FAMOXADONE (208)

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EXPLANATION

Famoxadone is an oxazolidinedione fungicide belonging to the quinol inhibitor family, which inhibits mitochondrial respiration of fungi. The compound was originally scheduled for the 2004 JMPR, by the 32nd Session of the CCPR (ALINORM 01/24), but was listed as a candidate new compound by the 33rd Session of the CCPR (ALINORM 01/24A), for evaluation by 2003 JMPR. Data on metabolism and environmental fate; methods of residue analysis; supervised trials on grapes, melon, cucumber, tomato, potato, barley and wheat; a cow feeding study; and on the fate of residues in processing were provided. Some information on GAP and national MRLs were submitted by the governments of Germany, the Netherlands and Poland.

IDENTITY

ISO common name: famoxadone

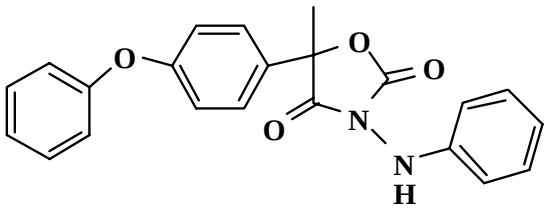
Chemical names

IUPAC: 3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione

Chemical Abstracts: 5-methyl-5-(4-phenoxyphenyl)-3-(phenylamino)-2,4-oxazolidinedione

CAS number: 131807-57-3

Structural formula:



Molecular formula: $C_{22}H_{18}N_2O_4$

Molecular weight: 374.4

Physical and chemical properties

Pure active ingredient

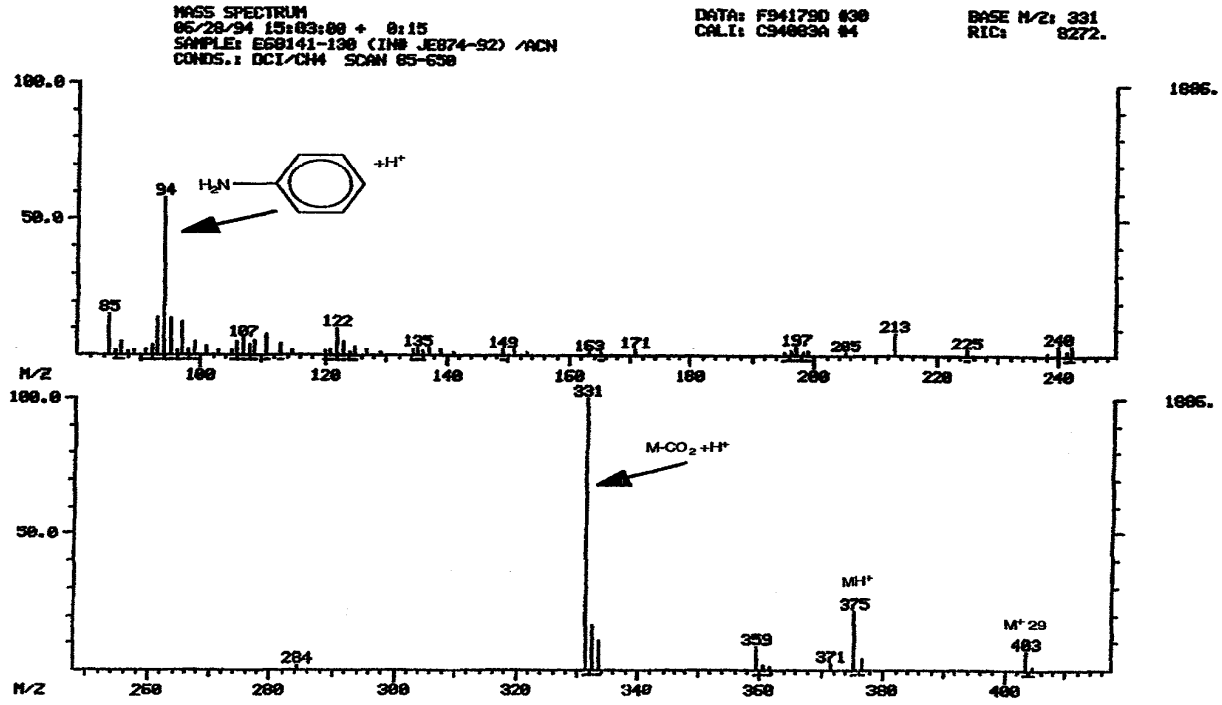
Physical state	Powder (Bates, 1994)
Colour:	Pale cream (Bates, 1994)
Odour:	Vanilla (Bates, 1994)
Relative density ($D^{20,4}$):	1.310 (Bates, 1994)
Vapour pressure:	6.4×10^{-7} Pa at 20°C (Bates, 1994)
Henry's Law constant	4.6×10^{-3} Pa m^3 mol^{-1} at 20°C (Bates, 1994)
Octanol-water partition coefficient:	Log P_{ow} 4.65 (pH 7, 25°C) (Bates, 1994)
Melting point:	141.3-142.3°C (Moore, 2001)
pH (1% aqueous suspension):	6.56 (Schmuckler, 1997)
Solubility in water (pH 7.8-8.9)	52 µg/1000 g (Bates, 1994)
Solubility in organic solvents:	(Bates, 1994)
acetone	274 g/l
acetonitrile	125 g/l
dichloromethane	239 g/l
ethyl acetate	125 g/l
hexane	0.0476 g/l
methanol	10.0 g/l
octan-1-ol	1.78 g/l
toluene	13.3 g/l

Hydrolysis: pH 5 pH 7 pH 9	DT_{50} at 25°C (Jernberg, 1996a) 41 d 2 d 0.0646 d (1.55 hr)
Dissociation characteristics:	Not determinable in technical material by potentiometric titration, conductometric or spectroscopic techniques, nor inferable from aqueous solubility or partition coefficient data.
Flammability:	Non-flammable (Gravell, 1996)
Auto-flammability:	Negative. Conducted in a 100-mm mesh cube at 140°C (Gravell, 1996)
Explosive properties:	Negative, thermal (with respect to explosion), impact, or friction (Gravell, 1996)
Oxidizing/reducing properties:	Solid famoxadone is non-oxidizing, based on structural evidence (Gravell, 1996)

