

## FENPYROXIMATE(193)

### EXPLANATION

Fenpyroximate was first evaluated by the 1995 JMPR, which allocated an ADI of 0-0.01 mg/kg bw. The Meeting estimated a maximum residue level of 0.2 mg/kg for apples but this could not be recommended for use as an MRL owing to the lack of critical supporting data.

The manufacturer provided new residue data for oranges, grapes and hops, a feeding study on cows, metabolism studies on goats and rats, and a processing study on apples.

Information on national MRLs and GAP were provided by the governments of Australia, Germany, Poland, The Netherlands and the UK.

### Animal metabolism

The 1995 JMPR considered the need for a livestock metabolism study in accordance with FAO guidelines in future submissions. The present Meeting received reports of a goat metabolism study. A poultry metabolism study was not reported because byproducts of citrus, apples, grapes and hops, on which fenpyroximate is used, are not included in poultry feed.

Two lactating goats were dosed orally twice daily for 3 consecutive days by gelatin capsule with either [*pyrazole-3-<sup>14</sup>C*]fenpyroximate (10 ppm fenpyroximate in the diet = 0.5 mg/kg bw/day) or [*U-benzyl-<sup>14</sup>C*]fenpyroximate (10 ppm in the diet = 0.3 mg/kg bw/day) (Jalali and Gibson, 1999a,b). The body weights of the goats were 34 and 41 kg, and the feed intakes 1.6 and 1.4 kg animal/day (dry weight). Milk and faeces were sampled twice daily and urine once daily, and the goats were slaughtered approximately 22 hours after the final dose.

The total recovery of radioactivity was 80% for the pyrazole label and 84% for the benzyl label. Excretion in the faeces and urine was found to be a significant route of elimination of fenpyroximate. The recovery of radioactivity from the urine was 32% of the pyrazole label and 12% of the benzyl label. The faeces accounted for 32% of the pyrazole label and 45% of the benzyl label. Less than 0.2% of the dose was excreted in the milk by both goats. The tissues contained small amounts of radioactivity, 3.3% of the total dose from the pyrazole label and 6.0% from the benzyl label. The highest levels of <sup>14</sup>C in the tissues were found in the livers and kidneys. The distribution of <sup>14</sup>C in the tissues, milk and excreta is shown in Table 1.

Table 1. Distribution of the total radioactive residue (TRR) in the tissues, milk and excreta from lactating goats dosed for 3 consecutive days with either [*pyrazole-3-<sup>14</sup>C*]fenpyroximate (10 ppm in the diet) or [*U-benzyl-<sup>14</sup>C*]fenpyroximate (10 ppm in the diet) and slaughtered 22 hours after the final dose (Jalali and Gibson, 1999a,b).

Sample	Pyrazole label		Benzyl label	
	TRR, mg/kg <sup>1</sup>	% of total dose	TRR, mg/kg <sup>1</sup>	% of total dose
Liver	1.2	1.7	1.3	2.7
Kidney	1.1	0.2	2.1	0.7
Muscle	0.021	0.7	0.024	1.1
Fat	0.082	0.6	0.14	1.4

Sample	Pyrazole label		Benzyl label	
	TRR, mg/kg <sup>1</sup>	% of total dose	TRR, mg/kg <sup>1</sup>	% of total dose
Blood	0.026	0.1	0.034	0.1
Milk	0.004-0.033	0.2	0.008-0.031	0.1
Urine	1.1-4.4	25	0.4-1.3	11
Cage wash	0.26	7.3	0.035	1.0
Faeces	0.01-10	31	0.000-11	40
Cage solid	0.48	2	4.3	4.3
Bile	2	0.1	6.2	<0.1
Gastrointestinal tract	0.64	11	0.87	22
Total	–	79.9	–	84.5

<sup>1</sup> As fenpyroximate

The samples were extracted with hexane, acetonitrile and acetonitrile/water. The liver, kidney and fat samples were then hydrolyzed with HCl, NaOH and/or protease. The extracts were analysed by HPLC, TLC and LC-MS.

Over 90% of the <sup>14</sup>C was extracted from the liver, kidney and muscle of both goats and from the fat of the goat dosed with the phenyl label; 81% from the fat of the other goat. The radioactivity extracted from the milk ranged from 67% to 96% of the pyrazole label and 85% to 136% of the benzyl label. Metabolism was rapid. Traces of fenpyroximate were found in the fat, kidneys, muscle and milk. Ten metabolites (G-1-G-10) were identified or characterized. The major compounds found were G-4, (*E*)- $\alpha$ -(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethyleneamino-oxy)-*p*-toluic acid (identified as C in the 1995 evaluation) and G-7 (Y in 1995) (*E*)- $\alpha$ -(3-methyl-5-phenoxy-pyrazol-4-ylmethyleneamino-oxy)-*p*-toluic acid in the liver and kidneys, G-2 (*1*-hydroxymethyl-1-methylethyl (*E*)- $\alpha$ -(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethyleneamino-oxy)-*p*-toluate) and G-4 in muscle and fat, and fenpyroximate, G-2 and G-9 (S) (*4*-cyano-1-methyl-5-phenoxy-pyrazole-3-carboxylic acid) in the milk. M-8 (H) (*1,3*-dimethyl-5-phenoxy-pyrazole-4-carboxylic acid) and G-9 (S) were the major components in the urine. The faeces contained fenpyroximate and G-2. The metabolite G-1 (A) is the (*Z*)- stereoisomer of the parent fenpyroximate. The compounds detected in the tissues and milk are shown in Tables 3 and 4.

Metabolites G-4 (C), G-7 (Y) and G-9 (S) were reported in the 1995 monograph to be found in rats. Metabolite G-2 was considered to be an intermediate in the hydrolysis of fenpyroximate to G-4 (C) and was detected in the liver and plasma of rats (Motoba, 1992). It was therefore considered that there were no essential differences between metabolism in rats and goats. The proposed metabolic pathways are shown in Figure 1.

Table 2. Metabolites identified in the tissues and milk of a goat dosed with [*pyrazole-3-<sup>14</sup>C*]fenpyroximate (10 ppm in the diet) for 3 days and slaughtered 22 hours after the final dose (Jalali and Gibson, 1999a).

Sample	<sup>14</sup> C expressed as fenpyroximate, mg/kg									
	TRR	Fenpyro-ximate	G-1 (A)	G-2	G-3 (T)	G-4 (C)	G-7 (Y)	G-9 (S)	G-6	G-10
Liver	1.21	<0.001	<0.001	0.042	0.053	0.609	0.265	0.016	0.023	0.042
Kidney	1.10	0.005	<0.001	0.016	0.094	0.462	0.305	0.023	0.050	0.044
Muscle	0.024	0.006	<0.001	0.014	<0.001	0.002	<0.001	<0.001	<0.001	<0.001
Fat	0.082	0.035	<0.001	0.029	<0.001	0.006	<0.001	<0.001	<0.001	<0.001

Sample	<sup>14</sup> C expressed as fenpyroximate, mg/kg									
	TRR	Fenpyro -ximate	G-1 (A)	G-2	G-3 (T)	G-4 (C)	G-7 (Y)	G-9 (S)	G-6	G-10
Milk 0-8hr	0.004									
8-24hr	0.020	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.011	<0.001	<0.001
24-32hr	0.026	0.005	<0.001	0.003	<0.001	<0.001	<0.001	0.011	<0.001	<0.001
32-48hr	0.028	0.003	<0.001	0.002	<0.001	<0.001	<0.001	0.010	<0.001	<0.001
48-56hr	0.033	0.008	<0.001	0.003	<0.001	<0.001	<0.001	0.015	<0.001	<0.001
56hr-	0.030	0.001	0.001	0.001	<0.001	<0.001	<0.001	0.011	<0.001	<0.001

Table 3. Metabolites identified in the tissues and milk of a goat dosed with [U-*benzyl*-<sup>14</sup>C]fenpyroximate (10 ppm in the diet) for 3 days and slaughtered 22 hours after the final dose ( Jalali and Gibson, 1999b).

