PIRIMIPHOS-METHYL (086)

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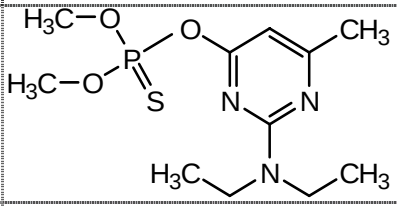
EXPLANATION

Pirimiphos-methyl, a broad spectrum organophosphorus insecticide, was first evaluated in 1974 for toxicology and residues. Subsequently, it was reviewed for toxicology in 1976 and 1992 and for residues in 1976, 1977, 1979, 1983, 1985 and 1994. The current ADI of 0-0.03 mg/kg body weight was recommended by the 1992 JMPR. Currently there are 44 Codex MRLs: for plant commodities and derived products resulting from pre- and post-harvest uses; and for meat, milk and dried fish.

The 30th Session of the CCPR identified pirimiphos-methyl as a priority compound for periodic re-evaluation by the present Meeting.

The Meeting received data on metabolism, analytical methods, storage stability, supervised field trials, processing and farm animal feeding and information on use pattern.

IDENTITY

ISO Common name:	pirimiphos-methyl
Chemical name	
IUPAC:	*O*-(2-diethylamino-6-methylpyrimidin-4-yl) *O*,*O*-dimethylphosphorothioate
CAS:	*O*-(2-diethylamino-6-methyl-4-pyrimidin) *O*,*O*-dimethylphosphorothioate
CAS Registry No.:	29232-93-7
CIPAC No.:	239a
Synonyms and trade names:	PP511; Actellic
Structural formula:	
Molecular formula:	$C_{11}H_{20}N_3O_3PS$
Molecular weight:	305.4

Physical and chemical properties

Pure active ingredient

Purity	99.6% minimum
Appearance:	White solid; clear liquid at temperatures above the freezing point.
Vapour pressure:	2.0 mPa at 20ºC (Husband, 1997)
Freezing point:	20.8ºC; super-cooling was observed, with the temperature dropping to about 17ºC prior to solidification (Husband, 1997).
Relative density:	1.17 g/cm^3 at 20ºC (Husband, 1997).
Henry's law constant:	6 x 10^{-2} Pa·m^3·mol^{-1} at 20ºC in purified water and water buffered at pH 5, 7 and 9 (Husband, 1997).
Octanol-water partition coefficient:	log P_{ow} = 3.90 at 20ºC in water buffered at pH 4, 5 and 7 and in purified water (Husband, 1997).
Solubility at 20ºC:	Water, 10 mg/l in purified water; 11 mg/l at pH 5; 10 mg/l at pH 7; and 9.7 mg/l at pH 9 (Husband, 1997).
Hydrolysis at 25ºC:	Half-life in sterile aqueous buffer solutions: 2 days at pH 4; 7 days at pH 5; 117 days at pH 7; 75 days at pH 9 (Hand, 1996).

Photolysis at 25ºC:	Half-life in sterile aqueous buffer solutions: 0.46 hours at pH 5; 0.47 hours at pH 7. Main photolysis product: 2-diethylamino-6-methylpyrimidin-4-ol (63% applied radioactivity) (Powell, 1999).
Dissociation constant:	pK_a 4.30 at 20ºC (Husband, 1997).

Technical material

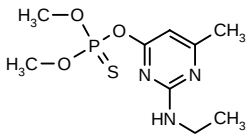
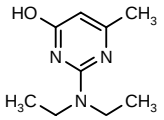
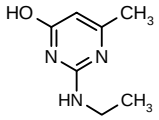
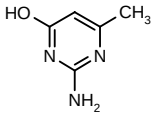
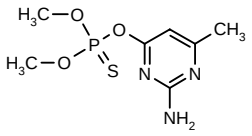
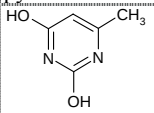
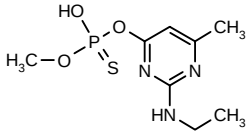
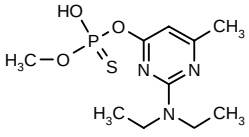
Purity:	≥88%; impurities total ≤12%.
Appearance:	Pale yellow, slightly turbid, mobile liquid (Husband, 1998).
Odour:	Strong mercaptan-like odour (Husband, 1998).
Density:	1.16 g/cm^3 at 20ºC (Husband, 1998).
Freezing point:	17.5ºC; existing as a super-cooled liquid at temperatures substantially lower than 1.75ºC (Husband, 1998).
Solubility:	Acetone, >250 g/kg (>200 g/l); 1,2-Dichloroethane, >250 g/kg (>200 g/l); Ethyl acetate, >250 g/kg (>200 g/l); *n*-Heptane, 249 g/kg (189 g/l); Methanol, >250 g/kg (>200 g/l); Xylene, >250 g/kg (>200 g/l) (Husband, 1998).
Stability:	≥ 14 days at 54ºC; ≥ 2 years at ambient temperature

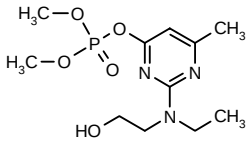
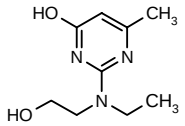
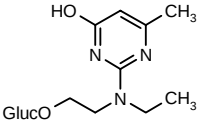
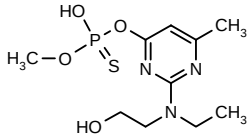
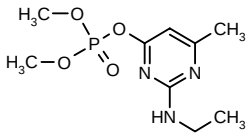
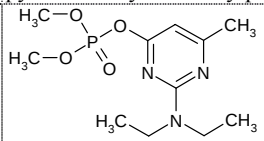
Formulations

Emulsifiable concentrates (EC), in various concentrations, and 2% dustable powder (DP).

METABOLISM AND ENVIRONMENTAL FATE

The codes, chemical names and structures of metabolites are shown below.

Metabolite	Structure and Name	Metabolite	Structure and Name
R36341	 *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphorothioate	R46382	 2-diethylamino-4-hydroxy-6-methylpyrimidine
R35510	 2-ethylamino-6-methyl pyrimidin-4-ol	R4039	 2-amino-4-hydroxy-6-methyl-pyrimidine
R31528	 *O*-2-amino-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphorothioate	R4041	 2-hydroxy-6-methylpyrimidin-4-ol
Desethyl R402186	 *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*-methyl phosphorothioate	R402186	 *O*-2-diethylamino-6-methyl-pyrimidin-4-yl *O*-methyl phosphorothioate

Metabolite	Structure and Name	Metabolite	Structure and Name
R290480	 *O*-2-(ethyl-(2-hydroxyethyl)amino)-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphate	R290481	 2-(ethyl-(2-hydroxyethyl)amino)-4-hydroxy-6-methylpyrimidine
R290481-ethoxy-glucuronide	 2-(ethyl-(2-glucuronylethyl)amino)-4-hydroxy-6-methylpyrimidine	R290483	 *O*-2-(ethyl-(2-hydroxyethyl)amino)-6-methyl pyrimidin-4-yl *O*-methylphosphorothioate
R74947	 *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*,*O*-dimethylphosphate	R35311	 *O*-2-diethylamino-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphate

Animal metabolism

The Meeting received information on the fate of orally-dosed pirimiphos-methyl in rats, a lactating goat and laying hens.

Rats

In order to determine the metabolic pathway of pirimiphos-methyl in the rat, metabolites of pirimiphos-methyl present in urine, bile and faeces were studied (Macpherson, 1998). A single dose of 50 mg/kg [2-^{14}C]pirimiphos-methyl was administered, by gavage, to male and female Alpk;AP$_f$SD rats, fitted with a bile duct cannula. Bile was collected at 2, 4, 6, 8, 12, 24, 36 and 48 hours; urine and faeces were collected at 6, 12, 24, 36 and 48 hours. For the quantification of metabolites in urine and faecal samples, male and female rats without surgical treatment were administered by gavage a single dose of 1 mg/kg or 250 mg/kg [2-^{14}C]pirimiphos-methyl alone, or 1 mg/kg [2-^{14}C]pirimiphos-methyl following 14 daily doses of 1 mg/kg unlabelled compound. Urine and faeces samples were collected for 48 hours after dosing the radio-labelled compound. Metabolites isolated from bile, urine and faeces were characterized by mass spectrometry, proton nuclear magnetic resonance spectroscopy and co-chromatography with reference standards. Metabolites were quantified by HPLC.

Two male and two female rats, each fitted with a bile duct cannula, excreted 38% and 33%, respectively, of the administered 50 mg/kg [2-^{14}C]pirimiphos-methyl in urine; 17% and 21%, respectively, via bile; and 30% and 16%, respectively, in faeces, within 48 hours of dosing. The total radioactivity recovered was 85% from male rats and 69% from female rats.

When dosed at the same time as the bile duct cannulated rats, non-cannulated male and female rats (5 each) excreted 50% and 49%, respectively, of the 50 mg/kg [2-^{14}C]pirimiphos-methyl dose respectively in urine; and 22% (both male and female) in faeces in 48 hours. The total radioactivity recovered was 75% from male rats and 74% from female rats (values include the terminal cage wash). However, in additional tests, the same non-cannulated rats excreted 61-76% of the dose in urine and 15-29% in faeces, with the total recovered radioactivity up to 93-98% (including the terminal cage wash).

The quantities and nature of pirimiphos-methyl metabolites in bile, urine and faeces in the three different dosing studies are summarized in Tables 1 and 2.

At the lower dose of 1 mg/kg, either with a single radio-labelled dose or following repeated non-labelled doses, the major metabolite was R35510 in both male and female rats. At the higher dose level of 250 mg/kg, the major metabolites differed between male and female rats: in male rats the major

metabolite in urine was desethyl R402186 and R35510, while in female rats the major metabolite was R402186 and desethyl R402186.

From the results of studies using bile duct cannulated rats, it was speculated that pirimiphos-methyl metabolites found in bile were re-absorbed and eventually excreted predominantly in urine, because the radioactivity in faeces (29% of the administered dose for males and 15% for females; Table 1) of bile duct cannulated rats was exclusively in the form of the unchanged parent compound. However, the radioactivity in faeces (4-15% of the administered dose for males and 3-15% for females; Table 2) of non-cannulated rats was attributed to several different metabolites and the percentage of the parent compound in faeces was, on average, lower. No parent compound was present in the urine and bile of the bile duct cannulated rats, nor was it present in the urine of the non-cannulated rats, which indicates that the absorbed pirimiphos-methyl was completely metabolized. Extensive metabolism of the absorbed pirimiphos-methyl is indicated by the range of metabolites detected.

Table 1. Quantification of pirimiphos-methyl and its metabolites in bile, urine and faeces of bile duct cannulated rats administered a single oral dose of 50 mg/kg [2-^{14}C]pirimiphos-methyl (expressed as % of the administered radioactivity) (Macpherson, 1998).

Metabolite	Status	Bile		Urine		Faeces	
		Male	Female	Male	Female	Male	Female
Pirimiphos-methyl	Identified					28.65	14.97
R36341	Identified	3.15	1.77				
R31528	Identified	0.18					
R46382	Identified	0.55	0.78	0.96	4.65		
R35510	Identified	1.46	0.64	14.41	4.95		
R4039	Tentatively identified	0.30		0.68	0.10		
desethyl R402186	Identified	3.02	1.68	11.68	6.50		
A	Unknown	0.50	2.06				
R402186	Identified	0.14	0.28	0.46	10.82		
R290480	Identified						
B	Unknown			0.52	1.00		
R290481	Identified	0.37		1.80	0.66		
R290481-ethoxy-glucuronide	Identified			0.66	0.22		
R46382-*O*-glucuronide	Identified	6.00	11.84	3.36	2.21		
R290483	Identified			0.24	0.45		
R74947	Identified						
C	Unknown	0.50		1.59	0.53		
		Male		Female			
% of excreted dose characterized		91.8		90.8			
% of administered dose characterized		78.1		62.5			

Table 2. Quantification of pirimiphos-methyl and its metabolites in urine and faeces of male and female rats after receiving an oral dose of [2-^{14}C]pirimiphos-methyl (expressed as % of the administered radioactivity) (Macpherson, 1998).

Metabolite	Status	Single 1 mg/kg radio-labelled dose				14 x unlabelled 1 mg/kg doses followed by a single 1 mg/kg radio-labelled dose				single 250 mg/kg radio-labelled dose			
		Male		Female		Male		Female		Male		Female	
		Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces
Pirimiphos-methyl	Identified		12.90		14.86		15.08		4.59		3.74		2.74
R36341	Identified												
R31528	Identified		0.55						0.37				
R46382	Identified	2.63		4.13		3.19	0.63	5.64	0.50	7.08		8.97	
R35510	Identified	28.39	2.36	28.28	3.10	29.95	6.82	28.28	2.50	15.19	6.36	8.14	4.25
R4039	Tentatively identified	2.46	5.76	0.96	4.54	1.20	5.25	1.45	3.04	0.51	5.41		2.25
desethyl R402186	Identified	8.01		5.04		9.56		10.15		23.90		12.66	

Metabolite	Status	Single 1 mg/kg radio-labelled dose				14 x unlabelled 1 mg/kg doses followed by a single 1 mg/kg radio-labelled dose				single 250 mg/kg radio-labelled dose			
		Male		Female		Male		Female		Male		Female	
		Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces	Urine	Faeces
A	Unknown												
R402186	Identified			1.72				2.33		2.51		34.51	
R290480	Identified									trace			
B	Unknown	1.82		1.73		2.43		3.50		2.03		2.73	
R290481	Identified	4.54		3.71		7.97		5.00		4.12		2.67	
R290481-ethoxy-glucuronide	Identified	3.35		1.34		2.16		1.53		1.34			
R046382- *O*-glucuronide	Identified	3.51		4.22	0.61	1.47	0.75	4.8	0.51	4.68	2.69	5.82	0.86
R290483	Identified			0.71		0.50		0.52		0.41			
R74947	Identified									trace			
C	Unknown	10.8		4.20		5.00		5.40		1.84		0.79	
D	Unknown								0.79				
E	Unknown								1.18				
F	Unknown										1.97		
% of excreted dose characterized		78.7		78.7		86.3		75.4		81.7		88.7	
% of administered dose characterized		74.5		73.2		84.5		71.2		77.9		82.9	

Lactating goat

An adult female goat was dosed orally with [2-^{14}C]pirimiphos-methyl in gelatine capsules, twice daily after milking for 7 days, at a rate equivalent to 45 ppm in the diet (Skidmore, *et al*., 1985). Urine and faeces samples were collected after dosing. Sixteen hours after the final dose, the goat was killed with an intravenous barbiturate injection. Fat (subcutaneous and peritoneal fats combined for analysis), meat (forequarter and hindquarter combined for analysis), liver and kidneys were collected for residues analysis. For the determination of the nature of residues in milk, a composite sample was formed by combining 100 ml aliquots of milk obtained in the afternoon of day 6 and in the morning and afternoon of day 7.

The majority (89.4%) of the administered dose was excreted in the urine and faeces, while a further 0.2% was recovered in the milk. The quantities and nature of radioactive residues are summarized in Table 3, in which the residues are expressed as pirimiphos-methyl equivalents. In fat samples, the major radioactive components of the residue were pirimiphos-methyl and R36341, whereas, in other tissues and milk, they were R35510, R4039 and R46382. Liver and kidney samples contained conjugated components: R46382 conjugates and R35510 conjugates in liver; and R46382 conjugates in kidney.

Approximately 32% of the TRR in liver was unextracted and therefore a second sample was prepared, to investigate the nature of residues in the unextracted fraction (post-extraction solids, PES) of the liver. In the second sample, the TRR was 0.33 mg/kg equivalent, of which the unextracted fraction represented 34.4.%. Refluxing the PES with 4M HCl extracted a further 27% of the TRR (Table 4), leaving a residual 7.4% of the TRR in the post-hydrolysis solids.

Radioactivity in the milk increased sharply after the first dose, it reached a peak in the afternoon of day 2, then decreased slightly and became reasonably constant by day 4 (Table 5).

Table 3. Quantification of pirimiphos-methyl and its metabolites in tissues and milk of a lactating goat (residues are expressed as pirimiphos-methyl equivalents) (Skidmore, *et al*., 1985).

Component	Fat (TRR: 0.067 mg/kg)		Meat (TRR: 0.042 mg/kg)		Liver (TRR: 0.32 mg/kg)			
					Pre acid hydrolysis		Post acid hydrolysis	
	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg
Pirimiphos-methyl	55.2	0.037	4.1	0.002	1.8	0.006	-	-
R36341	17.1	0.011	1.0	<0.001	1.9	0.006	-	-
R31528	0.8	<0.001			0.04	<0.001	-	-
R46382	1.6	0.001	4.7	0.002	3.4	0.011	8.3	0.027
R35510			23.5	0.010	11.6	0.037	17.1	0.055
R4039			20.1	0.008	7.1	0.023	7.3	0.023
R4041			7.8	0.003	1.4	0.004	2.0	0.006
Unknown					-	-	0.8	0.003
Polar material +TLC origin			9.9	0.004	21.5	0.069	6.6	0.021
Remainder (TLC streaking)	5.6	0.004	0.9	<0.001	3.6	0.012	2.7	0.009
Aqueous soluble			8.3	0.003	4.8	0.015	4.8	0.015
Unexamined hexane soluble	4.9	0.003			0.3	0.001	0.3	0.001
Solid precipitate					0.8	0.003	0.8	0.003
Solid residue					-	-	4.5	0.014
Unextracted	17.3	0.012	11.4	0.005	31.9	0.102	31.9	0.102
Residue from hydrolysis								
Losses during workup			8.3	0.004	9.9	0.032	12.9	0.042

Component	Kidney (TRR: 0.50 mg/kg)				Milk (TRR: 0.184 mg/kg)	
	Pre acid hydrolysis		Post acid hydrolysis			
	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg
Pirimiphos-methyl					4.2	0.008
R36341					0.3	<0.001
R31528						
R46382	2.6	0.013	14.0	0.070	4.5	0.008
R35510	35.1	0.174	36.9	0.185	31.8	0.059
R4039	13.4	0.066	9.0	0.045	14.3	0.026
R4041	1.9	0.009	1.6	0.008	3.1	0.006
Unknowns					A:3.9 B:1.9	A:0.007 B:0.003
Polar material +TLC origin	26.2	0.130	7.4	0.037	9.4	0.017
Remainder (TLC streaking)	1.4	0.007	1.7	0.009	0.6	0.001
Aqueous soluble	6.2	0.030	6.2	0.031	10.9	0.020
Unexamined hexane soluble	3.4	0.017	3.4	0.017	0.1	-
Solid precipitate						
Solid residue						
Unextracted	4.1	0.020	4.1	0.020	2.7	0.005
Residue from hydrolysis	-	-	5.0	0.025		
Losses during workup	5.7	0.028	10.7	0.054	12.2	0.022

Table 4. Radioactive residues released from the unextracted fraction of a second sample of goat liver, by refluxing in 4M HCl (TRR in liver, 0.33 mg/kg; unextracted fraction, 0.11mg/kg) (Skidmore, *et al*., 1985).

