information on aerobic degradation in soil, photolysis on soil surface and hydrolytic degradation study.

In soil under the aerobic conditions, the DT_{50} ranged from 1–70 days at 20 °C. Many minor degradation products were detected in the extracts during the study. Most of the radioactivity was

recovered from natural components. Mineralization was up to 45%. Minor degradates were identified as W 625, WOS 2379, piperazine and W 1069, but all of them were less than 3% TAR.

In soil photolysis study, the degradation was biphasic. The photodegradation half-life of triforine was 11 hours of artificial sunlight or 0.5 natural sunlight days for phase 1 (hours 0 to 8). For phase 2 (hours 8 to 48), the half-life was 71 hours of artificial sunlight equivalent to 3.2 natural sunlight days.

In summary, triforine was rapidly and completely degraded in soil and is unlikely to be taken up by crops from the soil after soil treatment.

Methods of analysis

The Meeting received description of validation data on analytical methods for residues of triforine in plant and animal commodities.

In most of the methods for the determination of triforine in plant, homogenized samples were extracted with acetone, and the extract was partitioned into organic solvent and the active substance was degraded by heating with dilute sulphuric acid. Chloral hydrate thus formed was determined by GC-ECD. The methods of analysis with GC-ECD for a range of matrices were validated with acceptable recoveries with the LOQs of 0.01 mg/kg for triforine.

New methods using LC-MS or LC-MS/MS were developed for analysing triforine directly. In the methods, homogenized samples were extracted with acetone, and the extract was purified with SPE cartridge clean-ups. The methods of analysis with LC-MS or LC-MS/MS for a range of matrices were validated with acceptable recoveries with the LOQs of 0.01 mg/kg except for tomato paste for which the LOQ was 0.05 mg/kg.

In the methods for animal commodities, homogenized samples were extracted with acetone, or were diluted with water. Triforine and possible metabolites containing the Cl_3C-CH group in the acetone extract or diluted homogenate were degraded by heating with dilute sulphuric acid. Chloral hydrate thus formed was determined by GC-ECD. These methods were validated with acceptable recoveries with the LOQ of 0.001–0.003 mg/kg for milk and animal tissues, and 0.01 mg/kg for egg.

The Meeting was aware that the QuEChRS-multi residue method was validated for most plant matrices with LOQs of 0.01–0.02 mg/kg for triforine.

Stability of residues in stored analytical samples

The Meeting received information on the freezer storage stability of triforine in plant (apples, cherries, plums, peaches, blueberries and hops) and their processed (beer) commodities. Analysis was done by the common moiety method.

Using the common moiety method, storage stability results indicated that residues with common moiety including triforine were stable for at least 1 month in processed hops (beer), at least 6 months in plums and hops (dried cones), at least 12 months in apples, cherries, peaches and blueberries. However, according to the result of plant metabolism study on tomato, triforine seems stable for at least 5 months.

Definition of the residue

In the lactating goat metabolism studies, TRRs in liver and kidney were higher than those in milk, muscle and fat. Triforine, WOS 2379 and W 1084 accounted for 15%, 15% and 13% TRR in liver, and 19%, 8.4% and 19% TRR in kidney. The polar unknown fraction M1 represented 18% TRR in liver and 31% TRR in kidney. In the laying hen metabolism studies, TRR in liver was also higher than those in other tissues. In the study using [side chain-^{14}C]-triforine, the trichloroethanol sulphate conjugate and W 1069 were the main components in muscle (22% TRR) and egg yolk (10–25% TRR).

The analytical methods for animal commodities provided determine only the residues of triforine and metabolites containing the Cl_3C-CH group converted to chloral hydrate which is formed

by heating in acidic condition. No method of analysis was available for quantification of triforine alone.

The Meeting decided that triforine and its metabolites containing the Cl_3C-CH group were suitable analytes for enforcement purposes and dietary risk assessment for animal commodities.

The octanol/water coefficient (log P_{ow}) of triforine was 2.2 at 20 °C. In the lactating goat and the laying hen metabolism studies, triforine and its metabolites found in muscle were 2–100 times higher than those in fat. Fractionation of whole milk showed that 32% of the radioactivity was found in cream and 76% was found in skim milk. In the lactating goat feeding study, triforine and its metabolites were detected at 0.003–0.007 mg/kg in liver, kidney and muscle but less than LOQ (< 0.003 mg/kg) in fat. The Meeting considered the residue of triforine is not fat soluble.