Sample	<sup>14</sup> C expressed as fenpyroximate, mg/kg									
	TRR	Fenpyro -ximate	G-1 (A)	G-2	G-3 (T)	G-4 (C)	G-7 (Y)	G-6	G-5 (E)	G-8
Liver	1.25	<0.001	0.070	0.068	0.073	0.74	0.25	<0.001	0.036	0.014
Kidney	2.08	0.022	<0.001	0.054	0.140	0.98	0.55	0.10	0.11	0.060
Muscle	0.024	0.002	<0.001	0.020	<0.001	0.009	<0.001	<0.001	<0.001	<0.001
Fat	0.14	0.049	<0.001	0.024	<0.001	0.019	0.003	<0.001	<0.001	<0.001
Milk 0-8hr	0.008									
8-24hr	0.013	0.003	0.005	0.003	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
24-32hr	0.024	0.006	<0.001	0.006	<0.001	0.002	<0.001	<0.001	<0.001	<0.001
32-48hr	0.025	0.004	<0.001	0.004	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
48-56hr	0.031	0.008	<0.001	0.007	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
56hr-	0.022	0.003	<0.001	0.006	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

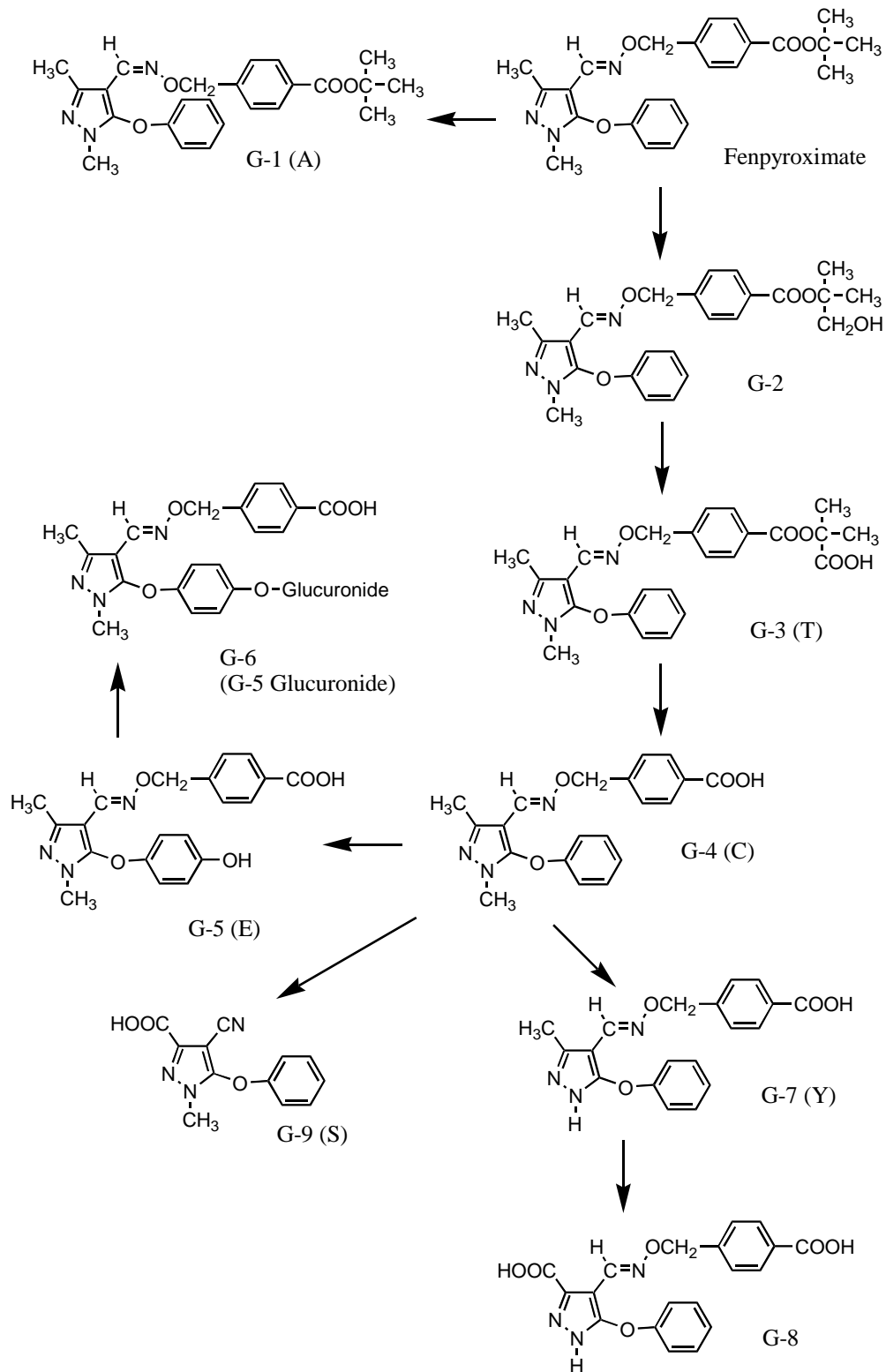
## METHODS OF RESIDUE ANALYSIS

### Analytical method

The Meeting received information on methods of analysis for fenpyroximate in crops, processed commodities, meat and milk.

A method was developed to determine residues of fenpyroximate in orange pulp, orange peel, grapes, and fresh and dried hops in supervised trials (Todd, 1999).

Figure 1. Proposed metabolic pathways of fenpyroximate in goats.



Oranges and grapes. Homogenized sub-samples of orange pulp, orange peel or grapes are extracted twice with acetone/water and centrifuged. The supernatants are collected and adjusted to a volume with acetone/water. An aliquot of the extract is partitioned with dichloromethane (oranges) or ethyl acetate (grapes) after the addition of sodium chloride. The organic layer is collected and the solvent evaporated. The residue is dissolved in diethyl ether/hexane (1:19) and cleaned up on a silica solid phase extraction (SPE) cartridge, eluting with acetone/hexane (1:1). The eluate is reconstituted in acetonitrile/water (7:3) for quantification by LC-MS.

The method was validated over the range of 0.01-0.5 mg/kg for orange pulp and grapes and 0.05-1.0 mg/kg for orange peel. The recoveries from orange pulp, orange peel and grapes were 80-100%, 81-92% and 78-106% respectively, with LODs of 0.01, 0.05 and 0.01 mg/kg respectively (Table 4).

Hops. Sub-samples of dried hops are homogenized twice with ethyl acetate and water, and centrifuged to separate the phases. The organic phases are collected and the solvent evaporated. The residue is dissolved in methanol and an aliquot is partitioned twice with 2,2,4-trimethylpentane with water and saturated sodium carbonate solution. The organic layer is collected and the solvent evaporated. The residue is dissolved in acetonitrile/water (3:10) and cleaned up on a C-18 SPE cartridge, eluting with acetonitrile. The eluate is reconstituted in acetone/water (7:3) for quantification by LC-MS.

The method was validated over the range of 0.05-1.0 mg/kg, giving recoveries of fenpyroximate of 82-96%, with an LOD in dried hops of 0.05 mg/kg (Table 4).

Table 4. Recoveries and limits of determination of fenpyroximate.

Sample	Fortification level, mg/kg	Recovery, %	Mean recovery, %	SD, %	Limit of quantification, mg/kg
Orange pulp	0.01	100, 97, 80	94	7.0	0.01
	0.05	100, 100, 93			
	0.5	92, 97, 86			
Orange peel	0.05	81, 84, 88	87	3.4	0.05
	0.25	86, 86, 85			
	1.0	92, 91, 88			
Grapes	0.01	78, 79, 87	90	11	0.01
	0.05	80, 83, 94			
	0.5	97, 106, 102			
Dried hops	0.05	94, 96, 82	91	4.2	0.05
	0.25	94, 92, 87			
	1.0	89, 90, 91			

In a method for whole apples, apple juice and apple pomace (Hatfield, 1996) homogenized samples were extracted by blending with aqueous ethyl acetate and celite. After filtration and evaporation nearly to dryness the sample was dissolved in an ethyl acetate/cyclohexane mixture, and cleaned up by GPC. The GPC eluate was further cleaned up by SPE with elution with toluene/acetone(95:5). The eluate was concentrated and analysed by gas chromatography with a mass-selective detector.

The method was validated over the range of 0.05-0.5 mg/kg giving recoveries of fenpyroximate and G-1 of 92-123 % and 82-118% (Table 5). The limits of determination were approximately 0.05 mg/kg for both compounds.

Table 5. Recoveries of fenpyroximate and G-1 from apples (Hatfield, 1996).

Sample	Fortification level, mg/kg	Fenpyroximate recovery, %	Mean recovery, % (SD, %)	G-1 recovery, %	Mean recovery, % (SD, %)
Apple	0.05	98, 116, 95	101 (11) n = 9	82, 106, 117	103 (13) n = 9
	0.25	95, 97, 123		118, 109, 110	
	0.5	92, 102, 90		93, 101, 89	

Milk, muscle, kidney, fat, and liver (Baker *et al.*, 1999). Milk and muscle samples were extracted with acetone and then acetone/water (2:1). The combined extracts were acidified, concentrated to remove acetone, and the aqueous solution extracted with ethyl acetate. The ethyl acetate extract was partitioned with aqueous sodium carbonate. The ethyl acetate fraction contained fenpyroximate and G-2, and the aqueous fraction contained G-4 and G-9. The ethyl acetate fraction was concentrated and the residue extracted with acetonitrile, and the acetonitrile replaced with hexane/diethyl ether (9:1) for clean-up on a silica SPE cartridge, eluting with diethyl ether. Fenpyroximate and G-2 in the eluate were both hydrolyzed to G-4, which was methylated with diazomethane. The reaction solvent was evaporated, the residue was dissolved in hexane/diethyl ether (9:1), cleaned up on a silica SPE cartridge, and eluted with diethyl ether. The eluate was reconstituted in acetone for GLC with an NPD. The aqueous fraction containing G-4 and G-9 was acidified and extracted with ethyl acetate, the analytes were methylated with diazomethane, and the analysis completed as above.

Fat samples were extracted twice with acetone, and the combined extracts concentrated and dissolved in hexane. The hexane solution was partitioned with aqueous sodium carbonate or ammonium hydroxide. The hexane fraction contained fenpyroximate and G-2, and the aqueous fraction contained G-4. The hexane and aqueous fractions were cleaned up and analysed as described for milk and muscle.

Liver and kidney samples were homogenized twice with acetonitrile/water (4:1). An aliquot of the combined supernatant fractions was partitioned with acetic acid and the aqueous fraction extracted with acetonitrile. The acetonitrile contained fenpyroximate, G-3, G-4 and G-7. The two acetonitrile fractions were combined and reconstituted in ethyl acetate. The ethyl acetate solution was cleaned up by gel permeation chromatography and the eluate methylated with diazomethane and reconstituted in acetonitrile for analysis by LC-MS-MS.