Component	% of TRR	Residue, mg/kg
R046382	1.7	0.006
R035510	4.2	0.014
R004039	1.8	0.006
R004041	1.0	0.003
Unknown	1.5	0.005
>700 molecular weight	6.5	0.021
Non-extracted	7.4	0.024
Polar material +TLC origin	1.0	0.003
Remainder (TLC streaking)	0.7	0.002
Aqueous soluble	5.2	0.017
Losses during workup	3.4	0.011

Table 5. Total radioactive residues (TRR) in goat milk, expressed as pirimiphos-methyl (Skidmore, *et al*., 1985).

Day	Time	TRR, mg/kg	Day	Time	TRR, mg/kg
1	am	<0.001	5	am	0.143
	pm	0.139		pm	0.157
2	am	0.169	6	am	0.152
	pm	0.208		pm	0.148
3	am	0.164	7	am	0.145
	pm	0.187		pm	0.180
4	am	0.149	8	am	0.131
	pm	0.154		pm	-

Hens

Three laying hens, aged about 35 weeks at the beginning of the study, were dosed orally with [2-^{14}C]pirimiphos-methyl in gelatine capsules, twice daily for 14 days, at a rate (2.5 mg/dose) equivalent to 50 ppm in the diet (Skidmore and Tagela, 1985). A fourth hen was used as a control. Eggs were collected from all hens from 2 days before the first dose and throughout the dosing period. Total excreta from each hen were collected separately, at 24-hour intervals. Hens were sacrificed 16 hours after the last dose and liver, kidneys, subcutaneous and peritoneal fat (combined for analysis), leg muscle, breast muscle and skin were collected. Metabolism cages were thoroughly washed with water and the washings retained. The nature of the radioactive residues in the eggs and tissues were investigated after combining sub-samples of the eggs and tissues from the three treated hens.

Radioactivity in the excreta collected over 14 days accounted for a mean of 97.5% of the total administered radioactivity. The quantities and nature of radioactive residues were summarized in Table 6. All residues levels are expressed as pirimiphos-methyl equivalents.

Pirimiphos-methyl was the predominant component of the radioactive residue in fat (subcutaneous and peritoneal fat combined), and was also present in egg yolk, but was not found in muscle, liver or egg albumen.

R35510 and R4039 were major components of the radioactive residues in liver, egg yolk and egg albumen. Conjugated forms of these compounds were present in the liver, while a conjugated form of R4039 was the major component of residues in the leg and breast muscle tissues. Fractionation and TLC analysis of the muscle extracts indicated that the majority of the radioactive residue in these tissues was of highly polar material. Following acid hydrolysis, 70 and 76% of the radioactive residue in the breast and leg muscles respectively were identified by TLC.

Table 6. Quantification of pirimiphos-methyl and its metabolites in tissues and eggs of laying hens (residues were expressed as pirimiphos-methyl) (Skidmore and Tagela, 1985).

Component	Fat (TRR: 0.077 mg/kg)		Breast muscle (TRR: 1.3 mg/kg)		Leg muscle (TRR: 0.67 mg/kg)	
	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg
Pirimiphos-methyl	72.5	0.056				
R36341	5.5	0.004				
R46382						
R35510			1.4	0.018	2.3	0.015
R4039			68.9	0.90	73.2	0.49
R4041						
Unknown			0.7	0.009	0.8	0.005
Polar material + TLC origin			0.7	0.009	0.8	0.005
Hexane soluble			0.5	0.007	1	0.007
Aqueous soluble	5	0.004				
Precipitate and salts						
Unextracted	15	0.012	11	0.143	7	0.047
Solid residues produced during fractionation			2	0.026	3	0.020
Other						
Losses during workup	2	0.001	14.8	0.192	11.9	0.080

Component	Liver (TRR: 0.20 mg/kg)				Egg yolk (TRR: 0.23 mg/kg)		Egg albumen (TRR: 0.17 mg/kg)	
	Pre acid hydrolysis		Post acid hydrolysis					
	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg	% of TRR	Residue mg/kg
Pirimiphos-methyl					9.5	0.022	-	-
R36341								
R46382	0.4	0.001	0.4	0.001	4.5	0.010	3.8	0.007
R35510	11.8	0.024	10.5	0.021	33.8	0.076	43.2	0.073
R4039	6.1	0.012	8.4	0.017	11.3	0.025	21.6	0.037
R4041	1.9	0.004	0.4	0.001	3.0	0.007	3.8	0.007
Unknown	A:11.0	A:0.022	A:10.9	A:0.022	A:6.8	A:0.015	A:12.2	A:0.021
Polar material + TLC origin	6.5	0.013	4.6	0.009	11.8	0.027	10.3	0.017
Hexane soluble	5	0.010	5	0.010	8.0	0.018	-	-
Aqueous soluble	5	0.010	5	0.010				
Precipitate and salts	2	0.004	4	0.008				
Unextracted	44	0.088	44	0.088	8.0	0.018	6	0.010
Solid residues produced during fractionation								
Other					3.0	0.007	-	-
Losses during workup	6.3	0.012	6.8	0.014	0.3	<0.001	-	-

Note. Large amounts of co-extractives prevented the chromatography of hexane- and aqueous extracts of the liver.

The liver extracts were subjected to acid hydrolysis, to release bound or conjugated radioactivity, and, consequently, 56% of the radioactive residue in the liver was extracted into organic solvent. No significant changes were observed in the proportions of the radioactive components following acid hydrolysis of the sample. The majority of radioactivity (39% of the TRR in liver) remaining in the liver in the extraction debris was solubilized by refluxing in acid. TLC revealed that the major components of this extract were R35510 and R4039 (Table 7).

Table 7. Radioactive residues released from the unextracted residue fraction of liver (Table 6) by acid reflux (Skidmore and Tagela, 1985).

Component	% of previously unextracted TRR	Residue, mg/kg
R46382	0.4	0.001
R35510	24.0	0.048
R4039	20.1	0.040
R4041	0.4	0.001
Unknown A	10.9	0.022
Polar material + TLC origin	9.7	0.019
Hexane soluble	5	0.010

Component	% of previously unextracted TRR	Residue, mg/kg
Aqueous soluble	5	0.010
Salts	11	0.022
Unextracted	3	0.006
Losses during workup	10.5	0.021

Radioactive residues in eggs reached a plateau on approximately day 6 after which the residues remained reasonably constant (0.17-0.23 mg/kg in the yolk and 0.13-0.20 mg/kg in the albumen). The trend in total radioactive residues in eggs during the 14-day period is shown in Figure 1.

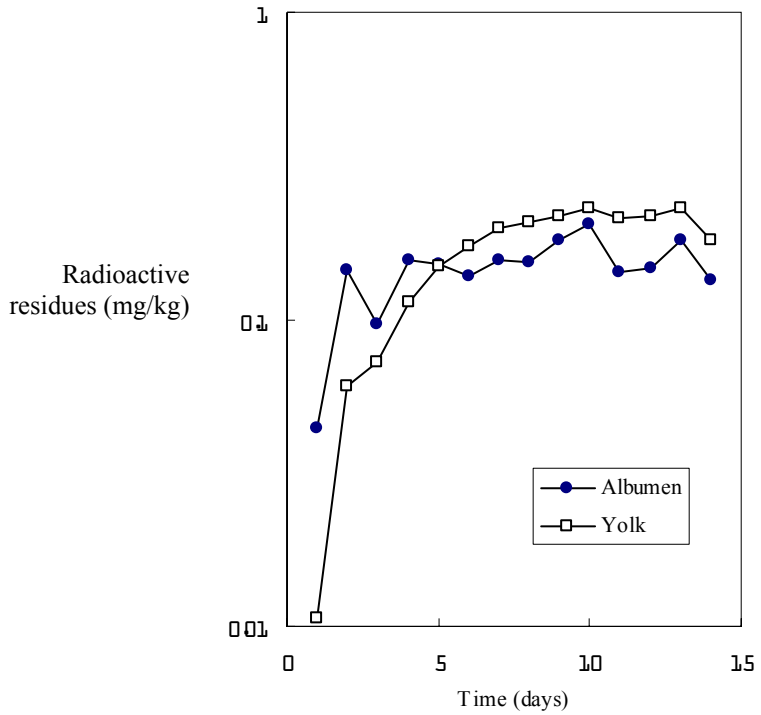


Figure 1. Radioactive residue levels in eggs during the 14-day study (N.B. Values of day 3 and day 14 were from only one hen).

Proposed metabolic pathway

In all tissues (except fat), milk and eggs, the main metabolites were the hydroxypyrimidines, R46382, R35510, R4039 and R4041, with R35510 and R4039 predominating. Residues of pirimiphos-methyl were very low (<5%) or not present, except in egg yolk, where it constituted 9.5% of the TRR, and in fat where it was the predominant component of residues (55% and 73% of the TRR in goats and hens, respectively). R36341, containing the phosphorothioate moiety, was found at 5.5% of the TRR in chicken fat and 17.1% of the TRR in goat fat. It was also found in lower proportions (less than 2% of the TRR) in other goat tissues and milk (0.3% of TRR).

Pirimiphos-methyl was absorbed and then extensively metabolized. In the metabolism of pirimiphos-methyl in animals, five transformation processes seem to occur: hydrolysis of the dimethyl phosphorothioate moiety, de-ethylation of *N*-diethyl group, conjugation with glucuronic acid or other biological compounds, de-methylation of dimethylphosphorothioate group, and phosphorothioate oxidation (replacement of the sulfur atom with oxygen). Through these reactions, the metabolites identified in Tables 1, 2, 3, 4, 6 and 7 were produced.

The removal of the dimethyl phosphorothioate group from the parent compound produced R46382, found in goat, hens and rats. R46382 underwent hydroxylation of one of the *N*-ethyl groups to produce R290481 (found in rat urine) and, following removal of the hydroxyethyl group, formed R35510 (found in goat, hens and rats). The removal of the second ethyl side chain formed R4039, also

found in goat, hens and rats, and subsequent replacement of amino group by a hydroxyl group gave R4041, found in goat and hens. Conjugates of R35510 and R4039 were found in goat and hens.

Metabolites R36341 and R31528, found in goat, hens and rats, were produced by de-ethylation of the diethylamino group of the parent compound. The removal of one ethyl moiety produced R36341 and the removal of both resulted in R31528.

In rats, cleavage of one methyl moiety from the dimethyl phosphorothioate group led to R402186; subsequent hydroxylation of one of the *N*-ethyl groups produced R290483; and removal of the hydroxyethyl group produced desethyl-R402186. Also in rats, phosphorothioate oxidation and hydroxylation of *N*-ethyl group of the side chain of the parent compound formed R290480 and subsequent loss of the hydroxylated side chain gave R74947. A proposed metabolic pathway is shown in Figure 2.

Plant metabolism

Stored wheat and rice grain

To investigate the degradation of pirimiphos-methyl after application to stored grains, 70 g of wheat (var., Manitoba) grain, rice grain (with husk; variety not reported) and husked rice were treated with a 2% dust formulation containing [2-^{14}C]pirimiphos-methyl at 4 mg/kg (g/t) or 8 mg/kg (g/t), which were within the application rates approved in many countries (Bowker & Hughes, 1973). Treated grain was stored at 25°C for 8 months in the dark, in dishes over concentrated sulphuric acid solutions in desiccators, to maintain low (12-15%) or high (17-20%; not normal practice) moisture contents. Samples were taken at 0, 2, 4, 8 and 16 weeks after treatment and also at 32 weeks in the case of wheat. Samples of the grain were ground to fine powder and extracted with methanol. Methanol extracts were analyzed by TLC, using with reference standards. Phosphorothioate or phosphate esters were hydrolyzed with 5N HCl and the resultant hydroxypyrimidines were also identified with TLC. In some instances, further confirmation of the identity of phosphorus-containing compounds was obtained using GC with a flame-photometric detector (FPD).

Tables 8 and 9 indicate that, at 25°C, the rate of degradation of pirimiphos-methyl was heavily dependent on the moisture content of the grain. On wheat grains treated at 4 mg/kg and maintained under optimum storage conditions, i.e., at the lower moisture content, the maximum concentration of hydroxypyrimidine degradation products was less than 0.3 mg/kg. Pirimiphos-methyl declined slowly from the maximum of 2.7 mg/kg (week 2) to 2.1 mg/kg at 32 weeks. The percentage of unextracted radioactivity increased from 0.7 to 4.0% of the TRR at 32 weeks after treatment. Major metabolites were products of hydrolysis: the hydroxypyrimidines, R46382, R35510 and R4039, with R46382 representing at least 90% of these.

On the other hand, pirimiphos-methyl on grain treated at 4 mg/kg and maintained under unfavourable storage conditions, i.e., at the higher moisture content, decreased from 2.7 mg/kg at week 2 to 0.4 mg/kg at week 32. The increase in unextracted radioactivity was correspondingly much faster than that in grain with the lower moisture content: 1.6 mg/kg at week 32, compared with 0.11 mg/kg in grain with the lower moisture content.

In both cases, the major metabolite was R46382, which increased gradually over 8 months, the fastest increase being in the grain with the higher moisture content. Under optimum storage conditions, the maximum level of R46382 following treatment at 4 mg/kg was 0.17 mg/kg. Under unfavourable storage conditions, the maximum level of R46382 was 0.62 mg/kg.

Radioautograms showed that the radioactivity was found to concentrate in the pericarp of treated grain of wheat, indicating that residues in white flour and bread would be lower than in bran and wholemeal products.

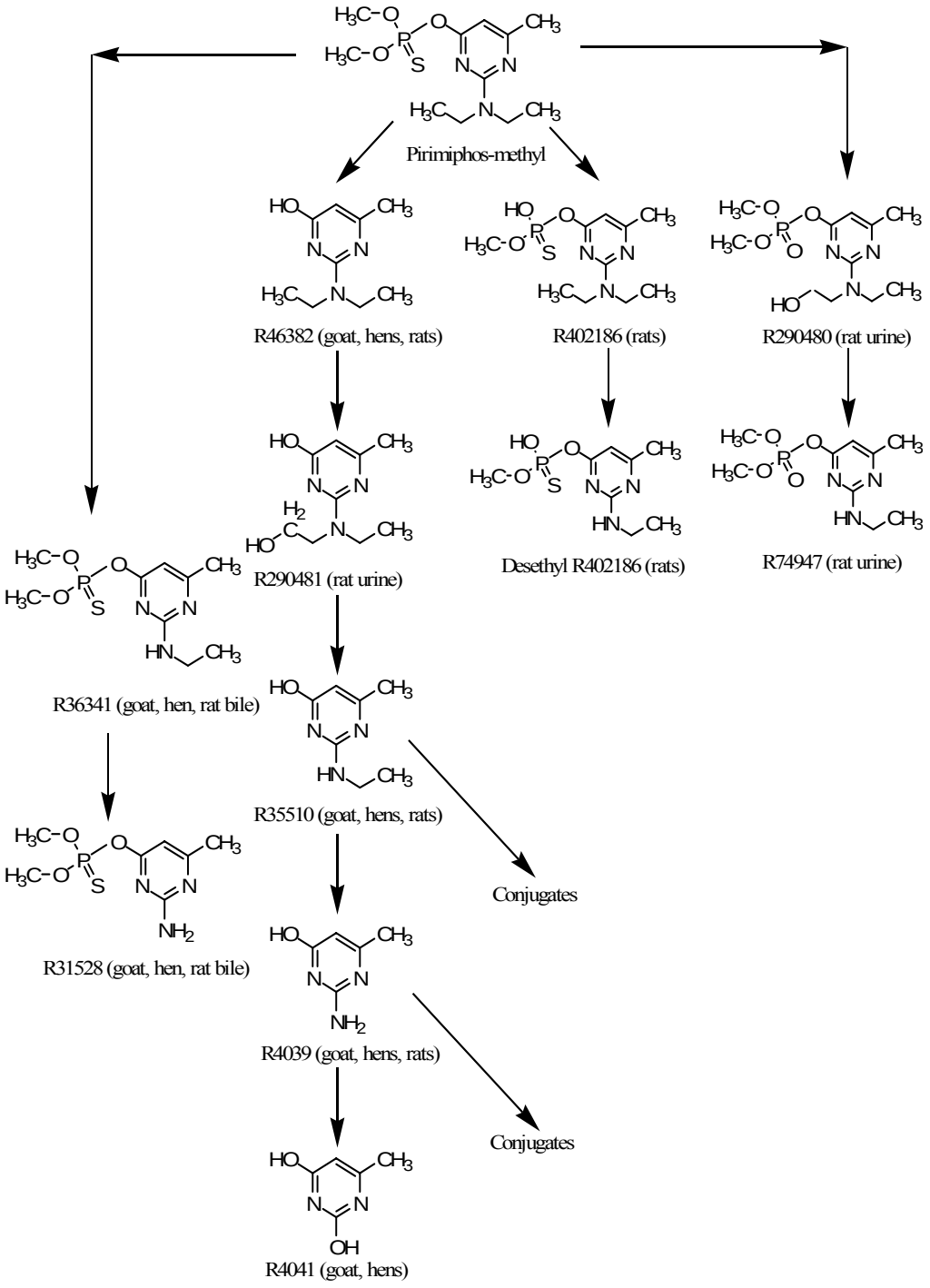


Figure 2. Proposed metabolic pathway of pirimiphos-methyl in animals.

Table 8. Radioactive residues in treated wheat grains expressed as pirimiphos-methyl equivalents, in mg/kg (Bowker & Hughes, 1973).

Treatment	Moisture content, %	Component	Storage time, weeks					
			0	2	4	8	16	32
4 mg/kg	13.2-15.0	Pirimiphos-methyl	2.16	2.66	2.05	2.66	2.32	2.08
		R36341 + unidentified [1/]	0.04	0.04	0.04	0.06	0.04	-
		R46382 + R35510 + R4039	<0.01	0.07	0.08	0.17	0.21	0.29
		TLC origin	<0.01	<0.01	0.04	0.04	0.08	0.26
		Unextracted	0.02	0.05	0.02	0.08	0.14	0.11
		Total	2.29	2.83	2.43	3.00	2.88	2.73
4 mg/kg	18.1-19.9	Pirimiphos-methyl	2.36	2.73	1.12	0.80	0.79	0.38
		R36341 + unidentified [1/]	0.05	0.03	0.03	0.03	0.03	0.03
		R46382 + R35510 + R4039	-	0.49	0.56	1.05	0.92	0.66
		TLC origin	-	-	0.21	0.03	0.16	0.14
		Unextracted	0.05	0.22	0.48	0.87	0.94	1.60
		Total	2.46	3.47	2.46	2.78	2.99	2.81
8 mg/kg	11.6-13.5	Pirimiphos-methyl	4.03	5.46	3.80	4.64	5.53	5.37
		R36341 + unidentified [1/]	0.12	0.08	0.08	0.11	0.04	0.10
		R46382 + R35510 + R4039	-	0.15	0.11	0.16	0.32	0.59
		TLC origin	-	-	0.02	0.03	0.04	0.22
		Unextracted	0.05	0.11	0.31	0.19	0.30	0.50
		Total	4.18	5.75	4.31	5.15	6.27	6.79
8 mg/kg	17.0-20.1	Pirimiphos-methyl	4.44	5.64	2.93	2.84	2.19	1.28
		R36341 + unidentified [1/]	0.69	0.27	0.08	0.99	0.05	0.04
		R46382 + R35510 + R4039	-	0.98	0.99	1.61	1.89	1.61
		TLC origin	-	-	0.41	0.06	0.24	0.27
		Unextracted	0.16	0.28	0.71	1.00	1.82	2.52
		Total	4.60	7.15	5.12	5.60	6.40	5.85

[1/] The unidentified component occurred only in trace amounts.