In plant metabolism studies, parent triforine was the major component (43–93% TRR) in apple, tomato, cucumber and barley. Several metabolites identified accounted for < 10% TRR.

In most of the analytical methods for triforine in plant, since chloral hydrate formed by heating with dilute sulphuric acid was quantified with GC-ECD, triforine and its metabolites containing piperazine ring were simultaneously measured. As the predominant residue was the parent compound in the plant metabolism study, using the common moiety method would result in only slight over-estimation of residues if PHI was short. Recently LC-MS and LC-MS/MS methods were available for determining triforine only.

The Meeting decided that parent triforine was a suitable analyte for enforcement purposes and dietary risk assessment in plant commodities.

The Meeting recommended the following residue definition:

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant commodities: *Triforine*

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for animal commodities: *Triforine and its metabolites determined as chloral hydrate expressed as triforine*

The residue is not fat soluble

Residue of supervised residue trials on crops

The Meeting received supervised trial data for the foliar application of triforine on apple, pear, cherry, plum, apricot, nectarine, peach, raspberry, blueberry, black currant, grape, cranberry, strawberry, cucumber, squash, melon, peppers, eggplant, tomato, common bean, barley and wheat. Residue trials were conducted in Australia, Brazil, Canada, Denmark, France, Germany, Greece, Hungary, Italy, Japan, Mexico, New Zealand, South Africa, South Korea, the United Kingdom (UK) and the USA. Most of the supervised residue trials employed the common moiety method, while the results of plant metabolism studies showed that triforine was the main component of residues in crops.

Labels were available from a number of countries in North and South America, Africa, Asia and Oceania describing the registered uses of triforine.

Pome fruits

Apple

Data were available from supervised trials conducted on apples in the USA, Canada, Australia, Germany, France and Brazil.

The GAP on apples in Canada was five foliar applications at a maximum rate of 0.475 kg ai/ha between tight cluster and petal fall stage. Trials in the USA and Canada on apples were conducted with foliar applications of EC formulation. Triforine residues in apple from the trials in Canada matching GAP of Canada were (n=1): 0.041 mg/kg.

Trials in Australia on apples were conducted with one to ten foliar applications of EC formulation (GAP: four foliar applications at a maximum spray concentration of 0.023 kg ai/hL with a PHI of 1 day). Triforine residue trials on apples in the Australia did not match the GAP of Australia.

Trials in Germany and France on apples were conducted with foliar applications of EC formulation. No GAP from European countries was available for apple.

The GAP on apples from Brazil was three foliar applications at a maximum concentration of 0.024 kg ai/hL with a PHI of 5 days. Triforine residues in apple from the trials in Brazil matching Brazilian GAP were (n=2): < 0.02 mg/kg (2).

As the data were insufficient for estimating a maximum residue level, the Meeting agreed to withdraw its previous recommendation for apple.

Pear

Data were available from a supervised trial on pears in Australia. No GAP from Australia was available for pear.

The Meeting agreed that estimation of maximum residue level was not possible for pear.

Stone fruits

Cherry

Data were available from supervised trials on cherries conducted in the USA, Canada and Germany.

The GAP on cherries in Canada was for three foliar applications at a maximum spray concentration of 0.014 kg/hL or a rate of 0.475 kg ai/ha between early and full bloom stages. Triforine residue in cherries from the trials in Canada and the USA matching GAP of Canada was (n=1): 0.007 mg/kg.

Trials in Germany on cherries were conducted with foliar applications of an EC formulation. No GAP from European countries was available for cherries.

The Meeting agreed to withdraw its previous recommendation for cherries.

Plum

Data were available from supervised trials on plums conducted in the USA, Canada, Germany, France and South Africa.

The GAP on plums in Canada is for three foliar applications at a maximum spray concentration of 0.014 kg/hL or a rate of 0.475 kg ai/ha between early and full bloom stages. No trials on plums in Canada and the USA matched the GAP of Canada.

Trials in Germany and France were conducted with foliar applications of an EC formulation. No GAP from European countries was available for plums.

