PYRIPROXYFEN (200)

IDENTITY

ISO common name: pyriproxyfen (draft E-ISO)

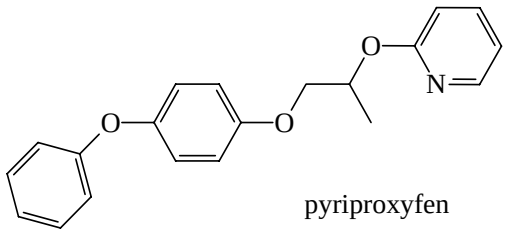
BSI name: pyriproxyfen

Chemical name
IUPAC: 4-phenoxyphenyl (*RS*)-2-(2-pyridyloxy)propyl ether
CA: 2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine

CAS No.: 95737-68-1 (unstated stereochemistry)

Synonyms: Company code numbers: S-31183, S-71639
Trade names: Admiral, Atominal, Juvinal, Knack, Nemesis, Prempt, Tiger

Structural formula:



pyriproxyfen

Molecular formula: $C_{20}H_{19}NO_3$

Molecular weight: 321.37

Physical and chemical properties

Pure active ingredient

Appearance: white odourless solid.

Vapour pressure: $<1.0 \times 10^{-7}$ mm Hg ($<1.3 \times 10^{-5}$ Pa) at 22.8°C. Vapour pressure was measured by the gas saturation procedure, but test material was not detected in the trapping tubes.

Melting point: 48.0-50.0°C

Octanol/water partition coefficient: $P_{ow} = 2.36 \times 10^5$ (log P = 5.37) at 25 ± 1°C.

Solubility:

water	0.367 ± 0.004 mg/l at 25 ± 1°C.
acetone	>150 g/100 g at 20°C
acetonitrile	>150 g/100 g at 20°C
hexane	6.97 (SD 0.460) g/100 g at 20°C
methanol	5.56 (SD 0.181) g/100 g at 20°C
methylene chloride	>150 g/100 g at 20°C

n-octanol	6.85 (SD 0.894) g/100 g at 20°C

Hydrolysis:

pyriproxyfen was stable in aqueous buffers in the dark at pH 4.0, 7.0 and 9.0 at 50°C and at pH 5.0, 7.0 and 9.0 at 25°C. Takahashi *et al.* (1989a,b) dissolved [*phenyl*-^{14}C]pyriproxyfen and [*pyridyl*-^{14}C]pyriproxyfen in sterile aqueous buffer solutions with 1% acetonitrile as co-solvent at 0.1 mg/l and analysed the solutions at intervals during 7 days at 50°C and 30 days at 25°C. No decrease of pyriproxyfen could be detected after 7 days at 50°C. Calculated half-lives were more than 200 days.

Technical material

Purity: minimum 95.0%

Stability: technical grade material stored at ambient temperature (19 - 35°C) for one year showed no change when analysed by HPLC.

Technical grade pyriproxyfen was also tested for stability when exposed to iron, elevated temperatures and sunlight. There was no degradation when the technical grade as a 1% solution containing either 0.1% ferric chloride hexahydrate or 0.025% iron powder was stored for 14 days at 20°C, or the product was held in a sealed bottle at 54°C for 14 days or exposed to sunlight in a transparent glass ampoule for 14 days.

METABOLISM AND ENVIRONMENTAL FATE

Studies of metabolic and environmental fate identified the compounds shown in Figure 1 and their conjugates.

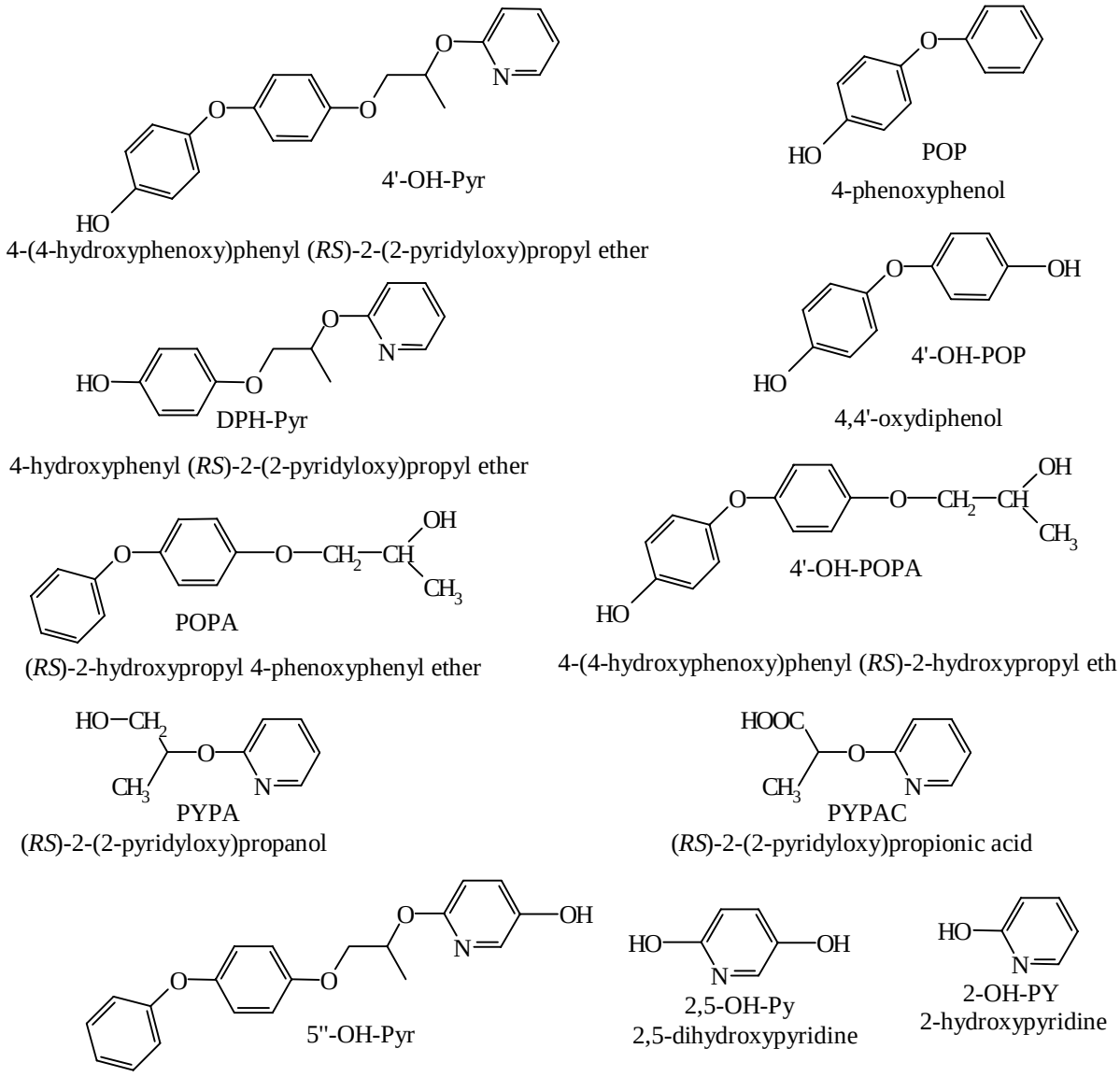
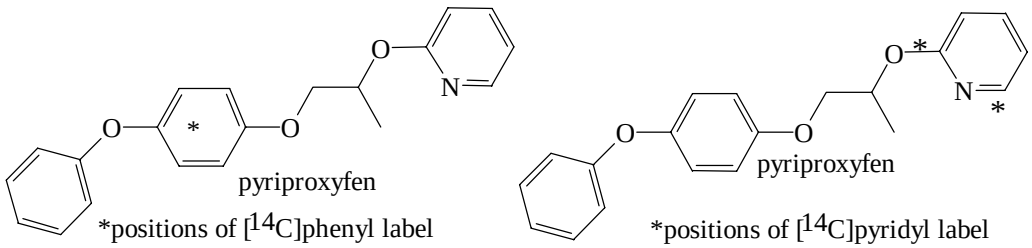


Figure 1. Structures, names and abbreviations of metabolites and degradation products found in studies of metabolism and environmental fate.

For the studies of metabolism and environmental fate pyriproxyfen was labelled either uniformly in the proximal ring of the phenoxyphenyl moiety or in positions 2 and 6 of the pyridine ring.



Animal metabolism

The Meeting received information on the metabolism of pyriproxyfen in rats, lactating goats and laying hens.

Isobe *et al.* (1988a) administered a single oral dose of [*phenyl*-^{14}C]pyriproxyfen to rats at 2 mg/kg bw (low dose) and 1000 mg/kg bw (high dose). Rats were also dosed orally with unlabelled pyriproxyfen at 2 mg/kg bw/day for 14 consecutive days followed by a single oral dose of labelled pyriproxyfen at the same rate. ^{14}C excretion was rapid, accounting for 88-96% in 2 days and 92-98% within 7 days. ^{14}C levels were higher in the fat than in other tissues. The main metabolite identified in the faeces was 4'-OH-Pyr, accounting for 25-54% of the dose; pyriproxyfen in the faeces accounted for 7-37% of the dose.

Isobe *et al.* (1988b) examined the distribution of ^{14}C in the tissues from the rats administered the single oral dose of 2 mg/kg bw of [*phenyl*-^{14}C]pyriproxyfen. Rats were killed for tissue collection 2, 4, 8, 12, 24, 48 and 72 hours after dosing. The radiolabel levels were higher in the liver than in other tissues for the first 8 hours after dosing, but higher in the fat than in other tissues after 72 hours. The radiolabel reached maximum levels in the liver, kidneys and muscle at 4-8 hours after dosing, and in fat at 12-24 hours. The highest levels of metabolites were of 4'-OH-Pyr sulfate and 5'',4'-OH-Pyr sulfate in the liver (Table 1). Yoshino (1993a) examined the distribution of ^{14}C in the tissues from the rats receiving the high dose (1000 mg/kg bw). Initially ^{14}C levels were higher in the liver than in other tissues but after 24 hours the levels were highest in the fat. The times to reach a maximum in each tissue were muscle and liver 2-8 h, kidneys 4-8 h and fat 12-24 h. The estimated biological half-life of ^{14}C in the fat was 36 hours. The metabolism studies on rats have subsequently been published (Matsunaga *et al.*, 1995).

Table 1. Maximum levels of ^{14}C expressed as pyriproxyfen associated with identified compounds in kidneys and liver of rats dosed orally with 2 mg/kg bw of [*phenyl*-^{14}C]pyriproxyfen, and time after dosing to reach maximum (Isobe *et al.*, 1988b).

Compound	Kidneys		Liver	
	max. ng/g	time, h	max, ng/g	time, h
Pyriproxyfen	39	2-4	63	2
4'-OH-Pyr	12	4	340	4-8
4'-OH-Pyr sulfate	80	4-8	770	2-8
4'-OH-POPA			15	8
4'-OH-POPA sulfate	34	8	160	8
5'',4'-OH-Pyr			21	8
5'',4'-OH-Pyr sulfate	153	4-8	735	8
4'-OH-POP sulfate	50	8	88	8

Yoshino (1993b) administered a single oral dose of [*pyridyl*-^{14}C]pyriproxyfen to rats at 2 mg/kg bw (low dose) and 1000 mg/kg bw (high dose). Excretion of ^{14}C accounted for 89-93% in 2 days and 92-99% within 7 days. ^{14}C levels were higher in the fat than in other tissues. The main metabolite identified in the faeces was 4'-OH-Pyr, accounting for 23-47% of the dose; pyriproxyfen accounted for 21-35%.

The rates of excretion and metabolic pathways of pyriproxyfen in rats and mice were shown to be similar (Yoshino *et al.*, 1995).

Studies of the metabolism of [*phenyl*-^{14}C] and [*pyridyl*-^{14}C] pyriproxyfen in lactating goats and laying hens were reported. A subsequent study of freezer storage stability (Green, 1997) showed

that pyriproxyfen and its metabolites in some animal substrates had limited storage stability at –20ºC. No data were available on the storage stability in milk or eggs. Samples of goat and chicken tissues, milk and eggs were generally extracted 60-90 days after collection in the four studies. Pyriproxyfen could have decreased by 35-45% in this time, 4'-OH-Pyr by less than 30%, 2,5-OH-Py by 60-70%. The studies should be interpreted in the light of the stability during freezer storage.

Residues in tissues, milk and excreta were measured in two lactating dairy goats, each weighing 51-57 kg, dosed orally for 5 consecutive days by capsule with 20 mg [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996a). The feed intake was 1.43-2.17 kg/animal/day. The two goats produced averages of 800 and 3200 g milk per day. Milk and excreta were collected throughout, and the animals were slaughtered 6 hours after the final dose for tissue collection (rear leg and loin muscle, omental and perirenal fat, liver, kidneys, heart and blood). The identified residues in the milk and tissues are shown in Tables 2 and 3.

Most of the radiolabel was accounted for by the faeces (58%), urine (17-18%) and GI tract (24%). Milk accounted for 0.29% and 0.79% of the dose in the two animals, while the livers contained 0.45% and 0.29%.

Pyriproxyfen was a minor component of the residue in the milk, accounting for 5-15% of the ^{14}C. The main residue was 4'-OH-Pyr sulfate accounting for about 50%, while POP sulfate, 4'-OH-POP sulfate and DPH-Pyr each accounted for between 5 and 10% of the total ^{14}C.

Pyriproxyfen was the major component in the fat, accounting for 50-79% of the ^{14}C. The residues in omental and perirenal fat were qualitatively and quantitatively similar. Pyriproxyfen was also the main residue component in muscle but the levels were very low. It was a very minor component of the residue in both kidneys and liver, accounting for 1-4% of the ^{14}C. The main residue in the kidneys was POP sulfate; 4'-OH-Pyr sulfate, 5''-OH-Pyr sulfate and 4'-OH-POP each exceeded 5% of the ^{14}C. The total residue level was higher in the liver than in other tissues; the main compounds were 4'-OH-Pyr sulfate, POPA, 4'-OH-Pyr and 4'-OH-POPA. The heart contained 0.035 and the blood 0.039 mg/kg of ^{14}C expressed as pyriproxyfen.

Table 2. Pyriproxyfen and identified metabolites in the milk of goats dosed orally for 5 consecutive days by capsule with [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996a). Residue levels are ^{14}C expressed as pyriproxyfen, mg/kg.

Compound	Day 2 milk				Day 4 milk			
	Goat A		Goat B		Goat A		Goat B	
	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C
pyriproxyfen	0.005	5.4	0.009	15	0.005	5.7	0.006	10
4'-OH-Pyr sulfate	0.044	50	0.025	45	0.049	51	0.028	49
4'-OH-Pyr	0.001	0.88	0.002	3.0	0.002	1.9	0.001	1.5
POP sulfate	0.009	10	0.005	9.0	0.010	10	0.006	9.7
4'-OH-POP sulfate	0.007	8.2	0.004	7.4	0.008	8.3	0.005	7.9
4'-OH-POPA sulfate	0.002	2.8	0.001	2.5	0.003	2.9	0.002	2.7
DPH-Pyr	0.007	8.1	0.004	7.2	0.008	8.2	0.004	7.8
TOTAL	0.090	100	0.060	100	0.096	100	0.058	100

Table 3. Pyriproxyfen and identified metabolites in the tissues of goats dosed orally for 5 consecutive days by capsule with [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996a). The residues in the 2 goats are shown separately.

Compound	^{14}C as pyriproxyfen, mg/kg					
	Kidneys	Liver	Loin muscle	Leg muscle[1]	Omental fat	Perirenal fat
pyriproxyfen	0.003 0.003	0.010 0.012	0.007 0.008	0.004	0.014 0.043	0.023 0.050
4'-OH-Pyr sulfate	0.052 0.029	0.121 0.078	0.002 0.002	0.001	0.001 0.002	0.001 0.002
4'-OH-Pyr	0.001 -	0.068 0.017	0.002 0.002	<0.001	0.007 0.004	0.008 0.003
5''-OH-Pyr		0.027 0.006				
5''-OH-Pyr sulfate	0.040 0.023	0.004 0.015				
POP sulfate	0.093 0.057					
POP	0.002 0.002	0.017 0.009	0.001 0.001	<0.001	0.001 0.001	0.001 0.001
4'-OH-POP	0.024 0.014		0.001 0.001	<0.001	<0.001 0.001	<0.001 0.001
4'-OH-POP sulfate	0.003 0.003					
POPA	0.008 0.004	0.076 0.039				
4'-OH-POPA	0.007 0.004	0.051 0.026				
DPH-Pyr	0.005 0.003	0.032 0.016				
TOTAL[2]	0.262 0.162	0.492 0.288	0.021 0.019	0.010	0.029 0.054	0.038 0.050

[1]Components of residue in leg muscle of goat B were not determined because total residue was <0.001 mg/kg
[2]Total residue measured by combustion analysis

Two other lactating dairy goats, each weighing 39-47 kg, were dosed orally daily for 5 consecutive days by capsule with 14.9 mg [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996b). The feed intake was 1.09-1.77 kg/animal/day. The goats produced averages of 1270 and 1410 g milk per day. Milk and excreta were collected throughout, and the animals were slaughtered 6 hours after the final dose for tissue collection as before.

Most of the ^{14}C (62-70%) was excreted in the faeces and urine with about 31% in the gastrointestinal tract and contents. Less than 2% was distributed in the milk and tissues: 0.44% and 0.84% in the milk, 0.46% and 0.81% in the liver, 0.04% and 0.06% in the kidneys, 0.02 and 0.03% in muscle, 0.05% and 0.05% in fat. The residues in the milk and tissues are shown in Tables 4 and 5. Heart samples contained 0.029-0.039 and blood 0.038-0.041 mg/kg ^{14}C expressed as pyriproxyfen, representing 0.01% and <0.01% of the dose respectively. The administered ^{14}C was quantitatively recovered (95-102%).

Pyriproxyfen was a minor component of the residue in the milk accounting for 3.2-5.6% of the ^{14}C. The major residues were 4'-OH-Pyr sulfate (29-42%) and 2,5-OH-Py conjugate(s) (19-30%).

Pyriproxyfen was the main residue in fat, with essentially the same levels in the omental and perirenal fat, and was generally the major identified compound in muscle with the metabolites 4'-OH-Pyr sulfate, 2-OH-PY and PYPA conjugate(s) contributing 6-15% of the residue. The levels of pyriproxyfen were less than 10% of its levels in the fat, as would be expected for a fat-soluble compound.

Pyriproxyfen was a very minor part of the residue in the liver and kidneys (between about 0.3 and 1.4% of the total ^{14}C). 4'-OH-Pyr sulfate was the major identified component (22-39% in the kidneys and 7-20% in the liver), with 2,5-OH-Py and PYPA conjugates contributing about 7-13%. The total residues in the liver and kidneys were much higher than in the other tissues. About half the ^{14}C in the liver was unextractable. This was examined further by enzyme and acid hydrolysis but none of the known or expected metabolites were released. The chromatographic behaviour of the released ^{14}C suggested that it had been incorporated into natural products such as proteins or polysaccharides.

Table 4. Pyriproxyfen and identified metabolites in the milk of goats dosed orally for 5 consecutive days by capsule with [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996b). Residue levels are ^{14}C expressed as pyriproxyfen, mg/kg.

Compound	Day 2 milk				Day 4 milk			
	Goat A		Goat B		Goat A		Goat B	
	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C	mg/kg	% of total ^{14}C
pyriproxyfen	0.003	4.2	0.003	3.2	0.004	5.6	0.003	3.0
4'-OH-Pyr sulfate	0.028	42	0.037	35	0.020	29	0.041	35
4'-OH-Pyr	0.001	0.76	<0.001	0.21	<0.001	0.4	<0.001	0.05
2,5-OH-Py conjugate	0.013	19	0.033	30	0.019	27	0.033	29
DPH-Pyr	0.004	6.4	0.006	5.5	0.003	4.5	0.006	5.6
TOTAL	0.063	100	0.111	100	0.071	100	0.121	100

Table 5. Pyriproxyfen and identified metabolites in the tissues of goats dosed orally for 5 consecutive days by capsule with [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996b). The residues in the 2 goats are shown separately.