The limits of determination in the milk and the tissues were 0.005 and 0.01 mg/kg respectively. All residues were corrected for concurrent recoveries from fortified samples if these were below 100%.

### Stability of residues in stored analytical samples

Samples of milk, muscle, liver and kidney were fortified separately with fenpyroximate and appropriate metabolites as identified in the study of metabolism in goats, and stored frozen for periods of 49-79 days. Analytical recoveries from the stored samples were compared with recoveries from freshly fortified samples. Recoveries of fenpyroximate, G-2 and G-9 from milk were 89, 83 and 65% after frozen storage for 73-79 days. Recoveries of fenpyroximate, G-2 and G-4 from muscle were 60, 68 and 47% after storage for 51-56 days. Recoveries of fenpyroximate, G-2 and G-4 from fat were 67, 37 and 54% after storage for 49-54 days. Again the recoveries from unstored samples were low. After 53-55 days frozen storage, recoveries of fenpyroximate, G-7, G-4 and G-3 were 105, 99, 121 and 107% from liver, and 86, 88, 81 and 89% from kidney. The results are shown in Table 6.

Table 6 Recoveries of fenpyroximate and its metabolites from samples fortified at 0.1 mg/kg after frozen storage.

Sample	Storage period, days	Recovery, %											
		Freshly fortified						After storage					
		Fenpyroximate	G-2	G-9	G-3	G-4	G-7	Fenpyroximate	G-2	G-9	G-3	G-4	G-7
Milk	73	90						89					
	77		92						83				
	79			99						65			
Muscle	51	68	72					60	68				
	56					56						47	
Fat	49					60						54	
	54	76	62					67	37				
Liver	53	99			111	106	117	105			107	121	99
Kidney	55	94			93	87	108	86			89	81	88

### Definition of the residue

The current definition is "fenpyroximate". In new animal metabolism and feeding studies the metabolite G-4 was found in the liver and kidneys and G-2 was found in muscle, fat and milk. However, since toxicity studies on fenpyroximate would include these metabolites they indicate that the metabolites would have little or no potential for toxicity.

The Meeting concluded that the current residue definition is suitable both for compliance with MRLs and for the estimation of dietary intake.

The octanol-water partition coefficient and the results of the animal feeding studies indicate that fenpyroximate is fat-soluble.

### USE PATTERN

The Meeting received updated information on the registered uses of fenpyroximate on selected crops, shown in Table 7.

Table 7. Registered uses of fenpyroximate on citrus fruits, pome fruits, grapes, and hops (5% SC formulation, foliar application). Entries in bold indicate changes from Table 19 of the 1995 JMPR residue evaluation.

Crop	Country	Application			PHI, days
		kg ai/ha	kg ai/hl	No.	
Citrus fruits	Brazil	<b>0.05-0.12</b>	<b>0.005</b>	<b>NS</b> <sup>1</sup>	15
	Chile		0.0025	1	14
	Greece	<b>0.1-0.2</b>	0.004-0.005	<b>NS</b>	14
	Italy	0.1	0.005	1	<b>30</b>
	Japan		0.003-0.005	1	14
	Spain			<b>0.005-0.0075</b>	1
Pome fruits	Argentina		0.0025-0.0037	1	14
	<b>Belgium</b>		<b>0.004-0.005</b> <sup>2</sup>		<b>7</b>
	Chile		0.0025	1	21
	<b>Germany</b>	<b>0.12</b>	<b>0.0075</b>	<b>1</b>	<b>21</b>
	Malaysia	0.01-0.02	0.005	1	7
	New Zealand	0.05-0.075	0.0025	1	<b>28</b>
	Portugal	0.05-0.075	0.005-0.0075	1	14

Crop	Country	Application			PHI, days
		kg ai/ha	kg ai/hl	No.	
	Spain		<b>0.0075-0.01</b>	1	7
	Switzerland	<b>0.075-0.1</b>	<b>0.005</b>	1	21
Apples	<b>Australia<sup>3</sup></b>	<b>0.075-0.175</b>	<b>0.005</b>	<b>1</b>	<b>14</b>
	<b>Australia<sup>4</sup></b>	<b>0.038-0.088</b>	<b>0.0025</b>	<b>1</b>	<b>14</b>
	Brazil	0.06	0.005	1	15
	France	0.06-0.08	0.008	1	21
	Germany	0.12	0.0075	1	21
	Greece	0.06-0.11	0.004-0.005	1	7
	Italy	0.075	0.005	1	14
	Japan		0.003-0.005	1	14
	<b>Poland</b>	<b>0.06-0.08</b>	<b>0.006-0.016</b>	<b>1-2</b>	<b>7</b>
	Portugal	0.05-0.075	0.005-0.0075	1	<b>14</b>
	UK	0.1		1	14
Grapes	Chile		0.0025	1	30
	Germany	0.092-0.123	0.008	1	35
	Italy	0.05	<b>0.005</b>	1	<b>28</b>
	Japan		0.003-0.005	1	14
	Portugal	<b>~ 0.075</b>	<b>0.005-0.0075</b>	1	14
	Spain	<b>~ 0.1</b>	<b>0.0075-0.01</b>	1	14
	Switzerland	<b>0.1</b>	<b>0.005</b>	1	21
Hops	Germany	0.225-0.263	0.0075	1	21
	Japan		0.005	1	14

<sup>1</sup> Not specified

<sup>2</sup> 0.004 kg ai/hl in summer

<sup>3</sup> Without integrated pest management (IPM)

<sup>4</sup> With IPM

## RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised field trials in Spain and Italy on oranges and grapes and in Germany on hops. Trials on these commodities and on apples were reviewed by the 1995 JMPR, and the results are reproduced together with new information in Tables 8-11.

Table 8	Oranges
Table 9	Apples
Table 10	Grapes
Table 11	Hops

Fenpyroximate (5% SC) was applied by backpack lance sprayers in trials on oranges in Italy (compressed air) and Spain (motorized). The plots were single rows of 24 to 30 m, and the row spacing was 4.5 to 7 m. Triplicate samples taken from each row were >6 kg (36 fruit in Spain, 48 in Italy) corrected. Samples were separated into peel and pulp in the field, and stored in a freezer for 29 to 49 days in Spain and 23 to 25 days in Italy before analysis.



Grapes were treated by similar sprayers in Italy and Spain. The plot sizes were 3 rows of 15 m, spaced 2.5 to 3 m apart and each field contained one control and two treated plots. Samples >2 kg (>12 bunches) from each row in Spain and 3.7 to 5 kg (>12 bunches) from each row in Italy. The samples were shipped frozen to the analytical laboratories and stored in a freezer for 5 weeks in Spain and 3 weeks in Italy before analysis.

All applications in the trials on hops were made with commercial airblast sprayers towed by tractors. The plots were 6 rows of 20 m, with 3.1 to 3.3 m spacing, and 1 control and 2 treated plots in each field. Samples were >1 kg of fresh and 0.38 to 0.80 kg of dry hops (equivalent to 1.5 to 2.4 kg of fresh). Samples were shipped to the analytical laboratories in dry ice by air. The hops were dried at 63°C in research kilns for 6 h.

Table 8. Residues of fenpyroximate in oranges in supervised trials in Spain and Italy in 1998, and in citrus in trials reviewed by the 1995 JMPR. Residues in replicate field samples from the same plot in each trial are shown separately. Underlined residues are from treatments according to GAP and were used to estimate maximum residue and STMR levels.

Country, Location, (variety)	Form	Application				Sample	PHI, days	Residues, mg/kg		Ref.
		No	kg ai/ha	water l/ha	kg ai/hl			replicates	mean	
Spain, Lepe (Salustiano)	SC	1	0.14	2001	0.007	pulp	14	<0.01(3)	<0.01	Wilson, 1998, NHH092/983274
				2007		peel		0.17,0.18,0.19	0.18	
						whole	14	0.05,0.05,0.06	<u>0.05</u>	
						pulp		<0.01(3)	<0.01	
Spain, Cantillana (Valencia late)	SC	1	0.14	2006	0.007	pulp	14	<0.01(3)	<0.01	
				2004		peel		0.13,0.14,0.22	0.16	
		1	0.14	2004	0.005	whole	14	0.03,0.03,0.05	<u>0.04</u>	
						pulp		<0.01(3)	<0.01	
Italy, Catania (Tarocco comune)	SC	1	0.1	2000	0.005	pulp	30	<0.01(3)	<0.01	
				2000		peel		0.17,0.13,0.09	0.13	
		1	0.1	2000	0.005	whole	30	0.05,0.04,0.03	<u>0.04</u>	
						pulp		<0.01(3)	<0.01	
Palagonia (Tarocco comune)	SC	1	0.1	2000	0.005	peel	31	0.13,0.12,0.10	0.12	
				2000		whole		0.04,0.04,0.03	<u>0.04</u>	
		1	0.1	2000	0.005	pulp	31	<0.01(3)	<0.01	
						peel		0.10,0.13,0.15	0.13	
whole	0.04,0.04,0.05	<u>0.04</u>								
						pulp		<0.01(3)	<0.01	
						peel		0.12,0.09,0.13	0.11	
						whole		0.04,0.03,0.05	<u>0.04</u>	