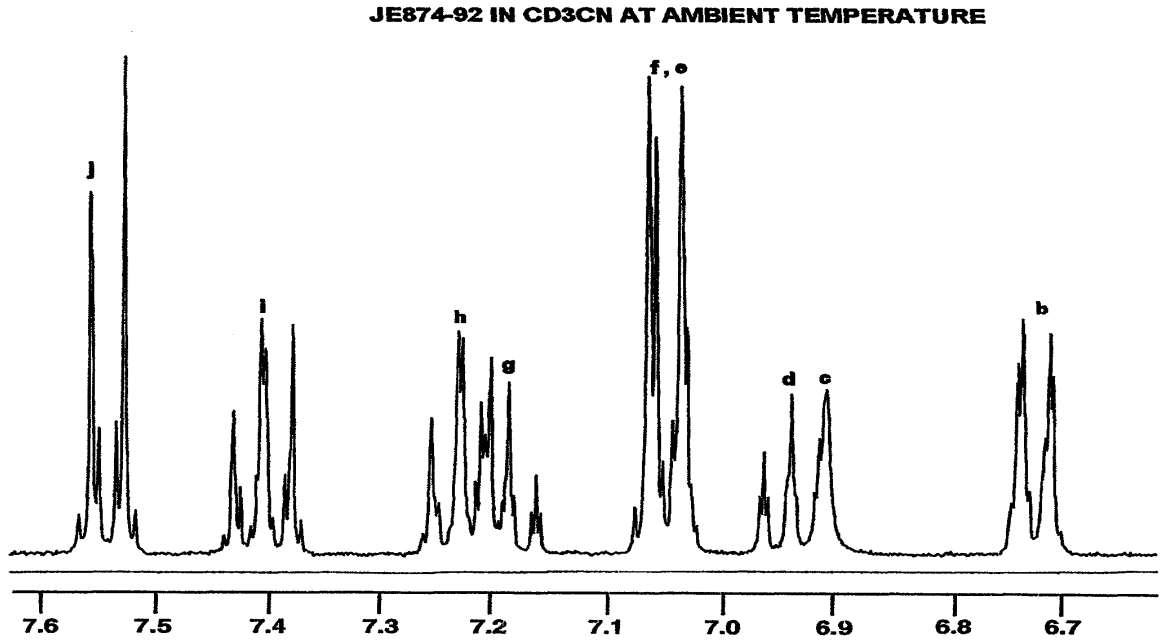
Spectral data for the pure active ingredient (99.6% purity) (Schmuckler, 1996)

UV/visible absorption spectrum**:** maximum absorption at 231 nm, with molar extinction coefficient of 553 (solvent: acetonitrile/pH 3 water/, 2 + 3).

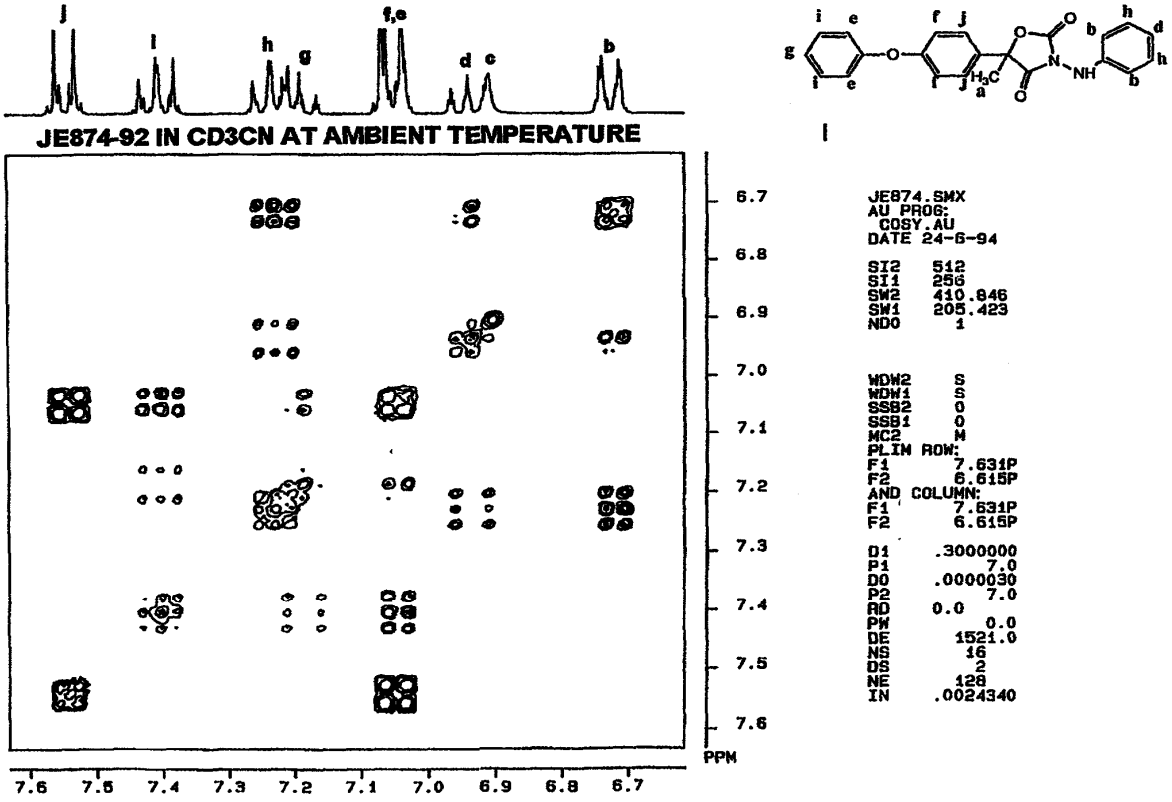
Mass spectrum (CH_4^+ chemical ionization):



Proton NMR spectrum:



COSY NMR



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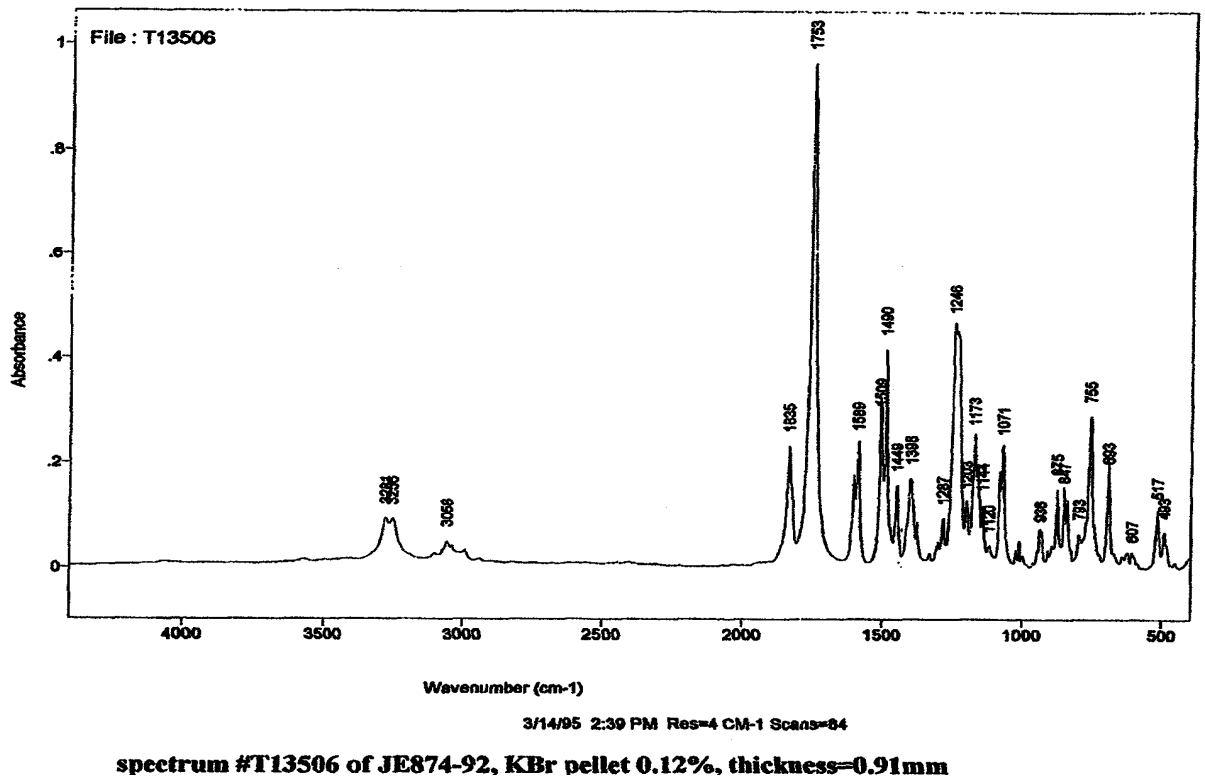
Infra-red spectrum