Compound	^{14}C as pyriproxyfen, mg/kg					
	Kidneys	Liver	Loin muscle	Leg muscle	Omental fat	Perirenal fat
pyriproxyfen	0.001 0.001	0.006 0.004	0.003 0.001	0.003 0.003	0.039 0.033	0.033 0.033
4'-OH-Pyr sulfate	0.088 0.065	0.085 0.060	0.001 0.002	0.001 0.002	0.001 0.001	0.002 0.002
4'-OH-Pyr	0.002 0.002	0.016 0.018	<0.001 0.001	<0.001 0.001	0.008 0.004	0.007 0.003
5"-OH-Pyr	0.001 0.001	0.009 0.011				
PYPA conjugate	0.022 0.039					
2,5-OH-Py conjugate	0.017 0.030	0.031 0.058				
PYPAC	0.005 0.009		<0.001 <0.001	<0.001 -		
PYPA conjugate		0.027 0.049	0.001 0.001	0.001 0.002		
2-OH-PY			0.002 0.001	0.002 -		
2,5-OH-Py			- <0.001			
TOTAL [1]	0.226 0.290	0.433 0.829	0.012 0.015	0.015 0.020	0.061 0.045	0.069 0.049

[1] Total residue measured by combustion analysis

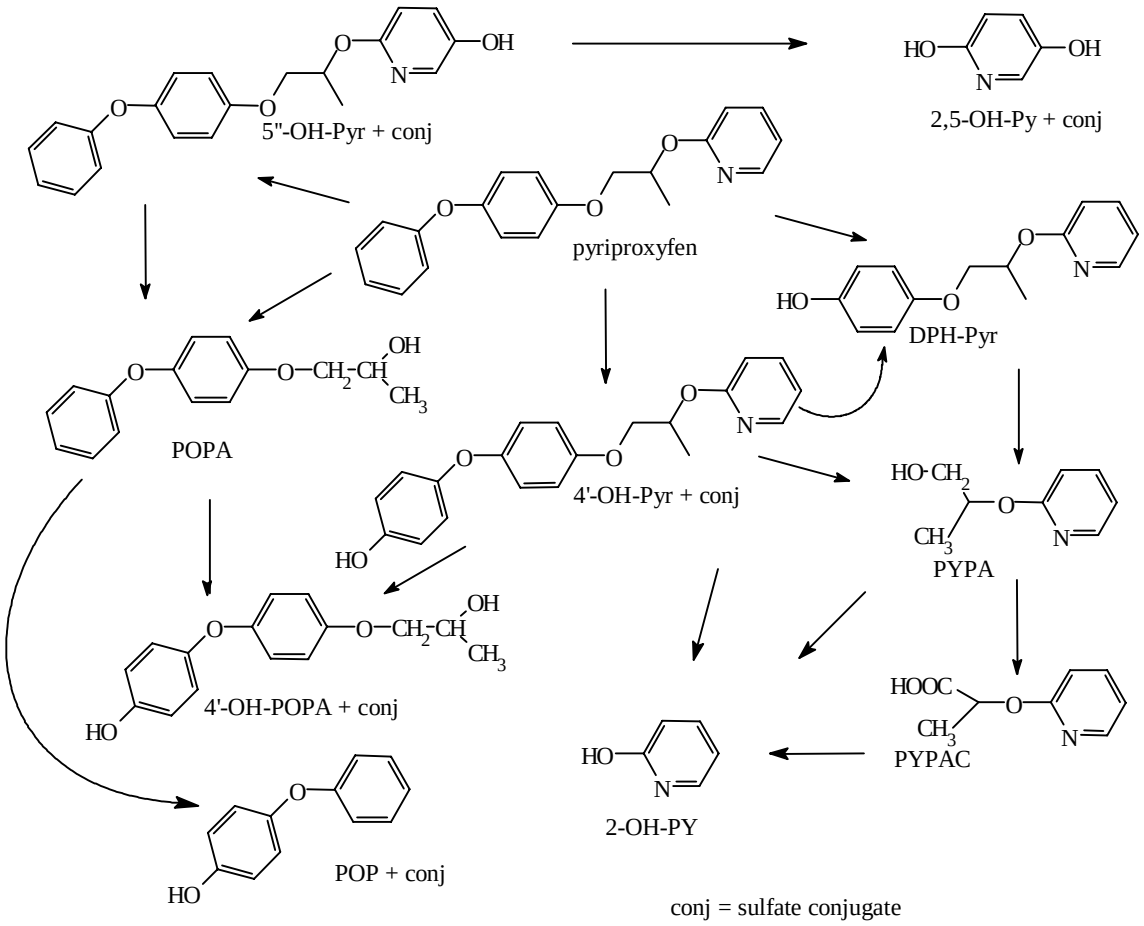


Figure 2. Metabolic fate of pyriproxyfen in lactating goats.

Ten Leghorn laying hens, each bird weighing 1.48-1.77 kg, were dosed orally daily for 8 consecutive days by capsule with 1.26 mg [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996c). The feed intake was 108-139 g/bird/day. Eggs and excreta were collected throughout, and birds were slaughtered within 4 hours of the final dose for tissue collection.

Approximately 96% of the ^{14}C was accounted for, with 89% in the excreta including the cage wash, 4.3% in the GI tract and contents, 2.6% in other tissues and 0.18% in eggs. The residue level in the gizzard was higher than in other tissues. The major identified residue in the excreta was 4'-OH-Pyr. The distribution of the radiolabel in the tissues and eggs is shown in Table 6 and the distribution of the identified compounds in Table 7.

Residue levels were very low in the egg white and apparently reached a plateau in the yolk in 6 days. Pyriproxyfen represented 55% of the ^{14}C in 7-day yolks with 4'-OH-Pyr accounting for 21% and 4'-OH-Pyr sulfate for 10%. Minor metabolites identified in egg yolk included DPH-Pyr, 4'-OH-POP and 4'-OH-POPA. The residue levels in muscle were lower than in the other tissues; pyriproxyfen accounted for 56% and 77% of the residue in breast and thigh muscles respectively. Residues in the fat were much higher than in the muscle, suggesting a fat-soluble residue; pyriproxyfen constituted 94% and 71% of the residue in the abdominal fat and the skin with fat respectively, and the level of pyriproxyfen in abdominal fat was 4.6 times the level in skin with fat. Pyriproxyfen was a minor component of the residue in the liver, in which 4'-OH-Pyr sulfate was the major component, accounting for 40% of the ^{14}C.

Table 6. Distribution of ^{14}C in the tissues and eggs of laying hens dosed for 8 days with [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996c).

Sample	^{14}C as pyriproxyfen, mg/kg		^{14}C as % of dose
Muscle, breast	0.033		0.02
Muscle, thigh	0.085		0.06
Fat, abdominal	0.88		0.06
Fat, skin attached	0.21		0.03
Kidneys	0.86		0.13
Liver	0.75		0.39
Heart	0.23		0.02
Blood	0.17		0.36
Gizzard	3.91		1.23
GI tract	3.51		4.32
Reproductive organs	0.20		0.26
Eggs	yolk	white	0.18
day 1	0.016	0.001	
day 2	0.021	0.004	
day 4	0.16	0.004	
day 6	0.30	0.006	
day 7	0.23	0.003	

Table 7. Pyriproxyfen and identified metabolites in the tissues of laying hens dosed for 8 days with [*phenyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996c).

Compound	^{14}C as pyriproxyfen, mg/kg							
	Kidneys	Liver	Breast muscle	Thigh muscle	Abdominal fat	Skin with fat	Gizzard	Egg yolk
pyriproxyfen	0.057	0.046	0.014	0.069	0.79	0.17	1.8	0.13
4'-OH-Pyr sulfate	0.089	0.27	0.002	0.005		0.012	0.57	0.024
4'-OH-Pyr	0.012	0.029	0.001	0.003	0.031	0.009	0.035	0.049
POP sulfate		0.022				0.006		
POP					0.005			
4'-OH-POP	0.031			0.001	0.001		0.058	0.001
4'-OH-POP sulfate	0.073	0.044				0.003		
POPA		0.035			0.001	0.008	0.089	
4'-OH-POPA	0.022		0.001	0.001		0.006	0.059	0.002
4'-OH-POPA-sulfate	0.073	0.025						
DPH-Pyr	0.011	0.036	0.002	0.002	0.001		0.094	0.009
TOTAL [1]	0.75	0.68	0.025	0.090	0.84	0.24	4.4	0.24

[1] Sum of bound and extractable ^{14}C

Ten Leghorn laying hens, each weighing 1.31-1.78 kg were similarly dosed for 8 days with 1.26 mg [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed or a mean daily dose of 0.78 mg/kg bw (Panthani *et al.*, 1996d). The average feed intake was 110-138 g/bird/day. Samples were taken as before.

Approximately 88% of the ^{14}C was accounted for, with 84% of the dose in the excreta including the cage wash, 1.6% in the GI tract and contents, 2.3% in other tissues and 0.29% in eggs. The residue level in the gizzard was higher than in other tissues. The major identified residues in the excreta were PYPAC and 4'-OH-Pyr. The distribution of ^{14}C in the tissues and eggs is shown in Table 8 and that of the identified compounds in Table 9.

Residue levels were low in the egg white; residues in the yolk had almost reached a plateau by day 7. Pyriproxyfen accounted for 41 of the ^{14}C in 7-day yolks with 4'-OH-Pyr sulfate accounting

for 29%. Residue levels in muscle were lower than in the other tissues; pyriproxyfen accounted for 30% and 54% of the residue in muscle. Residues in the fat were much higher, with pyriproxyfen amounting to 87 and 62% of the residue in the abdominal fat and the skin with fat; the level of pyriproxyfen in the abdominal fat was 7 times its level in the skin with fat. Pyriproxyfen was a minor component (0.44%) of the residue in the liver, in which 4'-OH-Pyr sulfate was the major component accounting for 26% of the ^{14}C.

Table 8. Distribution of ^{14}C in the tissues and eggs of laying hens dosed for 8 days with [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996d).

Tissue	^{14}C as pyriproxyfen, mg/kg		^{14}C as % of dose
Muscle, breast	0.054		0.04
Muscle, thigh	0.11		0.07
Fat, abdominal	0.93		0.03
Fat, skin attached	0.27		0.03
Kidneys	0.80		0.12
Liver	0.69		0.34
Heart	0.27		0.03
Blood	0.28		0.60
Gizzard	1.8		0.60
GI tract	1.14		1.6
Reproductive organs	0.34		0.45
Eggs	yolk	white	0.29
Day 1	0.002	0.002	
Day 2	0.012	0.013	
Day 4	0.19	0.017	
Day 6	0.38	0.020	
Day 7	0.41	0.019	

Table 9. Pyriproxyfen and identified metabolites in the tissues of laying hens dosed for 8 days with [*pyridyl*-^{14}C]pyriproxyfen equivalent to 10 ppm pyriproxyfen in the feed (Panthani *et al.*, 1996d).

Compound	^{14}C as pyriproxyfen, mg/kg							
	Kidneys	Liver	Breast muscle	Thigh muscle	Abdominal fat	Skin with fat	Gizzard	Egg yolk (day 7)
pyriproxyfen	0.041	0.011	0.013	0.047	0.92	0.13	0.48	0.17
4'-OH-Pyr sulfate	0.057	0.18	0.003	0.002		0.023	0.17	0.12
4'-OH-Pyr	0.006	0.015	0.001	0.001	0.030	0.005	0.043	0.012
5"-OH-Pyr		0.003						
5"-OH-Pyr sulfate		0.011						
PYPA							0.010	
DPH-Pyr	0.011		0.001	0.002	0.009			0.013
2-OH-PY	0.069	0.087	0.013	0.014		0.013	0.021	0.007
PYPAC	0.060	0.025	0.007	0.006	0.001	0.012	0.008	
TOTAL [1]	0.75	0.68	0.044	0.087	1.06	0.21	0.95	0.41

[1] Sum of bound and extractable ^{14}C

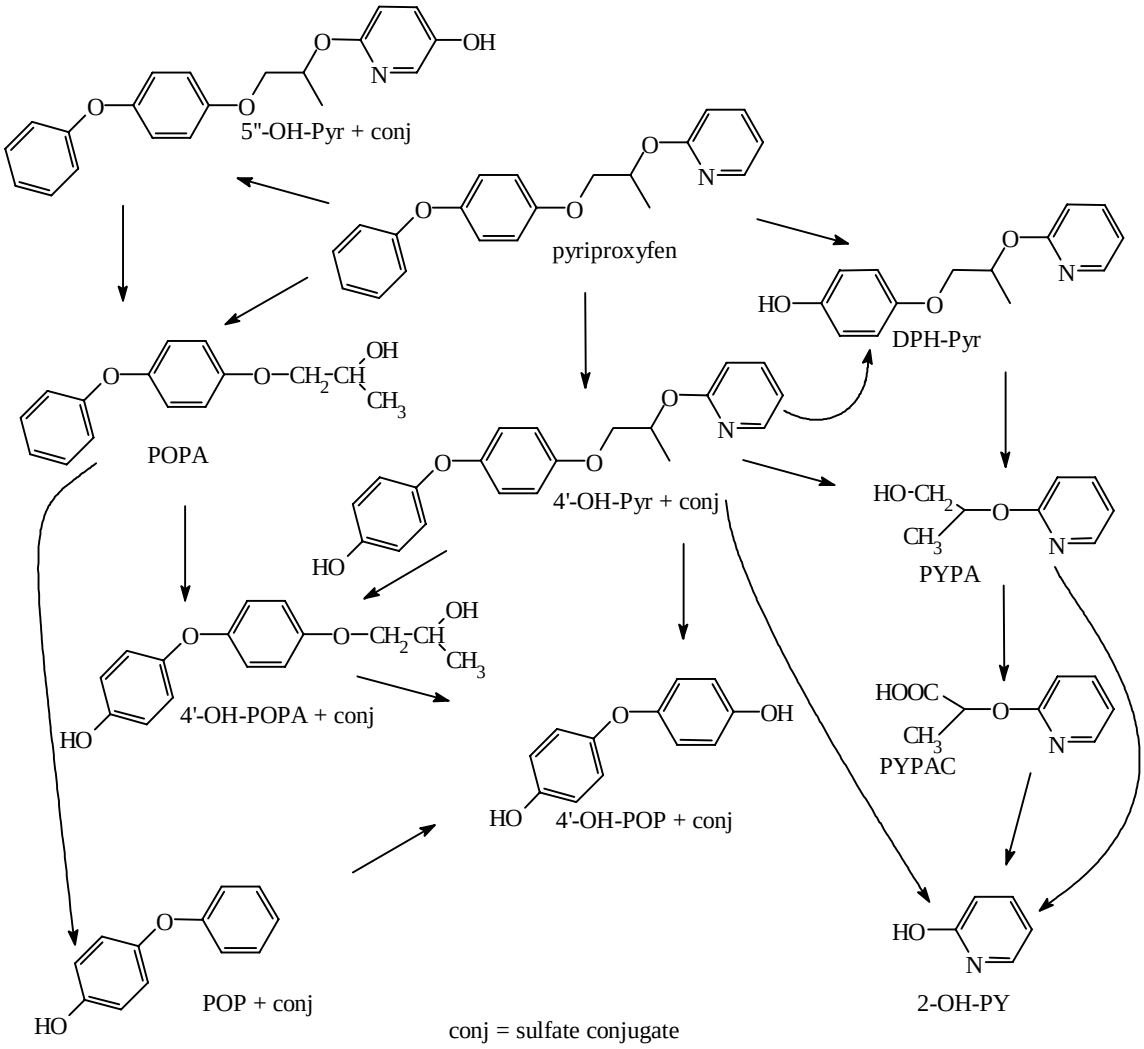


Figure 3. Metabolic fate of pyriproxyfen in laying hens

Plant metabolism

The Meeting received information on the metabolism of pyriproxyfen in apples, tomatoes and cotton.

Panthani and Walsh (1996) treated apple trees three times (soon after petal fall and at 60 and 40 days before harvest) with phenyl- and pyridyl-labelled pyriproxyfen at 150 g/ha. The residues found in mature apples are shown in Table 10.

A surface wash with acetonitrile removed 1.5-2.6% of the total residue. The washed apples were homogenized and centrifuged to produce juice and pomace. Juice fractions contained 6-14% of the ^{14}C and pomace 84-92%. About 70% of the ^{14}C in the pomace was extractable with methanol, with 12-15% unextractable after acid treatment and other extractions. Pyriproxyfen was not detectable (<0.001 mg/kg) in the juice, where the main identified residue was PYPA which accounted for 25% of the ^{14}C in the juice and 3.2% of that in the apples. Pyriproxyfen accounted for most of the ^{14}C in the pomace and for 52 and 54% of the total ^{14}C in the whole apples.

Table 10. Residues in mature apples from trees treated three times with phenyl- or pyridyl-labelled [^{14}C]pyriproxyfen at 150 g/ha and harvested 40 days after the final application (Panthani and Walsh, 1996).

Residue	^{14}C as pyriproxyfen, mg/kg	
	phenyl label	pyridyl label
Extractable [1]	0.16	0.16
Pyriproxyfen	0.097	0.101
4'-OH-Pyr [2]	0.021	0.017
PYPA [3]		0.012
DPH-Pyr [3]	0.006	0.003
POPA [3]	0.004	
4'-OH-POPA [4]	0.004	
POP [3]	0.002	
4'-OH-POP [4]	0.001	
5''-OH-Pyr [4]	0.001	<0.001
PYPAC [2]		0.003
Unextractable	0.028	0.023

[1] Including surface wash
[2] Free
[3] Sum of free and conjugated
[4] Conjugated

Panthani and DiFrancesco (1997) treated tomato plants three times (35, 21 and 7 days before harvest) with phenyl- or pyridyl-labelled pyriproxyfen at 150 g/ha. The residues in the tomatoes are shown in Table 11. A surface wash with acetonitrile removed 1.8-3.3% of the total residue. The washed tomatoes were homogenized and centrifuged to produce juice and pomace. Juice fractions contained 14% and 33% of the ^{14}C from the phenyl and pyridyl label respectively, and the pomace 82% and 65%. Approximately 92-95% of the ^{14}C in pomace was extractable with acetonitrile/water.

Pyriproxyfen was not detectable in the tomato juice, where the main identified residues were PYPA (free 0.007 mg/kg, conjugated 0.018 mg/kg), PYPAC (free 0.010 mg/kg, conjugated 0.008 mg/kg) and 2-OH-PY (conjugated 0.013 mg/kg) accounting for 29%, 21% and 15% of the ^{14}C respectively. Pyriproxyfen accounted for most of the residue in the pomace and for 68% and 50% of the total phenyl and pyridyl labels respectively in the whole tomatoes.

Table 11. Residues in tomatoes from plants treated three times with phenyl- or pyridyl-labelled [^{14}C]pyriproxyfen at 150g/ha and harvested 7 days after the final application (Panthani and DiFrancesco, 1997).

Residue	^{14}C as pyriproxyfen in tomatoes, mg/kg	
	phenyl label	pyridyl label
Extractable [1]	0.34	0.25
Pyriproxyfen	0.24	0.13
4'-OH-Pyr	0.020	0.012
PYPAC [2]		0.021
PYPA [3]		0.029
2-OH-PY [3]		0.013
4'-OH-POPA [2]	0.009	
DPH-Pyr [3]	0.008	0.005
4'-OH-POP [2]	0.007	
Unextractable	0.016	0.014

[1] including surface wash
[2] sum of free and conjugated
[3] conjugated

Panthani *et al.* (1996e) treated field cotton plants 43 and 28 days before harvest at 150 g/ha, and glasshouse plants at 590 g/ha 42 and 28 days before harvest, with phenyl- or pyridyl-labelled pyriproxyfen. The higher rate was to provide a source of material for the identification of metabolites. The residues in the cotton seed and gin trash are shown in Table 12.

Pyriproxyfen was metabolized to polar compounds in the plants, with most of the residue remaining in the foliage. Pyriproxyfen was the main residue component in the gin trash. Residues were much lower in the seed than in the gin trash, suggesting little if any translocation of residue from leaf to seed. Pyriproxyfen constituted only 3.9% and 0.6% of the residue in the seed, where the main identified residue was PYPAC in free and conjugated forms. Much of the residue in the cotton seed (49 and 55%) was unextractable; about half of this was associated with the protein fraction and the remainder with carbohydrate and lignin.

Table 12. Residues in cotton seed and gin trash from cotton plants treated twice with phenyl- or pyridyl-labelled [^{14}C]pyriproxyfen at 150g/ha and harvested 28 days after the second application (Panthani *et al.*, 1996e).