#### Trials reviewed by 1995 JMPR.

Country, Year, Crop	Application			PHI, days	Fenpyroximate, mg/kg			Ref.
	No.	kg ai/ha	kg ai/hl		Pulp	Peel	Whole	
Brazil, 1989-1990 Oranges	2	0.08	0.005	15	<0.05	0.2		

				30	<0.05	<0.05		R-08
	2	0.16	0.01	15	<0.05	0.1		R-09
	2	0.18	0.005	30	<0.05	<0.05		
				16	<0.05	0.38		R-10
				29	<0.05	0.18		
		0.36	0.01	16	0.08	0.73		R-11
						0.85		
				29	<0.05	0.59		
Greece, 1992 Oranges	1	0.15	0.005	0	<0.01	0.35	0.12	
				2	<0.01	0.37	0.11	R-12
				9	<0.01	0.3	0.11	
				16	<0.01	0.26	<u>0.09</u>	
				22	<0.01	0.13	0.05	
				28	<0.01	0.18	0.07	
	1	0.31	0.01	0	<0.01	0.31	0.11	R-13
				2	<0.01	0.28	0.12	
				9	<0.01	0.19	0.07	
				16	<0.01	0.24	0.08	
				22	<0.01	0.19	0.07	
				28	<0.01	0.23	0.08	
Italy, 1990 Oranges	2	0.077	0.0075	21	0.05	0.38		
				64	<0.05	0.39		R-14
				113	<0.05	0.35		
	2	0.077	0.0075	21	<0.05	0.3		R-15
				63	<0.05	0.26		
				105	<0.05	0.36		
	2	0.077	0.0075	21	0.06	0.54		R-16
				63	<0.05	0.53		
				84	<0.05	0.4		
	2	0.15	0.015	21	0.08	0.73		R-17
				64	<0.05	0.77		
				113	<0.05	0.62		
	2	0.15	0.015	21	<0.05	0.96		R-18
				63	<0.05	0.57		
				105	<0.05	0.71		
				21	0.08	0.83		R-19
				43	<0.05	0.75		
				84	<0.05	0.72		
Italy, 1991 Mandarins	1	0.1	0.006	28	0.01	0.35		R-01
	1	0.2	0.013	28	<0.01	0.42		R-03
					0.03	0.78		R-02
					0.03	0.86		R-04
	1	0.1	0.006	0	0.03	0.52		R-05
				5	0.02	0.5		
				10	<0.01	0.36		
				14	<0.01	0.34		
				25	0.02	0.24		
				28	<0.01	0.13		
	1	0.2	0.013	0	0.05	0.45		R-06
				5	0.06	0.63		
				10	0.03	0.57		
				14	0.03	0.83		
				25	0.02	0.59		
				28	0.01	0.59		
Japan, 1989	1	0.25	0.005	7	0.006	0.15	0.028	R-07
					0.006	0.14		
Mandarins,				14	<0.005(2)	0.15	0.026	
						0.14		

Greenhouse	1	0.5	0.005	21	0.009(2)	0.08 0.068	0.019
				30	0.008 0.007	0.17(2)	0.037
				44	0.007(2)	0.21 0.18	0.04
				7	0.027 0.024	0.99 0.96	0.20
				14	0.023 0.019	0.98 0.97	0.21
				21	0.01 0.01	0.69 0.66	0.15
				30	0.01 0.01	0.67 0.65	0.12
				44	<0.005(2)	0.72 0.68	0.13

Table 9. Trials on apples reviewed by 1995 JMPR.

Country, Year	Application			PHI, days	Fenpyroximate, mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl			
Australia, 1992	1	0.083	0.005	0	0.09, 0.07, 0.1, 0.13	R-20
				7	0.08, 0.10, 0.05, 0.06	
				14	<u>0.14</u> , <u>0.12</u> , 0.08, <u>0.18</u>	
				24	0.06(2), 0.03, <u>0.17</u>	
	1	0.16	0.01	0	0.34, 0.30, 0.23(2)	
				7	0.19, 0.33, 0.29, 0.22	
				14	0.19(2), 0.18, 0.17	
				24	0.12, 0.19, 0.08(2)	
Belgium, 1991	1	0.090	0.006	7	0.12	R-21
				14	0.10	
				21	<u>0.08</u>	
				28	0.05	
	1	0.18	0.012	7	0.19	
				14	0.17	
				21	0.14	
				28	0.18	
France, 1989	1	0.06	0.006	0	0.1	R-22
				7	0.08	
				14	0.03	
				21	0.02	
				29	<u>0.03</u>	
	2	0.06		48	0.05	
				53	0.07	
				69	0.03	
	2	0.08	0.008	48	0.08	
				53	0.03	
				69	0.04	
France, 1990	1	0.08	0.008	0	0.11, 0.12	R-22
				7	0.05, 0.08	
				14	0.06, 0.10	
				20-21	0.05, <u>0.09</u>	
				29	0.03, <u>0.06</u>	
	2	0.06	0.006	24	<u>0.11</u>	
				68	0.05	
	2	0.08	0.008	24	<u>0.16</u>	
				68	0.07	
	2	0.17	0.006	45	0.08	
	2	0.23- 0.24	0.008	45	0.19	

Country, Year	Application			PHI, days	Fenpyroximate, mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl			
France, 1991	1	0.08	0.008	30	0.03	R-23
				50	0.03	
				75	<0.02	
				106	<0.02	
				120	<0.02	
				144	<0.02	
Germany, 1989	2	0.1125	0.0075	0	0.1, 0.19	R-24
				7	0.12, 0.18	
				14	0.11, 0.1	
				21	<u>0.1, 0.09</u>	
	2	0.0643- 0.0868	0.0075- 0.0073	0	0.12	
				7	0.12	
				14	0.08	
				21	<u>0.09, 0.12</u>	
	2	0.1- 0.115	0.0075- 0.0076	0	0.21	
				7	0.19	
				14	0.15	
				21	<u>0.16</u>	
	2	0.15	0.001	0	0.23, 0.24	R-25
				7	0.23	
				14	0.24	
				21	0.24	
	2	0.095,0. 132	0.01	0	0.12	
				7	<0.01(2)	
				14	0.12	
				21	<u>0.12</u>	
Germany, 1990	1	0.064	0.0075	0	0.15	R-26
				7	0.11	
				14	0.16	
				28	0.12	
				42	0.09	
				56	0.06	
				70	<0.05	
				81	<0.05	
				92	<0.05	
	1	0.1125	0.0075	0	0.13	
				7	0.14	
				14	0.11	
				28	0.08	
				42	0.06	
				56	<0.05	
				70	<0.05	
				84	<0.05	
				91	<0.05	
	2	0.075	0.0075	0	0.13	
				7	0.08	
				14	0.08	
				21	<u>0.06</u>	
				28	<0.05	
	2	0.081	0.0075	0	0.24	
				7	0.21	
				14	0.18	
				21	<u>0.15</u>	
				28	0.13	

Country, Year	Application			PHI, days	Fenpyroximate, mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl			
	2	0.1125	0.0075	0 7 14 21 28	0.21 0.17 0.13 <u>0.08</u> 0.11	
	2	0.114	0.0076	0 7 14 21 28	0.05 <0.05 <0.05 <u>&lt;0.05</u> <0.05	
Japan, 1990	1	0.14	0.005	15 30 45 60	<u>0.11</u> 0.08 <u>0.034</u> <u>0.042</u>	R-28
	1	0.25	0.005	15 30 45 60	<u>0.048</u> 0.028 0.007 <u>&lt;0.005</u>	
New Zealand, 1991/92	1		0.0025 (3 trials)	7-9 14 28 42-43	0.07, 0.09, 0.12 0.12, 0.13, 0.03 <u>&lt;0.01(3)</u> <u>&lt;0.01(2), 0.01</u>	R-29
	1		0.005 (3 trials)	7-9 14 21 28 42-43 52-56	0.1, 0.07, 0.06 <u>0.05, 0.04</u> , 0.02 <0.01 <u>0.03(2)</u> , <0.01 <0.01(2), 0.01 <0.01(3)	
New Zealand, 1993/94	1		0.0025 (4 trials)	7-9 14 21 28 35 42-43 49 52-56	0.05, 0.06, 0.01(2) 0.03(2), <0.01, 0.04 0.04(2), 0.02, <0.01 0.03, 0.02, <0.01(2) 0.02(2), 0.01, <0.01 0.02(3), <0.01 0.02, 0.01, <0.01 0.01, <0.01(2)	R-30
	1		0.005 (4 trials)	7-9 14 21 28 35 42-43 49 52-56	0.11, 0.07, 0.06, 0.05 <u>0.08, 0.06(2)</u> , 0.03 0.03, 0.04, 0.05, <u>0.06</u> 0.03(2), 0.05, 0.02 0.03(2), 0.04, 0.01 0.04, 0.03(2), <0.01 0.03, 0.02, 0.01 0.03, 0.01, <0.01	

Table 10. Residues of fenpyroximate in grapes from supervised trials in Spain and Italy in 1998 (Wilson, 1999a), and in trials reviewed by the 1995 JMPR. Residues in replicate field samples from the same plot in each trial are shown separately. Underlined residues are from treatments according to GAP and were used to estimate maximum residue and STMR levels.