The GAP on plums in South Africa was two foliar applications at a rate of 0.87 kg ai/ha with a PHI of 3 days. No trials for plums in South Africa matched the GAP of South Africa.

The Meeting agreed to withdraw its previous recommendation for plums.

Apricot

Data were available from supervised trials on apricots from the USA, France, Greece and Italy.

Trials in the USA on apricots were conducted with one to three foliar applications of an EC formulation at a spray concentration of 0.018 kg ai/hL. No GAP of the USA was available.

Trials in France, Greece and Italy on apricots were conducted with three foliar applications of DC formulation at a spray concentration of 0.038 kg ai/hL. No GAP from European countries was available for apricots.

The Meeting agreed that estimation of maximum residue level was not possible for apricots.

Nectarine

Data were available from supervised trials on nectarines from the USA.

Trials in the USA on nectarines were conducted with one to four foliar applications of an EC formulation at a spray concentration of 0.015–0.018 kg ai/hL. No GAP from the USA was available.

The Meeting agreed that the estimation of maximum residue level was not possible for nectarines.

Peach

Data were available from supervised trials on peaches from the USA, Canada, France, Greece, Japan, Brazil and South Africa.

The GAP on peaches in Canada is three foliar applications at a maximum spray concentration of 0.014 kg/hL or a rate of 0.475 kg ai/ha between early and full bloom stages. Triforine residue in peaches from trials in Canada and the USA matching GAP of Canada was (n=1): 0.02 mg/kg.

The GAP on peaches in Brazil is for three foliar applications at a maximum spray concentration of 0.024 kg ai/hL with a PHI of 3 days. Triforine residues in peaches from trials in Brazil matching GAP were (n=2): < 0.01 and 9.4 mg/kg.

Trials in France and Greece on peaches were conducted with one to eight foliar applications of a DC formulation at a rate of 0.36–0.38 kg ai/ha. No GAP from European countries was available for peaches.

The GAP on peaches in South Africa is two foliar applications at a maximum rate of 0.67 kg ai/ha with a PHI of 3 days. No trials from South Africa on peaches matched the GAP of South Africa.

The GAP on peaches in Japan is five foliar applications at a maximum spray concentration of 0.018 kg ai/hL with a PHI of 1 day. Triforine residues in peaches from the trials in Japan matching GAP of Japan were (n=2): 0.77 and 1.4 mg/kg.

The Meeting considered the data insufficient for the estimation of a maximum residue level, and agreed to withdraw its previous recommendation for peaches.

Berries and other small fruits

Raspberries, Red, black

Data were available from supervised trials on raspberries in France. No GAP from European countries was available for raspberry.

The Meeting agreed that estimation of maximum residue level was not possible for raspberry.

Blueberries

Data were available from supervised trials on blueberries in Canada.

The GAP on blueberries in Canada (except for Eastern Canada) is four foliar applications at a maximum rate of 0.570 kg ai/ha from bud break to 10–14 days after early bloom with a PHI of 60 days. Triforine residues in blueberries from the trials conducted in Canada (except for Eastern Canada) matching this GAP were (n=2): < 0.01 and 0.015 mg/kg.

The GAP for Eastern Canada (only) is three foliar applications at a maximum rate of 0.570 kg ai/ha from leaf-bud break to pink-bud stage with a PHI of 60 days. Triforine residues in blueberries from the trials conducted in Eastern Canada matching this GAP were (n=3): < 0.01(3) mg/kg.

Based on the trials on blueberries in Canada, the Meeting estimated a maximum residue level of 0.03 mg/kg to replace its previous recommendation (1 mg/kg) for blueberry. The Meeting also estimated an STMR and an HR for triforine in blueberry of 0.01 and 0.018 mg/kg, respectively. The highest residue concentration in an individual sample was selected for HR.

Currant, Black

Data were available from supervised trials on black currants in Germany and UK. No GAP from European countries was available for black currants.

The Meeting agreed to withdraw its previous recommendation for black currants.

Grapes

Data were available from supervised trials on grapes from Germany, Mexico and New Zealand.

Trials in Germany on grapes were conducted with one to three foliar applications of an EC formulation at a rate equivalent to 0.28–0.57 kg ai/ha. No GAP from European countries was available for grapes.