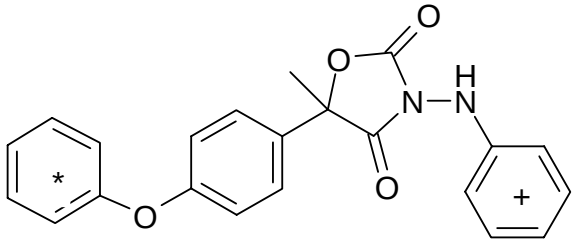
Technical material

Stability	(Moore, 1998)
Solid technical material	Stable for at least 14 d in the dark, at 25°C and 54°C
Solid technical material	Stable for at least 14 d in the dark, at 25°C and 54°C, when exposed to aluminium or iron metal foil
In aqueous solution	Stable for at least 14 d in the dark, at 25°C, in solutions containing 0.0005 M aluminum chloride or 0.0005 M ferric chloride

METABOLISM AND ENVIRONMENTAL FATE

In various studies reported to the Meeting, famoxadone was labelled at one of two positions, as indicated in Figure 1.

Figure 1. Radio-labelled famoxadone used in metabolism and environmental fate studies.



* denotes [^{14}C-phenoxyphenyl]famoxadone (^{14}C POP)
+ denotes [^{14}C-phenylamino]famoxadone (^{14}C PA)

Animal metabolism

Rats

The absorption, distribution, metabolism and elimination of ^{14}C-famoxadone (^{14}C-POP and ^{14}C-PA) in male and female rats were examined, following single or multiple oral dosing at 5 and 100 mg/kg

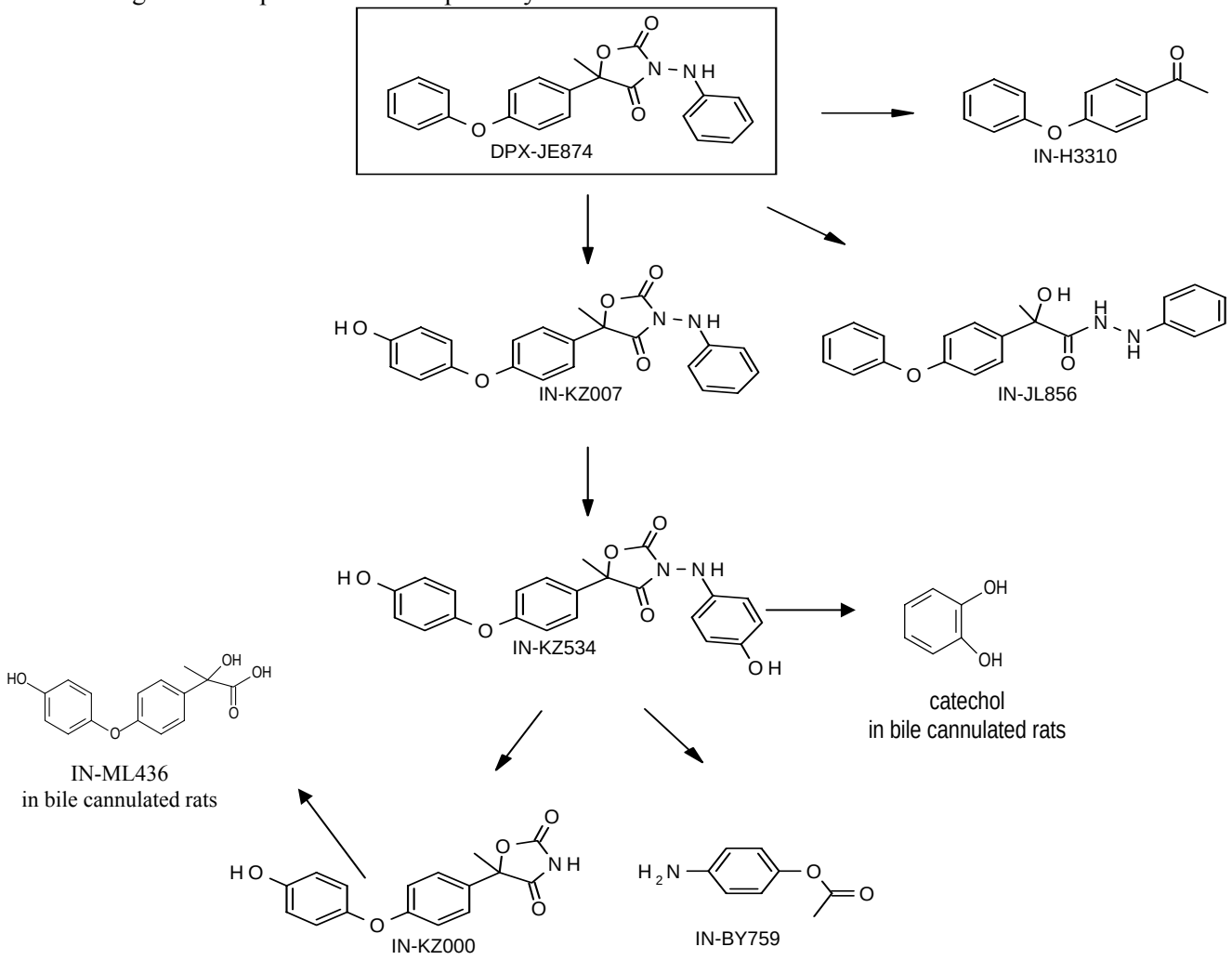
body weight dose levels (Savides, *et al*., 1995), using 4 or 5 animals per sex per group (total of 9 groups). $^{14}CO_2$ was not observed in the expired air collected from the pilot groups. Between 88.8 and 96% of the administered radioactive dose was recovered in the faecal excreta, with over 80% within the first 24 hours after dosing. Urinary elimination ranged from 3% in the 100 mg/kg bw dose groups to 12% of the administered radioactive dose in the 5 mg/kg dose groups. Over 70% of the administered dose that was eliminated in urine (<10%) occurred within the initial 24 hours. No significant difference was found in the elimination profile under single and multiple dose regimens.

Unmetabolized ^{14}C-famoxadone was the major component recovered in the faeces, with the hydroxylated metabolites (IN-KZ007 or IN-KZ534) identified as major metabolites (up to 13% of the administered dose) (Figure 2). In urine, only hydrolytic (IN-JL856) and the hydrolysis cleavage products (IN-KZ000, IN-BY759 and IN-H3310) were detected (up to 7% of the administered dose). After 36-48 hours, tissue/blood concentration ratios were ≤ 0.5 for all tissues, except liver which showed ratios of 1.8 and 1 in the lower and higher dose groups, respectively.

The biliary excretion of famoxadone was investigated in bile duct-cannulated male and female Sprague-Dawley rats, following a single oral dose of 5 mg/kg bw ^{14}C-POP or ^{14}C-PA labelled test material (5 animals/sex/group). Urine, bile and faeces were collected continuously for 48 hours post-dosing. The average amount of radio-label excreted in the bile ranged from 30 to 39% and in the faeces from 56 to 65% of the administered dose. The average amount of radioactivity absorbed was 40% of the administered dose, in both the ^{14}C-POP and ^{14}C-PA groups (sum of the radioactivity measured in the bile, urine, cage wash, blood and carcass). There was no difference between males or females for absorption and elimination in the bile or excreta (Savides *et al*., 1997).