Residue	^{14}C as pyriproxyfen, mg/kg			
	Cotton seed		Gin trash	
	phenyl label	pyridyl label	phenyl label	pyridyl label
Extractable	0.016	0.069	1.4	3.6
Pyriproxyfen	0.0012 [3]	0.0009 [4]	0.76	1.5
4'-OH-Pyr	0.0001	0.0001	0.13	0.27
DPH-Pyr [1]			0.13	0.32
OH-pyriproxyfen [2]			0.032	0.17
PYPAC [1]		0.020		0.20
PYPA [1]		0.0059		0.093
POPA			0.044	
4'-OH-POPA			0.035	
POP			0.019	
Unextractable	0.015	0.084	0.39	0.81

[1] sum of free and conjugated
[2] sugar sulfate conjugate of pyriproxyfen hydroxylated in the pyridine ring
[3] 28% in the surface rinse
[4] 35% in the surface rinse

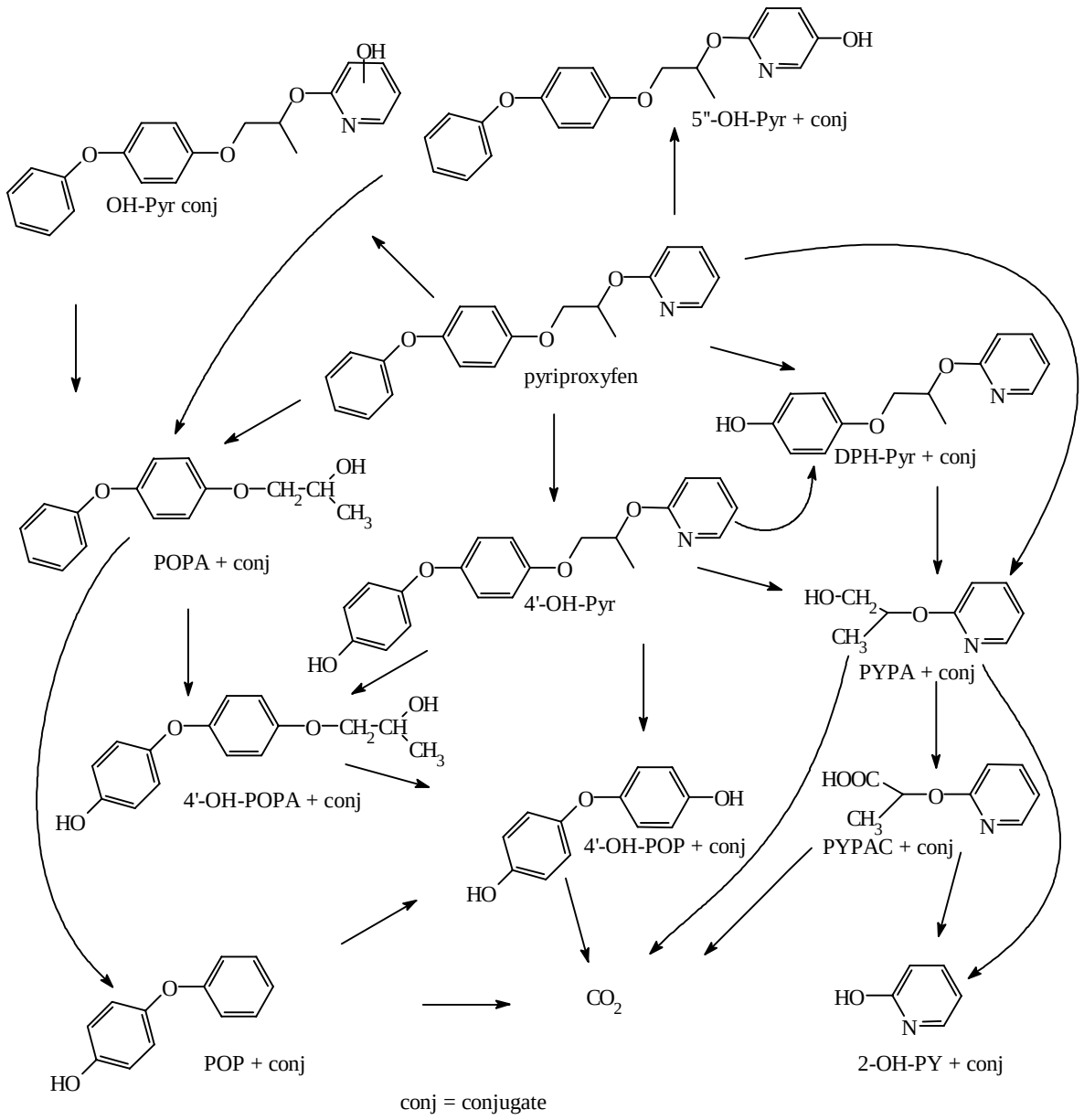


Figure 4. Metabolic fate of pyriproxyfen in apples, tomatoes and cotton.

Environmental fate in soil

Kouno *et al.* (1990a) incubated [*phenyl*-^{14}C]pyriproxyfen and [*pyridyl*-^{14}C]pyriproxyfen in a sandy clay loam soil (73% sand, 8% silt, 19% clay, 2.4% organic content, pH 5.7) at 0.5 mg/kg under aerobic conditions at 25°C in the dark for 30 days. The recovery of ^{14}C, including volatiles, was in the range 91-103%. The residues are shown in Table 13. Pyriproxyfen disappeared rapidly in the initial stages, but later more slowly: its estimated half-life after the first 7 days was 28 days. The estimated mineralization half-lives were 68 and 139 days for the pyridyl and phenyl labels respectively, with an indication that mineralization was slower after longer intervals. The main identified residue was 4'-OH-Pyr. Other minor products were PYPAC, DPH-Pyr and 4'-OH-POPA. A substantial part of the ^{14}C quickly became bound in the soil organic matter.

Table 13. Residues found during aerobic degradation of phenyl- and pyridyl-labelled pyriproxyfen in a sandy clay loam soil (Kouno *et al.*, 1990a). The recorded results are means of two separate experiments with each label.

Days	^{14}C, % of applied								
	pyriproxyfen		CO_2		4'-OH-Pyr [1]		PYPAC [1]	Bound	
	phenyl label	pyridyl label	phenyl label	pyridyl label	phenyl label	pyridyl label	pyridyl label	phenyl label	pyridyl
0	95	95						0.8	0.9
1	87	93			1.5	1.1		4.7	3.0
3	63	64	4.1	3.6	2.5	3.7	1.0	20	17
7	45	46	8.3	12.6	2.8	4.2	0.7	36	31
14	38	36	11	18	2.6	3.2	0.9	42	38
30	25	25	17	28	2.7	2.7		46	34

[1] Additional amounts were identified in the fulvic acid fraction of the bound residues

Kouno *et al.* (1990b) carried out an identical experiment with sandy loam soil (54% sand, 36% silt, 10% clay, 0.8% organic content, pH 6.5) but continued the incubation for 91 days. The recovery of ^{14}C, including volatiles, was in the range 88-106%. The residues are shown in Table 14. The estimated half-lives of pyriproxyfen were 8.2 days during days 1-14 and 20 days during days 14-91. The rates for the phenyl and pyridyl labels were very similar. The estimated mineralization half-lives (calculated from the rates of $^{14}CO_2$ production) were 112 and 82 days for the phenyl and pyridyl labels respectively.

PYPAC was the main identified product, with the sum of free and bound PYPAC exceeding pyriproxyfen from day 28. 4'-OH-Pyr was a minor product, at its highest on day 1 and decreasing with estimated half-lives of 29 and 39 days for the phenyl and pyridyl labels respectively. Bound residues accounted for approximately 50% of the applied ^{14}C by day 28. Other identified products representing 0.1-0.2% of the applied ^{14}C were detected intermittently.

Table 14. Residues found during aerobic degradation of phenyl- and pyridyl-labelled pyriproxyfen in a sandy loam soil (Kouno *et al.*, 1990b). The recorded results are means of two separate experiments with each label.

Days	^{14}C, % of applied									
	pyriproxyfen		CO_2		4'-OH-Pyr		PYPAC free	PYPAC bound	Bound	
	phenyl label	pyridyl label	phenyl label	pyridyl label	phenyl label	pyridyl label	pyridyl label	pyridyl label	phenyl label	pyridyl label
0	94	96	0.0	0.0	0.3	0.3	0.0	0.0	2.1	2.0
1	77	84	1.9	0.2	0.9	0.8	1.1	0.0	9.5	9.4
3	66	70	5.8	1.6	0.9	0.7	2.5	3.7	19	18
7	49	51	11.2	5.1	0.7	0.6	3.7	6.2	25	27
14	27	29	19	10.9	0.5	0.5	6.3	7.6	40	37
28	8.7	13.0	30	24	0.4	0.4	5.4	9.5	52	50
59	3.0	3.6	38	46	0.2	0.2	2.8	3.3	50	45
91	1.5	2.3	43	50	0.1	0.2	1.7	2.8	51	40

Fathulla *et al.* (1994) incubated [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen aerobically in a sandy loam soil (pH 7.6, organic matter 0.87%, clay 8.4%) at 0.6 mg/kg in the dark at 25°C for 6 months and measured the evolved CO_2 and the levels of pyriproxyfen and identifiable products. The recoveries of ^{14}C were in the range 94% to 108%. The results are shown in Tables 15 and 16.

Mineralization was slow with 13.9% of the ^{14}C from the phenyl label and 31.1% from the pyridyl label evolved as CO_2 after 180 and 189 days, equivalent to mineralization half-lives of 850 and 330 days. Pyriproxyfen disappeared quickly in the first 14 days with estimated initial half-lives of

6.3 and 9.1 days for the phenyl and pyridyl labels, but much more slowly between 2 and 6 months, with estimated half-lives of 120 and 77 days for the phenyl and pyridyl labels respectively.

Identified products were generally minor proportions of the residue; 4'-OH-Pyr and PYPAC reached their highest measured levels on day 14 and then decreased. The polar material, which accounted for 22-23% of the applied ^{14}C after 6 months, could not be identified but was characterized as a mixture of high-molecular-weight compounds, suggesting incorporation or binding to natural products.

Table 15. Aerobic degradation of [*phenyl*-^{14}C]pyriproxyfen incubated with sandy loam soil at 0.6 mg/kg in the dark at 25°C for 6 months (Fathulla *et al.*, 1994).

Days	^{14}C, % of applied				
	Pyriproxyfen	Polar material [1]	4'-OH-Pyr	DPH-Pyr	CO_2
0	104	nd	nd	nd	
1	100	nd	nd	nd	<0.1
3	87	5.8	nd	nd	0.1
7	47	10	2.2	nd	0.5
14	24	18	3.3	0.4	3.5
31	13	16	2.6	0.1	5.7
62	10.3	23	1.3	0.2	8.8
94	7.5	26	0.8	0.1	10.7
122	6.7	27	0.6	0.1	11.5
150	6.9	26	0.5	0.1	12.8
180	5.0	23	0.4	<0.1	13.9

[1] Material remaining at TLC origin

Table 16. Aerobic degradation of [*pyridyl*-^{14}C]pyriproxyfen incubated with sandy loam soil at 0.6 mg/kg in the dark at 25°C for 6 months (Fathulla *et al.*, 1994).

Day	^{14}C, % of applied					
	Pyriproxyfen	Polar material [1]	PYPAC	4'-OH-Pyr	DPH-Pyr	CO_2
0	102	nd	nd	nd	nd	
1	104	nd	nd	nd	nd	0.1
3	88	nd	1.0	5.3	nd	0.6
7	66	13.5	3.1	nd	nd	1.6
14	36	12.6	7.6	6.3	0.3	4.6
30	23	16	4.9	2.7	0.2	12.5
59	11.4	18	1.4	1.8	0.2	20
92	7.7	20	0.6	1.6	0.1	24
120	6.3	21	0.4	1.0	0.1	27
149	7.1	16	0.5	0.9	nd	29
189	4.5	22	0.3	0.9	nd	31

[1] Material remaining at TLC origin

Mikami *et al.* (1989) determined the leaching of [*phenyl*-^{14}C]pyriproxyfen freshly mixed at 1 mg/kg with a silt soil (43% sand, 47% silt, 10% clay, 7.6% organic matter, pH 7.0) and a sandy loam (72% sand, 17% silt, 11% clay, 0.9% organic matter, pH 7.2) and applied to 30 cm x 3 cm i.d. columns of the untreated soils. The columns were leached with water (360 ml) at 69 mm/day for 8 days. Most of the ^{14}C (89% for the silt soil and 84% for the sandy loam) still remained in the treated portion at the top of the soil columns, with 5% in the 0-5 cm untreated layer of both soils. Small amounts of ^{14}C were detected throughout the columns with 0.1% and 2.8% in the eluates from the silt and sandy loam respectively. Most of the extractable residue was pyriproxyfen (Table 17) with bound ^{14}C in the humin, humic acid and fulvic acid fractions. Small amounts of DPH-Pyr and 4'-OH-Pyr were identified in the extracted and fulvic acid fractions. Pyriproxyfen is unlikely to be leached and its degradation products become substantially bound in the soil organic matter.

Table 17. ^{14}C residues in two soil columns after leaching fresh [*phenyl*-^{14}C]pyriproxyfen for 8 days (Mikami *et al.*, 1989).

Residue	^{14}C, % of applied	
	Silt soil	Sandy loam soil
Extracted ^{14}C	31	43
pyriproxyfen	25	34
DPH-Pyr	0.9	0.7
4'-OH-Pyr	2.9	1.8
Bound ^{14}C	58	39
fulvic acid	14	9.4
DPH-Pyr	1.9	1.1
4'-OH-Pyr	0.7	0.5
humic acid	16	10.6
humin	28	19

Fathulla *et al.* (1993a) incubated [*phenyl*-^{14}C]pyriproxyfen and [*pyridyl*-^{14}C]pyriproxyfen with a sandy loam soil (pH 8.1, organic matter 0.79%, clay 23%) under aerobic conditions in the dark at 25°C for 14 days and used the treated soil after 9 days for leaching experiments. The composition of the residues during the incubation is shown in Tables 18 and 19. The half-life of pyriproxyfen was 7.5 and 9.5 days and the mineralization half-life was 170 and 140 days in the two systems.

Glass columns (5.1 cm i.d.) that could be separated into six 6 cm sections were used for the leaching experiments. A 3-cm layer of soil with aged residue was placed on top of the soil column and the column was leached with 1030 ml of 0.015N $CaCl_2$. In the experiment with the phenyl label 86% of the ^{14}C remained in the treated soil (top 3 cm), with 2.3% in section 2 (3-9 cm), 0.13-0.54% in the other sections and 1.0% in the leachate, giving a total recovery of 90%. Most of the residue consisted of pyriproxifen (26%) and bound material (44.5%). With the pyridyl label, 88.5% of the ^{14}C remained in the top 3 cm, with 1.4% in the 3-9 cm section, 0.13-0.44% in the other sections and 7.6% in the leachate: a total recovery of 98.6%. Most of the ^{14}C was associated with pyriproxyfen (35%) and bound residue (41%). PYPAC was the main residue in the leachate, 6.5 of the 7.6%. The leaching of pyriproxyfen is slight but PYPAC, constituting only a few per cent of the residue, is apparently mobile.

Table 18. Residues resulting from aerobic incubation at 25°C of [*phenyl*-^{14}C]pyriproxyfen with a sandy loam soil at 0.6 mg/kg (Fathulla, 1993a).

Days	Distribution of ^{14}C, % of applied.						
	Pyriproxyfen	Unidentified P1	DPH-Pyr	4'-OH-Pyr	Total unidentified	Unextractable	CO_2
0	95	0.09	0.10	0.19	1.9	3.0	0
2	71	0	0.64	6.3	4.7	8.0	0.27
4	64	0.72	1.9	8.2	4.8	20	1.1
7	44	0.78	1.6	5.3	9.4	29	2.6
9	39	0.54	1.4	5.1	7.7	37	3.5
9 [1]	41	0.34	1.8	4.4	8.5	41	3.5
11	31	1.4	2.0	5.5	8.9	42	4.3
14	26	0.77	1.5	3.6	8.3	48	5.3

[1] Beginning of leaching experiment

Table 19. Residues resulting from aerobic incubation at 25°C of [*pyridyl*-^{14}C]pyriproxyfen with a sandy loam soil at 0.6 mg/kg (Fathulla, 1993a).

Days	Distribution of ^{14}C, % of applied.						
	Pyriproxyfen	PYPAC	DPH-Pyr	4'-OH-Pyr	Total unidentified	Unextractable	CO_2
0	95	0.15	0.05	0.24	1.8	2.4	0
2	84	0.68	0.79	5.4	1.8	6.7	0.01
4	72	1.4	1.1	4.4	3.7	16	1.1
7	55	2.1	1.3	4.4	3.6	29	3.1
9	48	1.8	0.81	3.4	2.9	36	4.2
9 [1]	51	1.5	0.37	2.2	2.6	36	4.2
11	42	4.3	0.72	3.1	3.1	39	4.9
14	36	4.4	0.44	3.3	4.8	48	6.2

[1] Beginning of leaching experiment

Nambu *et al.* (1989) measured the adsorption and desorption of [*phenyl*-^{14}C]pyriproxyfen with 4 soils, a loam, clay loam, sandy loam and sand, after determining the water solubility to be 0.54 mg/l at 20°C. Adsorption and desorption measurements were made with 0.01 M $CaCl_2$ solutions of pyriproxyfen in equilibrium with the soils at 25°C in the dark (Table 20). K_{oc} values were calculated from the K_d and the percentage of organic carbon. The measured K_d and K_{oc} values suggest that pyriproxyfen is unlikely to be leached into ground-water. Cohen *et al.* (1984) interpreted K_d values below 1-5 and K_{oc} values below 300-500 as indicating potential leaching if other requirements, such as environmental persistence, are met.

Table 20. Properties and adsorption and desorption constants of pyriproxyfen for four soils (Nambu *et al.*, 1989).

Soil	Soil properties						Adsorption		Desorption	
	sand	silt	clay	organic matter	pH	CEC, meq/100 g	K_d	K_{oc}	K_d	K_{oc}
Loam	56%	30%	15%	8.2%	7.1	32	614	13000	755	16000
Clay loam	55%	26%	19%	1.9%	7.0	6.3	637	58000	925	84000
Sandy loam	72%	18%	11%	0.9%	7.2	2.8	142	27000	182	35000
Sand	98%	0.8%	1.5%	<0.1%	6.6	4.9	25	-	36	-

Fathulla *et al.* (1991) measured the adsorption and desorption of [*phenyl*-^{14}C]pyriproxyfen with 5 agricultural soils and a lake sediment. Pyriproxyfen at 1-50 ng/g dissolved in 10 ml aqueous 0.01M $Ca(NO_3)_2$ was added to 2 g of soil or sediment and shaken at 24.3°C for 2 hours. ^{14}C levels were measured in 7 ml of clear solution after centrifugation, and adsorption to the soil or sediment was calculated. To measure desorption, 7 ml aqueous 0.01M $Ca(NO_3)_2$ was added to the same tube with further shaking for 2 hours at 24.3°C. ^{14}C was measured in the clear solution after centrifugation and desorption was calculated. The results are shown in Table 21. Pyriproxyfen was soluble and stable at the concentrations tested. The recovery of ^{14}C ranged from 90% to 107% showing that losses by volatilization or adsorption to the containers were minimal. Pyriproxyfen was rated as essentially immobile and unlikely to be leached from most agricultural soils.

Table 21. Properties and adsorption and desorption constants of pyriproxyfen for a sediment and 5 agricultural soils (Fathulla *et al.*, 1991).

Soil	Soil properties						Adsorption		Desorption	
	sand	silt	clay	organic matter	pH	CEC, meq/100 g	K_d	K_{oc}	K_d	K_{oc}
Lake sediment	97%	1%	2%	0.4%	7.6	4	11.7	4980	10.0	4260
Sand	97%	1%	2%	0.3%	5.4	1.1	20.4	11600	25.1	14300
Sandy loam	60%	25%	15%	1.65%	8.0	9.7	126	12600	141	14100
Silt loam	29%	58%	13%	1.1%	7.0	13	174	26900	178	27500
Silty clay loam	7%	53%	49%	1.4%	7.8	27	282	34200	275	33400
Clay loam	21%	47%	32%	5.0%	7.0	21	324	11000	457	15500

Fathulla *et al.* (1995a,b) measured the adsorption and desorption of 4'-OH-Pyr and PYPAC on four agricultural soils and a lake sediment. In initial experiments, the solubility of 4'-OH-Pyr was measured as 1.1 µg/ml at 25°C and that of PYPAC as 89.1 mg/ml at .21.4°C.

[*Pyridyl*-^{14}C]4'-OH-Pyr at 25, 50, 250 and 500 ng/g dissolved in 10 ml aqueous 0.01M $CaCl_2$ was added to 2 g of soil or sediment and shaken at 25°C for 2 hours. ^{14}C levels were measured in the clear solution removed after centrifugation, and adsorption to the soil or sediment was calculated. Desorption was measured by adding 10 ml aqueous 0.01M $CaCl_2$ to the same tube with further shaking for 2 hours at 25°C. ^{14}C was measured after centrifugation and desorption was calculated. The results are shown in Table 22. Recoveries of ^{14}C ranged from 101% to 109%.

On the basis of the K_{oc} values 4'-OH-Pyr was rated as having slight to low mobility in most agricultural soils and having a slight chance of leaching.

Table 22. Properties and adsorption and desorption constants of 4'-OH-Pyr for a sediment and four agricultural soils (Fathulla *et al.*, 1995a).

Soil	Soil properties						Adsorption		Desorption	
	sand	silt	clay	organic matter	pH	CEC, meq/100 g	K_d	K_{oc}	K_d	K_{oc}
Lake sediment	93%	6.0%	1.2%	0.17%	8.2	0.85	2.76	2760	47.5	47500
Sand	92%	3.6%	4.4%	0.22%	6.0	0.82	5.50	4250	36.3	28050
Sandy loam	75%	18%	7.2%	0.96%	6.9	6.6	21.5	3810	164	29100
Silt loam	35%	54%	11%	1.8%	6.9	8.9	32.8	3060	386	36000
Clay loam	33%	28%	39%	2.1%	7.9	15.8	11.5	920	239	19100

[*Pyridyl*-^{14}C]PYPAC at 20, 100, 200 and 1000 ng/g dissolved in 10 ml aqueous 0.01M $CaCl_2$ was added to 4.9 g of soil or sediment and shaken at 25°C for 8 hours. Adsorption and desorption were determined as before (Table 23). Recoveries of ^{14}C ranged from 100% to 106%.

