ETOXAZOLE (241)

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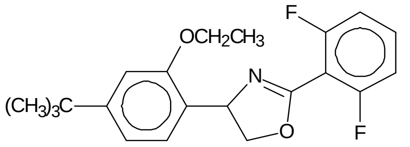
EXPLANATION

Etoxazole is an acaricide (miticide/ovicide) belonging to the diphenyloxazoline group of chemicals. It controls mites through inhibition of chitin biosynthesis and by causing adults to lay sterile eggs. At the Forty-first session of the CCPR (2009), etoxazole was scheduled for the evaluation as a new compound by 2010 JMPR.

The Meeting received information on identity, animal and plant metabolism, environment fate in soil, rotational crops, analytical methods, storage stability, use patterns, supervised trials, farm animal feeding studies and fates of residues in processing

IDENTITY

Common name	Etoxazole
Chemical name	
IUPAC:	*(RS)*-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl] phenetole
CAS:	2-(2,6-difluorophenyl-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole
CAS number:	153233-91-1
Synonyms:	V-1283, S-1283, YI-5301, SCAL-5001
Structural formula:	



Molecular formula:	$C_{21}H_{23}F_2NO_2$
Molecular weight:	359.4

PHYSICAL AND CHEMICAL PROPERTIES

Pure active ingredient

Property	Results	Reference
Appearance	White N 9.5/ with 90% reflectance free flowing crystalline powder	Betteley, 1997 (SKP-0005)
Odour	No obvious odour	Betteley, 1997 (SKP-0005)
Melting point	101.5–102.5 °C	Betteley, 1997 (SKP-0005)

Property	**Results**	**Reference**
Relative density	1.2389 kg/m^3	Betteley, 1997 (SKP-0005)
Vapour pressure	7.0 × 10^{-6} Pa at 25 °C	Betteley, 1997 (SKP-0005)
Volatility (Henry's law constant)	Henry's law constant (calculated) 3.6 × 10^{-2} Pa m^3/mole at 20–25 °C	Betteley, 1997 (SKP-0005)
Solubility in water	3.99 × 10^{-5} g/L in distilled water at 10 °C 7.04 × 10^{-5} g/L in distilled water at 20 °C 6.69 × 10^{-5} g/L in distilled water at 30 °C The effect of pH was not determined as the test material has no ionisable groups or dissociation constant.	Betteley, 1997 (SKP-0005)
Partition coefficient n-octanol/water	Log Pow = 5.52 ± 0.58 at 20 °C The effect of pH was not determined as the test material has no ionisable groups or dissociation constant.	Betteley, 1997 (SKP-0005)
Hydrolysis	DT_{50} values: Test period: 21 days for pH5, 20 °C, 30 days for pH 7 and 9, 20 °C pH Half-life (days) Rate constant (/day) pH 5 9.57 @ 20 °C 0.0724 pH 7 161 @ 20 °C 0.0043 147 @ 20 °C* 0.0047 7.96 @ 50 °C 0.0871 3.15 @ 60 °C 0.2198 1.48 @ 70 °C 0.4667 pH 9 165 @ 20 °C 0.0042 217 @ 20 °C* 0.0032 9.49 @ 50 °C 0.0730 3.90 @ 60 °C 0.1777 1.61 @ 70 °C 0.4307 In buffers of acidic pH, etoxazole is hydrolysed to R-7 and in neutral or basic pH to R-4. * determined by extrapolation of Arrhenius plot	Elsom, 1996 (SKM-0014)
Photolysis	[^{14}C-oxazole]etoxazole: Half-life = 15.9 days summer sunlight equivalents at latitude 40°N; [^{14}C-*tert*-butylphenyl]etoxazole: Half-life = 17.4 days summer sunlight equivalents at latitude 40°N Major degradates were identified as R-3, R-11, R-12 and R-15.	Elsom, 1997 (SKM-0032)
Quantum yield	The quantum yield was determined to be 0.026. A theoretical halftime was 5.56 days (half-life 3.85 days) at latitude of 40°N in the summer at a depth of 30 cm.	Elsom, 1997 (SKM-0032)
Dissociation constant	pKa - no measurable value	Betteley, 1997 (SKP-0005)

Technical material

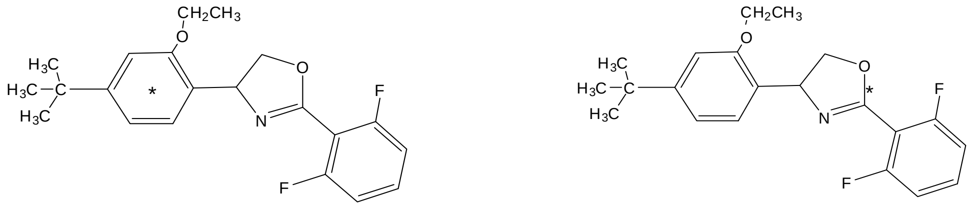
Property	Results	Reference
Minimum concentration	94.8%	
Appearance	Lumpy powder at 20 °C with a Munsell colour notation of N9.5	Betteley, 1996 (SKP-0003)
Odour	Musty odour	Betteley, 1996 (SKP-0003)
Solubility in organic solvents	Acetone: 309 g/L at 20 °C 1,2-dichloroethane: 402 g/L at 20 °C Ethyl acetate: 249 g/L at 20 °C n-heptane: 18.7 g/L at 20 °C Methanol: 104 g/L at 20 °C Xylene: 252 g/L at 20 °C	Betteley, 1996 (SKP-0003)

FORMULATIONS

Formulation	Active ingredient content
Suspension concentrate (SC)	360 g ai/L, 100 g ai/L or 110 g ai/L
Wettable powder (WP)	800 g ai/kg
Water dispersible granule (WG)	720 g ai/kg or 50 g ai/kg
Emulsifiable concentrate (EC)	a mixture of pyriproxyfen + etoxazole
	100 g ai/L + 160 g ai/L or
	200 g ai/L + 160 g ai/L

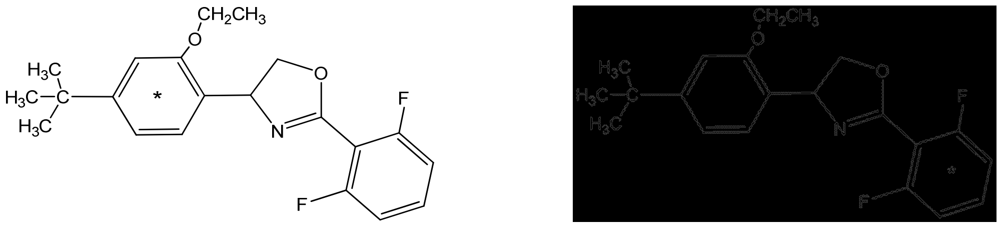
METABOLISM AND ENVIRONMENTAL FATE

The metabolism of etoxazole has been investigated in animals and plants. The crops selected represent those for which supervised trials have been provided. The fate and behaviour of etoxazole in animals, plants and the environment was investigated using the [^{14}C] labelled test materials shown in Figures 1 and 2.



[^{14}C-*tert*-butylphenyl]etoxazole [^{14}C-oxazole]etoxazole

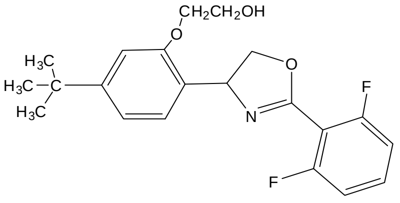
Figure 1 [^{14}C]-Labelled test materials used in apple, orange, eggplant and rat metabolism studies

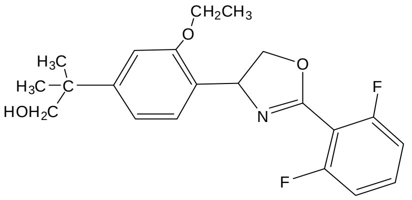
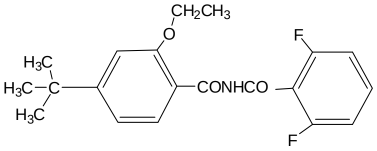
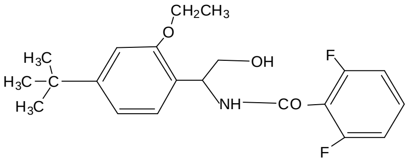
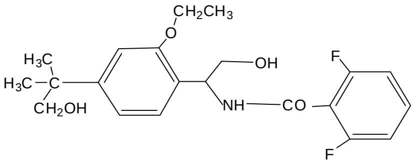
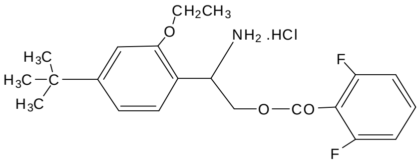
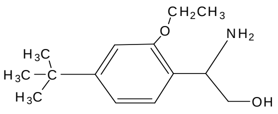
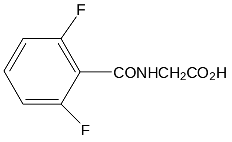
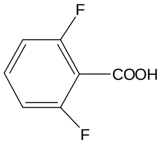
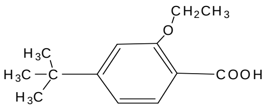


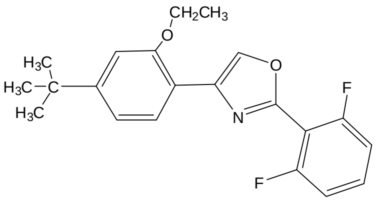
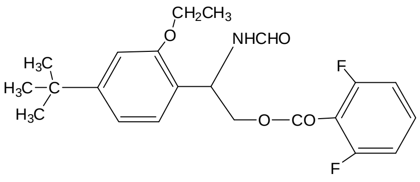
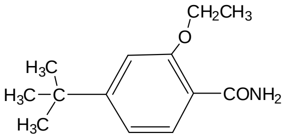
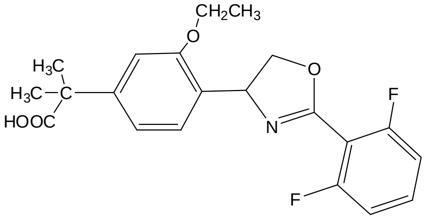
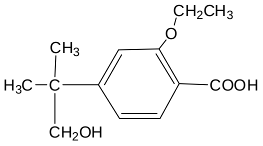
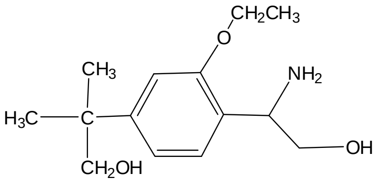
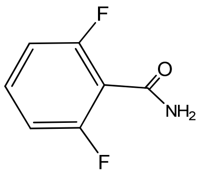
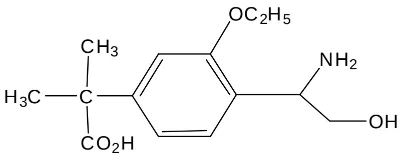
[^{14}C-*tert*-butylphenyl]etoxazole [^{14}C-difluorophenyl]etoxazole

Figure 2 [^{14}C]-Labelled test materials used in cotton, lactating goat, and laying hen metabolism as well as in degradation in soil and water, and rotational crops studies

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

Compound name	Structure	Found in metabolism studies
R-1: 4-[4-*tert*-butyl-2-(2-hydroxyethoxy)phenyl]-2-(2,6-difluorophenyl)- 4,5-dihydrooxazole		Plants, Livestock

Compound name	Structure	Found in metabolism studies
R-2: 2-(2,6-difluorophenyl)-4-[2-ethoxy-4-(1-hydroxymethyl-1-methylethyl)phenyl]-4,5-dihydrooxazole		Plants, Livestock, Rats
R-3: *N*-(2,6-difluorobenzoyl)-4-*tert*- butyl-2-ethoxybenzamide		Plants, Soil, Water, Rats
R-4: *N*-(2,6-difluorobenzoyl)-2-amino- 2-(4-*tert*-butyl-2-ethoxyphenyl) ethanol		Plants, Soil, Rats
R-6: *N*-(2,6-difluorobenzoyl)-2-amino- 2-[2-ethoxy-4-(1-hydroxymethyl-1-methylethyl)phenyl]ethanol		Rats
R-7: 2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethyl 2,6-difluorobenzoate hydrochloride		Plants, Livestock, Soil, Rats
R-8: 2-amino-2-(4-*tert*-butyl-2-ethoxy-phenyl)ethanol		Plants, Livestock, Soil
R-10: *N*-(2,6-difluorobenzoyl)glycine		Livestock
R-11: 2,6-difluorobenzoic acid		Plants, Livestock, Soil, Water, Rats
R-12: 4-*tert*-butyl-2-ethoxybenzoic acid		Plants, Water, Rats

Compound name	Structure	Found in metabolism studies
R-13: 4-(4-*tert*-butyl-2-ethoxyphenyl)-2-(2,6-difluorophenyl)oxazole		Plants, Livestock, Soil, Rats
R-14: *N*-formyl-2-amino-2-(4-*tert*-butyl-2-ethoxyphenyl)ethyl 2,6-difluorobenzoate		Plants
R-15: 4-*tert*-butyl-2-ethoxybenzamide		Plants, Soil, Water, Rats
R-16: 2-(2,6-difluorophenyl)-4-[2-ethoxy-4-(1-carboxy-1-methylethyl)phenyl]-4,5-dihydrooxazole		Livestock, Rats
R-20: 2-ethoxy-4-(1-hydroxymethyl-1-methylethyl)benzoic acid		Livestock
R-24: 2-amino-2-[2-ethoxy-4-(1'-hydroxymethyl-1'-methylethyl)-phenyl]ethanol		Livestock, Rats
DFB 2,6-difluorobenzamide		Plants, Livestock
Meta-bolite 1 2-amino-2-(2-ethoxy-4-(1'-hydroxycarbonyl-1'-methylethyl)phenyl)ethanol		Livestock, Rats

Animal metabolism

The Meeting received studies on the metabolism of etoxazole in rats, lactating goats and laying hens. The study on rats was evaluated by the WHO Core Assessment Group of the 2010 JMPR. A summary of the rat metabolism is given in this section.

Rats

The absorption, distribution, metabolism and excretion studies for rats were conducted with two labelled forms of etoxazole, using [*tert*-butylphenyl-U-^{14}C]-labelled etoxazole and [oxazole-^{14}C]-labelled etoxazole.

The excretion results from the study have shown that oral doses of etoxazole are quickly eliminated at both the high and low dose level. The concentration of radioactivity in tissues was highest in the gastrointestinal tracts and livers at almost all sacrifice times with significantly higher concentrations being found in male rats compared to females. In tissues with significant concentrations, males were often two-fold higher than the corresponding tissues from females.

Etoxazole was metabolised principally by hydroxylation of the 4,5-dihydrooxazole ring followed by cleavage of the molecule and hydroxylation of the tertiary-butyl side chain. There was a significant difference in the proportions of metabolites excreted in the urine of male and female rats. The major component in male rat urine was 2-amino-2-(2-ethoxy-4-[1'-hydroxycarbonyl-1'-methyl-ethyl]phenyl)ethanol (Metabolite 1) and in female urine was 2-amino-2-(2-ethoxy-4-[1'-hydroxymethyl-1'- methylethyl]phenyl)ethanol (R-24).

Lactating goat

The metabolism of etoxazole in the lactating goat has been studied using etoxazole labelled separately with ^{14}C in the difluorophenyl and *tert*-butylphenyl positions (Figure 2). The radiolabelled materials were administered orally (in capsules) to two separate British Saanen goats for 4 consecutive days. The goats received mean daily doses of 20 mg of etoxazole per day, equivalent to a daily intake of total diet containing etoxazole at a level of approximately 10 ppm in the diet.

Urine and faeces were collected in the 24-hour period preceding administration of the first dose and then during the 24-hour intervals afterwards up to 23 hours after the final dose. Cages were rinsed with about 2 L of water at the end of each 24 hour collection period, immediately prior to dosing. Milk samples were collected twice daily, immediately prior to dosing and in the afternoon after an interval of approximately 6 hours, commencing from the afternoon preceding the first dose until 23 hours after the last dose. Whole blood samples were taken from each animal just prior to sacrifice. At sacrifice, approximately 23 hours after the final dose, the following tissues were collected: liver, kidneys, heart, bile, rumen, reticulum and contents, omasum, abomasum and contents, intestines and contents, samples of muscle (rump and foreleg) and fat (subcutaneous and peritoneal).

Radioactivity was measured by liquid scintillation counting. Solid samples were combusted in oxygen using an automatic sample oxidiser. The combustion products were absorbed into Carbosorb and mixed with scintillation cocktail and radiocounted.

Metabolites were characterised and identified following sample extraction and co-chromatography with known reference materials using thin-layer chromatography and high-performance liquid chromatography. The possible presence of conjugated metabolites in the urine and kidney was investigated via enzyme hydrolysis (β-glucuronidase/sulfatase or β-glucuronidase). Bile samples (difluorophenyl label only) were subjected to acid hydrolysis and neutralisation to detect corresponding liver metabolites. Mass spectrometry (direct infusion and HPLC-electrospray) was used to identify the metabolites.

Recovery of radioactivity in the urine and faeces from the *tert*-butylphenyl radiolabel was 1.9% and 17% of the dose, respectively. A further 80% of the dose was recovered in the gastro-intestinal contents. In the difluorophenyl radiolabel, totals of 1.5% and 54% of the dose were recovered in the urine and faeces, respectively. The gastro-intestinal contents accounted for 29% of the dose. Overall recoveries of the administered dose were 99% (*tert*-butylphenyl label) and 85% (difluorophenyl label). Table 1 summarises the results from administration of both radiolabelled compounds.

Table 1 Excretion and retention of radioactivity by goats after oral administration of ^{14}C-etoxazole at a nominal dietary concentration of 10 ppm for four days (percentage of cumulative dose)

Sample	[^{14}C-*tert*-butylphenyl]etoxazole	[^{14}C-difluorophenyl]etoxazole
Urine	1.89	1.48
Cage wash	0.02	0.08
Faeces	16.98	53.89
Rumen	42.18	18.65
Omasum/Abomasum	4.46	2.50
Intestinal contents	33.11	7.99
Milk	0.01	0.03
Liver	0.31	0.08
Kidney	0.19	< 0.01
Total Recovery	99.15	84.70

Total radioactive residues were highest in the bile from both labels (3.46 mg/kg, *tert*-butylphenyl; 0.317 mg/kg difluorophenyl) and kidneys and liver from the *tert*-butylphenyl radiolabel (0.938 mg/kg and 0.230 mg/kg, respectively) and liver from the difluorophenyl radiolabel (0.063 mg/kg). Radioactive residues in the *tert*-butylphenyl plasma, whole-blood and heart were 0.01-0.02 mg/kg. Total radioactive residues in all other tissues and milk from both radiolabels were < 0.008 mg/kg. The concentration of radioactive residues in tissues is summarised in Table 2.

Concentrations of radioactivity in the kidney from the difluorophenyl radiolabel were 0.007 mg/kg. Concentrations of radioactivity in fat and muscle after administration of both radiolabelled forms etoxazole were < 0.001–0.008 mg/kg. Concentrations of radioactivity in the heart from the *tert*-butylphenyl label were 0.011 mg/kg. After partitioning the organic extract with an aqueous phase, most of the heart radioactivity was extracted with the aqueous phase

Table 2 Concentration of radioactivity (expressed as parent etoxazole) in tissues of goats sacrificed 23 hours after 4 daily oral doses of ^{14}C-etoxazole at a nominal 10 ppm

Tissue	[^{14}C -*tert*-butylphenyl]etoxazole mg/kg	[^{14}C -difluorophenyl]etoxazole mg/kg
Fat – subcutaneous	0.006	0.005
Fat peritoneal	0.007	0.008
Heart	0.011	0.002
Kidneys	0.938	0.007
Liver	0.230	0.063
Muscle – rump	0.006	0.001
Muscle – foreleg	0.006	< 0.001
Bile	3.46	0.317
Plasma	0.024	0.005
Whole- blood	0.021	0.004

During administration of [*tert*-butylphenyl-^{14}C] etoxazole, mean daily milk concentrations increased from 0.001 ppm during Day 1 to 0.004 ppm on Day 4. During administration of [difluorophenyl-^{14}C] etoxazole, mean daily milk concentrations increased to a plateau of 0.002 ppm during Days 2 to 4. The concentration of radioactive residues in milk is summarised in Table 3.

Table 3: Concentration of radioactivity in milk from goats during oral administration of ^{14}C-etoxazole at a nominal 10 ppm for 4 days

Treatment	Time (hours after first dose)	Mean daily concentration [a]
[^{14}C -*tert*-butylphenyl]etoxazole	0–24	0.001
	24–48	0.001
	48–72	0.003

Treatment	Time (hours after first dose)	Mean daily concentration [a]
	72–95	0.004
[^{14}C -difluorophenyl]etoxazole	0–24	0.001
	24–48	0.002
	48–72	0.002
	72–95	0.002

Residues are expressed as parent etoxazole μg equivalents/ml milk

[a] Averaged for the total 24 hours collection; values below LOQ were considered equal to LOQ.

Parent etoxazole accounted for a total of 63-65% dose in the faeces and gastro-intestinal tract. The major urinary metabolite in the *tert*-butylphenyl radiolabel accounted for 1.4% dose and was identified as Metabolite 1 by mass spectrometry. This metabolite also accounted for 11.7% of the radioactive residue in the liver and 81% of the radioactive residue in the kidney. Metabolite 1 co-chromatographed with a major rat urine metabolite by reversed phase HPLC and normal phase TLC. The major urinary metabolites in the difluorophenyl radiolabel corresponded to R-11 (0.5% dose) and R-10 (0.8% dose). Table 4 presents a summary of residues in liver and kidney.

Table 4: Distribution of metabolites in goat liver and kidney

	Liver				Kidney	
	^{14}C -*tert*-butylphenyl		^{14}C –difluorophenyl		^{14}C -*tert*-butylphenyl	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
TRR	0.230		0.063		0.938	
Extracted ^{14}C[a]	0.198	86.3	0.030	48.2	0.929	99.0
Etoxazole	0.009	3.8	0.002	2.8	-	
Metabolite 1	0.027	11.7	nd	-	0.760	81.0
R-20	0.026	11.5	nd	-	-	-
Metabolite 3 (tBLi17)	0.033	14.5[b]	nd	-	-	-
Metabolite 4 (dFPLi3)	ND	-	0.021	32.8[c]	-	-
Unidentified	0.019	8.2	na	-	0.042	4.5
Base Treatment	0.019	8.2	0.025	39.4[d]	na	-
Unextracted	0.012	5.4	0.008	12.4	0.009	1.0

na Not applicable

nd Not observable with the radiolabelled form

[a] Sum of solvent and protease extracts for liver; solvent alone for kidney

[b] Unstable component which degraded to Metabolite 1 on storage at <-15 °C

[c] Water-soluble at pH 2, 7, and 12

[d] Contains a number of components

The results of this study indicate very low potential for transfer of residues of etoxazole and/or its metabolites to milk, meat or meat by-products in ruminants after dietary exposure to etoxazole. The proposed metabolic pathway is shown in Figure 3.

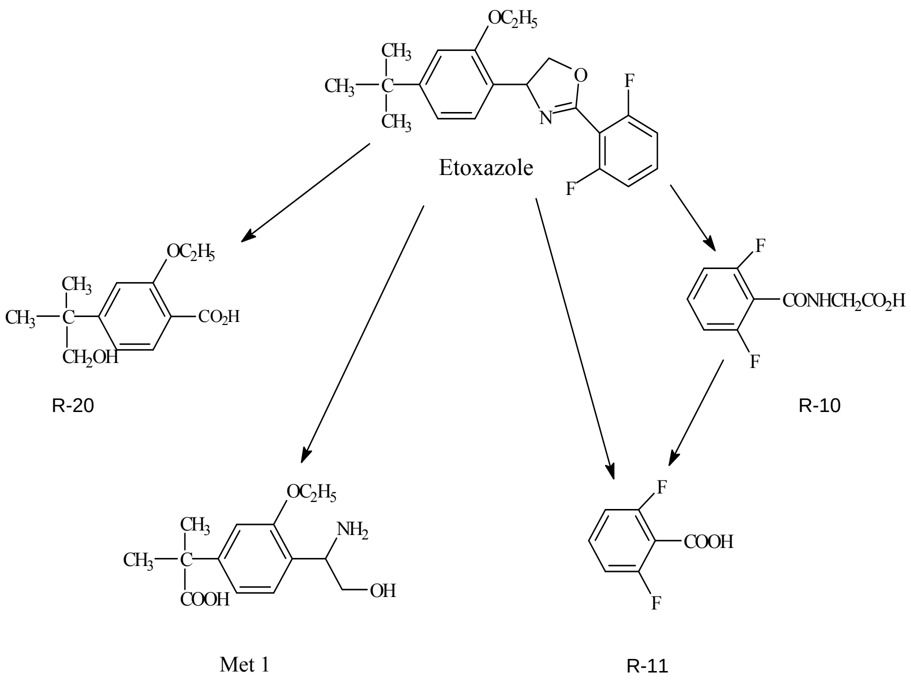


Figure 3 Proposed Metabolic Pathway of Etoxazole in Lactating Goats

Laying hen

The metabolic fate of etoxazole in laying hens has been studied using test materials separately labelled with ^{14}C in the difluorophenyl and the *tert*-butylphenyl rings (Figure 2). Each radiolabelled test material was administered orally to White Leghorn laying hens twice daily for 4½ consecutive days. The average dietary dose was equivalent to 12 ppm for the [*tert*-butylphenyl-^{14}C] etoxazole, and 11 ppm for the [difluorophenyl-^{14}C] etoxazole. Eggs were collected twice daily prior to dosing. Excreta were collected on Day 4 and pooled from all groups. The hens were sacrificed approximately 4 hours after the last dosing, and tissue samples were collected for analysis.

The total radioactive residues (TRR) increased gradually with time to a maximum of 0.23-0.27 mg/kg in egg yolks and 0.008–0.013 mg/kg in egg whites on the last day of dosing. The total residue levels in tissues, determined by combustion analysis, were similar in the two radiolabels, and varied from a high of 2.4 mg/kg in liver to a low of 0.015 mg/kg in breast muscle. The excreta samples were not analysed since sufficient residue was present in the egg and tissue samples.

The majority (84.4–99.8%) of the radioactive residue in egg yolk, egg white, abdominal and skin fat, thigh muscle, breast muscle and liver were extracted with organic (hexane and acetonitrile) and aqueous (water and methanol) solvents. The bound residue in the post-extraction solids (PES) of liver was approximately 0.29 mg/kg. The amounts of unextracted residues in all other samples were less than 0.03 mg/kg. The distribution of the radioactive residues is summarised in Table 5.

Table 5 Distribution of TRR in eggs and tissues

Sample	[^{14}C -*tert*-butylphenyl]etoxazole mg/kg, (% TRR)			[^{14}C -difluorophenyl]etoxazole mg/kg, (% TRR)		
	Extractable	PES	Total	Extractable	PES	Total
Egg yolk (day 4+5)	0.157 (84.4)	0.029 (15.6)	0.186	0.157 (87.5)	0.022 (12.5)	0.179
Egg white (day 4+5)	a	a	0.008	0.011 (94.8)	0.001 (5.2)	0.011
Fat (abdominal + skin)	0.611 (99.8)	0.001 (0.2)	0.612	0.750 (99.8)	0.002 (0.2)	0.751
Thigh muscle	0.077 (97.9)	0.002 (2.1)	0.078	0.089 (98.1)	0.002 (1.9)	0.091

Sample	[^{14}C -*tert*-butylphenyl]etoxazole mg/kg, (% TRR)			[^{14}C -difluorophenyl]etoxazole mg/kg, (% TRR)		
	Extractable	PES	Total	Extractable	PES	Total
Breast muscle	0.014 (93.4)	0.001 (6.6)	0.015	0.015 (92.5)	0.001 (7.5)	0.016
Liver	1.64 (85.2)	0.285 (14.8)	1.93	2.11 (88.0)	0.287 (12.0)	2.40

[a] not extracted due to low residue level.

Parent etoxazole was the major ^{14}C residue in egg yolk, abdominal and skin fat, thigh muscle, and breast muscle. Its concentration in isolated egg yolk was approximately 0.1 mg/kg. However, the whole egg, which had a yolk to white ratio of 31:69 w/w, contained etoxazole at a much lower concentration (< 0.036 mg/kg). Etoxazole accounted for only about 3% of TRR in liver (0.057–0.078 mg/kg), but 90–92% of TRR in the composite fat (0.55–0.69 mg/kg). The distribution of ^{14}C residue components in egg and tissue samples is presented in Table 6.

Table 6 Distribution of metabolites in egg and tissue samples

Component	Egg yolk		Egg white		Abdominal & skin fat		Thigh muscle		Breast muscle		Liver	
	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR	mg/kg	%TRR
[^{14}C -*tert*-butylphenyl-]etoxazole												
Etoxazole	0.104	55.9	A		0.550	89.9	0.065	82.7	0.008	51.7	0.057	3.0
R-2	0.007	3.6	-		0.023	3.8	0.004	5.2	0.001	8.6	0.020	1.0
R-7	0.002	1.0	-		0.010	1.7	-	-	-	-	0.026	1.4
R-7-COOH	-	-	-		-	-	-	-	-	-	0.030	1.5
R-8	-	-	-		-	-	-	-	-	-	0.014	0.7
R-13	0.007	3.7	-		0.013	2.1	0.003	3.7	-	-	-	-
R-16	0.002	0.9	-		0.006	1.0	0.004	4.9	0.003	18.6	1.13	58.6
R-24	-	-	-		-	-	-	-	-	-	0.031	1.6
Others [b]	0.036	19.3	-		0.008	1.3	0.001	1.3	0.003	14.6	0.336	17.3
Unextracted	0.029	15.6	-		0.001	0.2	0.002	2.1	0.001	6.6	0.285	14.8
Total	0.186	100	-		0.612	100	0.078	100	0.015	100	1.93	100
[^{14}C -difluorophenyl-]etoxazole												
Etoxazole	0.111	62.0	0.003	22.5	0.692	92.1	0.078	85.5	0.008	50.7	0.078	3.2
R-2	0.008	4.5	0.003	27.0	0.028	3.8	0.004	4.8	0.002	9.6	0.028	1.2
R-7	0.002	1.1	0.003	24.4	0.003	0.4	-	-	-	-	0.028	1.1
R-7-COOH	-	-	-	-	-	-	-	-	-	-	0.025	1.0
R-13	0.007	3.9	-	-	0.014	1.8	0.002	1.8	< 0.001	2.2	-	-
R-16	0.002	1.3	-	-	0.007	0.9	0.005	5.1	0.003	19.1	1.59	66.2
Others [b]	0.027	14.7	0.003	20.9	0.005	0.8	0.001	0.8	0.002	0.8	0.366	15.2
Unextracted	0.022	12.5	0.001	5.2	0.002	0.2	0.002	1.9	0.001	7.5	0.287	12.0
Total	0.179	100	0.011	100	0.751	100	0.091	100	0.016	100	2.40	100

[a] not extracted due to a low residue level.

[b] total unidentified extractable compounds, each < 0.05 mg/kg.

Most of ^{14}C residue in liver was metabolite R-16, a *tert*-butyl methyl group oxidation product of etoxazole. R-16 was also observed in minor quantities in all tissues except egg white. Another metabolite, R-2, in which one of the *tert*-butyl methyl groups was oxidized to a CH_2OH group, was present in trace amounts (< 0.03 mg/kg) in eggs and tissues. Metabolite R-7, a product with opened dihydrooxazole ring, was also present in small quantities in a number of tissues. The analogous dihydrooxazole ring-opened product of R-16, designated as R-7-CO_2H, was observed only in liver. Another minor metabolite, R-13, which was formed by reduction of the dihydrooxazole ring of etoxazole to an oxazole ring, was observed in egg yolk, fat and muscle samples. Other minor metabolites observed in liver extracts were R-8 and R-24 (*tert*-butylphenyl label only).

The liver contained unextracted ^{14}C residues in both radiolabel treatments (0.29 mg/kg or 12–15% of TRR). The majority (about 80%) was protein-bound and could be solubilised by treatment with protease. Minor amounts of R-16, R-10 and R-11 were released from the bound residues of the difluorophenyl label, and R-16, R-8, R-20 and R-24 from those of the *tert*-butylphenyl label.

Etoxazole was extensively metabolized by the laying hen. About ten metabolites were identified from eggs and various tissues. The major metabolic processes were oxidation of the *tert*-butyl moiety, and hydrolysis of the dihydrooxazole ring. Based on the findings, the proposed metabolic pathway of etoxazole in hens is shown in Figure 4. The metabolic routes in hen were similar to those observed in rat and goat.

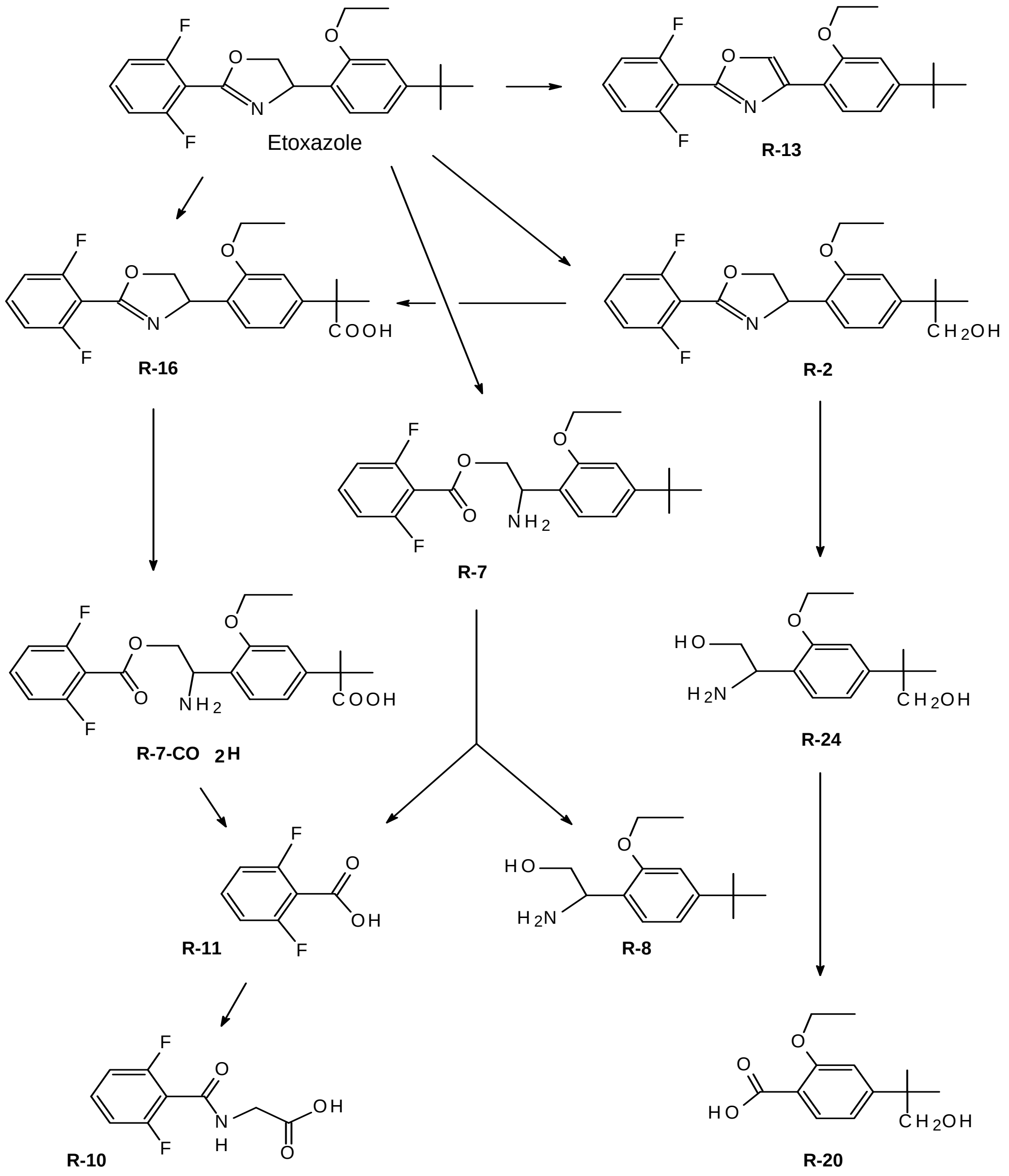


Figure 4 Proposed metabolic pathway for etoxazole in hens

Summary of animal metabolism

Metabolism of ^{14}C-etoxazole labelled in the *tert*-butylphenyl or difluorophenyl rings has been studied in lactating goats and laying hens. In both studies, etoxazole was metabolized to several metabolites. The metabolic routes are similar. The major metabolic processes were oxidation of the *tert*-butyl moiety, and the hydrolysis of the hydrooxazole ring. Ruminant and poultry metabolism studies demonstrated that transfer of administered ^{14}C residues to milk, eggs, and tissues is low. No information was available on metabolism and environmental persistence of the individual enantiomers. It is not clear if one enantiomer is more biologically active than the other.