The degradation pattern of pirimiphos-methyl and the quantities of degradation products in rice grain (with husk) and husked rice were similar to those observed in wheat grain. The main metabolite was R46382. Husked rice, derived from rice grain (in husk) treated with pirimiphos-methyl at 4 mg/kg, generally contained less than 1 mg/kg pirimiphos-methyl, before and after parboiling. Other minor hydroxypyrimidine metabolites were present at less than 0.05 mg/kg.

Table 9. Radioactive residues in treated husked rice expressed as pirimiphos-methyl equivalents, in mg/kg (Bowker & Hughes, 1973).

Treatment	Moisture content, %	Component	Storage time, weeks				
			0	2	4	8	32
4 mg/kg	12.2-13.2	Pirimiphos-methyl	2.13	2.31	2.06	2.19	-
		R36341 + unidentified [1/]	<0.01	<0.01	<0.01	0.07	-
		R46382 + R35510 + R4039	0.05	0.11	0.06	0.10	-
		TLC origin	0.01	0.07	0.23	0.07	0.02
		Unextracted	0.25	0.20	0.17	0.18	0.12
		Total	2.44	2.70	2.54	2.64	2.05
4 mg/kg	16.5-18.4	Pirimiphos-methyl	1.89	1.99	1.50	1.17	0.76
		R36341 + unidentified [1/]	<0.01	<0.01	<0.01	0.12	<0.01
		R46382 + R35510 + R4039	0.06	0.17	0.34	0.24	0.33
		TLC origin	0.01	0.12	0.26	0.27	0.17
		Unextracted	0.20	0.17	0.19	0.30	0.15
		Total	2.16	2.44	2.30	2.44	2.41
8 mg/kg	12.2-13.2	Pirimiphos-methyl	3.7	4.37	4.1	3.73	2.99
		R36341 + unidentified [1/]	<0.01	<0.01	<0.01	0.11	0.09
		R46382 + R35510 + R4039	0.10	0.18	0.11	0.34	0.17
		TLC origin	0.03	0.13	0.36	0.23	0.06
		Unextracted	0.72	0.24	0.23	0.50	0.78
		Total	4.55	4.93	4.80	5.07	4.13

Treatment	Moisture content, %	Component	Storage time, weeks				
			0	2	4	8	32
8 mg/kg	16.5-18.4	Pirimiphos-methyl	3.11	3.68	1.55	2.3	1.58
		R36341 + unidentified [1/]	<0.01	<0.01	<0.01	0.21	0.11
		R46382 + R35510 + R4039	0.06	0.32	0.10	0.86	0.45
		TLC origin	0.02	0.19	1.48	0.43	0.06
		Unextracted	0.47	0.35	0.31	0.40	1.07
		Total	3.67	4.55	3.94	4.22	3.40

[1/] The unidentified component occurred only in trace amounts.

Wheat grain (var. Hustler), rice grain (with husk) and husked rice (var. Labelle) were treated with an aqueous dilution of an EC formulation containing [2-^{14}C]pirimiphos-methyl, at a rate equivalent to 15 mg/kg (g/t) (wheat) or 22.5 mg/kg (g/t)(rice) (Curl & Leahey, 1980). The grain was stored in the dark, in dishes over concentrated sulphuric acid solutions in desiccators, to keep them at low (10-14%) or high (19-24%) moisture content, for up 24 weeks at 20°C. Samples were taken for analysis at 12 and 24 weeks. A summary of the total radioactive residues (TRR) on the grain is shown in Table 10. The degradation pattern of pirimiphos-methyl and the quantities of degradation products were similar between wheat and rice (grains with husks and husked rice).

Pirimiphos-methyl constituted the major component of the radioactive residue; major degradation products were R46382 and an unknown compound (Unknown X), which was hydrolyzed by acid reflux to release R46382. Pirimiphos-methyl accounted for 50-95% of the radioactive residues on/in the grain and R46382 and Unknown X accounted for 70-85% of the remaining radioactivity. Other, minor, compounds found in the grain were R36341, R35510 and R4039.

Table 10. Comparison of mean total radioactive residues in wheat and rice grain, expressed as pirimiphos-methyl equivalents, in mg/kg (Curl & Leahey, 1980).

Grain	Moisture content, %	Treatment, mg/kg	Storage, weeks		
			0	12	24
Wheat grain	11.9-13.5	15	10.8	10.9	9.8
Wheat grain	18.8-20.4	15	12.0	12.3	12.3
Rice grain (with husk)	10.4-12.5	22.5	20.7	14.3 [1/]	14.0
Rice grain (with husk)	21.5-21.8	22.5	18.7	15.3	14.8
Husked rice	11.3-12.9	22.5	16.1	15.8 [1/]	15.1
Husked rice	20.8-23.8	22.5	16.0	16.5	17.3

[1/] Samples taken at 13 weeks after treatment.

Stored maize grain

A study was conducted to determine the fate of ^{14}C-pirimiphos-methyl on stored maize grain, treated at exaggerated levels (Hauswald, 1993). Two portions of maize grain (var. Agrigene), with 14% moisture content, were sprayed three times with an EC formulation containing [^{14}C]pirimiphos-methyl, each application being made at a rate of approximately 47 mg a.i./kg grain. This resulted in a total application rate of 96 mg a.i./kg. Treated maize was maintained at about 14% moisture content for 0, 12 and 24 weeks after treatment, when samples were removed and frozen until the determination of TRR and the nature of residues. The total radioactive residues in maize grain are shown in Table 11. In the first 12 weeks, a decline in radioactivity corresponding to 44-63% of the initial dose was observed but the reason for this decline was unknown. No significant additional losses were observed in the second 12 weeks. The majority of the radioactivity in the grain was extractable with methanol, with 6% of the total radioactive residues remaining unextracted from the maize grain at 0, 12 and 24 weeks following the final application.

Table 11. Total radioactive residues (TRR) in methanol extracts of maize grain, expressed as mg pirimiphos-methyl/kg (Hauswald, 1993).

Sample	Storage, weeks		
	0	12	24
A	91.5	49.3	-
B	97.8	-	43.9

Grain samples having residue levels equal to or greater than 0.01 mg radioactive pirimiphos-methyl/kg were further characterized by TLC. The nature of the extractable residue is summarized in Table 12. In all samples, the methanol-soluble radioactivity was predominantly associated with metabolites that were closely related to pirimiphos-methyl, rather being incorporated into natural products.

Table 12. Residues extracted from maize grain and analyzed by TLC, expressed as % of TRR (Hauswald, 1993).

Component	Storage, weeks		
	0	12	24
Pirimiphos-methyl	86-92	71-74	60-64
R36341	5-7	4-6	4-7
R46382	1-3 [1/]	9-12	13-18
R35510	-	2-5	4-8
R4039 or R4041	0	0-1	0-1
Unknown	0-4	2-3	2-4

[1/] Chromatography indicated that this could be either R046382 or R035510.

Proposed metabolic pathway in cereal grains

The metabolism studies on stored grains that were submitted to the current Meeting showed similar metabolite profiles. The predominant component of residues was the unchanged parent compound, which formed not less than 60% of the TRR at the end of each storage experiment. The remainder was mainly comprised of the hydroxypyrimidines, R46382, R35510 and R4039. These hydroxypyrimidines were derived from the parent compound through hydrolysis and subsequent *N*-dealkylation of the side chain. The most abundant hydroxypyrimidine was R46382, which was present at up to 10% of the TRR under conditions reflecting current GAP. Some unknown components were also present in wheat grain, which could be converted to R46382 by hydrolysis. R35510 and R4039 were present at <5% of the TRR. R36341 was also detected in small amounts and resulted from the loss of one *N*-ethyl group from the parent compound. A proposed metabolic pathway is shown in Figure 3.

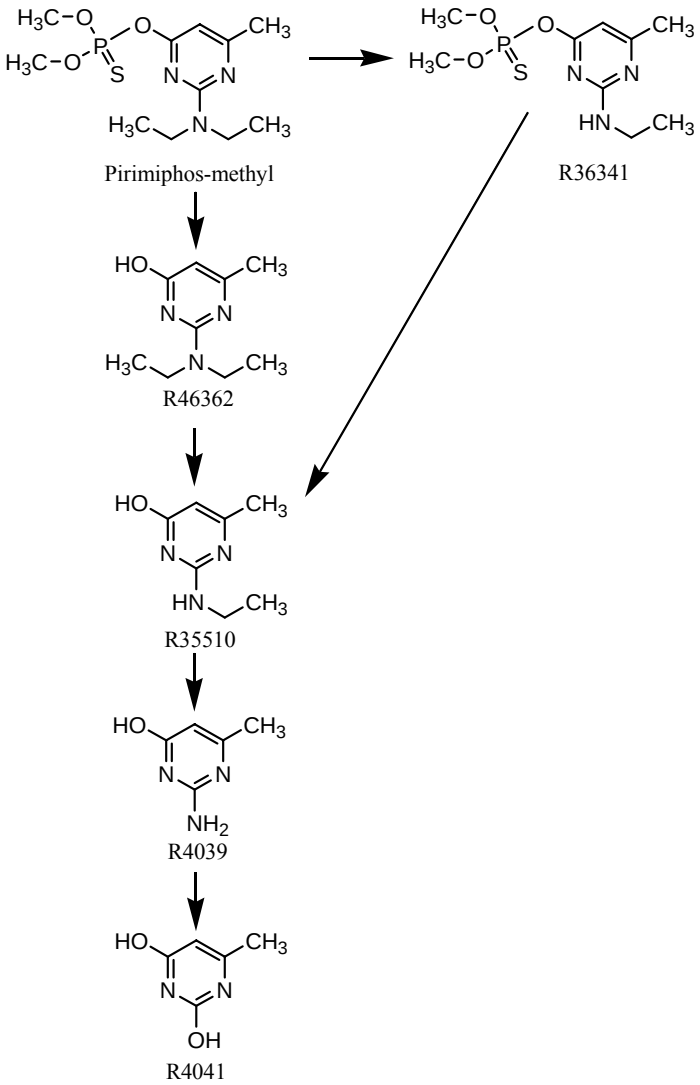


Figure 3. Proposed metabolic pathway of pirimiphos-methyl in cereal grains.

Environmental fate in soil, water-sediment systems and rotational crops

No studies were reported.

RESIDUE ANALYSIS

Analytical methods

The Meeting received information on analytical methods for pirimiphos-methyl in a variety of fruit, vegetables, wheat and, for pirimiphos-methyl and its metabolites in animal tissues, milk and eggs. The limits of quantification and recoveries of each analytical method are summarized in Table 13.

Wilson (1997) and Anderson and Wilson (1997) developed and validated gas-chromatographic methods for the determination of pirimiphos-methyl in various crops. Test matrices were selected from different Codex food categories, as shown in Table 13. Portions of prepared samples, with or without fortification with pirimiphos-methyl at 0.05-8.0 mg/kg, were extracted with acetone/hexane (2:8 v/v) followed by maceration, addition of ultra-pure water, shaking and centrifugation. The upper (hexane) layer was analyzed by GC, using either a nitrogen-selective thermionic-specific detector (GC-TSD) or a mass selective detector (GC-MSD) (ion monitored, *m/z* 290 and 305). Except for cotton seed and olive samples analyzed by GC-MSD, the mean detector response obtained from 3 injections was linear for all matrices between 0.0125 and 2.0 µg/ml (i.e. 3.75-600 pg of pirimiphos-methyl injected onto GC-TSD or 12.5-2000 pg injected onto GC-MSD. As the MSD response to pirimiphos-methyl in cotton seed and olive extracts was not linear, it was recommended that

GC-TSD method should be used in these cases. The limit of detection, defined as four times baseline noise, was around 0.01 mg/kg but dependent on the sample matrix. Orange peel tended to produce recovery values >100%.

Robinson (2000) examined the suitability of a GC-MSD method, similar to that above, for determination of residues of pirimiphos-methyl in animal matrices. Pirimiphos residues were extracted by homogenizing samples with acetone/hexane (1:4), shaking the homogenates with water then separating the phases by centrifugation. Aliquots of the upper (hexane) layer, resulting from the extraction of milk, egg, liver, kidney and muscle samples were subjected a clean-up process using a silica solid phase extraction column. The hexane layer obtained from the extraction of fat samples was subjected, prior to solid phase extraction clean-up, to an additional hexane/acetonitrile liquid-liquid partition procedure. Final extracts were analyzed by GC-MSD (ions monitored: target ion, *m/z* 290; qualifier ions, *m/z* 276 and 305). The linearity of the GC-MSD response to the pirimiphos-methyl standard was linear between 0.001 to 1.0 µg/ml, equivalent to 2 to 2000 pg injected. The limit of detection, corresponding to 4 times background noise in a blank sample, was estimated to be 0.003 mg/kg.

Swaine and Pain (1980) examined the suitability of a GC-MS (ions monitored, *m/z* 224, 210 and 254) method for the determination of hydroxypyrimidine metabolites of pirimiphos-methyl, in a variety of animal tissues, milk and eggs. Tissue samples were extracted by homogenizing in methanol/2N HCl (1:1). After centrifugation, an aliquot was shaken with hexane and then evaporated to remove methanol. The aqueous extract (containing residual HCl) was refluxed to hydrolyze hydroxypyrimidine conjugates, then neutralized, buffered and then cleaned up with an Extrelut column, eluting with *n*-butanol. Hexane extracts were cleaned up using adsorption chromatography with Fractosil. The final extracts were analyzed by GC-MS following trimethylsilylation of the hydroxypyrimidines with *N,O*-bis(trimethylsilyl)-trifluoroacetamide in pyridine. Milk samples were extracted by blending with concentrated HCl/methanol/hexane (1:5:6). An aliquot of the aqueous phase was evaporated, neutralized and cleaned up using an Extrelut column and the organic phase was cleaned up on a Fractosil column.. Egg samples were extracted by blending with methanol/2N HCl (9:1), to remove protein by precipitation. For both milk and egg samples, the hydrolysis step was omitted. The recovery of R4039 in animal tissue samples was lower (65 ± 13%) than in other matrices, or for other compounds in all matrices, and this was attributed to the lower yield of the TMS derivative in derivatization reaction. To compensate for this, R31680 as added an internal standard. The validity of the use of the internal standard was demonstrated by the linear calibration graphs with 0.1-1.0 mg/kg of R4039 (5 mg/kg R31680 added) and with 0.01-0.10 mg/kg of R4039 (0.5 mg/kg R31680 added).

Table 13. Summary of the performance of analytical methods.

Method and reference	LOQ, mg/kg	LOD, mg/kg	Matrix	Fortification mg/kg	Recovery, %		CV, %
					Mean	Range	
Pirimiphos-methyl							
GC-TSD Wilson, 1997; Anderson and Wilson, 1997	0.05	*ca*. 0.01	Apple	0.05-8.0	98	94-115	9
			Strawberry		99	88-115	9
			Melon		79	70-90	8
			Orange flesh		106	93-117	8
			Orange skin		96	89-103	8
			Tomato		100	88-117	9
			Lettuce		94	85-106	7
			Nectarine		99	86-109	10
			Carrot		94	80-98	7
			Cotton seed		81	61-109	17
			Olive		81	69-95	13
			Wheat		86	69-102	12

Method and reference	LOQ, mg/kg	LOD, mg/kg	Matrix	Fortification mg/kg	Recovery, %		CV, %
					Mean	Range	
GC-MSD Wilson, 1997; Anderson and Wilson, 1997	0.05	*ca*. 0.01	Apple	0.05-8.0	86	76-101	12
			Strawberry		100	93-109	5
			Melon		81	75-84	5
			Orange flesh		105	97-109	5
			Orange skin		98	90-118	9
			Tomato		101	96-109	4
			Lettuce		94	86-107	9
			Nectarine		98	83-106	9
			Carrot		96	88-101	5
			Cotton seed		84	72-92	11
			Olive		85	74-100	10
			Wheat		79	65-87	8
GC-MSD, with automated extraction Wilson, 1997; Anderson and Wilson, 1997	0.05	*ca*. 0.01	Apple	0.05-8.0	84	76-89	7
			Strawberry		82	70-90	8
			Melon		102	95-111	6
			Orange flesh		88	72-107	13
			Orange skin		104	92-123	8
			Tomato		81	65-107	14
			Lettuce		76	67-88	10
			Nectarine		78	60-90	13
			Carrot		98	92-108	5
GC-MSD Robinson, 2000	0.01	0.003	Milk	0.01-0.1	90	85-96	4
			Liver		94	86-98	5
			Kidney		91	87-96	3
			Muscle		97	95-99	2
			Fat		77	73-81	4
			Hens' eggs		87	76-93	6
R46382							
GC-MS [1/] Swaine and Pain, 1980	0.01 (4x baseline noise)	-	Animal tissue incl. chicken muscle, cow muscle, liver and kidney	0.10-5.0	81	62-101	11
			Cows' milk	0.0025-1.0	87	63-114	16
			Hens' eggs	0.05	97	76-106	16
R35510							
GC-MS [1/] Swaine and Pain, 1980	0.01 (4x baseline noise)	-	Animal tissue incl. chicken muscle, cow muscle, liver and kidney	0.10-5.0	81	60-111	13
			Cows' milk	0.0025-1.0	95	55-120	14
			Hens' eggs	0.05	86	67-112	17
R4039							
GC-MS [1/] Swaine and Pain, 1980	0.01 (4x baseline noise)	-	Animal tissue incl. chicken muscle, cow muscle, liver and kidney	0.10-5.0	64	48-93	13
			Cows' milk	0.0025-1.0	85	63-119	18
			Hens' eggs	0.05	86	65-106	15

[1/] Same method.

Stability of pesticide residues in stored analytical samples

Anderson and Butters (1999) investigated the stability of pirimiphos-methyl in barley, carrot, lettuce, olive and tomato matrices, stored frozen for 24 months. Samples of these commodities were fortified with pirimiphos-methyl at 0.5 mg/kg and stored in a freezer at <-16°C. Duplicate samples were removed after 4, 12, 18 and 24 months and analyzed for pirimiphos-methyl. Barley and olive samples were also analyzed at 724 and 216 days, respectively, to confirm the 739 day results (barley) and 124 day results (olives). Samples were analyzed using the GC method developed and validated by Wilson (1997), which has an LOQ of 0.05 mg/kg (see table 13).

Table 14 shows that no significant loss in residues of pirimiphos-methyl occurred during 24 months storage of barley, carrots, lettuce or tomatoes at <-16°C. Residue data are not corrected for recovery. Mean recovery of pirimiphos-methyl, added to samples of barley, carrots, lettuce, olives and tomatoes at 0.5 mg/kg, was 83, 98, 98, 79 and 97%, respectively. However, these recovery data were

generated separately from the storage experiment and procedural recovery was not checked at each individual time point in the experiment.

Table 14. Storage stability of pirimiphos-methyl in plant samples fortified at 0.5 mg/kg and stored at below -16°C (Anderson and Butters, 1999).