The results indicated that PYPAC had a high or very high mobility with a high potential to leach to ground-water on the basis of the interpretations of K_d and K_{oc} by Cohen *et al.* (1984). PYPAC is quite soluble in water, so weak sorption by soil is not surprising. Whether the potential to be leached is realised will depend on the persistence of PYPAC in soil and the prevailing field conditions.

Table 23. Adsorption and desorption constants of [*pyridyl*-^{14}C]PYPAC on the sediment and soils of Table 22 (Fathulla *et al.*, 1995b).

Soil	Adsorption		Desorption	
	K_d	K_{oc}	K_d	K_{oc}
Lake sediment	0.12	120	0.88	881
Sand	0.11	85	0.45	350
Sandy loam	0.12	21	0.84	148
Silt loam	0.34	32	1.05	98
Clay loam	0.11	9	0.72	57

Takahashi *et al.* (1988) exposed [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen on upland sandy loam and silt loam soils at approximately 100 mg/m^2 to natural sunlight for 8 weeks. The soils were in layers of approximately 0.5 mm. Volatiles were collected and soil samples were taken at intervals for analysis and identification of the residues by TLC. In control samples (vials wrapped in aluminium foil) run simultaneously, 87% or more of the applied ^{14}C was still in pyriproxyfen after the 8 weeks. In the sandy loam soil pyriproxyfen disappeared with half-lives of 12.5 weeks for the phenyl label and 10.3 weeks for the pyridyl label. The mineralization half-life (production of $^{14}CO_2$) was 37 weeks for the phenyl label and 350 weeks for the pyridyl label. In the silt loam soil pyriproxyfen disappeared very quickly in the first week, but with half-lives after the first week of 18 and 21 weeks for the phenyl and pyridyl labels respectively. The corresponding mineralization half-lives were 51 and 150 weeks. The identified decomposition products of pyriproxyfen were all minor and may have arisen from other routes of degradation as well as photolysis: 4'-OH-Pyr, DPH-Pyr, POPA, POP and 2-OH-PY.

Fathulla *et al.* (1995e) irradiated phenyl- and pyridyl-labelled pyriproxyfen on a sandy loam soil at approximately 0.3 mg/kg with artificial sunlight (xenon lamp) for 20 and 18 days (12 hours irradiation per day). Volatiles were collected and soil samples taken at intervals for analysis by TLC. Control samples stored in the dark at 25°C were run simultaneously. Recoveries of ^{14}C were between 92% and 106%. The results are shown in Tables 24 and 25.

Degradation was faster in the irradiated soils than in the controls. Half-lives of [*phenyl*-^{14}C]pyriproxyfen were 16 days irradiated and 27 days dark, and of [*pyridyl*-^{14}C]pyriproxyfen 6.8 days irradiated and 13 days dark. PYPAC was identified as a degradation product reaching its maximum level on day 10. The levels of 4'-OH-Pyr after 10 days were lower in the irradiated soil than in the control, so if it was formed by photolysis it was also degraded by photolysis. The production of volatile ^{14}C was negligible. The main degradation products were, or were incorporated into, polar and unextractable compounds.

Table 24. Degradation of [*phenyl*-^{14}C]pyriproxyfen at 0.3 mg/kg on a sandy loam soil during irradiation with simulated sunlight (Fathulla *et al.*, 1995e).

Days	^{14}C, % of applied							
	pyriproxyfen		polar		4'-OH-Pyr		unextractable	
	irradiated	dark	irradiated	dark	irradiated	dark	irradiated	dark
0	100	100	nd	nd	nd	nd	0.8	0.8
2	90	95	nd	nd	nd	nd	9.1	4.2
4	90	94	2.7	nd	0.6	nd	4.4	6.3
7	65	92	10.6	1.9	2.8	2.4	14	8.4
10	44	79	22	6.3	3.5	1.9	26	12.4
14	57	81	11.5	4.4	1.3	2.0	21	10.9
20	45	57	9.1	18	1.4	2.4	35	19

Table 25. Degradation of [*pyridyl*-^{14}C]pyriproxyfen at 0.3 mg/kg on a sandy loam soil during irradiation with simulated sunlight (Fathulla *et al.*, 1995e).

Days	^{14}C, % of applied											
	pyriproxyfen		polar		PYPAC		4'-OH-Pyr		DPH-Pyr		unextractable	
	irradiated	dark	irradiated	dark	irradiated	dark	irradiated	dark	irradiated	dark	irradiated	dark
0	101	101	nd	nd	nd	nd	nd	nd	nd	nd	0.6	0.6
3	93	98	nd	nd	nd	nd	nd	nd	nd	nd	7.1	3.5
6	67	95	8.4	1.7	9.8	0.5	nd	nd	nd	nd	9.3	7.4
10	49	80	11	6.8	13	3.8	nd	nd	nd	nd	19	9.9
14	25	63	19	10	5.9	5.4	0.7	1.3	nd	nd	41	15
18	18	36	18	18	2.6	7.6	1.0	5.6	0.3	0.6	45	25

In a confined rotational crop study, Waller (1996) applied [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen to a sandy loam soil at 0.20 kg ai/ha, and after an ageing interval of 30 days sowed lettuce, radish and wheat seed. Levels of ^{14}C were measured in the crops at harvest (Table 26). The levels in lettuce leaves, radish roots and leaves, and wheat forage were very low, suggesting that residue uptake was negligible. The ^{14}C residues in wheat grain, straw and chaff were investigated further. The grain was extracted with hexane/methanol, but 89% of the residue was unextractable. Mild acid hydrolysis of the extracted grain released little ^{14}C. Hydrolysis at 80°C in 6N HCl released most of the ^{14}C, but it was not organosoluble and pyriproxyfen and its immediate degradation products were not detectable, suggesting that the ^{14}C had been incorporated into proteins and carbohydrates. Extraction and hydrolysis of wheat straw and chaff gave similar results. Residues of pyriproxyfen and its immediate degradation products should not occur above negligible levels in rotational crops following the use of pyriproxyfen on the previous crop.

Table 26. Levels of ^{14}C in rotational crops sown 30 days after treatment of the soil with ^{14}C-pyriproxyfen (Waller, 1996).

Sample	Interval from sowing to harvest, days		^{14}C as pyriproxyfen, mg/kg	
	phenyl label	pyridyl label	phenyl label	pyridyl label
Lettuce leaf	43	45	0.0034	0.0065
Radish root	50	52	0.0018	0.0049
Radish leaf	50	52	0.0043	0.011
Wheat forage	36	38	0.0051	0.011
Wheat grain	123	137	0.081	0.059
Wheat straw	123	137	0.032	0.059
Wheat chaff	123	137	0.040	0.082

In a field dissipation study, pyriproxyfen as an EC formulation was applied twice at 0.15 kg ai/ha to bare ground at a field site in California intended for cotton production (Pensyl, 1995a). Soil cores (90 cm depth) were taken at intervals and sections of the cores were analysed for pyriproxyfen, 4'-OH-Pyr and PYPAC. The test area was flat with no appreciable slope. The top 30 cm of the soil was classified as a sandy loam (60% sand, 28% silt, 12% clay, 0.6% organic matter, pH 8.6) and the 30-60 cm depth as a loam. Rainfall was supplemented by irrigation and during the 7 months of the study the total rainfall plus irrigation was 30 cm.

Pyriproxyfen was detected essentially only in the top 7.5 cm of soil, apart from traces appearing in the 7.5-15 cm segment on the day of the second treatment and the following day (Table 27). The estimated half-life of pyriproxyfen in the top 7.5 cm of the soil was 16 days. Pyriproxyfen residues did not migrate down the soil profile. All the core samples analysed for pyriproxyfen were also analysed for PYPAC and 4'-OH-Pyr. PYPAC was not detected (<0.01 mg/kg) in any sample, and 4'-OH-Pyr was detected only in one sample at 0.01 mg/kg in the 7.5-15 cm layer immediately after the second application.

Table 27. Residues of pyriproxyfen in the soil profile after two applications to bare ground at 0.15 kg ai/ha in California (Pensyl, 1995a). Three soil cores were analysed on each occasion.

Day[1]	Pyriproxyfen, mg/kg, at depths of			
	0-7.5 cm	7.5-15 cm	15-30 cm	30-90 cm
-13	0.11 0.12 0.12	<0.01 (3)	<0.01 (3)	
0	0.08 0.12 0.07	<0.01 0.02 <0.01	<0.01 (3)	<0.01 (3)[2]
1	0.12 0.14 0.26	0.02 <0.01 <0.01	<0.01 (3)	
3	0.05 0.08 0.01	<0.01 (3)	<0.01 (3)	
7	0.04 0.06 0.03	<0.01 (3)	<0.01 (3)	
10	0.03 0.02 0.03	<0.01 (3)	<0.01 (3)	
14	0.05 0.04 0.09	<0.01 (3)	<0.01 (3)	
28	0.04 0.07 0.03	<0.01 (3)	<0.01 (3)	
40	0.01 (3)	<0.01 (3)	<0.01 (3)	
60	<0.01 (3)	<0.01 (3)	<0.01 (3)	
91	0.01 0.01 <0.01	<0.01 (3)	<0.01 (3)	<0.01 (3)[2]
119	<0.01 (3)	<0.01 (3)	<0.01 (3)	
184	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)[2]

[1] The first application of pyriproxyfen was on day -13 and the second on day 0
[2] Not detected (<0.01 mg/kg) in the soil layers 30-45 cm, 45-60 cm, 60-75 cm and 75-90 cm

An identical study was carried out at a field site intended for cotton production in Mississippi (Pensyl, 1995b). The treated test plot was approximately 10 m × 10 m and the area was relatively flat with 0.5-2% slope. The top 30 cm of the soil was classified as a silt loam (32% sand, 52% silt, 16% clay, 0.8% organic matter, pH 5.9) and the 30-60 cm depth as a clay loam. Rainfall was supplemented by irrigation and during the 2 months of the study the total rainfall plus irrigation was 17 cm.

Pyriproxyfen disappeared quickly from the top 7.5 cm of soil with an estimated half-life of 3.5 days. Residues were not detected further down the profile, implying that it was rapidly degraded rather than lost by mobility and dilution. PYPAC was detected at 0.01 mg/kg in only one sample, a surface soil on the day of the second application. 4'-OH-Pyr was present at 0.02 mg/kg in 2 of 3 surface core samples on day 10, at 0.02 mg/kg in 1 core sample at 30-45 cm on day 7 and at 0.01 mg/kg in 1 core, also on day 7. These sporadic occurrences of 4'-OH-Pyr at levels near the LOD are difficult to interpret as the result of systematic persistence and mobility down the soil profile.

Table 28. Residues of pyriproxyfen in the soil profile after two applications to bare ground at 0.15 kg ai/ha in Mississippi (Pensyl, 1995b). Three soil cores were analysed on each occasion.

Day[1]	Pyriproxyfen, mg/kg, at depths of			
	0-7.5 cm	7.5-15 cm	15-30 cm	30-45 cm
-14	0.06 0.06 0.06	<0.01 (3)	<0.01 (3)	
0	0.17 0.15 0.12	<0.01 (3)	<0.01 (3)	<0.01 (3)
1	0.36 0.20 0.10	<0.01 (3)	<0.01 (3)	
3	0.13 0.10 0.11	<0.01 (3)	<0.01 (3)	
7	0.02 0.06 0.05	<0.01 (3)	<0.01 (3)	
10	0.03 0.01 0.04	<0.01 (3)	<0.01 (3)	
14	<0.01 (3)	<0.01 (3)	<0.01 (3)	
28	<0.01 (3)	<0.01 (3)	<0.01 (3)	
42	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)

[1] The first application of pyriproxyfen was on day -14 and the second on day 0.

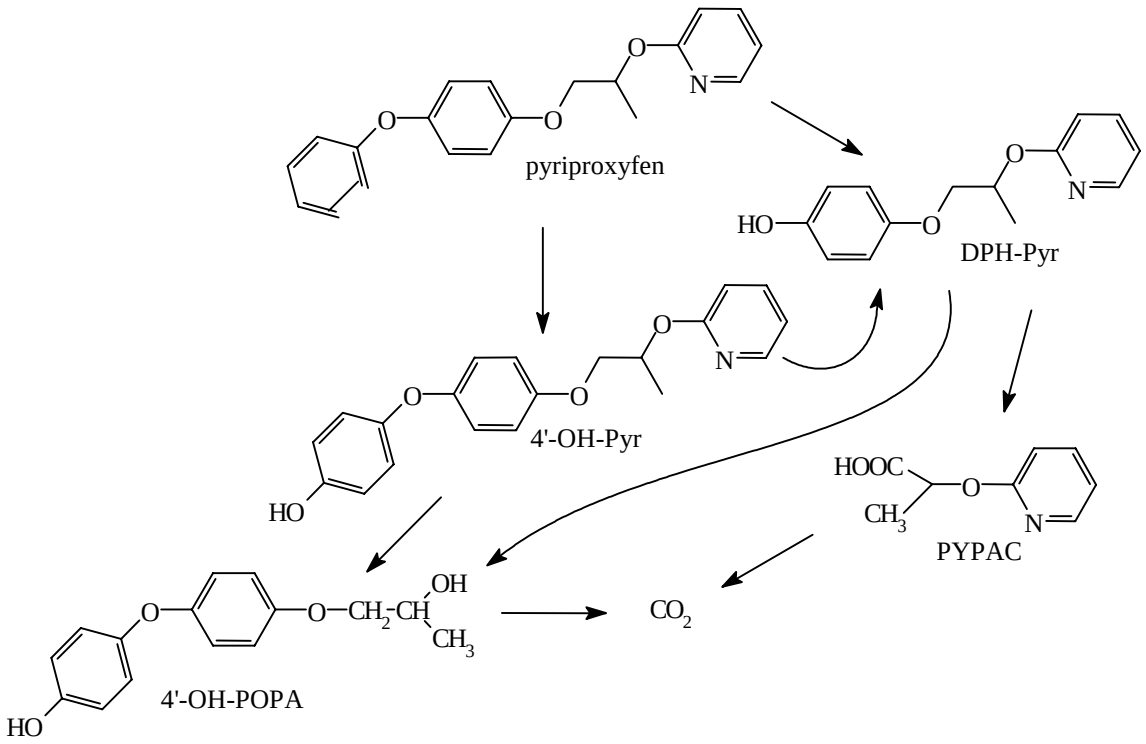


Figure 5. Fate of pyriproxyfen in soil.

Environmental fate in water/sediment systems

Fathulla *et al.* (1993b) incubated lake water (20 ml) and lake sediment (2 g) with [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen at approximately 0.3 µg/g sediment in the dark at 25°C under aerobic conditions for 31 and 28 days. The sediment and water contained a large number of aerobic micro-organisms. The pH of the lake water was 8.0 with an alkalinity of 205 mg/l as $CaCO_3$. Residues were identified by HPLC and two-dimensional TLC. Recoveries of ^{14}C in the two experiments were in the range 89-105%.

The half-life of [*phenyl*-^{14}C]pyriproxyfen was 16 days. Pyriproxyfen itself was the main residue component in the sediment throughout the study (Table 29). A mixture of unidentified polar compounds accounted for 35% of the original ^{14}C by day 31. The main identified product in both water and sediment was 4'-OH-Pyr.

The half-life of [*pyridyl*-^{14}C]pyriproxyfen was 21 days. Levels of the parent compound and 4'-OH-Pyr (Table 30) were in general agreement with those from the phenyl label. From day 12 PYPAC became a substantial part of the residue in the water phase.

Table 29. Residues in a lake sediment and water resulting from aerobic incubation at 25°C with [*phenyl*-^{14}C]pyriproxyfen at approximately 0.3 µg/g sediment (Fathulla 1993b).

Days	^{14}C, % of applied.								
	Pyriproxyfen		Unidentified polar		DPH-Pyr		POP	4'-OH-Pyr	
	water	sed	water	sed	water	sed	water	water	sed
0	68	23	nd		nd		nd	nd	nd
1	52	34	nd		nd		nd	nd	nd
2	18	57	nd		nd		nd	3.8	4.5
4	19	59	nd		nd		nd	4.3	5.2
7	16	58	3.7		nd		nd	3.9	5.6
14	7.3	46	12	0.6	1.4	1.4	1.0	0.6	6.4
21	0.3	28	20	8.8	1.6	nd	0.6	2.9	10.7
31	nd	27	24	11.3	nd	nd	nd	nd	3.6

nd: not detected

Table 30. Residues in a lake sediment and water resulting from aerobic incubation at 25°C with [*pyridyl*-^{14}C]pyriproxyfen at approximately 0.3 µg/g sediment (Fathulla 1993b).

Days	^{14}C, % of applied.							
	pyriproxyfen		PYPAC		DPH-Pyr		4'-OH-Pyr	
	water	sed	water	sed	water	sed	water	sed
0	23	64	nd	nd	nd		0.2	nd
1	52	40	nd	nd	nd		0.3	nd
2	34	53	nd	4.1	nd	nd	nd	0.4
4	39	53	nd	1.7	nd	nd	1.0	0.5
7	20	65	nd	0.5	0.6	nd	4.4	3.1
12	9.3	52	11.7	0.9	nd	0.2	1.2	2.8
21	0.5	37	30	3.7	2.3	0.5	nd	4.0
28	0.3	46	25	2.8	nd	0.5	2.3	0.5

nd: not detected

An essentially identical experiment (Fathulla *et al.,* 1995c) was carried out under anaerobic conditions for 1 year. The sediment and water contained a large number of aerobic micro-organisms and some anaerobic spores. The lake water had an alkalinity of 205 mg/l expressed as $CaCO_3$. The sediment was extracted with methanol/water and acetone/water for analysis by HPLC and two-dimensional TLC as before. Recoveries of ^{14}C were in the range 90-107%. The results are shown in Tables 31 and 32.

Pyriproxyfen was the main residue in both labelled systems throughout the studies and was mainly in the sediment rather than the water. Pyriproxyfen in the phenyl-label experiment appeared to be degraded in two phases, slowly for 180 days (estimated half-life 750 days) and then more quickly for the next 6 months (estimated half-life 105 days). The likely explanation is the adaptation of the anaerobic organisms to the conditions and substrate during the 6 months. The estimated half-life of the pyridyl-labelled pyriproxyfen was 280 days. There may again have been a two-phase degradation with the second phase beginning after 9 months, but such an interpretation would rely on only the analysis at 12 months. The identified products were mainly at very low levels. PYPAC accounted for 16% of the dose after a year; because of its solubility it was mainly in the water. Volatile ^{14}C, including $^{14}CO_2$, was negligible. Much more polar material was formed from the phenyl-labelled compound, suggesting that the phenolic compounds released after the separation of PYPAC were incorporated into the humin in the sediment.

Table 31. Residues in a lake sediment and water resulting from anaerobic incubation at 25°C with [*phenyl*-^{14}C]pyriproxyfen at 0.28 µg/g sediment (Fathulla *et al.*, 1995c).

Days	^{14}C, % of applied									
	pyriproxyfen		Polar		4'-OH-Pyr		DPH-POPA		DPH-Pyr	
	water	sed	water	sed	water	sed	water	sed	water	sed
0	28	74	nd	nd	nd	nd	nd	nd	nd	nd
7	13.4	90	nd	nd	nd	nd	nd	nd	nd	nd
14	7.5	87	nd	nd	nd	nd	nd	nd	nd	nd
32	5.5	92	nd	nd	nd	nd	nd	nd	0.5	nd
61	2.1	92	0.3	nd	nd	nd	nd	nd	0.2	nd
91	2.7	89	0.1	nd	nd	nd	nd	nd	0.1	nd
120	3.1	90	0.4	0.8	nd	0.2	nd	nd	0.1	0.1
180	3.4	80	0.7	0.1	nd	0.2	nd	nd	0.1	0.1
273	5.9	52	0.9	1.1	2.2	5.2	0.5	nd	2.8	0.4
368	nd	24	13.5	0.8	nd	2.4	nd	0.2	nd	1.1

nd: not detected

Table 32. Residues of pyriproxyfen and metabolites in a lake sediment and water resulting from anaerobic incubation at 25°C of [*pyridyl*-^{14}C]pyriproxyfen at 0.28 µg/g sediment (Fathulla *et al.*, 1995c).