Plant metabolism

Plant metabolism studies were performed on apples, oranges and eggplants using the *tert*-butylphenyl- and oxazole-U-^{14}C-labeled etoxazole, on cotton using the *tert*-butylphenyl- and difluorophenyl-U-^{14}C -labelled etoxazole.

Apples

The metabolism of etoxazole was studied in container grown apple trees using [^{14}C-*tert*-butylphenyl] and [^{14}C-oxazole] etoxazole (Figure 1). Each radiolabelled form, as a suspension concentrate (SC), was applied separately to apple trees maintained outdoors in the UK. A single application was made about 4 weeks before harvest at a nominal rate of 0.15 kg ai/ha. Samples of fruit and leaves were taken for analysis at Day 0, 14 or 15, 21 and 30. To provide information on the translocation of radiolabelled material, selected branches bearing fruit were covered with polyethylene during the application.

Concentrations of radioactivity (total radioactive residues, TRR) in fruit declined from 0.46 mg/kg immediately after application with [^{14}C-*tert*-butylphenyl] to 0.13 mg/kg at harvest. For apples treated with [^{14}C-oxazole] etoxazole, the TRR declined from 0.18 mg/kg immediately after application to 0.09 mg/kg at harvest. Similarly, the TRR in leaves declined from 14.9 to 2.5 mg/kg and 11.8 to 0.7 mg/kg from treatment with the phenyl- and oxazole- labelled etoxazole, respectively. Concentrations of radioactivity at harvest, in fruit of plants in which the fruits were covered during application were 0.010 mg/kg (*tert*-butylphenyl-labelled) and 0.004 mg/kg (oxazole-labelled), indicating that translocation was minimal. The results are summarised in Table 7.

Table 7 Total radioactive residues in apple fruit and leaves following application of ^{14}C-*tert*-butylphenyl] etoxazole or [^{14}C-oxazole] etoxazole

Fraction	Sampling time (days)							
	[^{14}C-*tert*-butylphenyl]etoxazole				[^{14}C-oxazole]etoxazole			
	0	14	21	30	0	15	21	30
Fruit [%TRR (mg/kg)]								
Surface wash	99.4 (0.453)	68.8 (0.023)	66.1 (0.044)	59.5 (0.079)	98.8 (0.176)	70.4 (0.109)	73.9 (0.069)	61.1 (0.054)
Peel extracts	0.5 (0.002)	10.6 (0.004)	12.6 (0.008)	19.7 (0.026)	0.9 (0.002)	13.5 (0.021)	6.8 (0.006)	14.7 (0.013)
Flesh extracts	< 0.2 (< 0.001)	2.6 (0.001)	< 5.1 (< 0.003)	4.8 (0.006)	< 1.7 (< 0.003)	1.4 (0.002)	< 5.5 (< 0.005)	9.9 (0.009)
Total extracts	0.5 (0.002)	13.2 (0.004)	12.6 (0.008)	22.5 (0.030)	0.9 (0.002)	14.9 (0.023)	6.8 (0.006)	15.5 (0.014)
Peel residue	0.1 (< 0.001)	19.0 (0.006)	19.9 (0.013)	21.7 (0.029)	0.4 (0.001)	13.2 (0.020)	18.5 (0.017)	21.9 (0.019)
Unextracted flesh residue	< 0.1 (< 0.001)	1.6 (0.001)	1.5 (0.001)	1.4 (0.002)	< 1.0 (< 0.002)	1.5 (0.002)	0.9 (0.001)	1.6 (0.001)
Total unextracted residue	0.2 (< 0.001)	20.1 (0.007)	21.4 (0.014)	23.1 (0.030)	0.4 (0.001)	14.7 (0.023)	19.4 (0.018)	23.5 (0.021)
Total fruit	(0.456)	(0.034)	(0.066)	(0.132)	(0.178)	(0.155)	(0.093)	(0.088)
Leaves [%TRR (mg/kg)]								
Surface wash	99.8 (14.91)	86.8 (2.267)	82.4 (1.819)	64.3 (1.622)	99.1 (11.679)	80.4 (2.320)	83.7 (2.777)	55.7 (0.382)
Leaf extract	0.3	5.7	6.0	19.5	0.9	10.8	5.8	26.2

Fraction	Sampling time (days)							
	[^{14}C-*tert*-butylphenyl]etoxazole				[^{14}C-oxazole]etoxazole			
	0	14	21	30	0	15	21	30
	(0.045)	(0.149)	(0.132)	(0.492)	(0.106)	(0.312)	(0.192)	(0.179)
Leaf residue	0.1 (0.015)	7.5 (0.196)	11.6 (0.256)	16.2 (0.409)	0.1 (0.012)	8.8 (0.254)	10.6 (0.351)	18.1 (0.124)
Total leaf	(14.94)	(2.612)	(2.208)	(2.522)	(11.79)	(2.886)	(3.318)	(0.685)

Results expressed as % fruit and leaf radioactivity (ppm, as etoxazole, in parentheses)

Results from the use of either radiolabelled forms of etoxazole showed that the major radioactive component was the parent compound and only very small amounts of metabolites, common to both forms, were found. The mean concentrations of radioactivity in fruit and leaves immediately after application were 0.32 mg/kg and 13 mg/kg, respectively. At harvest, the mean concentration of radioactivity in fruits and leaves were 0.11 mg/kg and 1.6 mg/kg, respectively. At all sampling times, the major radioactive residues were located in surface washes of fruit and leaves, indicating that penetration of radioactivity into the fruit or leaves was minimal (< 9% of the radioactivity in the fruit at harvest occurred in the flesh).

Characterisation of the radioactivity in fruit and leaves indicated that parent etoxazole was the only component that exceeded 10% of the TRR at all sampling times. In fruit, etoxazole accounted for 94% of the radioactivity immediately after application and 42% at harvest. In leaves, etoxazole accounted for 99% of the radioactivity immediately after application and 30% at harvest. Table 8 summarises distribution of radioactive components in fruit and leaves at harvest.

Table 8 Summary of distribution of radioactivity in apples following treatment with [^{14}C-*tert*-butylphenyl] etoxazole or [^{14}C-oxazole] etoxazole

	Fruit		Leaves	
	mg/kg	% of TRR	mg/kg	% of TRR
Total Radioactive Residue (TRR)	0.11	-	1.604	-
Extracted Radioactivity [a]	0.089	79.3	1.338	82.9
Parent Etoxazole	0.047	41.7	0.556	30.3
R-3	0.004	4.0	0.048	3.2
R-7	0.010	8.2	0.087	6.3
R-11[b]	0.001	0.9	0.002	0.3
R-13	0.001	1.1	0.001[e]	0.1
R-8[c]	-	-	0.025	1.0
R-15[d]	< 0.001	0.9	-	-
Maximum unidentified	0.004	3.2	0.117	8.5
Unextracted Radioactivity	0.007	6.2	0.130	6.4

[a] Sum of surface washes and total extracts

[b] oxazole label; present in surface washes of fruit at 15 days and in leaf extracts

[c] phenyl label; only detected on TLC

[d] phenyl label, only present at 14 days

[e] oxazole label only

Metabolites accounting for 0.001–0.010 mg/kg (0.4–8.2% fruit radioactivity) were characterised by co-chromatography (HPLC and TLC) and included R-3, R-7, R-13, R-11 (oxazole label), R-12 (*tert*-butylphenyl label), and R-15 (*tert*-butylphenyl label). R-3 and R-7 were further characterised by mass spectrometry. Treatment of peel residues with alkali released components corresponding to R-11 (oxazole label) and R-12 (*tert*-butylphenyl label) implying that these components existed in the peel residue as conjugates. Concentration of radioactivity in fruit which had been covered during application was 0.007 ppm indicating that translocation of radioactivity was limited.

The stability of metabolites in apple fruit samples during freezer storage was determined by reanalysis and comparison of the radioresidue profiles to chromatographic profiles generated earlier in the study. For apple fruit labelled in both the *tert*-butylphenyl and oxazole rings, the amounts of radioactivity extracted and the percentage of the major metabolites identified was similar after 8-9 months of storage.

Oranges

The metabolism of etoxazole was studied in orange trees using [^{14}C-*tert*-butylphenyl] and [^{14}C-oxazole] etoxazole (Figure 1). Orange trees maintained outdoors in California were treated separately with SC formulations of each of these test materials at about 90 days before harvest at a nominal rate of 0.4 kg ai/ha. Samples of fruit and leaves were taken immediately after application and at 21, 30, 60, and 90 days after application. Oranges were peeled and the peel and fruit analysed separately. To provide information on the translocation of radiolabelled material, selected branches bearing fruit were covered during the application.

Concentrations of radioactivity (total radioactive residues, TRR) in orange fruit declined from 0.25 mg/kg immediately after application with [^{14}C-*tert*-butylphenyl] to 0.11 mg/kg at harvest. For oranges treated with [^{14}C-oxazole] etoxazole, the TRR declined from 0.27 mg/kg immediately after application to 0.07 mg/kg at harvest (90 days later). Similarly, the TRR in leaves declined from 9.3 to 0.81 mg/kg and 17.9 to 2.7 mg/kg from treatment with the phenyl- and oxazole- labelled etoxazole, respectively. The results are summarised in Table 9.

Table 9 Total radioactive residues in orange fruit and leaves following application of [^{14}C-*tert*-butylphenyl] etoxazole or [^{14}C-oxazole] etoxazole

Fraction	Sampling time (days)									
	[^{14}C-*tert*-butylphenyl]etoxazole					[^{14}C-oxazole]etoxazole				
	0^{a}	21	30	60	90	0	21	30	60	90
Fruit [%TRR (mg/kg)]										
Surface wash	99.1 (0.245)	86.2 (0.131	87.0 (0.139)	74.7 (0.134)	69.0 (0.075)	98.5 (0.267)	55.6 (0.129)	66.0 (0.092)	47.9 (0.072)	37.5 (0.025)
Peel extracts	0.9 (0.002)	9.7 (0.015)	9.4 (0.015)	17.0 (0.030)	20.4 (0.022)	1.5 (0.004)	32.3 (0.075)	24.0 (0.033)	35.6 (0.054)	35.2 (0.023)
Flesh extracts	< 0.4 (< 0.001)	0.4 (0.001)	0.8 (0.001)	0.7 (0.001)	2.2 (0.002)	< 0.3 (< 0.001)	3.5 (0.008)	3.1 (0.004)	0.9 (0.001)	9.0 (0.006)
Total extracts	0.9 (0.002)	10.1 (0.015)	10.2 (0.016)	17.7 (0.032)	22.6 (0.024)	1.5 (0.004)	35.8 (0.083)	27.1 (0.038)	36.5 (0.055)	44.2 (0.029)
Unextracted peel residue	0.1 (< 0.001)	3.6 (0.005)	2.8 (0.004)	7.5 (0.013)	7.7 (0.008)	0.1 (< 0.001)	7.4 (0.017)	6.2 (0.009)	15.8 (0.024)	14.8 (0.010)
Unextracted flesh residue	< 0.3 (< 0.001)	0.3 (< 0.001)	< 0.1 (< 0.001)	0.3 (0.001)	0.7 (0.001)	0.2 (0.001)	1.3 (0.003)	0.8 (0.001)	< 0.2 (< 0.001	3.6 (0.002)
Total unextractable residue	0.3 (< 0.001)	3.7 (0.006)	2.8 (0.004)	7.8 (0.014)	8.4 (0.009)	0.2 (0.001)	8.7 (0.020)	6.9 (0.010)	15.8 (0.024)	18.4 (0.012)
Total fruit	(0.247)	(0.152)	(0.160)	(0.179)	(0.108)	(0.271)	(0.232)	(0.139)	(0.151)	(0.066)
Leaves [%TRR (mg/kg)]										
Surface wash	99.4 (9.293)	85.9 (1.630)	79.5 (1.167)	nd ^{b}	77.9 (0.629)	99.6 (17.813)	77.2 (2.460)	60.3 (1.975)	nd ^{b}	64.4 (1.761)
Leaf extract	0.5 (0.047)	9.2 (0.175)	11.7 (0.172)	90.6 (0.009)	11.1 (0.090)	0.4 (0.072)	15.5 (0.494)	24.7 (0.809)	81.1 (0.012)	16.3 (0.446)
Leaf residue	0.2 (0.019)	5.0 (0.095)	8.9 (0.131)	21.3 (0.002)	11.1 (0.090)	0.1 (0.018)	7.4 (0.236)	15.1 (0.495)	18.9 (0.003)	19.4 (0.531)
Total leaf	(9.349)	(1.897)	(1.468)	(0.010	(0.807	(17.885)	(3.187	(3.276	(0.015)	(2.735

Fraction	Sampling time (days)									
	[^{14}C-*tert*-butylphenyl]etoxazole					[^{14}C-oxazole]etoxazole				
	0[a]	21	30	60	90	0	21	30	60	90
				)	)		)	)		)

Results expressed as % fruit and leaf radioactivity (ppm as etoxazole in parentheses)

nd: not detected

[a] Sample was taken at 2 hours after application

[b] Values for samples taken at 60 days were considered anomalous and samples were not analysed further

Results from the use of either radiolabelled forms of etoxazole showed that the major radioactive component was the parent compound and only very small amounts of metabolites, common to both forms, were found. The mean concentrations of radioactivity in fruit and leaves immediately after application were 0.26 mg/kg and 14 mg/kg, respectively. At harvest, the mean concentration of radioactivity in fruits and leaves were 0.09 mg/kg and 1.8 mg/kg, respectively. At all sampling times, the radioactive residues in fruit and leaves were found in surface washes. In the fruit itself, residues concentrated in the peel, with pulp extracts accounting for 2.2% fruit radioactivity (0.002 mg/kg) in the phenyl label and 9.0% (0.006 mg/kg) in oxazole label.

Concentrations of radioactivity in fruit and leaves that had been covered during application were 0.007 mg/kg and 0.06 mg/kg respectively at harvest indicating that translocation of radioactivity was minimal.

Characterisation of the radioactivity in fruit and leaves indicated that parent etoxazole was the only component that exceeded 10% of the TRR at all sampling times. Etoxazole and metabolites R-3, R-7, R-13, R-14, and R-15 were identified by co-chromatography with authentic reference standards using both reversed phase HPLC (with ion pairing reagents) and normal phase TLC.

The unextracted residue from the oxazole label was subjected to base hydrolysis, acidified and partitioned into ethyl acetate. The major component in the ethyl acetate extract co-chromatographed with R-11 with normal phase TLC and accounted for 0.004 mg/kg at harvest. R-11 formed after base hydrolysis was identified by mass spectrometry. Table 10 summarises that distribution of radioactive components in orange fruit and leaves at harvest.

Table 10: Summary of distribution of radioactivity in oranges at harvest, following treatment with [^{14}C-*tert*-butylphenyl] etoxazole or [^{14}C-oxazole] etoxazole

	Fruit		Peel		Leaves	
	mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR
Total radioactive residue	0.087	-	0.023	-	1.77	-
Extracted radioactivity [a]	0.077	86.7	0.023	27.8	1.46	84.9
Parent, etoxazole	0.044	47.7	0.004	4.8	0.83	51.7
R-3	0.003	2.8	0.001	1.0	0.03	1.6
R-7	0.003	3.1	0.003	3.1	0.02	0.6
R-11[b]	< 0.001	0.6	ND	-	0.07	2.6
R-13	0.001	1.4	< 0.001	0.4	0.03	1.3
R-14	0.003	2.4	0.001	0.9	0.06	3.2
R-15[c]	0.004	3.4	0.003	2.6	0.02	2.2
Maximum unidentified [d]	0.008	11.4	0.006	9.6	0.39	14.2
Unextracted radioactivity	0.011	13.4	0.009	11.3	0.31	15.3

[a] Sum of surface washes and peel extracts. Pulp extracts accounted for 2.2% fruit radioactivity (0.002 mg/kg) in phenyl label and 9.0% (0.006 mg/kg) in oxazole label

[b] oxazole label

[c] phenyl label

[d] polar fraction from oxazole radiolabel excluding value for R-11. No component accounted for > 10% TRR.

The stability of metabolites in oranges during freezer storage was determined by reanalysis and comparison of the radioresidue profiles to chromatographic profiles generated earlier in the study. For oranges treated with both [^{14}C-*tert*-butylphenyl] etoxazole and [^{14}C-oxazole] etoxazole, the amounts of radioactivity extracted and the percentage of the major metabolites identified was similar after five months of freezer storage.

Eggplants

The metabolism of etoxazole has been studied in eggplants using [^{14}C-*tert*-butylphenyl] and [^{14}C-oxazole] etoxazole (Figure 1). Eggplants maintained under controlled conditions in a plant growth room were treated separately with formulations of each of these test materials at about 4 weeks before harvest at a nominal rate of 0.2 kg ai/ha. Samples of fruit were taken immediately after application at 1 day, and 2 and 4 weeks after application. Samples of leaves were taken immediately after application at 1 day and 4 weeks after application. To provide information on the translocation of radiolabelled material, fruit of selected plants was covered during the application so that only the leaves of these plants were treated.

Concentration of radioactivity (total radioactive residues, TRR) in eggplant fruit declined from 0.161–0.203 mg/kg immediately after application to 0.096–0.195 mg/kg at harvest (nominally 4 weeks after application). At harvest, concentration of radioactivity in leaves was 4.4–6.5 mg/kg. The results are summarised in Table 11.

Table 11 Total radioactive residues in eggplant fruit and leaves following application of [^{14}C-*tert*-butylphenyl] etoxazole or [^{14}C-oxazole] etoxazole

Fraction	Sampling time (days)					
	[^{14}C-*tert*-butylphenyl]etoxazole			[^{14}C-oxazole]etoxazole		
	0[a]	14	27	0	14	27
Fruit [%TRR (mg/kg)]						
Surface wash	95.7 (0.194)	83.7 (0.168)	70.2 (0.067)	87.4 (0.141)	64.4 (0.092)	68.3 (0.133)
Peel extracts	3.4 (0.007)	10.8 (0.022)	14.9 (0.014)	4.4 (0.007)	26.3 (0.038)	20.6 (0.040)
Flesh extracts	0.6 (0.001)	1.5 (0.003)	6.1 (0.006)	6.6 (0.011)	2.1 (0.003)	3.0 (0.006)
Total extracts	3.5 (0.007)	12.3 (0.025)	20.7 (0.020)	11.0 (0.018)	28.4 (0.041)	23.5 (0.046)
Unextracted peel residue	0.7 (0.001)	3.6 (0.007)	5.9 (0.006)	1.1 (0.002)	6.6 (0.009)	8.0 (0.016)
Unextracted flesh residue	0.2 (< 0.001)	0.4 (< 0.001)	2.9 (0.003)	0.7 (0.001)	0.6 (< 0.001)	0.3 (< 0.001)
Total unextracted residue	0.8 (0.002)	4.0 (0.008)	8.8 (0.008)	1.7 (0.003)	7.2 (0.010)	8.2 (0.016)
Total fruit	(0.203)	(0.201)	(0.096)	(0.161)	(0.143)	(0.195)
Leaves [%TRR (mg/kg)]						
Surface wash			88.1 (3.911)			82.3 (5.322)
Leaf extract			8.9 (0.395)			12.9 (0.834)
Unextracted leaf residue			3.0 (0.133)			4.7 (0.304)
Total leaf			(4.439)			(6.467)

Results expressed as % fruit and leaf radioactivity (ppm in parentheses)

[a] 0 days is a mean of samples at 2 hours and 24 hours after application

The mean concentration of radioactivity in fruit and leaves after application were 0.18 mg/kg and 17 mg/kg, respectively. At harvest, the mean concentration of radioactivity in fruit and leaves had declined to 0.15 mg/kg and 6 mg/kg, respectively. At all sampling times, the major radioactive residues were located in surface washes of fruit and leaves, indicating minimal penetration of radioactivity into the fruit or leaves, i.e., < 10% of the radioactivity in the fruit at harvest occurred in the flesh.

Concentrations of radioactivity in fruit which had been covered during application to leaves were < 0.001–0.002 mg/kg, indicating that translocation of radioactivity was minimal.

Characterisation of the radioactivity in fruit and leaves indicated that parent etoxazole was the only component that exceeded 10% of the TRR at all sampling times. Metabolites accounting for 0.001–0.004 mg/kg (0.3–1.8% fruit radioactivity) were characterised by co-chromatography with authentic reference standards using both reverse phase HPLC (with ion pairing reagents) and normal phase TLC and included R-2, R-3, R-7, R-13 (both radiolabels), R-11 (oxazole radiolabel), and R-12 (*tert*-butylphenyl radiolabel). Table 12 summarises distribution of radioactive components in fruit and leaves at harvest.

Table 12 Summary of distribution of radioactivity in eggplants at harvest, following treatment with [^{14}C-*tert*-butylphenyl] etoxazole and [^{14}C-oxazole] etoxazole

	[*tert*-butylphenyl-^{14}C] Etoxazole		[oxazole-^{14}C] Etoxazole	
	mg/kg	% TRR	mg/kg	% TRR
Fruit				
Total radioactive residue	0.096	-	0.195	-
Extractable Activity	0.081	85.1	0.179	91.9
Parent Etoxazole	0.066	68.5	0.144	74.0
R-2	< 0.002	1.10	0.001	0.8
R-3	0.001	0.60	0.002	1.1
R-7	0.001	1.4	0.002	1.1
R-13	0.001	1.4	0.001	0.7
R-12	ND [b]	-	ND	-
R-11	ND	-	< 0.001	0.4
Maximum unidentified	0.002	2.5	0.004[c]	2.2
Unextracted Radioactivity	0.008	8.8	0.016	8.3
Leaves [a]				
Total radioactive residue	4.44	-	6.47	-
Extractable Activity	4.31	97.0	6.16	95.2
Parent Etoxazole	3.32	74.7	4.54	70.2
R-2	0.071	1.6	0.084	1.3
R-3	0.044	1.0	0.097	1.5
R-7	0.057	1.3	0.078	1.2
R-13	0.053	1.2	0.045	0.7
R-12	ND	-	ND	-
R-11	ND	-	0.007	0.1
Maximum unidentified	0.142	3.2	0.239	3.7
Unextracted Radioactivity	0.133	3.0	0.304	4.7

Totals may not sum to 100% due to rounding. ND = Not Detected.

[a] Values taken from whole plant application.

[b] Detected only as a transient component at 14 days.

[c] Polar fraction from the oxazole radiolabel (excluding R-11).

The stability of metabolites in eggplant fruit samples during freezer storage was determined by reanalysis and comparison of the radioresidue profiles to chromatographic profiles generated earlier in the study. For fruit labelled in both the *tert*-butylphenyl and oxazole rings, the amounts of radioactivity extracted and the percentage of the major metabolites identified was similar after 5 months of storage.

Cotton

The metabolism and distribution of [^{14}C] etoxazole, labelled in the difluorophenyl-ring and *tert*-butylphenyl-ring positions (Figure 2), was studied in cotton plants. Two foliar treatments of [^{14}C] etoxazole were applied to cotton plants at a rate of approximately 0.1 kg ai/ha (0.09 lb ai/A) at 42 and

21 days prior to harvest (21 day PHI). Cottonseed (ginned from open cotton bolls) and gin trash were harvested for radioresidue analysis.

Combustion analysis of whole cottonseed samples gave total radioactive residues (TRR) of 0.031 mg/kg and 0.020 mg/kg for the [difluorophenyl-^{14}C] and [*tert*-butylphenyl-^{14}C] etoxazole treated plant samples, respectively. Surface residues were rinsed off the seeds with methanol and the seeds extracted to yield hexane, acetonitrile, aqueous and post extraction solid (PES) fractions. Metabolites in the fractions containing the greatest activity (methanol rinse and acetonitrile fractions) were quantitated by TLC with radiographic analysis. Parent etoxazole and the metabolites DFB and R-3 were the major residues detected (all present at < 0.01 mg/kg). The distribution of etoxazole residues in treated cottonseed is presented in Table 13.

Table 13 Distribution of metabolites in cottonseed (Concentrations of ^{14}C are expressed as parent etoxazole.)

	[Difluorophenyl-^{14}C] Etoxazole		[*tert*-Butylphenyl-^{14}C] Etoxazole	
	% TRR	mg/kg	% TRR	mg/kg
TRR[a]		0.031		0.020
Extracted Activity [b]	76.6	0.024	78.2	0.016
Unextracted Activity (PES)	23.4	0.007	21.8	0.004
Parent Etoxazole	4.9	0.002	19.9	0.004
DFB	20.1	0.006	NA	NA
R-3	4.6	0.001	7.2	0.001
R-4	0	0	0	0
R-7	0	0	0	0
R-8	NA	NA	0	0
R-11	0.8	< 0.001	NA	NA
R-12	NA	NA	0	0
R-13	0	0	0	0
R-14/R-15	0.9	< 0.001	2.7	< 0.001
TRR Identified	31.3	0.010	29.8	0.006
Unknown Activity (TLC)	12.3	0.004	18.3	0.004
Hexane Soluble Activity	12.1	0.004	9.4	0.002
Aqueous Soluble Activity	17.8	0.006	16.1	0.003
TRR Characterised	42.2	0.015	43.8	0.009
TRR Identified/Characterised	73.5	0.025	73.6	0.015

Totals may not sum to 100% due to rounding. NA = Not Applicable.

[a] TRR = extracted and unextracted activity at first extraction step.

[b] Extracted activity is a sum of the four extracted fractions: methanol rinse, hexane, acetonitrile and aqueous. The methanol rinse and acetonitrile fractions were analysed by TLC to yield identified and characterised activity. The hexane and aqueous soluble fractions and PES were not analysed.

Cottonseed contained low amounts of activity, with TRR values of 0.031 and 0.020 mg/kg for difluorophenyl and *tert*-butylphenyl cottonseed, respectively. Therefore only limited analyses were performed to identify the most significant organosoluble metabolites – parent etoxazole and DFB. The total amount of the TRR identified in cottonseed was 31.3% and 29.8%, for the difluorophenyl and *tert*-butylphenyl labels, respectively. An additional 42.2% (difluorophenyl label) and 43.8% (*tert*-butylphenyl label) was characterised but not identified as either TLC unknowns or hexane soluble or aqueous soluble activity.

Combustion analysis of homogenized gin trash samples gave TRR values of 6.9 and 5.3 mg/kg for the [difluorophenyl-^{14}C] and [*tert*-butylphenyl-^{14}C] etoxazole treated plant samples, respectively. The majority of the radioactivity in gin trash was extracted (88.6% and 85.1%, respectively for [difluorophenyl-^{14}C] and [*tert*-butylphenyl-^{14}C] etoxazole gin trash) to yield hexane, acetonitrile and aqueous fractions. The hexane fraction was partitioned to yield hexane soluble and acetonitrile soluble radioactivity, while the acetonitrile fraction was analysed directly. The aqueous fraction was acid hydrolysed to break aglycones (conjugates) and the organosoluble radioactivity partitioned into ethyl acetate prior to analysis. The remaining aqueous fraction was neutralized with base and repartitioned with ethyl acetate to yield organosoluble and aqueous radioactivity prior to analysis. The unextracted residues in gin trash represented 11.5 and 14.9% of the TRR from [difluorophenyl-^{14}C] and [*tert*-butylphenyl-^{14}C] etoxazole gin trash, respectively.

The unextracted gin trash residues were characterised by several sequential procedures: cellulase digestion, lignin solubilisation, 2M HCl hydrolysis and 2M NaOH hydrolysis. Radioactivity released by the cellulase digestion and lignin solubilisation was partitioned into organosoluble and aqueous fractions. The organosoluble radioactivity released by the lignin solubilisation was analysed by TLC with radiographic analysis, while all other fractions were characterised by LSC. Treatment of the unextracted residues by sequential enzymatic and chemical procedures allowed an additional 10% of the TRR to be identified as distinct metabolites or characterised as associated activity (accessible cellulose, accessible lignin etc.). Metabolites were quantitated or confirmed using liquid chromatography/liquid scintillation counting (LC/LSC) and/or TLC with radiographic analysis. The percentages of the total radioactive residue (TRR) identified (HPLC and/or 2DTLC analyses) in the extracted and unextracted fractions from difluorophenyl and *tert*-butylphenyl treated gin trash are presented in Table 14. The major residues identified in gin trash were parent etoxazole (36–44% of TRR) and R-3 (16–18% of TRR).

Table 14 Distribution of metabolites in cotton gin trash (Concentrations of ^{14}C are expressed as parent etoxazole.)

	[Difluorophenyl-^{14}C] Label		[*tert*-Butylphenyl-^{14}C] label	
	% TRR	mg/kg	% TRR	mg/kg
TRR[a]	-	5.93	-	4.47
Extracted Activity [b]	88.6	5.25	85.1	3.81
Unextracted Activity (PES)	11.5	0.683	14.9	0.665
Parent Etoxazole	36.3	2.15	43.9	1.96
DFB	2.6	0.153	NA	NA
R-3	18.1	1.07	16.0	0.714
R-4	0.8	0.051	1.1	0.045
R-7	3.3	0.186	2.7	0.119
R-8	NA	NA	2.2	0.102
R-11	7.4	0.441	NA	NA
R-12	NA	NA	1.2	0.052
R-13	2.1	0.122	3.4	0.144
R-14	2.9	0.168	2.4	0.109
R-15	NA	NA	1.6	0.073
TRR identified	73.5	4.35	74.4	3.32
Unknown Activity (HPLC)[c]	15.1	0.900	12.4	0.557
Unknown Activity (TLC)[c]	2.5	0.145	3.4	0.144
PES Characterised	6.1	0.364	7.3	0.328
TRR Identified/Characterised	97.2	5.76	97.5	4.35

Totals may not sum to 100% due to rounding. NA = Not Applicable.

[a] TRR = extracted and unextracted activity at first extraction step.

[b] Extracted activity is a sum of the three extracted fractions: hexane, acetonitrile and aqueous. These fractions were analysed by HPLC and TLC to yield identified and characterised activity.

[c] Summation of approximately 40 separate areas of activity in the difluorophenyl label (highest 3% of TRR, 0.175 ppm) and approximately 42 separate areas of activity in the *tert*-butylphenyl label (highest 3% of TRR, 0.136 ppm).

[d] Activity characterised as cellulase organosoluble, cellulase aqueous soluble (accessible cellulose), lignin organosoluble, lignin aqueous soluble (accessible lignin), protein associated, hemicellulose associated, or insoluble lignin, cellulose.

The total amount of the TRR identified in the extractable and PES fractions from difluorophenyl and *tert*-butylphenyl gin trash was 73.5% and 74.4%. Parent etoxazole and R-3 were the most significant organosoluble metabolites (> 10% of the TRR). An additional 6.1–7.3% of the TRR was characterised as associated with various plant constituents (accessible cellulose, accessible lignin, protein-associated etc.). The balance of the TRR was spread across numerous unidentified TLC areas or HPLC peaks.

The stability of metabolites in cottonseed and gin trash samples under freezer storage was determined by re-extraction and comparison of the radioresidue profiles to chromatographic profiles generated earlier in the study. For both [difluorophenyl-^{14}C] and [*tert*-butylphenyl-^{14}C] etoxazole treated cottonseed and gin trash, the amounts of radioactivity extracted and the percentage of the major metabolites identified was similar after 12–13 months of freezer storage.

Summary of plant metabolism

Metabolism of ^{14}C-etoxazole labelled in the *tert*-butylphenyl, difluorophenyl, or oxazole rings has been studied in apples, oranges, eggplants, and cotton. In all plants investigated, etoxazole was metabolized to several metabolites. Even with exaggerated treatment, individual metabolites and parent were only found at very low concentrations. In all studies, the residue remained mainly in the surface and penetration into fruit was minimal and metabolic pathways were similar. Figure 5 presents the proposed metabolism pathway for etoxazole in plants. No information was available on metabolism and environmental persistence of the individual enantiomers. It is not clear if one enantiomer is more biologically active than the other.