Storage days	Mean residue of pirimiphos-methyl, mg/kg (n = 2)				
	Barley	Carrots	Lettuce	Olives	Tomatoes
0	0.47	0.51	0.47	0.39	0.54
120	-	0.53	0.51	-	-
124	0.41	-	-	0.33	0.48
216	-	-	-	0.40	-
350	0.40	-	-	-	-
359	-	-	-	0.38	-
370	-	0.49	0.53	-	0.49
572	-	0.53	0.49	-	0.49
573	0.39	-	-	-	-
582	-	-	-	0.43	-
735	-	0.45	0.45	-	0.45
739	0.32	-	-	0.36	-
747	0.37	-	-	-	-

Wilson (1997) tested the stability of pirimiphos-methyl in analytical extracts of plant samples. Final, cleaned-up extracts were stored in vials at 5-7°C and, in this matrix, pirimiphos-methyl was evidently stable for up to 7 days (the maximum storage time), if quantified against standards in solvent that had been stored in the same conditions.

No data were submitted on the storage stability of pirimiphos-methyl and its metabolites in animal tissues or eggs. For milk, see the section on farm animal feeding studies.

USE PATTERN

Pirimiphos-methyl is registered in many countries for control of insect infestation in crops, stored grain and storage facilities, as well as for public health purposes. Official labels or official use instructions from Brazil, China, Georgia, Slovenia, Thailand and Vietnam were provided to the Meeting by the manufacturer, with English translations. Labels/instructions from Albania, Algeria, Argentina, Australia, Cameroon, Columbia, Czech Republic, Ecuador, Italy, Côte d'Ivoire, former Yugoslav Republic of Macedonia, Mexico, New Zealand, Paraguay, Poland, Slovak Republic, South Africa and Spain were provided only in the original languages. Information on uses was also provided by Australia, France, Germany and the Netherlands and was also obtained from the official web sites of the Governments of Japan and the USA.

In addition to post-harvest uses, shown in Table 15, pirimiphos-methyl is registered in many countries for pre-harvest uses on a variety of fruit, vegetables and cereals, including asparagus, beans, broccoli, Brussels sprouts, cabbages, cacao, carrots, cauliflowers, cashew nuts, cereals, Chinese chives, citrus fruit, coconut palm, cucumbers (field & glasshouse), other cucurbits (greenhouse), custard apples, egg plant, garlic, kiwi fruit, komatsuna, lettuce, maize, melons, oil palm, olives, peas, peppers (field & glasshouse), potatoes, rice, sugar beet, tea, tomatoes (field & greenhouse), watermelons, wheat, wine grapes, winter cereals and alfalfa. It is also registered in the USA for use on beef and non-lactating dairy cattle and calves, as ear tags (2 ear tags/animal; concentration, 14 or 20%). The information available to the Meeting on post-harvest uses on cereal grains and peanuts is summarized in Table 15.

Table 15. Registered post-harvest uses of pirimiphos-methyl on cereal grains.

Crop	Country	Formulation		Application				PHI, days
		Type	Conc g a.i./l	Method	Spray conc. kg a.i./hl	Vol. l/t	Rate	
Cereal grains in bulk	Algeria	EC	500				5 g a.i./t [1/]	
Cereal grains in bulk	Argentina	EC	210	Admixture			4 g a.i./t	[2/]
Cereal grains in bulk	Argentina	EC	210	Admixture			2 g a.i./t	[3/]
Cereal grains in bulk	Argentina	EC	500	Admixture			3-5 g a.i./t	
Cereal grains in bags	Argentina	EC	500	Spraying			0.25-0.5 g a.i./m^2 surface	

Crop	Country	Formulation		Application				PHI, days
		Type	Conc g a.i./l	Method	Spray conc. kg a.i./hl	Vol. l/t	Rate	
Cereal grains in bulk	Australia		900	Admixture			4 g a.i./t	[4/]
Peanuts in bulk	Australia		900	Admixture			19.8 g a.i./t	
Cereal grains in bulk	Brazil	EC	500	Admixture			4-8 g a.i./t	30 [5/]
Cereal grains in bags	Brazil	EC	500	Spraying			0.25 g a.i./m^2 of surface	[6/]
Cereal grains in bulk	Cameroon	DP	2%	Admixture			10 g a.i./t	
Cereal grains in bulk	Chile	EC	500	Admixture			4-10 g a.i./t	
Cereal grains in bags	Chile	EC	500	Spraying			0.25 g a.i./m^2 of surface	
Cereal grains in bulk	China	EC	500	Spraying			5-10 g a.i./t	
Potato in bulk	Columbia	EC	500	Spraying	0.25-0.5			[7/]
Cereal grains in bags	Columbia	EC	500	Spraying			0.5 g a.i./ m^2 of surface	[8/]
Cereal grains in bulk	Côte d'Ivoire	DP	2%	Dusting			5-10 g a.i./t	
Cereal grains in bulk	Georgia	EC	500	Admixture			8 g a.i./t	
Cereal grains in bulk	France	EC	725	Admixture			4 g a.i./t	
Cereal grains in bulk except maize	Germany	EC	500	Spraying on conveyer belt		5	4 g a.i./t	
Cereal grains in bulk	Italy		50	Spraying			4-8 g a.i./t	
Cereal grains in bulk	Italy	EC	440	Spraying			4.1-7.5 g a.i./t	
Cereal grains in bulk	Italy	EC	250	Spraying			4-8 g a.i./t	
Cereal grains in bags	Italy	EC	440	Spraying			0.26-0.62 g a.i./m^2	
Cereal grains in bags	Italy	EC	250	Spraying			0.25-0.63 g a.i./m^2	
Cereal grains	Italy	DP	2%	Dusting			4-8 g a.i./t	
Cereal grains in bulk	Mexico	EC	500	Admixture			4-8 g a.i./t	
Cereal grains in bulk	Netherlands	EC	500	Spraying			4 g a.i./t	
Cereal grains in bulk	New Zealand	DP	2%	Admixture			4 g a.i./t	
Cereal grains in bulk	New Zealand	EC	500	Admixture			4 g a.i./t	
Cereal grains in bags	New Zealand	DP	2%	Dusting			0.7 g a.i./m^2	
Cereal grains in bags	New Zealand	EC	500	Spraying			0.25-0.5 g a.i./m^2	
Cereal grains in bulk	Paraguay	EC	500	Admixture			4-8 g a.i./t	30
Cereal grains in bags	Paraguay	EC	500	Admixture			0.25 g a.i./m^2	30
Cereal grains in bulk	Slovenia	EC	500	Admixture			4 g a.i./t	
Wheat in bulk	South Africa	EC	400	Spraying	1.6			
Wheat in bags	South Africa	EC	400	Spraying			1.6 g a.i./m^2	
Cereal grains in bulk	Spain	DP	2%	Dusting			3-8 g a.i./t	21
Cereal grains in bulk	Uruguay	EC	400	Admixture			3.2-5.6 g a.i./t	
Corn in bulk	USA	EC	570	Admixture			5-7 g a.i./t	
Corn in bulk	USA	EC	570	Top dress			0.52 g a.i./m^2	
Sorghum in bulk	USA	EC	570	Admixture			5-7 g a.i./t	
Sorghum in bulk	USA	EC	570	Top dress			0.54 g a.i./m^2	

[1/] Per tonne of grain.
[2/] For 6 months.
[3/] For 3 months.
[4/] For rice, apply only to paddy rice prior to milling.
[5/] Period between the treatment of stored grains and commercialization. Rice and barley, in hulls.
[6/] Rice and barley, in hulls.
[7/] Repeat, if necessary or one week later, with 8 g a.i./t to be applied directly on grain.
[8/] Repeat applications one or two times a week during storage.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Pirimiphos-methyl is used for the control of a broad spectrum of insects and is applied either directly to stored commodities or to the storage facilities. The Meeting received information from the manufacturer on supervised trials conducted on stored cereal grains. The results of these trials are shown in Table 16. Many pre-harvest uses have been registered in many countries but no supervised trial studies on pre-harvest uses were submitted.

Residue values from trials conducted according to GAP were used for the estimation of maximum residue levels. These results are double underlined.

Laboratory reports included method validation data, with recovery experiments conducted at levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of

sample storage were also provided. Most reports provided information on the methods of application, grain weights, application dates, residue sample sizes and sampling dates. Residue data are recorded unadjusted for recovery.

Table 16. Residues in stored cereal grains from supervised trials conducted in Germany and the United Kingdom.

Grain, (Variety), Reference	Location, Year	Formulation	Application g a.i./t	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
Wheat (Chalk) RIC2913	Crondall, Hampshire, UK 1973	EC 25%	4	0	Grain	2.6
					Bran	6.0
					Fine offal	1.8
					Flour	0.27
					Bread	0.17
				4	Grain	1.9
					Flour [2/]	1.7
					Bread [2/]	0.87
				8	Grain	2.0
					Flour [2/]	1.6
					Bread [2/]	0.91
				12	Grain	1.9
					Flour [2/]	1.6
					Bread [2/]	0.85
Wheat (Capelle) RIC2913	Brown Candover, Hampshire, UK 1973	EC 25%	4	0	Grain	2.3
					Bran	7.0
					Fine offal	4.3
					Flour	0.79
					Bread	0.21
				2	Grain	1.4
					Bran	5.6
					Fine offal	4.8
					Flour	0.52
					Bread	0.24
Wheat (Maris Huntsman) RIC2913	Brown Candover, Hampshire, UK 1973	EC 25%	4 (applied at 0.85 l/t)	0	Grain	3.8
					Bran	7.8
					Fine offal	3.1
					Flour	0.51
					Bread	0.25
				3.5	Grain	3.6
					Bran	5.0
					Fine offal	5.0
					Flour	0.51
					Bread	0.28
				8	Grain	3.7
					Bran	5.4
					Fine offal	3.7
					Flour	0.52
					Bread	0.30
				12	Grain	2.4
					Bran	4.2
					Fine offal	3.8
					Flour	0.57
					Bread	0.48
Wheat (Maris Huntsman) RIC2913	Brown Candover, Hampshire, UK 1973	EC 25%	4 (applied at 1.7 l/t)	0	Grain	2.9
					Bran	8.0
					Fine offal	3.0
					Flour	0.59
					Bread	0.23
				3.5	Grain	3.3
					Bran	4.7
					Fine offal	4.4
					Flour	0.69
					Bread	0.32

Grain, (Variety), Reference	Location, Year	Formulation	Application g a.i./t	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
				8	Grain	3.7
					Bran	5.1
					Fine offal	3.6
					Flour	0.48
					Bread	0.30
				12	Grain	3.3
					Bran	5.2
					Fine offal	4.1
					Flour	0.60
					Bread	0.49
Wheat (Desprez) RIC2913	Dummer, Hampshire, UK 1973	EC 25%	4	0	Grain	1.9
					Flour [2/]	1.2
					Bread [2/]	0.60 [3/]
				3.5	Grain	1.3
					Flour [2/]	1.9
					Bread [2/]	0.80
				8	Grain	1.5
					Flour [4/]	0.26
					Bread [4/]	0.22
					Bread [2/]	0.95
				12	Grain	1.2
					Flour [2/]	1.1
					Bread [2/]	0.70
Wheat (Kleiber) RIC2913	Hackwood, Hampshire, UK 1973	EC 25%	4	0	Grain	4.5
					Bran	12 [3/]
					Fine offal	4.5 [3/]
					Flour	0.33 [3/]
					Bread	0.17 [3/]
				4	Grain	3.3
					Bran	11
					Fine offal	4.5
					Flour	0.54
					Bread	0.33
				8	Grain	2.2
					Bran	8.9
					Fine offal	3.8
					Flour	0.58
					Bread	0.41
Wheat (Kleiber) RIC2913	Hackwood, Hampshire, UK 1973	DP 2%	4	0	Grain	2.3
					Bran	5.5 [5/]
					Fine offal	2.01 [5/]
					Flour	0.3.
					Bread	0.22 [5/]
				4	Grain	3.2
					Bran	6.0
					Fine offal	3.2
					Flour	0.40
					Bread	0.20
				8	Grain	2.2
					Bran	3.8
					Fine offal	2.7
					Flour	0.50
					Bread	0.28
				12	Grain	2.2
					Bran	2.7
					Fine offal	2.5
					Flour	0.34
					Bread	0.19
Wheat (Widgeon) RIC2913	Windsor, Berkshire, UK 1973	EC 25%	4	0	Grain	3.2
					Flour [2/]	0.98
					Bread [2/]	0.65
				4	Grain	2.8
					Flour [2/]	1.7
					Bread [2/]	0.73

Grain, (Variety), Reference	Location, Year	Formulation	Application g a.i./t	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
				8	Grain	2.5
					Flour [2/]	1.9
					Bread [2/]	0.87
				12	Grain	2.4
					Flour [2/]	1.9
					Bread [2/]	0.60
Wheat (Widgeon) RIC2913	Windsor, Berkshire, UK 1973	DP 2%	4	0	Grain	2.2
					Flour [2/]	1.1
					Bread [2/]	0.48
				4	Grain	1.9
					Flour [2/]	0.99
					Bread [2/]	0.50
				8	Grain	1.4
					Flour [2/]	1.0
					Bread [2/]	0.54
				12	Grain	1.3
					Flour [2/]	0.90
					Bread [2/]	0.47
Wheat RIC2912	Abingdon, Oxon, UK 1972	EC 25%	3	0	Grain	1.8
				2		0.87
				4		0.64
				8		1.5
				16		0.52
				20		1.1
Spring wheat M4944B RS-8834 B2	Gödensdorf/ Salzhousen, Germany 1988	EC 50%	4	Untreated	Grain	<0.05
				0		1.8
				1		2.3
				4		2.2
				8		1.8
				24.5		2.1
Winter wheat (Urban) M4944B RS-8834 E1	Kapellen-Drusweiler, Germany 1988	EC 50%	4	Untreated	Grain	<0.05
				0		1.9
				1		2.3
				4		1.8
				8		1.8
				26		2.6
Barley RIC2912	Abingdon, Oxon, UK 1972	EC 25%	3 (solid stream)	0	Grain	2.8
				2		2.7
				4		1.2
				8		1.6
				16		1.0
				20		1.3
			2 (solid stream)	0	Grain	0.84
				2		0.90
				4		0.47
				8		0.56
				16		0.63
				20		0.70
			3 (50% spray)	1 day	Grain	1.3
				2		0.99
				4		0.73
				8		0.70
				16		0.63
				20		1.1
			2 (50% spray)	0	Grain	0.72
				2		0.67
				4		0.47
				8		0.42
				16		0.58
				20		0.45

Grain, (Variety), Reference	Location, Year	Formulation	Application g a.i./t	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
Barley RIC2912	Cliddesdon, UK 1972	DP 2%	3	0 5 days 6 days 2 4 8 12 13	Grain	0.36 (16) 0.38 (2) 0.34 (2) 0.35 (4) 0.32 (4) 0.80 (2) 0.41 (2) 0.51 (2)
Barley RIC2912	Stalham, Norfork, UK 1971	EC 25%	4	0 2 4 8 12	Grain	0.83 (17) 1.1 (15) 2.0 (10) 0.74 (15) 0.62 (15)
Barley RIC2912	Stalham, Norfork, UK 1971	EC 25%	8	0 2 4 8 12	Grain	1.4 (8) 1.7 (10) 3.7 (7) 1.5 (8) 1.7 (10)
Barley RIC2912	Woodmancote, UK 1972	EC 25%	4 (full cover)	0 2.5 4 6 10 12	Grain	1.5 (10) 1.1 1.5 1.2 0.44 (2) 0.48
			4 (solid stream)	0 1 3 5 9 11	Grain	2.6 (10) 2.5 3.1 3.1 1.8 (2) 1.3
			4 (50% cover)	0 1.5 3.5 5.5 9 11.5	Grain	1.1 (10) 0.96 1.3 2.7 0.80 1.2
			3 (full cover)	0 2 4 6 10 12	Grain	0.92 (10) 0.85 1.3 1.0 0.66 0.62
			3 (50% cover)	0 1.5 3 5 9 11	Grain	2.3 (10) 2.16 2.4 2.1 1.7 1.7
			2 (full cover)	0 2 4 6 10 12	Grain	0.92 (10) 0.69 0.98 0.97 0.62 0.33
Barley RIC2912	Polesdon Lacey, Surrey, UK 1971	DP 2%	3	0 2 3.5 8 12	Grain	0.68 (6) 0.69 (15) 0.74 (15) 0.37 (15) 0.55 (15)
			4	0 2 3.5 8 12	Grain	1.4 (6) 0.99 (15) 0.71 (15) 0.76 (15) 0.16 (15)

Grain, (Variety), Reference	Location, Year	Formulation	Application g a.i./t	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
Barley RIC2912	Polesdon Lacey, Surrey, UK 1971	DP 2%	4	0 2 3.5 8 12	Grain	1.0 (5) 1.0 (15) 0.84 (15) 0.42 (15) 0.12 (10)
			8	0 2 3.5 8 12	Grain	1.5 (5) 2.6 (15) 1.1 (15) 1.7 (15) 1.3 (15)
Winter barley M4944B RS-8834 B1	Klein-Zecher, Germany 1988	EC 50%	4	Untreated Untreated Untreated 0 1 4 6 25 14 14	Grain Husk Kernel Grain Grain Grain Grain Grain Husk Kernel	<0.05 <0.05 <0.05 1.0 0.82 0.73 0.60 0.19 1.0 0.09
Spring barley (Arena) M4944B RS-8834 G1	Moosburg, Germany 1988	EC 50%	4	Untreated Untreated Untreated 0 1 4 8 9.5 9.5	Grain Husk Kernel Grain Grain Grain Grain Husk Kernel	<0.05 <0.05 <0.05 1.5 1.6 1.4 1.4 3.3 0.06
Oats (Lorenz) M4944B RS-8834 E2	Pirmasens-Windsberg, Germany 1988	EC 50%	4	Untreated Untreated Untreated Untreated Untreated 0 1 4 8 25 13 13 13 13	Grain Husk Kernel [6/] Kernel [7/] Rolled oat Grain Grain Grain Grain Grain Husk Kernel [6/] Kernel [7/] Rolled oat	<0.05 <0.05 <0.05 <0.05 <0.05 2.5 2.0 2.0 2.3 2.9 3.8 0.25 0.10 0.07
Rye M4944B RS-8834 G2	Velder, Germany 1988	EC 50%	4	Untreated 0 1 4 8	Grain Grain Grain Grain Grain	<0.05 1.7 1.7 1.8 1.9
Maize (Zeamx) M4944B RS-8834 G3	Rudelhausen, Germany 1988	EC 50%	4	Untreated 0 1 4.5 8	Grain Grain Grain Grain Grain	<0.05 2.2 2.0 2.4 2.4

In all cases, the LOQ was 0.01 mg/kg.

Note. Residue value for barley arising from trials in the UK is the average of replicate samples. The number of samples is in brackets following the value.

[1/] Where bran and fine offal are not indicated, grains were milled to wholemeal flour.

[2/] Wholemeal flour and whole wheat bread.

[3/] Control sample analysis gave positive result.

[4/] White flour and white bread.

[5/] Control sample analysis gave positive result but the re-analysis gave result of <LOQ.

[6/] Pre-dry.

[7/] Post-stream.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In storage

See plant metabolism section, under stored wheat and rice and stored maize.

In processing

The Meeting received information on the fate of incurred residues of pirimiphos-methyl during the processing of cereal grain. Some information on the fate of pirimiphos-methyl residues in wheat and oats is also presented in Table 16.