Country,	Form.	Application	PHI	Residues	Ref.
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		No.	kg ai/ha	Water, l/ha	kg ai/hl	days	mg/kg	
Spain, Bollulos (Cardinal)	SC	1	0.10	991 1007	0.01	14	<u>0.04</u> <u>0.06</u>	Wilson, 1999a, NHH093/985072
Spain, Los Palacios (Cardinal)	SC	1	0.10	1014 1029	0.01	14	<u>0.04</u> <u>0.04</u>	
Italy, Granieri (Italia)	SC	1	0.05	1014 1002	0.005	28	<u>0.04</u> <u>0.02</u>	
Italy, Mazzarrone (Italia)	SC	1	0.05	999 1002	0.005	28	<u>0.04</u> <u>0.03</u>	

**Trials reviewed by 1995 JMPR**

Country, Year Location	Application			PHI days	Fenpyroximate mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl			
France, 1989	1	0.06	0.006	0	0.05	R-31
				7	<0.02	
				14	<u>&lt;0.02</u>	
				21	<0.02	
				29	<0.02	
	2		0.006	36	0.05	R-31
				37	0.07	
				47	<0.02	
France, 1990	2	0.06	0.006	42	0.05	R-31
				46	0.07	
				55	0.06	
France, 1990	1	0.08	0.008	0	0.1	R-31
				7	0.05	
				14	0.05	
				21	<u>0.08</u>	
				30	0.07	
France, 1989	2	0.08	0.008	36	<0.02	R-31
				37	0.14	
				47	<0.02	
France, 1990	2	0.08	0.008	42	0.08	R-31
				46	0.05	
				55	0.04	
Germany, 1989 Mussbach	2	0.14	0.023	0	0.17	R-32
				7	0.12	
				14	0.11	
				28	0.09	
				35	0.06	
Germany, 1989 Kappelrodeck	2	0.14	0.023	0	0.41	R-33
				7	0.41	
				14	0.27, 0.34	
				28	0.32	
				35	0.4	
Germany, 1989 Pfeddersheim	2	0.18	0.03	0	0.2	R-34
				7	0.12, 0.17	
				14	0.14	
				28	0.21	
				35	0.15	
Willsbach	2	0.18	0.03	0	0.19(2)	R-35
				7	0.18	
				14	0.24	
				28	0.16	

Country, Year Location	Application			PHI days	Fenpyroximate mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl			
				35	0.13, 0.14	
Germany, 1989 Mussbach	2	0.18	0.03	0 7 14 28 35	0.26 0.16 0.1(2) 0.13 0.13	R-36
Germany, 1989 Kappelrodeck	2	0.18	0.03	0 7 14 28 35	0.29 0.3(2) 0.18 0.12 0.16	R-37
Germany, 1991 Nittel	2	0.045-0.035	0.015-0.225	0 7 14 28 35	0.22 0.16 0.16 0.1 0.08	R-38
Muhlhofan	2	0.045-0.135	0.015-0.225	0 7 14 28 35	0.36 0.29 0.17 0.12 0.11	
Italy, 1991	1 1 1 1 1 1	0.081 0.16 0.094 0.19 0.064 0.13	0.0062 0.012 0.0063 0.013 0.0064 0.013	14 14 14 4 14 14	<u>0.47</u> <u>0.57</u> <u>0.17</u> 0.52 <u>0.07</u> <u>0.19</u>	R-39 R-40 R-41
Japan, 1988	1	0.2	0.005	14 21	0.38, <u>0.41</u> <u>0.45</u> , 0.41	R-42
greenhouse				30 60	0.36, 0.33 0.062, 0.058	
Japan, 1989 greenhouse	1 2	0.2	0.005 0.005	13 20 29 13 20	0.43(2) <u>0.53</u> , 0.5 <u>0.51</u> , 0.49 1.1, 1.2 1.1, 1.2	R-43 R-43

Table 11. Residues of fenpyroximate in hops from supervised trials in Germany in 1998 (Wilson, 1999b), and in trials reviewed by the 1995 JMPR. Residues in replicate field samples from the same plot in each trial are shown separately. Underlined residues are from treatments according to GAP and were used to estimate maximum residue and STMR levels.

Country, Year Location	Form	Application				Sample	PHI, days	Residues, mg/kg	Report
		No.	kg ai/ha	water, l/ha	kg ai/hl				
Germany, Wolnzach (Perle)	SC	1	0.27 0.26	3526 3431	0.008	fresh	21	1.6 1.9	Wilson, 1999b. NHH094/98 4984
						dry	21	<u>4.4</u> <u>5.0</u>	
Germany, Wolnzach (Magnum)	SC	1	0.28 0.28	3677 3641	0.008	Fresh	21	1.7 1.8	
						dry	21	<u>5.9</u> <u>8.4</u>	
Germany,	SC	1	0.26	3446	0.008	fresh	21	1.9	

Wolnzach (Hersbrucker)		0.27	3542				1.9
					dry	21	<u>7.4</u> <u>6.2</u>

**Trials on hops reviewed by the 1995 JMPR**

Country, Year Location	Application			PHI, days	Sample	Fenpyroximate, mg/kg	Ref.
	No.	kg ai/ha	kg ai/hl				
Germany, 1989, Gambach	1	0.375	0.0125	0 7 14 21 21	green    dry	5.2, 7.6 1.6, 3.8 0.9, 3.1 0.8, 3.2 6.4, <1	R-44,R-45
Oberrunseried	1	0.375	0.0086	0 7 14 21 21	green    dry	2.7, 2.6 1.6, 1.1 1.5, 1.1 0.5, 0.8 <u>2.1, 2.1</u>	R-46,R-47
Germany, 1990, Gambach	1	0.375	0.0188	0 7 14 21 21	green    dry	3.1, 1.8 3.7, 2.1 3.7, 2.5 1.1, <0.5 6.8, 8.2	R-48
Germany, 1990, Gambach	1	0.75	0.0375	0 7 14 21 21	green    dry	11.6 11.3 15.8 10.4 28.7	R-48
Germany, 1990, Tannant Red	1	0.375	0.015	0 7 14 21 21	green    dry	5.3 2.5 2.4 2.1 7.0	R-48
Germany, 1990, Lindau-Bodenegg	1	0.375	0.0094	0 7 14 21 21	green    dry	4.7 3.5 13.7 4.9 <u>≤1</u>	R-48
Germany, 1990, Lindau-Bodenegg	1	0.75	0.0188	0 7 14 21 21	green    dry	25.9 24.1 12.1 9.2 25	
Germany, 1991	1	0.23	0.0075	0 7 14 21 21	green    dry	11.3, 6.6, <0.5 1.5, 2.3, 2.6 <0.5, 1.2, 1.7 <0.5, 0.7, 1.6 <u>1.2, 3.7, 4.3</u>	R-49
Germany, 1991	1	0.46	0.015	0 7 14 21 21	green    dry	9.8, 6.8, 14.7 4.2, 4.0, 4.0 1.3, 2.5, 2.3 0.6, 1.5, 3.1 2.5, 4.9, 3.6	

**Livestock feeding trials**



The Meeting received information on a lactating dairy cow feeding study on fenpyroximate. (Baker, 1999)

Three groups of three Holstein dairy cows were dosed orally by gelatin capsules once daily for 29 consecutive days with fenpyroximate at rates equivalent to approximately 1, 3, and 10 ppm dry weight in the diet (19, 57 and 190 mg of fenpyroximate per cow per day). There was one control cow. Milk was collected in the morning and evening on days 0, 1, 3, 7, 11, 14, 18, 21, 24 and 28 and stored frozen until analysis. All the cows were slaughtered between 15 and 22 hours after their final doses and samples of liver (~1 kg), both kidneys, composite round and loin muscle (~1 kg), and composite omental and permental fat (~1 kg) were collected. Tissue samples were homogenized frozen and stored frozen up to 63 days before extraction and analysis. Milk samples were stored frozen for a maximum of 82 days between collection and extraction. The cows were fed a combination of roughage (hay) and high-protein dairy concentrate. In the acclimatization day all the cows were fed 18.7-18.9 kg/day (6.4 kg concentrate and 12.3-12.5 kg hay). During the dosing period the mean feed consumption was 18.7 kg/day for the control cow and 18.9, 19.0 and 19.0 for the 1 ppm, 3 ppm and 10 ppm dose groups. There was little change in the body weights between acclimatization and slaughter. The control cow lost 3 kg, the low-dose group lost a mean 1 kg, the 3 ppm group gained 8 kg and the high-dose group gained 7 kg.

The residues found in the 10 ppm, 3 ppm and 1 ppm dose groups are shown in Tables 13, 14 and 15 respectively.

Milk. The mean residues of fenpyroximate plus G-2 in the 10 ppm dose group reached a maximum of 0.017 mg/kg 1 day after the first dose (the highest individual residue was 0.022 mg/kg after 3 days) and then generally decreased except for a residue of 0.016 mg/kg at 21 days. Residues of G-9 in the 10 ppm group were below the LOD until 24 days and were then 0.005 mg/kg. Milk from the 3 ppm dose group was analysed at 3, 14 and 21 days and contained <0.005-0.011 mg/kg of fenpyroximate plus G-2; residues of G-9 were either not detected or less than 0.005 mg/kg. It was considered that the analyses of milk from the 1 ppm dose group were not necessary.

Muscle. The mean residues in muscle of fenpyroximate plus G-2 in the 10 ppm, 3 ppm and 1 ppm dose groups were 0.038, 0.015 and <0.01 mg/kg respectively (the range was <0.01 to 0.049 mg/kg). The residues of G-4 in the 10 ppm and 3 ppm dose groups were either not detected or less than 0.01 mg/kg.