Days	^{14}C, % of applied											
	pyriproxyfen		polar		PYPAC		PYPA		4'-OH-Pyr		DPH-Pyr	
	water	sed	water	sed	water	sed	water	sed	water	sed	water	sed
0	20	78	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
7	13.3	83	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
14	13.3	77	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
30	5.2	89	nd	nd	nd	nd	0.2	nd	nd	nd	nd	nd
59	2.6	90	0.1	nd	<0.1	nd	0.1	nd	nd	nd	nd	nd
91	1.7	89	0.8	1.5	1.0	nd	1.3	nd	nd	nd	0.4	nd
120	2.5	82	2.4	2.2	1.2	nd	1.0	0.3	nd	nd	nd	nd
175	3.9	66	0.9	1.0	4.7	nd	1.8	0.4	nd	0.8	0.1	0.3
268	5.5	62	0.4	1.5	1.8	nd	1.0	0.7	1.4	1.4	3.6	nd
363	nd	34	1.6	1.0	16.4	0.3	nd	nd	nd	1.6	nd	0.7

nd: not detected

Itoh *et al.* (1988a) dissolved [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen at nominal concentrations of 0.2 mg/l in the presence of Tween 85 at 7.5 mg/l in sterilized distilled water and sterilized Muko River water and exposed the solutions to sunlight for about 8 h/day for 5 weeks at Hyogo, Japan, approximately 40° N. Pyriproxyfen was degraded with half-lives of 17.5 and 21 days in the distilled water and river water respectively, and was essentially stable in the dark controls. A theoretical half-life of 16 days was calculated for 40° N latitude from the quantum yield for pyriproxyfen photolysis. The main photoproducts were PYPA and CO_2, accounting for 16-30% and 11-29% of the applied ^{14}C respectively. POPA, POP and DPH-Pyr were minor identified products.

Fathulla *et al.* (1995d) exposed [*phenyl*-^{14}C] and [*pyridyl*-^{14}C]pyriproxyfen dissolved at 0.1 mg/kg in sterile aqueous buffer solutions at pH 7 to continuous artificial sunlight (xenon lamp, filtered to restrict UV light below 290 nm) for 14 days at 25°C. Recoveries of ^{14}C at the various sampling times ranged from 92% to 107%. Photolysis products were identified by TLC. Negligible amounts of volatile ^{14}C, including $^{14}CO_2$, were produced.

Pyriproxyfen decreased to 24% of the phenyl and 4.7% of the pyridyl-labelled compound by day 14, with estimated half-lives of 6.4 and 3.7 days respectively. No significant degradation was observed in the dark controls. The only major identified product was PYPA, accounting for 26% of

the initial ^{14}C on day 4 and 70% on day 14. Other photolytic products were not identified but consisted of a mixture of polar materials, probably polymerised phenolic and quinonoid compounds.

METHODS OF RESIDUE ANALYSIS

Analytical methods

Methods of residue analysis for pyriproxyfen and its degradation products in crops, animal products, soils and water were reported.

Gardner (1997) described analytical procedure CHE 33383-02R for pyriproxyfen in citrus peel and pulp. Samples were extracted with acetone, the extract was diluted with sodium chloride solution and partitioned with dichloromethane. This solution was cleaned up by column chromatography, on silica gel for peel and on Florisil for pulp. The eluates were evaporated and the residues taken up in toluene for analysis by GLC with an NPD. The LOD was 0.01 mg/kg.

Benwell (1997a) validated the method. Analytical recoveries from peel and pulp fortified at 0.01, 0.10 and 1.00 mg/kg were mean 95%, range 90-102% (n = 9) for peel and mean 84%, range 73-96% (n = 9) for pulp.

Van Zyl (1997) used the analytical method described by Kakuta *et al.* (1989) for pyriproxyfen in citrus whole fruit, peel and pulp in the South African citrus trials. The method was essentially that described by Gardner (1997). Analytical recoveries from samples fortified at 0.01-1.00 mg/kg were whole fruit mean 94%, range 70-108% (n = 5), peel mean 91%, range 82-108% (n = 13) and pulp mean 102%, range 87-110% (n = 13). The LOD was 0.01 mg/kg.

Orpella *et al*. (1997) used a method similar to CHE 33383-02R with the Florisil clean-up for the determination of pyriproxyfen residues in tomatoes. Analytical recoveries from tomatoes fortified at 0.01, 0.10 and 1.00 mg/kg were mean 102%, range 92-109% (n = 15). The LOD was 0.01 mg/kg.

Kruplak (1996a) described method RM-33P-2-2 (a modification of RM-33/P-2; see below) for pyriproxyfen and PYPAC residues in cotton seed. The residues were extracted in a blender with acetonitrile/water (4:1) and the filtrate was mixed with ethyl acetate to prevent foaming during rotary evaporation to an aqueous phase. This was diluted with 5% aqueous sodium chloride and the pyriproxyfen was extracted into dichloromethane; PYPAC remained in the water. The dichloromethane was evaporated to leave a residue which was taken up in hexane and acetonitrile. The acetonitrile layer was evaporated and the residue taken up in hexane and cleaned up on a silica gel column. Pyriproxyfen was determined by GLC with an NP detector. The aqueous phase containing PYPAC was acidified and the PYPAC extracted into ethyl acetate. The solvent was evaporated just to dryness and the PYPAC methylated by treatment with methyl iodide in methanolic tetrabutylammonium hydroxide at 45-50°C for 2 hours. After careful evaporation of the solvent the residue was taken up in hexane/ethyl acetate and cleaned up on a disposable silica gel column for GLC with an NP detector. The validated LOD for both compounds was 0.02 mg/kg. A trained analyst could analyse a set of 8 samples for pyriproxyfen and PYPAC in approximately 16 hours. Analytical recoveries from cotton seed fortified at 0.02 and 0.1 mg/kg were pyriproxyfen mean 87%, range 81-89% (n = 4); PYPAC mean 83%, range 72-95% (n = 4).

Pensyl (1996a) validated method RM-33P-2 for pyriproxyfen and PYPAC in cotton seed. RM-33P-2 was modified successively to RM-33P-2-3 after experience and suggestions from an independent laboratory. The LOD for both analytes was 0.02 mg/kg. Analytical recoveries from cotton seed fortified at 0.02 and 0.1 mg/kg were pyriproxyfen mean 76%, range 67-90% (n = 9); PYPAC mean 81%, range 79-90% (n = 9). Pensyl (1996b) used method RM-33P to determine

pyriproxyfen, PYPAC and DPH-Pyr in samples from the US supervised trials on cotton in 1994 and 1995. The results, corrected for control values, are shown in Table 33.

Table 33. Procedural recoveries of pyriproxyfen and metabolites from samples from the US supervised cotton trials in 1994 and 1995 (Pensyl, 1996b).

Compound	Sample	Fortification, mg/kg	Mean recovery, %	Range, %	No. of analyses
Pyriproxyfen	cotton seed	0.02	88	74-102	14
Pyriproxyfen	cotton seed	0.10	88	68-136	20
PYPAC	cotton seed	0.02	77	62-105	15
PYPAC	cotton seed	0.10	79	66-99	21
Pyriproxyfen	gin trash	0.02	100	47-119	5
Pyriproxyfen	gin trash	0.10	91	81-99	10
DPH-Pyr	gin trash	0.02	96	77-124	7
DPH-Pyr	gin trash	0.10	102	86-146	11
Pyriproxyfen	meal	0.02, 0.10		75-76	2
Pyriproxyfen	hulls	0.02, 0.10		70-75	2
Pyriproxyfen	crude oil	0.02, 0.10	89	75-101	6
Pyriproxyfen	refined oil	0.02, 0.10		97	2
PYPAC	meal	0.02, 0.10		64-78	2
PYPAC	hulls	0.02, 0.10		69-73	2
PYPAC	crude oil	0.02, 0.10	75	72-80	6
PYPAC	refined oil	0.02, 0.10		51-64	2

Green (1997) analysed milk for pyriproxyfen, POP and 4'-OH-Pyr by method RM-33G-2 and for 2,5-OH-Py by RM-33G-3. The methods include an acid hydrolysis step to release POP and 4'-OH-Pyr from conjugates. In G-2 milk was extracted with an ethyl acetate/methanol mixture, and the solvent evaporated to leave an aqueous solution which was extracted with ethyl acetate. The residue in the ethyl acetate was further cleaned up by acetonitrile/hexane partitioning and an aliquot was purified on an alumina column and analysed for pyriproxyfen by GLC with an NPD. A second portion of the aqueous residue after evaporation of the original ethyl acetate/methanol extract was hydrolysed with 1N HCl for 2 hours to convert the conjugates to free POP and 4'-OH-Pyr, which were cleaned up on a silica gel column and determined by HPLC with a UV detector (275 nm). Analytical recoveries from 22 samples of milk fortified at 0.02 or 0.10 mg/kg were pyriproxyfen mean 90%, range 71-104%, POP mean 93%, range 76-115% and 4'-OH-Pyr mean 84%, range 69-105%.

RM-33G-3 for 2,5-OH-Py and its conjugates was similar to RM-33G-2, except that the extract was cleaned up on a benzenesulfonic acid column after hydrolysis. Free 2,5-OH-Py was then determined by HPLC with fluorescence detection (excitation 320 nm, emission 395 nm). Recoveries from milk fortified at 0.02 and 0.10 mg/kg were mean 96%, range 66-129% (n = 24).

Green (1997) also analysed muscle, fat, liver and kidneys for pyriproxyfen by method RM-33T-1 and for 4'-OH-Pyr by RM-33T-2, and liver and kidneys for POP by RM-33T-3 and for 2,5-OH-Py by RM-33T-4. These methods are essentially identical to RM-33-G2 and -G3 except that the HPLC of POP was with fluorescence detection (excitation 235, emission 327 nm). Analytical recoveries at 0.02 and 0.10 mg/kg were pyriproxyfen mean 93%, range 87-99% (n = 8); 4'-OH-Pyr mean 81%, range 68-88% (n = 8); POP mean 83%, range 69-106% (n = 8); 2,5-OH-Py mean 86%, range 73-96% (n = 6). The LODs were typically 0.01-0.02 mg/kg.

Pensyl (1994a,b) described method RM-33S-1 for pyriproxyfen and PYPAC, and RM-33S-2 for 4'-OH-Pyr in soil. In 33S-1 residues were extracted with methanol/0.1N NaOH and the methanol evaporated. The remaining aqueous solution was diluted with sodium chloride solution and the pyriproxyfen extracted with dichloromethane; PYPAC remained in the aqueous phase. The dichloromethane was evaporated and the residues were taken up in hexane/ethyl acetate and cleaned

up on an alumina column for GLC with an NPD. The aqueous solution containing PYPAC was acidified with hydrochloric acid and extracted with ethyl acetate. The extract was evaporated, the residue methylated with methyl iodide in methanolic tetrabutylammonium hydroxide and, after evaporations and extractions, taken up in hexane/ethyl acetate for GLC with an NPD. Care must be taken during evaporation of methyl PYPAC or residues will be lost. The LOD for both analytes was 0.01 mg/kg. Analytical recoveries from soil fortified at 0.02 and 0.1 mg/kg were pyriproxyfen mean 91%, range 88-95% (n = 9); PYPAC mean 74%, range 69-79% (n = 12); 4-OH-Pyr mean 94%, range 74-105% (n = 12). RM-33S-2 was superseded by RM-33S-3-3, described below.

Pensyl (1995a,b) used methods RM-33S-1 and RM-33S-2 for soil analyses in field dissipation studies. The procedural recoveries are shown in Table 34.

Table 34. Procedural recoveries of pyriproxyfen and degradation products from soil in field dissipation studies (Pensyl, 1995a,b).

Compound	Location	Fortification, mg/kg	Mean recovery, %	Range, %	No. of analyses
Pyriproxyfen	CA	0.02	97	73-146	19
Pyriproxyfen	MS	0.02	86	66-106	15
Pyriproxyfen	CA	0.10	106	74-129	20
Pyriproxyfen	MS	0.10	101	78-119	15
PYPAC	CA	0.02	67	52-87	16
PYPAC	MS	0.02	72	59-90	14
PYPAC	CA	0.10	73	49-97	15
PYPAC	MS	0.10	83	66-100	14
4'-OH-Pyr	CA	0.02	107	80-168	16
4'-OH-Pyr	MS	0.02	80	62-134	18
4'-OH-Pyr	CA	0.10	113	98-131	17
4'-OH-Pyr	MS	0.10	105	81-123	18

Kruplak (1996b) validated method RM-33S-1-5 for pyriproxyfen and PYPAC in soil. The residues were extracted with methanol/0.1N NaOH, the methanol was evaporated and the extract diluted with water, adjusted to pH 7 and extracted with dichloromethane. Pyriproxyfen was in the dichloromethane phase and PYPAC in the aqueous phase. The remainder of the procedure followed that of RM-33P-2-2 for cotton seed. The author stressed the care necessary during the evaporation of solutions of methylated PYPAC, which may easily be lost because of its volatility. Analytical recoveries from soil fortified at 0.02 and 0.1 mg/kg were pyriproxyfen mean 91%, range 88-92% (n = 4); PYPAC mean 97%, range 85-115% (n = 4).

Kruplak (1996c) described method RM-33S-3-3, a development of RM-33S-2, for the determination of 4'-OH-Pyr. Soil was extracted with a methanol/phosphate buffer and the filtrate evaporated to yield an aqueous concentrate which was mixed with sodium chloride solution and extracted with ethyl acetate. The ethyl acetate was evaporated to leave a residue that was taken up in hexane/ethyl acetate for clean-up on a disposable silica gel column. The eluate was evaporated to dryness and the residue taken up in methanol/water for reversed-phase HPLC analysis with fluorescence or UV detection. The LOD was 0.02 mg/kg. A trained analyst can complete the analysis of a set of 8 samples in about 8 hours. Analytical recoveries from soil fortified at 0.02 and 0.1 mg/kg were mean 92%, range 78-99% (n = 4).

Nandihalli (1996) determined the recoveries of pyriproxyfen and PYPAC by an FDA multi-residue GLC method from fortified cotton seed and apple samples, representing fatty and non-fatty foods. Adequate recoveries of pyriproxyfen were achieved at 0.05 and 0.5 mg/kg, but PYPAC was not recovered from the Florisil column clean-up.

Schuster (1989) validated the analytical method for pyriproxyfen in aquarium water used in the ecotoxicology tests. The residues were extracted with dichloromethane, the dichloromethane was

evaporated and the residue was taken up in hexane for analysis by GLC with an NPD. The validated LOD was 1 µg/l. Recoveries over the concentration range 1.15 µg/l to 11.5 mg/l were mean 105%, range 102-111% (n = 10).

Stability of pesticide residues in stored analytical samples

Green (1997) stored cattle tissue samples fortified with pyriproxyfen and metabolites at -20ºC (Table 35). When pyriproxyfen was stored with liver, fat and muscle for 1 month the estimated times for 30% decrease were 45, 55 and 68 days respectively. 4'-OH-Pyr was stored 96 days in fat and 71 days in muscle where the estimated times for 30% decrease were 200 and 90 days respectively. 4'-OH-Pyr sulfate and POP sulfate were stored with liver for about 2 months; the estimated times for 30% decrease of the conjugate + free metabolite were 110 days and 66 days respectively. 2,5-OH-Py in kidneys decreased by 30% in an estimated 24 days.

Table 35. Freezer storage stability of pyriproxyfen and metabolites in muscle, fat, liver and kidneys fortified at 0.1 mg/kg and stored at –20ºC (Green, 1997). The % remaining is not corrected for the corresponding procedural recovery.

Compound	Sample	Storage period, days	Procedural recovery, %	% remaining	Estimated time for 30% decrease, days
Pyriproxyfen	liver	0	86	100, 103	
Pyriproxyfen	liver	15	104	90 86	
Pyriproxyfen	liver	32	105	79 79	45 days
Pyriproxyfen	muscle	0		91 95	
Pyriproxyfen	muscle	16	88	71 80	
Pyriproxyfen	muscle	31	102	82 76	68 days
Pyriproxyfen	fat	0		90 93	
Pyriproxyfen	fat	14	96	86 86	
Pyriproxyfen	fat	33	103	78 70	55 days
4'-OH-Pyr	fat	0		76 78	
4'-OH-Pyr	fat	13	70	66 67	
4'-OH-Pyr	fat	96	74	56 67	200 days
4'-OH-Pyr	muscle	0	82	75 84	
4'-OH-Pyr	muscle	14	84	80 79	
4'-OH-Pyr	muscle	30	75	72 72	
4'-OH-Pyr	muscle	71	70	64 58	90 days
4'-OH-Pyr conj [1]	liver	0		81 84	
4'-OH-Pyr conj [1]	liver	15	70	76 77	
4'-OH-Pyr conj [1]	liver	28	77	77 76	
4'-OH-Pyr conj [1]	liver	57	66	69 67	110 days
POP conj [2]	liver	0		76 74	
POP conj [2]	liver	29	80	74 81	
POP conj [2]	liver	51	67	63 69	
POP conj [2]	liver	72	68	43 59	66 days
2,5-OH-Py	kidneys	0		86 86	
2,5-OH-Py	kidneys	22	83	71 65	
2,5-OH-Py	kidneys	53	88	48 60	
2,5-OH-Py	kidneys	119	70	16 14	24 days

[1] Fortified with the sulfate conjugate at 0.10 mg/kg expressed as 4'-OH-Pyr
[2] Fortified with the sulfate conjugate at 0.10 mg/kg expressed as POP

Goller (1998) stored tomato homogenate spiked with pyriproxyfen at 0.10 mg/kg at -18°C for 12 months. Samples were analysed by method NNA-90-0016, similar to CHE 333/83-02R. The initial acetone extract was evaporated to an aqueous solution, which was mixed with 5% sodium chloride and extracted with dichloromethane. The dichloromethane extract was evaporated and the residue taken up in hexane, cleaned up on a Florisil column and analysed by GLC with a thermionic detector. The LOD was 0.01 mg/kg.

Pyriproxyfen was stable for at least the 12 months of the study (Table 36).

Table 36. Stability of pyriproxyfen in tomato homogenate fortified at 0.10 mg/kg and stored at –18ºC (Goller, 1998). The % remaining is not corrected for the corresponding procedural recovery.

Storage period, months	Procedural recovery, %	% remaining
0	93	105, 102
1	92	89, 97
3	104	96, 101
6	84	73, 75
12	86	96, 98

Pensyl (1996b) determined the stability of pyriproxyfen, PYPAC and DPH-Pyr added to cotton seed, gin trash and oil at 0.1 mg/kg and stored at -20°C (Table 37) in conjunction with supervised residue trials on cotton. The compounds were stable for the periods tested, except that DPH-Pyr was of marginal stability in gin trash for 6 months, decreasing by 30% in about 150 days.

Table 37. Stability of pyriproxyfen and metabolites in cotton seed, gin trash and crude oil fortified at 0.1 mg/kg and stored at –20ºC (Pensyl, 1996b). The % remaining is not corrected for the corresponding procedural recovery.

Compound	Sample	Storage period, days	Procedural recovery, %	% remaining (2 stored samples)
Pyriproxyfen	cotton seed	0	89	77 83
Pyriproxyfen	cotton seed	29	136	101, 126
Pyriproxyfen	cotton seed	91	87	98, 86
Pyriproxyfen	cotton seed	395	86	75, 71
PYPAC	cotton seed	0	95	97, 99
PYPAC	cotton seed	31	83	83, 90
PYPAC	cotton seed	141	71	70, 78
PYPAC	cotton seed	380	84	83, 84
Pyriproxyfen	gin trash	0	99	89, 88
Pyriproxyfen	gin trash	71	99	106, 93
Pyriproxyfen	gin trash	231	99	72, 75
DPH-Pyr	gin trash	0	86	90, 92
DPH-Pyr	gin trash	89	102	64, 60
DPH-Pyr	gin trash	178	81	62, 55
Pyriproxyfen	cotton seed oil, crude	0	95	89, 87
Pyriproxyfen	cotton seed oil, crude	32	101	99, 99
PYPAC	cotton seed oil, crude	0	74	72, 80
PYPAC	cotton seed oil, crude	32	74	84, 82

Pensyl (1995a,b) determined the stability of pyriproxyfen, PYPAC and 4'-OH-Pyr added to California and Mississippi soil and stored at a nominal -20°C (Table 38) in conjunction with dissipation studies. The California soil was classified as a sandy loam (60% sand, 28% silt, 12% clay, 0.6% organic matter, pH 8.6) and the Mississippi soil as a silt loam (32% sand, 52% silt, 16% clay, 0.8% organic matter, pH 5.9).

Pyriproxyfen and PYPAC were stable for the periods tested (210-218 days). 4'-OH-Pyr was stable in the California soil for the 168 days of the trial, but unstable in the Mississippi soil with about half of the original concentration remaining after 3 and 7 days. All the samples of Mississippi soil analysed for 4'-OH-Pyr in the dissipation trial were therefore extracted within 3-5 days of sampling.

Table 38. Stability of pyriproxyfen and metabolites in soil samples fortified at 0.1 mg/kg and stored at –20ºC (Pensyl, 1995a,b). The % remaining is not corrected for the corresponding procedural recovery.