Famoxadone was the only radio-labelled component in solvent extracts of faeces and it was not detected in bile samples. The main metabolites released in bile samples treated with β-glucuronidase/sulfatase were: IN-KZ007 (up to 5.2% of the administered dose); a catechol (1,2 dihydroxybenzene) (up to 4.6%) and IN-ML436 (up to 3.6%) (Figure 2).

Figure 2. Proposed metabolic pathway of famoxadone in rats.



Goats

The metabolism of [^{14}C]famoxadone was studied in three lactating goats (two receiving [^{14}C]famoxadone and one control), dosed orally for 7 days, at the equivalent of 10 ppm in feed, with either [^{14}C] POP or [^{14}C] PA (Lee and Hashinger, 2001). Samples of milk, urine and faeces were collected during the dosing period. The animals were sacrificed within 23 ± 1 hours and tissue samples were collected.

The majority of radioactivity (>80% of the administered radioactive dose) was excreted via the faeces (Table 1). Radioactive residues in milk reached a plateau during the day 6-7 period, at an average of 0.018 mg/kg ^{14}C famoxadone equivalents.

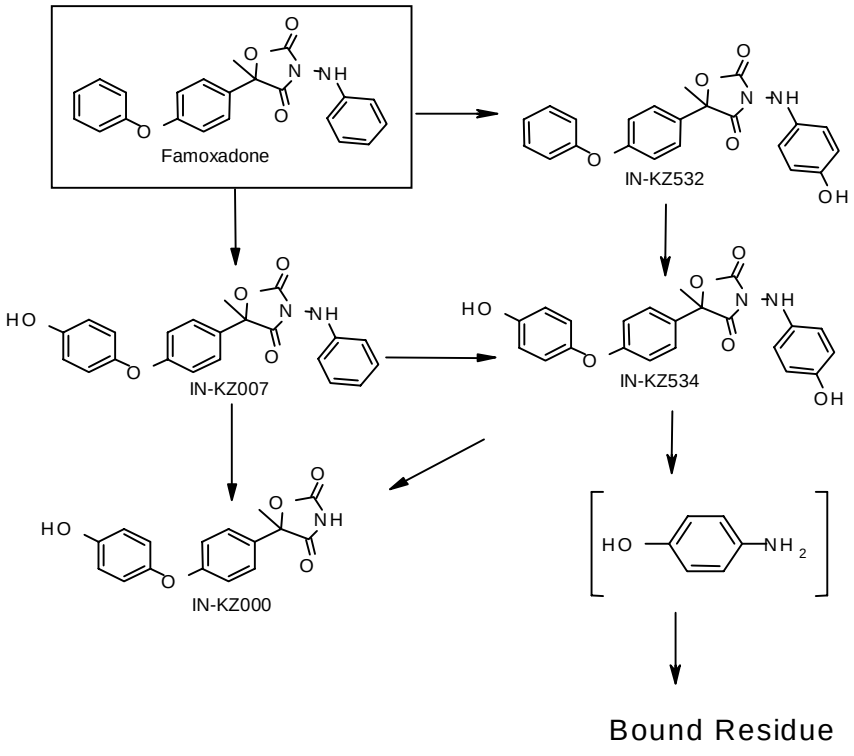
Famoxadone was the major detectable radioactive component of residues in milk and tissues. The metabolic pathway of famoxadone involved hydroxylation of the phenoxyphenyl or phenylamino rings, followed by cleavage of the hydrazine bond. In milk, no individual radioactive components were present at greater than 0.01 mg/kg, with famoxadone representing, on average, 42%TRR (Table 1). IN-KZ007 and IN-KZ000 were detected in liver tissue and IN-KZ534 and IN-KZ007 were detected in faeces (Table 1, Figure 3). The unextractable fraction of residues in liver tissues was partly released by protease digestion. The individual components released and the remaining unextractable residues were at levels <0.05 mg/kg.

Table 1. Total residues and the distribution of famoxadone and metabolites in goats treated with of [^{14}C]famoxadone (Lee and Hashinger, 2001).

Matrix	PA label		POP label	
	TRR, mg/kg	% total dose	TRR, mg/kg	% total dose
Milk [1/]	0.021	0.10	0.011	0.06
Famoxadone	0.007		0.005	
Liver	0.207	0.18	0.107	0.07
Famoxadone	0.023		0.028	
IN-KZ007	<0.005		0.005	
IN-KZ532	<0.005		<0.005	
IN-KZ000	0.005		0.006	
Kidney	0.060	0.01	0.033	<0.01
Famoxadone	0.008		0.014	
Muscle	0.018	0.01	0.018	0.01
Famoxadone	0.007		0.011	
Fat	0.133	0.04	0.168	0.08
Famoxadone	0.067		0.105	
Faeces [1/]	7.90	82.4	11.5	89.8
Famoxadone	5.59		9.39	
IN-KZ534	0.06		0.16	
IN-KZ007	0.29		0.21	
Bile	1.57	0.03	0.952	0.03
Urine [1/]	0.317	4.64	0.144	1.24
Cage wash	0.038	0.06	0.021	0.04
Total		87.4		91.4

[1/] Composite sample from days 3 to 7.

Figure 3. Proposed predominant metabolic pathway of famoxadone in goats.



Poultry

Laying hens were dosed for 7 consecutive days at a dietary level of 10-mg famoxadone/kg feed (Powles *et al*., 1996), using either ^{14}C-POP or ^{14}C-PA famoxadone (5 hens/group). Eggs were collected daily and liver, skin, fat and muscle tissues were sampled at termination (Table 2; Figure 4).

The major route of elimination of the administered radioactivity was *via* the excreta (>88%) and low levels were found in the cage wash (<1%). Residues in eggs and tissues are shown in