Laboratory-scale processing of wheat

Bullock *et al*. (1976) studied the fate of pirimiphos-methyl residues in wheat flour during baking on a laboratory scale. Wheat flour (white and wholemeal) was spread out as a thin layer onto which [2-^{14}C]pirimiphos-methyl dissolved in diethyl ether was applied uniformly. After the solvent had evaporated, the flour was mixed and used for baking bread and biscuits. Representative samples (50 g) of flour, bread and biscuits were extracted by maceration with methanol. Soxhlet extraction with methanol was employed for further extraction. Unextracted radioactivity was measured by combustion of the post-extraction solids and the extracts were analyzed by TLC. Radioactive volatiles, potentially generated during baking, were trapped by passing a stream of nitrogen slowly through the oven and collecting the effluent gas in a series of traps, containing solid CO_2-acetone, ethanolamine, methyoxyethanol and 0.1 N sulfuric acid.

Extraction of the flour, bread or biscuits with methanol recovered about 98% of the applied radioactivity. Combustion of the post-extraction solids showed that only 1-2% of the applied radioactivity was unextracted. Although pirimiphos-methyl is known to be relatively volatile, no significant radioactivity was detected in the traps. The total recovery of radioactivity from the baked products was more than 98% of that applied to the flour used. Analysis of slices, crusts and crumbs showed that the distribution of radioactivity within the bread was reasonably uniform. The quantities of radioactive compounds present in the methanol extracts are shown in Table 17. Pirimiphos-methyl was found to be relatively stable during the baking process. The parent compound accounted for 75, 90 and 87% of the radioactivity in the white bread, wholemeal bread and biscuits, respectively; the lower value apparent in white bread was not explained. Metabolites R46382 and R4039 accounted for 3-10% of the radioactivity in the final products.

Another experiment was conducted, using [2-^{14}C]R46382 added to white flour to make white bread, because this metabolite is usually present after pirimiphos-methyl has been applied to plants. After baking, 94% of the applied radioactivity was recovered from the bread. TLC chromatograms of methanolic extracts of the bread showed that R46382 was also stable to the baking process and accounted for 92% of the radioactivity present in the bread. R35510 accounted for approximately 4% and R4039 approximately 1%.

Table 17. Degradation of pirimiphos-methyl during the baking of treated wheat flour into white bread, wholemeal bread and biscuits: TLC analysis of compounds extracted with methanol (Bullock *et al*., 1976).

Compound	Radioactivity (expressed as % of total applied to chromatogram)							
	White Bread				Wholemeal bread			
	Flour	Slice	Crust	Crumb	Flour	Slice	Crust	Crumb
Unknown	2	1	1	1	-	-	-	-
Pirimiphos-methyl	94	75	59	74	97	90	87	89
R36341	2	2	1	3	-	-	-	-
R35311	-	1	1	1	-	-	-	-
R46382	2	9	25	5.5	2	3	5	4.5
R35510	-	1	1	1	-	-	-	-
R4039	-	7	9	11.5	0.5	3	4	4
Origin	-	3	3	1	0.5	2	3	2
Areas between radioactive bands	-	-	-	-	-	2	1	0.5

Compound	Radioactivity (expressed as % of total applied to chromatogram)	
	Flour	Biscuits
Pirimiphos-methyl	94.7	86.9
R36341	0.5	1.2
R35311	0.1	0.8
R46382	0.5	4.5
R35510	-	0.2
R4039	1.0	3.0

The order of compounds is that observed in the chromatogram, in descending order of Rf value.
- = Not significantly above background.

Commercial-scale processing of wheat

Bullock (1974) investigated the fate of pirimiphos-methyl residues in commercial milling and baking practice. Pirimiphos-methyl was applied as a 25% EC or 2% dust formulation to 50 tonnes of wheat, at a rate of 4 g/t, at six different sites in the United Kingdom. For details of varieties and sites, refer Table 15 under RIC2913. Treated grain was milled and baked at the Flour Milling and Baking Research Association, Rickmansworth, UK. Samples were analyzed for residues of pirimiphos-methyl, R36341 and hydroxypyrimidines. The limit of detection was 0.01 mg/kg. The residues of pirimiphos-methyl in bran, flour (white and wholemeal), offal and bread (white and wholemeal) are shown in Table 16.

The average residue level in unprocessed grain used to make white bread was 2.9 mg/kg and that in the grain used to make wholemeal bread was 1.9 mg/kg. Most of the residue (80-90%) was separated into the bran, during the milling process to prepare white flour. Further losses occurred during baking, so that the residue level in the bread was markedly lower than in the flour. The average residues of pirimiphos-methyl in the bran, fine offal, white flour, white bread, wholemeal flour and wholemeal bread were 6.3, 3.6, 0.96, 0.28, 1.4 and 0.69 mg/kg respectively. The overall average processing factors of pirimiphos-methyl were calculated to be 2.2 for grain to bran, 1.3 for grain to fine offal, 0.33 for grain to white flour, 0.097 for grain to white bread, 0.71 for grain to wholemeal flour, and 0.36 for grain to wholemeal bread. In stored grain, the levels of pirimiphos-methyl were known to decrease by volatilization and hydrolysis and the consequent average residues of hydroxypyrimidines were not expected to exceed 0.15 mg/kg in white bread and 0.55 mg/kg in wholemeal bread. R36341 was not detected in any sample. Residues of pirimiphos-methyl declined gradually during the 3-month storage period but time, formulation or grain variety had no major influence on residues.

Hayward (1990) carried out a commercial processing study in which a single application of an EC formulation (25% pirimiphos-methyl) was made to wheat grain (var. Apostle), at a rate of 10 mg/kg. The wheat grain was milled and processed into white, wholemeal and high-fibre bread by a commercial producer. Half of the treated sample was processed 5 days after application and the other half 7 months (*ca.* 230 days) after application, to observe the extent of any degradation. Although nominally treated at a rate of 10 mg/kg, the unprocessed grain was found to contain 4.6-4.7 mg/kg immediately after and 3.3 mg/kg at 5 and 232 days after the treatment. Total metabolites in these samples were <0.05 mg/kg. Table 18 shows that a concentration of the pirimiphos-methyl residue was observed on processing grain to bran and offal (4x and 2.3x respectively) but a reduction in the residue concentration was found on processing into white flour and wholemeal flour (0.18x and 0.74x). A reduction in residue concentration of up to 30% was found to occur when the flour and bran fractions were blended and baked into bread. An overall decrease in residue levels was observed in the milled fractions and bread when the grain had been stored under controlled conditions for 7 months after treatment. No residues of R36341 were detected in any sample analyzed. A reduction of >90% of the residue of pirimiphos-methyl was observed on processing treated wheat grain to white bread. Reductions of 70-75% were also observed in wholemeal and high-fibre bread.

Table 18. Total pirimiphos-methyl and R36341 residues in milled flour fractions (Hayward, 1990).

Flour fraction	Days after application	Residue, mg/kg	
		Pirimiphos-methyl	R36341
Straight run white	5	1.2	<0.05
Straight run white	232	0.6	<0.05
3rd Break flour	5	2.7	<0.05
3rd Break flour	232	1.2	<0.05

Bran	5	16.3	<0.05
Bran	232	10.1	<0.05
Offal	5	6.7	<0.05
Offal	232	8.3	<0.05
Wholemeal	5	3.2	<0.05
Wholemeal	232	2.5	<0.05
High-fibre	5	4.6	<0.05
High-fibre	232	3.2	<0.05

Table 19. Pirimiphos-methyl and R36341 residues in bread (Hayward, 1990).

Type of bread	Days after application	Residue, mg/kg	
		Pirimiphos-methyl	R36431
White	7	0.8	<0.05
White	233	0.4	<0.05
Wholemeal	7	2.6	<0.05
Wholemeal	233	2.3	<0.05
High-fibre	7	3.1	<0.05
High-fibre	233	2.3	<0.05

Hayward (1989) investigated the fate of pirimiphos-methyl during processing of wheat grain into bran breakfast cereals. A commercial processing study was carried out in the United Kingdom in 1987, in which a single application of pirimiphos-methyl (in 25% EC formulation) was applied to wheat grain (var. Moulin) at a rate of 10 mg a.i./kg. Samples of treated wheat grain were milled and processed into bran breakfast cereals by a commercial producer. Samples of the grain and products were analyzed for pirimiphos-methyl, with a limit of quantification of 0.05 mg/kg. The average residue of pirimiphos-methyl in the treated grain was 7.8 mg/kg. A concentration of pirimiphos-methyl residue was observed in the fine and light bran fractions, which contained 13.5 and 12.2 mg/kg pirimiphos-methyl, respectively, but a reduction in residue level was observed in the heavy bran, which contained 5.5 mg/kg. An overall reduction of the pirimiphos-methyl residue levels was observed during the production of bran breakfast cereals from bran fractions, if the process involved cooking. The pirimiphos-methyl level in breakfast cereal made from mixed heavy- and light bran (3.4:1) was 1.7 mg/kg, whereas the product made from fine bran only contained 3.4 mg/kg. No significant residues (<0.1 mg/kg) of R36341 or any other metabolites were found in the treated grain or the manufactured products. A processing factor of 2.3-4.6x was estimated for the process of converting treated grain into bran breakfast cereal.

Processing of barley

Bonner and Bullock (1979) treated malting barley (vars. Ark Royal, Proctor, Athos, Golden Promise, Maris Otter) or malt with a 25% EC or 2% dust formulation of pirimiphos-methyl, at a rate of 3.1-6.8 mg/kg. Samples were taken for analysis and the remaining material was used for brewing into beer. The limit of quantification was 0.01 mg/kg. Table 20 shows that beer brewed from treated grain or treated malt, using a single brewing process, contained very low levels of pirimiphos-methyl, with the majority of the residues being less than 0.01 mg/kg. Residue loss occurred mainly at the malting stage and in the wort.

Table 20. Pirimiphos-methyl residues in barley grain and its brewing products (single brew) (Bonner and Bullock, 1979).

Sample	Pirimiphos-methyl, mg/kg			
	25% EC application to:		2% Dust application to:	
	Grain	Malt	Grain	Malt
Grain	3.1-6.40	-	4.39-6.01	-
Malted grain	0.27-0.65	5.14-6.13	0.25-0.84	6.04-6.82
Spent Grain	0.27-1.47	2.7, 3.4	0.36-1.15	2.5, 2.6
Wort	<0.01 (5)-0.03	<0.01 (2)	<0.01 (4)-0.09	<0.01 (3)
Beer	<0.01 (8)-0.08 [1/]	<0.01 (2)	<0.01 (10)	<0.01 (3)

Note. The values, except <0.01 mg/kg, appeared to have been corrected for recovery but no original data or recovery factors were available.

[1/] Among 10 samples, one was found to contain 0.01 mg/kg and another 0.08 mg/kg.

In a sequential brewing process (Bonner and Bullock, 1979), barley with initial residues of pirimiphos-methyl at 6.40 mg/kg (25% EC) and 4.98 mg/kg (2% dust) was malted and 8 consecutive batches were fermented, using yeast recovered from the previous brew for the second and subsequent batches Residues in most wort samples (total of 16 samples) were in the range <0.01 (9) to 0.04 mg/kg but one sample contained 0.14 mg/kg. Residues in the beer (16 samples in total) were <0.01 (8) to 0.04 mg/kg. As with a single-brew process, the most significant reduction in residues occurred during the malting and wort-making procedures in sequential brewing.

Anderson and Hayward (1990) conducted a study on the transfer of pirimiphos-methyl residues from barley, treated with a 50% EC formulation of pirimiphos-methyl, to its processed fractions. Two trials were carried out in Germany during 1989. Malting barley (vars. Arena and Ballerina) was treated with a single application of pirimiphos-methyl at 4 g a.i./t. Samples of the treated grain were collected for residue analysis, before the remainder was sent for processing into beer. Samples of the beer and other processed fractions, namely, malt, malt germ and spent malt, were analyzed for residues of pirimiphos-methyl and metabolites. The limit of quantification was 0.01 mg/kg. Table 21 indicates that residues of pirimiphos-methyl in the grain immediately after treatment were not more than half the nominal application rate and that residue levels were considerably lower in the malt 24 days after treatment. Compared with the malt at 24 days, slightly higher residues were found in spent malt, 30 or 31 days after treatment. No residues of pirimiphos-methyl were detected in the beer 73 days after treatment of the barley. The major metabolite, R36341, was not present above 0.01 mg/kg in any of the grain or processed fractions after treatment. Both pirimiphos-methyl and R36341 were below the limit of quantification of 0.01 mg/kg in untreated grain and its fractions, so there was no evidence of interference in the analyses.

Table 21. Residues in barley grain and its products in brewing (application rate, 4 g a.i./t) (Anderson and Hayward, 1990).

Sample	Days after application	Residues, mg/kg	
		Pirimiphos-methyl [1/]	R36341 [1/]
Grain	0	1.0, 2.0	0.01, <0.01
Malt	24	0.05, 0.06	<0.01, <0.01
Malt germ	24	0.05, 0.07	<0.01, <0.01
Spent malt	30 - 31	0.10 - 0.08	<0.01, <0.01
Beer	73	<0.01, <0.01	<0.01, <0.01

[1/] Values are for the varieties Arena (1st value) and Ballerina (2nd value).

Processing of oats

Hayward and Harradine (1989) carried out seven residue trials on barley, maize, oats, rye and wheat in Germany in 1988, using a 50% EC formulation at a rate of 4 g a.i./t (see Table 16 under M4944B, RS-8834 E2). Sub-samples of the oat (var. Lorenz) grain were sent for processing into various fractions (husk, kernel and rolled oats) and the processed fractions were analyzed for residues of pirimiphos-methyl and R36341. Ninety-one days after application, the whole oats contained pirimiphos methyl at 2.2-3.2 mg/kg and, after processing, the majority of the residue remained with the husk, resulting in a concentration of residues in this processed fraction. Correspondingly significant reductions in residue level were observed in the kernels throughout the processing. A 10x reduction was seen on removal of the husk; a further 2x reduction was seen after steam treatment of the kernels; and a further 3.5x reduction was seen in the production of the rolled oats, such that this processed fraction contained 0.08 mg/kg or less than 4% of the residue levels in whole grain. Low-level residues of R36341 (0.06 mg/kg) were observed in some of the grain samples and appeared to be associated with the husk only. No residues, at or above 0.05 mg/kg of pirimiphos-methyl or R36341, were detected in any of the untreated samples of grain or processed fractions.

Residues in the edible portion of food commodities

Supervised trials conducted in Germany (Hayward and Harradine, 1989) investigated residue concentrations in the husk and kernel of various types of grain, treated with pirimiphos-methyl at a rate of 4 g/t (Table 22).

Table 22. Residue concentrations of pirimiphos-methyl in the husks and kernels of grain treated with pirimiphos-methyl at 4 g/t (Hayward and Harradine, 1989).

Grain (Variety)	Sampling interval, weeks	Portion analyzed [1/]	Pirimiphos-methyl, mg/kg
Winter barley	14	Husks	1.0
	14	Kernels	0.09
Spring barley	9.5	Husks	3.3
(Arena)	9.5	Kernels	0.06
Oats	13	Husks	3.8
(Lorenz)	13	Kernels [1/]	0.25
	13	Kernels [2/]	0.10

Residues in untreated grain, husks and kernels were below the limit of quantification of 0.05 mg/kg.
[1/] Pre-dry.
[2/] Post-steam.

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

Metabolism studies on a goat and hens showed that in muscle, liver, kidney, milk and eggs, little or no pirimiphos-methyl was detectable and that the major metabolites were hydroxypyrimidines, though in fat the predominant residue was pirimiphos-methyl. For this reason, animal feeding studies were conducted using dairy cows and laying hens, dosed with pirimiphos-methyl, to determine the residues of pirimiphos-methyl and the hydroxypyrimidines, R46382, R35510 and R4039, in milk, eggs and edible tissues.

Lactating cows

Bullock *et al*. (1974) fed four groups of three Friesian cows for 30 days on diets containing 0, *ca.* 5, 15 and 50 ppm (dry weight basis) of pirimiphos-methyl. The diet consisted of 8 kg/day (4 kg twice a day) of commercially available concentrate nuts, treated with pirimiphos-methyl, with silage to make up the remainder of the diet. Within four hours of the last feeding, two cows per group were slaughtered. The remaining cows were fed on untreated feed for an additional 10 days before slaughter. Milk samples were taken three times each week for analysis. The cows accepted the diet and were in good health throughout the trial. There were no visible pathological effects attributable to pirimiphos-methyl at the end of the trial and post-mortem examination showed no histological effects due to pirimiphos-methyl. At slaughter, samples of tissues were taken for analysis and these were stored at -14°C within 6 hours of slaughter.

Samples were analyzed using a GC-FPD method, with limits of detection of 0.005 mg/kg for pirimiphos-methyl in milk and 0.01 mg/kg for pirimiphos-methyl in tissues. Pirimiphos-methyl and R35311, added to milk and milk fat, at 0.01 or 0.1 mg/kg, were stable for 2 months at -14°C. However, R36341, similarly added to milk and stored at -14°C, showed significant degradation to <0.005 mg/kg at 2 months, while it was shown to be stable for 2 months when similarly added to milk fat. Only very low level residues of pirimiphos-methyl were present in milk samples taken at 3-day intervals during the trial. Residue concentrations higher than those found in samples from untreated control cows (mostly undetectable but two samples produced finite values) were seen only in milk from cows given the 15 ppm diet (up to 0.02 mg/kg) and the 50 ppm diet (up to 0.03 mg/kg). Pirimiphos-methyl concentrations were below 0.01 mg/kg in milk from cows given the 5 ppm diet. No trend of accumulation in milk was observed. No residues of R36341 or R35311 were detected (<0.005 mg/kg). Butter prepared from the milk of cows on the highest rate diet also contained low-level residues of pirimiphos-methyl (0.02-0.04 mg/kg). Residues of pirimiphos-methyl, R36341 and R35311 were below the limit of quantification (<0.01 mg/kg) in all tissues (heart, liver, kidney, fat, adductor muscle and pectoral muscle) from all cows tested, including those on the 50 ppm diet.

Swaine (1982) dosed 12 Jersey cows, separated into 4 groups, twice a day for 30 consecutive days with a grass nuts feed onto which molasses containing pirimiphos-methyl was sprinkled, to give a feed concentration of 0, 8.3, 31 and 94 ppm. Milk was collected from 4 days before dosing started, until 8 days after dosing terminated. The evening milk was bulked with that from the following morning for each cow. Samples were kept at -18°C until analysis. After 30 days of feeding, two cows were

sacrificed from each group. The remaining cows were fed untreated control diets for an additional 9 days before being slaughtered. Samples of pectoral, adductor and cardiac muscle, liver, kidney, peritoneal and subcutaneous fat were taken from each animal and stored at -18°C until analysis. Samples were analyzed for residues of hydroxypyrimidines using a GC-MS method, with a limit of quantification of 0.01 mg/kg for R46382, R35510 and R4039.

Residues in milk and in cardiac, pectoral and adductor muscle were very low, generally <0.01 mg/kg. Residues of the hydroxypyrimidines, R46382, R35510 and R4039, were extremely low in milk, even in animals that received the highest dose; residues above the LOQ of 0.01 mg/kg were found only in isolated cases. The highest residue found was 0.02 mg/kg of R35510 in a day 24 sample. Traces of all three hydroxypyrimidines, i.e. up to 0.03 mg/kg, were found in the liver. Slightly higher concentrations of these compounds were observed in the kidney, especially R46382 (up to 0.16 mg/kg) and R35510 (up to 0.14 mg/kg). Residues of hydroxypyrimidines in the tissues from animals dosed with pirimiphos-methyl at 94 ppm in the diet are presented in Table 23. No measurable residues of any metabolites were found in the tissues of a cow which had been allowed a 9-day recovery period. No data were available for tissues from cows dosed with pirimiphos-methyl at lower rates.