Compound	Location	Storage period, days	Procedural recovery, %	%, remaining, (2, stored, samples)
Pyriproxyfen	CA	0	87	74, 86
Pyriproxyfen	CA	29	86	88, 88
Pyriproxyfen	CA	116	87	94, 84
Pyriproxyfen	CA	211	106	89, 102
PYPAC	CA	0	88	72, 86
PYPAC	CA	56	98	83, 88
PYPAC	CA	150	65	73, 74
PYPAC	CA	218	84	82, 79
4'-OH-Pyr	CA	0	97	98, 106
4'-OH-Pyr	CA	1	93	91, 89
4'-OH-Pyr	CA	7	116	117, 125
4'-OH-Pyr	CA	15	125	108, 105
4'-OH-Pyr	CA	29	105	103, 110
4'-OH-Pyr	CA	99	100	111, 114
4'-OH-Pyr	CA	168	139	81, 99
Pyriproxyfen	MS	0	118	118, 120
Pyriproxyfen	MS	29	94	88, 85
Pyriproxyfen	MS	116	96	63, 69
Pyriproxyfen	MS	210	110	75, 64
PYPAC	MS	0	80	84, 79
PYPAC	MS	56	87	90, 82
PYPAC	MS	149	71	69, 63
PYPAC	MS	218	79	86, 88
4'-OH-Pyr	MS	0	87	96, 98
4'-OH-Pyr	MS	1	80	60, 62
4'-OH-Pyr	MS	3	93	52, 50
4'-OH-Pyr	MS	7	107	46, 43
4'-OH-Pyr	MS	20	118	35, 44
4'-OH-Pyr	MS	36	107	29, 26

Definition of the residue

The main residue in the metabolism studies on plant commodities was pyriproxyfen itself. In cotton seed the levels of free + conjugated PYPAC and PYPA exceeded that of pyriproxyfen, which was very low, probably because the metabolites were translocated more readily. PYPAC in cotton seed in the metabolism study was about 60% free and 40% conjugated, but in the trials on cotton free PYPAC was generally undetected and lower than pyriproxyfen in the seed.

The residue can be defined as pyriproxyfen for enforcement in crops.

In animal commodities the composition of the residue varies in different tissues. Pyriproxyfen itself is fat-soluble (log P_{OW} 5.37) so it predominates in fat. In muscle all the residues are very low, but pyriproxyfen is again the main component. In milk and liver 4'-OH-Pyr with its sulfate conjugate are the main residues, while in kidneys POP is the main residue with 4'-OH-Pyr also a significant component. Pyriproxyfen predominates in eggs.

The feeding study on dairy cows suggests that the residues in milk and tissues will generally be undetectable or very low whatever the residue definition, except pyriproxyfen itself in fat and the fat of milk at the higher dietary burdens. The Meeting agreed it would be unpractical to define the residue to include metabolites and their conjugates in liver and kidneys for undetectable residues; it would create a pointless additional analytical expense.

Pyriproxyfen is also a suitable definition of the residue for dietary intake estimates.

Proposed definition of the residue (for compliance with MRLs and for the estimation of dietary intake): pyriproxyfen.

The residue is fat-soluble.

USE PATTERN

Pyriproxyfen is an insect growth regulator with insecticidal activity against public health insect pests: houseflies, mosquitoes and cockroaches. In agriculture and horticulture pyriproxyfen has registered uses for the control of scale, whitefly, bollworm, jassids, aphids and cutworms. Registered uses of pyriproxyfen are shown in Table 39.

Table 39. Registered uses of pyriproxyfen.

Crop	Country	Form	Application					PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hl	Water vol l/ha	No.	
Apple	Israel	EC	foliar		0.015	1500-2000	1	[1]GS
Bean	Brazil	EC	foliar	0.1		200-250	2	14
Cabbage	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Cabbage	Israel	EC	foliar	0.075		80-100		14
Carrot	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Citrus	Brazil	EC	foliar		0.005-0.0075	10 l/tree	2	14
Citrus	Cyprus	EC	foliar		0.005-0.0075		2	30
Citrus	Israel	EC	foliar	0.25-0.40	0.01	2500-4000		[2]GS
Citrus	Lebanon	EC	foliar		0.0075			30
Citrus	South Africa	EC	foliar		0.0030		3	[3]90
Citrus	Spain	EC	foliar		0.0025-0.0075		2	30
Citrus	Turkey	EC	foliar		0.005			30
Citrus	UAE	EC	foliar		0.0025-0.0075		1	[4]GS
Citrus	Zimbabwe	EC	foliar		0.0075		1	[5]90
Citrus	Zimbabwe	EC	foliar		0.0030		2	[6]90
Cotton	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Cotton	El Salvador	EC	(a) foliar	0.05		15-27	2	30
Cotton	El Salvador	EC	foliar	0.05		290	2	30
Cotton	Israel	EC	(a) foliar	0.075		30-200		30
Cotton	Israel	EC	foliar	0.075		30-200		30
Cotton	Pakistan	[8]EC	foliar	0.038-0.05				
Cotton	Sudan	[7]EC	(a) foliar	0.044		23	2	
Cotton	Turkey	EC	foliar		0.005			30
Cotton	Turkey	[8]EC	foliar	0.05				15
Cotton	USA	EC	(a) foliar	0.059-0.075		28-94	1	28
Cotton	USA	EC	foliar	0.059-0.075		94-470	1	28

[1] Until fruit set or after picking

[2] End of May in varieties picked until end of December. End of June in varieties picked after the end of December.

[3] First spray late November or December, second spray at bud burst, third spray at 80-100% petal drop or shortly thereafter.

[4] Apply at bud burst or petal drop.

[5] Apply at bud burst or at 80-100% petal drop or shortly thereafter.

[6] First spray at bud burst. Second spray at 80-100% petal drop or shortly thereafter.

[7] Formulation contains pyriproxyfen + fenpropathrin

[8] Formulation of fenpropathrin (150 g/l) and pyriproxyfen (50 g/l)

Crop	Country	Form	Application					PHI, days
			Method	Rate, kg ai/ha	Spray conc. kg ai/hl	Water vol l/ha	No.	
Cucumber	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Egg plant	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Egg plant	Israel	EC	foliar	0.075		80-100		14
Egg plant	Lebanon	EC	foliar		0.0075			30
Egg plant	Netherlands	EC	foliar	0.013-0.038	0.0025	500-1500	2 g	3
Grape-vine	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Melon	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Melon	Israel	EC	foliar	0.075		80-100		14
Okra	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Olive	Israel	EC	foliar		0.010-0.015	2000-2500		[1]GS
Peach	Israel	EC	foliar		0.015	1500-2000	1	[1]GS
Pear	Israel	EC	foliar		0.015	1500-2000	1	[1]GS
Pear	Lebanon	EC	foliar		0.0075			45
Peppers	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Peppers, sweet	Netherlands	EC	foliar	0.013-0.038	0.0025	500-1500	2 g	3
Persimmon	Israel	EC	foliar		0.007	1500		[9]GS
Plum	Israel	EC	foliar		0.015	1500-2000	1	[1]GS
Pumpkin	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Soybean	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14
Tomato	Brazil	EC	foliar		0.005-0.01	800-1000	2	7
Tomato	Lebanon	EC	foliar		0.0075			30
Tomato	Netherlands	EC	foliar	0.013-0.038	0.0025	500-1500	2 g	3
Tomatoes	Turkey	EC	foliar		0.0038		1	15
Watermelon	Brazil	EC	foliar	0.05-0.1	0.005-0.01		2	14

(a) aerial application
g: glasshouse use
GS growth stage

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised field trials on citrus and cotton.

Table 40 Citrus fruits (mandarin, orange, grapefruit). *Israel, Italy, South Africa, Spain.*
Table 41 Cotton seed. *USA.*
Table 42 Cotton gin trash. *USA.*

Where residues were not detected they are recorded in the Tables as below the limit of determination (LOD), e.g. <0.01 mg/kg. Residues, application rates and spray concentrations have generally been rounded to 2 significant figures or, for residues near the LOD, to 1 significant figure. Although trials included control plots, control residues are recorded in the Tables only if they exceeded the LOD. Residues are recorded uncorrected for recovery.

Oranges and mandarins were treated with pyriproxyfen in trials in Spain in 1991 by a knapsack motorised hand-lance sprayer. The plots were single trees and field samples of 1 kg or 5 fruits were harvested for analysis. Fruit were stored in a freezer for approximately 4 months before analysis. Orange trials in Spain in 1992 were similar except that the trees were sprayed to run-off and field samples of 2 kg were stored for 7-8 weeks before extraction and analysis. The field reports for the trials in study NNR-31-0021 were very brief.

[9] Until middle of June

Single mandarin trees were sprayed with a motor pump in supervised trials in Spain in 1992. Field samples of 2 kg were stored for 24 weeks before analysis. Procedural recoveries were in the range 47-78%.

In Italian trials on mandarins and oranges in 1991, pyriproxyfen was applied by knapsack motor sprayer to plots of 6 trees. Field samples of 12 fruits or 2 kg were stored for 101-117 days before analysis.

Pyriproxyfen was applied to orange and mandarin trees with a diaphragm pump and spray gun in Spain in supervised trials in 1997. Plot sizes were 8-20 trees and field samples of 2 kg or 12 fruit were analysed after very short periods in storage.

Mandarin and orange trees were treated by hand gun sprayer in South African trials in 1997. Plots were of 6 trees, and field samples of 2 kg (12-24 fruit) were stored for 14 weeks before analysis. In orange trials in 1998, plots of 4 rows of 8-10 trees were sprayed with a high-pressure pump and spray gun. Field samples of at least 2 kg (12-24 fruit) were stored for 15 weeks before analysis.

In a series of grapefruit trials in Israel in 1997 pyriproxyfen was applied by high-pressure spray gun to plots of 5 rows of 10 trees. Field samples of 13 fruits or 2 kg were stored for 233-375 days before analysis. Residues in the mature fruit were calculated from separate analyses of peel and pulp. Peel constituted 37-45% of the weight of the fruit. The trees were treated from 4 June to 10 June in the 5 trials and grapefruit were harvested from 7 October to 19 October. This is not strictly in accord with the label instructions which permit application until the end of May for varieties picked until the end of December and application until the end of June for varieties picked after the end of December. The time for a 30% residue decrease was estimated from three decline trials as 27, 51 and 75 days, demonstrating quite a slow decrease and hence sufficient latitude to interpret the timing as matching GAP conditions.

Fifteen trials on cotton in 1994 and 1995 were geographically distributed to represent 97% of the commercial cotton production area in the USA. Tractor-mounted boom sprays were used in all trials except the Californian trials in 1994 and trial V-11117-E in 1995 where backpack sprayers with hand-held booms were used. The plot sizes ranged from 4 rows of 30 m to 12 rows of 70 m. The field samples were at least 1.2 kg of undelinted seed. The longest periods of frozen storage of the samples were 157 days for pyriproxyfen determination and 180 days for PYPAC determination.

In six trials in 1995, unginned cotton (20 kg) was harvested and processed to produce gin trash (plant residues from ginning cotton - burrs, leaves, stems, lint, immature seeds), which is used as an animal feed (Table 42). Residues were determined in the samples as received, but moisture levels were measured and are recorded in Table 42.

Table 40. Pyriproxyfen residues in citrus fruit resulting from supervised trials in Israel, Italy, South Africa and Spain from 1991 to 1998. Double-underlined residues were from treatments according to GAP and are valid for the estimation of maximum residue levels.

Location, year (variety)	Application					PHI, days	Pyriproxifen, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	kg ai/ha			
MANDARIN								
Italy (Marina), 1996 (Clementina)	EC	0.075	0.0075	1000	1	44 60	peel 0.23 pulp <0.01 wf 0.08 [2] peel 0.11 pulp <0.01 wf 0.04 [2]	NNR-0047 Pyriproxyfen-IT-1996-3
South Africa (Cape Province), 1997 (Clementine Nules)	EC	0.36	0.003	12000	1 2	63 0 30 60 90 120	0.03 0.03 0.23 0.28 0.09 0.11 0.04 0.06 peel 0.065 pulp <0.01 wf <u>0.02</u> peel 0.045 pulp <0.01 wf 0.01	NNR-0048 IK30196/97
Spain (Valencia), 1991 (Fortuna)	EC	0.08	0.005	1600	1	31 45 61	<u>0.069</u> 0.057 0.062	NNR-21-0018 S/SP/E/91971
Spain (Betera), 1992 (Fortuna)	EC		0.005		1	17 31 45 60	0.14 <u>0.20</u> 0.19 0.15	NNR-31-0022[3] S/SP/M/92163
Spain (Rafeguaraf), 1992 (Fortuna)	EC		0.005		1	16 31 45 60	0.20 <u>0.33</u> 0.30 0.28	NNR-31-0022[3] S/SP/M/92160
Spain (Murcia), 1997 (Clemenules)	EC	0.23	0.0075	3000	1 GS 77	0 60	0.48 0.03	NNR-0054S R10.A.97.026
Spain (Murcia), 1997 (Marisol)	EC	0.23	0.0075	3000	1 GS 78	0 15 30 45 60	0.23 0.18 0.09 <u>0.10</u> 0.06	NNR-0054S R10.A.97.027
ORANGE								
Italy (Marina), 1996 (Navalin)	EC	0.075	0.0075	1000	1	0 14 28 44 60	peel 0.31 pulp <0.01 wf 0.11 [2] peel 0.14 pulp <0.01 wf 0.04 [2] peel 0.12 pulp <0.01 wf 0.04 [2] peel 0.10 pulp <0.01 wf 0.03 [2] peel 0.15 pulp <0.01 wf <u>0.06</u> [2]	NNR-0047 Pyriproxyfen-IT-1996-1
Italy (Marina), 1996 (Navalin)	EC	0.075	0.0075	1000	1	44 60	peel 0.11 pulp <0.01 wf 0.04 [2] peel 0.08 pulp <0.01 wf 0.02 [2]	NNR-0047 Pyriproxyfen-IT-1996-2

Location, year (variety)	Application					PHI, days	Pyriproxifen, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	kg ai/ha			
South Africa (Cape province), 1997 (Navel)	EC	0.36	0.003	12000	1 2	64 0 30 60 90 120	<0.01 (2) 0.10 0.11 0.03 0.03 0.02 0.02 peel 0.045 pulp <0.01 wf 0.01 peel 0.085 pulp <0.01 wf 0.02	NNR-0048 IK30296/97
South Africa (Hazyview Mpumalanga), 1998 (Valencia)	EC	0.36	0.003	12000	1 2	105 0 30 60 90 120	<0.01 0.09 0.06 peel 0.12 pulp <0.01 wf 0.04 [2] peel 0.16 pulp <0.01 wf 0.05 [2] peel 0.18 pulp <0.01 wf 0.05 [2]	NNR-0060 311P130
South Africa (Karino Irial Mpumalanga), 1998 (Valencia)	EC	0.36	0.003	12000	1 2	105 0 30 60 90 120	<0.01 0.09 0.05 peel 0.12 pulp <0.01 wf 0.04 [2] peel 0.19 pulp <0.01 wf 0.05 [2] peel 0.20 pulp <0.01 wf 0.06 [2]	NNR-0060 311P130
Spain (Valencia), 1991 (Navelate)	EC	0.08	0.005	1600	1	31 45 61	0.12 0.11 0.08	NNR-21-0018 S/SP/E/91972
Spain (Albalat), 1992 (Navel)	EC		0.005	runoff	1	17 31 45 61	0.25 0.25 0.20 0.18	NNR-31-0021 S/SP/M/92161
Spain (Betera), 1992 (Navelate)	EC		0.005	runoff	1	17 31 45 60	0.25 0.22 0.25 0.20	NNR-31-0021 S/SP/M/92162
Spain (Murcia), 1997 (Navelina)	EC	0.23	0.0075	3000	1 GS 77	0 15 30 45 60	0.17 0.10 0.06 0.08 0.04	NNR-0054S R10.A.97.025
Spain (Murcia), 1997 (New Hall)	EC	0.23	0.0075	3000	1 GS 78	0 60	0.25 0.03	NNR-00548S R10.A.97.024
GRAPEFRUIT								
Israel (Mazkeret Batyia), 1997 (Sweetie)	EC	0.35	0.01	3500	1 4 June	137 19 Oct	peel 0.07 pulp <0.01 wf 0.03 [2]	NNR-0059 1628/1
Israel (Gimzo), 1997 (Sweetie)	EC	0.4	0.01	4000	1 4 June	63 98 125 130 12 Oct	0.06 0.07 0.04 peel 0.08 pulp <0.01 wf 0.04 [2]	NNR-0059 1628/1

Location, year (variety)	Application					PHI, days	Pyriproxifen, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	kg ai/ha			
Israel (Mesilot), 1997 (Sweetie)	EC	0.3	0.01	3000	1 8 June	0 59 94 121 7 Oct	0.37 0.13 0.09 peel 0.21 pulp <0.01 wf 0.08 [2]	NNR-0059 1628/1
Israel (Hadasim), 1997 (Sweetie)	EC	0.4	0.01	4000	1 8 June	59 94 121 126 12 Oct	0.04 0.04 0.03 peel 0.07 pulp <0.01 wf 0.03 [2]	NNR-0059 1628/1
Israel (Hadera), 1997 (Sweetie)	EC	0.35	0.01	3500	1 10 June	124 12 Oct	peel 0.06 pulp <0.01 wf 0.03 [2]	NNR-0059 1628/1

[1] wf: whole fruit
[2] Residues in whole fruit calculated from residues in peel and pulp.
[3] Analytical recoveries in this trial were in the range 47-78%. Residues, as in the other trials, are not corrected for recoveries.

Table 41. Pyriproxyfen and PYPAC residues in cotton seed resulting from supervised trials in the USA in 1994 and 1995 (Pensyl, 1996b). Double-underlined residues were from treatments according to GAP and were used to estimate an STMR and a maximum residue level.

Location year (variety)	Application					PHI, days	Pyriproxyfen, mg/kg	PYPAC, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	no.				
AZ, 1994 (Delta Pine 50)	EC	0.10	0.053 +0.051	189 +196	2	29	<0.01	<0.01	NNR-0035 V-10946-A
AZ, 1994 (Delta Pine 50)	EC	0.19	0.10 +0.097	189 +196	2	29	0.02	0.01	NNR-0035 V-10946-A
CA, 1994 (Malla)	EC	0.097	0.040	240	2	29	0.02	<0.01	NNR-0035 V-10946-B
CA, 1994 (Malla)	EC	0.20	0.083	240	2	29	0.02	<0.01	NNR-0035 V-10946-B
TX, 1994 (MD51)	EC	0.10	0.053	186	2	29	<0.01	<0.01	NNR-0035 V-10946-C
TX, 1994 (MD51)	EC	0.20	0.11	187	2	29	<0.01	<0.01	NNR-0035 V-10946-C
GA, 1995 (DES 119)	EC	0.049 +2×0.074	0.034 +2×0.052	143	3	28	<0.01	<0.01	NNR-0035 V-11117-A
AR, 1995 (Stoneville 453)	EC	0.049 +2×0.074	0.035 +2×0.053	140	3	28	0.03	<0.01	NNR-0035 V-11117-B
TX, 1995 (Quickie)	EC	0.050 +2×0.074	0.035 +2×0.053	140	3	28	0.03	<0.01	NNR-0035 V-11117-C

Location year (variety)	Application					PHI, days	Pyriproxyfen, mg/kg	PYPAC, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	no.				
TX, 1995 (HS-200)	EC	0.050 +2×0.074	0.035 +2×0.053	140	3	28	0.01	<0.01	NNR-0035 V-11117-D
TX, 1995 (Paymoster 145)	EC	0.049 +2×0.075	0.036 +2×0.053	136 +140 +140	3	30	0.04	<0.01	NNR-0035 V-11117-E
TX, 1995 (Alltex Quickie)	EC	0.050 +2×0.075	0.035 +2×0.053	142 +142 +139	3	30	0.03	<0.01	NNR-0035 V-11117-F
TX, 1995 (MD 51)	EC	0.049 +2×0.075	0.035 +2×0.053	138 +144 +140	3	28	<0.01	<0.01	NNR-0035 V-11117-G
AZ, 1995 (Delta Pine 20)	EC	0.050 +2×0.074	0.035 +2×0.053	142 +141 +140	3	28	0.03	<0.01	NNR-0035 V-11117-H
LA, 1995 (DPL 51)	EC	0.050 +0.079 +0.075	0.035 +2×0.052	145 +152 +146	3	21 28 35	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	NNR-0035 V-11117-I
LA, 1995 (DPL 51)	EC	0.10 +0.16 +0.15	0.069 +2×0.10	144 +156 +145	3	28	<0.01	0.01[2]	NNR-0035 V-11117-I
CA, 1995 (Maxxa)	EC	0.049 +2×0.074	0.034 +2×0.052	144	3	21 28 35	<0.01 <0.01 <0.01	<0.01 <0.01 <0.01	NNR-0035 V-11117-J
CA, 1995 (Maxxa)	EC	0.10 +2×0.15	0.069 +2×0.10	143	3	28	0.02	<0.01	NNR-0035 V-11117-J
MS, 1995 (Delta Pine 50)	EC	0.050 +2×0.074	0.035 +2×0.053	141	3	28	<0.01	<0.01	NNR-0035 V-11117-K
AZ, 1995 (DP 5415)	EC	0.049 +2×0.072	0.035 +2×0.053	139	3	28	0.03	<0.01	NNR-0035 V-11117-M
AZ, 1995 (DP 5415)	EC	0.25 +2×0.36	0.17 +2×0.26	141 +138 +136	3	28	0.1	<0.01	NNR-0035 V-11117-N

[1] Unconjugated.
[2] <0.01 mg/kg on confirmatory GLC column.