Etoxazole

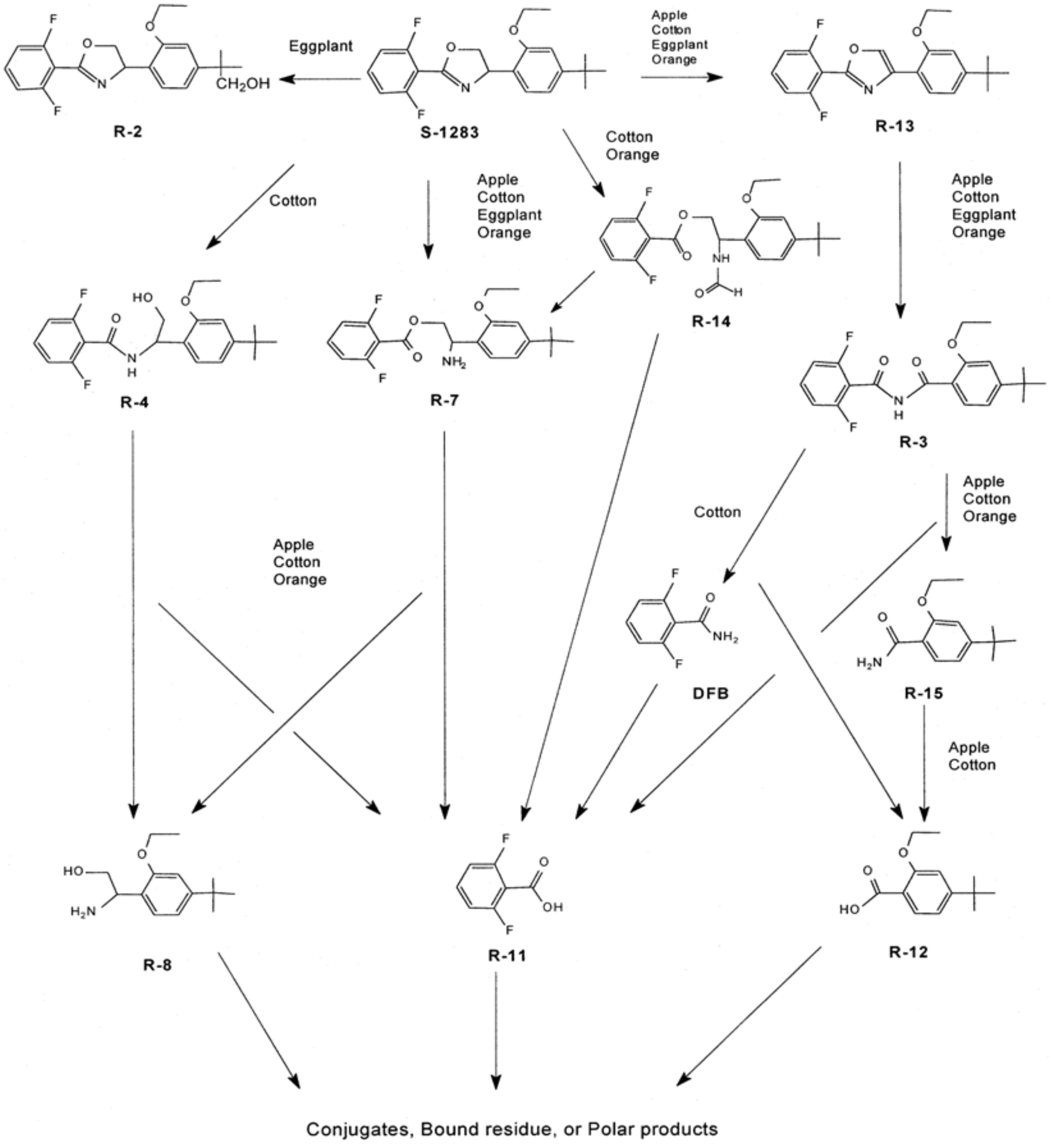


Figure 5 Proposed metabolic pathway of etoxazole in plants

Environmental fate in soil

The Meeting received information on aerobic and anaerobic degradation in soil, photolysis on soil surface, field dissipation and confined rotational crop study. Because etoxazole is intend for use as a foliar treatment, only aerobic degradation, hydrolytic degradation and the rotational crop study relevant to the current evaluations were reported below (FAO Manual 2009).

The fate and behaviour of etoxazole in soils were investigated using [^{14}C-*tert*-butylphenyl] and [^{14}C-difluorophenyl] labelled compounds.

Aerobic degradation

The metabolism and degradation of etoxazole has been studied in a sand loam soil under aerobic conditions at a nominal average temperature of 20 °C for 269 days. Two labelled forms of etoxazole,

[^{14}C-*tert*-butylphenyl] etoxazole and [^{14}C-difluorophenyl] etoxazole were used. These were applied separately to the soil at a nominal rate of 0.15 mg/kg which is equivalent to the use rate of 0.15 kg ai/ha. Soil samples were incubated (in darkness, in a temperature controlled room) before and after dose application. From the initiation of incubation to the termination of the study (269 days) the mean temperature was 20.4 ± sd 0.7 °C. The air flow through the system was approximately 60 mL/min. A single dish of soil for each radiolabelled form of ^{14}C-etoxazole was taken for analysis at 0, 1, 3, 7, 14, 30, 60, 90, 120, 180 and 269 days. The 0 day samples were taken immediately after application of the test compound.

Mean recoveries were 99.3 and 98.6% of applied radioactivity (AR) for soil treated with [^{14}C-*tert*-butylphenyl] etoxazole and [^{14}C-difluorophenyl] etoxazole, respectively. The recoveries of all samples at all sampling times were greater than 95% of AR.

Table 15 Extraction and recovery of radioactivity from aerobic soil after application of [^{14}C] etoxazole

Time (days)	^{14}C-label							
	[^{14}C-*tert*-butylphenyl]				[^{14}C-difluorophenyl]			
	Extracts	Cumulative volatiles	Residues	Total	Extracts	Cumulative volatiles	Residues	Total
0	97.91	na	1.83	99.74	99.54	na	2.05	101.59
1	94.39	nd	5.42	99.81	93.82	0.11	6.61	100.54
3	94.37	0.02	5.72	100.11	92.94	1.29	7.08	101.31
7	93.46	0.19	4.78	98.43	87.02	4.66	8.65	100.33
14	92.08	0.77	5.91	98.76	71.04	12.83	13.42	97.29
30	84.70	2.61	10.94	98.25	43.19	30.33	21.58	95.10
60	78.28	4.48	16.86	99.62	27.62	43.49	26.29	97.40
90	74.43	6.95	18.61	99.99	24.71	48.00	25.55	98.26
120	66.18	9.33	22.97	98.48	21.75	50.34	25.66	97.75
180	61.35	12.51	25.80	99.66	20.48	53.26	23.83	97.57
269	55.93	15.78	27.51	99.22	18.36	56.40	23.04	97.80

Results are expressed as % applied radioactivity

Totals of 15.8% and 56.4% of AR were evolved as volatile radioactivity during 269 days in soil treated with [^{14}C-*tert*-butylphenyl] etoxazole and [^{14}C-difluorophenyl] etoxazole, respectively. Most of the radioactivity was detected in the potassium hydroxide traps. The contents of these traps were identified as $^{14}CO_2$. The daily CO_2 production was identified as greatest during 14 to 22 days.

Table 16 Formation and decline of [^{14}C-*tert*-butylphenyl] etoxazole and its degradates in aerobic soil at 20 °C

Radioactive component	Time after application (days)										
	0	1	3	7	14	30	60	90	120	180	269
Etoxazole	95.7	81.9	74.5	60.1	40.6	12.6	4.3	2.2	2.0	1.5	0.9
R-8	*	0.6	1.6	7.7	20.1	38.4	44.8	40.2	36.0	31.1	28.6
R-7	0.5	5.5	7.3	11.5	11.3	9.5	5.5	4.4	3.2	2.4	3.3
R-4	*	0.5	0.9	1.7	0.6	1.2	3.5	4.4	3.8	2.7	1.0
R-3	*	*	*	1.0	0.9	1.0	1.0	1.1	1.5	1.0	0.7
R-13	*	2.2	4.0	5.9	7.3	8.6	11.7	9.8	8.9	9.2	7.1
R-15	*	*	*	0.5	0.2	0.7	2.3	1.8	2.2	2.8	3.2
R-12	*	*	0.8	1.1	1.4	2.4	2.3	1.7	2.8	3.1	4.0

Results are expressed as % applied radioactivity

* No discrete peak detected

Table 17 Formation and decline of [^{14}C-difluorophenyl] etoxazole and its degradates in aerobic soil at 20 °C

Radioactive component	Time after application (days)										
	0	1	3	7	14	30	60	90	120	180	269
Etoxazole	97.8	82.6	75.8	50.1	37.2	11.2	4.1	2.2	1.8	1.4	1.2
R-7	0.3	5.0	6.4	21.6	16.7	9.5	5.9	3.1	2.9	2.3	3.2

R-4	*	0.4	0.6	0.8	1.2	0.9	0.9	0.8	0.5	1.5	0.8
R-3	*	*	*	0.6	0.7	1.2	0.8	1.0	1.5	1.2	0.9
R-13	*	2.2	4.0	5.4	8.7	8.4	10.9	9.1	8.3	8.0	7.2
R-11	*	*	*	*	*	2.1	*	0.4	*	0.1	0.2

Results are expressed as % applied radioactivity

No discrete peak detected

Radioactivity was extracted from soil using methanol/water, methanol/0.1M HCl mixtures and by Soxhlet extraction with acetone. HPLC and TLC showed that the major degradates apart from CO_2 were R-7, R-8 and R-13. Minor degradates identified were R-3, R-4, R-11, R-12 and R-15.

After application the proportion of etoxazole declined rapidly from 95.7 and 97.8% of AR at 0 day for ^{14}C-tert-butylphenyl and ^{14}C-difluorophenyl-compounds respectively to 12.6 and 11.2% of AR respectively at 30 days. The proportion of component R-13 rose to 11.7 and 10.9% of AR respectively at 60 days, declining to about 7% of AR at 269 days. The degradate R-7 reached a maximum proportion of 11.5 and 21.6% of AR respectively after 7 days. The proportion declined to 5.5 and 5.9% of AR respectively at 60 days, and 3.3 and 3.2% of AR respectively at 269 days. The proportion of R-8 reached a peak level of 44.8% AR at 60 days and was still relatively great (28.6% AR) at 269 days. The proportion of the minor components R-3, R-4, R-12 and R-15 were never greater than 1.5, 4.4, 4.0 and 3.2% AR respectively. Several minor unidentified metabolites were detected by HPLC. One unidentified minor metabolite reached a maximum proportion of 5.4% AR at 30 days. Another accounted for 3.2% AR or less. Other unidentified minor metabolites each accounted for less than 2% AR.

The degradation of etoxazole was calculated. First order analyses were obtained for data recorded over the phase of the experiment during which approximately 90% of etoxazole was degraded (0–30 days). For ^{14}C-tert-butylphenyl etoxazole application, a DT_{50} of 10.6 days and a DT_{90} of 35.2 days were yielded. For ^{14}C-difluorophenyl etoxazole application, a DT_{50} of 9.9 days and a DT_{90} of 33.0 days were yielded.

Residues in rotational crops

A confined accumulation study on rotational crops was conducted with [difluorophenyl-^{14}C]etoxazole and [*tert*-butylphenyl-^{14}C]etoxazole using wheat, lettuce and radish. The test material was uniformly applied to bare plots containing a sandy loam soil, at an application rate of 0.11 kg ai/ha. The designated planting intervals were 30 days after treatment (DAT), 120 DAT, and 360 DAT. All 30 DAT plots were seeded as scheduled. The germinated radish and lettuce grew normally and provided the 30 DAT samples. Wheat germinated poorly, but the plot was seeded again within a week. The replanted wheat grew normally and provided the 30 DAT samples.

The total radioactive residues (TRR) were determined by combustion of homogenized rotational crop samples. The TRR results of these samples are presented in Table 18.

Table 18 Total radioactive residues (TRR) of 30 DAT rotational crop samples planted after soil application of [^{14}C-difluorophenyl] etoxazole and [^{14}C-*tert*-butylphenyl] etoxazole

Commodity	[^{14}C -difluorophenyl] etoxazole		[^{14}C -*tert*-butylphenyl] etoxazole	
	dpm/g	mg/kg	dpm/g	mg/kg
Radish tops	< 239	< 0.0009	325	0.0012
Radish roots	< 233	< 0.0009	238	0.0009
Lettuce	< 69	< 0.0003	< 268	< 0.0010
Wheat forage	518	0.0019	466	0.0017
Wheat hay	627	0.0023	624	0.0023
Wheat straw	1,333	0.0049	1,133	0.0042
Wheat grain	272	0.0010	< 254	< 0.0009

The total radioactive residues in the 30 DAT rotational crop samples from the treated plots were below 0.005 mg/kg, and in many cases, below the minimum detection or quantification limits. The TRR levels in all the control samples were below detection limit (< 0.0005 mg/kg). Since all of the TRR values in the treated samples were well below the significant residue level of 0.01 mg/kg, these samples were not analysed any further. Based on the observation that etoxazole was not taken up significantly by the rotational crops planted at 30 DAT, the field phase of the study was terminated, further processing and analysis of collected 120 DAT samples were not carried out, and the 360 DAT plots were left fallow.

Uptake and accumulation of etoxazole-related radioactive residues is very low (< 0.005 mg/kg) in rotational crops of radish, lettuce and wheat planted at the earliest plant-back interval (30 DAT).

Environmental fate in water systems

Hydrolysis

The hydrolysis of etoxazole in sterile aqueous buffer solutions of pH 1.2, pH 5, pH 7 and pH 9 has been investigated using [^{14}C-*tert*-butylphenyl] etoxazole. Etoxazole was added to buffer solutions at a rate of 0.037 mg/L which corresponded to half of its reported water solubility at 20 °C. pH 1.2 samples were incubated at 37 °C for 1.5 hours, pH 5 test samples at 20 °C for 21 days, pH 7 and pH 9 test samples at 20 °C (30 days), 50 °C (16 and 18 days), 60 °C (168 and 192 hours), and 70 °C (48 and 60 days).

Table 19 The hydrolysis rate constants and corresponding half-lives of etoxazole in aqueous buffer

pH	Incubation Temperature (°C)	Rate constant (day^{-1})	Regression coefficient	Half life (days)
1.2	37	0.9446[a]	0.9945	0.734[b]
5.0	20	0.0724	0.9646	9.57
7.0	20	0.0043	0.8484	161
	20	0.0047[c]	-	147
	25	0.0079[c]	-	87.7
	50	0.0871	0.9996	7.96
	60	0.2198	0.9995	3.15
	70	0.4667	0.9919	1.48
9.0	20	0.0042	0.7977	165
	20	0.0032[c]	-	217
	25	0.0056[c]	-	124
	50	0.0730	0.9970	9.49
	60	0.1777	0.9977	3.90
	70	0.4307	0.9982	1.61

[a] rate constant is hour^{-1}

[b] half life is in hours

[c] determined by extrapolation of Arrhenius plot of rate constants at 50 °C, 60 °C and 70 °C. All other kinetic parameters were determined experimentally

Due to insufficient hydrolysis of etoxazole at 20 °C in pH 7 and pH 9 buffers, the hydrolysis rate constants at 20 °C in pH 7 and pH 9 buffers were obtained by extrapolation of an Arrhenius plot generated from the results at 50 °C, 60 °C and 70 °C. The Arrhenius plots were also used to determine the hydrolysis rate constants at 25 °C.

At 20 °C, the extrapolated hydrolysis rate constants of etoxazole in pH 7 and pH 9 buffers were 0.0047 and 0.0032/day^{-} respectively. The corresponding half-lives were 147 and 217 days respectively. At 25 °C, the extrapolated hydrolysis rate constants of etoxazole in pH 7 and pH 9 buffers were 0.0079 and 0.0056/day^{-} respectively. The corresponding half-lives were 87.7 and 124 days respectively.

In pH 1.2 buffer at 37 °C ,and in pH 5 buffer at 20 °C, etoxazole was hydrolysed to R-7, while in pH 7 and pH 9 buffer, it was hydrolysed to R-4. No other radioactive products were detected in quantities greater than 6% of the recovered radioactivity.

At 20 °C the hydrolytic stability of etoxazole in aqueous buffer is of the order pH 9 > pH 7 > pH 5. In buffers of acidic pH, etoxazole is hydrolysed to R-7 and in neutral or basic pH to R-4.

Photolysis

The photolysis of etoxazole in water was investigated using a Suntest Accelerated Exposure Unit in which light of < 290 nm was excluded. [^{14}C-*tert*-butylphenyl] or [^{14}C-oxazole] etoxazole was added to pH 9 buffer containing 10% acetonitrile at a rate of 5 µg/L. Test solutions were irradiated continuously using a xenon arc simulated sunlight source for periods of up to 361.61 hours (approx. 47 days equivalent summer sunlight at latitude 40°N). All test solutions were maintained at 20 ± 1 °C during the study. Further test solutions were incubated in the dark and acted as control. Samples were taken immediately after dosing, and at 71.56, 143.53, 216.24, 288.46 and 361.61 hours after treatment. Recovery of radioactivity from test solutions was determined by liquid scintillation counting and proportions of radioactive components in the test solutions at each analysis time were determined by HPLC.

Recoveries from both irradiated and non-irradiated samples were in the range 95.1–99.4% of applied radioactivity. No significant degradation of etoxazole was observed in the dark control samples. The quantities of radioactive components in irradiated test solutions incubated for periods up to 46.99 days equivalent summer sunlight at latitude 40°N are summarised in Table 20.

Table 20 Quantities of radioactive components in irradiated test solutions of pH 9 buffer (containing 10% acetonitrile) treated with ^{14}C-etoxazole at a rate of 5 µg/L and incubated for periods up to 46.99 days equivalent summer sunlight at latitude 40°N

Component	R_T (mins)	Reference Standard	Days equivalent summer sunlight at latitude 40°N				
			8.58	17.57	24.28	38.24	45.71
[^{14}C-oxazole]etoxazole							
Ox/A	5-6	DFB	ND	ND	ND	ND	ND
Ox/B	7-9	R-11	14.8	29.2	62.6	64.0	61.2
Ox/C	17-19	Unknown	ND	11.8	4.2	4.0	4.2
Ox/D	21-23	R-4	ND	ND	ND	ND	ND
Ox/E	25-26	R-3	ND	7.7	7.6	7.1	5.6
Ox/F	27-29	Etoxazole	83.9	38.6	17.0	15.2	17.1
Others	-	-	0.7	8.3	5.4	6.6	7.9
Component	R_T (mins)	Reference Standard	Days equivalent summer sunlight at latitude 40°N				
			8.08	16.77	25.09	32.80	46.99
[^{14}C-*tert*-butylphenyl]etoxazole							
Polars	2-11	Unknown	ND	2.3	ND	ND	2.9
Bu/A	17-18	Unknown	ND	6.3	ND	ND	ND
Bu/B	18-19	R-12	7.2	6.5	7.4	20.4	30.6
Bu/C	21-23	R-15	ND	7.9	12.2	25.0	29.5
Bu/D	25-26	R-3	10.6	11.6	9.1	11.7	12.1
Bu/E	27-29	Etoxazole	75.1	54.2	55.4	24.9	14.9
Others	-	-	2.8	9.6	11.6	14.1	5.6

DFB 2,6-difluorobenzamide

Ox/C was not a clearly resolved peak indicating that more than one component was present

ND Not detected

'Others' refers to radioactivity not associated with specific compounds of which no individual component accounted for > 5% applied radioactivity

Table 21 Kinetic parameters for the half-life of etoxazole (5 µg/L) in pH 9 buffer (containing 10% acetonitrile)

Kinetic parameter	Actual irradiation time (hours)	Summer sunlight equivalents at latitude 40°N (days)

	[^{14}C-oxazole]	[^{14}C-*tert*-butylphenyl]	[^{14}C-oxazole]	[^{14}C-*t*ert-butylphenyl]
r^2	0.862	0.912	0.829	0.933
Rate constant	0.0057/hour	0.0050/hour	0.0436/day	0.0398/day
Half-life	121.6 hours	138.6 hours	15.9 days	17.4 days

The quantum yield of etoxazole was found to be 0.026. The theoretical lifetime obtained using modelling programme was 5.56 days (half-life 3.85 days) at latitude of 40°N in the summer at a depth of 30 cm. The corresponding lifetimes in spring were 7.19 days. The photolytic half-life of etoxazole in pH 9 buffer was found to be 15.9 days summer sunlight equivalents at latitude 40°N (oxazole label) and 17.4 days summer sunlight equivalents at latitude 40°N (*tert*-butylphenyl label). The major degradates were identified as R-3, R-11, R-12 and R-15.

METHODS OF RESIDUE ANALYSIS

Analytical methods

Descriptions of analytical methods together with validation data for residues of etoxazole in plant, animal, soil and water matrices were submitted to the Meeting. The methods rely on an initial extraction, usually with acetone for non-fat samples or ethyl acetate for fatty samples. After solvent partition cleanup, the etoxazole residues are prepared for gas chromatography or undergo further cleanup prior to GC analysis. Etoxazole residues can be measured either by flame thermionic (FTD), nitrogen-phosphorous (NPD) or mass selective detectors (MSD), typically to an LOQ of 0.01 mg/kg. Since the methods use standard extraction solvents and standard detection techniques, they have the potential to be incorporated into existing multi-residue methods.

The trials carried out in the USA, Australia, and Japan used methods based on the original method developed by Sumitomo, ER-MT-9512 (SKA-0002). These methods, referred to as methods RM-37, RM-37HM, RM-37GT, or ALM-030, follow similar procedures as the original method, with slight modifications depending on the matrices analysed.

Detailed descriptions of all these analytical methods are presented below.

Plant matrices

Method ER-MT-9512, with modifications

Non-fatty commodities/ Apple (SKA-0002)

Analyte:	Etoxazole	GC-FID	Method ER-MT-9512
LOQ:	0.01 mg/kg		
Description	Etoxazole residues are extracted from homogenized apples using acetone. The extract is partitioned with hexane and 5% aqueous sodium chloride solution. The organic phase is concentrated by rotary evaporation, the concentrated residue is dissolved in hexane/ethyl acetate (9/1), and cleaned up using a silica gel column, eluted with hexane/ethyl acetate. The eluate is concentrated, and residues of etoxazole are determined by gas chromatography (GC) equipped with a flame thermionic detector (FTD) and a fused silica capillary column.		

Apple, apple juice, pear, grapes (SKA-0012)

Analyte:	Etoxazole	GC-NPD	Method ER-MT-9512
LOQ:	0.01 mg/kg		
Description	Apple (fruit and juice), pear, and grapes samples were extracted with acetone, solvent partitioned, and cleaned up using silica gel. Grape extracts were additionally cleaned up over activated charcoal following clean-up over silica gel. Residues of etoxazole in apple fruit and juice, pear and grape were quantified by gas-liquid chromatography (GLC) equipped with a thermionic detector (N/P detection).		

Grape wine, must, pomace (SKA-0012)

Analyte:	Etoxazole	GC-MS-MS	Method ER-MT-9512
LOQ:	0.01 mg/kg		

Description Grape wine, must, wet and dry pomace samples were extracted with acetone, and solvent partitioned. Residues of etoxazole in wine, must, wet and dry pomace were quantified using GLC equipped with a mass spectrometry/mass spectrometry (MS/MS) detector.

Methods RM-37, RM-37HM, RM-37GT and modifications

Cottonseed (SKA-0048)
Analyte: Etoxazole GC-NPD Method: RM-37
LOQ: 0.01 mg/kg
Description: Residues of etoxazole are extracted from cottonseed samples with acetone and liquid-liquid partitioned with dichloromethane/water. The organic phase is evaporated and partitioned with acetonitrile/hexane to remove oils. The acetonitrile from this step is evaporated and the residue quantified by gas chromatography using a nitrogen-phosphorous specific flame ionization detector (NPD) following clean-up using a silica gel Sep-Pak.

Cucumber (SKR-0154, Analytical Report)
Analyte: Etoxazole GC-MSD Method: RM-37
LOQ: 0.01 mg/kg
Description: Etoxazole residues are extracted from homogenized sample using acetone and then partitioned with dichloromethane/water. The organic phase containing etoxazole residues is evaporated and cleaned up by a tandem Si/carbon solid phase extraction cartridge system. Etoxazole is determined by gas chromatography using mass selective detection.

Hops, dry (SKR-0128/ Analytical Report)
Analyte: Etoxazole GC-NPD Method: RM-37
LOQ: 0.2 mg/kg
Description: Etoxazole residues are extracted using acetone. The acetone is evaporated and the sample is cleaned-up using a silica gel column. The residues are quantified by gas chromatography using a nitrogen-phosphorous detector.

Mint tops and oil (SKR-0156, Analytical Report)
Analyte: Etoxazole GC-MSD Method: Modified RM-37
LOQ: 0.01 mg/kg for mint tops, 0.02 mg/kg for mint oil
Description: Etoxazole residues are extracted from mint tops using acetone. The extract is then filtered and partitioned with dichloromethane/water. The organic phase is evaporated and etoxazole quantified by gas chromatography using a mass selective detector following a tandem clean-up procedure consisting of a Si SPE column coupled to a charcoal SPE column. For mint oil, the clean-up procedure consists of a Si SPE column followed by a Florisil column.

Strawberry (SKR-0102, Analytical Report)
Analyte: Etoxazole GC-NPD Method: Modified RM-37HM
LOQ: 0.002 mg/kg
Description: Etoxazole residues are extracted from strawberries using acetone and then partitioned with dichloromethane/water. The organic phase, containing the etoxazole residues, is evaporated and partitioned with acetonitrile/hexane. The sample is cleaned-up with a silica gel Sep-Pak solid phase extraction column. Etoxazole residues are determined by gas chromatography using a nitrogen-phosphorous detector.

Tea (SKR-0160 to SKR-0163, Analytical Section)
Analyte: Etoxazole GC-NPD Method: Based on RM-37
LOQ: 0.02 mg/kg
Description: Etoxazole residues are extracted from homogenised samples using acetone and then partitioned with dichloromethane/water. The organic phase is then dehydrated with anhydrous sodium sulphate, concentrated and cleaned up by silica gel column using hexane as eluate. A further clean-up in Florisil mini column is made prior to analysis by gas chromatography equipped with nitrogen-phosphorous detector.

Tomato (SKR-0155, Analytical Report)
Analyte: Etoxazole GC-MSD Method: Modified RM-37
LOQ: 0.01 mg/kg
Description: Etoxazole residues are extracted from samples of homogenized tomato using acetone, and then partitioned with dichloromethane/water. The organic phase, containing etoxazole, is evaporated and further cleaned up by a tandem Si/Carbon solid phase extraction cartridge system. Etoxazole residues were determined by gas chromatography using a mass selective detector.

Tree nuts nutmeat/ almonds (SKR-0138, Analytical Report), pecans (SKR-0140, Analytical Report)

Analyte: Etoxazole GC-NPD Method: Modified RM-37
LOQ: 0.01 mg/kg
Description: Residues of etoxazole are extracted from nutmeat samples with acetone and after evaporating off the solvent, the sample is re-dissolved in dichloromethane and partitioned into 5% NaCl aqueous. The organic phase is dried through a bed of sodium sulphate, and evaporated. The residues are re-dissolved in hexane saturated with acetonitrile and partitioned into acetonitrile. The acetonitrile portion is evaporated to dryness, dissolved in hexane and cleaned up with a silica Sep-Pak cartridge, using ethyl acetate/hexane as eluants. The eluate is evaporated to dryness and the residue taken up in toluene for analysis using gas chromatography with a nitrogen-phosphorous detector.

Apple (SKR-0100/ Analytical Report), Pears (SKR-0101/ Analytical Report)
Analyte: Etoxazole GC-NPD Method RM-37HM
LOQ: 0.002 mg/kg
Description Etoxazole residues are extracted from apple samples using acetone, then partitioned with dichloromethane/water. The organic phase containing the etoxazole residues, is evaporated and partitioned with acetonitrile/hexane. The acetonitrile from this step is evaporated and the residues quantified by gas chromatography using a nitrogen-phosphorous specific flame ionization detector (NPD) following clean-up using a silica gel Sep-Pak.

Apple juice, pomace (SKR-0100/ Analytical Report)
Analyte: Etoxazole GC-NPD Method RM-37HM-1
LOQ: 0.002 mg/kg
Description This method is a revision of method RM-37HM. Etoxazole residues are extracted from the samples using acetone, then partitioned with dichloromethane/water. The organic phase containing the etoxazole residues, is evaporated and the residues quantified by gas chromatography using a nitrogen-phosphorous specific flame ionization detector (NPD) following clean-up using a silica gel Sep-Pak.

Grapes, juice, raisins (SKR-0151, Analytical Report)
Analyte: Etoxazole GC-MSD, NPD Method: RM-37HM-1
LOQ: 0.01 mg/kg (grapes); 0.005 mg/kg (juice); 0.01 mg/kg (raisins)
Description Samples are extracted with acetone, partitioned with dichloromethane and sodium chloride aqueous solution. The dichloromethane fraction is dried in a bed of sodium sulphate and evaporated. Residues are re-dissolved in hexane and passed through a silica Sep-Pak cartridge using ethyl acetate/hexane solution as eluant. The sample is evaporated and re-dissolved in toluene for analysis with GC with MSD or NPD detector.

Peach (SKR-0153/Analytical Report)
Analyte: Etoxazole GC-MSD Method: RM-37HM-1
LOQ: 0.01 mg/kg
Description: Etoxazole residues are extracted from the samples using acetone. Samples are partitioned with dichloromethane/water and cleaned by a tandem Si/ carbon solid phase extraction cartridge system. The organic phase containing the etoxazole residues, is evaporated and the residues quantified by gas chromatography using mass selective detection.

Cotton gin trash (SKA-0051)
Analyte: Etoxazole GC-MSD Method: RM-37GT
LOQ: 0.2 mg/kg
Description Samples are extracted with acetone and filtered. An aliquot is concentrated, the residue re-dissolved in sodium chloride solution and partitioned first, into hexane then into acetonitrile. The acetonitrile solution is concentrated and the residue re-dissolved in hexane and cleaned up with alumina column chromatography. The sample is then concentrated prior to clean-up with ENVI-carb carbon SPE column. Etoxazole residues are quantified using gas chromatography with mass selective detection.

Hulls, almond (SKR-0138, Analytical Report)
Analyte: Etoxazole GC-MSD Method: Modified RM-37GT
LOQ: 0.05 mg/kg
Description: Residues of etoxazole are extracted from nutmeat samples with acetone and after evaporating off the solvent, the sample is re-dissolved in an aqueous 5% NaCl solution and partitioned into hexane. The organic phase is dried through a bed of sodium sulphate, and evaporated. The residues are partitioned into acetonitrile. The acetonitrile portion is evaporated to dryness, and the residues dissolved in hexane. The sample is cleaned up using an alumina column and etoxazole residues are eluted with hexane/ethyl acetate solution. The eluants is evaporated to dryness and the residue taken up in hexane/acetone solution and further cleaned up using an ENVI-Carb solid phase extraction cartridge using hexane/acetone as eluants. The eluant is evaporated to dryness and the residue taken up in toluene for analysis using gas chromatography with a mass selective detector.

Method ALM-030

Stone fruit (SKR-0143)

Analyte:	Etoxazole	GC-MS	Method: ALM-030
LOQ:	0.01 mg/kg		
Description:	Residues of etoxazole are extracted from stone fruit samples with acetone, liquid-liquid partitioned with dichloromethane/aqueous sodium chloride solution followed by a SPE cleanup. The instrumental analyses involve chromatographic separation of the target analytes via Gas Chromatography and identification and quantitation of residues via (ion-trap) mass spectrometry.		

Method DFG S 19 with modifications

Fruits with high acid content/ Citrus (SKA-0037)

Analyte:	Etoxazole	GC-MSD	Method: Modified DFG S19
LOQ:	0.01 mg/kg		
Description:	Sodium hydrogen carbonate is added prior to extraction to the samples of mandarin peel and pulp to adjust the pH (at least pH 8). Residues of etoxazole are extracted with acetone, adding water to maintain a ratio of acetone:water of 2:1 (v:v). The extract is partitioned with ethyl acetate/cyclohexane (1+1) and sodium chloride is then added. After repeated mixing, water is separated and the evaporated residue of an aliquot of the organic phase is cleaned up by gel permeation chromatography using a mixture of ethyl acetate/cyclohexane as eluants. The residue containing fraction is concentrated and analysed for residues of etoxazole by GC using mass selective detection (MSD). This same method was used for determination of etoxazole in peaches (see SKR-0076), tomato (see EU trials)		

Commodities with high water content/ Melons (SKA-0055)

Analyte:	Etoxazole	GC-MSD	Method: Modified DFG S19
LOQ:	0.01 mg/kg		
Description	Sample is extracted with acetone. Water is added before-hand to the homogenized sample in an amount that takes account of the natural water content of the sample so that during extraction the acetone/water ratio remains constant at 2:1 (v:v). For liquid-liquid partition, ethyl acetate/ cyclohexane (1:1, v:v) and sodium chloride are added and after mixing, water is separated. The organic phase is evaporated and the residue cleaned up by gel permeation chromatography using a mixture of ethyl acetate/cyclohexane as eluants. The residue-containing fraction is concentrated and analysed for residues of etoxazole by gas chromatography using mass selective detection.		

Commodities with high fat content /Cottonseed (SKA-0038)

Analyte:	Etoxazole	GC-MSD	Method: Modified DFG S19
LOQ:	0.01 mg/kg		
Description:	Samples are mixed with acetonitrile + acetone (9+1) and with synthetic calcium silicate and the suspension filtered. After evaporating an aliquot of the filtrate, the residue is dissolved in ethyl acetate/cyclohexane and cleaned up by gel permeation chromatography. The residue-containing fraction is concentrated and after supplemental clean-up on a silica gel column the solution is analysed for etoxazole residues by gas chromatography using mass selective detection.		

Hops (SKA-0056)

Analyte:	Etoxazole	GC-MSD	Method: Modified DFG S19
LOQ:	0.5 mg/kg		
Description:	Sample is extracted with acetone. Water is added before-hand to the homogenized sample in an amount that takes account of the natural water content of the sample so that during extraction the acetone/water ratio remains constant at 2:1 (v:v). For liquid-liquid partition, ethyl acetate/ cyclohexane (1:1, v:v) and sodium chloride are added and after mixing, water is separated. The organic phase was concentrated and cleaned up by gel permeation chromatography. The residue-containing fraction was further cleaned up first, by Florisil/aluminium oxide column then by silica gel mini column. Residues of etoxazole were determined by gas chromatography using mass selective detection.		

Hops, green and dry (SKA-0057)

Analyte:	Etoxazole	GC-MSD	Method: Modified DFG S19
LOQ:	0.1mg/kg (green hops), 0.5 mg/kg (dry hops)		
Description:	Sample is extracted with acetone/water 2+1 (v+v) with subsequent extraction with ethyl acetate/ cyclohexane 1+1 (v+v) and partition into acetone/cyclohexane/ethyl acetate. The extracts are cleaned up by gel permeation chromatography, followed by Florisil/aluminium oxide column and an additional clean up on a mini silica gel column. Residues of etoxazole were determined by gas chromatography using mass selective detection.		

Validation data for methods on plant matrices are summarised in Table 22.