Trials in Mexico on grapes were conducted with one foliar application of EC formulation at a rate equivalent to 0.28 kg ai/ha. No GAP from Mexico was available for grapes.

The GAP on grapes in New Zealand is four foliar applications at a rate of at least 0.38 kg ai/ha with a PHI 14 days. No trials in New Zealand on grapes matched the GAP of New Zealand.

The Meeting agreed that estimation of maximum residue level was not possible for grapes.

Cranberry

Data were available from supervised trials on cranberries from the USA.

The GAP on cranberries in Canada was three foliar applications at a maximum rate of 0.570 kg ai/ha with a PHI of 60 days. No trials for cranberries from the USA matching the GAP of Canada were available.

The Meeting agreed that estimation of maximum residue level was not possible for cranberry.

Strawberry

Data were available from supervised trials on strawberries from Mexico, Brazil and Japan.

The GAP on strawberries in Mexico was four foliar applications at a maximum rate of 0.19 kg ai/ha with a PHI of 14 days. Triforine residue in strawberries from the trials in Mexico matching GAP of Mexico was (n=1): 0.57 mg/kg.

The GAP on strawberries in Brazil was four foliar applications at a maximum rate of 0.23 kg ai/ha with a PHI of 2 days. No trials in Brazil on strawberries matched the GAP of Brazil.

The GAP on strawberries in Japan is five foliar applications at a spray concentration equivalent to 0.009 kg ai/hL with a PHI of 1 day. Triforine residues in strawberries from the trials in Japan matching GAP of Japan were (n=4): 0.20, 0.39, 0.48 and 0.78 mg/kg.

The Meeting considered that the data was insufficient for estimating a maximum residue level, the Meeting agreed to withdraw its previous recommendation for strawberry.

Gooseberry

No supervised trials on gooseberry were available.

The Meeting agreed to withdraw its previous recommendation for gooseberry.

Brassica vegetables

Brussels sprouts

No supervised trials on Brussels sprouts were available.

The Meeting agreed to withdraw its previous recommendation for Brussels sprouts.

Fruiting vegetables, Cucurbits

Cucumber

Data were available from supervised trials on cucumbers from the USA, Canada, Mexico, Hungary, France and Germany.

Trials from the USA on cucumbers were conducted with four or five foliar applications of an EC formulation at a rate equivalent to 0.29–0.57 kg ai/ha. No GAP from the USA was available for cucumber.

One trial in Canada on cucumbers was conducted with one foliar application of an EC formulation at a rate of 0.29 kg ai/ha. No GAP from Canada was available for cucumber.

The GAP on cucumbers in Mexico is three foliar applications at a maximum rate of 0.29 kg ai/ha with a PHI of 7 days. Triforine residue in cucumber from a trial in Mexico matching the GAP of Mexico was (n=1): 0.066 mg/kg.

Trials in Hungary, France and Germany on cucumbers were conducted but no GAP from European countries were available.

The Meeting considered that the data was insufficient for estimating a maximum residue level for cucumbers.

Squash

Data were available from supervised trials on summer squash and winter squash from the USA, France and Germany. No GAP from the USA or European countries was available for squash.

The Meeting agreed that estimation of maximum residue level was not possible for squash.

Melon

Data were available from supervised trials on melon from the USA, Mexico, France, Italy and Japan.

Trials in the USA on melons were conducted with one or five foliar applications of an EC formulation at a rate of 0.23–0.46 kg ai/ha. No GAP from the USA was available for melons.

The GAP on melons in Mexico is three foliar applications at a maximum rate of 0.29 kg ai/ha with a PHI of 7 days. Triforine residue in melon from one trial in Mexico matching GAP of Mexico was (n=1): 0.039 mg/kg.

Trials from Italy and France on melon were conducted with one or four foliar applications of an EC formulation at a rate of 0.20–0.29 kg ai/ha. No GAP from European countries was available for melons.

The GAP on melon in Japan is six foliar applications at a spray concentration of 0.009 mg/hL with a PHI of 1 day. Triforine residues in melon from the trials in Japan were (n=2): < 0.005 and 0.006 mg/kg.

The Meeting considered the data was insufficient for estimating a maximum residue level for melons.