Fat. The mean residues of fenpyroximate plus G-2 in the 10 ppm, 3 ppm and 1 ppm dose groups were 0.1, 0.056 and 0.015 mg/kg respectively, with a range of 0.01 to 0.16 mg/kg. Residues of G-4 in the 10 ppm and 3 ppm dose groups were all less than 0.01 mg/kg .

Liver. The mean residues of G-4 in the 10 ppm, 3 ppm and 1 ppm dose groups were 0.80, 0.37 and 0.19 mg/kg respectively. Residues of fenpyroximate plus G-2, G-7 and G-3 were  $\leq$ 0.01 mg/kg in the 10 ppm dose group and not detected in the other groups.

Kidneys. The mean residues of fenpyroximate plus G-2 were 0.014 mg/kg in the 10 ppm dose group, <0.01 mg/kg in the 3 ppm dose group and undetected in the 1 ppm dose group. The mean residues of G-4 were 0.40, 0.29 and 0.20 mg/kg. G-7 and G-3 were undetectable in all three groups.

Table 12. Residues in the milk and tissues of cows dosed at 10 ppm.

Sample	Residues, mg/kg				
	Fenpyroximate/G-2	G-9	G-4	G-7	G-3
Milk/ Day 0	ND, <0.005(2)	ND, <0.005(2)	-	-	-
Day 1	0.017, 0.014, 0.021	ND(3)	-	-	-

Sample	Residues, mg/kg				
	Fenpyroximate/G-2	G-9	G-4	G-7	G-3
Day 3	0.022, 0.015, 0.014	ND(3)	–	–	–
Day 7	0.007, 0.019, 0.015	ND(2), <0.005	–	–	–
Day 11	0.010(2), 0.017	ND(3)	–	–	–
Day 14	0.012(2), 0.014	ND(3)	–	–	–
Day 18	0.007, 0.013, 0.014	ND(2), <0.005	–	–	–
Day 21	0.013, 0.019, 0.015	<0.005(2), ND	–	–	–
Day 24	0.006, 0.007, 0.008	0.005(3)	–	–	–
Day 28	0.015, 0.008, 0.007	<0.005(3)	–	–	–
Liver	<0.010(2), 0.011	–	0.90, 0.70, 0.80	ND(2), <0.01	<0.01, ND(2)
Kidney	0.009, 0.014, 0.019	–	0.35, 0.44, 0.41	ND(3)	ND(3)
Muscle	0.024, 0.040, 0.049	–	ND(2), <0.010	–	–
Fat	0.046, 0.136, 0.12 (0.052, 0.115, 0.159)	–	ND(2), <0.01 (<0.01(3))	–	–

–: not determined ND: not detected

Values in parentheses are from analysis of a second set of samples

Table 13. Residues in the milk and tissues of cows dosed at 3 ppm.

Sample	Residues, mg/kg				
	Fenpyroximate/G-2	G-9	G-4	G-7	G-3
Milk/ Day 3	<0.005(3)	ND(3)	–	–	–
Day 14	0.007, 0.006, 0.011	<0.005(2)	–	–	–
Day 21	0.007, 0.005, <0.005	<0.005(2), ND	–	–	–
Liver	ND(3)	–	0.42(2), 0.28	ND(3)	ND(3)
Kidney	ND(2), <0.01	–	0.35, 0.29, 0.23	ND(3)	ND(3)
Muscle	0.012, 0.017, 0.015	–	ND(3)	–	–
Fat	0.025, 0.073, 0.071	–	ND, 0.01(2)	–	–

–: not determined. ND: not detected

Table 14. Residues in the tissues of cows dosed at 1 ppm.

Sample	Residues, mg/kg				
	Fenpyroximate/G-2	G-9	G-4	G-7	G-3
Liver	ND(3)	–	0.2, 0.16, 0.22	ND(3)	ND(3)
Kidney	ND(3)	–	0.18, 0.23, 0.2	ND(3)	ND(3)
Muscle	<0.01(3)	–	–	–	–
Fat	0.018, 0.016, 0.01	–	–	–	–

–: not determined.

## FATE OF RESIDUES IN STORAGE AND PROCESSING

## Processing

Apples. In four field trials apples were sprayed twice  $21 \pm 1$  days and 7 days before maturity, at 0.15 kg ai/ha (0.008 kg ai/hl) before maturity. The apples were processed to juice and pomace at A.C.D.S. Research Inc. by procedures that simulated commercial processing.

Fresh, unwashed apples were ground in a hammer-mill and the resulting wet mash was pressed to 155-211 kg/cm<sup>2</sup> for five minutes in one or more cloth stacks in a hydraulic press. The wet pomace remained as a cake after juice extraction. The residues, and the processing factors for pomace, are shown in Table 15. Processing factors could not be calculated for juice because all the residues were below the LOD.

Table 15. Residues of fenpyroximate and G-1 in apples and their processed fractions, USA, 1994.

Location	Fresh apples		Juice		Wet pomace			
	Fenpyroximate, mg/kg	G-1, mg/kg	Fenpyroximate, mg/kg	G-1, mg/kg	Fenpyroximate		G-1	
					mg/kg	PF <sup>1</sup>	mg/kg	PF <sup>1</sup>
MI	0.21, 0.15	<0.05(2)	<0.05	<0.05	0.93	5.17	0.07	1.4
NY	0.10, 0.15	<0.05(2)	<0.05	<0.05	0.65	5.20	<0.05	-
PA	0.06, 0.10	<0.05(2)	<0.05	<0.05	0.48	6.0	<0.05	-
WA	0.10, 0.09	<0.05(2)	<0.05	<0.05	0.38	4.0	<0.05	-

<sup>1</sup> Processing factor

## RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

No information.

## NATIONAL MAXIMUM RESIDUE LIMITS

National MRLs in Australia were reported. The Table below shows these and the national MRLs previously listed in the 1995 evaluation.

Country	Commodity	MRL, mg/kg
Australia	Apple	0.3
	Pear	0.3
Belgium	Pome fruits	0.2
	Others	0.01
Brazil	Citrus fruits	0.5
	Apple	0.1
France	Apple	0.2
	Grapes	0.2
Japan	Satsuma mandarin	0.5
	Citrus fruits (except Satsuma mandarin)	1
	Apple	1
	Grapes	2
	Hops	15
Spain	Citrus fruits	0.3
	Pome fruits	0.3
	Grapes	0.3
Switzerland	Apples	0.2
	Grapes	0.2

## APPRAISAL

Fenpyroximate was first evaluated for toxicity and residues by the 1995 JMPR, which allocated an ADI of 0-0.01 mg/kg bw. That Meeting estimated a maximum residue level of 0.2 mg/kg for apples but this could not be recommended for use as an MRL owing to the lack of critical supporting data.

The Meeting received information on analytical methods with supplementary residue data on oranges, grapes and hops, animal metabolism studies on goats and rats, and an animal feeding study on cows.

### Animal metabolism

The metabolism of fenpyroximate in goats was rapid. Small traces of fenpyroximate were found in fat, kidney, muscle and milk. Ten metabolites were identified or characterized. The main compounds found were G-4 ((*E*)- $\alpha$ -(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethylene-amino-oxy)-*p*-toluic acid) and G-7 ((*E*)- $\alpha$ -(3-methyl-5-phenoxy-pyrazol-4-ylmethylene-amino-oxy)-*p*-toluic acid) in the liver and kidneys, fenpyroximate, G-2 (1-hydroxymethyl-1-methylethyl (*E*)- $\alpha$ -(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethylene-amino-oxy)-*p*-toluate) and G-4 in muscle and fat, fenpyroximate, G-2 and G-9 (4-cyano-1-methyl-5-phenoxy-pyrazole-3-carboxylic acid) in milk and M-8 (1,3-dimethyl-5-phenoxy-pyrazole-4-carboxylic acid) and G-9 in urine. The faeces contained fenpyroximate and G-2.

### Analytical methods

Analytical methods for fenpyroximate and its isomer were described in the 1995 evaluation. They were based on extraction with methanol and acetone, partitioning with hexane and acetonitrile and clean-up with some combination of C-18 cartridges, gel permeation, silica gel and alumina columns. Determination was by GLC and HPLC. The limits of determination were 0.01 mg/kg for green peppers by HPLC, and 0.1 and 0.2 mg/kg for fruit and tea by GLC.

In the analytical method used for the supervised field trials homogenized orange pulp, orange peel and grapes are extracted with acetone/water twice and centrifuged to separate the phases. The supernatants are collected and adjusted to a volume with acetone/water. An aliquot of the extract is partitioned with dichloromethane (oranges) and ethyl acetate (grapes) after addition of sodium chloride. The organic layer is collected and evaporated. The residue is dissolved in diethyl ether/hexane (1:19) and cleaned up on a silica solid phase extraction (SPE) cartridge, eluted with acetone/hexane (1:1). The eluate is reconstituted in acetonitrile/water (7:3) for quantification by LC-MS. The limits of determination in orange pulp, orange peel and grapes are 0.01, 0.05 and 0.01 mg/kg.