Table 42. Pyriproxyfen and DPH-Pyr residues in cotton gin trash resulting from supervised trials in the USA 1995 (Pensyl, 1996b) and ginning of 20 kg lots of seed cotton. Residues are expressed on samples as received.

Location, year (variety)	Application					PHI, days	Pyriproxyfen, mg/kg	DPH-Pyr mg/kg	Moisture, %	Ref
	Form	kg ai/ha	kg ai/hl	water, l/ha	no.					
GA, 1995 (DES 119)	EC	0.049 +2×0.074	0.034 +2×0.052	143	3	28	0.45 c 0.04	0.04	21.8%	NNR-0035 V-11117-A
TX, 1995 (Quickie)	EC	0.050 +2×0.074	0.035 +2×0.053	140	3	28	0.68	0.03	29.8%	NNR-0035 V-11117-C
TX, 1995 (HS-200)	EC	0.050 +2×0.074	0.035 +2×0.053	140	3	28	0.35	0.08	30.3%	NNR-0035 V-11117-D
TX, 1995 (Paymoster 145)	EC	0.049 +2×0.075	0.036 +2×0.053	136 +140 +140	3	30	0.66	<0.01	21.8%	NNR-0035 V-11117-E
MS, 1995 (Delta Pine 50)	EC	0.050 +2×0.074	0.035 +2×0.053	141	3	28	1.4	0.06	14.9%	NNR-0035 V-11117-K
AZ, 1995 (DP 5415)	EC	0.049 +2×0.072	0.035 +2×0.053	139	3	28	2.3	0.07 c 0.07	13.8%	NNR-0035 V-11117-M

c: control

Groups of 3 lactating dairy cows (each weighing 400-620 kg and producing approximately 15 kg milk per day) were dosed with pyriproxyfen by gelatin capsule at 0.13, 0.38 or 1.17 mg/kg bw/day, equivalent to nominal feed levels of 3, 9 and 30 ppm in the diet on a dry weight basis for 28 days (Green, 1997). Milk was collected from two milkings each day for analysis. Each animal consumed 8.0 kg prepared feed, 16 kg alfalfa hay cubes and 2 kg bailed hay as the basal daily feed (Helsten, 1996). The animals were slaughtered on day 29. Muscle samples were composites of hind quarter, pectoral and abductor muscle in equal proportions, and fat samples of perirenal, abdominal and subcutaneous fat in equal proportions. Milk and tissues were analysed for pyriproxyfen and the major metabolites identified in the metabolism studies (Tables 43 and 44). Analyses for the metabolites included a hydrolysis step, so the recorded residues include both free and conjugated compounds. LODs were generally 0.01 mg/kg, but sometimes 0.02 mg/kg because of interference. In the studies of goat metabolism free and conjugated 4'-OH-Pyr was generally the main identified metabolite; other metabolites would not be expected to be detectable in its absence. In the kidneys of the cows in the 30 ppm group however, 2,5-OH-Py was detected when 4'-OH-Pyr was not.

The residues in the milk from the 30 ppm feeding group are shown in Table 43. Milk samples up to day 14 from the other two groups were also analysed, but residues were not detected. Residues of pyriproxyfen, but not the metabolites, were detected in the cream of milk from the 30 ppm group taken on day 24, implying that pyriproxyfen is fat-soluble. Pyriproxyfen was not detected (<0.01 mg/kg) in the cream of milk from the 9 ppm group taken on day 24.

In the tissues pyriproxyfen itself was detected only in the fat, again confirming its classification as a fat-soluble compound. Mean residues of 0.058 mg/kg in the 30 ppm group and 0.018 mg/kg in the 9 ppm group suggested that residues would be proportional to the doses.

Milk samples were extracted and analysed within 5 days of collection, so the residues would be stable. Pyriproxyfen residues in the tissues were determined within 9-23 days after sampling, and had been shown to be stable for this period by the storage stability studies. POP residues in the liver

and kidneys were extracted 49 and 67 days after sampling. Storage stability trials showed that the sulfate conjugate of POP would decrease by about 30% in 66 days, so the results could be accepted. Storage periods for residues of 4'-OH-Pyr in the tissues were 45-70 days, shorter than the demonstrated periods of stability. Samples were stored for 109-113 days before analysis for 2,5-OH-Py. Stability trials showed considerable losses of free 2,5-OH-Py by this time and no data were available for its conjugates. Studies of the storage stability of free POP and 4'-OH-Pyr in the liver were abandoned when significant degradation was observed within about 2 months.

Table 43. Residues of pyriproxyfen and metabolites in milk from dairy cows dosed with pyriproxyfen at the equivalent of a nominal feed level of 30 ppm dry weight for 28 days (Green, 1997). Metabolite residues include free and conjugated compounds.

Day	Sample	Residues, mg/kg, in milk from 3 cows			
		pyriproxyfen	POP	4'-OH-Pyr	2,5-OH-Py
1	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
2	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
4	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
7	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
10	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
14	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
17	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
21	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
24	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
28	whole milk	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
24	skimmed milk	<0.01 (3)	<0.01 (3)	<0.02 (3)	<0.01 (3)
24	cream	0.012 0.015 0.014	<0.02 (3)	<0.02 (3)	<0.02 (3)

Table 44. Residues of pyriproxyfen and metabolites in the tissues from dairy cows dosed with pyriproxyfen equivalent to nominal feed levels of 3, 9 or 30 ppm dry weight for 28 days (Green, 1997). Metabolite residues include free and conjugated compounds.

Sample	Dose groups, ppm	Residues, mg/kg, from 3 cows			
		pyriproxyfen	POP	4'-OH-Pyr	2,5-OH-Py
Muscle	30	<0.01 (3)		<0.01 (3)	
Liver	30	<0.01 (3)	<0.01 (3)	<0.01 (3)	<0.01 (3)
Kidneys	9	<0.01 (3)			<0.01 (3)
Kidneys	30	<0.01 (3)	<0.02 (3)	<0.01 (3)	0.017 0.014 0.016
Fat	3	<0.01 (3)			
Fat	9	0.025 0.011 0.019			
Fat	30	0.058 0.046 0.072		<0.01 (3)	

Residues in animal commodities

The Meeting estimated the dietary burden (Table 45) of pyriproxyfen for beef and dairy cattle from the diets in Appendix IX of the FAO Manual, the recommended MRLs for cotton gin trash and cotton seed, and the maximum residue level for cotton seed meal derived from the recommended MRL for cotton seed and the relevant processing factor (0.1). These three commodities from cotton were the only feed items considered. The dietary burden for both beef and dairy cattle is equivalent to 1.1 ppm pyriproxyfen and is suitable for estimating maximum residue levels for meat, offal and milk.

A similar calculation from the STMR levels for the feed commodities gives a dietary burden of 0.21 ppm pyriproxyfen, which is suitable for estimating STMRs for animal commodities.

Table 45. Estimated dietary burden of pyriproxyfen for beef and dairy cattle calculated from recommended MRLs, STMRs and standard animal diets. DM is dry matter. MRL/DM is MRL expressed on the dry matter. The residues in cotton gin trash are already expressed on a dry matter basis, so no adjustment is needed.

Commodity	MRL, mg/kg	Processing factor[1]	DM, %	MRL/DM, mg/kg	%, of diet		Pyriproxifen in diet, ppm	
					Beef	Dairy	Beef	Dairy
Cotton gin trash	5		100	**5.00**	20	20	1.00	1.00
Cotton seed (undelinted)	0.05		88	**0.057**	25	25	0.01	0.01
Cotton seed meal	0.005	0.1	89	**0.006**				
							1.0	**1.0**
	STMR			STMR/DM				
Cotton gin trash	0.91		100	**0.91**	20	20	0.18	0.18
Cotton seed (undelinted)	0.01		88	**0.011**	25	25	0.00	0.00
Cotton seed meal	0.001	0.1	89	**0.001**				
							0.18	**0.18**

[1] The processing factor for cotton seed meal in a processing trial was 0 (<0.1), taken as 0.1 for the calculation. The cotton seed meal "MRL" of 0.005 mg/kg is calculated from the recommended MRL for cotton seed and the processing factor.

Interpretation of residue trials

Table 46. Interpretation table for pyriproxyfen residues in citrus fruits, cotton seed and cotton gin trash. GAP and trial conditions are compared for treatments considered valid for the estimation of maximum residue levels and STMRs.

Crop	Country	Use pattern				Trial	Pyriproxyfen, mg/kg
		kg ai/ha	kg ai/hl	No of appl	PHI, days[1]		
CITRUS FRUIT							
Citrus GAP	Israel	0.25-0.40	0.01		GS		
Grapefruit trial	Israel	0.35	0.01	1	137	1628/1	0.03 pulp <0.01
Grapefruit trial	Israel	0.4	0.01	1	130	1628/1	0.04 pulp <0.01
Grapefruit trial	Israel	0.3	0.01	1	121	1628/1	0.08 pulp <0.01
Grapefruit trial	Israel	0.4	0.01	1	126	1628/1	0.03 pulp <0.01
Grapefruit trial	Israel	0.35	0.01	1	124	1628/1	0.03 pulp <0.01
Citrus GAP	SA		0.0030	3	90		
Mandarin trial	SA	0.36	0.003	2	90	IK30196/97	0.02 pulp <0.01
Orange trial	SA	0.36	0.003	2	90	IK30296/97	0.02 pulp <0.01
Orange trial	SA	0.36	0.003	2	120 (90)	311P130	0.05 pulp <0.01
Orange trial	SA	0.36	0.003	2	120 (90)	311P130	0.06 pulp<0.01
Citrus GAP	Spain		0.0025-0.0075	2	30		
Mandarin trial	Spain	0.08	0.005	1	31	S/SP/E/91971	0.069
Mandarin trial	Spain		0.005	1	31	S/SP/M/92163	0.20
Mandarin trial	Spain		0.005	1	31	S/SP/M/92160	0.33
Mandarin trial	Spain	0.23	0.007	1	45 (30)	R10.A.97.027	0.10
Orange trial	Spain	0.08	0.005	1	31	S/SP/E/91972	0.12
Orange trial	Spain		0.005	1	31	S/SP/M/92161	0.25
Orange trial	Spain		0.005	1	45 (31)	S/SP/M/92162	0.25
Orange trial	Spain	0.23	0.007	1	45 (30)	R10.A.97.025	0.08

Crop	Country	Use pattern				Trial	Pyriproxyfen, mg/kg
		kg ai/ha	kg ai/hl	No of appl	PHI, days[1]		
Orange trial	Italy	0.07	0.007	1	60 (28)	Pyriproxyfen-IT-1996-1	0.06 pulp <0.01
COTTON SEED							
Cotton GAP	USA	0.059-0.075		1	28		
Cotton seed trial	USA	0.10	0.053 +0.051	2	29	V-10946-A	<0.01
Cotton seed trial	USA	0.097	0.040	2	29	V-10946-B	0.02
Cotton seed trial	USA	0.10	0.053	2	29	V-10946-C	<0.01
Cotton seed trial	USA	0.049 +2×0.074	0.034 +2×0.052	3	28	V-11117-A	<0.01
Cotton seed trial	USA	0.049 +2×0.074	0.035 +2×0.053	3	28	V-11117-B	0.03
Cotton seed trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-C	0.03
Cotton seed trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-D	0.01
Cotton seed trial	USA	0.049 +2×0.075	0.036 +2×0.053	3	30	V-11117-E	0.04
Cotton seed trial	USA	0.050 +2×0.075	0.035 +2×0.053	3	30	V-11117-F	0.03
Cotton seed trial	USA	0.049 +2×0.075	0.035 +2×0.053	3	28	V-11117-G	<0.01
Cotton seed trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-H	0.03
Cotton seed trial	USA	0.050 +0.079 +0.075	0.035 +2×0.052	3	28	V-11117-I	<0.01
Cotton seed trial	USA	0.049 +2×0.074	0.034 +2×0.052	3	28	V-11117-J	<0.01
Cotton seed trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-K	<0.01
Cotton seed trial	USA	0.049 +2×0.072	0.035 +2×0.053	3	28	V-11117-M	0.03
COTTON GIN TRASH							
Cotton GAP	USA	0.059-0.075		1	28		
Cotton gin trash trial	USA	0.049 +2×0.074	0.034 +2×0.052	3	28	V-11117-A	0.58 [2]
Cotton gin trash trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-C	0.97 [2]
Cotton gin trash trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-D	0.50 [2]
Cotton gin trash trial	USA	0.049 +2×0.075	0.036 +2×0.053	3	30	V-11117-E	0.84 [2]
Cotton gin trash trial	USA	0.050 +2×0.074	0.035 +2×0.053	3	28	V-11117-K	1.65 [2]
Cotton gin trash trial	USA	0.049 +2×0.072	0.035 +2×0.053	3	28	V-11117-M	2.67 [2]

[1] A shorter PHI in parentheses is the GAP PHI, but the residue was higher at the longer PHI and was used for the evaluation.
[2] expressed on a dry weight basis

FATE OF RESIDUES IN STORAGE AND PROCESSING

In storage

No information.

In processing

Cotton was treated three times with pyriproxyfen at an exaggerated rate and harvested 28 days after the final application for processing (Pensyl, 1996b). The residue trial is included in Table 41 (trial V-11117-N). The processing procedure is shown in Figure 6. Pyriproxyfen residues of 0.10 mg/kg in cotton seed produced residues of 0.02 mg/kg in the crude and refined oil, but no residues (<0.01 mg/kg) in the meal (Table 47). PYPAC residues were below the LOD (0.01 mg/kg) in both the raw and processed commodities.

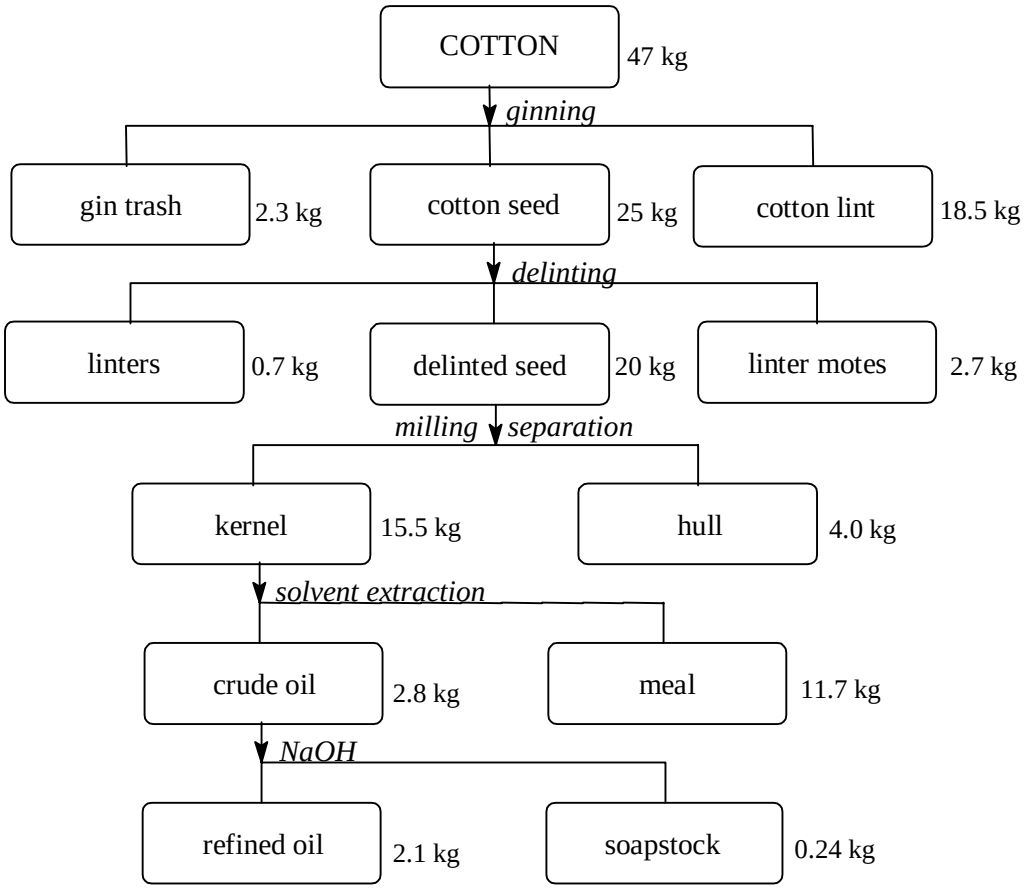


Figure 6. Cotton seed processing (Pensyl, 1996b).

Table 47. Residues in cotton seed and its processed fractions from cotton treated at a fivefold rate, 0.25 + 0.37 + 0.37 kg ai/ha, and harvested 28 days after the final application in the USA (Pensyl, 1996b).

Commodity	Pyriproxyfen, mg/kg	PYPAC, mg/kg
Cotton seed	0.10	<0.01
Solvent-extracted meal	<0.01	<0.01
Cotton hulls	<0.01	<0.01
Crude oil	0.02	<0.01

Commodity	Pyriproxyfen, mg/kg	PYPAC, mg/kg
Refined oil	0.02	<0.01

Residues in the edible portion of food commodities

Pyriproxyfen residues were not detected (<0.01 mg/kg) in the edible pulp in 24 citrus trials. The calculated factors for transfer to the pulp are based on the level in the whole fruit and the LOD so that the real factors, if residues enter the pulp, are somewhat lower. The mean and minimum factors were 0.33 and 0.09 respectively. The mean factor was used in the estimation of the STMR for citrus fruits.

In a processing trial on cotton seed the processing factor for both crude and refined cotton seed oil was 0.2. The Meeting applied this factor to the STMR for cotton seed to calculate the STMR for cotton seed oils.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

The Meeting received information from The Netherlands on pyriproxyfen residues in food in commerce in 1997. The residues were below the LOD (0.02 mg/kg) in 172 of the 175 tomato samples analysed and did not exceed the MRL (0.1 mg/kg) in the remaining 3 samples.

NATIONAL MAXIMUM RESIDUE LIMITS

The Meeting was aware that the following national MRLs had been established.

Country	MRL, mg/kg	Commodity
Brazil	0.1	bean
Brazil	0.1	citrus fruits
Brazil	0.5	tomato
Netherlands [1]	0.1	solanaceae
Netherlands	0.02*	other food commodities
Spain	0.5	citrus fruits
USA	0.05	cotton seed
USA	2	gin trash

[1] Residue definition: parent compound, expressed as pyriproxyfen

APPRAISAL

Pyriproxyfen is an insect growth regulator with insecticidal activity against public health insect pests: houseflies, mosquitoes and cockroaches. In agriculture and horticulture pyriproxyfen has registered uses for the control of scale, whitefly, bollworm, jassids, aphids and cutworms.

The Meeting received extensive information on pyriproxyfen metabolism and environmental fate, methods of residue analysis, freezer storage stability, national registered use patterns, supervised trials, farm animal feeding studies, fate of residues in processing and national MRLs.

Animal metabolism

When rats were dosed orally with [^{14}C]pyriproxyfen excretion of the ^{14}C was rapid, accounting for 88-96% in 2 days. ^{14}C levels were higher in the fat than in other tissues and slightly more persistent. The

estimated biological half-life for ^{14}C depletion in fat was 36 hours. The main metabolite in the faeces was 4-(4-hydroxyphenoxy)phenyl (*RS*)-2-(2-pyridyloxy)propyl ether (4'-OH-Pyr).

When lactating goats were dosed with [^{14}C]pyriproxyfen, labelled in either the phenyl or the pyridyl ring, at the equivalent of 10 ppm in the feed for 5 consecutive days most of the dose was accounted for by residues in the excreta and the contents of the GI tract. Pyriproxyfen (0.003-0.009 mg/kg) was a minor component of the milk residue (3-15%) with the main metabolite 4'-OH-Pyr sulfate constituting about 30-50%. Parent pyriproxyfen (0.014-0.050 mg/kg) was the main residue in fat with essentially the same levels in omental and perirenal fat. Pyriproxyfen was the main residue in muscle but levels were very low. It was a very minor component of the residues in the kidneys and liver. The main identified residue in the liver was 4'-OH-Pyr sulfate, while in the kidneys the main identified residues were 4'-OH-Pyr sulfate and 4-phenoxyphenyl sulfate (POP sulfate).