Table 22 Summary of Method Validation Data for etoxazole fortified into plant matrices

Commodity	Fortification mg/kg	N	Range Recovery (%)	Mean recovery (%)	% RSD	Method	Reference
Plant commodities							
Almond hulls	0.05–0.50	13	67–108	88	14.0	RM-37GT	SKR 0138/AR
Almond nutmeats	0.01–0.10	15	73–112	86	12.8	RM-37	SKR-0138/AR
Apple	0.01–0.1	4	90–97	94	3.1	ER-MT-9512	SKA-0002
Apple juice, pomace	0.002–0.01	4	70–82	75	7.4	RM-37HM-1	SKR-0100
Apple, juice	0.01–0.02	3	75–86	79	7.4	ER-MT-9512	SKA-0012
Apples	0.01–0.20	9	74–107	86	11.5	ER-MT-9512	SKA-0012
Apples	0.002–0.01	26	70–123	91	11.0	RM-37HM	SKR-0100
Cotton gin trash (ILV)	0.2–1.0	4	82–86	83	1.8	RM-37GT	SKA-0051
Cottonseed	0.02	4	84–96	91	5.6	RM-37	SKA-0048
Cucumber	0.01–1.0	9	89–126	109	10.7	RM-37	SKR-0154/AR
Dry pomace	0.01	2	73–75	74	1.9	ER-MT-9512	SKA-0012
Grapes	0.01–0.10	4	94–108	100	5.9	ER-MT-9512	SKA-0012
Grapes	0.002–0.50	26	62–119	93	17	RM-37HM-1	SKR-0151/AR
Grape juice	0.005–0.20	5	85–96	90	5.6	RM-37HM-1	SKR-0151/AR
Grape raisins	0.01–0.50	5	87-100	96	6.2	RM-37HM-1	SKR-0151/AR
Dried hops cones	0.2–1.0	5	87-103	95	6.8	RM-37	SKR-0128/AR
Mint tops	0.01–1.0	14	84–128	104	14.3	RM-37	SKR-0156/AR
Mint oil	0.02–1.0	9	86–125	103	14.7	RM-37	SKR-0156/AR
Must	0.01	2	73–76	75	2.8	ER-MT-9512	SKA-0012
Peach	0.01–1.0	9	80–103	92	7.1	RM-37HM-1	SKR-0153/AR
Pears	0.01–0.10	4	86–106	92	13.2	ER-MT-9512	SKA-0012
Pears	0.002–0.01	12	82–114	95	10.1	RM-37HM	SKR-0101
Pecans	0.01–0.05	6	87–110	99	10.0	RM-37	SKR 0140/AR
Stone fruit	0.01–0.25	4	82–106	94	12.4	ALM-030	SKR-0143 /AR
Strawberry	0.002–0.01	18	71–97	80	7.2	RM-37HM	SKR-0102
Tomato	0.01–1.0	9	91-109	100	6.0	RM-37	SKR-0155/AR
Wet pomace	0.01	2	74–87	81	11.4	ER-MT-9512	SKA-0012
Wine	0.01–0.02	3	75–76	75	0.77	ER-MT-9512	SKA-0012
Multi-residue method							
Cottonseed	0.01-0.10	10	75–100	85	9.6	DFG S19	SKA-0038
Cottonseed (ILV)	0.01–0.10	10	90–101	97	4.0	DFG S19	SKA-0040
Cottonseed (ILV)	0.01–0.10	10	71–103	82	12	DFG S19	SKA-0042
Dry hops (m/z = 300)	0.5– 20	10	80-115	96	11	DFG S19	SKA-0056
Dry hops(m/z = 141)	0.5– 20	10	80–109	93	8.4	DFG S19	SKA-0056
Dry hops (m/z = 204)	0.5–20	10	79–108	92	8.3	DFG S19	SKA-0056
Dry hops (m/z = 141)	0.5– 20	10	79–113	95	11.1	DFG S19	SKA-0057
Dry hops (m/z = 204)	0.5– 20	10	77–114	95	12.5	DFG S19	SKA-0057
Dry hops (m/z = 300)	0.5– 20	10	80–109	93	10.3	DFG S19	SKA-0057
Green hops (m/z = 141)	0.10–1.0	10	75–102	90	9.1	DFG S19	SKA-0057
Green hops (m/z = 204)	0.10–1.0	10	77–99	91	7.5	DFG S19	SKA-0057
Green hops(m/z = 300)	0.10–1.0	10	73–102	88	8.9	DFG S19	SKA-0057
Mandarin peel	0.01–2.0	15	84–105	91	6.4	DFG S19	SKA-0037
Mandarin peel (ILV)	0.01–0.10	10	92–105	99	5.0	DFG S19	SKA-0041/50
Mandarin peel (ILV)	0.01–2.0	10	81–109	97	10	DFG S19	SKA-0043
Mandarin pulp	0.01–2.0	15	70–89	82	7.7	DFG S19	SKA-0037
Mandarin pulp (ILV)	0.01–0.10	10	77–101	91	12	DFG S19	SKA-0041/50
Mandarin pulp (ILV)	0.01–0.10	10	91–105	99	4.3	DFG S19	SKA-0043
Melon (ILV)	0.01-0.10	10	91–115	103	7.9	DFG S19	SKA-0055

Animal matrices

Methods initially developed by Sumitomo (ER-MT-XXXX)

Bovine meat (SKA-0014, SKA-0026) and Poultry meat (SKA-0029)
Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9723

LOQ: 0.01 mg/kg

Description Residues of etoxazole in bovine meat and poultry meat are mixed with anhydrous sodium sulphate, extracted with ethyl acetate and filtered. After the filtrate is concentrated and mixed with hexane and acetonitrile, the compound is partitioned with acetonitrile. The acetonitrile layer is concentrated and the residue cleaned up on a Mega Bond Elut column SI connected with a Mega Bond Elut column Jr. PSA for determination by gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Milk (SKA-0015, SKA-0025)

Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9724

LOQ: 0.01 mg/kg

Description Residues of etoxazole in milk are extracted with acetone using a mechanical shaker. The mixture is centrifuged and the supernatant is mixed with 5% sodium chloride aqueous solution and partitioned with dichloromethane. The concentrated dichloromethane layer is cleaned up on a Mega Bond Elut SI column connected with a Mega Bond Elut Jr. PSA amine column conditioned with hexane. Residues of etoxazole are eluted with hexane:ethyl ether (2:1 v/v), concentrated using a rotary vacuum evaporator and dissolved in hexane. Determination is carried out using gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Bovine liver (SKA-0016, SKA-0033), Bovine kidney (SKA-0034) and Poultry liver (SKA-0035)

Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9727

LOQ: 0.01 mg/kg

Description Residues of etoxazole in bovine liver, kidney and poultry liver are mixed with anhydrous sodium sulphate, extracted with ethyl acetate and filtered. After the filtrate is concentrated, and mixed with hexane and acetonitrile, the compound is partitioned with acetonitrile. The concentrated acetonitrile layer is cleaned up on a Mega Bond Elut SI column connected with a Mega Bond Elut Jr. PSA amine column conditioned with hexane. Residues of etoxazole are eluted with hexane:ethyl ether (2:1 v/v), concentrated and dissolved in hexane. Determination is carried out using gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Bovine fat (SKA-0017, SKA-0027/ SKA-0058) and Poultry fat (SKA-0028)

Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9728

LOQ: 0.01 mg/kg

Description Residues of etoxazole in bovine fat and poultry fat are mixed with anhydrous sodium sulphate, extracted with ethyl acetate and filtered. After the filtrate is concentrated, and mixed with hexane and acetonitrile, the compound is partitioned with acetonitrile. The concentrated acetonitrile layer is cleaned up on a Mega Bond Elut SI column connected with a Mega Bond Elut Jr. PSA amine column conditioned with hexane. Residues of etoxazole are eluted with hexane:ethyl ether (2:1 v/v), concentrated using a rotary vacuum evaporator and dissolved in hexane. Determination is carried out using gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Egg yolk (SKA-0019, SKA-0030)

Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9733

LOQ: 0.01 mg/kg

Description Residues of etoxazole in egg yolk are mixed with anhydrous sodium sulphate, extracted with ethyl acetate and filtered. After the filtrate is concentrated, and mixed with hexane and acetonitrile, the compound is partitioned with acetonitrile. The concentrated acetonitrile layer is cleaned up on a Mega Bond Elut SI column connected with a Mega Bond Elut Jr. PSA amine column conditioned with hexane. Residues of etoxazole are eluted with hexane:ethyl ether (2:1 v/v), concentrated and dissolved in hexane. Determination is carried out using gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Egg white (SKA-0020, SKA-0030)

Analyte: Etoxazole GC-FTD, NPD Method ER-MT-9734

LOQ: 0.01 mg/kg

Description Residues of etoxazole in egg white are mixed with anhydrous sodium sulphate, extracted with ethyl acetate and filtered. The filtrate is concentrated and dissolved in hexane. Clean up is achieved on a Mega Bond Elut SI column conditioned with hexane. Residues of etoxazole are eluted with hexane:ethyl ether (2:1 v/v), concentrated and dissolved in hexane. Determination is carried out using gas chromatography equipped with a flame thermionic detector (FTD) or a nitrogen-phosphorous detector (NPD).

Methods RM-37L, RM-37M, RM-37MT, and their modifications

Bovine liver and kidney (SKR-0099)

Analyte: Metabolite 1 and R-20 HPLC-MS-MS Method: RM-37L

LOQ: 0.02 mg/kg for both analytes

Description:	Residues of Metabolite1 and R-20 are extracted from tissues using methanol followed by a mixture of methanol plus water. The methanol is removed and residue diluted with additional water. The sample is cleaned with a styrene divinyl benzene polymer (PPL) SPE column and eluted with methanol/water. The sample is concentrated and brought up in a mixture of methanol/acetic acid/water for analysis by ion trap HPLC/MS/MS.		

Milk (SKR-0099)

Analyte:	Etoxazole	GC-NPD	Method: RM-37M
LOQ:	0.01 mg/kg		
Description:	Etoxazole residues are extracted from the milk using acetone, then partitioned with dichloromethane/water. The organic phase containing the etoxazole residues is evaporated and the sample is partitioned with acetonitrile/hexane. The acetonitrile is evaporated and the sample is cleaned-up using a silica gel SPE column. The etoxazole residues are then quantified by gas chromatography using a nitrogen-phosphorous detector.		

Bovine tissues – muscle, fat, liver, kidney (SKR-0099)

Analyte:	Etoxazole	GC-NPD or GC-MSD	Method RM-37MT
LOQ:	0.01 mg/kg (muscle, liver, kidney); 0.02 mg/kg (fat)		
Description:	Etoxazole residues are extracted from the tissue using ethyl acetate. The ethyl acetate is evaporated and the sample is partitioned with acetonitrile/hexane. The acetonitrile containing etoxazole is evaporated and cleaned-up using a silica gel SPE column. The etoxazole residue in muscle is quantified by gas chromatography using a nitrogen-phosphorous detector. The etoxazole residues in liver, kidney and fat are determined by gas chromatography using a mass selective detector.		

Validation data for methods on animal matrices are summarised in Table 21.

Table 23 Summary of Method Validation Data for etoxazole fortified into animal matrices

Commodity	Fortification mg/kg	N	Range Recovery (%)	Mean recovery (%)	% RSD	Method	Reference
Animal commodities							
Bovine fat	0.01–1.0	9	87–109	99	7.5	ER-MT-9728	SKA-0017
Bovine fat (ILV)	0.01–1.0	9	84–109	98	8.7	ER-MT-9728	SKA-0027/58
Bovine kidney (ILV)	0.01–1.0	9	75–106	85	13.0	ER-MT-9727	SKA-0034
Bovine liver	0.01–1.0	9	95–105	99	3.7	ER-MT-9727	SKA-0016
Bovine liver (ILV)	0.01–1.0	9	77-103	88	9.8	ER-MT-9727	SKA-0033
Bovine meat	0.01–1.0	9	88–101	91	6.4	ER-MT-9723	SKA-0014
Bovine meat (ILV)	0.01–1.0	9	85–101	91	5.7	ER-MT-9723	SKA-0026
Bovine meat (GC-NPD)	0.01–0.05	9	80–104	94	8.2	RM-37MT	SKR-0099
Bovine meat (GC-MSD)	0.01–0.05	9	89–115	101	8.3	RM-37 MT	SKR-0099
Egg white	0.01–1.0	9	87–100	95	5.0	ER-MT-9734	SKA-0020
Egg white (ILV)	0.01–1.0	9	71–95	85	9.8	ER-MT-9734	SKA-0030
Egg yolk	0.01–1.0	9	90–110	99	6.8	ER-MT-9733	SKA-0019
Egg yolk (ILV)	0.01–1.0	9	77–108	84.	11.2	ER-MT-9733	SKA-0030
Milk	0.01–1.0	9	92–106	99	5.4	ER-MT-9724	SKA-0015
Milk (ILV)	0.01–1.0	9	74–91	83	8.2	ER-MT-9724	SKA-0025
Milk	0.01–0.05	9	76-97	86	6.8	RM-37M	SKR-0099
Poultry fat (ILV)	0.01–1.0	9	77–103	88	12.4	ER-MT-9728	SKA-0028
Poultry liver (ILV)	0.01–1.0	9	71–117	93	17.4	ER-MT-9727	SKA-0035
Poultry meat (ILV)	0.01–1.0	9	85–94	90	3.5	ER-MT-9723	SKA-0029

Multi-residue Method

As previously indicated, the examination of the applicability of the multi-residue method, DFG S 19, for the determination and monitoring of etoxazole residues was investigated. Slight modifications have been introduced for each commodity analysed and the methods validated with acceptable range of recoveries (70–120%) and relative standard deviations (RSD = < 15%).

Analytical methods for determination of etoxazole in soil

Soil (SKA-0010)			
Analyte:	Etoxazole	GC-NPD	Method: ER-MT-9615
LOQ:	0.01 mg/kg		
Description:	Residues of etoxazole are extracted from soil using acetone. The extract is partitioned with hexane and 5% aqueous sodium chloride solution. The organic phase is concentrated by rotary evaporation, the concentrated residue is dissolved in hexane/ethyl acetate (9/1), and cleaned up using a silica gel column eluted with hexane/ethyl acetate. The eluate is concentrated and residues of etoxazole are determined by gas chromatography with nitrogen-phosphorous detector.		

Table 24 Summary of Method Validation Data for soil

Commodity	Fortification mg/kg	N	Range Recovery (%)	Mean recovery (%)	% RSD	Method	Reference
Soil	0.01–1.0	9	76–94	87	6.1	ER-MT-9615	SKA-0010

Stability of pesticide residues in stored analytical samples

The Meeting received data on the stability of etoxazole residues in apple, orange, hop, cotton seed and cotton gin trash samples for plant and animal commodities stored frozen.

The stability study of etoxazole was conducted on apple stored frozen at approximately -18 °C (Maestracci, 1996: SKR-0021). About 20 g (accurately weighed) of ground apple (commercial source) were placed in a 150 mL glass jar and fortified with etoxazole at a level of 0.1 mg/kg. The apple samples were immediately homogenized for about 1 min and then stored at -18 °C in the dark. The analyses of etoxazole were performed at 0, 1, 3, 7, 9 and 12 months after freezing. For each timing, one untreated sample, spiked just before the analysis at 0.10 mg/kg (Quality control sample), and two samples, stored at -18 °C until analysis, were analysed. The residues of etoxazole were determined using GC-FTD (ER-MT-9512). The LOQ was 0.010 mg/kg.

The results demonstrate that etoxazole is stable when stored at -18 °C in apple samples for 7 months. However, following storage for 9 months or more, degradation of etoxazole was observed, reaching < 50% of the original concentration.

Table 25 Stability of etoxazole in apple samples

Time stored (month)	Procedural recovery (%)	Etoxazole after storage (% remaining)
0	87	90, 86
1	73	75, 72
3	97	73, 75
7	74	78
9	72, 74*, 72*	43, 43, 51*, 46*
12	84	45, 40

* Complementary samples for confirmation

A freezer storage stability study, utilizing laboratory-fortified samples, was conducted to verify that etoxazole is stable in/on apples for the storage intervals (Schreier, 2001: SKR-0103). The samples were fortified with 0.01 mg/kg etoxazole. Three aliquots of the fortified matrix were immediately extracted and analysed to establish initial recovery; the remaining bags were placed in a freezer (nominally -20 °C) and stored for the duration of the study. At periodic intervals duplicate samples were removed from storage and analysed along with an untreated control and a freshly fortified sample. The residues of etoxazole were determined using GC-NPD (RM-37HM). The LOQ for etoxazole in this study was 0.002 mg/kg.

The results indicate that etoxazole is stable in/on apples under frozen conditions even for a period of at least 41 days.

Table 26 Freezer storage stability of etoxazole in apples

Time stored (days)	% Recovery (0.01 mg/kg fortification)			
	Freshly fortified recovery	Stored Sample A	Stored Sample B	% remaining
0	90, 92, 75			
41	89	67	72	70
107	85	62	68	65
183	81	58	55	57
369	94	44	52	48

The study was examined the stability of etoxazole fortified at 0.1 mg/kg in mandarin peel and pulp stored frozen at ≤-18 °C for 0, 3, 6, 9 and 12 months (Grolleau, 2000: SKR-0075). The control (untreated) samples and freshly fortified samples were analysed in single determination whereas the aged fortified samples were analysed in duplicate. The samples were analysed for etoxazole using GC-MSD (DFG Method S 19 with modified alkaline extraction). The LOQ was 0.01 m/kg.

The test results indicate that etoxazole is more decreasing in aged mandarin pulp samples than in aged peel samples under these conditions, because the remaining percentage of etoxazole fall below the 70%-level for mandarin pulp after 9 months whereas for mandarin peel the 70%-level is not reached after 12 months.

Table 27 Freezer storage stability of etoxazole in mandarin peel and pulp

Time stored (months)	Mandarin peel		Mandarin pulp	
	Fresh fortification recovery (%)	Aged fortification remaining (%)	Fresh fortification recovery (%)	Aged fortification remaining (%)
0	94	100	92	100
3	94	105	91	99
6	84	99	92	78
9	91	93	91	62
12	90	82	86	56

A freezer storage stability study was conducted on strawberries (Schreier, 2001: SKR-0102). Aliquots of a control strawberry were weighed into storage bags. Each aliquot was fortified with a solution of etoxazole at 0.01 mg/kg. The storage bags were placed in a freezer (nominally -20ºC) and stored for the duration of the study. At periodic intervals duplicate samples were removed from storage and analysed along with an untreated control and a freshly fortified sample. The samples were analysed by GC-NPD, using the analytical method of RM-37HM. The LOQ was 0.002 mg/kg.

Table 28 Freezer storage stability of etoxazole in strawberries

Time stored (days)	% Recovery (0.01 mg/kg fortified)			% remaining
	Freshly Fortified [a]	Stored [b] Sample A	Stored [b] Sample B	
0	83, 95, 97			
32	85	62	64	63
60	77	54	56	55
90	83	46	54	50

[a] Sample fortified and extracted on same day

[b] Sample fortified and stored at -20 ºC until analysis

A freezer storage stability study was conducted on cantaloupe for the storage intervals which occurred between sample collection and extraction for analysis of the study samples (Leonard, 2006: SKR-0139). Aliquots of control samples of cantaloupe were weighed into storage bags. Each aliquot was fortified with a solution of etoxazole at 0.10 mg/kg. The storage bags were placed in a freezer (nominally -20 ºC) and stored for the duration of the study. The samples were analysed by GC-NPD, using the analytical method of RM-37. The LOQ was 0.01 mg/kg.

Table 29 Freezer storage stability of etoxazole in cantaloupe

Time stored (days)	% Recovery (0.01 mg/kg fortified)				% remaining
	Freshly Fortified [a]	Stored [b] Sample A	Stored [b] Sample B	Stored [b] Sample C	
0	83, 84, 80				
50	85	63	53	48	55
126	90	56	69	63	63

[a] Sample fortified and extracted on same day

[b] Sample fortified and stored at -20 ºC until analysis

Stones were removed from stone fruits. Samples were stored for 84–278 days, depending on the storage period of field samples. Stability data are summarised in Table 30.

Table 30 Storage stability of etoxazole in plant commodities

Commodity	Fortification level (mg/kg)	Storage time (days)	Storage temp. (ºC)	Concurrent recovery (%)	% remaining	Reference
Cherry	0.10	193	< -20	98, 100, 103	60, 63, 68	SKR-0141
Plum (fresh)	0.10	207	< -20	97, 100, 101	43, 45, 41	SKR-0152
Plum (dried)	0.10	167	< -20	112, 107, 111	105, 105, 103	SKR-0152
Stone fruit (peach or nectarine)	0.10	134–203	-15	78 (0.01 mg/kg) 84 (0.5 mg/kg)	82, 92	SKR-0144
Peach	0.10	278	< -20	92, 96, 94	45, 53, 52	SKR-0153
Cucumber	0.10	158	< -20	96, 97, 95	83, 88, 82	SKR-0154
Pepper and Tomato	0.10	188–198	-22	99, 99, 94, 98 (0.01 mg/kg) 103, 102, 102, 102 (0.5 mg/kg)	100, 97, 99, 100	SKR-0142
Tomato	0.10	214	< -20	104, 101, 103	87, 87, 88	SKR-0155
Mint (tops)	0.10	154	< -20	125, 103, 109	102, 106, 102	SKR-0156
Mint (oil)	0.10	173	< -20	76, 79, 79	84, 79, 86	SKR-0156
Hop (dried cones)	1.0	84	-20	90, 102, 94, 88	89, 89	SKR-0128
Tea	0.8	49 56	-20	92, 87	88, 85 85, 83	SKR-0160
	0.4	21 29	-20	84, 80	72, 71 74, 70	SKR-0161
	0.8	308 308	-20	92, 87	81, 77 79, 78	SKR-0162
	0.4	275 276	-20	93, 92	83, 81 86, 81	SKR-0163

The storage stability of etoxazole in grapes, raisins and juice samples stored under frozen conditions, was evaluated by extracting samples that had been previously analysed and stored frozen (nominally -20 ºC) between analyses. Samples from this study were extracted within 64 days from sampling.

Table 31 Storage stability of etoxazole in extraction of grapes, raisins and juice

Sample	Initial extraction		Re-extraction		Storage interval (days)[b]	% remaining
	Fortified recovery (%)[a]	Residues, mg/kg	Fortified recovery (%)[a]	Residues, mg/kg		
Grapes	83	0.103, 0.105	85	0.109, 0.108	256	104
Juice	90	0.170, 0.165	90	0.181, 0.190	138	110
Raisins	96	0.127, 0.098	90	0.090, 0.102	108	85

[a] Average recovery from fortified samples analysed concurrently.

[b] Days between initial extraction and re-extraction

The storage stability of etoxazole and its R-3 metabolite in almond hulls stored under frozen conditions was evaluated by extracting samples that had been previously analysed and stored frozen (nominally -20 ºC) between analyses.

Table 32 Storage stability of etoxazole and R-3 in extraction of almond hulls

Storage interval (days)[a]	Initial extraction				Re-extraction				% remaining	
	Fortified recovery (%)[b]		Residues, mg/kg		Fortified recovery (%)[b]		Residues, mg/kg			
	etoxazole	R-3	etoxazole	R-3	etoxazole	R-3	etoxazole	R-3	etoxazole	R-3
182	100	70.5	0.57	0.03	73.8	91.1	0.42	0.05	74	167
			0.55	0.03			0.41	0.05	75	167
			0.34	0.03			0.30	0.04	88	133
			0.71	0.06			0.43	0.05	61	83

[a] Days between initial extraction and re-extraction

[b] Average recovery from fortified samples analysed concurrent set

A deep-freezer storage stability study was conducted with etoxazole in/on hops (Rzepka, 2006: SKR-0132). Samples of hops were fortified with etoxazole at a level of 1.0 mg/kg. The samples were stored in amber-glass bottles at <-18 ºC and were analysed at the nominal storage intervals of 0, 60 and 83 days. Concurrent recovery experiments were conducted at all storage intervals except day 0 by spiking control samples. The samples were analysed by GC-MSD, using the extended revision of the DFG Method S 19 with an additional clean up step. The LOQ was 0.50 mg/kg.

All recoveries were well above 70%, so that residues of etoxazole can be considered stable during storage in sample material of hops for 83 days in frozen state.

Table 33 Freezer storage stability of etoxazole in hops

Time stored (days)	Procedural recovery (%)	Etoxazole after storage (% remaining)
0	120, 92, 88	
60	107	97, 112, 112
83	76	113, 101, 96

Freezer storage stability studies, utilizing laboratory-fortified samples were conducted concurrently with the field trial study. These studies were conducted to verify that etoxazole and R-3 are stable in/on the cotton matrices for the storage intervals which occurred between sample collection and extraction for analysis of study samples (Schreier, 2000: SKR-0090). Aliquots of each matrix were weighed into storage bags. Each aliquot was fortified with a solution of etoxazole or R-3 in acetone. For ginned cottonseed, 10 g sub-samples were fortified at 1.0 mg/kg with etoxazole. For gin trash, 5 g sub-samples were fortified at 1.0 mg/kg with both etoxazole and R-3. Three aliquots of each matrix/analyte combination were immediately extracted and analysed to establish initial (Day 0) recovery. The remaining bags were placed in a freezer (nominally -20 ºC) and stored for the duration of the study. At periodic intervals duplicate samples were removed from storage and analysed along with an untreated control and a freshly fortified sample. The etoxazole and R-3 were quantified by GC-MSD (RM-37GT-1). The LOQ of etoxazole in cottonseed in this study was 0.01 mg/kg. The LOQ of etoxazole and R-3 in gin trash was 0.2 mg/kg.

The results indicate that etoxazole is stable in/on ginned cottonseed during the period studied, with 77% of the etoxazole of the remaining after 513 days. For cotton gin trash, the results indicate that R-3 is stable during the period studied, with 81% of the R-3of the etoxazole of the remaining after 188 days, whereas etoxazole is unstable with 66% of the etoxazole at 31 days storage period.

Table 34 Freezer storage stability of etoxazole in/on cottonseed and cotton gin trash

Time stored (days)	% Recovery (1.0 mg/kg fortified)			% remaining
	Freshly Fortified [a]	Stored [b] Sample A	Stored [b] Sample B	
Cottonseed				
0	93, 90, 87			
28	88	67	66	67
59	82	71	69	70
91	104	77	84	81
178	90	69	75	72
513	87	74	80	77
Cotton gin trash				
0	82, 72, 74			
31	77	66	66	66
94	91	64	70	67
188	91	59	70	65

[a] Sample fortified and extracted on same day

[b] Sample fortified and stored at -20 ºC until analysis.

Table 35 Freezer storage stability of R-3 in/on cotton gin trash

Time stored (days)	% Recovery (1.0 mg/kg fortified)			% remaining
	Freshly Fortified [a]	Stored [b] Sample A	Stored [b] Sample B	
Cotton gin trash				
0	118, 98, 100			
31	92	72	74	73
94	120	79	83	81
188	116	72	89	81

[a] Sample fortified and extracted on same day

[b] Sample fortified and stored at -20 ºC until analysis.

Freezer storage stability studies, utilizing laboratory-fortified samples were conducted concurrently with the cattle feeding study. This storage stability study was conducted to verify that etoxazole and its metabolites are stable in animal matrices for storage intervals, in excess of 30 days, that occurred between sample collection and extraction for analysis of study samples (Schreier, 2002: SKR-0099). All milk, fat, muscle, liver and kidney were extracted for etoxazole analysis within 30 days of collection; consequently no storage stability data was required. The stability of etoxazole in cream, Metabolite R-20 in liver, and Metabolite 1 in liver and kidney were determined through the storage and periodic analysis of laboratory spiked samples. Aliquots of a control sample were weighed into storage bags. Each aliquot was fortified at 0.1 mg/kg with solutions of etoxazole, Metabolite R-20 and Metabolite 1 as appropriate. Three aliquots of the spiked matrix were immediately extracted and analysed to establish initial (Day 0) recovery. The remaining bags were placed in a freezer (nominally -20 ºC) and stored for the duration of the study. At an interval sufficient to cover the period of storage of the treated samples, duplicate stability samples were removed from storage and analysed along with an untreated control and a freshly fortified sample.

Residues of etoxazole in milk cream were determined to be stable with 92% remaining following a period of 64 days of frozen storage.

Metabolite R-20 and Metabolite 1 were determined to be stable under frozen condition for the period that the samples were stored. The stability of Metabolite R-20 in liver under frozen condition was determined to be 72% following 60 days of storage. The stability of Metabolite 1 in liver under frozen condition was determined to be 108% following 60 days of storage.

The stability of Metabolite 1 in kidney under frozen condition was evaluated. Metabolite 1 was determined to be stable with 82% of the material remaining after 60 days of storage.

Table 36 Storage stability of etoxazole in cream, Metabolite R-20 in liver, and Metabolite1 in liver and kidney

Analyte in Sample	Time stored (days)	Freshly Fortified [a]	Stored [b] Sample A	Stored [b] Sample B	% remaining
Etoxazole in Cream	0	115, 113, 115			
	64	99	86	97	92
Metabolite R-20 in Liver	0	88, 90, 77			
	60	88	62	81	72
Metabolite 1 in liver	0	81, 81, 72			
	60	88	89	127	108
Metabolite 1 in kidney	0	77, 88, 87			
	60	86	77	87	82

[a] Sample fortified and extracted on same day

[b] Sample fortified and stored at -20 ºC until analysis.

USE PATTERN

Etoxazole is registered in many countries for control of mites on fruits, vegetables, oilseeds, herbs and forage crops. It is commonly applied as a foliar treatment. The Meeting received labels in many countries in Europe, North America, Latin America, Asia and Australia. The information available to Meeting on registered uses of etoxazole is summarised in Table 32.

Table 37 Registered uses of etoxazole relevant to the review

Crop	Country	Formulation		Application					PHI days
		Type	Conc. of etoxazole	Method	Rate kg ai/ha	Volume L/ha	Spray conc. kg ai/hL	Number max	
Citrus	Australia	SC	110 g/L	Foliar	0.077–0.15	2000–4000	0.0039	1	28
Citrus	Brazil	SC	110 g/L	Foliar	0.045	1800–2000	0.0050	2	14
Citrus	Greece	SC	110 g/L	Foliar	0.055	2000–3000	0.0018–0.0028	1	14
Citrus [b]	Israel	SC	110 g/L	Foliar		To run off	0.0014	1	21
Citrus	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	14
Citrus	Japan	SC	100 g/L	Foliar	0.067–0.35	2000–7000	0.0033–0.005	2	21
Citrus [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025		0.002–0.005	2	21
Citrus [b]	Lebanon	SC	110 g/L	Foliar			0.0028–0.0055	1	7
Citrus [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	14
Citrus [b]	South Africa	SC	100 g/L	Foliar			0.0030–0.0050	1	28
Citrus	Spain	SC	110 g/L	Foliar	0.055		0.0014–0.0055	1	14
Citrus [b]	Turkey	SC	100 g/L	Foliar			0.0025	1	21
Citrus [b]	UAE	SC	100 g/L	Foliar	0.035	1000	0.0035	2	21
Pome fruit									
Pome fruit	Australia	SC	110 g/L	Foliar	0.029–0.077	750–2000	0.0039	1	21
Pome fruit	USA	WP	720 g/kg	Foliar	0.10–0.15	> 934		1	14
Apple [b]	Egypt	SC	100 g/L	Foliar			0.0025	1	15
Apple	France	SC	110 g/L	Foliar			0.0055	1	42
Apple	Greece	SC	110 g/L	Foliar	0.055	1000–1500	0.0037–0.0055	1	28
Apple [b]	Israel	SC	110 g/L	Foliar		1500–2000	0.0028	1	14
Apple	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	28
Apple	Japan	SC	100 g/L	Foliar	0.067–0.35	2000–7000	0.0033–0.005	2	14
Apple [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	14
Apple [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	14
Apple [b]	South Africa	SC	100 g/L	Foliar			0.0035	1	42
Apple	Spain	SC	110 g/L	Foliar	0.055		0.0028–0.0055	1	28
Apple [b]	Switzerland	SC	110 g/L	Foliar	0.053	600–1000	0.0053–0.0088	1	-
Apple [b]	Turkey	SC	100 g/L	Foliar			0.0025	1	14
Pear	France	SC	110 g/L	Foliar			0.0055	1	42

Crop	Country	Formulation		Application					PHI days
		Type	Conc. of etoxazole	Method	Rate kg ai/ha	Volume L/ha	Spray conc. kg ai/hL	Number max	
Pear	Greece	SC	110 g/L	Foliar	0.055	1000–1500	0.0037–0.0055	1	28
Pear	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	28
Pear	Japan	SC	100 g/L	Foliar	0.10–0.35	2000–7000	0.005	2	14
Pear [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	14
Pear [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	14
Pear [b]	South Africa	SC	100 g/L	Foliar			0.0035	1	42
Pear [b]	Switzerland	SC	110 g/L	Foliar	0.053	600–1000	0.0053–0.0088	1	-
Stone fruit									
Stone fruit (except cherries)	Australia	SC	110 g/L	Foliar	0.029–0.077	750–2000	0.0039	1	21
Stone fruit	USA	WP	720 g/kg	Foliar	0.10–0.15	> 467		2	7
Cherry	Japan	SC	100 g/L	Foliar	0.10–0.35	2000–7000	0.005	1	14
Cherry [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	14
Apricot	France	SC	110 g/L	Foliar			0.0055	1	14
Apricot	Greece	SC	110 g/L	Foliar	0.055	1000–1500	0.0037–0.0055	1	14
Apricot	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	14
Nectarine	Greece	SC	110 g/L	Foliar	0.055	1000–1500	0.0037–0.0055	1	14
Nectarine	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	14
Peach	France	SC	110 g/L	Foliar			0.0055	1	14
Peach	Greece	SC	110 g/L	Foliar	0.055	1000–1500	0.0037–0.0055	1	14
Peach	Italy	SC	110 g/L	Foliar	0.055		0.0055	1	14
Peach	Japan	SC	100 g/L	Foliar	0.10–0.35	2000–7000	0.005	2	7
Peach [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	7
Peach [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	14
Peach	Spain	SC	110 g/L	Foliar	0.055		0.0028–0.0055	1	14
Plum	France	SC	110 g/L	Foliar			0.0055	1	45
Berries and other small fruit									
Grapes	Australia	SC	110 g/L	Foliar	0.029–0.077	750–2000	0.0039	1	21
Grapes	France	SC	110 g/L	Foliar			0.028 0.055	1 1	35 120
Grapes	Greece	SC	110 g/L	Foliar	0.028	500–1000	0.0028–0.0055	1	28
Grapes	Italy	SC	110 g/L	Foliar	0.028		0.0028	1	A
Grapes	Japan	SC	100 g/L	Foliar	0.10–0.35	2000–7000	0.005	1	7
Grapes [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	7
Grapes [b]	Lebanon	SC	110 g/L	Foliar			0.0028–0.0055	1	7
Grapes [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	14
Grapes	USA	WP	720 g/kg	Foliar	0.10–0.15	234–1868		1	14
Strawberry [b]	Egypt	SC	100 g/L	Foliar			0.0025	1	15
Strawberry	Japan	SC	100 g/L	Foliar	0.075–0.18	1500–3500	0.005	1	1
Strawberry [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	1
Strawberry [b]	Mexico	SC	110 g/L	Foliar	0.022–0.050			2	-
Strawberry	USA	WP	720 g/kg	Foliar	0.10–0.15	934–2802		1	1
Fruiting vegetables, cucurbits									
Cucumber [b]	Israel	SC	110 g/L	Foliar	0.028	300–1000		1	7
Cucumber	Japan	SC	100 g/L	Foliar	0.075–0.18	1500–3500	0.005	1	1
Cucumber [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	1
Cucumber [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	1
Cucumber [b]	UAE	SC	100 g/L	Foliar	0.035	1000	0.0035	2	1
Cucumber	USA	WP	720 g/kg	Foliar	0.10–0.15	> 467		2	7
Melons [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	1
Melons [b]	UAE	SC	100 g/L	Foliar	0.035	1000	0.0035	2	1
Melons incl watermelon	Japan	SC	100 g/L	Foliar	0.075–0.18	1500–3500	0.005	2	1