Dried hops are homogenized and extracted with ethyl acetate twice after the addition of water and centrifuged to separate the phases. The organic phases are collected and evaporated. The residue is dissolved in methanol. An aliquot of the extract is partitioned twice with 2,2,4-trimethylpentane after the addition of water and saturated sodium carbonate solution. The organic layer is collected and evaporated. The residue is dissolved in acetonitrile/water (3:10) and cleaned up on a C-18 SPE cartridge, eluted with acetonitrile. The eluate is reconstituted in acetone/water (7:3) for quantification by LC-MS. The limit of determination is 0.01 mg/kg.

In the analytical method used for the processing study on apples homogenized samples of apples, apple juice or apple pomace are extracted by blending with aqueous ethyl acetate and celite. After filtration the extract is evaporated nearly to dryness. The sample is dissolved in ethyl acetate/cyclohexane mixture and cleaned up by GPC. The GPC eluate is further cleaned up on an SPE cartridge eluted with toluene/acetone(95:5). The eluate is concentrated and analysed by gas chromatography with a mass selective detector. The limits of determination are approximately 0.05 mg/kg.

In the analytical methods for animal products used in the animal processing study milk and muscle samples are extracted with acetone and then acetone/water (2:1). The combined extracts are acidified and concentrated to remove acetone, the aqueous solution is extracted with ethyl acetate and the extract partitioned with aqueous sodium carbonate. The ethyl acetate fraction contains fenpyroximate and G-2, while the aqueous fraction contains G-4 and G-9. The ethyl acetate fraction is concentrated and the residue extracted with acetonitrile. The acetonitrile extract is reconstituted in hexane/diethyl ether (9:1) and cleaned up on a silica SPE cartridge, eluted with diethyl ether. Fenpyroximate and G-2 in the eluate are hydrolysed to the common product G-4 which is subsequently methylated with diazomethane. The reaction solution is evaporated and the residue dissolved in hexane/diethyl ether (9:1) and cleaned up on a silica SPE cartridge, eluted with diethyl ether. The eluate is reconstituted in acetone for analysis by GLC with an NPD. The aqueous fraction containing G-4 and G-9 is acidified and extracted with ethyl acetate. The ethyl acetate extract is methylated with diazomethane. The reaction solution is reconstituted in hexane/diethyl ether (9:1) and cleaned up on a silica SPE cartridge eluted with diethyl ether. The eluate is reconstituted in acetone for GLC analysis.

Fat samples are extracted twice with acetonitrile. The combined extracts are concentrated and dissolved in hexane. The hexane solution is partitioned with aqueous sodium carbonate and ammonium hydroxide. The hexane fraction contains fenpyroximate and G-2, while the aqueous fraction contains G-4. The hexane and aqueous fractions are cleaned up and analysed as described for milk and muscle.

Liver and kidney samples are homogenized twice with acetonitrile/water (4:1). The combined supernatant fractions are made up to a volume. An aliquot is partitioned with acetic acid and the aqueous fraction is extracted with acetonitrile. The acetonitrile fraction contains fenpyroximate, G-3 ((E)-2-[4-(1,3-dimethyl-5-phenoxy-pyrazol-4-ylmethyleneaminoxy)methyl]benzoyloxy]-2-methylpropionic acid), G-4 and G-7. The acetonitrile fractions are reconstituted in ethyl acetate. The ethyl acetate solution is cleaned up by GPC and the eluate is methylated with diazomethane and reconstituted in acetonitrile for LC-MS-MS analysis. The limits of determination in the milk and tissues are 0.005 and 0.01 mg/kg.

### **Stability of residues in stored analytical samples**

Animal commodities. Samples were fortified separately with fenpyroximate and various metabolites at 0.1 mg/kg.

Milk was stored frozen for 73-79 days. Recoveries of fenpyroximate, G-2 and G-9 were 89, 83 and 65%. Recoveries of fenpyroximate, G-2 and G-4 were 60, 68 and 47% from muscles stored for 51-56 days, and 67, 37 and 54% from fat stored for 49-54 days. Liver and kidney samples were stored frozen for 53 and 55 days. Recoveries of fenpyroximate, G-7, G-4 and G-3 were 105, 99, 121 and 107% from liver and 86, 88, 81 and 89% from kidneys.

Plant commodities. The storage stability of fenpyroximate in plant commodities was reported in the 1995 monograph. After about 3 years approximately 65% of the initial residue remained on apples and grapes stored at -20°C. In citrus samples fortified with fenpyroximate 65% remained in the pulp stored for 140 days and 72% in peel stored for 188 days. About 100% of the fenpyroximate remained in hops stored at -18°C for 2 years, about 100% of the residues remaining. No new studies were reported.

### **Definition of the residue**

The current residue definition is "fenpyroximate". In new animal metabolism and feeding studies the metabolite G-4 was found in the liver and kidneys and G-2 was found in muscle, fat and milk. However, since toxicity studies on fenpyroximate would include these metabolites they indicate that the metabolites would have little or no potential for toxicity.

The Meeting concluded that the current residue definition is suitable both for compliance with MRLs and for the estimation of dietary intake.

The octanol-water partition coefficient and the results of the animal feeding studies indicate that fenpyroximate is fat-soluble.

### Use pattern

Fenpyroximate is an acaricide. National registrations specify only one application per season to avoid the development of resistance.

For tree crops, spray concentration (kg ai/hl) rather than application rate (kg ai/ha) is the prime determinant of GAP for the use of fenpyroximate.

### Results from supervised trials

Oranges. Fenpyroximate may be used at 0.005 kg ai/hl (0.1 kg ai/ha) on oranges in Italy with a PHI of 30 days. The residues in whole oranges in four trials in Italy under these conditions were all 0.04 mg/kg and in one trial in Greece in accordance with Italian GAP the residue was 0.07 mg/kg. The residues in the pulp in all five trials were <0.01 mg/kg.

Fenpyroximate may be used at 0.005-0.0075 kg ai/hl on oranges in Spain with a PHI of 14 days. The residues in whole oranges from four trials in Spain and one in Greece under these conditions were 0.04 (2), 0.05 (2) and 0.09 mg/kg. The residues in the pulp were all <0.01 mg/kg.

In Japan, fenpyroximate may be used on mandarins at 0.003-0.005 kg ai/hl with a PHI of 14 days. The residues in mandarins in two trials 14 or more days after treatment according to GAP were 0.04 and 0.21 mg/kg (1995 JMPR).

The residues in oranges from Italy, Spain and Greece were within the same population.

The residues in the whole oranges from 4 Italian trials, 4 Spanish trials and 1 Greek trial according to GAP in rank order were 0.04 (6), 0.05 (2) and 0.09 mg/kg. All the 9 residues in the pulp were <0.01 mg/kg.

The Meeting estimated a maximum residue level and an STMR level for fenpyroximate in oranges of 0.2 mg/kg and 0.01 mg/kg respectively.

Apples. Fenpyroximate may be used at 0.008 kg ai/hl (0.06-0.08 kg ai/ha) on apples in France with a PHI of 21 days. The residues in apples from five French trials, ten German trials and one Belgian trial in accordance with French GAP were 0.03, 0.09, 0.06, 0.11, 0.16, 0.1, 0.09 (2), 0.12, 0.16, 0.12, 0.06, 0.15, 0.08 and <0.05 mg/kg.

Fenpyroximate may be used at 0.005 kg ai/hl (0.075-0.175 kg ai/ha) on apples in Australia with a PHI of 14 days. The residues in apples from four Australian trials were 0.18, 0.14, 0.12 and 0.17 mg/kg and from seven trials in New Zealand in accordance with Australian GAP were 0.05, 0.04, 0.03, 0.08 and 0.06 (3) mg/kg.

Fenpyroximate may be used at 0.0025 kg ai/hl (0.05-0.075 kg ai/ha) on apples in New Zealand with a PHI of 28 days. The residues in apples from seven trials in New Zealand meeting these conditions were <0.01 (2), 0.01, 0.03 and 0.02 (3) mg/kg.

The residues from France and Australia, and those from New Zealand complying with Australian GAP, were in a single population, but those from trials according to New Zealand GAP cannot be combined with the others since the PHI is longer and the spray concentration is lower.

The fenpyroximate residues in trials according to French and Australian GAP in rank order (median underlined) were <0.05, 0.03 (2), 0.04, 0.05, 0.06 (5), 0.08 (3), 0.09 (3), 0.1, 0.11, 0.12 (3), 0.14, 0.15, 0.16 (2), 0.17 and 0.18 mg/kg

The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR of 0.09 mg/kg for fenpyroximate in apples.

Grapes. Fenpyroximate may be used at 0.005 kg ai/hl (0.05 kg ai/ha) on grapes in Italy with a PHI of 28 days. The residues in the grapes from four trials in Italy meeting these conditions were 0.02, 0.03 and 0.04 (2) mg/kg. Fenpyroximate is not registered in France but one trial at the spray concentration of 0.006 kg ai/hl was considered to be in accordance with Italian GAP. The residue was <0.02 mg/kg.

Fenpyroximate may be used at 0.0075-0.01 kg ai/hl (0.1 kg ai/ha) on grapes in Spain with a PHI of 14 days. The residues in grapes from four trials in Spain meeting these conditions were 0.06 and 0.04 (3) mg/kg. Two trials in France at 0.006 and 0.008 kg ai/hl and five trials in Italy at 0.0062-0.013 kg ai/hl were considered to be in accordance with Spanish GAP. The residues were <0.02, 0.07, 0.08, 0.17, 0.19, 0.47 and 0.57 mg/kg.