Table 23. Residues of hydroxypyrimidines in tissues of two cows dosed with pirimiphos-methyl at 94 ppm in the diet (Swaine, 1982).

Tissue	Hydroxypyrimidines, mg/kg [1/]		
	R46382	R35510	R4039
Pectoral muscle	<0.01, <0.01	0.01, <0.01	<0.01, <0.01
Adductor muscle	<0.01, <0.01	<0.01, <0.01	<0.01, <0.01
Cardiac muscle	<0.01, <0.01	0.01, <0.01	<0.01, <0.01
Liver	0.03, <0.01	0.02, <0.01	0.02, <0.01
Kidney [2/]	0.05, 0.16	0.08, 0.12	0.04, 0.03

[1/] Residue data from two different cows.
[2/] Each value was the mean of duplicate determinations.

Laying hens

Green *et al.* (1973) conducted a study on Warren Hybrid hens (30 weeks old) dosed with radio-labelled and/or non-labelled pirimiphos-methyl in gelatin capsules, mixed into a powder diet. Eggs were collected throughout each of the four studies described below and stored deep-frozen until analysis. On termination of the third and fourth studies, all six birds were killed and samples of leg and breast muscle were taken for analysis. Pirimiphos-methyl was determined using a GC method with phosphorus thermionic detection. No gross toxic symptoms were apparent in any of the birds fed at 1, 4, 8 and 32 mg/kg for 7 to 28 days. Feed consumption and egg production were not affected by treatment with pirimiphos-methyl.

In the first study, three hens were given a single oral dose of [2-^{14}C]-labelled and unlabelled pirimiphos-methyl (5 μCi + 9 mg, 7 μCi + 20 mg or 14 μCi + 2 mg). Eggs collected over 11 days following dosing were analyzed for radioactivity. The level of radioactivity in eggs, following single doses, was dose-dependent, as shown in Table 24. The total transfer to eggs was 0.16, 0.32 and 0.26% of the administered radioactivity for the 2, 9 and 20 mg doses respectively. The level of radioactivity in the eggs was too low to allow identification of metabolites. However, chromatographic analysis of the 24-hour excreta, containing more than 70% of the administered radioactivity, indicated the presence of parent (4.7% of dose), R35510 (25% of dose) and R4039 (31% of dose).

Table 24. Recovery of radioactivity, expressed as mg pirimiphos-methyl/kg, from hens' eggs following a single dose of pirimiphos-methyl (Green *et al.*, 1973).

Days after dosing	Pirimiphos-methyl, mg/kg in eggs		
	Hen 1, given 2 mg + 14 μCi	Hen 2, given 9 mg + 5 μCi	Hen 3, given 20 mg + 7 μCi
1	0.04	-	0.67
2	-	0.33	0.14
3	0.004	0.08	0.11
4	0.004	0.06	0.10
5	-	0.05	0.07
6	0.006	0.06	

7	0.002	-	
8	<0.001	0.04	
9		0.03	
10		0.01	
11		0.01	
Total recovery of dose, %	0.164	0.325	0.261

- =No egg.

In the second study, groups of 3 hens were each given doses equivalent to dietary concentrations of 0, 1, 4 or 8 ppm unlabelled pirimiphos-methyl, for a period of 18 days. Among the 103 eggs laid during the experimental period, only 13 contained pirimiphos-methyl above 0.001 mg/kg, the highest residue being 0.008 mg/kg. Due to great variability among the birds, a dose-response relationship could not be established for the excretion of pirimiphos-methyl into eggs. R35311 was not detected (LOQ, 0.001 mg/kg).

In the third study, three hens were given daily doses of [2-^{14}C]pirimiphos-methyl (0.91 μCi) for 28 days, at a rate equivalent to a dietary concentration of 4 ppm. During the first few days of the experiment, radioactivity in egg white tended to be higher than in yolk. Thereafter, the radioactivity levels in egg white and yolk increased steadily, at similar rates, reaching a maximum (0.04 mg/kg) 15 days after the start of dosing, after which the levels of radioactivity remained constant at about 0.026-0.028 mg/kg, expressed as pirimiphos-methyl. In egg yolks, which were bulked from days 1-9 and days 10-28 for analysis, levels of pirimiphos-methyl did not exceed 0.001 mg/kg. Similar results were found for egg whites. No radioactivity was found in the shells. The mean TRR, expressed as pirimiphos-methyl, was 0.21 mg/kg in breast muscle and 0.11 mg/kg in leg muscle. The possibility that the parent compound was present in eggs as a conjugate could not be excluded, as the aqueous extracts of egg yolks and whites contained 86% and 90% of the radioactivity, respectively.

In the fourth study, a dose equivalent to a dietary concentration of 32 ppm unlabelled and 0.77 μCi [2-^{14}C]pirimiphos-methyl was given to three hens, daily for 7 days. In the egg whites, pirimiphos-methyl was present at 0.001-0.007 mg/kg and remained constant, while in the yolk the pirimiphos-methyl concentration increased to a maximum of 0.012 mg/kg at day 6. No radioactivity was detected in any of the shells. A dose-response relationship was observed in the eggs, as the total radioactivity in the eggs after 8 days administration at 4 ppm in the third study was one-eighth of that found with the 32 ppm dose after the same period. Neither pirimiphos-methyl nor R35311 was found in any of the muscle samples taken at the end of the study. The mean TRR in breast muscle and leg muscle was 0.36 and 0.29 mg/kg, respectively. There was no evidence of accumulation of residues in eggs.

Earl *et al*. (1990) fed Light Sussex hens with pirimiphos-methyl in the diet and determined hydroxypyrimidine metabolites in the tissues and eggs. Four groups hens (25 hens in each group) were given diets containing pirimiphos-methyl at rates 0, 3.3, 11 or 38 ppm for 28 days and then allowed a 14-day recovery period on an untreated diet. No effects were observed on body weight, feed consumption, egg production or general behaviour which were attributable to the presence of pirimiphos-methyl in the diet.. Breast muscle, liver and eggs were taken from hens sacrificed after treatment periods of 21 or 28 days and following 7- or 14-day recovery periods. Whites and yolks of eggs were separated and bulked each day (except for day 25), frozen until analysis, when the bulked whites and yolks were recombined. Breast muscle samples were combined prior to analysis. Analysis for residues of hydroxypyrimidines (free and conjugated) was carried out using a GC-MS method, with a limit of quantification of 0.01 mg/kg for all analytes. No residues were detected in the control samples. Results for the hydroxypyrimidine metabolites, R46382, R35510 and R4039, in tissues and eggs are shown in Table 25. Residues of R4039 were approximately proportional to dose. The 3.3 ppm dose egg samples were not analyzed, due to the extremely low or undetectable residues found in the 11 ppm dose samples. The study report provided no information on pirimiphos-methyl residue concentrations in the tissues and eggs.

Table 25. Residues of the hydroxypyrimidines, R46382, R35510 and R4039, in tissues and eggs from hens fed pirimiphos-methyl in the diet (Earl *et al.*, 1990).

Dose	Compound	Residue concentration, mg/kg

		Day 21	Day 28	Day 35	Day 42
Breast muscle					
38 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01
	R4039	0.86	0.96	0.70	0.47
11 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01
	R4039	0.34	0.27	0.31	0.27
3.3 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01
	R4039	0.08	0.08	0.03	<0.01
Untreated control	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01
	R4039	<0.01	<0.01	<0.01	<0.01
Liver					
38 mg/kg diet	R46382	0.02	<0.01	<0.01	<0.01
	R35510	0.05	0.06	<0.01	<0.01
	R4039	0.05	0.02	0.03	0.01
11 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01
	R4039	0.02	0.02	0.03	0.01
3.3 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.02	<0.02	<0.02	<0.02
	R4039	<0.01	<0.01	<0.01	<0.01
Untreated control	R46382	<0.01	<0.01	<0.01	<0.01
	R35510	<0.02	<0.02	<0.02	<0.02
	R4039	<0.01	<0.01	<0.01	<0.01

Whole eggs									
		Day -3	Day 3	Day 7	Day 14	Day 21	Day 28	Day 39	Day 42
38 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	0.04	0.03	0.04	0.03	0.04	<0.01	<0.01
	R4039	<0.01	0.02	0.02	0.02	0.02	0.03	<0.01	<0.01
11 mg/kg diet	R46382	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
	R35510	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
	R4039	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

Note. For one series of liver samples the limit of quantification for R35510 was 0.02 mg/kg, rather than 0.01mg/kg, due to an instrumental error.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

Residue monitoring data were provided by the government of Australia, as shown in Table 26.

Table 26. Residue monitoring data from the Australian Residue Survey: results for 2001-2002 (AFFA, 2002).

Commodity	LOR, mg/kg	MRL, mg/kg	No. samples	No. with residues	No. with residues exceeding MRL
Barley	0.1	7	1170	2	0
Bran	0.1	20	109	5	0
Canola	0.1	not set	265	0	0
Chickpeas	0.1	not set	36	0	0
Field peas	0.1	not set	159	0	0
Flour	0.1	10	108	1	0
Lupin	0.1	not set	172	0	0
Oats	0.1	7	125	5	0
Sorghum	0.1	10	352	2	0
Wheat	0.1	10	3428	15	0

LOR = limit of reporting.

NATIONAL MAXIMUM RESIDUE LIMITS

National MRLs were reported by the manufacturer and by the governments of Australia, France and the Netherlands. The residue definition is pirimiphos-methyl for all of the following MRLs. The

information on MRLs in Japan and the USA was obtained from official publications and official web sites.

Table 27. National maximum residue limits.

Country	Commodity	MRL mg/kg
Australia	Barley	7
	Bran, unprocessed of cereal grain	20
	Maize	7
	Millet	10
	Oats	7
	Peanuts	5
	Peanut oil, Edible	15
	Rice	10
	Rice, husked	2
	Rice, polished	1
	Rye	10
	Sorghum	10
	Wheat	10
	Wheat germ	30
Japan	Almonds	0.10
	Apples	1.0
	Apricots	1.0
	Artichokes	1.0
	Asparagus	1.0
	Avocado	0.10
	Banana	0.10
	Barley	1.0
	Blackberries	0.10
	Blueberries	0.10
	Broccoli	1.0
	Brussels sprouts	1.0
	Buckwheat	1.0
	Burdock	1.0
	Button mushrooms	1.0
	Cabbages	1.0
	Carrots	1.0
	Cauliflower	5.0
	Celery	1.0
	Cherries	1.0
	Chestnuts	0.10
	Chicory	1.0
	Chinese cabbages	1.0
	Corn (including Maize, Sweet corn)	1.0
Japan	Cotton seed	0.10
	Cranberries	0.10
	Cucumbers (including Gherkins)	2.0
	Dates	0.10
	Egg plants	3.0
	Endive	1.0
	Garlic	1.0
	Ginger	1.0
	Ginkgo nut	0.10
	Grapes	1.0
	Grapefruit	5.0
	Guavas	0.10
	Horseradish	1.0
	Huckleberry	0.10
	Japanese pears	1.0
	Japanese persimmons	1.0
	Japanese plums (including Prunes)	1.0
	Japanese radishes (root and leaf)	1.0
	Kale	1.0
	Kidney beans (with pods, immature)	1.0

Country	Commodity	MRL mg/kg
Japan	Kiwifruit	1.0
	Komatsuna	1.0
	Kyona	1.0
	Lemons	5.0
	Lettuce (Cos lettuce, Leaf lettuce)	1.0
	Limes	5.0
	Loquats	1.0
	Makuwauri (a type of melon)	0.10
	Mangoes	0.10
	Melons	0.10
	Mitsuba	1.0
	Multiplying onion (including Shallot)	1.0
	Mume plums	1.0
	Natsudaidai (whole)	5.0
	Nectarines	0.10
	Okra	1.0
	Onions	1.0
	Oranges (including Navel)	5.0
	Oriental pickling melons (vegetable)	1.0
	Other berries	1.0
	Other cereal grains	1.0
	Other citrus fruits	5.0
	Other composite vegetables	1.0
	Other cruciferous vegetables	1.0
	Other cucurbitaceous vegetables	1.0
	Other fruits	1.0
	Other liliaceous vegetables	1.0
	Other mushrooms	1.0
	Other nuts	0.10
	Other oil seeds	0.10
	Other solanaceous vegetables	1.0
	Other umbelliferous vegetables	1.0
	Other vegetables	1.0
	Papayas	0.10
	Parsley	1.0
	Parsnips	1.0
	Passion fruit	0.10
	Peaches	0.10
	Peanuts (dry)	1.0
	Pears	1.0
	Peas (with pods, immature)	1.0
	Pecans	0.10
	Pineapples	0.10
	Potatoes	0.05
	Pumpkins (including Squash)	1.0
	Quinces	0.10
	Rape seeds	0.10
	Raspberries	1.0
	Rice (husked rice)	0.20
	Rye	1.0
	Safflower seeds	0.10
	Salsify	1.0
	Sesam seeds	0.10
	Shiitake mushrooms	1.0
	Shungiku (edible chrysanthemum leaf)	1.0
	Soya beans	1.0
	Spinach	1.0
	Strawberries	1.0
	Sunflower seeds	0.10
	Sweet pepper	1.0
	Tea (green, black, Oolong, Wulung tea)	10
	Tomatoes	2.0

Country	Commodity	MRL mg/kg
	Turnip (including rutabaga) (root and leaf)	1.0
	Unshu orange	0.10
	Walnuts	0.10
	Watermelons	0.10
	Watercress	1.0
	Welsh onions (including leeks)	1.0
	Wheat	1.0
USA	Cattle, fat	0.20
	Cattle, kidney	2.0
	Cattle, liver	2.0
	Cattle, meat	0.20
	Cattle, meat by-products	0.20
	Corn	8.0
	Goat, fat	0.20
	Goat, kidney	2.0
	Goat, liver	2.0
	Goat, meat by-products	0.20
	Hog, fat	0.20
	Hog, kidney	2.0
	Hog, liver	2.0
	Hog, meat by-products	0.20
	Horse, fat	0.20
	Horse, kidney	2.0
	Horse, liver	2.0
	Horse, meat by-products	0.20
	Kiwifruit	5.0
	Poultry, fat	0.20
	Sheep, fat	0.20
	Sheep, kidney	2.0
	Sheep, liver	2.0
	Sheep, meat by-products	0.20
	Sorghum, grain, grain	8.0
	Wheat, flour	8.0
EU	Brussels sprouts	2
	Carrots	1
	Cereal group	5
	Citrus fruit group	1
	Flowering brassica group	1
	Kiwi fruit	2
	Mandarins	2
Belgium	Brussels sprouts	2
	Cabbages	0.5
	Cabbages, red	0.5
	Carrots	1
Belgium	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit group	1
	Cucurbit Group	0.5
	Cucurbit group	0.5
	Flowering brassica group	1
	Fruiting vegetable group	0.5
	Head brassica group	0.5
	Herb group	1
	Kiwi fruit	2
	Kohlrabi	0.5
	Leafy brassica group	0.5
	Lettuce group	1
	Mandarins	2
	Mushrooms	1
	Spinach group	1
	Stalk/stem vegetable group	1
	Tomatoes	1
Denmark	Brussels sprouts	2

Country	Commodity	MRL mg/kg
	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit, others, for EU use only	1
	Flowering brassica group	1
	Grapefruit	1
	Herb group	2
	Kiwi fruit	2
	Lemons	1
	Limes	1
	Mandarins	2
	Oranges	1
	Pummelos (pomelos)	1
	Stalk/stem vegetable group	0.05
Finland	Brussels sprouts	2
	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit, others, for EU use only	1
	Flowering brassica group	1
	Grapefruit	1
	Kiwi fruit	2
	Lemons	1
	Limes	1
	Mandarins	2
	Oranges	1
	Pummelos (pomelos)	1
France	Avocados	0.05
	Bananas	0.05
	Beet, red	0.05
	Berry/small fruit, others, for EU use only	0.05
	Brussels sprouts	2
	Bulb vegetable group	0.05
	Cabbages	0.05
	Cabbages, Savoy	0.05
	Cabbages, red	0.05
	Cane fruit group	0.05
	Carrots	1
	Celeriac	0.05
	Cereal grains	4
	Cereals, others, for EU use only	5
	Chicory, witloof	0.05
	Citrus fruit, others, for EU use only	1
France	Corn, sweet	0.05
	Cucurbit group	0.05
	Cumquat (kumquat)	0.05
	Dates	0.05
	Figs	0.05
	Flowering brassica group	1
	Fruiting vegetable group	0.05
	Grape group	0.05
	Grapefruit	1
	Head brassicas, others, for EU use only	0.05
	Hops	0.05
	Horseradish	0.05
	Jerusalem artichokes	0.05
	Kaki (persimmons)	0.05
	Kiwi fruit	2
	Kohlrabi	0.05
	Leafy brassica group	0.05
	Legume vegetable group	0.05
	Lemons	1
	Lettuce group	0.05

Country	Commodity	MRL mg/kg
	Limes	1
	Litchees	0.05
	Mandarins	2
	Mangoes	0.05
	Non-poultry	0.05
	Nut group	0.05
	Oil seed group	0.05
	Olives	0.05
	Oranges	1
	Oyster plant	0.05
	Parsley, turnip-rooted	0.05
	Parsnips	0.05
	Passion fruit	0.05
	Pineapples	0.05
	Pome fruit group	0.05
	Pomegranates	0.05
	Potatoes	0.05
	Poultry	0.05
	Pulse Group	0.05
	Pummelos (pomelos)	1
	Radishes	0.05
	Root/tuber vegetable, others, for EU use only	0.05
	Salsify	0.05
	Spinach group	0.05
	Stalk/stem vegetable group	0.05
	Stone fruit group	0.05
	Strawberry group	0.05
	Strawberry tree	0.05
	Sugar beet	0.05
	Swedes	0.05
	Sweet potatoes	0.05
	Tea group	0.05
	Tropical fruit, others, for EU use only	0.05
	Turnips	0.05
	Watercress	0.05
	Wheat bran	10
	Wheat flour, white	1
	Wheat wholemeal	2
	White bread	0.2
	Wholemeal bread	1
	Yams	0.05
Germany	Beans	0.5
	Brussels sprouts	2
	Bulb vegetable group	1
Germany	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit group	1
	Corn, sweet	0.05
	Cucurbit group	0.5
	Flowering brassica group	1
	Fruiting vegetable group	0.5
	Head brassica group	1
	Herb group	1
	Herb others, for EU use only	0.3
	Kale	2
	Kiwi fruit	2
	Kohlrabi	1
	Leafy brassica group	1
	Lettuce group	1
	Mandarins	2
	Mushrooms	0.5
	Peas	0.5