Crop	Country	Formulation		Application					PHI days
		Type	Conc. of etoxazole	Method	Rate kg ai/ha	Volume L/ha	Spray conc. kg ai/hL	Number max	
Melons incl watermelon [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	1
Melons incl watermelon	USA	WP	720 g/kg	Foliar	0.10–0.15	28–93 (air) 93–467 (ground)		1	7
Melons incl watermelon [b]	Israel	SC	110 g/L	Foliar	0.028	300–1000		1	7
Watermelon [b]	Turkey	SC	100 g/L	Foliar			0.0025	1	3
Fruiting vegetables other than cucurbits									
Eggplant	Greece	SC	110 g/L	Foliar	0.055	500–1000 (outdoor) 500–1500 (greenhouse)	0.0055–0.011 0.0037–0.011	1	3
Eggplant [b]	Israel	SC	110 g/L	Foliar	0.028	300–1000		1	3
Eggplant	Japan	SC	100 g/L	Foliar	0.075–0.18	1500–3500	0.005	1	1
Eggplant [b]	Jordan	SC	100 g/L	Foliar	0.020–0.025	1000–2000	0.002–0.005	2	1
Eggplant [b]	Netherlands	SC	110 g/L	Foliar	0.028–0.055	500–1000	0.0055	1	3
Eggplant [b]	Saudi Arabia	SC	100 g/L	Foliar			0.005	2	1
Eggplant	UK	SC	110 g/L	Foliar	0.014–0.050 0.019–0.039	500–1500 500–1000	0.0028–0.0033 0.0039	1	45–60
Peppers	Australia	SC	110 g/L	Foliar	0.019	500	0.0039	1	7
Peppers [b]	Israel	SC	110 g/L	Foliar	0.028	300–1000		1	3
Tomato	Australia	SC	110 g/L	Foliar	0.019	500	0.0039	1	7
Tomato	Brazil	SC	110 g/L	Foliar	0.025	1000	0.0028	2	1
Tomato	Greece	SC	110 g/L	Foliar	0.055	500–1000 (outdoor) 500–1500 (greenhouse)	0.0055–0.011 0.0037–0.011	1	3
Tomato [b]	Israel	SC	110 g/L	Foliar	0.028	300–1000		1	3
Tomato [b]	Netherlands	SC	110 g/L	Foliar	0.028–0.055	500–1000	0.0055	1	3
Tomato [b]	South Africa	SC	100 g/L	Foliar	0.020–0.080	500–2000	0.0040	1	3
Tomato [b]	Turkey	SC	100 g/L	Foliar			0.0035	1	3
Tomato	UK	SC	110 g/L	Foliar	0.014–0.050 0.019–0.039	500–1500 500–1000	0.0028–0.0033 0.0039	1	45–60
Tomato (indoor)	USA	WG	50 g/kg	Foliar	0.056–0.14			2	1
Tree nuts									
Tree nuts	USA	WP	720 g/kg	Foliar	0.10–0.15			1	28
Oilseeds									
Cotton	Australia	SC	110 g/L	Foliar	0.039			1	21
Cotton	Brazil	SC	110 g/L	Foliar	0.23	250–300	0.025	2	14
Cotton	Greece	SC	110 g/L	Foliar	0.033–0.041	500–800	0.0041–0.0083	1	35
Cotton	Spain	SC	110 g/L	Foliar	0.028–0.041			1	-
Cotton [b]	Turkey	SC	100 g/L	Foliar			0.0025–0.0050	1	21
Cotton	USA	WP	720 g/kg	Foliar	0.033–0.050	28–93 (air) 93–467 (ground)		1	28
Cotton [b]	Uzbekistan	SC	100 g/L	Foliar	0.025			2	30
Herbs, incl. Dried herbs and hops									
Hops	Japan	SC	100 g/L	Foliar	0.10–0.35	2000–7000	0.005	1	7
Hops	USA	WP	720 g/kg	Foliar	0.15–0.20	> 467		1	7
Mint	USA	WP	720 g/kg	Foliar	0.10–0.20	> 93 (air) > 467 (ground)	0.022–0.043	2	7
Tea									
Tea	Japan	SC	100 g/L	Foliar	0.067–0.40	2000–4000	0.0033–0.010	1	14

[a]: allowed to be treated in spring (before bud break)

-: PHI is not required

[b]: label is not submitted

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

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

Crop group	Commodity	Table
Citrus fruits	Mandarins & Oranges	Table 33
Pome fruits	Apples	Table 34, 35
	Pears	Table 36, 37
Stone fruits	Cherries	Table 38, 39
	Plums	Table 40, 41
	Nectarine	Table 42
	Peach	Table 43–45
Berries and other small fruits	Grapes	Table 46, 47
	Strawberry	Table 48
Fruiting vegetables, Cucurbits	Cantaloupe	Table 49
	Cucumber	Table 50
Fruiting vegetables, other than Cucurbits	Peppers	Table 51
	Tomato	Table 52–54
Tree nuts	Almonds	Table 55,56
	Pecan	Table 57
Oilseed	Cotton seed	Table 58–61
Herbs	Mints	Table 62
Dried herbs	Hops	Table 63, 64
Teas	Tea	Table 65

Each formulation of etoxazole, used in these trials, was applied as a foliar spray. In general, each of the field trial sites consisted of untreated control and treated plots. Application rates and spray concentrations have been rounded to two significant figures.

Residue values from the trials conducted according to maximum GAP have been used for the estimation of maximum residue levels and STMRs. Those results included in the evaluation 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 or duration of residue sample storage was also provided. Although trials included control plots, no control data are recorded in the tables except where residues were found in from control samples. 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.

Citrus fruits

Mandarins and Oranges

Etoxazole was applied to oranges at six trials and mandarins at eight trials in South Europe. Seven trials were conducted for decline curve studies and the other seven for harvest studies. Oranges and mandarins were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 38 Etoxazole residues on mandarins and oranges from supervised trials in Europe

Orange and Mandarin country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, Italy and Spain	*SC*	*0.055*	*0.0055*			*1*		*14*		
Italy, 1998 (Tarocco)	SC	0.055	0.0018	3000	79	1	peel	0 4 8 15	0.11 0.07 0.12 0.05	Grolleau, 1999, SKR-0064
							pulp	0 4 8 15	< 0.01 < 0.01 < 0.01 < 0.01	Maximum storage interval: 92 days
							whole fruit*	0 4 8 15	0.04 0.03 0.04 0.02	
Italy, 1998 (Tarocco)	SC	0.055	0.0018	3000	79	1	peel pulp whole fruit	14 14 14	0.06 < 0.01 0.02	Grolleau, 1999, SKR-0064 Storage interval: 77 days
Italy, 1998 (Mandarin Avana)	SC	0.055	0.0018	3000	79	1	peel	0 2 6 13	0.16 0.16 0.18 0.04	Grolleau, 1999, SKR-0065
							pulp	0 2 6 13	< 0.01 < 0.01 < 0.01 < 0.01	Maximum storage interval: 102 days
							whole fruit	0 2 6 13	0.03 0.03 0.04 0.02	
Italy, 1998 (Mandarin Avana)	SC	0.055	0.0018	3000	81	1	peel pulp whole fruit	14 14 14	0.23 < 0.01 0.04, 0.05	Grolleau, 1999, SKR-0065 Storage interval: 68 days
Italy, 1999 (Tarocco O.L)	SC	0.055	0.0022	2500	78	1	peel	0 2 8 14	0.13 0.05 0.05 0.02	Grolleau, 2000, SKR-0073
							pulp	0 2 8 14	< 0.01 < 0.01 < 0.01 < 0.01	Storage interval: 43–57 days
							whole fruit*	0 2 8 14	0.04 0.02 0.02 0.01	

Orange and Mandarin country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
Italy, 1999 (Tarocco O.L)	SC	0.055	0.0022	2500	79	1	peel pulp whole fruit*	14 14 14	0.15 < 0.01 0.05	Grolleau, 1999, SKR-0073 Storage interval: 38 days
Italy, 1999 (Mandarin Avana)	SC	0.055	0.0022	2500	78	1	peel	0 3 7 13 19	0.12 0.14 0.08 0.07 0.03	Grolleau, 2000, SKR-0074 Storage interval: 46–65 days
							pulp	0 3 7 13 19	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	
							whole fruit	0 3 7 13 19	0.04, 0.06 0.03, 0.03 0.04, 0.03 0.04, 0.03 < 0.01, 0.01	
Italy, 1999 (Mandarin Avana)	SC	0.055	0.0022	2500	78	1	peel pulp whole fruit	12 12 12	0.20 0.01 0.05, 0.05	Grolleau, 2000, SKR-0074 Storage interval: 45 days
Spain, 1998 (Mandarin Fortune)	SC	0.055	0.0018	3000	85	1	peel	0 4 7 14	0.10 0.09 0.08 0.05	Grolleau, 1999, SKR-0067 Maximum storage interval: 121 days
							pulp	0 4 7 14	< 0.01 < 0.01 < 0.01 < 0.01	
							whole fruit	0 4 7 14	0.03 0.02 0.03 0.01	
Spain, 1998 (Mandarin Clemenule)	SC	0.055	0.0018	3000	89	1	peel pulp whole fruit	14 14 14	0.04 < 0.01 0.02, 0.01	Grolleau, 1999, SKR-0067 Storage interval: 66 days
Spain, 1999 (Mandarin Clemenules)	SC	0.055	0.004	1500	81	1	peel	0 3 7 14 21	0.21 0.24 0.17 0.15 0.08	Grolleau, 2000, SKR-0082 Storage interval: 28–49 days
							pulp	0 3 7 14 21	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	
							whole fruit	0 3 7 14 21	0.10, 0.11 0.08, 0.06 0.06, 0.06 0.05, 0.05 0.04, 0.04	
Spain, 1999 (Mandarin Clemenules)	SC	0.055	0.004	1500	81	1	peel pulp whole fruit	14 14 14	0.12 < 0.01 0.03, 0.05	Grolleau, 2000, SKR-0082 Storage interval: 22 days

Orange and Mandarin country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
Spain, 1999 (Navelina)	SC	0.055	0.003	2000	81	1	peel	0 3 7 15	0.07 0.05 0.06 0.05	Grolleau, 2000, SKR-0084 Storage interval: 47–62 days
							pulp	0 3 7 15	< 0.01 < 0.01 < 0.01 < 0.01	
							whole fruit*	0 3 7 15	0.02 0.01 0.02 0.01	
Spain, 1999 (Navel 'New Hall')	SC	0.055	0.003	2000	81	1	peel pulp whole fruit*	15 15 15	0.07 < 0.01 0.02	Grolleau, 2000, SKR-0084 Storage interval: 47 days

* Whole fruit residues calculated from residues in peel and pulp, adjusted by the weight ratio of peel to pulp. Residues below LOQ were calculated as LOQ value.

Pome fruits

Apples

Etoxazole was applied to apples at 6 trials in Northern France (Northern Europe) and at eight trials in Southern France, Greece, Italy and Spain (Southern Europe). Seven trials were conducted for decline curve studies and the other seven for harvest studies. Apples were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 39 Etoxazole residues on apples from supervised trials in Europe

Apples country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, France	*SC*		*0.0055*			*1*		*42*		
GAP, Greece	*SC*	*0.055*	*0.0055*	1500		*1*		*28*		
GAP, Italy	*SC*	*0.055*	*0.0055*			*1*		*28*		
GAP, Spain	*SC*	*0.055*	*0.0055*			*1*		*28*		
Northern Europe										
North France, 1999 (Golden)	SC	0.055	0.0055	1000	77	1	whole fruit	0 7 14 28 43	0.02 < 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2000, SKR-0070 Storage interval: 48–115 days
North France, 1999 (Elstar)	SC	0.055	0.005	1100	77	1	whole fruit	0 7 14 28 42	0.04 0.03 0.02 < 0.01 < 0.01	
North France, 1999 (Starkrimson)	SC	0.055	0.0061	900	77	1	whole fruit	35	< 0.01	
North France, 2000 (Rouge Americaine)	SC	0.055	0.0069	800	79	1	whole fruit	0 7 13 28 42	0.06 0.03 0.03 0.01 0.01	Grolleau, 2001, SKR-0077 Storage interval:

Apples country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
North France, 2000 (Melrose)	SC	0.055	0.0069	800	77	1	whole fruit	0 7 14 27 42	0.04 0.02 0.02 < 0.01 < 0.01	26–58 days
North France, 2000 (Oregon)	SC	0.055	0.0069	800	79	1	whole fruit	34	< 0.01	
Southern Europe										
South France, 1999 (Golden)	SC	0.055	0.0055	1000	75	1	whole fruit	0 7 14 28 42	0.04 0.02 0.01 < 0.01 < 0.01	Grolleau, 2000, SKR-0070 Storage interval: 64–106 days
Greece, 2000 (Red Chief)	SC	0.055	0.0092	600	77-81	1	whole fruit	35	0.04	Grolleau, 2001, SKR-0077 Storage interval: 25 days
Italy, 1998 (Golden)	SC	0.055	0.01	1000	74	1	whole fruit	90	< 0.01	Grolleau, 1999, SKR-0063 Storage interval: 176 days
Italy, 1998 (Red Chief)	SC	0.055	0.01	1000	74	1	whole fruit	90	< 0.01	
Italy, 1999 (Golden)	SC	0.055	0.0037	1500	77	1	whole fruit	35	< 0.01	Grolleau, 2000, SKR-0071 Storage interval: 75 days
Italy, 2000 (Golden Delicious)	SC	0.055	0.0055	1000	81	1	whole fruit	0 7 13 28 42	0.05 0.02 0.01 < 0.01 < 0.01	Grolleau, 2001, SKR-0077 Storage interval: 27–69 days
Spain, 1999 (Golden)	SC	0.055	0.0037	1500	78-79	1	whole fruit	0 7 14 28 42	0.04 0.02 0.01 < 0.01 < 0.01	Grolleau, 2000, SKR-0081 Storage interval: 86–128 days
Spain, 2000 (Starking)	SC	0.055	0.0037	1500	76	1	whole fruit	35	< 0.01	Grolleau, 2001, SKR-0087 Storage interval: 14 days

The Meeting received sixteen trials on apple which were conducted in USA in California, Colorado, Idaho, Michigan, New York, Oregon, Virginia, Washington and Pennsylvania. Five trials conducted in CO, ID, MI, NY and WA received two applications of the WP formulation containing nominally 800 g/kg etoxazole at a rate of 0.15 kg ai/ha. Eight trials conducted in CA, ID, MI, NY, OR, PA, VA and WA received two applications of the WG formulation containing nominally 720 g/kg etoxazole at a rate of 0.15 kg ai/ha for a seasonal total of 0.30 kg ai/ha. Both applications were foliar air blast sprays. At one test site (CO), additional plots were treated with a total seasonal rate of 0.20 kg ai/ha (0.67× rate), and 0.60 kg ai/ha (2× rate). At one test site (WA), additional plot was treated with a total seasonal rate of 1.5 kg ai/ha (5× rate). The 5× samples from this trial utilized for production of processed products. All study samples were stored at nominally -20 ºC until analysis. The maximum storage interval from sample collection to extraction for analysis was 65 days.

The analytical method was validated with analyses by spiking control samples with etoxazole at fortification levels ranging from 0.002 to 0.010 mg/kg. The limit of quantification (LOQ) was 0.002 mg/kg.

Table 40 Etoxazole residues on apples from supervised trials in USA

Apples	Application	Portion	PHI	Residues,	Ref

country, year (variety)	Form	kg ai/ha	kg ai/hL	water, L/ha	no.	analysed	Days	mg/kg	
GAP, USA	*WP*	*0.15*		*> 934*	*1*		*14*		
USA/MI, 1999 (MacIntosh)	WP	0.15		1336 (air blast)	2	whole fruit	14 20 27 34	0.060, 0.056 0.061, 0.042 0.059, 0.062 0.040, 0.061	Schreier, 2002 SKR-0100
USA/ ID, 1999 (Rome)	WP	0.15		925, 934 (air blast)	2	whole fruit	28	0.035, 0.036	Storage interval: 8–65 days
USA/NY, 1999 (Rome)	WP	0.15		1130, 1121 (air blast)	2	whole fruit	28	0.028, 0.028	
USA/CO, 1999 (Golden Delicious)	WP	0.10		1410, 1400 (air blast)	2	whole fruit	28	0.040, 0.031	
		0.15		1410, 1400 (air blast)	2		28	0.062, 0.059	
		0.30		1410, 1400 (air blast)	2		28	0.15, 0.13	
USA/WA,1999 (Red Delicious)	WP	0.15		1205, 1280 (air blast)	2	whole fruit	28	0.044, 0.050	
		0.75		1205, 1280 (air blast)	2		28	0.43, 0.35	
USA/NY, 2000 (Red Delicious)	WG	0.15		942, 934 (air blast)	2	whole fruit	28	0.065, 0.033	
USA/PA, 1999 (Red Delicious)	WG	0.15		976, 999 (air blast)	2	whole fruit	28	0.037, 0.048	
USA/VA, 2000 (Red Delicious)	WG	0.15		941, 928 (air blast)	2	whole fruit	28	0.049, 0.049	
USA/MI, 2000 (Jonathan)	WG	0.15		938, 947 (air blast)	2	whole fruit	28	0.017, 0.036	
USA/CA, 2000 (Granny)	WG	0.15		928, 928 (air blast)	2	whole fruit	28	0.037, 0.036	
USA/OR, 2000 (Jonagold)	WG	0.15		927, 948 (air blast)	2	whole fruit	14 21 28 35	0.019, 0.048 0.021, 0.028 0.022, 0.019 0.014, 0.017	
USA/WA,2000 (Red Delicious)	WG	0.15		933, 927 (air blast)	2	whole fruit	28	0.066, 0.070	
USA/ID, 2000 (Red Delicious)	WG	0.15		917, 895 (air blast)	2	whole fruit	28	0.040, 0.034	

Pears

Etoxazole was applied to pears at two trials in Northern France (Northern Europe) and at two trials in Southern France, Greece (Southern Europe). One trial was conducted for decline curve study and the other three for harvest studies. Pears were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 41 Etoxazole residues on pears from supervised trials in Europe

Pears	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
country, year (variety)	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, France *GAP, Greece*	*SC* *SC*	 *0.055*	*0.0055* *0.0055*	 *1500*		*1* *1*		*42* *28*		
Northern Europe										
North France, 1999	SC	0.055	0.0055	1000	75	1	whole fruit	35	< 0.01	Grolleau, 2000, SKR-0070

Pears country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
(William)										Storage interval: 91 days
North France, 2000 (Highland)	SC	0.055	0.0069	800	75	1	whole fruit	35	< 0.01	Grolleau, 2001, SKR-0077 Storage interval: 39 days
Southern Europe										
South France, 1999 (Alexandrine)	SC	0.055	0.0069	800	75	1	whole fruit	35	< 0.01	Grolleau, 2000, SKR-0070 Storage interval: 95 days
Greece, 2000 (Cristali)	SC	0.055	0.0044	1263	74 - 75	1	whole fruit	0 7 14 28 42	0.02 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2001, SKR-0077 Storage interval: 30–72 days

The Meeting received seven trials on pear which were conducted in USA in California, Oregon, Washington and Pennsylvania. Four trials conducted in CA, OR, PA and WA received two applications of the WP formulation containing nominally 800 g/kg etoxazole at a rate of 0.15 kg ai/ha. Three trials conducted in CA, OR and WA received two applications of the WG formulation containing nominally 720 g/kg etoxazole at a rate of 0.15 kg ai/ha for a seasonal total of 0.30 kg ai/ha. Both applications were foliar air blast sprays. At one test site (WA), additional plots were treated with a total seasonal rate of 0.20 kg ai/ha (0.67× rate), and 0.60 kg ai/ha (2× rate).

The analytical method was validated with analyses by spiking control samples with etoxazole at fortification levels ranging from 0.002 to 0.010 mg/kg. The LOQ was 0.002 mg/kg.

Table 42 Etoxazole residues on pears from supervised trials in USA

Pears country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*> 934*	*1*		*14*		
USA/PA, 1999 (Bartlett)	WP	0.15		1602, 1698 (air blast)	2	whole fruit	14 21 28 35	0.040, 0.068 0.041, 0.036 0.023, 0.028 0.014, 0.015	Schreier, 2002 SKR-0101 Storage interval: 14–63 days
USA/ CA,1999 (Bartlett)	WP	0.15		935, 932 (air blast)	2	whole fruit	28	0.045, 0.045	
USA/OR, 1999 (Starkrimson)	WP	0.15		1226, 1201 (air blast)	2	whole fruit	28	0.015, 0.017	
USA/WA,1999 (D' Anjou)	WP	0.10		930, 959 (air blast)	2	whole fruit	28	0.027, 0.037	
		0.15		963, 951 (air blast)	2		28	0.062, 0.047	
		0.30		888, 959 (air blast)	2		28	0.13, 0.13	
USA/CA, 2000 (Bartlett)	WG	0.15		934, 968 (air blast)	2	whole fruit	28	0.032, 0.038	
USA/WA,2000 (D' Anjou)	WG	0.15		931, 936 (air blast)	2	whole fruit	14 21 28 35	0.14, 0.14 0.13, 0.13 0.11, 0.094 0.081, 0.087	
USA/OR, 2000 (Red Clapp)	WG	0.15		1268, 1224 (air blast)	2	whole fruit	28	0.041, 0.032	

Stone fruits

Cherries

Thirteen field trials (seven in tart cherries and six in sweet cherries) were conducted during the 2004 growing season in the USA. At each trial, two foliar directed airblast (or equivalent) applications of the WG formulation, containing nominally 720 g/kg, at a rate of approximately 0.15 kg ai/ha were targeted at 14 days (± 1 day) intervals for a seasonal total of 0.30 kg ai/ha.

Control samples were fortified with etoxazole and analysed both prior to and concurrently with field-treated samples. Fortification levels ranged from 0.01 to 1 mg/kg. Method validation recoveries ranged from 89 to 98%. The LOQ was statistically calculated as 0.0037 mg/kg. The maximum storage interval for field-treated samples in this study was 179 days. Storage stability samples fortified at 0.10 mg/kg etoxazole were analysed after 193 days and yielded recoveries (% remaining) that averaged 64%.

Table 43 Etoxazole residues on cherries from supervised trials in USA

Cherries country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*> 467*	*2*		*7*		
USA/NJ, 2004 (North Star)	WG	0.15		897, 943	2	pitted fruit	6	0.20, 0.20	Leonard, 2006 SKR-0141 Storage interval: 123–179 days
USA/ MI, 2004 (Montmorency)	WG	0.15		953, 934	2	pitted fruit	7	0.24, 0.24	
USA/MI, 2004 (Montmorency)	WG	0.15		971, 953	2	pitted fruit	7	0.26, 0.21	
USA/MI, 2004 (Montmorency)	WG	0.15		962, 953	2	pitted fruit	7	0.38, 0.34	
USA/MI, 2004 (Montmorency)	WG	0.15		943, 943	2	pitted fruit	3 7 10 14	0.24, 0.22 0.22, 0.21 0.19, 0.17 0.14, 0.16	
USA/CO, 2004 (Montmorency)	WG	0.15		1149, 1093	2	pitted fruit	7	0.34, 0.31	
USA/ID, 2004 (Montmorency)	WG	0.15		934, 934	2	pitted fruit	8	0.36, 0.76	
USA/MI, 2004 (Heidelfingen)	WG	0.15		943, 943	2	pitted fruit	7	0.18, 0.16	
USA/MI, 2004 (Heidelfingen)	WG	0.15		953, 934	2	pitted fruit	7	0.089, 0.12	
USA/OR, 2004 (Bing and Ranier)	WG	0.15		1663, 1691	2	pitted fruit	6	0.17, 0.14	
USA/WA,2004 (Brooks)	WG	0.15		1373, 1392	2	pitted fruit	2 8 10 13	0.14, 0.17 0.081, 0.11 0.081, 0.075 0.063, 0.096	
USA/CA,2004 (Kings)	WG	0.15		1224, 1224	2	pitted fruit	7	0.10, 0.10	
USA/CA, 2004 (Brooks)	WG	0.15		1233, 1168	2	pitted fruit	8	0.15, 0.13	

The duplicate residues recorded in the table originate from duplicate field samples.

Two supervised field trials were conducted in Spain (Southern Europe) involving a single foliar application with the SC formulation, containing 110 g/L etoxazole, at a rate of 0.055 kg ai/ha.

The storage stability of etoxazole in sample extracts was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 44 Etoxazole residues on cherries from supervised trials in Europe

Cherries country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
Spain, 2007 (Heidelfingen)	SC	0.055	0.0046	1200	85	1	cherry flesh after stoning	0 3 7	0.02 < 0.01 0.01	Grolleau, 2008, SKR-0136 Storage interval: 168–176 days
							whole fruit assuming no residue in stone	0 3 7	0.02 < 0.01 < 0.01	
Spain, 2007 (Starking)	SC	0.055	0.0055	1000	85	1	cherry flesh after stoning	0 3 7	0.02 < 0.01 0.01	
							whole fruit assuming no residue in stone	0 3 7	0.02 < 0.01 < 0.01	

Plums

A total of twelve supervised trials on plums were conducted in Europe. Six trials on plums were conducted in Northern France (Northern Europe), four in Southern France and two in Spain (Southern Europe) at a rate of 0.055 kg ai/ha using an SC formulation containing 110 g/L etoxazole.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 45 Etoxazole residues on plums from supervised trials in Europe

Plums country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, France	*SC*		*0.0055*			*1*		*45*		
Northern Europe										
North France, 2004 (Mirabelle)	SC	0.055	0.006	1000	75	1	flesh	47	0.01	Bousquet, 2004, SKR-0112 Storage interval: 24–25 days
							whole fruit (calculated)	47	< 0.01	
North France, 2004 (Stanley)	SC	0.055	0.006	1000	75	1	flesh	47	< 0.01	
							whole fruit (calculated)	47	< 0.01	
North France, 2001 (Mirabelle de Nancy)	SC	0.055	0.006	1000	75	1	flesh after flesh/ stone separation	45	< 0.01	Grolleau, 2002, SKR-0121 Storage interval; 24–39 days
							whole fruit (calculation based on ratio flesh/ stone)	45	< 0.01	
North France, 2001 (Mirabelle de Nancy)	SC	0.055	0.006	1000	77	1	flesh after flesh/ stone separation	45	< 0.01	
							whole fruit (calculation based on ratio flesh/ stone)	45	< 0.01	
North France, 2001 (Reine Claude	SC	0.055	0.006	1000	75	1	flesh after flesh/ stone separation	44	< 0.01	

Plums country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
veritable)							whole fruit (calculation based on ratio flesh/ stone)	44	< 0.01	
North France, 2001 (Reine Claude)	SC	0.055	0.006	1000	75	1	flesh after flesh/ stone separation	44	< 0.01	
							whole fruit (calculation based on ratio flesh/ stone)	44	< 0.01	
Southern Europe										
South France, 2001 (Reine Claude 1119-veritable)	SC	0.055	0.006	1000	75	1	flesh after flesh/ stone separation	47	< 0.01	Grolleau, 2002, SKR-0121 Storage interval: 11–61 days
							whole fruit (calculation based on ratio flesh/ stone)	47	< 0.01	
South France, 2001 (President)	SC	0.055	0.006	1000	75	1	flesh after flesh/ stone separation	46	< 0.01	
							whole fruit (calculation based on ratio flesh/ stone)	46	< 0.01	
South France, 2001 (Prune d'ente)	SC	0.055	0.006	1000	77	1	flesh after flesh/ stone separation	44	< 0.01	
							whole fruit (calculation based on ratio flesh/ stone)	44	< 0.01	
South France, 2001 (Prune d'ente)	SC	0.055	0.006	1000	78	1	flesh after flesh/ stone separation	43	< 0.01	
							whole fruit (calculation based on ratio flesh/ stone)	43	< 0.01	
Spain, 2007 (Black Gold)	SC	0.055	0.0046	1200	81-85	1	flesh after stoning	0 3 7	0.03 0.02 0.02	Grolleau, 2008, SKR-0137 Storage interval: 137–159 days
							whole fruit assuming no residue in/ stone	0 3 7	0.03 0.02 0.02	
Spain, 2007 (Frias)	SC	0.055	0.0046	1200	85	1	flesh after stoning	0 3 7	0.01 < 0.01 < 0.01	
							whole fruit assuming no residue in/ stone	0 3 7	< 0.01 < 0.01 < 0.01	

Six residue trials on plums were conducted during the 2005 growing season in the USA. At each trial, two foliar directed airblast (or equivalent) applications of the WG formulation, containing nominally 720 g/kg ,at a rate of approximately 0.15 kg ai/ha were targeted at 14 days (± 1 day) intervals for a seasonal total of approximately 0.30 kg ai/ha.

Control samples were fortified with etoxazole and analysed both prior to and concurrently with field-treated samples. Fortification levels ranged from 0.01 to 1 mg/kg. Method validation recoveries ranged from 79 to 99%. The LOQ for fresh plums was statistically calculated as 0.004 mg/kg. The LOQ for dried plums was statistically calculated as 0.003 mg/kg. The maximum storage interval for field-treated samples in this study was 225 days in fresh plum fruit and 180 days in dried plum fruit. Storage stability samples of fresh fruits and dried plums fortified at 0.10 mg/kg etoxazole were analysed after 207 days and 167 days, and yielded recoveries (% remaining) that averaged 43% for fresh fruits and 104% for dried plums.

Table 46 Etoxazole residues on plums from supervised trials in USA

Plums country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*> 467*	*2*		*7*		
USA/MI, 2005 (Early Golden)	WG	0.15		953, 943	2	pitted fresh fruit	7	0.038, 0.044	Leonard, 2007 SKR-0152 Storage interval: 162–225 days
USA/ OR, 2005 (Brooks)	WG	0.15		1588, 1616	2	pitted fresh fruit	6	< 0.01, < 0.01	
USA/CA, 2005 (Hiromi)	WG	0.15		925, 943	2	pitted fresh fruit	7	0.014, 0.011	
USA/CA, 2005 (Angelino)	WG	0.15		663, 701	2	pitted fresh fruit	7	< 0.01, < 0.01	
USA/CA, 2005 (French)	WG	0.15		943, 943	2	pitted fresh fruit	7	0.012, 0.017	
USA/CA, 2005 (Casselman)	WG	0.15		1756, 1765	2	pitted fresh fruit	7	< 0.01, < 0.01	

The duplicate residues recorded in the table originate from duplicate field samples.

Nectarines

Five supervised field trials on nectarines were conducted in Australia. Two treatments of the SC formulation, containing 110 g/L etoxazole or the EC formulation containing 200 g/L pyriproxyfen and 160 g/L etoxazole, were applied. The average recovery of etoxazole from untreated samples fortified at 0.01 mg/kg and 0.25 mg/kg was 93.9%. The LOQ was 0.01 mg/kg.

Fortified samples were not extracted and analysed due to the samples being processed within 3 months of sample receipt (SKR-0143).

Table 47 Etoxazole residues on nectarines from supervised trials in Australia

Nectarines country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.077*	*0.0039*	*2000*	*1*		*21*		
Australia/NSW, 2005 (August Red)	SC		0.0039	To run off 1000–2000	2	whole fruit	0 7 14 21 28 42 56	0.05 0.03 0.02 0.01 < 0.01 < 0.01 < 0.01	Mitchell, 2006 SKR-0143 Storage interval: < 3 months
Australia/NSW, 2005	EC		0.004	To run off 1000–2000	2	whole fruit	0 7	0.03 0.02	

Nectarines country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
(August Red)							14 21 28 42 56	0.01 < 0.01 < 0.01 < 0.01 < 0.01	
Australia/WA, 2006 (Arctic Snow)	SC		0.0039	2437, 3801	2	whole fruit	7 14 28 42 56	0.01 < 0.01 < 0.01 < 0.01 < 0.01	Burn, 2006 SKR-0144 Storage interval: 134–202 days
Australia/VIC, 2006 (Arctic Snow)	SC		0.0039	1000, 1333	2	whole fruit	7	0.12	
Australia/QLD, 2006 (Summer Blush)	SC		0.0039	2408, 2465	2	whole fruit	7	0.01	

Peaches

Etoxazole was applied to peaches at two trials in Northern France (Northern Europe) and at eleven trials in Southern France, Greece, Italy and Spain (Southern Europe). Seven trials were conducted as decline curve studies and the other six as single point harvest studies. Peaches were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts, frozen or refrigerated, was confirmed by procedural recoveries which were analysed in parallel with the field samples.

Table 48 Etoxazole residues on peaches from supervised trials in Europe

Peaches country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, France	*SC*		*0.0055*			*1*		*14*		
GAP, Greece	*SC*	*0.055*	*0.0055*	*1500*		*1*		*14*		
GAP, Italy and Spain	*SC*	*0.055*	*0.0055*			*1*		*14*		
Northern Europe										
North France, 2000 (Springcrest)	SC	0.055	0.0055	1000	85	1	flesh after flesh/ stone separation	13	0.02	Grolleau, 2001, SKR-0086 Storage interval: 46–62 days
							whole fruit (calculation based on ratio flesh/ stone)	13	0.02	
North France, 2000 (Dixired)	SC	0.055	0.0055	1000	77	1	flesh after flesh/ stone separation	13	0.02	
							whole fruit (calculation based on ratio flesh/ stone)	13	0.02	
Southern Europe										
South France, 1999 (Flowercrest)	SC	0.055	0.0069	800	75	1	flesh after flesh/ stone separation	0 4 8 14	0.11 0.04 0.03 0.02	Grolleau, 2000, SKR-0083 Storage interval:
							whole fruit (calculation	0 4	0.09 0.04	

Peaches country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
							based on ratio flesh/ stone)	8 14	0.03 0.02	117–153 days
South France, 1999 (Elegant Lady)	SC	0.055	0.0069	800	77	1	flesh after flesh/ stone separation	13	0.02	
							whole fruit (calculation based on ratio flesh/ stone)	13	0.02	
South France, 1999 (Tendresse)	SC	0.055	0.0069	800	75	1	flesh after flesh/ stone separation	13	0.02	
							whole fruit (calculation based on ratio flesh/ stone)	13	0.02	
South France, 2002 (Summer Lady)	SC	0.055	0.0046	1200	73-81	1	flesh	14 27 34 40	< 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2003, SKR-0123
							whole fruit (theoretical residue assuming no residue in/ stone)	14 27 34 40	< 0.01 < 0.01 < 0.01 < 0.01	Storage interval: 21–22 days
South France, 2002 (Opale)	SC	0.055	0.0046	1200	73-77	1	flesh	13 28 35 41	0.02 < 0.01 0.01 0.01	
							whole fruit (theoretical residue assuming no residue in/ stone)	13 28 35 41	0.02 < 0.01 0.01 0.01	
South France, 2002 (July Lady)	SC	0.055	0.0046	1200	73-76	1	flesh	14 28 35 42	0.02 0.01 < 0.01 < 0.01	
							whole fruit (theoretical residue assuming no residue in/ stone)	14 28 35 42	0.02 0.01 < 0.01 < 0.01	
Greece, 2000 (Maria Blanca)	SC	0.055	0.0069	800	75-77	1	flesh after flesh/ stone separation	0 3 7 14 21	< 0.01 0.02 < 0.01 < 0.01 < 0.01	Grolleau, 2001, SKR-0076
							whole fruit (calculation based on ratio flesh/ stone)	0 3 7 14 21	< 0.01 0.02 < 0.01 < 0.01 < 0.01	Storage interval: 41–99 days
Italy, 2000	SC	0.055	0.0055	1000	81	1	flesh after	0	0.22	

Peaches country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
(Cresthaven)							flesh/ stone separation	3 7 14 21	0.10 0.14 0.05 0.04	
							whole fruit (calculation based on ratio flesh/ stone)	0 3 7 14 21	0.20 0.09 0.13 0.04 0.04	
Italy, 2000 (Fayette)	SC	0.055	0.0055	1000	81	1	flesh after flesh/ stone separation	14	0.06	
							whole fruit (calculation based on ratio flesh/ stone)	14	0.06	
Spain, 2000 (Andros)	SC	0.055	0.005	1100	75	1	flesh after flesh/ stone separation	0 3 7 14 21	0.15 0.11 0.073 0.020 0.021	Grolleau, 2001, SKR-0088 Storage interval: 36–57 days
							whole fruit (calculation based on ratio flesh/ stone)	0 3 7 14 21	0.12 0.09 0.06 0.02 0.02	
Spain, 2000 (Carson)	SC	0.055	0.0055	1000	75	1	flesh after flesh/ stone separation	15	0.039	
							whole fruit (calculation based on ratio flesh/ stone)	15	0.04	

Twelve residue trials on peaches were conducted in the USA during the 2005 growing season. At each trial, two foliar directed airblast (or equivalent) applications of the WG formulation, containing nominally 720 g/kg, at a rate of approximately 0.15 kg ai/ha were targeted at 14 days (± 1 day) intervals for a seasonal total of approximately 0.30 kg ai/ha.