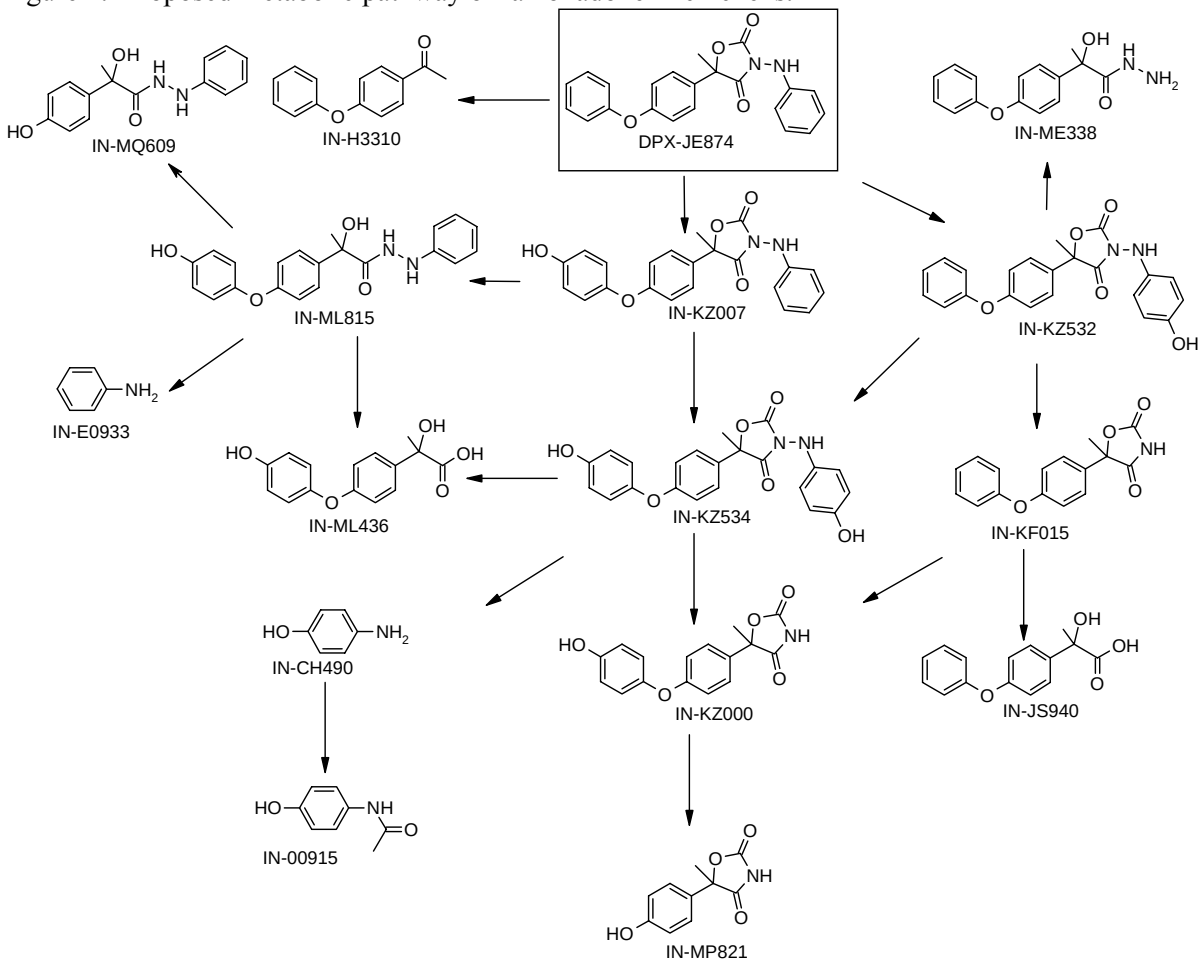
Table 2. Famoxadone was the major residue component in excreta (up to 17.8% TRR) but 15 metabolites were also identified. With the exception of the polar metabolite, IN-MP821 (15.4% TRR), all other metabolites were present at <5% of the administered dose (Figure 3). Stereo-selective metabolism of famoxadone enantiomers in egg-laying hens was not evident. The most abundant radioactive compound in liver and egg yolk was IN-KZ007, although the former also contained measurable quantities of IN-KZ534. No famoxadone was detected in liver.

Table 2. ^{14}C residues observed in hens treated with [^{14}C]famoxadone (Powles *et al.*, 1996).

Matrix	Residues, in mg equivalents /kg	
	POP label	PA label
Egg yolk (composite)	0.060	0.064
Famoxadone	0.003	0.002
IN-KZ532	0.004	0.007
IN-KZ007	0.016	0.015
Others [1/]	0.027	0.024
Liver	0.069	0.521
Famoxadone	<0.001	<0.001
IN-KZ532	<0.001	0.003
IN-KZ007	0.019	0.079
IN-KZ534	0.005	0.05
Others [1/]	0.029	0.160
Egg white	<0.01	<0.01
Fat	<0.01	<0.01
Muscle	<0.01	<0.01
Skin	<0.01	0.02

[1/] Includes all minor metabolites and background radioactivity.

Figure 4. Proposed metabolic pathway of famoxadone in chickens.



Plant metabolism

Grapes

The metabolism of [^{14}C]famoxadone (POP or PA label) in grapes was evaluated in a greenhouse study, with the pesticide applied directly onto grape foliage and immature berries (2 applications of 0.3kg famoxadone/ha), using a simulated a WG dispersed in water (Korsch and Lee, 1996). Leaves and grapes were sampled immediately after each application and at one and two weeks after the second application.

The majority of the [^{14}C]-residue was removed from leaves with a surface rinse of aqueous acetonitrile (Table 3). An average of >95% of the recovered radiolabelled residue was identified as famoxadone, in both leaves and fruit. In fruit tissues, famoxadone residues reached a maximum of 0.03 mg/kg. IN-H3310 (1-(4-phenoxyphenyl)ethanone) was observed as a minor component of the surface residues of leaves and fruits (Table 4).

Table 3. Distribution of total [^{14}C]famoxadone equivalents in treated grape plants (Korsch and Lee, 1996).

Sampling interval, days	^{14}C-POP				^{14}C-PA			
	Surface		Plant material		Surface		Plant material	
	mg/kg eq	%TRR	mg/kg eq	%TRR	mg/kg eq	%TRR	mg/kg eq	%TRR
Leaves								
0 (1st application)	35.9	98.0	0.75	2.0	25.9	97.0	0.81	3.0
7 (2nd application)	73.6	92.4	6.1	7.6	71.4	94.6	4.1	5.4
14	62.1	89.4	7.3	10.6	46.2	87.8	6.4	12.2
21	66.0	94.9	3.52	5.1	39.2	93.2	2.85	6.8
Grapes								
0 (1st application)	0.37	97.1	0.01	2.9	0.17	97.9	<0.01	2.1
7 (2nd application)	0.86	86.5	0.03	3.5	0.46	96.4	0.02	3.6
14	0.14	79.0	0.04	21.0	0.34	91.8	0.03	8.2
21	0.30	87.4	0.04	12.6	0.23	92.1	0.02	7.9

Table 4. Average percentage of radioactivity (%TRR) as famoxadone (from ^{14}C-POP and PA) and the metabolite IN-H3310 (1-(4-phenoxyphenyl)ethanone) in surface rinses and plant material extracts of leaves and grapes (Korsch and Lee, 1996).

Sampling interval (days), sample	Famoxadone		IN-H3310	
	Surface	Plant material	Surface	Plant material
0				
Leaves	99.5	71.8	<0.1	NA
Grape	95.7	0.0		NA
7				
Leaves	99.0	68.4	1.3	NA
Grape	100	41.6		NA
14				
Leaves	98.8	80.1	1.4	NA
Grape	100	0.0		NA
21				
Leaves	99.7	68.4	0.5	NA
Grape	100	62.5		NA

NA = not analyzed.

Tomatoes

The metabolism of famoxadone in tomatoes was evaluated in a field study (Freeman and Young, 1999). [^{14}C]Famoxadone (POP or PA label) was applied twice (14-day interval) as a direct foliar application, using a simulated a WG dispersed in water, at a rate of 0.63 kg/ha. Tomato fruit samples were taken at 0, 14, and 17 days after initial treatment.

The tomato fruit samples were homogenized in 0.05 M phosphate buffer, pH 3, and the extract decanted and filtered. Acetone was added to the aqueous extract which was then partitioned against ethyl acetate. The residual tomato solids were then extracted with acetone and the majority of

the radioactivity was recovered in this acetone extract (Table 2), with >90% of it identified as famoxadone. Less than 10% of the TRR was retained in the post-acetone-extraction solids from the treated sample and no attempt was made to identify residue components which were not extracted by the aqueous buffer or acetone.