Country	Commodity	MRL mg/kg
	Spinach group	2
	Stalk/stem vegetable group	1
	Tea group	0.05
	Tomatoes	1
Italy	Almonds	0.05
	Apples	0.5
	Aubergines	0.05
	Beans	0.5
	Beet, spinach	0.05
	Bell pepper	0.5
	Berry/small fruit, others, for EU use only	0.05
	Brussels sprouts	2
	Bulb vegetable, others, for EU use only	0.05
	Cane fruit group	0.05
	Carrots	1
	Celery	0.5
	Cereal group	5
	Cereals, others, for EU use only	5
	Chicory, Witloof	0.05
	Citrus fruit, others, for EU use only	1
	Corn, sweet	0.05
	Cotton	0.05
	Cucumbers	0.5
	Cucurbit, others, for EU use only	0.05
	Flowering brassica group	1
	Fruiting vegetable, others, for EU use only	0.05
	Grape group	0.5
	Hazelnuts	0.05
	Head brassica, others, for EU use only	0.5
	Herb group	0.5
	Hops	0.05
	Kiwi fruit	2
	Kohlrabi	0.5
	Leafy brassica group	0.5
	Legume vegetable, others, for EU use only	0.5
	Lettuce	0.5
	Lettuce, others, for EU use only	0.05
	Linseed	0.05
	Mandarins	2
	Mushrooms	0.05
	Mushroom group	0.05
	Nut others, for EU use only	0.05
	Oil seed, others, for EU use only	0.05
Italy	Olives	0.05
	Onions	0.5
	Peas	0.05
	Peanuts	0.05
	Pears	0.5
	Pistachios	0.05
	Plums	0.5
	Pome fruit, others, for EU use only	0.05
	Potatoes	0.05
	Pulse, others, for EU use only	0.05
	Rape	0.05
	Root/tuber vegetable, others, for EU use only	0.05
	Soya beans	0.05
	Spinach	0.5
	Spinach, others, for EU use only	0.05
	Stalk/stem vegetable, others, for EU use only	0.05
	Stone fruit, others, for EU use only	0.05
	Strawberry group	0.5
	Sugar beet	0.5
	Sunflower	0.05

Country	Commodity	MRL mg/kg
	Tea group	0.05
	Tomatoes	0.5
	Tropical fruit, others, for EU use only	0.05
	Walnuts	0.05
	Watercress	0.05
	Watermelons	0.5
Luxembourg	Barley	5
	Brussels sprouts	2
	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit group	1
	Cucurbit group	0.5
	Flowering brassica group	1
	Fruiting vegetable group	0.5
	Head brassica group	0.5
	Herb group	1
	Kiwi fruit	2
	Kohlrabi	0.5
	Leafy brassica group	0.5
	Lettuce group	1
	Maize	5
	Mandarins	2
	Mushrooms	1
	Oats	5
	Rice	5
	Rye	5
	Sorghum	5
	Spinach group	1
	Stalk/stem vegetable group	1
	Tomatoes	1
	Wheat	5
Netherlands	Brussels sprouts	2
	Carrots	1
	Cereals	5
	Cucumbers	0.1
	Flowering brassica	1
	Kiwi fruit	2
	Mandarins, clementines	2
	Melons	1
	Mushrooms (cultivated)	2
	Other citrus fruits	1
	Peppers, sweet	1
	Tomatoes	1
Netherlands	Wine grapes	2
	Other vegetables	0.05*
Portugal	Barley	5
	Maize	5
	Oats	5
	Rye	5
	Wheat	5
Spain	Almonds	0.5
	Aubergines	0.5
	Bell peppers	1
	Brussels sprouts	2
	Carrots	1
	Cereal group	5
	Citrus fruit, others, for EU use only	1
	Cucurbit group	0.2
	Flowering brassica Group	1
	Grape group	0.5
	Hazelnuts	0.5

Country	Commodity	MRL mg/kg
	Head brassica, others, for EU use only	1
	Kiwi fruit	2
	Kohlrabi	1
	Leafy brassica group	1
	Legume vegetable, others, for EU use only	0.5
	Lettuce group	1
	Mandarins	2
	Olives	0.5
	Pistachios	0.5
	Pome fruit group	0.5
	Spinach group	1
	Stone fruit group	0.5
	Strawberry group	0.5
	Tomatoes	0.5
	Walnuts	0.5
Sweden	Beans	1
	Beans, Lima	1
	Brussels sprouts	2
	Bulb vegetable group	1
	Cabbages	1
	Cabbages, Savoy	1
	Cabbages, red	1
	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit, others, for EU use only	1
	Cucurbit group	1
	Flowering brassica group	1
	Fruiting vegetable group	1
	Grape group	1
	Grapefruit	1
	Head brassica, others, for EU use only	1
	Kiwi fruit	2
	Legume vegetable others, for EU use only	1
	Lemons	1
	Lettuce group	1
	Limes	1
	Mandarins	2
	Mushrooms	1
	Olives	1
	Oranges	1
	Peas	1
	Pome fruit group	1
	Pummelos (pomelos)	1
	Spinach group	1
Sweden	Stone fruit group	1
	Strawberry group	1
United Kingdom	Brussels sprouts	2
	Buckwheat, common	5
	Carrots	1
	Cereal group	5
	Cereals, others, for EU use only	5
	Citrus fruit group	1
	Flowering brassica group	1
	Kiwi fruit	2
	Mandarins	2
	Mushrooms	2

APPRAISAL

Pirimiphos-methyl, a broad-spectrum insecticide, was first evaluated in 1974 for toxicology and residues. Subsequently, it was reviewed for toxicology in 1976 and 1992 and for residues in 1976, 1977, 1979, 1983, 1985 and 1994. The current ADI of 0-0.03 mg/kg body weight was established by

the 1992 JMPR. Currently there are 44 Codex MRLs for residues resulting from pre- and post-harvest uses of pirimiphos-methyl.

The 30th Session of the CCPR identified pirimiphos-methyl as a priority compound for periodic re-evaluation by the present Meeting.

The Meeting received data on metabolism, analytical methods, storage stability, supervised field trials, processing and farm animal feeding trials. The manufacturer and the governments of Australia, France, Germany and The Netherlands provided information on use patterns.

Animal metabolism

When a single dose of 50 mg/kg [2-^{14}C]pirimiphos-methyl was administered by gavage to rats fitted with a bile duct cannula, 33-38% of the administered radioactivity was excreted in urine, 17-21% in the bile, and 16-30% in the faeces within 48 h. Uncannulated rats receiving the same dose excreted 61-76% of the administered radioactivity in urine and 15-29% in faeces in 48 h.

After a single dose of 1 mg/kg given to normal rats, the main urinary metabolite was 2-ethylamino-6-methylpyrimidin-4-ol (R35510). At a single dose of 250 mg/kg, the main metabolites were *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*-methyl *O*-hydrogen phosphorothioate (desethyl-R402186) and R35510 in male rats, and *O*-2-diethylamino-6-methylpyrimidin-4-yl *O*-methyl *O*-hydrogen phosphorothioate (R402186) and desethyl R402186 in female rats. No parent compound was present in urine or bile. Faeces of bile-cannulated rats contained only pirimiphos-methyl while those of normal rats also contained several metabolites.

These results indicate that pirimiphos-methyl was incorporated, metabolized, and eventually excreted in urine. Re-absorption of pirimiphos-methyl metabolites from bile appeared to occur.

A lactating goat, dosed with 50 mg/kg [2-^{14}C]pirimiphos-methyl in gelatin capsules twice daily for 7 days at a rate equivalent to 45 ppm in the diet, excreted 89% of the administered dose in urine and faeces and 0.2% in milk. In fat samples (TRR 0.067 mg/kg pirimiphos-methyl equivalents), the major residue components were pirimiphos-methyl (55% of the TRR) and *O*-2-ethylamino-6-methylpyrimidin-4-yl *O*,*O*-dimethyl phosphorothioate (R36341) (17% of the TRR). In other tissues (TRR 0.042 mg/kg in meat, 0.32 mg/kg in liver and 0.50 mg/kg in kidney as pirimiphos-methyl) and milk (TRR 0.18 mg/kg pirimiphos-methyl equivalents), they were R35510 (12-35% of the TRR), 2-amino-6-methylpyrimidin-4-ol (R4039) (7-20% of the TRR) and 2-diethylamino-6-methylpyrimidin-4-ol (R46382) (3-5% of the TRR). Conjugates of R46382 and R35510 were found in liver and kidney. Up to 32% of the total radioactive residues were unextracted from liver. Refluxing the unextracted material in 4M HCl released 27% of the TRR originally in the liver.

Radioactivity in the milk increased sharply after the first dose and reached a peak in the afternoon of day 2. After some decrease, it stabilized on day 4.

Laying hens were dosed with [2-^{14}C]pirimiphos-methyl in gelatin capsules twice daily for 14 days, at a rate equivalent to 50 ppm in the diet, and 97.5% of the administered radioactivity was recovered from excreta collected over 14 days. Pirimiphos-methyl was the predominant residue component in the fat (73% of the TRR; 0.056 mg/kg) and was also present in egg yolk (9.5% of the TRR; 0.022 mg/kg) but was not found in muscle, liver or egg albumen.

R35510 and R4039 were the major residue components in liver (12 and 6% of the TRR), egg yolk (34 and 11% of the TRR) and egg albumen (43 and 22% of the TRR). Conjugates of these compounds were present in liver while a conjugate of R4039 was the major component of the leg and breast muscle. Some 39% of the TRR in liver was unextracted. After refluxing the unextracted material in acid, TLC of the extract showed that the major components were R35510 and R4039.

Radioactivity in eggs reached a plateau after about 6 days.

Pirimiphos-methyl was absorbed and extensively metabolized. Five transformation processes seemed to occur: hydrolysis of a methyl ester group, de-ethylation of the *N*-diethyl group, conjugation

with glucuronic acid or other biological compounds, hydrolysis of the pyrimidinyl group, and oxidation of phosphorothioate to phosphate.

Plant metabolism

Wheat grains, rice grains (with husk) and husked rice (70 g each) were treated with a 2% dust formulation containing [2-^{14}C]pirimiphos-methyl at 4 or 8 mg/kg (g/t). The treated grains were stored at 25°C for 8 months at low (12-15%) or high (17-20%) moisture content. In 32 weeks on wheat grains treated at 4 mg/kg, pirimiphos-methyl decreased from the maximum of 2.7 mg/kg to 2.1 mg/kg at the lower moisture content and to 0.4 mg/kg at the higher moisture. Over the same period, the unextracted radioactivity increased from 0.02 to 0.11 mg/kg (lower moisture content) and to 1.60 mg/kg (higher moisture content), expressed as pirimiphos-methyl. The main products were pyrimidinols, R46382, R35510 and R4039, with R46382 representing at least 90%. In all samples, the main product was R46382 which increased gradually over 8 months to a maximum of 0.17 mg/kg (lower moisture content) or 0.62 mg/kg (higher moisture content).

The degradation pattern of pirimiphos-methyl and the quantities of degradation products in rice and wheat were similar. The main product was R46382.

Radioautograms showed that radioactivity was concentrated in the pericarp of treated grain, indicating that residues in white flour and bread would be lower than in bran and wholemeal products.

Wheat, rice with husk, and husked rice grains were treated with aqueous formulations containing [2-^{14}C]pirimiphos-methyl at rates equivalent to 15 mg/kg (g/t) (wheat) or 22.5 mg/kg (rice) and stored in the dark in desiccators to keep them at low (10-14%) or high (19-24%) moisture content for 24 weeks at 20°C. The degradation pattern and quantities of degradation products were similar in wheat and rice. Pirimiphos-methyl accounted for 50-95% of the radioactive residues and R46382 and an unknown compound which was hydrolyzed to it by refluxing with acid accounted for 70-85% of the remaining radioactivity. Other minor products were R36341, R35510 and R4039.

Duplicate samples of maize grain, at 14% moisture, were sprayed three times with an EC formulation containing ^{14}C-pirimiphos-methyl, each at a rate of approximately 47 mg ai/kg grain. This resulted in a total application rate of 96 mg ai/kg, an exaggerated rate. The treated grain was stored under conditions that maintained the moisture content at about 14%. In the first 12 weeks, a decrease of radioactivity corresponding to 44-63% of that applied occurred for unknown reasons. Most of the radioactivity in the grain was extractable with methanol, with 6% of the total radioactivity remaining unextracted at 0, 12 and 24 weeks after the last application. The predominant residue component (no less than 60% of the TRR in week 24) was the parent compound, with up to 18% of R46382, R46382 and R35510.

The studies on stored grains showed similar profiles. The predominant residue component was the unchanged parent compound, which accounted for no less than 60% of the TRR at the end of each experiment. The major components of the remainder were the pyrimidinols R46382, R35510 and R4039. These were derived from the parent compound by the same transformation processes as in animals. The main pyrimidinol was R46382, which was present at up to 10% of the TRR under conditions reflecting current GAP. Unknown compound(s) also present in wheat grain were converted to R46382 by hydrolysis. R35510 and R4039 were present only at <5% of the TRR. R36341, resulting from the loss of one *N*-ethyl group from the parent compound, was also detected in small amounts.

Environmental fate in soil and in water-sediment systems

No studies of environmental fate in soil, in water-sediment systems or in rotational crops were reported. The supervised trials data were only on stored cereal grain, where use is only indoors, with little or no impact on the environment or succeeding crops. Although pre-harvest uses are registered in many countries, because pirimiphos-methyl is susceptible to photolysis (half-life in sterile aqueous buffer solution is 0.46 h at pH 5 and 0.47 h at pH 7), it was considered that its impact on the environment might not be significant.

Methods of analysis

The Meeting received information on gas chromatographic methods for determining residues of pirimiphos-methyl in a variety of fruits and vegetables and wheat, and both pirimiphos-methyl and its metabolites in animal tissues, milk and eggs.

All methods for the determination of pirimiphos-methyl involved extraction with acetone/hexane (2:8), maceration, addition of water, shaking and centrifugation. The resulting hexane layer derived from plant samples was analyzed directly by gas chromatography, and that from animal tissues, milk or eggs underwent clean-up on a silica solid-phase extraction column. The hexane layer from fat samples was subjected to an additional hexane/acetonitrile partition procedure before clean-up.

A gas chromatographic method using thermionic specific detection showed linearity between 0.0125 and 2.0 µg/ml in the final extract (3.75-600 pg injected) for all plant samples tested including wheat. The limit of quantification was 0.05 mg/kg and the average recovery within an acceptable range (70-110%) although individual recovery values were 60-117%. Gas chromatographic methods using mass-selective detection showed linearity between 0.0125 and 2.0 µg/ml (12.5-2000 pg injected) for all plant samples except cotton seed and olives, and between 0.001 and 1.0 mg/kg (2-2000 pg injected) for animal samples. The limit of quantification was 0.05 mg/kg for plant samples and 0.01 mg/kg for animal samples, and the average recovery was within an acceptable range although individual recovery values were 65-118% for plant samples. The methods were therefore suitable for analyzing both plant and animal samples.

A method for the determination of pyrimidinols in animal samples involved extraction of animal tissues with methanol/2N HCl (1:1), centrifugation, extraction with hexane, evaporation of methanol, hydrolysis of the aqueous extract in acid, butanol partition and clean-up by adsorption chromatography. Milk samples were extracted with concentrated HCl, methanol and hexane, and egg samples with methanol/2N HCl (9:1) to remove protein. No hydrolysis was used for egg or milk samples. The final extract was analyzed by gas chromatography with mass spectrometric detection after trimethylsilylation. The method showed a limit of quantification of 0.01 mg/kg and an average recovery within the acceptable range for R46382 and R35510. The recovery of R4039 from animal tissues was lower (65 ± 13%) than from other samples. As this was attributed to the inhibition of trimethylsilylation, R31680 was added as an internal standard. The validity of using R31680 was confirmed by the linear calibration for 0.1-1.0 mg/kg and 0.01-0.10 mg/kg of R4039 with the addition of R31680 at 5 mg/kg and 0.5 mg/kg, respectively. The modified method was shown to be suitable for determining pyrimidinols in animal tissues, milk and eggs.

Stability of residues in stored analytical samples

The stability of pirimiphos-methyl in barley, carrot, lettuce, olive and tomato stored at <-16°C for 24 months was investigated. No significant loss of pirimiphos-methyl residues occurred during the 24-month storage. Analytical extracts of plant samples (the final extracts for GC with thermionic or MS detection) retained in vials and stored at 5-7°C were stable for 7 days, the maximum tested period.

No data on the storage stability of pirimiphos-methyl or its main metabolites in animal tissues or eggs were provided. A storage stability study for 2 months showed that pirimiphos-methyl and R35311, added to milk and milk fat at 0.01 or 0.1 mg/kg, was stable for 2 months at -14°C. When R36341 was added to milk at the same fortification level, it was degraded to below the LOQ of 0.005 mg/kg after 2 months but it was shown to be stable for 2 months when added to milk fat.

Definition of the residue

Pirimiphos-methyl is metabolized in plants and animals through two major biotransformation routes: hydrolysis of the phosphorothioate group to produce the pyrimidinol R46382, and successive loss of the two *N*-ethyl groups. In muscle, liver, kidney, milk and eggs, and in plants, the main metabolites were the pyrimidinols R46382, R35510 and R4039.

The present Meeting received supervised trials data only on stored grains, in which the predominant residue component was pirimiphos-methyl.

In animal fat, the predominant residue component was pirimiphos-methyl. Little or no pirimiphos-methyl was found in animal tissues, other than fat, or in milk and eggs, although no storage

stability studies were conducted on pirimiphos-methyl or its metabolites in animal commodities except milk. A feeding study on cows indicated that pirimiphos-methyl residues were below the limit of quantification in all tissues analyzed, including fat. In another study, pyrimidinols were also below the limit of quantification or very low. A feeding study on hens showed 0.03-0.96 mg/kg R4039 in the muscle of hens dosed with 3.3-38 mg/kg pirimiphos-methyl. The other two pyrimidinols (R46483 and R35510) were in most cases below the limit of quantification or less than 0.06 mg/kg (R35510 in liver). These pyrimidinols were thought to be of much lower toxicity than the parent and their analysis required a different method from that for pirimiphos-methyl.

The definition of the residue in all the countries whose national MRLs were reported to the Meeting is pirimiphos-methyl.

Pirimiphos-methyl has a log P_{ow} of 3.90 at 20°C and in animals was found only in fat and egg yolk, indicating that pirimiphos-methyl should be categorized as fat-soluble.

The Meeting agreed that the definition of the residue for plant and animal commodities should be pirimiphos-methyl, for compliance with MRLs and for the estimation of dietary intake.

The residue is fat-soluble.

Results of supervised trials on crops

Supervised post-harvest trials on stored cereal grains were conducted in Germany and the UK. Approved application rates for stored cereal grains are in general 4-8 g ai/t. Only three of 20 countries whose information was available approved rates outside this range.

In wheat trials in Germany and the UK, pirimiphos-methyl residues resulting from 12 trials using rates within the range mentioned above were 1.8, 1.9, 2.2, 2.3 (2), 2.6 (2), 3.2 (2), 3.7, 3.8 and 4.5 mg/kg, and those from 16 barley trials within the same range were 0.74, 0.80, 1.0 (2), 1.3 (2), 1.4, 1.5, 1.6, 2.0, 2.4, 2.6, 2.7, 2.8, 3.1 and 3.7 mg/kg.

Trials on oats, rye and maize were conducted in accordance with the GAP of many countries. The residues were 2.9 mg/kg in oats, 1.9 mg/kg in rye and 2.4 mg/kg in maize. Only a single trial on each crop was reported, but in the studies on the fate of pirimiphos-methyl in stored grain it was estimated that the degradation profiles after the application of pirimiphos-methyl were similar qualitatively and quantitatively among the grains analyzed, namely wheat, rice and maize. The Meeting therefore agreed to combine the results of these trials, to recommend a group MRL for cereal grains.