Control samples were fortified with etoxazole and analysed both prior to and concurrently with field-treated samples. Fortification levels ranged from 0.01 to 1 mg/kg. Method validation recoveries ranged from 80 to 103%. The LOQ for fresh peaches was statistically calculated as 0.016 mg/kg. The maximum storage interval for field-treated samples in this study was 267 days in fresh peach fruit. Storage stability samples fortified at 0.10 mg/kg etoxazole were analysed after 278 days and yielded recoveries (% remaining) that averaged 50%.

Table 49 Etoxazole residues on peaches from supervised trials in USA

Peaches country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*> 467*	*2*		*7*		
USA/NJ, 2005 (Dixie Red)	WG	0.15		598, 887	2	pitted fresh fruit	6	0.12, 0.12	Leonard, 2007 SKR-0153
USA/ NJ, 2005 (Suncrest)	WG	0.15		962, 934	2	pitted fresh fruit	7	0.17, 0.13	

Peaches country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	Water, L/ha	no.				
USA/NY, 2005 (Harcrest)	WG	0.15		953, 934	2	pitted fresh fruit	8	0.17, 0.26	Storage interval: 143–267 days
USA/NC, 2005 (Contender)	WG	0.15		1046, 1025	2	pitted fresh fruit	7	0.06, 0.11	
USA/NC, 2005 (Emery)	WG	0.15		1065, 1055	2	pitted fresh fruit	6	0.17, 0.16	
USA/MI, 2005 (Elberta)	WG	0.15		962, 925	2	pitted fresh fruit	8	0.16, 0.22	
USA/TN, 2005 (Red Skin)	WG	0.15		551, 560	2	pitted fresh fruit	7	0.061, 0.062	
USA/TX, 2005 (Gold Prince)	WG	0.15		514, 514	2	pitted fresh fruit	7	0.11, 0.084	
USA/CA, 2005 (Flavorcrest)	WG	0.15		747, 738	2	pitted fresh fruit	7	0.15, 0.14	
USA/CA, 2005 (Henry)	WG	0.15		1990, 2018	2	pitted fresh fruit	7	0.070, 0.094	
USA/CA,2005 (May Sun)	WG	0.15		2186, 2130	2	pitted fresh fruit	6	0.094, 0.12	
USA/CA, 2005 (Last Chance)	WG	0.15		953, 934	2	pitted fresh fruit	7	0.12, 0.13	

The duplicate residues recorded in the table originate from duplicate field samples.

Five supervised field trials on peaches were conducted in Australia. The treatment were uniformly applied to peaches on two occasions using the SC formulation containing 110 g/L etoxazole or the EC formulation containing 200 g/L pyriproxyfen and 160 g/L etoxazole. The average recovery of etoxazole from untreated samples fortified at 0.01 mg/kg and 0.25 mg/kg was 93.9%. The LOQ was 0.01 mg/kg.

Fortified samples were not extracted and analysed due to the samples being processed within 3 months of sample receipt (SKR-0143).

Table 50 Etoxazole residues on peaches from supervised trials in Australia

Peaches country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.077*	*0.0039*	*2000*	*1*		*21*		
Australia/VIC, 2005 (Taylor Queen)	SC		0.0039	To run off 1000–2000	2	whole fruit	0 7 14 21 28	0.22 0.12 0.08 0.05 0.02	Mitchell, 2006 SKR-0143 Storage interval: < 3 months
Australia/VIC, 2005 (Taylor Queen)	EC		0.004	To run off 1000–2000	2	whole fruit	0 7 14 21 28	0.12 0.08 0.05 0.04 0.01	
Australia/VIC, 2006 (Taylor Queen)	SC		0.0039	1600	2	whole fruit	7 14 28 42 56	0.01 < 0.01 < 0.01 < 0.01 < 0.01	Burn, 2006 SKR-0144 Storage interval: 134–203 days
Australia/QLD, 2006 (Late Cling)	SC		0.0039	1300, 1763	2	whole fruit	7	< 0.01	
Australia/SA, 2006 (Tasty Zee)	SC		0.0039	1616	2	whole fruit	7	0.01	

Berries and other small fruits

Grapes

Etoxazole was applied to grapes at eight trials in Northern France (Northern Europe) and at eight trials in Southern France (Southern Europe). Eight trials were conducted for decline curve studies and the other eight for harvest studies. Grapes were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 51 Etoxazole residues on grapes from supervised trials in Europe

Grapes country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, France	*SC*	*0.055* *0.028*				*1* *1*		*120* *35*		
Northern Europe										
North France, 1996 (Pinot noir)	SC	0.054		297		1	fruit	35 55 83 129	< 0.010 < 0.010 < 0.010 < 0.010	Maestracci, 1997 SKR-0017 Storage interval: 3–6 months
North France, 1996 (Chenin blanc)	SC	0.056		288		1	fruit	28 48 77 127	0.085 < 0.010 < 0.010 < 0.010	
North France, 1996 (Gamay)	SC	0.058		291		1	fruit	116	< 0.010	Maestracci, 1997 SKR-0018 Storage interval: 3 months
North France, 1996 (Meunier)	SC	0.057		288		1	fruit	124	< 0.010	
North France, 2000 (Chenin)	SC	0.028	0.009	300	85	1	berries	0 7 14 28 42	0.01 < 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2001, SKR-0089 Storage interval: 25–67 days
North France, 2000 (Cabernet Franc)	SC	0.028	0.009	300	83 - 85	1	berries	29	< 0.01	
North France, 2000 (Chenin)	SC	0.028	0.009	300	87	1	berries	28	< 0.01	
North France, 1999 (Chenin (White cultivar)) -Wine grape-	SC	0.025	0.0063	400	71 - 83	1	berries	20 29 42 60 90	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2000, SKR-0080 Storage interval: 38 days
Southern Europe										
South France, 1996 (Cabernet franc)	SC	0.060		339		1	fruit	36 58 86 140	0.018 < 0.010 < 0.010 < 0.010	Maestracci, 1997 SKR-0017 Storage interval; 3–6 months
South France, 1996 (Grenache)	SC	0.055		279		1	fruit	26 48 77 119	0.051 < 0.010 < 0.010 < 0.010	
South France, 1996 (Cabernet Sauvignon)	SC	0.052		323		1	fruit	134	< 0.010	Maestracci, 1997 SKR-0018

Grapes country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
South France, 1996 (Aubun)	SC	0.052		318		1	fruit	118	< 0.010	Storage interval: 3 months
South France, 2000 (Ugni Blanc)	SC	0.028	0.009	300	83	1	berries	0 7 14 28 40	0.02 < 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2001, SKR-0089 Storage interval: 25–67 days
South France, 2000 (Merlot)	SC	0.028	0.009	300	83	1	berries	28	< 0.01	
South France, 2000 (Tannat)	SC	0.028	0.009	300	83	1	berries	27	< 0.01	
South France, 1999 (Merlot (Red cultivar) -Wine grape-	SC	0.025	0.0063	400	71 - 83	1	berries	21 28 41 60 89	< 0.01 0.01 < 0.01 < 0.01 < 0.01	Grolleau, 2000, SKR-0080 Storage interval: 38 days

Twelve residue trials were established in typical grape growing areas in USA, using commercially available varieties of grapes. The WG formulation, containing nominally 720 g/kg, was applied in a two-application program. Treatments consisted of foliar spray applications, applying approximately 0.15 kg ai/ha, made 35 and 14 days before normal harvest. At one trial, the grapes were treated at an exaggerated rate (5×, 2 applications × 0.30 kg ai/ha, 14 day PHI), harvested samples were used for processing into juice and raisins.

Residue analyses were conducted by gas chromatography using a mass selective detector (MSD) or a nitrogen-phosphorous detector (NPD). Approximately one-third of the samples were analysed with at a LOQ of 0.002 mg/kg. The remaining sets were analysed with at a LOQ of 0.01 mg/kg. The stability of etoxazole in grapes samples, stored under frozen conditions, was evaluated by extracting samples that had been previously analysed and stored frozen between analyses. Samples from this study were extracted within 64 days from sampling. Recoveries of etoxazole from the fortified samples averaged 92.6 ± 16.8% for grapes, demonstrating the stability of etoxazole residues in the sample extracts during the frozen storage.

Table 52 Etoxazole residues on grapes from supervised trials in USA

Grapes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*234–1868*	*1*		*14*		
USA/NY, 2002 (Concord)	WG	0.15		948, 949	2	fruit	7 10 14 21	0.031, 0.034 0.027, 0.030 0.045, 0.054 0.036, 0.061	Schreier, 2003 SKR-0151
USA/ PA, 2002 (Concord)	WG	0.15		914, 903	2	fruit	14	0.035, 0.031	Storage interval: 42–64 days (harvest to extraction)
USA/CA, 2002 (Flame Seedless)	WG	0.15		931, 931	2	fruit	7 14 20	0.10, 0.10 0.034, 0.032 0.033, 0.040	
USA/OR, 2002 (Chardonnay)	WG	0.15		952, 970	2	fruit	14	0.028, 0.031	
		0.30		936, 969	2	fruit	14	0.073, 0.068	
USA/CA, 2002 (Crimson)	WG	0.15		918, 954	2	fruit	14	0.033, 0.040	

Grapes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/CA, 2002 (Thompson Seedless)	WG	0.15		926, 934	2	fruit	14	0.037, 0.039	
USA/CA, 2002 (Centurion)	WG	0.15		935, 932	2	fruit	14	0.014, 0.010	
USA/CA, 2002 (Thompson Seedless)	WG	0.15		937, 976	2	fruit	13	0.045, 0.039	
USA/CA, 2002 (Cabernet)	WG	0.15		964, 950	2	fruit	14	0.10, 0.10	
USA/CA, 2002 (Chardonnay)	WG	0.15		980, 941	2	fruit	13	0.21, 0.33	
USA/ ID, 2002 (Concord)	WG	0.15		948, 930	2	fruit	13	0.051, 0.040	
USA/CA, 2002 (Thompson Seedless)	WG	0.15		948, 942	2	fruit	14	< 0.005, 0.008	
		0.75		953, 943	2	fruit	14	0.096, 0.11	

The duplicate residues recorded in the table originate from duplicate field samples.

Strawberry

A total of nine supervised trials were conducted on strawberries in 1999 and 2000 in the USA. At four trials etoxazole was applied using a WP formulation containing 800 g/kg etoxazole, in the remaining trials the WG formulation, containing 720 g/kg etoxazole, was used. Two applications of etoxazole at 0.15 kg ai/ha per application were made 21 days apart with samples collected 1 day after the last application. At one test site, additional plots were treated with a total seasonal rate of 0.20 kg ai/ha (0.67× rate), and 0.60 kg ai/ha (2× rate).

The analytical method was validated with analyses by spiking control samples with etoxazole at fortification levels ranging from 0.002 to 0.01 mg/kg. The LOQ was 0.002 mg/kg. The maximum interval from harvest to extraction for analysis for etoxazole on strawberries was 51 days. Residues of etoxazole were found to be stable in/on strawberries with 55% remaining of the applied material recovered following frozen storage for a period of 60 days.

Table 53 Etoxazole residues on strawberries from supervised trials in USA

Strawberries country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*934–2802*	*1*		*1*		
USA/NC, 1999 (Chandler)	WP	0.15		621, 628	2	fruit	0 1 2 4	0.12, 0.082 0.14, 0.14 0.093, 0.075 0.061, 0.071	Schreier, 2001 SKR-0102 Storage interval: 8–51 days
USA/ OH, 1999 (All Star)	WP	0.15		508, 498	2	fruit	1	0.15, 0.13	
USA/CA, 1999 (Camarosa)	WP	0.15		1501, 687	2	fruit	1	0.13, 0.12	
USA/OR, 1999 (Totem)	WP	0.10		476, 482	2	fruit	1	0.051, 0.047	
		0.15		476, 482	2	fruit	1	0.084, 0.069	
		0.30		476, 482	2	fruit	1	0.099, 0.076	
USA/PA, 2000 (Earliglow)	WG	0.15		1031, 1029	2	fruit	0 1 2 4	0.037, 0.037 0.031, 0.028 0.038, 0.029 0.026, 0.032	

Strawberries country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	Kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/FL, 2000 (Camarosa)	WG	0.15		1295, 1372	2	fruit	1	0.037, 0.068	
USA/CA, 2000 (PSI Variety #592)	WG	0.15		1410, 1401	2	fruit	1	0.29, 0.32	
USA/CA, 2000 (Seascape)	WG	0.15		1111, 1118	2	fruit	1	0.080, 0.13	
USA/OR, 2000 (Selva)	WG	0.15		1403, 1396	2	fruit	1	0.072, 0.094	

The duplicate residues recorded in the table originate from duplicate field samples.

Fruiting vegetables, Cucurbits

Cantaloupe

Nine supervised trials on cucumbers were conducted during the 2004 growing season, in the USA. At each site, two broadcast foliar applications of the 720 g/kg WG formulation were made at a rate of approximately 0.15 kg ai/ha with a spray interval of 21 days (± 2 days) for a seasonal total of approximately 0.30 kg ai/ha.

Recovery values for spiked control cantaloupe fruit samples fortified at 0.01 and 0.1 mg/kg, prior to the analysis of study samples, were 87% ± 6%, and 84% ± 6%, respectively. The LOQ for cantaloupe fruit was statistically calculated as 0.0046 mg/kg. The maximum storage interval for field-treated samples in this study was 72 days. Storage stability samples fortified at 0.10 mg/kg etoxazole were analysed after 50 and 126 days and yielded recoveries (% remaining) that averaged 55% and 63%, respectively.

Table 54 Etoxazole residues on cantaloupe from supervised trials in USA

Cantaloupe country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*			*1*		*7*		
USA/MD, 2004 (Athena)	WG	0.15		337, 338	2	fruit	7	0.044, 0.046	Leonard, 2006 IR-4 PR No. 09018 SKR-0139 Maximum storage interval: 72 days
USA/GA, 2004 (Hales Best Jumbo)	WG	0.15		301, 305	2	fruit	5	0.022, 0.020	
USA/WI, 2004 (Sweet and Early)	WG	0.15		222, 218	2	fruit	8	0.067, 0.067	
USA/ TX, 2004 (Primo)	WG	0.15		263, 252	2	fruit	6	0.026, 0.036	
USA/TX, 2004 (Cruiser)	WG	0.15		320, 308	2	fruit	6	0.027, 0.044	
USA/NM, 2004 (Topmark)	WG	0.15		521, 544	2	fruit	7	0.020, 0.014	
USA/CA, 2004 (Hy-Mark)	WG	0.15		245, 219	2	fruit	6	0.016, 0.019	
USA/CA, 2004 (Western Sunrise)	WG	0.15		282, 280	2	fruit	7	0.080, 0.079	
USA/NM, 2004 (Topmark)	WG	0.15		134, 128	2	fruit	3 8 14	0.032, 0.036 0.015, 0.011 0.007, 0.005	

The duplicate residues recorded in the table originate from duplicate field samples.

Cucumber

Nine supervised trials on cucumbers were conducted during the 2005 growing season in the USA. At each trial, two foliar applications of the 720 g/kg WG formulation were made at a rate of approximately 0.15 kg ai/ha at an interval of 21 days (± 2 days) for a seasonal total of approximately 0.30 kg ai/ha.

Recovery values for spiked control cucumber fruit samples fortified at 0.01, 0.1 and 1.0 mg/kg prior to the analysis of study samples were 121% ± 4%, 109% ±2%, and 96% ± 7%, respectively. The LOQ for cucumber fruit was statistically calculated as 0.0052 mg/kg. The maximum storage interval for treated samples in this study was 136 days. Storage stability samples of cucumber fortified at 0.10 mg/kg etoxazole were analysed after 158 days and yielded recoveries (% remaining) that averaged 84%.

Table 55 Etoxazole residues on cucumber from supervised trials in USA

Cucumber country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	Kg ai/hL	Water, L/ha	no.				
GAP, USA	*WP*	*0.15*		*> 467*	*2*		*7*		
USA/MD, 2005 (Genuine)	WG	0.15		224, 224	2	fruit	3 7 9 14	0.020, 0.026 < 0.01, < 0.01 < 0.01, < 0.01 < 0.01, < 0.01	Leonard, 2008 SKR-0154 Storage interval: 111–136 days, 18 days (TX)
USA/MD, 2005 (Little Leaf)	WG	0.15		215, 224	2	fruit	6	< 0.01, < 0.01	
USA/NC, 2005 (Dasher II)	WG	0.15		318, 308	2	fruit	6	< 0.01, < 0.01	
USA/ FL, 2005 (Dasher II)	WG	0.15		290, 290	2	fruit	6	< 0.01, 0.013	
USA/TN, 2005 (Long Green)	WG	0.15		187, 187	2	fruit	7	< 0.01, < 0.01	
USA/WI, 2005 (Marketmore)	WG	0.15		205, 205	2	fruit	8	< 0.01, < 0.01	
USA/OH, 2005 (Regal)	WG	0.15		458, 467	2	fruit	7	< 0.01, < 0.01	
USA/TX, 2005 (Royal)	WG	0.15		355, 346	2	fruit	7	0.014, 0.010	
USA/CA, 2005 (SMR58)	WG	0.15		140, 224	2	fruit	3 7 10 14	< 0.01, < 0.01 < 0.01, < 0.01 < 0.01, < 0.01 < 0.01, < 0.01	

The duplicate residues recorded in the table originate from duplicate field samples.

Fruiting vegetables, other than Cucurbits

Peppers

Six supervised field trials on peppers were conducted in Australia. Treatments included two applications of the SC formulation containing 110 g/L etoxazole, the EC formulation containing 200 g/L pyriproxyfen and 160 g/L etoxazole or the EC formulation containing 100 g/L pyriproxyfen and 160 g/L etoxazole. The average recovery of etoxazole from untreated samples fortified at 0.01 mg/kg and 0.5 mg/kg was 99.9%. The LOQ was 0.01 mg/kg.

Table 56 Etoxazole residues on peppers from supervised trials in Australia

Tomatoes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.019*	*0.0039*	*500*	*1*		*7*		
Australia/QLD,	SC	0.040			2	whole	0	0.03	Burn, 2005

Tomatoes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
2004						fruit	1 3	0.03 0.03	SKR-0142
Australia/QLD, 2004	SC	0.080			2	whole fruit	0 1 3	0.07 0.06 0.06	Storage interval: 196 days
Australia/QLD, 2004	EC	0.040			2	whole fruit	0 1 3	0.04 0.03 0.04	
Australia/QLD, 2004	EC	0.080			2	whole fruit	0 1 3	0.08 0.08 0.08	
Australia/QLD, 2004	EC	0.080			2	whole fruit	0 1 3	0.08 0.08 0.08	
Australia/QLD, 2004	EC	0.16			2	whole fruit	0 1 3	0.14 0.14 0.11	

Tomato

A total of fourteen supervised trials on tomatoes were conducted during 2002, 2003 and 2007 in Europe. Etoxazole was applied to tomatoes in four outdoor trials in Greece, Italy and Spain (Southern Europe), and in ten indoor trials in Netherlands (Northern Europe), Southern France, Greece, Italy and Spain (Southern Europe). Six trials on cherry tomatoes were conducted in greenhouses (indoor). Eight trials were conducted for decline curve studies and the remainder for single point harvest studies. Tomatoes were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 57 Etoxazole residues on tomatoes from supervised trials in Europe

Tomatoes country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, Netherlands *GAP, Greece*	*SC* *SC*	*0.055* *0.055*	*0.0055* *0.011*	*500–1000* *500–1500*		*1* *1*		*3* *3*		
Open Field										
Greece, 2003 (Dual Large)	SC	0.055	0.011	504	85 - 86	1	whole fruit	0 3 7	< 0.01 0.01 0.02	Bousquet, 2004, SKR-0120 Storage interval: 16–25 days
Italy, 2002 (16-35)	SC	0.055	0.009	600	78	1	whole fruit	0 3 7	0.04 0.02, 0.03 < 0.01	Grolleau, 2002, SKR-0094 Storage interval: 24–31 days
Italy, 2003 (Ruphus)	SC	0.055	0.007	800	87	1	whole fruit	3	0.02	Bousquet, 2004, SKR-0105 Storage interval: 15 days
Spain, 2002 (Valentin)	SC	0.055	0.007	757	72 - 73	1	whole fruit	3	< 0.01, 0.01	Grolleau, 2002, SKR-0125 Storage

Tomatoes country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
										interval:33 days
Protected (Greenhouse)										
Netherlands, 2002 (Durinta)	SC	0.055	0.006	1000	60 - 89	1	whole fruit	0 3 7	0.02 0.02, 0.03 0.02	Grolleau, 2002, SKR-0095 Storage interval: 36–53 days
Netherlands, 2002 (Favorieta) -Cherry Tomato-	SC	0.055	0.006	1000	60 - 85	1	whole fruit	3	0.03, 0.02	
Netherlands, 2007 (Claree) -Cherry Tomato-	SC	0.055	0.0046	1200	60 - 85	1	whole fruit	0 3 7	0.03 0.03, 0.02 0.02	Grolleau, 2007, SKR-0134 Storage interval: 6–14 days
Netherlands, 2007 (Juanita) -Cherry Tomato-	SC	0.055	0.0046	1200	60 - 87	1	whole fruit	0 3 7	0.03 0.03, 0.03 0.01	
South France, 2003 (Alicia) -Cherry Tomato-	SC	0.055	0.005	1200	89	1	whole fruit	0 3 7	0.11 0.08, 0.03 0.05	Bousquet, 2003, SKR-0116 Storage interval: 50–57 days
Greece, 2003 (Noa)	SC	0.055	0.004	1354	80	1	whole fruit	3	< 0.01, 0.01	Bousquet, 2003, SKR-0117 Storage interval: 34 days
Italy, 2003 (Italdor)	SC	0.055	0.004	1500	76 - 79	1	whole fruit	0 3 7	0.03 0.03, 0.03 0.03	Bousquet, 2004, SKR-0106 Storage interval: 19–46 days
Italy, 2003 (Shyren) -Cherry Tomato-	SC	0.055	0.004	1500	76 - 79	1	whole fruit	3	0.03, 0.02	
Spain, 2002 (Brillante)	SC	0.055	0.0039	1400	82	1	whole fruit	0 3 6	0.01, 0.02 < 0.01, 0.02 0.01, < 0.01	Grolleau, 2002, SKR-0126 Storage interval: 19–25 days
Spain, 2002 (Valentin)	SC	0.055	0.0042	1300	81	1	whole fruit	3	0.01, 0.02	

Three greenhouse trials on tomatoes were conducted during the 2005–2006 growing season, one in New Jersey, one in Florida, and one in Colorado. At each trial, two foliar directed applications of the WG formulation containing 720 g/L etoxazole at a rate of approximately 0.15 kg ai/ha were targeted at 21 days (± 2 days) interval for a total of approximately 0.30 kg ai/ha per season.

Recovery values for spiked control tomato fruit samples fortified at 0.01, 0.1 and 1.0 mg/kg prior to the analysis of study samples were 104% ± 7%, 96% ± 6%, and 99% ± 4%, respectively. The LOQ for greenhouse tomato fruit was statistically calculated as 0.004 mg/kg. The maximum storage interval for greenhouse treated samples in this study was 207 days. Storage stability samples of greenhouse tomatoes fortified at 0.10 mg/kg etoxazole were analysed after 214 days and yielded recoveries (% remaining) that averaged 87%.

Table 58 Etoxazole residues on tomatoes from supervised trials in USA

Tomatoes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WG*	*0.14*			*2*		*1*		
USA/NJ, 2005 (Florida 47)	WG	0.15		673, 663	2	whole fruit	1	0.014, < 0.01	Leonard, 2008 SKR-0155 Storage interval: 180–207 days, 9 days (CO)
USA/CO, 2006 (Favorita F1)	WG	0.15		271, 290	2	whole fruit	1	0.053, 0.051	
USA/FL, 2005 (Florida 47)	WG	0.15		290, 271	2	whole fruit	1	0.046, 0.018	

The duplicate residues recorded in the table originate from duplicate field samples.

Six supervised field trials on tomatoes were conducted in Australia. The treatments consisted of two applications using the SC formulation containing 110 g/L etoxazole, the EC formulation containing 200 g/L pyriproxyfen and 160 g/L etoxazole or the EC formulation containing 100 g/L pyriproxyfen and 160 g/L etoxazole. The average recovery of etoxazole from untreated samples, fortified at 0.01 mg/kg and 0.5 mg/kg, was 99.9%. The LOQ was 0.01 mg/kg.

Table 59 Etoxazole residues on tomatoes from supervised trials in Australia

Tomatoes country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.019*	*0.0039*	*500*	*1*		*7*		
Australia/VIC, 2004	SC	0.040			2	whole fruit	0 1 3	0.03 0.03 0.02	Burn, 2005 SKR-0142 Storage interval: 188 days
Australia/VIC, 2004	SC	0.080			2	whole fruit	0 1 3	0.06 0.06 0.04	
Australia/VIC, 2004	EC	0.040			2	whole fruit	0 1 3	0.04 0.03 0.02	
Australia/VIC, 2004	EC	0.080			2	whole fruit	0 1 3	0.06 0.06 0.04	
Australia/VIC, 2004	EC	0.080			2	whole fruit	0 1 3	0.06 0.05 0.04	
Australia/VIC, 2004	EC	0.16			2	whole fruit	0 1 3	0.14 0.12 0.09	

Tree nuts

Almonds

Five residue trials were established in typical almond growing areas in the USA (California). The WG formulation containing 720 g/kg was applied in a two-application program. Treatments consisted of foliar spray applications, applying approximately 0.15 kg ai/ha, made 49 and 28 days before normal harvest. At one trial site, an additional plot was treated using a 2× rate of approximately 0.30 ai kg/ha per application.

The stability of etoxazole in almond nutmeat was evaluated by spiking untreated nutmeat samples with a known amount of etoxazole, storing the samples and analysing samples after 70 days of storage. Recoveries (% remaining after storage) from the fortified samples averaged 98.6–101%, demonstrating the stability of etoxazole residues in the sample extracts during frozen storage. For the etoxazole residue in the almond nutmeat, the LOQ was 0.01 mg/kg, and the limit of detection (LOD) was 0.005 mg/kg.

Table 60 Etoxazole residues on almonds from supervised trials in USA

Almonds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*			*1*		*28*		
USA/CA, 2002 (Non-Pareil)	WG	0.15		949, 928	2	nutmeats	28	< 0.005, < 0.005	Schreier, 2003 SKR-0138 Srotage interval: 53–59 days (harvest to extraction)
USA/CA, 2002 (Non-Pareil)	WG	0.15		938, 928	2	nutmeats	28	< 0.005, < 0.005	
USA/CA, 2002 (Non-Pareil)	WG	0.15		940, 968	2	nutmeats	28	< 0.005, < 0.005	
USA/CA, 2002 (Non-Pareil)	WG	0.15		945, 938	2	nutmeats	14 21 28 35	< 0.005,< 0.005 < 0.005,< 0.005 < 0.005,< 0.005 < 0.005,< 0.005	
USA/CA, 2002 (Carmel)	WG	0.15		938, 936	2	nutmeats	28	0.005, < 0.005	
		0.30		918, 932	2	nutmeats	28	< 0.005, < 0.005	

The duplicate residues recorded in the table originate from duplicate field samples.

Pecans

Five supervised trials on pecans were conducted in USA using a WG formulation containing 720 g/kg etoxazole. Applications were made in a two spray program at a rate of 0.15 kg ai/ha per application, and 0.30 kg ai/ha per application (2× plot). All applications were foliar airblast at a 21 day interval with the last application occurring 28 days before harvest, except one trial. In that trial, pecans were harvested 14, 21, 28 and 35 days after the last application.

The analytical method was validated with analyses by spiking control samples with etoxazole at 0.01 mg/kg and 0.05 mg/kg. The LOQ for pecans was 0.01 mg/kg, and the LOD was 0.005 mg/kg.

Table 61 Etoxazole residues on pecans from supervised trials in USA

Pecans country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*			*1*		*28*		
USA/GA, 2002 (Summer)	WG	0.15		921, 923	2	nutmeats	28	< 0.005,< 0.005	Schreier, 2003 SKR-0140 Storage interval: 33–70 days
USA/SC, 2002 (Desirables)	WG	0.15		917, 914	2	nutmeats	28	< 0.005,< 0.005	
		0.30		926, 916	2	nutmeats	28	< 0.005,< 0.005	
USA/MS, 2002 (Forkert)	WG	0.15		938, 926	2	nutmeats	28	< 0.005,< 0.005	
USA/OK, 2002 (Natives)	WG	0.15		959, 947	2	nutmeats	14 21 28 35	< 0.005,< 0.005 < 0.005,< 0.005 < 0.005,< 0.005 < 0.005,< 0.005	
USA/TX, 2002 (Western Schley)	WG	0.15		937, 921	2	nutmeats	28	< 0.005, < 0.005	

The duplicate residues recorded in the table originate from duplicate field samples.

Oilseed

Cotton seed

Etoxazole was applied to cotton at four trials in Greece and Spain (Southern Europe). Cotton was sprayed once at a rate of 0.033 kg ai/ha with a SC formulation containing 110 g ai/L.

The storage stability of etoxazole in sample extracts in freezer or refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 62 Etoxazole residues on cotton seeds from supervised trials in Europe

Cotton seeds country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
GAP, Greece *GAP, Spain*	*SC* *SC*	*0.041* *0.041*	*0.0083*	*500-800*		*1* *1*		*35* *-*		
Greece, 1999 (Bravo)	SC	0.033	0.0066	500	79	1	Seeds	34	< 0.01	Grolleau, 2000, SKR-0072 Storage interval: 81 days
Greece, 2000 (Midas)	SC	0.030	0.0043	700	78 - 79	1	Seeds	35	< 0.01	Grolleau, 2001, SKR-0078 Storage interval: 66 days
Spain, 1999 (La Chata)	SC	0.033	0.006	550	79	1	Seeds	36	< 0.01	Grolleau, 2000, SKR-0079 Storage interval: 84 days
Spain, 2000 (Crema 111)	SC	0.030	0.004	750	79	1	Seeds	35	< 0.01	Grolleau, 2001, SKR-0085 Storage interval: 45 days

Thirteen supervised residue trials on cotton were conducted in 1997, 1998 and 1999 in USA using either a SC formulation containing 360 g/L etoxazole or a WP formulation containing 800 g/L etoxazole. For all trials the application rate was 0.050 kg ai/ha per application. Two application were made 21 days apart with samples collected at 21 (1997 trials) and 28 (1998 and 1999 trials) days after the last application. Ginned cottonseed was collected from all trials. At three test sites, an additional test plot was treated with a total seasonal rate of 0.20 kg ai/ha (2× rate). At two test sites, an additional test plot was treated with a total seasonal rate of 0.50 kg ai/ha (5× rate).

The LOQ of etoxazole in cottonseed was 0.01 mg/kg, and the LOD was 0.005 mg/kg.

The laboratory spiked freezer storage stability studies of etoxazole in/on ginned cottonseed were conducted concurrently with the residue studies. The results indicate that etoxazole is stable in/on ginned cottonseed during the period studied, with 89% of the etoxazole remaining in ginned cottonseed after 513 days. The maximum storage interval from sample collection to extraction for analysis was 228 days for ginned cottonseed.

Table 63 Etoxazole residues on cotton seeds from supervised trials in USA

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.050*			*1*		*28*		
USA/GA, 1997 (Sure Grow 1001)	SC	0.05	0.038	134, 135	2	seed	20	0.008, 0.013	Schreier, 2000 SKR-0090 Storage interval:
USA/AR, 1997 (PM1215RR)	SC	0.05	0.038	143, 137	2	seed	20	< 0.005, < 0.005	
USA/CA, 1997 (Maxxa)	SC	0.05	0.038	139, 141	2	seed	20	0.014, 0.023	

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/TX, 1997 (Delta Pine 5415RR)	SC	0.05	0.038	146, 136	2	seed	21	< 0.005, < 0.005	76–228 days 7 days (TX,1997)
USA/TX, 1997 (HS-200)	SC	0.05	0.038	143, 140	2	seed	14 21 28	< 0.005, < 0.005 < 0.005, < 0.005 < 0.005, < 0.005	
USA/AZ, 1997 (Delta Pine 5461)	SC	0.05	0.038	142, 138	2	seed	21	< 0.005, < 0.005	
		0.11	0.076	139, 141	2	seed	21	< 0.005, < 0.005	
USA/CA, 1998 (Maxxa)	WP	0.05	0.036	136, 144	2	seed	28	0.007, 0.005	
USA/LA, 1998 (DP33B)	WP	0.05	0.036	140, 138	2	seed	27	< 0.005, < 0.005	
USA/MS, 1998 (ST474)	SC	0.05	0.036	141, 139	2	seed	28	0.006, 0.007	
	WP	0.05	0.036	141, 139	2	seed	20	< 0.005, < 0.005	
USA/TX, 1999 (PM 2326)	WP	0.05	0.035	139, 141	2	seed	28	< 0.005, < 0.005	
USA/TX, 1999 (Delta Pine 2156)	WP	0.05	0.030	181, 169	2	seed	28	0.017, 0.011	
USA/TX, 1999 (DP 2379)	WP	0.05	0.045	112, 116	2	seed	28	0.011, 0.013	
		0.10	0.090	112, 113	2	seed	28	0.044, 0.040	
		0.25	0.22	112, 114	2	seed	28	0.093, 0.14	
USA/TX, 1999 (PM2200RR)	WP	0.05	0.045	114, 115	2	seed	28	0.006, 0.010	
		0.10	0.090	114, 115	2	seed	28	0.015, 0.015	
		0.26	0.22	114, 114	2	seed	28	0.081, 0.084	

The duplicate residues recorded in the table originate from duplicate field samples.