The Meeting agreed to withdraw its previous recommendation for fruiting vegetables, cucurbits.

Fruiting vegetables, other than Cucurbits

Peppers

Data were available from supervised trials on peppers from Mexico, Japan and South Korea.

The GAP on peppers in Mexico is three foliar applications at a maximum rate of 0.29 kg ai/ha with a PHI of 14 days. Triforine residue in peppers from the trials in Mexico matching GAP of Mexico was (n=1): 0.12 mg/kg.

The GAP on peppers in Japan is three foliar applications at a spray concentration of 0.018 kg ai/hL with a PHI of 14 days. Triforine residues in peppers from trials in Japan matching GAP of Japan were (n=2): 0.06 and 0.22 mg/kg.

The GAP on chili peppers in South Korea is two foliar applications at a spray concentration equivalent to 0.019 kg ai/ha with a PHI of 7 days. Tis residue in peppers from the trial in South Korea matching GAP of South Korea was (n=1): 0.35 mg/kg.

The Meeting considered that the data was insufficient for estimating a maximum residue level for peppers.

Egg plant

Data were available from supervised trials on egg plants in Mexico and Japan.

The GAP on egg plants in Mexico is three foliar applications at a maximum rate of 0.29 kg ai/ha with a PHI of 15 days. Triforine residue in egg plants from a trial in Mexico matching GAP of Mexico was (n=1): 0.066 mg/kg.

The GAP on eggplants in Japan is five foliar applications at a spray concentration of 0.018 kg ai/hL with a PHI of 1 day. Triforine residues in egg plants from the trials in Japan matching GAP of Japan were (n=5): 0.25, 0.28, 0.29, 0.38 and 0.39 mg/kg.

Based on the trials on egg plants in Japan, the Meeting estimated a maximum residue level, an STMR and an HR for triforine in egg plants of 1, 0.29 and 0.39 mg/kg, respectively.

Tomato

Data were available from supervised trials on tomatoes in the USA, Mexico, Denmark and Japan.

One trial from Denmark on tomatoes was conducted with one foliar application of EC formulation at a rate equivalent to 0.95 kg ai/ha. No GAP of European countries were available for tomatoes.

The GAP on tomatoes in Japan was three foliar applications at a spray concentration of 0.018 kg ai/hL with a PHI of 1 day. Triforine residues in tomatoes from trials in Japan matching GAP of Japan were (n=5): 0.14, 0.17, 0.26, 0.28 and 0.56 mg/kg.

The GAP on tomatoes in Mexico is four foliar applications at a maximum rate of 0.38 kg ai/ha with a PHI of 3 days. Triforine residues in tomatoes from the trials in Mexico matching GAP of Mexico were (n=5): 0.083, 0.096, 0.13, 0.27 and 0.40 mg/kg.

Trials from the USA on tomatoes were conducted with four or five foliar applications of an EC formulation at a rate of 0.18–0.41 kg ai/ha. Triforine residues in tomatoes from the trials in the USA matching GAP of Mexico were (n=3): 0.072, 0.17 and 0.28 mg/kg.

The Meeting decided to use the triforine residue data from the trials in Mexico and the USA. Triforine residues in tomatoes from the trials in Mexico and the USA matching GAP of Mexico were (n=8): 0.072, 0.083, 0.096, 0.13, 0.17, 0.27, 0.28, 0.40 mg/kg.

Based on the data, the Meeting estimated a maximum residue level of 0.7 mg/kg to replace its previous recommendation (0.5 mg/kg). The Meeting also estimated an STMR and an HR for triforine in tomato of 0.15 and 0.40 mg/kg, respectively.

Legume vegetables

Common bean

Data were available from supervised trials on common beans from Brazil and South Africa.

The GAP on beans in Brazil is three foliar applications at a maximum rate of 0.29 kg ai/ha with a PHI of 10 days. Triforine residue in bean seeds from the trials in Brazil matching GAP of Brazil was (n=1): < 0.01 mg/kg.

The GAP on beans in South Africa is for foliar application(s) with spray at a rate of 0.29 kg ai/ha with a PHI of 3 days (the maximum numbers of applications not specified). Triforine residue in beans from one trial in South Africa matching GAP of South Africa was (n=1): 0.44 mg/kg.