The combined values in ranked order, median underlined, are 0.74, 0.80, 1.0 (2), 1.3 (2), 1.4, 1.5, 1.6, 1.8, 1.9 (2), 2.0, 2.2, <u>2.3</u> (2), 2.4 (2), 2.6 (3), 2.7, 2.8, 2.9, 3.1, 3.2 (2), 3.7 (2), 3.8 and 4.5 mg/kg.

The Meeting recommended an MRL of 7 mg/kg Po for cereal grains, to replace the existing CXL of 10 mg/kg Po. The STMR and HR were 2.3 and 4.5 mg/kg respectively.

No data on supervised trials were provided on the following commodities: apples, Brussels sprouts, head cabbages, carrots, cauliflowers, cherries, citrus fruits, common beans, cucumbers, blackcurrants, dates, dried fish, gooseberries, kiwifruit, lettuce, mushrooms, olives, peanuts, peanut oil, pears, peas, peppers, plums, potatoes, raspberries, spinach, spring onions, strawberries and tomatoes. The Meeting therefore decided to recommend withdrawal of the MRLs for these commodities.

Fate of residues during processing

In a laboratory scale baking of flour, treated with radiolabelled pirimiphos-methyl, into bread and biscuits there was little degradation of pirimiphos-methyl, with up to 10% of the TRR attributed to R46382 and R4039. R46382 was present at 25% of the TRR in bread crusts and R4039 at 12% in breadcrumbs.

Processing wheat grain treated at 4 g ai/t on a commercial scale resulted in a concentration of pirimiphos-methyl in bran and offal and a reduction in white and wholemeal flour and bread.

The calculated processing factors and STMR-Ps are shown in Table 28, below. A maximum residue level was calculated for bran (in which the highest concentration of pirimiphos-methyl was found) from the HR for wheat grain, 4.5 mg/kg.

The Meeting recommended an MRL of 15 mg/kg (PoP) for unprocessed wheat bran, to replace the existing CXL of 20 mg/kg, and recommended withdrawal of the existing CXLs for wheat wholemeal, wheat flour, white bread and wholemeal bread, as STMR-Ps were calculated for intake estimation.

Table 28. Processing factors for wheat products.

	Bran	Fine offal	Wholemeal flour	White flour	Wholemeal bread	White bread
Processing factor	2.2	1.3	0.71	0.17	0.36	0.097
MRL, mg/kg	15 (HR 9.9)	-	-	-	-	-
STMR-P, mg/kg	5.1	2.9	1.6	0.39	0.83	0.22

Note. Residues in the grain used for processing were: 1.9 mg/kg for preparing bran, offal, white flour and white bread; and 2.9 mg/kg for preparing wholemeal flour and wholemeal bread.

Processing wheat grain to milling fractions and to bran breakfast cereals on a commercial scale showed an increased concentration of pirimiphos-methyl in fine bran (PF 1.7) and light bran (PF 1.6) but a reduction in heavy bran (PF 0.70). The processing factor from grain to bran breakfast cereals was calculated to be 2.3-4.

Residues of pirimiphos-methyl were extremely low, close to or below the limit of quantification of 0.01 mg/kg, in beer produced from barley grain treated with pirimiphos-methyl at a normal rate. Only two of 22 samples, brewed separately in single brews in two experiments, contained pirimiphos-methyl above the LOQ, with one showing 0.08 mg/kg. In malt, malt germ, wort and spent malt, low-level residues were detected, showing significant degradation (more than 90%) of pirimiphos-methyl during malting. In 16 beer samples obtained from sequential brews pirimiphos-methyl residues were <0.01-0.04 mg/kg. The Meeting calculated a processing factor from these results of <0.002 and an STMR-P for beer of 0.01 mg/kg.

Less than 4% of the residue in treated oat grain was found in rolled oats but there were insufficient data to calculate a processing factor.

Studies with barley and oats indicated that no more than 10% (2-9%) of the pirimiphos-methyl residue in grain was found in the kernels of treated grains when the application rate was 4 g ai/t. Most of the residues were associated with the husks. There were too few trials to estimate the ratio of pirimiphos-methyl between the husks and kernels.

As no processing studies were available for rice or rye, the Meeting decided to recommend withdrawal of the existing CXLs for rice bran, unprocessed; rice, husked; rice, polished; and rye wholemeal.

Residues in animal commodities

Farm animal dietary burden

The Meeting estimated farm animal burdens of pirimiphos-methyl residues with the diets in Appendix IX of the FAO Manual. A plateau was reached rapidly in milk (4 days). In eggs, a metabolism study indicated that a plateau was reached in 6 days and feeding studies indicated 15 days and 6 days. The Meeting agreed that calculation from MRLs would provide the feed levels suitable for recommending animal commodity MRLs, and calculation from feed STMRs would be suitable for the estimation of animal commodity STMRs.

Table 29. Estimated dietary burdens of pirimiphos-methyl for farm animals.

Crop	MRL, mg/kg	Group	DM, %	MRL/DM, mg/kg	% of diet			Residue contribution, mg/kg		
					Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	7	GC	88	8.0						
Maize grain	7	GC	88	8.0	80			6.36		
Oats grain	7	GC	89	7.9						
Rice grain	7	GC	88	8.0						
Rye grain	7	GC	88	8.0						
Wheat grain	7	GC	89	7.9			80			6.29
Wheat bran	9.9 [1/]	CF	88	11.3		50			5.63	
Total								6.36	5.63	6.29
	STMR, mg/kg									
Barley grain	2.3	GC	88	2.6						
Maize grain	2.3	GC	88	2.6	80			2.09		
Oats grain	2.3	GC	89	2.6						
Rice grain	2.3	GC	88	2.6						
Rye grain	2.3	GC	88	2.6						
Wheat grain	2.3	GC	89	2.6			80			2.07
Wheat bran	5.1	CF	88	5.8		50			2.90	
Total								2.09	2.90	2.07

DM = dry matter.
[1/] FAO Manual requires use of the HR.

The pirimiphos-methyl dietary burdens for animal commodity MRL and STMR estimation are: beef cattle, 6.4 and 2.1 mg/kg; dairy cattle, 5.6 and 2.9 mg/kg; and poultry, 6.3 and 2.1 mg/kg.

Farm animal feeding studies

Milk obtained from lactating cows fed diets containing 0, 5, 15 or 50 ppm (dry weight basis) of pirimiphos-methyl for 30 days contained only very low concentrations of pirimiphos-methyl throughout the trial; residue concentrations higher than those found in controls were seen only in milk from cows given 15 ppm (<0.005 to 0.02 mg/kg) and 50 ppm in the diet (<0.005 to 0.03 mg/kg), and were below 0.01 mg/kg (<0.005-0.008 mg/kg) from 5 ppm. No trend of accumulation in milk was observed. Pirimiphos-methyl residues were below the limit of quantification in all tissues analyzed (heart, liver, kidney, fat, cardiac muscle, adductor and pectoral muscle) from all cows.

Lactating cows were fed twice a day for 30 days with feed containing 0, 8.3, 31 and 94 ppm of pirimiphos-methyl. Residues of the pyrimidinols R46382, R35510 and R4039 were extremely low in milk, even from animals that received the highest dose; residues above the LOQ of 0.01 mg/kg were found only in isolated cases. At 94 ppm, up to 0.03 mg/kg of these hydroxypirimidines were found in the liver and slightly higher concentrations in the kidneys, especially of R46382 (up to 0.16 mg/kg) and R35510 (up to 0.14 mg/kg).

Laying hens given single oral doses of [2-^{14}C]pirimiphos-methyl excreted only 0.16-0.33% of the administered radioactivity in eggs. With unlabelled doses of 1-8 mg/kg, 12% of the collected eggs contained pirimiphos-methyl above 0.001 mg/kg, the highest residue being 0.008 mg/kg. Radioactivity in egg albumen and yolk from hens given daily doses of [2-^{14}C]pirimiphos-methyl for 28 days at 4 mg/kg reached a maximum (0.04 mg/kg) 15 days after the start of dosing, and remained fairly constant thereafter. In egg yolks, pirimiphos-methyl did not exceed 0.001 mg/kg. Egg whites from hens receiving 32 ppm pirimiphos-methyl for 7 days contained pirimiphos-methyl at 0.001-0.007 mg/kg, which remained constant, while in the yolks the pirimiphos-methyl concentration increased to a maximum of 0.012 mg/kg at day 6. No pirimiphos-methyl was found in any of the muscle samples taken at the end of the study. There was no evidence of accumulation of residues in eggs.

Muscles from laying hens given 3.3-38 ppm pirimiphos-methyl in the diet for 28 days were found to contain 0.03-0.96 mg/kg of R4039. R35510 and R46382 were, in most cases, below the limit of quantification in muscle, liver and eggs. The highest residue was 0.06 mg/kg R35510 in liver from 38 ppm.

Maximum residue levels for animal commodities

As no data were reported on the storage stability of pirimiphos-methyl or its metabolites in animal tissues or eggs, the Meeting concluded that it could not exclude the possibility that the low or negligible

concentrations of pirimiphos-methyl and metabolites reported were due to the unstable nature of these compounds in the samples.

According to one feeding study, pirimiphos-methyl was present at <0.005-0.008 mg/kg (mean 0.0053 mg/kg calculated using 0.005 mg/kg instead of <0.005 mg/kg) in whole milk from cows fed at 5 ppm pirimiphos-methyl, and at <0.005-0.02 mg/kg (mean 0.0064 mg/kg) in whole milk from cows fed at 15 ppm. Pirimiphos-methyl was found to be stable in milk for two months when stored at -14°C. Concentrations of pirimiphos-methyl in butter prepared from the milk of cows fed at 50 ppm were on average twice those in whole milk, indicating that most of the pirimiphos-methyl residue was in the non-fat fraction of the milk.

At the calculated maximum dietary burden of 5.6 mg/kg, it is unlikely that whole milk would contain pirimiphos-methyl above 0.01 mg/kg and, at the STMR burden of 2.9 mg/kg STMR, its level was calculated to be less than 0.003 mg/kg.

The Meeting estimated a maximum residue level of 0.01 mg/kg for milks, recommended to replace the existing CXL of 0.05 mg/kg, and an STMR of 0.003 mg/kg. The Meeting concluded that any preferential solubility of pirimiphos-methyl in milk fat was insufficient to attach the suffix "F" to the maximum residue level.

The Meeting decided not to estimate maximum residues levels for animal commodities except milk, pending a storage stability study with animal commodities. It therefore recommended withdrawal of the CXLs for eggs at 0.05 mg/kg and meat (from mammals other than marine mammals) at 0.05 mg/kg.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels listed in Table 30 are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue for plant and animal commodities for compliance with MRLs and for estimation of dietary intake: *pirimiphos-methyl.*

The residue is fat-soluble.

Table 30. Summary of recommendations.

Commodity		Recommended MRL, mg/kg		STMR/ STMR-P, mg/kg	HR/HR-P, mg/kg
CCN	Name	New	Previous		
FP 0226	Apples	W	2		
VB 0402	Brussels sprouts	W	2		
VB 0041	Cabbages, head	W	2		
VR 0577	Carrots	W	1		
VB 0404	Cauliflowers	W	2		
GC 0080	Cereal grains	7 Po	10 Po	2.3	4.5
FS 0013	Cherries	W	2		
FC 0001	Citrus fruits	W	2		
VP 0526	Common bean (pods and/or immature seeds)	W	0.5		
VC 0424	Cucumbers	W	1		
FB 0278	Currants, black	W	1		
DF 0295	Dates, dried or dried & candied	W	0.5 Po		
MD 0180	Dried fish	W	8 Po		
PE 0112	Eggs	W	0.05		
FB 0268	Gooseberries	W	1		
FI 0341	Kiwi fruit	W	2		
VL 0482	Lettuce, head	W	5		
MM 0095	Meat (from mammals other than marine mammals)	W	0.05		
ML 0106	Milks	0.01	0.05	0.003	
VO 0450	Mushrooms	W	5		
FT 0305	Olives	W	5		
SO 0697	Peanuts	W	2 Po		
OC 0697	Peanut oil, crude	W	15 PoP		
OR 0697	Peanut oil, edible	W	15 PoP		
SO 0703	Peanut, whole	W	25 Po		
FP 0230	Pears	W	2		
VP 0063	Peas (pods and succulent, i.e. immature, seeds)	W	0.05		
VO 0051	Peppers	W	1		
FS 0014	Plums (including prunes)	W	2		
VR 0589	Potatoes	W	0.05		
FB 0272	Raspberries, red, black	W	1		
CM 0649	Rice, husked	W	2 PoP		
CM 1205	Rice, polished	W	1 PoP		
CM 1206	Rice bran, unprocessed	W	20 PoP		
CF 1251	Rye wholemeal	W	5 PoP		
VL 0502	Spinach	W	5		
VA 0389	Spring onions	W	1		
FB 0275	Strawberries	W	1		
VO 0448	Tomatoes	W	1		
CM 0654	Wheat bran, unprocessed	15 PoP	20 PoP	5.1	
CF 1211	Wheat flour	W	2 PoP	0.39	
CF 1212	Wheat wholemeal	W	5 PoP	1.6	
CP 1211	White bread	W	0.5 PoP	0.22	
CP 1212	Wholemeal bread	W	1 PoP	0.83	
	Beer			0.01	

FURTHER WORK OR INFORMATION

Desirable

1. A study on the storage stability of pirimiphos-methyl and metabolites in animal tissues and eggs.
2. Pirimiphos-methyl concentrations in fat in animal feeding studies.

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets, using the STMR for cereal grains and STMR-Ps for milks, beer and processed wheat products, estimated by the current Meeting (Table 31). The current ADI is 0-0.03 mg/kg bw and the calculated IEDIs were 10-50% of the maximum ADI. The Meeting concluded that the intake of residues of pirimiphos-methyl resulting from the uses considered by the current JMPR was unlikely to present a public health concern.

Table 31. International Estimated Dietary Intakes (IEDIs) for the five GEMS/Food regional diets (ADI = 0-0.03 mg/kg bw/day).

Code	Commodity	STMR or STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	Intake	diet	intake	diet	intake	diet	intake
GC 0080	Cereal grains (excluding wheat flour)	2.3	106.9	245.9	336.8	774.6	290.0	667.0	140.4	322.9	46.1	106.0
ML 0106	Milks	0.003	116.9	0.4	32.1	0.1	41.8	0.1	160.1	0.5	289.3	0.9
CM 0654	Wheat bran, unprocessed	5.1	-	-	-	-	-	-	-	-	-	-
CF 1212	Wheat wholemeal	1.6	-	-	-	-	-	-	-	-	-	-
CP 1211	White bread	0.22	215.3	47.4	76.0	16.7	18.9	4.2	37.3	8.2	117.2	25.8
CP 1212	Wholemeal bread	0.83	107.7	89.4	38.0	31.5	9.4	7.8	74.7	62.0	58.6	48.6
	Beer	0.01	-	-	-	-	-	-	-	-	-	-
Total intake (µg/person) =			383.0		823.0		679.1		393.6		181.3	
Bodyweight per region (kg bw) =			60		55		60		60		60	
ADI (µg/person) =			1800		1650		1800		1800		1800	
% ADI =			21.3%		49.9%		37.7%		21.9%		10.1%	
Rounded % ADI =			20%		50%		40%		20%		10%	

Note. As the consumption value for wheat flour is the sum of the consumption values of white bread and wholemeal bread, the intake of pirimiphos-methyl was calculated using the consumption and STMR-P values for white bread and wholemeal bread.

Short-term intake

International Estimated Short-Term Intakes (IESTIs) of pirimiphos-methyl by the general population and by children were calculated for commodities for which STMRs or STMR-Ps were estimated by the current Meeting (Tables 32 and 33). The Meeting considered that it might be necessary to establish an acute reference dose for pirimiphos-methyl but, as one has not been established, the short-term risk assessment for pirimiphos-methyl could not finalized.

Table 32. International Estimated Short-Term Intakes (IESTIs) of pirimiphos-methyl by the general population (acute RfD not established).

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P, mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	Large portion, g/person	Unit wt (g)	Country	Unit wt, edible portion (g)				
GC 0640	Barley (beer only)	0.01	-	AUS	67.0	528	-	-	-	-	3	0.08	-
GC 0640	Barley (fresh, flour, beer)		4.5	NLD	63.0	378	-	-	-	-	1	27.00	-
GC 0645	Maize (fresh, flour, oil)		4.5	FRA	62.3	260	-	-	-	-	1	18.77	-
ML 0106	Milks	0.003	-	USA	65.0	2466	-	-	-	-	3	0.11	-
GC 0647	Oats		4.5	FRA	62.3	305	-	-	-	-	1	22.05	-
GC 0649	Rice		4.5	FRA	62.3	312	-	-	-	-	1	22.50	-

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P, mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	Large portion, g/person	Unit wt (g)	Country	Unit wt, edible portion (g)				
GC 0650	Rye		4.5	NLD	63.0	77	-	-	-	-	1	5.49	-
GC 0654	Wheat		4.5	USA	65.0	383	-	-	-	-	1	26.51	-
CM 0654	Wheat bran, unprocessed	5.1	-	USA	65.0	80	-	-	-	-	3	6.27	-
CF 1211	Wheat flour	0.39	-	USA	65.0	365	-	-	-	-	3	2.19	-
CF 1212	Wheat wholemeal	1.6	-	USA	65.0	155	-	-	-	-	3	3.82	-
CP 1211	White bread	0.22	-	SAF	55.7	479	-	-	-	-	3	1.89	-
CP 1212	Wholemeal bread	0.83	-	SAF	55.7	395	-	-	-	-	3	5.89	-

Table 33. International Estimated Short-Term Intakes (IESTIs) of pirimiphos-methyl by children up to 6 years (acute RfD not established).

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P, mg/kg	Large portion diet			Unit weight			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	Large portion, g/person	Unit wt (g)	Country	Unit wt, edible portion (g)				
GC 0640	Barley (beer only)	0.01	-	AUS	19.0	12	-	-	-	-	3	0.01	-
GC 0640	Barley (fresh, flour, beer)		4.5	AUS	19.0	14	-	-	-	-	1	3.29	-
GC 0645	Maize (fresh, flour, oil)		4.5	FRA	17.8	148	-	-	-	-	1	37.49	-
ML 0106	Milks	0.003	-	USA	15.0	1286	-	-	-	-	3	0.26	-
GC 0647	Oats		4.5	USA	15.0	62	-	-	-	-	1	18.68	-
GC 0649	Rice		4.5	FRA	17.8	223	-	-	-	-	1	56.25	-
GC 0650	Rye		4.5	NLD	17.0	37	-	-	-	-	1	9.77	-
GC 0654	Wheat		4.5	USA	15.0	151	-	-	-	-	1	45.32	-
CM 0654	Wheat bran, unprocessed	5.1	-	USA	15.0	30	-	-	-	-	3	10.10	-
CF 1211	Wheat flour	0.39	-	AUS	19.0	194	-	-	-	-	3	3.99	
CF 1212	Wheat wholemeal	1.6	-	USA	15.0	74	-	-	-	-	3	7.86	
CP 1211	White bread	0.22	-	SAF	14.2	270	-	-	-	-	3	4.18	-
CP 1212	Wholemeal bread	0.83	-	SAF	14.2	240	-	-	-	-	3	14.03	-

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