Table 5. Distribution of total radioactive residues in tomato (Freeman and Young, 1999).

Sampling interval	POP ^{14}C famoxadone label, % TRR (mg/kg ^{14}C eq)			PA ^{14}C famoxadone label, % TRR (mg/kg ^{14}C eq)		
	Extractable		Unextractable	Extractable		Unextractable
	Buffer	Acetone		Buffer	Acetone	
Day 0	10.5 (0.02)	82.4 (0.17)	7.1 (0.01)	12.6 (0.02)	80 (0.14)	7.4 (0.01)
Famoxadone	10 (0.02) [1/]	77.1 (0.16)		12.3 (0.02) [1/]	79.1 (0.14)	
Day 14	13.9 (0.01)	81.0 (0.07)	5.0 (0.01)	5.8 (<0.01)	88.3 (0.07)	6.0 (0.01)
Famoxadone	6.9 (0.01) [2/]	79.4 (0.07)		-	84.9 (0.07)	
Day 17	13.6 (0.01)	78.4 (0.08)	8.0 (0.01)	9.0 (0.01)	80.5 (0.05)	10.5 (0.01)
Famoxadone	-	74.9 (0.07)		-	75.4 (0.05)	

1. Data represent the sum of ethyl acetate and aqueous fractions, after partitioning.
2. Aqueous fraction only, after partition with ethyl acetate.

Potatoes

The metabolism of famoxadone in potatoes was evaluated in a greenhouse study (Jernberg, 1996b). Using a simulated a WG dispersed in water, [^{14}C]famoxadone was applied directly to potato foliage (3 applications at 0.3 kg ai/ha). Samples (whole plants, green foliage, seed potatoes and/or mature tubers) were collected after the first and second applications (day 0 and day 30) and immediately before, and 14 days after, the last application (day 37 and day 51). The foliage was rinsed in acetone/water solution and, following air-drying and freezing with liquid nitrogen, was homogenized in 50 mM phosphate buffer (pH 3). The mixture was filtered and the solids extracted with ethyl acetate. The distribution of radioactivity in foliage is shown in Table 6. In the tubers of treated potato plants, the levels of radioactivity observed by combustion for determination of total radioactivity were equivalent to <0.01 mg famoxadone/kg. After 37 or 51 days, the majority of the radio-labelled residue was removable by rinsing the foliage surface with aqueous acetone, with 76-95% of this characterized as famoxadone (Table 6). Two minor hydrolytic metabolites, IN-H3310 and IN-JL856 (Table 11), were observed in the aqueous acetone rinse and the former was also identified in extracts of the leaves and stems but unextractable residues in the foliage were not identified or characterized.

Table 6. Distribution (%) of total ^{14}C residues in potato foliage treated with ^{14}C-famoxadone (Jernberg, 1996b).

Components found in:	^{14}C POP, % of total residue			^{14}C PA, % of total residue		
	Day 0	Day 37	Day 51	Day 0	Day 37	Day 51
Surface wash	96.1	83.6	52.2	97.3	89.4	71.4
Famoxadone	96.1	63.9	43.7	97.3	71.9	68.0
IN-H3310		4.9	3.2			
IN-JL856		2.2	1.2			
Others		12.6	4.1			
Foliage tissues	3.9	16.4	47.8	2.7	10.6	28.6
Famoxadone		9.6	22.2		4.8	17.7
IN-H3310		0.43	1.4			
Others		0.87	3.0		0.8	0.8
Water-soluble		0.22	0.21		0.40	0.96
Unextractable		5.3	21.0		4.6	9.1

Wheat

The metabolism of famoxadone in spring wheat was evaluated in a field study (Brown *et al*., 1996). [^{14}C]Famoxadone (POP and PA labels) was applied 3 times as a diluted EC formulation, at 0.2 kg ai/ha, directly onto wheat foliage. Samples were taken 0, 9, 22 and 72 days after the initial treatment. Samples were homogenized with 0.1 M phosphate buffer (pH 3), centrifuged, filtered and extracted with acetone or acetonitrile.

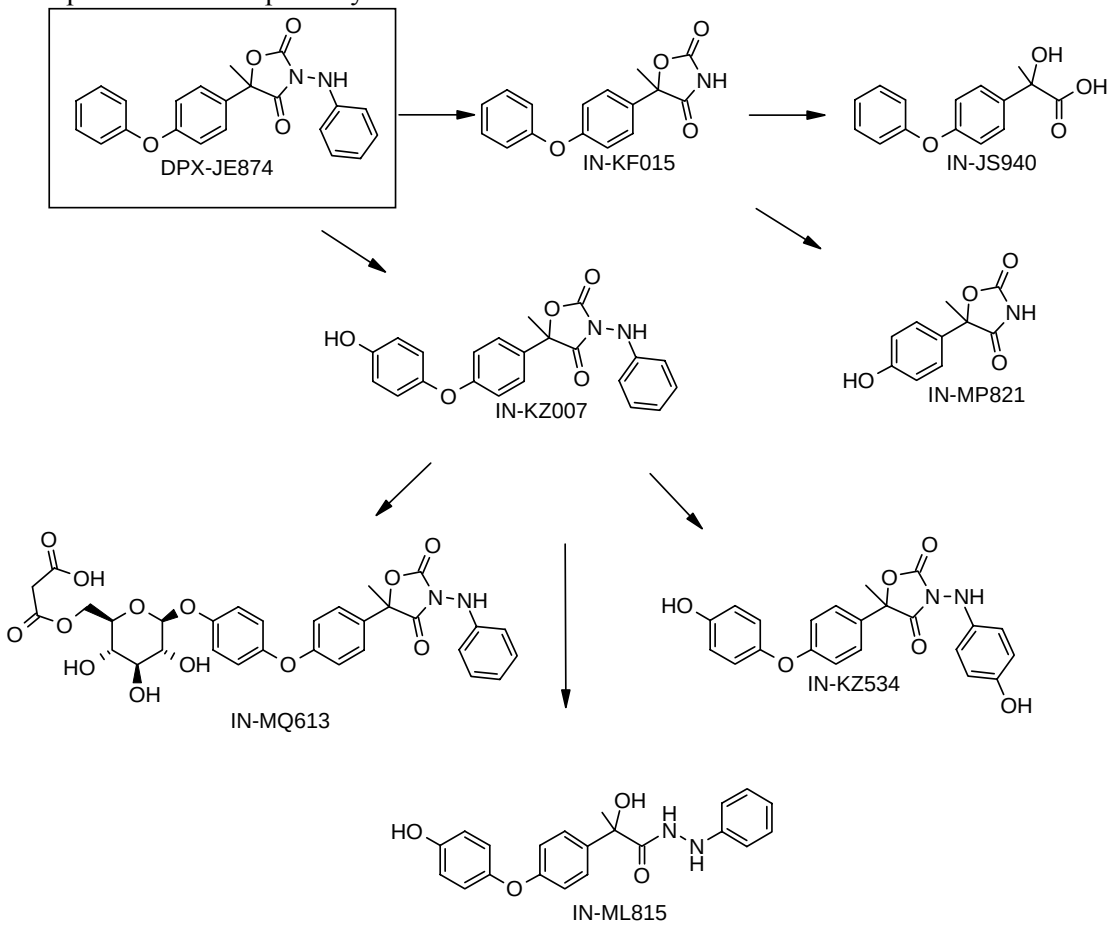
In mature wheat plants, harvested 50 days after the last application (72 days after the first application), low levels of [^{14}C] were detected in the grain (0.01-0.02 mg/kg, famoxadone equivalents) and chaff (0.11 and 0.13 mg/kg, famoxadone equivalents). The majority of the radio-labeled residues (>98%) were found in the straw. Famoxadone was the main component of the extractable residues in foliage and mature straw. Other components include hydroxylation, conjugation and the hydrolytic cleavage products (Table 7, Figure 5). The post-extraction solids were re-extracted (cellulase, 0.1 or 4 N NaOH and 1 N HCl) and the radioactivity measured (Table 7). Most of the unextractable radio-labelled residue was recovered by alkaline hydrolysis, with IN-JS940, an hydrolysis product of famoxadone, tentatively identified as a major component from [^{14}C-POP]-treated plant tissues. In a greenhouse study conducted at the same rate, in which mature wheat samples were taken at 64 days after initial treatment, the results were qualitatively the same as those from the field study.