Approximately 90% of the dose appeared in the excreta of laying hens dosed with [^{14}C]pyriproxyfen labelled in either the phenyl or pyridyl ring for 8 consecutive days at the equivalent of 10 ppm in the feed. The main identified residues in the excreta were 4'-OH-Pyr and (*RS*)-2-(2-pyridyloxy)propionic acid (PYPAC). The residues were very low in the egg whites and reached a plateau in the yolks in about 6 days in one experiment and had almost reached a plateau in the other. Parent pyriproxyfen (up to 0.17 mg/kg) was the main residue in egg yolk. The residues in muscle were below those in other tissues and pyriproxyfen was the main component of the residue. The residues in fat were much higher than in muscle, suggesting a fat-soluble compound, and pyriproxyfen was the main residue. Levels of pyriproxyfen in abdominal fat (0.79 and 0.92 mg/kg) were much higher than in the skin + fat (0.17 and 0.13 mg/kg). Pyriproxyfen was a minor component of the liver residue with 4'-OH- Pyr sulfate the main identified metabolite.

The Meeting concluded that the animal metabolism studies were marginally acceptable where data on freezer storage stability were available, but not for residues in milk and eggs. Summary information on the storage stability of pyriproxyfen and its metabolites in goat milk and egg yolk were provided at a late stage of the Meeting, which suggested that the residues were stable during freezer storage. The full report should be evaluated the next time pyriproxyfen is reviewed.

Plant metabolism

Pyriproxyfen accounted for most of the residue in apples when trees were treated with labelled pyriproxyfen soon after petal fall and twice more at 60 and 40 days before harvest. A surface wash accounted for only 1.5-2.6% of the total apple residue. Pyriproxyfen was not detectable in apple juice, where the main identified residue was (*RS*)-2-(2-pyridyloxy)propyl alcohol (PYPA). Pyriproxyfen was the main component of the residue in apple pomace.

When tomato plants were treated 3 times with ^{14}C-labelled pyriproxyfen 35, 21 and 7 days before harvest, a surface wash of the harvested fruit with acetonitrile accounted for 1.8-3.3% of the residues in the tomatoes. Pyriproxyfen was not detectable in the tomato juice, where the identified metabolites were PYPA, PYPAC and 2-hydroxypyridine (2-OH-PY) in free and conjugated form. Parent pyriproxyfen accounted for most of the residue in whole tomatoes and tomato pomace.

Pyriproxyfen was the main residue component in gin trash from cotton plants treated twice, 43 and 28 days before harvest, with ^{14}C-labelled pyriproxyfen. Levels of ^{14}C were much lower in the cotton seed than in the gin trash suggesting little, if any, translocation of the residue from leaf to seed. The main identified residue in cotton seed was free and conjugated PYPAC with pyriproxyfen constituting only 3.9% and 0.6% of the residue. Approximately half of the residue in cotton seed was unextractable and was associated with the protein, carbohydrate and lignin fractions.

Metabolic pathways in plants and animals are very similar.

Environmental fate in soil

Labelled pyriproxyfen disappeared rapidly in the first few days during aerobic degradation in soil but then more slowly, with an estimated half-life of 28 days from days 7 to 30 of the study. Half-lives for mineralization were 68 and 139 days for the pyridyl label and phenyl label respectively. The main identified residue was 4'-OH-Pyr, but it did not exceed 5% of the dose.

In a second study of aerobic soil degradation the half-lives for pyriproxyfen were 8.2 days for days 1-14 and 20 days for days 14-91, while mineralization half-lives were 82 and 112 days for the pyridyl and phenyl label respectively. PYPAC was the main identified product, reaching 15% of the dose with levels exceeding those of pyriproxyfen after day 28. In a further aerobic study for 6 months the results were generally consistent with the previous ones but mineralization was found to be very slow with estimated half-lives of 330 and 850 days.

The leaching of [^{14}C]pyriproxyfen was determined with columns of silt and sandy loam soils. Most of the ^{14}C (89% and 84%) remained in the treated soil at the top of the column. Pyriproxyfen is unlikely to be leached, and degradation products become substantially bound in the soil organic matter.

The leaching of residues aged by aerobic soil incubation for 9 days was also determined. Most of the residue (86-88.5%) remained in the applied soil at the top of the leaching column. PYPAC was mobile and constituted 6.5 of the 7.6% of the applied dose which appeared in the leachate.

After a series of adsorption-desorption studies, pyriproxyfen was rated as essentially immobile and unlikely to be leached from most agricultural soils. 4'-OH-Pyr was rated as having slight to low mobility in most agricultural soils or a slight chance of leaching. On the basis of its adsorption values, PYPAC was rated as having high or very high mobility with a high potential to be leached into ground water. Whether the potential to be leached is realized will depend on the persistence of PYPAC in the soil and the prevailing field conditions.

Pyriproxyfen disappeared more quickly from irradiated soil than from dark controls and produced polar and unextractable residues. However, the rate of photolysis was not so much faster than that of soil degradation as to suggest that photolysis would be a main mechanism of environmental degradation.

In a confined rotational crop study, lettuce, radishes and wheat seed were sown in a soil treated 30 days previously with [^{14}C]pyriproxyfen at 0.20 kg ai/ha. Levels of ^{14}C were negligible in lettuce leaves, radish roots and leaves and wheat forage from crops grown to maturity. The ^{14}C in wheat grain, straw and chaff was unextractable and found to be biochemically incorporated into proteins and carbohydrates. The residues of pyriproxyfen and its immediate metabolites or degradation products would not be expected above negligible levels in rotational crops.

In two field dissipation studies pyriproxyfen residues did not migrate down the soil profile and the disappearance half-lives in the top soil segment were 3.5 and 16 days. PYPAC was detected in only one sample, in the top segment of the soil. 4'-OH-Pyr was detected sporadically at concentrations close to the LOD, but the incidence could not be interpreted as evidence of systematic persistence or mobility down the soil profile.

Environmental fate in water-sediment systems

Pyriproxyfen disappeared from aerobic lake water-sediment systems with half-lives of 16 and 21 days. Pyriproxyfen was the main residue in the sediment during the 1-month studies, and 4'-OH-Pyr

accounted for 7.5% and 9.5% of the dose after 7 days. PYPAC was the main residue in the water phase after 12 days and accounted for 34% of the dose on day 21.

Pyriproxyfen was the main residue throughout 1-year studies of anaerobic lake water-sediment systems and most of the residue was in the sediment. PYPAC accounted for 16% of the dose after 1 year and, because of its water solubility, it was mainly in the aqueous phase. Mineralization was negligible. Pyriproxyfen appeared to be degraded slowly for the first 6 months and subsequently more quickly.

In a photolysis study, pyriproxyfen was exposed to sunlight in sterilized distilled water and sterilized lake water. The estimated photolytic half-lives were 17.5 and 21 days respectively. A theoretical half-life of 16 days was calculated for 40° N latitude. The main photoproducts were PYPA and CO_2 accounting for 16-30% and 11-29% of the initial ^{14}C respectively.

In a laboratory photolysis study pyriproxyfen in water was subjected to light from a xenon lamp with a filter to restrict light below 290 nm for 14 days. Estimated half-lives for photolytic disappearance were 6.4 and 3.7 days. The main photoproduct was PYPA. Negligible amounts of CO_2 were produced.

Analytical methods

Methods of analysis for pyriproxyfen and its metabolites in crops, processed commodities, animal commodities, soil and water were reported.

In a typical method pyriproxyfen residues are extracted with acetone, the extract is diluted with aqueous sodium chloride, and the residues are partitioned into dichloromethane. Column chromatography is used for clean-up and the residues are determined by GLC with an NPD. The LOD is usually about 0.02 mg/kg.

PYPAC remains in the aqueous phase during the extraction with dichloromethane. After acidification it is extracted into an organic phase such as ethyl acetate. PYPAC is methylated, cleaned up on a silica gel column and determined by GLC with an NPD. The LOD is about 0.02 mg/kg. Care must be exercised not to lose methyl PYPAC during the evaporation of its solutions because it is volatile.

An acid hydrolysis step is introduced into methods for POP (4-phenoxyphenol) and 4'-OH-Pyr in animal commodities to release conjugates. After clean-up, these metabolites are determined by HPLC with UV detection. 2,5-OH-Py (2,5-dihydroxypyridine) may be determined by HPLC with fluorescence detection.

Analytical methods for soils begin with various extractions and then follow the methods for crop residues. Typical LODs for pyriproxyfen and its degradation products in soils are 0.02 mg/kg. The validated LOD for a straightforward GLC method for pyriproxyfen in aquarium water was 1 µg/l.

Adequate recoveries of pyriproxyfen were achieved from apples and cotton seed fortified at 0.05 and 0.5 mg/kg with an FDA multi-residue method. PYPAC was not recovered from the Florisil column in this method.

Stability of pesticide residues in stored analytical samples

Pyriproxyfen and its metabolites were generally stable in crop and soil samples during freezer storage (-18°C to -20°C) for the periods tested.

Pyriproxyfen and some metabolites were of doubtful stability in animal commodities when stored for long periods.

Pyriproxyfen was stable in tomato homogenate for 12 months, cotton seed for 13 months, gin trash for 8 months, and soils for 7 months.

PYPAC was stable in cotton seed for 13 months and soils for 7 months. 4'-OH-Pyr was stable in fat for 14 weeks, muscle tissue for 10 weeks and one soil for 5 months, but decreased by 70% in another soil in 107 days. 4'-OH-Pyr sulfate was stable in cow liver for 8 weeks, but POP sulfate in cow liver decreased by about 30% in 72 days and 2,5-OH-Py in kidneys decreased by 85% in 70 days.

Definition of the residue

The main residue in the metabolism studies on plant commodities was pyriproxyfen itself. In cotton seed the levels of free + conjugated PYPAC and PYPA exceeded that of pyriproxyfen, which was very low, probably because the metabolites were translocated more readily. PYPAC in cotton seed in the metabolism study was about 60% free and 40% conjugated, but in the trials on cotton free PYPAC was generally undetected and lower than pyriproxyfen in the seed.

The residue can be defined as pyriproxyfen for enforcement in crops.

In animal commodities the composition of the residue varies in different tissues. Pyriproxyfen itself is fat-soluble (log P_{OW} 5.37) so it predominates in fat. In muscle all the residues are very low, but pyriproxyfen is again the main component. In milk and liver 4'-OH-Pyr with its sulfate conjugate are the main residues, while in kidneys POP is the main residue with 4'-OH-Pyr also a significant component. Pyriproxyfen predominates in eggs.

The feeding study on dairy cows suggests that the residues in milk and tissues will generally be undetectable or very low whatever the residue definition, except pyriproxyfen itself in fat and the fat of milk at the higher dietary burdens. The Meeting agreed it would be unpractical to define the residue to include metabolites and their conjugates in liver and kidneys for undetectable residues; it would be a pointless additional analytical expense.

Pyriproxyfen is also a suitable definition of the residue for dietary intake estimates.

Proposed definition of the residue (for compliance with MRLs and for the estimation of dietary intake): pyriproxyfen.

The residue is fat-soluble.

Residues resulting from supervised trials

Citrus fruits. Pyriproxyfen is registered for use on citrus fruit in Israel at 0.01 kg ai/hl with the final application at the end of May for varieties picked until the end of December and the end of June for those picked after the end of December. Five trials on grapefruit in substantial accord with Israeli GAP (sprayed in early June instead of the end of May) gave pyriproxyfen residues in the whole fruit of 0.03 (3), 0.04 and 0.08 mg/kg. The residues in the pulp were below the LOD (0.01 mg/kg).

South African GAP permits 3 applications of pyriproxyfen at a spray concentration of 0.0030 kg ai/hl with harvest 90 days after the final application. One trial on mandarins and 3 on oranges substantially complying with GAP (2 applications instead of 3) produced residues of 0.02 mg/kg in the mandarins and 0.02, 0.05 and 0.06 mg/kg in the oranges.

In Spain pyriproxyfen may be applied twice to citrus fruit at 0.0025-0.0075 kg ai/hl with harvest 30 days after the final application. Four trials on mandarins with 1 application of 0.005 and 0.007 kg ai/hl and harvest after 31 and 45 days (the residue at 45 days exceeded the residue at 30 days) were acceptably close to GAP and produced residues of 0.069, 0.10, 0.20 and 0.33 mg/kg. Recoveries in trial NNR-21-0018 were low and the results should be adjusted for the recovery (62.5%). The values 0.20 and 0.33, on adjustment, become 0.32 and 0.53 mg/kg. The residues in oranges from 4 trials in Spain and 1 in Italy substantially in line with Spanish GAP produced residues of 0.06, 0.08, 0.12, 0.25 and 0.25 mg/kg.

In summary, pyriproxyfen residues in the 18 trials according to GAP were Italy oranges 0.06 mg/kg, Israel grapefruit 0.03 3, 0.04, 0.08 mg/kg, South Africa mandarins 0.02 mg/kg, oranges 0.02, 0.05 and 0.06 mg/kg, and Spain mandarins 0.069, 0.10, 0.32, 0.53; oranges 0.08, 0.12, 0.25, 0.25 mg/kg.

The Meeting agreed that the residues arising from the Spanish GAP with the 30 days PHI seemed to be a different population from the residues from South African and Israeli GAP and that the higher population would be used for the estimation of an STMR and maximum residue level. The residues in rank order (median underlined) from the trials according to Spanish GAP were 0.06, 0.069, 0.08, 0.1, <u>0.12</u>, 0.25, 0.25, 0.32 and 0.53 mg/kg.

Because data were available for grapefruit, mandarins and oranges the Meeting agreed that an MRL for citrus fruits was appropriate. The Meeting estimated a maximum residue level for pyriproxyfen on citrus fruits of 1 mg/kg.

Pyriproxyfen residues were not detected (<0.01 mg/kg) in the edible pulp in 24 samples analysed during the citrus trials, but many of the samples did not reflect GAP conditions so the results could not be used directly, and the residues in the whole fruit only just exceeded the LOD. The mean ratio of the residue in the pulp to that in the whole fruit for the 3 samples with the highest residues in the whole fruit was 0.11, which is artificially high because it is largely an artefact of the LOD. The Meeting applied this factor to the median residue from the 9 relevant trials (0.12 mg/kg) to estimate an STMR of 0.013 mg/kg for pyriproxyfen in citrus fruits.

<u>Cotton seed</u>. Pyriproxyfen may be applied to cotton at 0.059-0.075 kg ai/ha with the crop harvested 28 days after the single application. In a series of trials in the USA in 1994 and 1995 pyriproxyfen was applied 2 or 3 times to cotton with the final application in the range 0.072-0.10 kg ai/ha, which was considered to comply with GAP for residue purposes. The pyriproxyfen residues in cotton seed in rank order (median underlined) in the 15 trials were <0.01 (7), <u>0.01</u>, 0.02, 0.03 (5) and 0.04 mg/kg.

The Meeting estimated a maximum residue level of 0.05 mg/kg and an STMR of 0.01 mg/kg for pyriproxyfen in cotton seed.

<u>Cotton gin trash</u>. In 6 of the US cotton trials in 1995 seed cotton (20 kg) was ginned to produce cotton seed and gin trash and pyriproxyfen residues were measured on the gin trash. The residues, expressed on a dry weight basis, in rank order (median underlined) were 0.50, 0.58, <u>0.84</u>, <u>0.97</u>, 1.7 and 2.7 mg/kg.

The Meeting estimated a maximum residue level and an STMR for pyriproxyfen in cotton gin trash of 5 and 0.91 mg/kg respectively.

<u>Feeding trials</u>

Pyriproxyfen and metabolites identified in the metabolism study were determined in the milk and tissues from dairy cows dosed for 28 days with pyriproxyfen at 0.13, 0.38 and 1.17 mg/kg bw/day, equivalent to 3, 9 and 30 ppm dry weight in the diet. In the 30 ppm group pyriproxyfen residues were not detected (<0.01 mg/kg) in whole milk, muscle, liver or kidney, but were present in cream from

day 24 milk (0.012-0.015 mg/kg) and in body fat (0.046-0.072 mg/kg). In the 9 ppm feeding group, pyriproxyfen residues were not detected in milk and kidney, but were present in body fat at 0.011-0.025 mg/kg. In the 3 ppm feeding group, pyriproxyfen residues were not detected (<0.01 mg/kg) in body fat, whole milk or the cream of day 24 milk.

The residues in the body fat in the 30 ppm group (mean 0.058 mg/kg) and the 9 ppm group (mean 0.018 mg/kg) were roughly proportional to the doses.

Residues in animal commodities

The dietary burden for estimating maximum residue levels for animal commodities for beef and dairy cattle is 1.0 ppm pyriproxyfen, calculated from the maximum residue levels estimated for cotton gin trash and cotton seed. This level is sufficiently close to be evaluated against the 3 ppm feeding level which did not produce pyriproxyfen residues above the LOD (0.01 mg/kg) in the animal commodities.

The dietary burden for estimating STMRs for products of beef and dairy cattle is 0.18 ppm pyriproxyfen, calculated from the STMRs estimated for cotton gin trash and cotton seed.

The Meeting estimated maximum residue levels of 0.01* mg/kg for cattle meat (fat), cattle edible offal and cattle milk. The Meeting noted that residues resulting from feeding dairy cows at 10 ppm were quite similar to those found in the 10 ppm goat metabolism study and agreed that the estimated maximum residue levels could be extended to milks and to goat meat (fat) and goat edible offal. However, the estimated maximum residue level for milks cannot be recommended for use as an MRL because the stability of pyriproxyfen and its metabolites in goat milk is yet to be confirmed.

The residues were below the LOD in the muscle, liver and kidneys at feeding levels of 3, 9 and 30 ppm. Residues of pyriproxyfen were detected in the fat at the 9 and 30 ppm feeding levels and in the fat of milk at the 30 ppm feeding level. The Meeting noted that the dietary burden of 0.18 ppm was much lower than the lowest feeding level and as an approximation assumed proportionality between likely tissue levels and dietary intake.

STMR (animal commodity) = LOD × (STMR dietary burden) ÷ (feeding level)

STMR for meat = 0.01 × 0.18 ÷ 30 = 0.00006 mg/kg (no detections at 30 ppm feeding level)

The same calculation applies for liver, kidneys and milk. The Meeting agreed that the calculated STMRs were low enough to be treated as effectively zero. The Meeting estimated STMR levels of 0 for cattle meat, goat meat, cattle edible offal, goat edible offal and milks, but could not recommend the use of the STMR for milks until the maximum residue level estimated for milks can be recommended for use as anMRL.

Processing

In a cotton seed processing trial pyriproxyfen residues of 0.1 mg/kg in cotton seed produced residues of 0.02 mg/kg in both crude and refined oil and no detectable residues in the meal (<0.01 mg/kg). The estimated processing factors for crude oil and refined oil are therefore 0.2 and the processing factor for cotton seed meal is 0 (<0.1).

The Meeting applied the processing factors to the maximum residue level and STMR for cotton seed to produce estimated maximum residue levels of 0.01 mg/kg and STMRs of 0.002 mg/kg for crude and edible cotton seed oil, and an estimated STMR for cotton seed meal of 0.001 mg/kg.

Similarly, the processing factor 0.2 applied to the maximum trials residue value for cotton seed (0.04 mg/kg) produced maximum trials residue values of 0.008 mg/kg for crude and edible cotton seed oils.

RECOMMENDATIONS

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

Definition of the residue (for compliance with MRLs and for estimation of dietary intake): pyriproxyfen.

The residue is fat-soluble.

Commodity		MRL, mg/kg	STMR, mg/kg
CCN	Name		
MM 0812	Cattle meat	0.01* (fat)	0
MO 0812	Cattle, Edible offal of	0.01*	0
FC 0001	Citrus fruits	1	0.013
	Cotton gin trash	5	0.91
SO 0691	Cotton seed	0.05	0.01
	Cotton seed meal		0.001
OC 0691	Cotton seed oil, crude	0.01	0.002
OR 0691	Cotton seed oil, edible	0.01	0.002
MM 0814	Goat meat	0.01* (fat)	0
MO 0814	Goat, Edible offal of	0.01*	0

FURTHER WORK OR INFORMATION

Desirable

1. Information on the fate of pyriproxyfen during the processing of oranges. At a late stage of the Meeting information on an orange processing study was provided. It should be evaluated the next time pyriproxyfen is reviewed.

2. Information on the freezer storage stability of pyriproxyfen and the main metabolites in milk and eggs is necessary to validate the data from the metabolism studies. At a late stage of the Meeting a

summary report on the freezer storage stability of residues in goat milk and egg yolk was provided. The full report should be evaluated the next time pyriproxyfen is reviewed.

DIETARY RISK ASSESSMENT

Chronic intake

Pyriproxyfen is a new compound and maximum residue and STMR levels were estimated for citrus fruits, cotton seed, animal commodities and some processed commodities. The dietary intake of pyriproxyfen is presented in Annex III.

International Estimated Daily Intakes for the 5 GEMS/Food regional diets, based on estimated STMRs, were effectively 0% of the ADI. The Meeting concluded that the intake of residues of pyriproxyfen resulting from its uses that have been considered by the JMPR is unlikely to present a public health concern

Acute intake

The Meeting concluded that an acute RfD for pyriproxyfen is unnecessary. This conclusion was based on a determination that the pesticide is unlikely to present an acute toxicological hazard and residues are therefore unlikely to present an acute risk to consumers.

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