As the available data was insufficient for estimating a maximum residue level, the Meeting agreed to withdraw its previous recommendation for common bean (pods and immature seeds).

Cereal grains

Data were available from supervised trials on barley in France. No GAP from European countries was available for barley.

Data were available from supervised trials on wheat in Austria, France, UK and Brazil. No GAP from European countries and Brazil was available for wheat.

No other information was available for any other cereal grains.

The Meeting agreed that the estimation of maximum residue level was not possible for cereal grains.

The Meeting agreed to withdraw its previous recommendation for cereal grains.

Animal feedstuffs

Barley straw and forage

Data were available from supervised trials on barley straw and forage in France. No GAP from European countries was available for barley straw and forage.

The Meeting agreed that the estimation of a maximum residue level was not possible for barley straw and forage.

Wheat straw and forage

Data were available from supervised trials on wheat straw and forage in France and UK. No GAP from European countries was available for wheat straw and forage.

The Meeting agreed that the estimation of a maximum residue level was not possible for wheat straw and forage.

Fate of residues during processing

Residues in processed commodities

The fate of triforine residues following the processing of plums, grapes and tomatoes was made available to the Meeting. Estimated processing factors and the derived STMR-Ps are summarized in the Table below.

Processing factors, STMR-P for food

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors [a]	PF (Mean or best estimate)	RAC STMR (mg/kg)	STMR-P (mg/kg)
Tomato	Juice	0.74 [b], 0.76 [b]	0.75	0.15	0.11
	Paste	< 0.008	< 0.008		< 0.001

Raw agricultural commodity (RAC)	Processed commodity	Calculated processing factors [a]	PF (Mean or best estimate)	RAC STMR (mg/kg)	STMR-P (mg/kg)
	Puree	0.14, 2.3 [b], 2.6 [b]	2.3		0.35
	Wet pomace	< 0.12	< 0.12		< 0.018
	Dry pomace	1.6	1.6		0.24

[a] Each value represents a separate study.
[b] RAC was dipped in EC formulation solution.

Residues in animal commodities

Estimated maximum and mean dietary burdens of farm animals

The maximum and mean dietary burdens were calculated using the median residue of triforine in dry tomato pomace estimated at the current Meeting on a basis of the OECD Animal Feeding Table.

Summary of livestock dietary burdens (ppm of dry matter diet)

Livestock dietary burden, triforine, ppm of dry matter diet								
	US-Canada		EU		Australia		Japan	
	Max	Mean	Max	Mean	Max	Mean	Max	Mean
Beef cattle	0	0	0	0	0.027 [a]	0.027 [b]	0	0
Dairy cattle	0	0	0	0	0.027	0.027 [c]	0	0
Broilers	0	0	0	0	0	0	0	0
Layers	0	0	0	0	0	0	0	0

[a] Highest maximum beef cattle dietary burden suitable for MRL estimates for mammalian meat, fat, edible offal and milk
[b] Highest mean beef cattle dietary burden suitable for STMR estimates for mammalian meat, fat and edible offal
[c] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk

Farm animal feeding studies

The Meeting received a lactating dairy goat feeding studies using triforine, which provided information on likely residues resulting in animal commodities and milk from triforine residues in the animal diet.

Lactating dairy goats

Lactating dairy goats were dosed with triforine for 30 days at doses equivalent to 5, 15 and 50 ppm in the diet. Residues of triforine were at or less than the LOQ (0.001 mg/L) in whole milk at the 5 ppm of feeding level except on sampling day 29 (< 0.001–0.003 mg/L). In the highest dose group (50 ppm feed), triforine residues in milk reached a plateau at the level of 0.002–0.010 mg/L after 3 days. In tissues, no measurable residues were found in fat, liver, kidney and muscle of the 5 ppm feed group. In the 15 ppm feed group, triforine concentration slightly exceeded the LOQ in several samples. In the 50 ppm feed group, residues were detected in all of the analysed tissues with exception of muscle in one animal and fat of all animals. The maximum values in kidney and liver were 0.009 and 0.012 ppm, respectively.

Animal commodities maximum residue levels

For MRL estimation, the residue in the animal commodities is triforine.