Table 7. Distribution of total [^{14}C]-residues in fractions of spring wheat foliage and straw after treatment of the growing plants with [^{14}C-POP] and [^{14}C-PA] famoxadone (Brown *et al*., 1996).

Fraction, component	% of the recovered radioactivity (mg/kg ^{14}C famoxadone equivalents)			
	Foliage at day 29		Straw at day 72	
	[^{14}C-POP]	[^{14}C-PA]	[^{14}C-POP]	[^{14}C-PA]
Solvent-extractables	48.9 (1.4)	47.2 (0.86)	40.2 (1.53)	22.0 (0.86)
Components extracted by organic solvent:				
Famoxadone	13.7 (0.39)	15.8 (0.29)	10.0 (0.38)	9.4 (0.37)
IN-KZ007	3.4 (0.10)	3.5 (0.06)	7.0 (0.27)	5.2 (0.20)
IN-KZ534	15.0 (0.43)	9.8 (0.18)	4.1 (0.16)	(<0.01)
Others [1/]	0.89 (0.02)	1.7 (0.03)	3.7 (0.14)	3.2 (0.12)
Components extracted by aqueous solvent:				
IN-MQ613	11.0(0.31)	10.9 (0.20)	3.6 (0.14)	0.7 (0.03)
Others [1/]	4.5 (0.13)	5.2 (0.09)	11.8 (0.45)	3.3 (0.13)
Post-extraction solids	37.4 (1.07)	28.7 (0.52)	20.4 (0.78)	56.1 (2.19)
Components extracted by treatment by:				
Cellulase	10.2 (0.29)	3.8 (0.07)	4.1 (0.16)	11.3 (0.44)
Alkaline extraction	24.8 (0.71)	23.8 (0.43)	15.3 (0.58)	41.4 (1.62)
Acid extraction	2.4 (0.07)	1.1 (0.02)	1.0 (0.04)	3.4 (0.13)
Unextractable fraction	13.8 (0.39)	24.0 (0.44)	39.4 (1.5)	21.9 (0.86)

[1/] Includes all minor metabolites shown in Figure 5.

Figure 5. Proposed metabolic pathway of famoxadone in wheat.



Environmental fate

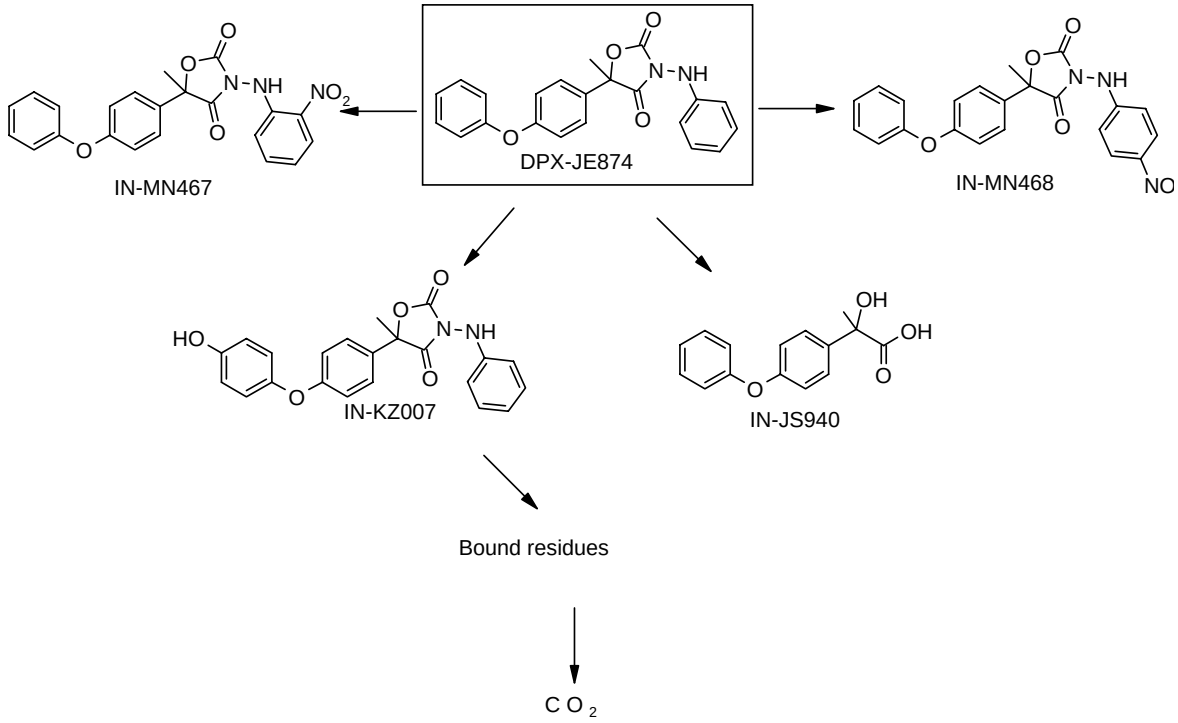
In soil

The fate of famoxadone ([^{14}C-POP] and [^{14}C-PA]) in aerobic soil metabolism was evaluated in a sandy loam soil (16 samples), pH 7.2, in a flow-through metabolism chamber connected to ethylene glycol and sodium hydroxide traps (Kaman, 1996a). The soil was adjusted to 40% of the maximum water-holding capacity (MWHC), after treatment with 0.3-mg famoxadone/kg, and incubated at 20°C. Samples were taken after treatment from day 0 to day 174 (12 sampling days).

Material balances ranged from 80 to 111% and radioactivity evolved as carbon dioxide and trapped in NaOH was 15-38% after 6 months. DT_{50} and DT_{90} values (time at which 50% and 90% of the applied famoxadone disappeared) were 6 and 134 days, respectively. Famoxadone was not detected in the unextractable residues subjected to strong acidic conditions. A high proportion (79.4-93.3%) of the parent compound remained after 90 days in sterile soil, indicating that famoxadone degradation in soil was mainly microbial.

The major route of transformation (Figure 6) was hydroxylation of the parent molecule, to give IN-KZ007, the major degradation product, which reached a peak of 7-16% within 4 days. IN-JS940 reached a peak of 11% in one soil and <5% in the other four soils. A minor pathway involves the formation of two nitro-analogues of famoxadone (IN-MN467 and IN-MN468), which were found at levels <10% in all soils.