Five supervised field trials on cotton were conducted in Australia. The treatments consisted of a single application of the SC formulation containing 110 g/L etoxazole. The average recovery of etoxazole from cotton substrates fortified at 0.01 mg/kg for cottonseedwas 103% ± 10%. The LOQ for cottonseed was 0.01 mg/kg.

Table 64 Etoxazole residues on cotton seeds from supervised trials in Australia

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.039*			*1*		*21*		
Australia/NSW, 2002 (Sicala V-2RR)	SC	0.039			1	seed	0 7 14 21 28 35	0.08 < 0.01 0.01 < 0.01 0.01 0.03	Litzow, 2002 SKR-0147/ Shields, 2002 SKR-0145
		0.077			1	seed	0 7 14 21 28	0.05 0.02 0.03 0.01 0.01	

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
							35	0.03	
Australia/NSW, 2002 (NuPearl)	SC	0.039			1	seed	0 7 14 21 28 35	< 0.01 < 0.01 0.03 < 0.01 < 0.01 < 0.01	Litzow, 2002 SKR-0148/ Shields, 2002 SKR-0145
Australia/NSW, 2002 (Sicala V-2RR)	SC	0.039			1	seed	0 6 13 21 28 35	0.13 0.03 0.04 < 0.01 0.07 0.02	Litzow, 2002 SKR-0150/ Shields, 2002 SKR-0145
Australia/QLD, 2002 (Sioka V16)	SC	0.039			1	seed	0 7 14 21 28 35	0.09 0.02 0.03 0.02 0.10 0.02	Litzow, 2002 SKR-0146/ Shields, 2002 SKR-0145
		0.077			1	seed	0 7 14 21 28 35	0.09 0.12 0.03 0.03 0.01 0.02	
Australia/QLD, 2002 (Sicot 189i)	SC	0.039			1	seed	0 7 14 21 28 35	0.03 0.02 0.03 0.02 < 0.01 < 0.01	Litzow, 2002 SKR-0149/ Shields, 2002 SKR-0145

Herbs

Mints

Five field trials on mints were conducted during the 2003 growing season, in the USA. At each trial, two foliar broadcast applications of a 720 g/kg WG formulation were made at a rate of approximately 0.22 kg ai/ha, for a seasonal total of approximately 0.45 kg ai/ha. The applications were made 20 to 22 days apart and timed so that commercially mature mint tops (leaves and stems) could be collected 6 to 7 days after the final application.

The maximum storage interval for field-treated samples in this study was 130 days (mint tops) and 155 days (mint oil). Storage stability testing was performed on mint tops after 154 days of storage and on mint oil after 173 days of storage. Recoveries (% remaining) of etoxazole from the samples were 102–106% for mint tops and 79–86% for mint oil. The LOQ was statistically calculated as 0.005 mg/kg for mint tops and as 0.0099 mg/kg for mint oil.

Table 65 Etoxazole residues on mints from supervised trials in USA

Mints country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.20*	*0.043*		*2*		*7*		
USA/WI, 2003 (Black Mitchem)	WG	0.23		242, 273	2	tops	6	3.3, 4.9	Dorschner, 2008 SKR-0156
USA/WI, 2003 (Scotch Spearmint)	WG	0.22		242, 273	2	tops	6	5.6, 4.9	Storage interval:

Mints country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/ID, 2003 (Black Mitchem)	WG	0.23		186, 186	2	tops	0[a] 7	0.01, 0.01 2.8, 3.1	111–130 days
USA/WA, 2003 (Native Spearmint)	WG	0.23		207, 212	2	tops	6	2.4, 3.2	
USA/WA, 2003 (Native Spearmint)	WG	0.23		231, 230	2	tops	7	5.6, 7.6	

[a] The samples were taken from control plot.

Miscellaneous fodder and forage crops

Cotton gin trash

Six supervised residue trials on cotton were conducted in 1998 and 1999 in USA using either a SC formulation containing 360 g/L etoxazole or a WP formulation containing 800 g/L etoxazole. For all trials the application rate was 0.050 kg ai/ha per application. Two applications were made 21 days apart with samples collected at 28 days after the last application. Gin trash was collected from all trials. At two test sites, an additional test plot was treated with a total seasonal rate of 0.20 kg ai/ha (2× rate). At two test sites, an additional test plot was treated with a total seasonal rate of 0.50 kg ai/ha (5× rate).

The analytical method for etoxazole and its metabolite (R-3) was validated with mean recoveries from fortified samples, analysed concurrently with the treated cottonseed, of 88% ± 12%. The mean recovery of R-3 from fortified samples analysed concurrently with the treated gin trash was 113% ± 8%. The LOQ of etoxazole and R-3 in gin trash was 0.2 mg/kg, and the LOD was 0.1 mg/kg.

The laboratory spiked freezer storage stability studies of etoxazole in/on gin trash were conducted concurrently with the residue studies. The results indicate that etoxazole is stable in/on gin trash during the period studied, with 71% of the etoxazole remaining in gin trash after 188 days. The laboratory spiked freezer storage stability studies of R-3 in/on gin trash were conducted concurrently with the residue studies. The results indicate that R-3 is stable in/on gin trash during the period studied, with 69% of the R-3 remaining in gin trash after 188 days. The maximum storage interval from sample collection to extraction for analysis was 187 days for gin trash.

Table 66 Etoxazole residues on cotton gin trash from supervised trials in USA

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.050*			*1*		*28*		
USA/CA, 1998 (Maxxa)	WP	0.05	0.036	136, 144	2	gin trash	28	0.60, 0.56	Schreier, 2000 SKR-0090 Storage interval: 46–187 days
USA/LA, 1998 (DP33B)	WP	0.05	0.036	140, 138	2	gin trash	27	0.13, 0.11	
USA/MS, 1998 (ST474)	SC	0.05	0.036	141, 139	2	gin trash	28	0.29, 0.25	
	WP	0.05	0.036	141, 139	2	gin trash	20	0.22, 0.25	
USA/TX, 1999 (Delta Pine 2156)	WP	0.05	0.030	181, 169	2	gin trash	28	0.40, 0.36	

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/TX, 1999 (DP 2379)	WP	0.05	0.045	112, 116	2	gin trash	28	0.38, 0.33	
		0.10	0.090	112, 113	2	gin trash	28	0.93, 0.90	
		0.25	0.22	112, 114	2	gin trash	28	2.6, 2.0	
USA/TX, 1999 (PM2200RR)	WP	0.05	0.045	114, 115	2	gin trash	28	0.32, 0.34	
		0.10	0.090	114, 115	2	gin trash	28	0.79, 0.96	
		0.26	0.22	114, 114	2	gin trash	28	2.7, 1.8	

The duplicate residues recorded in the table originate from duplicate field samples.

Table 67 Metabolite of etoxazole (R-3) residues on cotton gin trash from supervised trials in USA

Cotton gin trash country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.050*			*1*		*28*		
USA/CA, 1998 (Maxxa)	WP	0.05	0.036	136, 144	2	gin trash	28	0.14, 0.12	Schreier, 2000 SKR-0090 Storage interval: 46–187 days
USA/LA, 1998 (DP33B)	WP	0.05	0.036	140, 138	2	gin trash	27	< 0.1, < 0.1	
USA/MS, 1998 (ST474)	SC	0.05	0.036	141, 139	2	gin trash	28	< 0.1, < 0.1	
	WP	0.05	0.036	141, 139	2	gin trash	20	< 0.1, < 0.1	
USA/TX, 1999 (Delta Pine 2156)	WP	0.05	0.030	181, 169	2	gin trash	28	< 0.1, < 0.1	
USA/TX, 1999 (DP 2379)	WP	0.05	0.045	112, 116	2	gin trash	28	< 0.1, < 0.1	
		0.10	0.090	112, 113	2	gin trash	28	< 0.1, < 0.1	
		0.25	0.22	112, 114	2	gin trash	28	0.23, 0.23	
USA/TX, 1999 (PM2200RR)	WP	0.05	0.045	114, 115	2	gin trash	28	< 0.1, < 0.1	
		0.10	0.090	114, 115	2	gin trash	28	< 0.1, < 0.1	
		0.26	0.22	114, 114	2	gin trash	28	0.22, 0.16	

The duplicate residues recorded in the table originate from duplicate field samples.

Three supervised field trials on cotton were conducted in Australia. Treatments were uniformly applied to cotton using the SC formulation containing 110 g/L etoxazole. The average recovery of etoxazole from cotton substrates fortified at 0.2 mg/kg for gin trash was 93% ± 12%. The LOQ for cotton gin trash was 0.2 mg/kg.

Table 68 Etoxazole residues on cotton gin trash from supervised trials in Australia

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Australia	*SC*	*0.039*			*1*		*21*		
Australia/NSW, 2002 (Sicala V-2RR)	SC	0.039			1	gin trash	0 7 14 21 28	2.3 1.1 0.43 < 0.2 0.20	Litzow, 2002 SKR-0147/ Shields, 2002 SKR-0145

Cotton seeds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
							35	0.25	
Australia/NSW, 2002 (NuPearl)	SC	0.039			1	gin trash	0 7 14 21 28 35	0.47 0.27 0.17 0.23 0.40 0.28	Litzow, 2002 SKR-0148/ Shields, 2002 SKR-0145
Australia/QLD, 2002 (Sioka V16)	SC	0.039			1	gin trash	0 7 14 21 28 35	1.5 0.79 0.60 0.60 2.7 3.3	Litzow, 2002 SKR-0146/ Shields, 2002 SKR-0145

Dried herbs

Hops

A total of seven supervised trials on hops were conducted during 2005 and 2006 in Germany (Northern Europe). All trials were conducted as single point harvest studies. The hops were sprayed once at 0.055 kg ai/ha with a SC formulation containing 110 g ai/L. In these stidues the hops samples (green cones) were collected at commercial harvest, i.e., 27–29 days after application. Green cones were collected and processed into dried cones. Both green and dried cones were analysed. The LOQ for green cones was 0.10 mg/kg, and for dried cones was 0.50 mg/kg.

The storage stability of etoxazole in sample extracts in refrigerator was confirmed by procedural recoveries which was analysed in parallel with the field samples.

Table 69 Etoxazole residues on hops from supervised trials in Europe

Hops country, year (variety)	Application						Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	GS	no.				
Germany, 2005 (Magnum)	SC	0.055	0.0022	2500	82	1	green cones dried cones	27 27	< 0.10 < 0.50	Grolleau, 2005, SKR-0129 Storage interval: 34–49 days
Germany, 2005 (Hersbruck)	SC	0.055	0.0022	2500	61-63	1	green cones dried cones	28 28	< 0.10 < 0.50	
Germany, 2005 (Halletauer Tradition)	SC	0.055	0.0022	2500	63	1	green cones dried cones	28 28	< 0.10 < 0.50	
Germany, 2005 (Perle)	SC	0.055	0.0022	2500	63-65	1	green cones dried cones	28 28	< 0.10 < 0.50	
Germany, 2006 (Magnum)	SC	0.055	0.0028	2000	71-73	1	green cones dried cones	28 28	< 0.10 < 0.50	Grolleau, 2006, SKR-0130 Storage interval: 21–77 days
Germany, 2006 (Taurus)	SC	0.055	0.0028	2000	71-73	1	green cones dried cones	27 27	< 0.10 < 0.50	
Germany, 2006 (Northern Brewer)	SC	0.055	0.0028	2000	68-71	1	green cones dried cones	29 29	< 0.10 < 0.50	

Three supervised trials on hops were conducted in 2003, in the USA. Two foliar airblast applications of a 720 g/kg WG formulation were made at a rate of approximately 0.22 kg ai/ha. For one trial, a second plot was treated at 0.45 kg ai/ha (2× rate). In two trials the interval between the first and second applications ranged from 14 to 15 days with the second application made 6 to 7 days prior to hop cones harvest. In one trial, the cones were harvested 2, 6, 13 and 20 days after the last application.

A freezer storage stability study, utilizing laboratory-fortified samples, was also conducted on dried hop cones. Etoxazole residues on dried hop cones were found to be stable (89% remaining) for 84 days when stored at -20 ºC. The maximum interval from harvest to extraction for analysis for etoxazole on dried hop cones was 60 days.

Table 70 Etoxazole residues on hops from supervised trials in USA

Hops country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.20*		*> 467*	*1*		*7*		
USA/WA, 2003 (Warrior)	WG	0.21		885, 899	2	dried cones	6	2.0, 2.5	Kowalsky, 2006 SKR-0128
USA/ID, 2003 (Galena)	WG	0.22		920, 947	2	dried cones	7	4.2, 3.7	
		0.45		928, 934	2	dried cones	7	13, 13	
USA/OR, 2003 (Liberty)	WG	0.20		873, 868	2	dried cones	2 6 13 20	5.0, 4.2 4.1, 4.2 3.7, 3.5 4.3, 4.3	Storage interval: 42–60 days

The duplicate residues recorded in the table originate from duplicate field samples.

Tea

A total of eight supervised trials were conducted in 1995 and 1996 in Japan. In four trials treatments consisted of two foliar applications of either a 50 g/L SC formulation or 50 g/L WP formulation. In the remaining four trials one application was made at a rate of 0.40 kg ai/ha with a 50 g/L SC formulation.

The recoveries of etoxazole from dried green tea leaves fortified at 0.4 mg/kg were 82–92%, and at 0.8 mg/kg was 90%. A freezer storage stability study utilizing laboratory-fortified samples was also conducted on dried green tea leaves. Etoxazole residues on dried green tea leaves were found to be stable for 308 days when stored at -20 ºC. Recoveries (% remaining) of etoxazole from the samples were 78–79% for green tea leaves. The maximum interval from harvest to extraction for analysis on green tea leaves was 308 days.

Table 71 Etoxazole residues on tea from supervised trials in Japan

Tea country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, Japan	*SC*	*0.40*	*0.010*	*2000–4000*	*1*		*14*		
Japan, 1996 (Yabukita)	SC	0.40	0.01	4000	2	dried green tea leaves	7 14 21	20, 19 7.3, 7.0 0.83, 0.80	Hoshino, 1996 SKR-0160 Storage interval: 49–56 days
Japan, 1996 (Yabukita)	SC	0.40	0.01	4000	2	dried green tea leaves	7 14 21	15, 14 4.7, 4.1 0.76, 0.75	
Japan, 1996 (Yabukita)	WP	0.40	0.01	4000	2	dried green tea leaves	7 14 21	21, 20 8.0, 8.0 0.79, 0.76	Kato and Kobayashi, 1996 SKR-0161 Storage interval: 21–29 days
Japan, 1996 (KPTRI No. 129)	WP	0.40	0.01	4000	2	dried green tea leaves	7 14 21	13, 12 4.1, 3.9 0.79, 0.77	

Tea country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
Japan, 1995 (Yabukita)	SC	0.40	0.01	4000	1	dried green tea leaves	7 14 21	81, 75 2.7, 2.5 3.1, 2.1	Hoshino, 1996 SKR-0162 Storage interval: 308 days
Japan, 1995 (Yabukita)	SC	0.40	0.01	4000	1	dried green tea leaves	7 14 21	51, 44 6.4, 5.6 1.4, 1.3	
Japan, 1995 (Yabukita)	SC	0.40	0.01	4000	1	dried green tea leaves	7 14 21	57, 55 2.4, 2.3 1.2, 1.2	Kato and Kobayashi, 1996 SKR-0163 Storage interval: 275–276 days
Japan, 1995 (Yabukita)	SC	0.40	0.01	4000	1	dried green tea leaves	7 14 21	39, 39 4.8, 4.6 0.92, 0.90	

Almond hulls

Five residue trials in almonds were completed in the USA with a 720 g/kg WG formulation in a two spray program. Treatments consisted of two foliar applicationsat approximately 0.15 kg ai/ha, made 49 and 28 days before normal harvest. At one trial site, an additional plot was treated using a 2× rate of approximately 0.30 ai kg/ha per application.

The stability of etoxazole in almond hulls was evaluated by spiking untreated hull samples with a known amount of etoxazole, the analysing the stored samples after 70 days. Recoveries (% remaining after storage) from the fortified samples averaged 67.2–80.4% for etoxazole and 75.2–107% for R-3, demonstrating the stability of etoxazole and R-3 residues in the sample extracts during frozen storage. The LOQ for the etoxazole and R-3 residues in the almond hulls 0.05 mg/kg, and the LOD was 0.02 mg/kg.

Table 72 Etoxazole residues on almond hulls from supervised trials in USA

Almonds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*			*1*		*28*		
USA/CA, 2002 (Non-Pareil)	WG	0.15		949, 928	2	hulls	28	1.17, 1.79	Schreier, 2003 SKR-0138 Storage interval: 53–60 days (harvest to extraction)
USA/CA, 2002 (Non-Pareil)	WG	0.15		938, 928	2	hulls	28	0.23, 0.09	
USA/CA, 2002 (Non-Pareil)	WG	0.15		940, 968	2	hulls	28	0.16, 0.17	
USA/CA, 2002 (Non-Pareil)	WG	0.15		945, 938	2	hulls	14 21 28 35	0.57, 0.55 0.34, 0.71 0.39, 0.26 0.22, 0.23	
USA/CA, 2002 (Carmel)	WG	0.15		938, 936	2	hulls	28	0.13, 0.14	
		0.30		918, 932	2	hulls	28	0.38, 0.54	

The duplicate residues recorded in the table originate from duplicate field samples.

Table 73 Metabolite of etoxazole (R-3) residues on almond hulls from supervised trials in USA

Almonds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
GAP, USA	*WP*	*0.15*			*1*		*28*		
USA/CA, 2002 (Non-Pareil)	WG	0.15		949, 928	2	hulls	28	0.06, 0.12	Schreier, 2003

Almonds country, year (variety)	Application					Portion analysed	PHI Days	Residues, mg/kg	Ref
	Form	kg ai/ha	kg ai/hL	water, L/ha	no.				
USA/CA, 2002 (Non-Pareil)	WG	0.15		938, 928	2	hulls	28	0.03, < 0.02	SKR-0138
USA/CA, 2002 (Non-Pareil)	WG	0.15		940, 968	2	hulls	28	< 0.02, < 0.02	Storage interval: 53–60 days (harvest to extraction)
USA/CA, 2002 (Non-Pareil)	WG	0.15		945, 938	2	hulls	14 21 28 35	0.03, 0.03 0.03, 0.06 0.04, 0.04 < 0.02, 0.02	
USA/CA, 2002 (Carmel)	WG	0.15		938, 936	2	hulls	28	0.02, 0.02	
		0.30		918, 932	2	hulls	28	0.04, 0.05	

The duplicate residues recorded in the table originate from duplicate field samples.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In Processing

The Meeting received information on the fate of etoxazole residues during the processing of oranges, apples, plums, grapes, cotton seed and mint. On the basis of the data provided the Meeting calculated processing factors for etoxazole in citrus, apple, plum, grape, cotton seed and mint.

Citrus

In a trial in Spain, etoxazole was applied once to oranges using a 110 g/L SC formulation at a rate of 0.055 kg ai/ha. The fruit was collected at commercial harvest 13 days after the application. The harvested samples were then processed using normal processing procedures for commercially grown oranges.

Table 74 Etoxazole residues in processed commodities of citrus from supervised trials

Citrus country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	Form	kg ai /ha	water, L/ha	no.			mg/kg	Processing factor	
Spain, 1998 Orange (Navelino)	SC	0.055	3000	1	13	Peel	0.07		Grolleau, 1999 SKR-0066
						Pulp	< 0.01		
						Whole fruit*	0.02		
						Wet pomace	0.03	1.5	
						Dry pomace	0.03	1.5	
						Juice	< 0.01	< 0.5	
						Canned orange	< 0.01	< 0.5	
						marmalade	< 0.01	< 0.5	

* Whole fruit residues calculated from residues in peel and pulp, adjusted by the weight ratio of peel to pulp. Residues below LOQ were calculated as LOQ value.

Apple

In two trials in France, etoxazole was applied once to apples using a 110 g/L SC formulation at a rate of 0.055 kg ai/ha. The samples were harvested at 98 and 118 days after treatment. The apples were crushed then pressed with the resultant juice collected.

In a trial in USA, apples were treated with two foliar applications of a 800 g/kg WP formulation at total seasonal rate of 1.5 kg ai/ha (5× normal use rate) with a harvest interval of 28 days after the last application. The apples were washed, crushed by a hammer mill to a uniform consistency, and heated to 40–50 ºC. An enzyme was added and the apples allowed to set for two hours. Following enzyme treatment the apple pulp was pressed using a hydraulic style apple press to produce the apple juice.

Table 75 Etoxazole residues in processed commodities of apple from supervised trials

Apple country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	Form	kg ai /ha	water, L/ha	no.			mg/kg (mean)	Processing factor	
North France, 1996 (Starkrimson)	SC	0.050	913	1	98	fruit juice	< 0.010 < 0.010	 -	Maestracci, 1997, SKR-0020
South France, 1996 (Golden)	SC	0.055	1005	1	118	fruit juice	< 0.010 < 0.010	 -	
USA/WA, 1999 (Red Delicious)	WP	0.75	1209 1281	2	28	fruit pomace juice	0.256, 0.278 (0.267) 1.483, 1.565 (1.524) 0.0024, 0.0034 (0.0029)	 5.7 0.01	Schreier, 2001, SKR-0100

Plum

In a trial in USA, plums were treated with two foliar applications of a 720 g/kg WG formulation at a seasonal rate of 0.30 kg ai/ha and a harvest interval of 7 days after the last application. The treated fruit was pitted and dried according to commercial practice prior to collection for analysis.

Table 76 Etoxazole residues in processed commodities of plums from supervised trials

Plum country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	Form	kg ai /ha	water, L/ha	no.			mg/kg (mean)	Processing factor	
USA/CA, 2005 (Casselman)	WG	0.15	1756 1765	2	7	fresh fruit dried fruit	< 0.01, < 0.01 0.015	 > 1.5	Leonard, 2007 SKR-0152

Grape

In two trials in France, etoxazole was applied once to grapes using a 110 g/L SC formulation at a rate of 0.055 kg ai/ha. Samples were collected 138 and 148 days after treatment. The grapes were then crushed and placed into a glass demijohn. The samples were processed into wine, following commercial practices.

In a trial in the USA, grapes were treated with two foliar applications of a 720 g/kg WG formulation at a seasonal rate of 1.5 kg ai/ha (5× normal use rate) and harvested 14 days after the last application. Grape samples were processed to provide juice and raisins at the same facility that conducted the field trial. Juice processing was conducted on the same day the grapes were sampled by running the grapes through a crusher and collecting the resultant pulp. The pulp was then pressed to separate the juice and pulp. The resulting juice was filtered through cheesecloth, poured into sample containers and frozen. For raisins, the harvested grapes were laid out on paper trays and allowed to dry for 32 days. The raisins were run over a shaker and a small mesh screen to remove leaves, dirt and stems before sampling, and were then frozen.

Table 77 Etoxazole residues in processed commodities of grape from supervised trials

Grape country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	Form	kg ai /ha	water, L/ha	no.			mg/kg (mean)	Processing factor	
North France, 1995 (Sauvignon))	SC	0.056	242	1	138	fruit must wet pomace dry pomace wine	< 0.010 < 0.010 < 0.010 < 0.010 < 0.010	 - - - -	Maestracci, 1997, SKR-0015
South France, 1995 (Cabernet Sauvignon)	SC	0.057	328	1	148	fruit must wet pomace dry pomace wine	< 0.010 < 0.010 < 0.010 < 0.010 < 0.010	 - - - -	
USA/CA, 2002 (Thompson Seedless)	WG	0.75	953 943	2	14	fruit (field) fruit(processor) juice raisins	0.096, 0.11 (0.103) 0.034, 0.030 (0.032) 0.17, 0.17 (0.17) 0.13, 0.10 (0.115)	 1.7[a] (5.3)[b] 1.1[a] (3.6)[b]	Schreier, 2003 SKR-0151

[a] Processing factor based on mean grape residue found from field samples

[b] Processing factor based on mean grape residue found from processing facility

Cotton seed

In a trial in USA, cotton was treated with two foliar applications of a WP formulation containing 800 g/L etoxazole at a nominal rate of 0.50 kg ai/ha per season and harvested samples 28 days after the last application. The cotton samples were separated into seed and gin trash. The cottonseed was dried if necessary in a tower drier and then stick extracted in a stick extractor to remove burrs, sticks and other plant parts. The ginned cottonseed was delinted and processed into the commodities cotton hulls, solvent extracted meal, and refined oil.

Table 78 Etoxazole residues in processed commodities of cottonseed from processing trials

Cotton seed country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	Form	kg ai /ha	water, L/ha	no.			mg/kg (mean)	Processing factor	
USA/TX, 1999 (DP 2379)	WP	0.25	112 114	2	28	seed meal hulls oil	0.093, 0.14 (0.12) < 0.005, < 0.005(< 0.005) 0.047, 0.029 (0.038) 0.023, 0.024 (0.024)	 < 0.042 0.32 0.20	Schreier, 2000 SKR-0090
USA/TX, 1999 (PM2200RR)	WP	0.26	114 114	2	28	seed meal hulls oil	0.081, 0.084 (0.083) < 0.005, < 0.005(< 0.005) 0.007, 0.012 (0.010) 0.009, 0.010 (0.010)	 < 0.060 0.12 0.12	

Mint

In two trials in the USA, mint was treated with two foliar applications of a 720 g/kg WG formulation at a nominal rate of 0.45 kg ai/ha per season and harvested 6 days after the last application. Mint samples were distilled into oil.

Table 79 Etoxazole residues in processed commodities of mint from processing trials

Mint country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	F	kg ai /ha	water, L/ha	no			mg/kg (mean)	Processing factor	
USA/WI, 2003 (Scotch Spearmint)	WG	0.22	242 273	2	6	tops oil	5.6, 4.9 (5.3) 15, 16 (16)	 3.0	Dorschner, 2008 SKR-0156

Mint country, year (country)	Application				PHI Days	Commodity	Residues		Ref.
	F	kg ai /ha	water, L/ha	no			mg/kg (mean)	Processing factor	
USA/WA, 2003 (Native Spearmint)	WG	0.23	207 212	2	6	tops oil	2.4, 3.2 (2.8) 0.34, 0.74 (0.54)	0.19	Storage interval: 147–155 days (mint oil)

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

The Meeting received a dairy cow feeding study in which etoxazole was administered orally (within gelatin capsules) with a balling gun to lactating Holstein dairy cow (four to eight years old, 430 to 667 kg) for 28 consecutive days. The daily dose was administered twice daily following the am and pm milking. The daily doses equated to approximately 1, 3 and 10 ppm etoxazole in the diet. The actual daily dose, prepared on a weekly basis, was calculated based on each cows average feeding consumption (dry weight basis) from the seven days feed consumption recorded during the acclimation period. Milk samples were composites from the pm milking of one day and the am milking of the following day. On study Day 27, a portion of the remaining composite milk from each group was further processed and separated into skim milk and milk cream by centrifugation. Each cow was sacrificed within 24 hours of the final dose at the end of feeding period. The tissue samples (liver, kidney, muscle and fat) were collected from each cow immediately after termination. Milk, fat and muscle samples were analysed for parent etoxazole only. Kidney samples were analysed for etoxazole and Metabolite 1, liver for etoxazole, Metabolite 1 and R-20.

For the 3 ppm dosing group, only one cow produced milk that contained detectable residues of etoxazole. Residues were only found on Days 3 and 6. Because of the low level of etoxazole residues found in milk, analysis of the 1 ppm dosing group was limited to Days 3 and 6 with no detectable etoxazole residues being found. The etoxazole residues of the skim milk samples from the 10 ppm dosing group were all below the LOQ of 0.01 mg/kg. Consequently, skim milk samples from the 1 ppm and 3ppm dosing groups were not analysed.

No detectable residues of etoxazole were found in muscle samples from the 1 ppm and 3 ppm dose levels. For the 10 ppm dose level one of three samples contained the LOD residue of 0.005 mg/kg. Etoxazole residues were consistently found in fat from all dose levels. No detectable residues of etoxazole were found in liver samples from the 1 ppm dose levels. Etoxazole residues were found in all liver samples from the 3 ppm and 10 ppm dose levels. Residues of Metabolite 1 and R-20 of liver samples from all dose levels were below the LOQ of 0.02 mg/kg. Etoxazole residues of kidney samples from all dose levels were below the LOQ of 0.01 mg/kg. No residue of Metabolite 1 was found in kidney samples from the 1 ppm dose level. For the 3 ppm dose level, one sample contained a residue of the LOQ of 0.02 mg/kg. Residues of Metabolite 1 were found in all 10 ppm dose samples.

Table 80 Residue in milk of lactating dairy cows dosed with etoxazole at the equivalent of 1, 3 and 10 ppm in the diet

Study Day Sampled	Residues, mg/kg		
	Dosing, 1 ppm	Dosing, 3 ppm	Dosing, 10 ppm
	etoxazole	etoxazole	Etoxazole
3	< 0.005, < 0.005, < 0.005	0.008, < 0.005, < 0.005	0.007, < 0.005, 0.012
6	< 0.005, < 0.005, < 0.005	0.008, < 0.005, < 0.005	< 0.005, 0.006, 0.014
9	-*	< 0.005, < 0.005, < 0.005	0.006, 0.006, 0.010
13	-*	< 0.005, < 0.005, < 0.005	0.005, 0.006, 0.008
16	-*	< 0.005, < 0.005, < 0.005	0.006, 0.007, 0.011
20	-*	< 0.005, < 0.005, < 0.005	0.006, 0.008, 0.012
23	-*	< 0.005, < 0.005, < 0.005	0.008, 0.009, 0.011
27	-*	< 0.005, < 0.005, < 0.005	0.008, < 0.005, 0.008

The Limit of Quantification was 0.01 mg/kg, the Limit of Detection was 0.005 mg/kg.

* Sample from the 1 ppm treatment group were not analysed beyond study day 6 due to lack of residues in the 3 ppm treatment group.

Table 81 Residue in milk cream and skim milk of lactating dairy cows dosed with etoxazole at the equivalent of 1, 3 and 10 ppm in the diet

Study Day Sampled	Residues, mg/kg		
	Dosing, 1 ppm	Dosing, 3 ppm	Dosing, 10 ppm
	Etoxazole	etoxazole	Etoxazole
Cream[a]			
27	0.005, 0.009, 0.010	0.007, 0.018, 0.020	0.077, 0.048, 0.094
Skim milk[b]			
27	-	-	< 0.005, < 0.005, 0.006

[a] The Limit of Quantification was 0.02 mg/kg, the Limit of Detection was 0.005 mg/kg for milk cream.

[b] The Limit of Quantification was 0.01 mg/kg, the Limit of Detection was 0.005 mg/kg for skim milk.

Table 82 Residue in tissues of lactating dairy cows dosed with etoxazole at the equivalent of 1, 3 and 10 ppm in the diet

Tissues	Residues, mg/kg								
	Dosing, 1 ppm			Dosing, 3 ppm			Dosing, 10 ppm		
	etoxazole[a]	metabolite1[b]	R-20[b]	etoxazole[a]	metabolite1[b]	R-20[b]	etoxazole[a]	metabolite1[b]	R-20[b]
Muscle	< 0.005 < 0.005 < 0.005			< 0.005 < 0.005 < 0.005			< 0.005 0.005 < 0.005		
Liver	< 0.005 < 0.005 < 0.005	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	0.007 0.006 0.005	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	0.017 0.013 0.020	0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01
Kidney	< 0.005 < 0.005 < 0.005	< 0.01 < 0.01 < 0.01		< 0.005 < 0.005 < 0.005	0.018 < 0.01 < 0.01		< 0.005 0.005 < 0.005	0.117 0.060 0.029	
Fat	< 0.005 0.015 0.014			0.033 0.027 0.019			0.078 0.063 0.106		

[a] The Limit of Quantification was 0.01 mg/kg, the Limit of Detection was 0.005 mg/kg.

[b] The Limit of Quantification was 0.02 mg/kg, the Limit of Detection was 0.01 mg/kg.

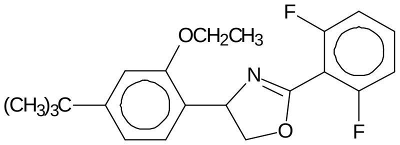
APPRAISAL

Residue and analytical aspects of etoxazole were considered for the first time by the present Meeting. The residue evaluation was scheduled for the 2010 JMPR by the Forty-first Session of the CCPR (ALINORM 09/32/24).

Etoxazole is an acaricide which belongs to the diphenyloxazoline group of chemicals, and controls mites by causing adults to lay sterile eggs and also inhibition of chitin biosynthesis. The Meeting received information on identity, animal and plant metabolism, environment fate in soil, rotational crops, analytical methods, storage stability, use patterns, supervised trials, farm animal feeding studies and fates of residues in processing.

The 2010 JMPR established an ADI for etoxazole of 0–0.05 mg/kg bw. For etoxazole the ARfD is unnecessary.

(*RS*)-5-*tert*-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole



Etoxazole is a 1:1 mixture of the enantiomers.

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

R-2	2-(2,6-difluorophenyl)-4-[2-ethoxy-4-(1-hydroxymethyl-1-methylethyl)phenyl]-4,5-dihydrooxazole
R-3	*N*-(2,6-difluorobenzoyl)-4-*tert*- butyl-2-ethoxybenzamide
R-4	*N*-(2,6-difluorobenzoyl)-2-amino- 2-(4-*tert*-butyl-2-ethoxyphenyl) ethanol
R-7	2-amino-2-(4-*tert*-butyl-2- ethoxyphenyl)ethyl 2,6-difluorobenzoate hydrochloride
R-7-CO$_2$H	2-amino-2-[2-ethoxy-4-(1-carboxy-1-methylethyl)phenyl]ethyl 2,6- difluorobenzoate hydrochloride
R-8	2-amino-2-(4-*tert*-butyl-2-ethoxy- phenyl)ethanol
R-10	*N*-(2,6-difluorobenzoyl)glycine
R-11	2,6-difluorobenzoic acid
R-12	4-*tert*-butyl-2-ethoxybenzoic acid
R-13	4-(4-*tert*-butyl-2-ethoxyphenyl)-2- (2,6-difluorophenyl)oxazole
R-15	4-*tert*-butyl-2-ethoxybenzamide
R-16	2-(2,6-difluorophenyl)-4-[2-ethoxy-4-(1-carboxy-1-methylethyl)phenyl]-4,5- dihydrooxazole
R-20	2-ethoxy-4-(1-hydroxymethyl-1- methylethyl)benzoic acid
R-24	2-amino-2-(2-ethoxy-4-[1'- hydroxymethyl-1'- methylethyl]phenyl)ethanol
DFB	2,6-difluorobenzamide
Metabolite 1	2-amino-2-(2-ethoxy-4-[1'-hydroxycarbonyl-1'-methyl-ethyl]phenyl)ethanol

Animal metabolism

The Meeting received animal metabolism studies with etoxazole in rats, lactating goats and laying hens. The metabolism and distribution of etoxazole in animals were investigated using the [U-^{14}C-difluorophenyl] and [U-^{14}C-*tert* butylphenyl]-labelled etoxazole.