The maximum dietary burden for beef and dairy cattle was 0.027 ppm. The maximum dietary burden for beef and dairy cattle was 0.54% of the lowest dose of 5 ppm in feed of the lactating goat feeding study. In the lactating goat feeding study at 5 ppm, triforine was at < 0.01 mg/kg in milk and < 0.01 mg/kg in liver.

The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR of 0 mg/kg in milk.

The Meeting estimated a maximum residue level of 0.01* mg/kg, an STMR of 0 mg/kg and an HR of 0 mg/kg in mammalian meat and fat.

The Meeting estimated a maximum residue level of 0.01* mg/kg, an STMR of 0 mg/kg and an HR of 0 mg/kg in mammalian edible offal.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed below are suitable for estimating maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for plant commodities: *Triforine.*

Definition of the residue (for compliance with the MRL and for estimation of dietary intake) for animal commodities: *Triforine and its metabolites determined as chloral hydrate expressed as triforine.*

The residue is not fat soluble.

Commodity		Recommended Maximum residue level, mg/kg		STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
CCN	Name	New	Previous		
FP 0226	Apple	W	2		
FB 0020	Blueberries	0.03	1	0.01	0.018
VB 0402	Brussels sprouts	W	0.2		
GC 0080	Cereal grains	W	0.1		
FS 0013	Cherries	W	2		
VP 0526	Common bean (pods and immature seeds)	W	1		
FB 0021	Currants, Black, Red, White	W	1		
VO 0440	Egg plant	1	–	0.29	0.39
VC 0045	Fruiting vegetables, Cucurbits	W	0.5		
FB 0268	Gooseberry	W	1		
FS 0247	Peach	W	5 Po		
FS 0014	Plums (including Prunes)	W	2		
FB 0275	Strawberry	W	1		
VO 0448	Tomato	0.7	0.5	0.15	0.40
MO 0105	Edible offal (Mammalian)	0.01 [a]	–	0	0
MF 0100	Mammalian fats (except milk fat)	0.01 [a]	–	0	0
MM 0095	Meat (from mammals except marine)	0.01 [a]	–	0	0
ML 0106	Milks	0.01 [a]	–	0	0

[a] At or about the LOQ.

Commodity	STMR or STMR-P, mg/kg	HR or HR-P, mg/kg
Name		
Tomato juice	0.11	
Tomato paste	< 0.001	
Tomato puree	0.35	
Tomato wet pomace	< 0.018	
Tomato dry pomace	0.24	

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Daily Intakes (IEDIs) of triforine were calculated for the 17 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting (Annex 3). The ADI is 0–0.03 mg/kg bw and the calculated IEDIs were 0–2% of the maximum ADI. The Meeting concluded

that the long-term intakes of residues of triforine, resulting from the uses considered by current JMPR, are unlikely to present a public health concern.

Short-term intake

The ARfD for triforine is 0.3 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for triforine were calculated for the food commodities for which STMRs or HRs were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4 of the 2014 JMPR Report. The IESTIs were 0–5% of the ARfD for children and the general population. The Meeting concluded that the short-term intake of residues of triforine from other uses that have been considered by the present Meeting is unlikely to present a public health concern.

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The annual Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues was held in Rome, Italy, from 16 to 25 September 2014. The FAO Panel of Experts had met in preparatory sessions from 11 to 15 September 2014. The Meeting was held in pursuance of recommendations made by previous Meetings and accepted by the governing bodies of FAO and WHO that studies should be undertaken jointly by experts to evaluate possible hazards to humans arising from the occurrence of pesticide residues in foods. During the meeting the FAO Panel of Experts was responsible for reviewing pesticide use patterns (use of good agricultural practices), data on the chemistry and composition of the pesticides and methods of analysis for pesticide residues and for estimating the maximum residue levels that might occur as a result of the use of the pesticides according to good agricultural use practices. The WHO Core Assessment Group was responsible for reviewing toxicological and related data and for estimating, where possible and appropriate, acceptable daily intakes (ADIs) and acute reference doses (ARfDs) of the pesticides for humans. This report contains information on ADIs, ARfDs, maximum residue levels, and general principles for the evaluation of pesticides. The recommendations of the Joint Meeting, including further research and information, are proposed for use by Member governments of the respective agencies and other interested parties.

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