In Japan, fenpyroximate may be used at 0.003-0.005 kg ai/hl on grapes with a PHI of 14 days. The residues in grapes from four trials meeting these conditions were 0.41, 0.45, 0.53 and 0.51 mg/kg.

The residues from the trials in Spain, France, Italy and Japan were in the same population.

The fenpyroximate residues in the combined Spanish, French, Italian and Japanese trials according to GAP in rank order (median underlined) were <0.02, 0.02, 0.03, 0.04(5), 0.06, 0.07, 0.08, 0.17, 0.19, 0.41, 0.45, 0.47, 0.51, 0.53 and 0.57 mg/kg.

The Meeting estimated a maximum residue level and an STMR level for fenpyroximate in grapes of 1 mg/kg and 0.07 mg/kg respectively.

Hops. Fenpyroximate may be used at 0.0075 kg ai/hl (0.225-0.263 kg ai/ha) on hops in Germany with a PHI of 21 days. The residues in hops from twelve trials in Germany meeting these conditions in rank order were <1, 1.2, 2.1(2), 3.7, 4.3, 4.4, 5.0, 5.9, 6.2, 7.4 and 8.4 mg/kg.

The Meeting estimated a maximum residue level of 10 mg/kg and an STMR of 4.4 mg/kg for fenpyroximate on hops.

## Processing

Apples. In four processing studies the mean processing factor from fresh apples to apple juice was 0.42 and that from apples to wet pomace was 5.1. The 1995 JMPR evaluated a processing study in which the residues in the fruit were 0.06 and 0.15 mg/kg and those in apple purée were <0.05 (2) mg/kg, giving processing factors for apple purée of <0.83 and <0.24 (mean <0.54). Since the estimated STMR for apples is 0.09 mg/kg, the calculated STMRs for apple juice and purée are  $0.09 \times 0.42 = 0.038$  and  $0.09 \times 0.54 = 0.049$ .

The Meeting estimated STMRs for apple juice of 0.04 mg/kg and for apple purée of 0.05 mg/kg.

Grapes. The processing study reported in the 1995 JMPR monograph showed residues in wine of <0.01 mg/kg from residues in fresh grapes of 0.15, 0.13 and 0.14 mg/kg, giving processing factors for wine of

<0.07, <0.08 and <0.07 (mean <0.07). The STMR for grapes is 0.07 mg/kg, so the calculated STMR for wine is  $0.07 \times 0.07 = 0.0049$  mg/kg.

**Hops.** In the processing study reported in 1995, beer containing residues of <0.01 mg/kg was brewed from dried hops containing residues of 6.4, 9.0, 11.4 and 37.4 mg/kg giving processing factors for beer of <0.0016, <0.0011, <0.0009 and <0.0003 (mean <0.001).

The Meeting estimated an STMR for beer of 0.0044 mg/kg from the STMR for hops of 4.4 mg/kg.

### Animal feeding studies

Dairy cattle dosed at a level equivalent to 1, 3 or 10 ppm in the feed showed mean total residues of fenpyroximate and its metabolite G-2 of <0.01, 0.015 and 0.038 mg/kg in muscle, 0.015, 0.056 and 0.11 mg/kg in fat, <0.003, <0.003 and <0.01 mg/kg in liver, and <0.003, <0.01 and 0.014 mg/kg in kidney. The residues in the milk of the high-dose group were 0.007 to 0.017 mg/kg.

The concentration factors for wet apple pomace from processing studies were 4.0 to 6.0 (mean 5.1).

Assuming a dry matter content of 40% in wet apple pomace and maximum incorporation rates of dry apple pomace of 20 and 40% in dairy and beef cattle diets respectively, the maximum feed intakes will be approximately 0.25 and 0.5 ppm.

$$0.09 \text{ mg/kg} \times 5.1/40\% \times 20\% (40\%) = 0.25 \text{ ppm} (0.5 \text{ ppm})$$

The residues were below the LOD in muscle at the 1 ppm feeding level, in kidneys at 1 and 3 ppm, and in liver at 1, 3 and 10 ppm. Residues were detected in the fat and milk at the 1, 3 and 10 ppm feeding levels. The Meeting noted that the calculated dietary burdens of 0.5 ppm for beef cattle and 0.25 ppm for dairy cattle were close the lowest feeding level of 1 ppm.

In the animal feeding study, the lowest feeding level showed <0.01 mg/kg in muscle, 0.018 mg/kg in fat and <0.003 mg/kg in kidney and liver. Milk from the low-dose group was not analysed. The calculated maximum dietary burden was 1/6th of the 3 ppm feeding level, in which the highest milk residue was 0.011 mg/kg. The calculated milk residue from the estimated dietary burden is therefore 0.002 mg/kg. Liver and kidney may contain residues of the polar metabolite G-4 at an estimated maximum of 0.1 mg/kg from the calculated dietary level.

The Meeting estimated maximum residue levels of 0.02 mg/kg for cattle meat (fat), 0.01\* mg/kg for cattle kidney and liver and 0.005\* mg/kg for cattle milk, and STMRs of 0.01 mg/kg for cattle meat, 0 mg/kg for cattle liver and kidney, and 0.002 mg/kg for cattle milk.

## RECOMMENDATIONS

On the basis of the available data on residues resulting from supervised trials the Meeting estimated the maximum residue and STMR levels listed below. The maximum residue levels are recommended for use as MRLs.

Definition of residue for compliance with the MRL and for estimation of dietary intake: fenpyroximate.

The residue is fat-soluble

Commodity		MRL, mg/kg	STMR, mg/kg	HR/HR-P, mg/kg <sup>1</sup>
CCN	Name			



Commodity		MRL, mg/kg	STMR, mg/kg	HR/HR-P, mg/kg <sup>1</sup>
CCN	Name			
FP 0226	Apple	0.3	0.09	0.18
JF 0226	Apple juice		0.04	<0.05
	Apple purée		0.05	<0.05
	Beer		0.005	<0.01
MO 1280	Cattle kidney	0.01*	0	
MO 1281	Cattle liver	0.01*	0	
MM 0812	Cattle meat	0.02(fat)	0.01	
ML 0812	Cattle milk	0.005* F	0.002	
FB 0269	Grapes	1	0.07	0.57
DH 1100	Hops	10	4.4	8.4
FC 0004	Oranges, Sweet, Sour	0.2	0.01	0.09
	Wine		0.004	<0.01

<sup>1</sup> HR: highest residue (edible portion) from supervised trials. HR-P: highest residue processed commodity, calculated from the HR of the raw agricultural commodity and the processing factor.

## FURTHER WORK OR INFORMATION

### Desirable

An additional study of processing grapes to wine and raisins.

The Meeting was informed that the results of a study of processing grapes to raisins, pomace, forage and juice would be available in the year 2000.

## DIETARY RISK ASSESSMENT

### Chronic intake

STMRs have been estimated for 9 commodities. The International Estimated Daily Intakes for the five GEMS/Food regional diets were in the range of 0-1% of the ADI. The Meeting concluded that the intake of residues of fenpyroximate resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern.

### Acute intake

The international estimated short-term intake (IESTI) for fenpyroximate was calculated as described in Section 3 for the commodities for which maximum residue levels and STMRs were estimated and for which consumption data (large portion consumption, unit weight) were available. The results are shown in Annex IV. The IESTI varied from 0 to 0.008 mg/kg bw in the general population and from 0 to 0.032 mg/kg bw in children. As no acute reference dose has been established, the risk assessment for fenpyroximate was not finalized.

## REFERENCES

Baker, F. C., Bacher, R. and Gibson, N. 1999. Magnitude of the Residue in Meat and Milk from Daily Cows Administrated Fenpyroximate. PTRL Report No. 1179E/301G. Unpublished.

Hatfield, M. W. 1996. Magnitude of the Residue of Fenpyroximate in Apple Raw Agricultural and Processed Commodities. American Agricultural Services Study No. AA940423. Unpublished.

Jalali, K. and Gibson, N. A. 1999a. The Metabolism of [pyrazole-3-<sup>14</sup>C]-Fenpyroximate in the Lactating Goat. PTRL Report No. 1109E/674W. Unpublished.

Jalali, K. and Gibson, N. A. 1999b. The Metabolism of [benzyl (U)-<sup>14</sup>C]-Fenpyroximate in the Lactating Goat. PTRL Report No. 1110E/675W. Unpublished.

Motoba, K. 1992. Rapid Hydrolysis Pathway for a Tertiary Alcohol Ester through Intermolecular Transesterification in Rats. *Biosci. Biotech. Biochem.*, **56**, 366-367.

Todd, M. 1999. The Development and Validation of Methodology for the Determination of Fenpyroximate Residues in Dried Hops, Grapes and Oranges (Pulp and Peel). Huntingdon Life Sciences Report No. NHH095/985009. Unpublished.

Wilson, A. J. 1998. Raw Agricultural Commodity Study with Miro and Kendo Applied to Oranges in Spain and Italy. Huntingdon Life Sciences Report No. NHH092/983274. Unpublished.

Wilson, A. J. 1999a. Raw Agricultural Commodity Study with Miro and Kendo Applied to Grapes in Spain and Italy. Huntingdon Life Sciences Report No. NHH093/985072. Unpublished.

Wilson, A. J. 1999b. Raw Agricultural Commodity Study with Kiron Applied to Hops in Germany. Huntingdon Life Sciences Report No. NHH094/984984. Unpublished.