Etoxazole was metabolised in rats principally by hydroxylation of the 4,5-dihydrooxazole ring followed by cleavage of the molecule and hydroxylation of the tertiary-butyl side chain. There was a significant difference in the proportions of metabolites excreted in the urine of male and female rats. The major component in male rat urine was Metabolite 1 and in female urine was R-24. Metabolism in rats was summarised and evaluated by the WHO panel of the JMPR in 2010.

When lactating goats were orally dosed with [^{14}C-*tert* butylphenyl]- and [^{14}C-difluorophenyl]-etoxazole at 20 mg/animal/day, equivalent to approximately 10 ppm in the feed for 4 consecutive days, most of the administered radioactivity was recovered in the gastro-intestinal contents (80% and 29%). Radioactivity was excreted in urine (1.9% and 1.5%) and faeces (17% and 54%). Overall recoveries of the administered dose were 99% and 85%. The Meeting considered that the result of studies using [^{14}C-*tert* butylphenyl]-etoxazole was unreliable, since most of radioactivity was recovered from the gastro-intestinal tracts. The result of studies using [^{14}C-difluorophenyl]-etoxazole are summarised below.

Radioactive residues were highest in the bile (0.317 mg/kg) and livers (0.063 mg/kg). Total radioactive residues in all other tissues and milk were < 0.008 mg/kg. Parent etoxazole accounted for a total of 63–65% dose in the faeces and gastro-intestinal tracts. The major urinary metabolites corresponded to R-11 (0.5% dose) and R-10 (0.8% dose).

Laying hens were orally dosed with [^{14}C-*tert*-butylphenyl]- or [^{14}C-difluorophenyl]-etoxazole at doses equivalent to 12 or 11 ppm in the feed for 8 consecutive days. The majority (84.4–99.8%) of the radioactive residues were extracted in egg yolk, egg white, abdominal and skin fat, thigh muscle, breast muscle and liver.

Parent etoxazole was the major ^{14}C residue in egg yolk, abdominal and skin fat, thigh muscle, and breast muscle. Its concentration in isolated egg yolk was approximately 0.1 mg/kg. It accounted for only about 3% of TRR in liver (0.057–0.078 mg/kg), but 90–92% of TRR in the composite fat (0.55–0.69 mg/kg). Most of ^{14}C residue in liver was metabolite R-16 (59–66% of TRR), a *tert*-butyl methyl group oxidation product of etoxazole. R-16 was also observed in minor quantities in all tissues except egg white. The analogous dihydrooxazole ring-opened product of R-16, designated as R-7-CO_2H, was observed only in liver. The liver contained unextracted ^{14}C residues in both radiolabel treatments (0.29 mg/kg or 12–15% of TRR). The majority (about 80%) was protein-bound and could be solubilised by treatment with protease.

Etoxazole was metabolized to several metabolites and the metabolic routes are similar in goats and hens. The major metabolic processes were oxidation of the *tert*-butyl moiety, and the hydrolysis of the hydrooxazole ring. Ruminant and poultry metabolism studies demonstrated that transfer of administered ^{14}C residues to milk, eggs, and tissues is low.

The metabolic pathway proposed for goats and hens is similar to that for rats. Some metabolites such as R-8 (0.7% TRR in poultry liver), R-10 (0.8% dose in goat urine), R-20 (11.5% TRR in goat liver) were observed in goat and hen metabolism studies, but not in rat studies.

Plant metabolism

The Meeting received plant metabolism studies performed on apples, oranges and egg plants using the tert-butylphenyl- and oxazole- U-[^{14}C] labelled etoxazole, and on cotton using the tert-butylphenyl- and difluorophenyl-U-[^{14}C] labelled etoxazole.

In an apple metabolism study, apple trees were treated once at a rate of 0.15 kg ai/ha. Samples of fruit and leaves were taken at Day 0, 14 or 15, 21 and 30 after application. The TRR in fruit declined from 0.46 to 0.13 mg/kg and 0.18 to 0.09 mg/kg from treatment with the tert-butylphenyl- and oxazole-labelled etoxazole, respectively. Similarly, the TRR in leaves declined from 14.9 to 2.5 mg/kg and 11.8 to 0.7 mg/kg. Parent etoxazole was the only component that exceeded 10% of the TRR in fruit (42% of TRR at harvest) and leaves (30% of TRR at harvest) at all sampling times. Metabolites accounting for 0.001–0.010 mg/kg (0.4–8.2% of TRR in fruit) were identified as R-3, R-7, R-13, R-11 (oxazole label), R-12 (tert-butylphenyl label), and R-15 (tert-butylphenyl label).

In an orange metabolism study, orange trees were treated at a rate of 0.4 kg ai/ha. Samples of fruit and leaves were taken immediately after application and at 21, 30, 60 and 90 days after application. The TRR in fruit declined from 0.25 to 0.11 mg/kg and 0.27 to 0.07 mg/kg from treatment with the tert-butylphenyl- and oxazole- labelled etoxazole, respectively. Similarly, the TRR in leaves declined from 9.3 to 0.81 mg/kg and 17.9 to 2.7 mg/kg from treatment. Parent etoxazole was the only component that exceeded 10% of the TRR in fruit (48% of TRR at harvest) and leaves (52% of TRR at harvest) at all sampling times. Etoxazole and metabolites R-3, R-7, R-13, R-14 and R-15 were identified by co-chromatography. The residue was a surface residue and translocation was minimal.

In an egg plant metabolism study, egg plants maintained under controlled conditions in a plant growth room were treated at a rate of 0.2 kg ai/ha. Samples of fruit were taken immediately after applications at 1 day, and 2 and 4 weeks. Samples of leaves were taken immediately after application at 1 day and 4 weeks. The TRR in fruit declined from 0.20 to 0.10 mg/kg from treatment with the tert-butylphenyl-labelled etoxazole, but for fruit-treated oxazole-labelled etoxazole the TRR did not decline (0.16 to 0.20 mg/kg). Parent etoxazole was the only component that exceeded 10% of the

TRR in fruit (69–74% of TRR at harvest) and leaves (70–75% of TRR at harvest) at all sampling times. Metabolites accounting for 0.001–0.004 mg/kg (0.3–1.8% fruit radioactivity) were identified as R-2, R-3, R-7, R-13 (both radiolabels), R-11 (oxazole radiolabel), and R-12 (tert-butylphenyl radiolabel). Again, the residue was a surface residue and translocation was minimal.

In a cotton metabolism study, two foliar treatments were applied to cotton plants at a rate of 0.1 kg ai/ha at 42 and 21 days prior to harvest. Cottonseed (ginned from open cotton bolls) and gin trash was harvested for analysis. Cottonseed contained low amounts of radioactivity, with TRR values of 0.031 and 0.020 mg/kg for difluorophenyl and tert-butylphenyl cottonseed, respectively. Cotton gin trash samples contained TRR values of 6.9 and 5.3 mg/kg for the difluorophenyl- and tert-butylphenyl-labelled etoxazole. The major residues identified in gin trash were parent etoxazole (36–44% of TRR) and R-3 (16–18% of TRR).

In the plant metabolism studies on apples, oranges, egg plants and cotton, the metabolic pathways were similar. Etoxazole was metabolized to several metabolites. In all plants investigated, the parent etoxazole was identified as the major component (30–75% of TRR). Metabolites were detected in concentrations < 10% of TRR in apples, oranges and egg plants. In cotton gin trash, the component (R-3) exceeded 10% of TRR. In all studies, the residue remained mainly in the surface, penetration into fruit was minimal and translocation was also minimal. The major metabolic processes were the hydrolysis and cleavage of the oxazole ring.

All plant metabolites identified except R-14 were found in rats, goats or hens. The structure of R-14 is similar to that of R-7 which was identified in rats and hens. These metabolites may be generated during the hydrolysis and cleavage of hydrooxazole ring.

The stabilities of metabolites in plant metabolism studies during freezer storage were determined by re-extraction and comparison of radioresidue profiles to chromatographic profiles. The amounts of radioactivity extracted and the percentages of the major metabolites identified were similar after freezer storage intervals (5–13 months).

Environmental fate in soil

The Meeting received information on aerobic soil metabolism and rotational crop study.

Aerobic soil metabolism and degradation study was conducted using [^{14}C-*tert*-butylphenyl] and [^{14}C-difluorophenyl]-etoxazole in a sand loam soil under aerobic conditions at a nominal average temperature of 20 °C for 269 days. Etoxazole declined rapidly from 95.7–97.8% of total applied radioactivity (TAR) at 0 day to 11.2–12.6% of TAR at 30 days. Totals of 15.8–56.4% of TAR were evolved as CO_2 during 269 days. Several degradates were observed during the incubation period. The degradate R-13 rose to 10.9–11.7% of TAR at 60 days, declining to about 7% of TAR at 269 days. The degradate R-7 reached a maximum proportion of 11.5–21.6% of TAR after 7 days, declined to 5.5–5.9% of TAR at 60 days. The degradate R-8 reached a peak level of 44.8% TAR at 60 days and was still relatively great (28.6% TAR) at 269 days. The minor components R-3, R-4, R-12 and R-15 were never greater than 1.5, 4.4, 4.0 and 3.2% TAR respectively. ^{14}C-etoxazole was degradated with a DT_{50} of 9.9 to 10.6 days.

In confined rotational crop study, radish, lettuce and wheat were designated for planting at 30, 120 and 360 days after treatment (DAT) at an application rate of 0.11 kg ai/ha with [^{14}C-*tert*-butylphenyl] and [^{14}C-difluorophenyl]-etoxazole. The TRR in the 30 DAT rotational crop samples from the treated plots were below the significant residue level of 0.01 mg/kg. Uptake and accumulation of etoxazole-related radioactive residues is very low (< 0.005 mg/kg) in rotational crops of radish, lettuce and wheat planted at the earliest plant-back interval (30 DAT).

Etoxazole residues are not expected to occur in succeeding crops.

Environmental fate in water systems

In the hydrolysis study with [^{14}C-*tert*-butylphenyl]-etoxazole conducted using sterile aqueous buffer solutions, the hydrolytic half-lives at 20 °C were found to be about 10 days at pH 5, 161 days at pH 7 and 165 days at pH 9. In pH 1.2 buffer at 37 °C and in pH 5 buffer at 20 °C, etoxazole was hydrolysed to R-7, while in pH 7 and pH 9 buffer, it was hydrolysed to R-4. No other radioactive products were detected in quantities greater than 6% of the recovered radioactivity. At 20 °C the hydrolytic stability of etoxazole in aqueous buffer is of the order pH 9 > pH 7 > pH 5. In buffers of acidic pH, etoxazole is hydrolysed to R-7 and in neutral or basic pH to R-4.

The photolysis study with [^{14}C-*tert*-butylphenyl] and [^{14}C-oxazole]-etoxazole was conducted using pH 9 buffer containing 10% acetonitrile. The photolytic half-life of etoxazole in pH 9 buffer was found to be 15.9–17.4 days summer sunlight equivalents at latitude 40 °N. The major degradates were identified as R-3, R-11, R-12 and R-15.

Methods of analysis

The Meeting received description and validation data for analytical methods for residues of parent etoxazole in raw agricultural commodities, processed commodities, feed commodities and animal commodities. In most of the methods for determination of etoxazole, homogenized samples were extracted with acetone (for plant materials) and ethyl acetate (for animal commodities), and the extract was cleaned up with liquid–liquid partition followed by column chromatography using SPE. Residues were determined by gas chromatography with FTD, NPD or MSD. The methods of analysis for a range of substrates were validated with LOQs of the 0.002–0.01 mg/kg range for etoxazole.

The multiresidue method DFG Method S19 (modified version) with GC-MS detection was validated for etoxazole in plant materials. LOQs were 0.01 mg/kg for etoxazole.

The Meeting received LC-MS/MS method of analysis for Metabolite 1 and R-20 in bovine liver and kidney. The method was validated with an LOQ of 0.02 mg/kg for both analytes.

Stability of residues in stored analytical samples

The Meeting received information on the freezer storage stability of etoxazole residues in plant commodities (apples, mandarin peel/pulp, strawberries, cantaloupes, grapes, almond hulls, hops, cotton seed/gin trash, cherries, plums fresh/dried, peaches, cucumbers, tomatoes, mint tops/oil and tea). The Meeting noted that the residue might be degradating during sample preparation. Spiking of chopped samples would not reveal this degradation. Nevertheless the Meeting decided to evaluate the results of residue trials, where the storage stability studies show adequate recoveries. Enforcement laboratories should be aware that special precautions may be necessary during sample preparations.

The Meeting received information on the freezer storage stability of etoxazole in milk cream, metabolite R-20 in liver, and Metabolite 1 in liver and kidney. The results of the studies showed that each compound is stable in each animal commodity tested for at least 2 months in frozen storage.

Definition of the residue

In the lactating goat metabolism study, TRRs in kidney (0.94 mg/kg) and liver (0.06–0.23 mg/kg) were higher than those in other tissues. Metabolite 1 is the major component of the residues in liver (12% TRR) and kidney (81% TRR). In the laying hen study, the major residue components are parent etoxazole (in all tissues) and R-16 (in muscle and liver). However, according to farm animal feeding studies, the parent, Metabolite 1 and R-20 are expected to be present at below the LOQ.

The Meeting decided that parent etoxazole is a suitable analyte for enforcement purposes and dietary risk assessment in animal commodities.

The octanol/water coefficient (log P_{ow}) of 5.5 for etoxazole suggests that etoxazole might be fat soluble. In the laying hen metabolism study, etoxazole found in the composite fat was 0.55–0.69 mg/kg and that in muscle was 0.01–0.08 mg/kg. In the dairy cow feeding study, the residue of etoxazole in fat was higher than that in other tissues. The ratio of etoxazole residues in muscle and fat observed in the laying hen metabolism study and the dairy cow feeding study indicates that etoxazole is fat soluble.

The plant metabolism studies of etoxazole were conducted with fruiting vegetables (egg plants), fruit crops (apples and oranges) and oilseed (cotton). Each study was conducted with both tert-butylphenyl- and oxazole-radio-labelled etoxazole for apples, oranges and egg plants, and with both tert-butylphenyl- and difluorophenyl-radio-labelled etoxazole for cotton. Parent etoxazole was always the major component (30–75% TRR). Metabolite R-14 was found in oranges and cotton at low levels (< 3.2% TRR) but not in rat metabolism studies. In cotton seed, DFB and R-3 were also identified as the major residue components, but the concentration of each residue was less than 0.01 mg/kg.

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

The Meeting recommended the following residue definition for plants and animals (for compliance with the MRL and for estimation of dietary intake): *etoxazole.*

The residue is fat-soluble.

Residues of supervised trials on crops

The Meeting received supervised trial data for the foliar application of etoxazole on citrus fruits (mandarins and oranges), apples, pears, cherries, plums, nectarines, peaches, grapes, strawberries, cantaloupes, cucumbers, peppers, tomatoes, almonds, pecans, cotton seed, mints, hops and tea. Residue trial data was made available from Australia, member states of the European Union, Japan and the USA.

Labels (or translation of labels) were available from Australia, Brazil, France, Greece, Italy, Japan, Spain, the UK and the USA describing the registered uses of etoxazole, and GAP information was also provided from Australia and the Netherlands.

The Meeting decided that an ARfD for etoxazole is unnecessary. Therefore, it is not necessary to estimate HR values for etoxazole in the commodities.

As noted above, the Meeting decided to use the results of only these residue trials, for which the storage stability of etoxazole during the respective storage interval was demonstrated, to estimate a maximum residue level. The Meeting therefore recommended the maximum residue levels for citrus, grapes, cucumbers, tree nuts, mint, hops and tea.

Citrus fruits

Data were available from supervised trials on mandarins and oranges in Italy and Spain.

In Italy and Spain, etoxazole is registered for use on citrus at a foliar application of 5.5 g ai/hL (a maximum rate of 0.055 kg ai/ha) with a PHI of 14 days. Residues in whole fruit of mandarins from trials matching GAP of Italy and Spain were (n = 8): 0.01, 0.02 (2), 0.04 and 0.05 (4) mg/kg. Residues in whole fruit of oranges from trials matching GAP of Italy and Spain were (n = 6): 0.01 (2), 0.02 (3) and 0.05 mg/kg. The residue populations for trials conducted on mandarins and oranges were not similar (Mann-Whitney U test). The Meeting decided to use the data on the crop with the highest residues (mandarins) to estimate a maximum residue level for the group. Residues in mandarin pulp from trials of Italy and Spain were (n = 8): < <u>0.01</u> (7) and <u>0.01</u> mg/kg. Residues in orange pulp from trials of Italy and Spain were (n = 6): < 0.01 (6) mg/kg.

Based on the trials for mandarins in Italy and Spain, the Meeting estimated a maximum residue level and an STMR value for etoxazole in citrus of 0.1 and 0.01 mg/kg respectively.

The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was 0.09 mg/kg (Mean + 3SD). Rounding-up of the value to 0.1 mg/kg coincides with the recommendation of the current Meeting.

Pome fruits

Data were available from supervised trials on <u>apples</u> in member states of the EU and the USA.

According to the freezer storage stability study on apples conducted in 2001, etoxazole is declining even after 41days storage interval. Insufficient data was available to demonstrate storage stability of pome fruits.

The Meeting could not estimate maximum residue levels for etoxazole in pome fruit.

Stone fruits

Cherries

Data were available from supervised trials on cherries in Spain and the USA.

Trials from the USA on cherries were reported for the foliar application of a WG formulation. However, the storage stability of etoxazole residues in the trials was unstable (60–68% remaining for 193 days storage interval). The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in cherries.

Residue trials were provided from Spain for use of etoxazole on cherries but no GAP was available.

The Meeting decided not to recommend a maxiumum residue level for etoxazole in cherries.

Plums

Trials were reported for plums from member states of the EU and the USA.

Trials from France on plums were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in plums.

Trials from the USA on plums were reported for the foliar application of a WG formulation. However, the storage stability of etoxazole residues in the trials was unstable (41–45% remaining for 207 days storage interval). The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in plums.

Nectarines

Trials on nectarines were reported from Australia (1 × 3.9 g ai/hL and PHI of 21 days). However, storage stability information was insufficient and the residue trials conducted in Australia did not match the GAP of Australia.

Peaches

Trials were reported for peaches from Australia, member states of the EU and the USA.

In Australia, etoxazole is registered for use on stone fruits at a foliar application of 3.9 g ai/hL with a PHI of 21 days. However, the residue trials on peaches conducted in Australia did not match the GAP of Australia.

Trials from France, Greece, Italy and Spain on peaches were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in peaches.

Trials from the USA on peaches were reported for the foliar application of a WG formulation. However, the storage stability of etoxazole residues in the trials was unstable (45–53% remaining for 278 days storage interval). The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in peaches.

Berries and other small fruits

Grapes

Data were available from supervised trials on grapes in France and the USA.

Trials from France on grapes were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in grapes.

Etoxazole is registered in the USA for use on grapes at a foliar application of a maximum rate of 0.15 kg ai/ha with a PHI of 14 days. Etoxazole residues in grapes from trials in the USA matching GAP were (n = 12): < 0.01, 0.01, 0.03, 0.04 (4), 0.05 (2), 0.06, 0.10 and 0.33 mg/kg. Adequate storage stability studies were available in the US trials.

Based on the US trials, the Meeting estimated a maximum residue level and an STMR value for etoxazole in grapes of 0.5 and 0.04 mg/kg respectively.

The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was 0.25 mg/kg (UCLMedian 95th), but this value was below the HR value and therefore disregarded.

Strawberry

Trials on strawberries were reported from the USA (GAP: one foliar application of a maximum rate of 0.15 kg ai/ha and PHI of 1 day). However, the storage stability of etoxazole residues in the trials was unstable (63% remaining for 32 days storage interval). The Meeting decided not to recommend a maximum residue level for etoxazole in strawberries

Fruiting vegetables—Cucurbits

Data were available from supervised trials on cantaloupe and cucumber in the USA.

Melons

Trials on cantaloupes were reported from the USA (two foliar applications of a maximum rate of 0.15 kg ai/ha and PHI of 7 days). However, the storage stability of etoxazole residues in the trials was unstable (55% remaining for 50 days storage interval). The Meeting decided not to recommend a maximum residue level for etoxazole in melons

Cucumber

The GAP on cucumbers of the USA is a maximum two foliar applications at a maximum rate of 0.15 kg ai/ha with a PHI of 7 days. Etoxazole residues in cucumbers from trials in the USA matching GAP were (n = 9): < 0.01 (7) and 0.01 (2) mg/kg. Adequate storage stability studies were available in the US trials.

Based on the US trials for cucumbers, the Meeting estimated a maximum residue level and an STMR value for etoxazole in cucumbers of 0.02 and 0.01 mg/kg respectively.

The NAFTA calculator could not be used, as residues from seven of the nine trials, matching GAP, were below the LOQs.

Fruiting vegetables, other than Cucurbits

Peppers

Trials from Australia on peppers were reported for the foliar application of a SC formulation. However, the residue trials conducted did not match the GAP on peppers in Australia. The Meeting could not estimate a maximum residue level for peppers.

Tomatoes

Data were available from supervised trials on tomatoes in Australia, member states of the EU and the USA.

Trials from France, Greece, Italy, Netherlands and Spain on tomatoes were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in tomatoes.

Trials from the USA on tomatoes were reported for the foliar application of a WG formulation (GAP: two foliar applications of a maximum rate of 0.14 kg ai/ha and PHI of 1 day). Etoxazole residues in tomatoes from trials in the USA matching GAP were (n = 3): 0.01 and 0.05 (2) mg/kg. Adequate storage stability studies were available in the US trials. However, the trials for tomatoes matching the US GAP were insufficient to estimate a maximum residue level for the commodity.

Trials from Australia on tomatoes were reported for the foliar application of a SC formulation. However, the residue trials conducted did not match the GAP on tomatoes in Australia.

The Meeting could not estimate a maximum residue level for etoxazole in tomatoes.

Tree nuts

Data were available from supervised trials on almonds and pecans in the USA.

Etoxazole is registered in the USA for use on tree nuts at a foliar application of a maximum rate of 0.15 kg ai/ha with a PHI of 28 days. Etoxazole residues in almond nutmeat from trials in the USA matching GAP were (n = 5): < 0.01 (5) mg/kg. Etoxazole residues in pecans from trials in the USA matching GAP were (n = 5): < 0.01 (5) mg/kg. Adequate storage stability studies were available in the US trials.

The use pattern in the USA is for tree nuts and the Meeting decided that trials in almonds and pecans could be used to support a group maximum residue level for tree nuts. The Meeting decided to combine the data for the purpose of estimating a maximum residue level for the group.

Based on the US trials for almond nutmeat and pecans, the Meeting estimated a maximum residue level of 0.01 (*) mg/kg, and an STMR value of 0 mg/kg for etoxazole in tree nuts.

The NAFTA statistical calculator was not used as all residues were below the LOQ.

Cotton seed

Data were available from supervised trials on cotton seeds in Australia, member states of the EU and the USA.

Trials from Greece and Spain on cotton seeds were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in cotton seeds.

Trials from the USA on cotton seeds were reported for the foliar application of a SC formulation or a WP formulation. Adequate storage stability studies were available in the US trials. However, the residue trials conducted in the USA did not match the GAP on cotton seeds in the USA.

Trials from Australia on cotton seeds were reported for the foliar application of a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate a maximum residue level for etoxazole in cotton seeds.

Mints

Data from the USA on mints were reported for the foliar application of a WG formulation.

Etoxazole is registered in the USA for use on mint at a maximum rate of 0.20 kg ai/ha and PHI 7 days with a maximum seasonal application of 0.40 kg ai/ha. Etoxazole residues in mints from trials in the USA matching GAP were (n = 5): 3.1, 3.2, 4.9, 5.6 and 7.6 mg/kg. Adequate storage stability studies were available in the US trials.

Based on the US trials, the Meeting estimated a maximum residue level and an STMR value for etoxazole in mints of 15 and 4.9 mg/kg respectively.

The normal Meeting procedure is to round values to the nearest units of 5 for maximum residue levels between 10 and 30 mg/kg. The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was 12 mg/kg (95/99 Rule). Rounding of the value to 15 mg/kg coincides with the recommendation of the current Meeting.

Hops

Data were available from supervised residue trials on hops in Germany and the USA.

Trials from Germany on hops were reported for the foliar application of a SC formulation. However, there was no approved GAP/label provided for hops.

Etoxazole is registered in the USA for use on hops at a foliar application of a maximum rate of 0.20 kg ai/ha with a PHI of 7 days. Etoxazole residues in dried cones of hops from trials in the USA matching GAP were (n = 3): 2.5, 4.2 and 4.3 mg/kg. Adequate storage stability studies were available in the US trials.

Based on the US trials, the Meeting estimated a maximum residue level and an STMR value for etoxazole in hops of 15 and 4.2 mg/kg respectively.

The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was 8.0 mg/kg (95/99 Rule), however, due to the small number of trials (n = 3) this value was considered unreliable.

Tea

Data from Japan on tea were reported for the foliar application of a SC formulation and a WP formulation.

Etoxazole is registered in Japan for use on tea at a foliar application of 10 g ai/hL (a maximum rate of 0.4 kg ai/ha) with a PHI of 14 days. Etoxazole residues in green tea from trials in Japan matching GAP were (n = 8): 2.4, 3.1, 4.1, 4.7, 4.8, 6.4, 7.3 and 8.0 mg/kg. Adequate storage stability studies were available in Japanese trials.

Based on Japanese trials, the Meeting estimated a maximum residue level and an STMR value for etoxazole in tea of 15 and 4.75 mg/kg respectively.

The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was 13 mg/kg (95/99 Rule). With rounding the value coincides with the recommendation of the current Meeting. The normal Meeting procedure is to round the value to the nearest units of 5 for maximum residue levels between 10 and 30 mg/kg.

Animal feedstuffs

Almond hulls

Trials on almond hulls were reported from the USA (GAP: a foliar application of a maximum rate of 0.15 kg ai/ha with a PHI of 28 days). Etoxazole residues in almond hulls from trials in the USA matching GAP were (n = 5): 0.14, 0.17, 0.23, 0.39 and 1.8 mg/kg. Adequate storage stability studies were available in the US trials.

The Meeting estimated a maximum residue level and an STMR value for etoxazole in almond hulls of 3 and 0.23 mg/kg respectively.

The maximum residue level estimate, derived from use of the NAFTA statistical calculator, was of 2.5 mg/kg (UCLMedian 95th), which when rounded-up is in agreement with the Meeting's estimation.

Cotton gin trash

Data were available from supervised residue trials on cotton gin trash in Australia and the USA

Trials from the USA on cotton gin trash were reported for the foliar application of a SC formulation or a WP formulation. However, storage stability information was insufficient and the residue trials conducted in the USA did not match the GAP on cotton gin trash in the USA.

Trials from Australia on cotton gin trash were reported for the foliar application of a SC formulation or a SC formulation. However, the storage stability of etoxazole residues in the trials was not clear. The Meeting could not use the results of the trials to estimate an STMR value for etoxazole in cotton gin trash.

Fate of residues during processing

The fate of etoxazole residues has been examined in oranges, apples, grapes, cotton seeds and mints processing studies. Processing studies were conducted for apples and grapes in France. However, RAC samples were below the LOQ (0.010 mg/kg), and no residues were found in any processed commodities. Based on the results of processing studies conducted in the USA, processing factors were calculated for apples and grapes. Estimated processing factors and the derived STMR-Ps are summarised in the Table below.

Processing factors and STMR-P for food and feed

Raw agricultural commodity	Processed commodity	Calculated processing factors[a]	PF (Mean or best estimate)	RAC STMR (mg/kg)	STMR-P (mg/kg)
Orange	Wet pomace	1.5	1.5	0.01 (for citrus)	0.015
	Dry pomace	1.5	1.5		0.015
	Juice	< 0.5	0.5		0.005
Grape	Juice	1.7	1.7	0.04	0.068
	Raisin	1.1	1.1		0.044
Mint	Oil	3.0, 0.19	1.6	4.9	7.8

[a] Each value represents a separate study. The factor is the ratio of the residue in processed commodity divided by the residue in the RAC.

The Meeting estimated an STMR-P of 0.015 mg/kg (0.01 × 1.5 = 0.015 mg/kg) for citrus dried pulp, 0.005 mg/kg (0.01 × 0.5 = 0.005 mg/kg) for citrus juice, 0.068 mg/kg (0.04 × 1.7 = 0.068 mg/kg) for grape juice, 0.044 mg/kg (0.04 × 1.1 = 0.044 mg/kg) for dried grapes and 7.8 mg/kg (4.9 × 1.6 = 7.8 mg/kg) for mint oil

Residue in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of etoxazole in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual 2009. Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed in a dry weight basis.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Appendix IX of the FAO manual. The calculations were made according to the animal diets from US/CAN, EU, Australia and Japan in the Table (Appendix IX of the FAO manual).

Livestock dietary burden, etoxazole, ppm of dry matter diet								
	US/CAN		EU		Australia		Japan	
	Max	mean	max	mean	Max	mean	max	Mean
Beef cattle	0.03	0.03	0.00	0.00	0.03[a]	0.03[b]	0.00	0.00
Dairy cattle	0.03	0.03	0.00	0.00	0.03[a]	0.03[bc]	0.00	0.00
Poultry-broiler	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Poultry-layer	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

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

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

[c] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk

Farm animal feeding studies

The Meeting received a lactating dairy cow feeding study, which provided information on likely residues resulting in animal commodities and milk from etoxazole residues in the animals' diets.

Lactating dairy cows

Holstein dairy cows were dosed with etoxazole for 28 days at the equivalent of 1, 3 and 10 ppm in the diet. Residues of etoxazole were below the LOQ (0.01 mg/kg) in whole milk at the 1 and 3 ppm feeding levels. At the 10 ppm level, etoxazole residues in milk were the LOQ level from day 3 to day 27. Cream (day 27) from the 3 ppm level contained at the LOQ (0.02 mg/kg) level of etoxazole residues. Kidney and muscle contained no residue (< 0.005 mg/kg) of etoxazole at 1 and 3 ppm feeding levels, and the LOQ level from only one cow at the 10 ppm level. Liver contained etoxazole residues of the LOQ at the 3 ppm level, and 0.01–0.02 mg/kg at the 10 ppm level. Fat contained etoxazole residues of 0.01–0.02 mg/kg at the 1 ppm, 0.02–0.03 mg/kg at the 3 ppm and 0.06–0.11 mg/kg at the 10 ppm level respectively.

At the 10 ppm feeding level at day 27, etoxazole residue levels in milk were approximately 10% of the levels in cream.

Animal commodities maximum residue levels

For the estimation of maximum residue levels, the residue in the animal commodities is etoxazole.

The maximum dietary burden for beef and dairy cattle is 0.03 ppm, allowing residue levels to be obtained from the 1 ppm feeding level. In a feeding study, in which etoxazole equivalent to 1 ppm in the diet was dosed to lactating cows for 28 consecutive days, no etoxazole residues were detected in liver, kidney and muscle (< 0.01 mg/kg) and milk (< 0.01 mg/kg). Etoxazole residues in fat were < 0.01, 0.014 and 0.015 mg/kg at the 1 ppm level. Therefore no residues (< LOQ) are to be expected at the maximum estimated dietary burden of 0.03 ppm feed for beef cattle and dairy cattle.

The Meeting estimated a maximum residue level of 0.01 (*) mg/kg in mammalian meat and mammalian edible offal, and 0.01 (*) mg/kg in milk.

The mean estimated dietary burden for dairy cattle is 0.03 ppm. No etoxazole residues (< 0.01 mg/kg) were found in any samples of milk at the 1 ppm feeding level. Therefore the Meeting estimated an STMR of 0 mg/kg in milk.

The mean estimated dietary burden for cattle is 0.03 ppm. In muscle, kidney and liver, no etoxazole residues (< 0.01 mg/kg) were detectable at the 1 ppm feeding level. In fat, etoxazole residues above the LOQ (0.01 mg/kg) were found at the 1 ppm level, but no residues (0.015 × 0.03 = 0.0005 mg/kg; LOD: 0.005 mg/kg) are expected to be detected in fat at the mean estimated dietary burden of 0.03 ppm. The Meeting estimated STMRs of 0 mg/kg in meat and offal and 0.0005 mg/kg of fat.

On the fat basis, the Meeting estimated a maximum residue level of 0.01 (*) mg/kg for meat (fat) from mammals (other than marine mammals) and an STMR value of 0.0005 mg/kg.

The maximum and mean dietary burden for broiler and layer poultry are 0.00 ppm. Therefore, no residues are to be expected at the estimated dietary burden for poultry.

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 plant and animal commodities (for compliance with the MRL and for estimation of dietary intake): *Etoxazole*

The residue is fat-soluble.

Commodity		Recommended maximum residue level, mg/kg	STMR or STMR-P, mg/kg
CCN	Name	New	
AM 0660	Almond hulls	3	0.23
FC 0001	Citrus fruits	0.1	0.01
JF 0001	Citrus juice		0.005
VC 0424	Cucumber	0.02	0.01
MO 0105	Edible offal (mammalian)	0.01*	0
FB 0269	Grapes	0.5	0.04
DF 0269	Dried grapes (= currants, Raisins and Sultanas)		0.044
JF 0269	Grape juice		0.068
DH 1100	Hops, dry	15	4.2
MM 0095	Meat (from mammals other than marine mammals)	0.01*(fat)	0
ML 0106	Milks	0.01*	0
HH 0738	Mints	15	4.9
	Mint oil		7.8
DT 1114	Tea, Green, Black (black, fermented and dried)	15	4.75
TN 0085	Tree nuts	0.01*	0

* at or about the LOQ.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) of etoxazole were calculated for the 13 GEMS/Food cluster diets using STMRs/STMR-Ps estimated by the current Meeting (Annex 3 of the 2010 JMPR Report). The ADI is 0–0.05 mg/kg bw and the calculated IEDIs were 0–1% of the maximum ADI (0.05 mg/kg bw). The Meeting concluded that the long-term intakes of residues of etoxazole, resulting from the uses considered by current JMPR, are unlikely to present a public health concern.

Short-term intake

The 2010 JMPR decided that an ARfD was unnecessary. The Meeting therefore concluded that the short-term intake of residues of etoxazole is unlikely to present a public health concern.

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