Figure 6. Proposed pathway for the degradation of famoxadone in soil under aerobic conditions.



The rate of famoxadone (^{14}C-POP) aerobic degradation was determined in another study in a loamy sand (pH 7.1, 1.1% organic matter), a silt loam (pH 8.0, 1.9% organic matter), and two sandy loam soils (pH 5.3-7.4, 1.9-2.9% organic matter), incubated at 20°C and at 50% MWHC (Kaman, 1996b). All soils were treated at a rate of 0.3 mg/kg. The famoxadone DT_{50} values were: 9 days in the loamy sand soil; 2 days in the silt loam soil; 3 and 11 days in the sandy loam soils.

The rate of degradation of IN-JS940 was determined in three soils, treated at 0.5 mg/kg and incubated at 20°C and 40-50% MWHC (Hatzenbeler, 2000). The DT_{50} values were: 20 hours in a sandy clay loam soil; 23 hours in a loam soil; and 6 hours in sandy loam soil. The DT_{50} values for IN-KZ007 under the same conditions (Theilacker and Van-Nguyen, 2000) were 1.5, 10.3 and 3.2 days in sandy clay loam, loam and sandy loam soils, respectively.

The degradation of famoxadone under field conditions was evaluated in three studies in the USA (McClory and Holt, 1999 and 2000; McClory, 2000) and one in Canada (Bechtel, 2000). The studies were conducted with a fungicide formulation containing 25% famoxadone and 25% cymoxanil, applied 1 or 3 times to bare soil, as a broadcast spray. Soil samples were collected to a depth of 45-90 cm, at a minimum of nine time points during the six months following the last application. No quantifiable residues of famoxadone were found below the 15 cm depth in the USA. In Canada, low levels of famoxadone were found down to 45 cm depth, corresponding to a maximum of 5.8% of the concentration found at 0-15 cm. The DT_{50} values are shown in Table 8.

Table 8. Half life (DT_{50}) of famoxadone in field soils (McClory and Holt, 1999 and 2000; McClory, 2000; Bechtel, 2000).

Reference/Country	Site	Soil (characteristics)	Rate, kg a.i/ha	DT_{50} (days)
McClory and Holt, 1999, USA	Maryland	Silt loam (pH 5.7, 1.6% OM)	3 x 0.296	6
	Florida	Loamy sand (pH 5.7, 0.7% OM)	3 x 3.92	12
	California	Silty clay loam (pH 7.2, 2.6% OM)	3 x 0.296	11
McClory and Holt, 2000, USA	Illinois	Clay loam (pH 5.0, 5.7% OM)	3 x 0.059	20
	Washington	Sandy soil (pH 6.7, 1.2% OM)	3 x 0.059	5
McClory, 2000, USA	Minnesota	Loam (pH 5.3, 3.8% OM)	1 x 1.77	26
	California	Sandy loam (pH 6.3, 0.3% OM)	1 x 1.77	28
Bechtel, 2000, Canada	Prince Edward Island	Sandy loam (pH 5.6, 0.2% OM)	1 x 1.68	26
	Manitoba	Loamy sand (pH 6.8, 2.6% OM)	1 x 1.68	13

Residues in rotational crops

Lettuce, sugar beet and wheat

The uptake and accumulation potential of famoxadone (^{14}C-POP and ^{14}C-PA) and/or its soil metabolites were studied in rotational crops at various intervals, under different soil application scenarios (Brown and Young, 1996; Young and Brown, 1997). [^{14}C]Famoxadone was applied to a bare loamy soil, either one or three times at 400 g a.i./ha. Treated soils were aged under greenhouse conditions for 30, 120 and 365 days prior to planting of lettuce, sugar beet or wheat. No residues of famoxadone (<0.05 mg/kg) were detected sugar beet tops or grain (Table 9).

Table 9 Residues of famoxadone equivalents in soil and crops after application to soil (Brown and Young, 1996; Young and Brown, 1997).

	[^{14}C-POP]famoxadone						[^{14}C-PA]famoxadone					
	30-Day [1]		120-Day [3]		365-day [4]		30-Day [1]		120-Day [3]		365-day [4]	
	mg/kg	Ratio [2]	mg/kg	Ratio [2]	mg/kg	Ratio [2]	mg/kg	Ratio [2]	mg/kg	Ratio [2]	mg/kg	Ratio [2]
Soil												
TRR	0.46	-	.19, 2.58	-	0.33	-	0.23	-	0.15, 2.82	-	0.34	-
Famox.	0.36	-	.04	-	-	-	0.15	-	0.03	-	-	-
Lettuce												
TRR	0.15	0.32	.02 (2)	0.11, 0.01	0.03	0.09	0.05	0.22	0.02 (2)	0.13,0.01	0.03	0.09
Famox.	0.04	0.11	0.01	-	-	-	<0.01	-	<0.01	-	-	-
Sugar beet tops												
TRR	0.03	0.06	.02, 0.03	0.11, 0.01	0.02	0.06	0.02	0.09	0.02, 0.04	0.13,0.01	0.02	0.06
Famox.	<0.01	-	0.01	-	-	-	<0.01	-	<0.01	-	-	-
Sugar beet roots												
TRR	0.17	0.37	.03, 0.06	0.16, 0.02	0.08	0.24	0.20	0.87	0.04, 0.08	0.26,0.03	0.08	0.23
Famox.	0.04	0.11	0.01	-	-	-	0.04	0.27	<0.01	-	-	-
Wheat foliage												
TRR	0.09	0.20	.04 (2)	0.21, 0.02	0.02	0.06	0.04	0.17	0.03, 0.04	0.2,0.01	0.02	0.06
Famox.	0.02	0.06	0.01	-	-	-	0.02	0.13	<0.01	-	-	-
Wheat straw												
TRR	0.28	0.61	.21, 0.37	1.1, 0.14	0.28	0.85	0.39	1.70	0.19, 0.37	1.27,0.13	0.33	0.97
Famox.	0.03	0.08	.06	1.5	-	-	0.06	0.40	0.01	0.33	-	-
Wheat grain												
TRR	0.06	0.13	.05, 0.07	0.26, 0.13	0.05	0.15	0.04	0.17	0.05 (2)	0.33,0.02	0.04	0.12
Famox.	<0.01	-	<0.01	-	-	-	<0.01	-	<0.01	-	-	-

TRR = total radioactive residue. Famox. = famoxadone (parent compound).

[1] Data after a single application.

[2] Ratio of mg famoxadone equivalents/kg tissue to mg equivalents/kg soil.

[3] First number after single application, second after 3 applications.

[4] Data after 3 applications.

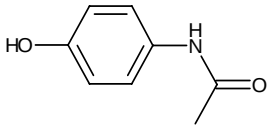
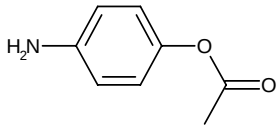
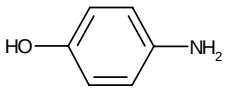
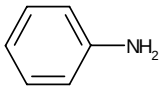
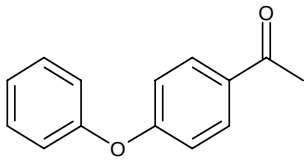
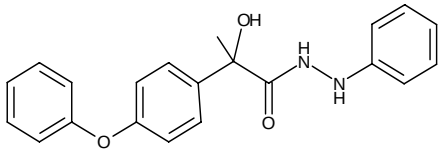
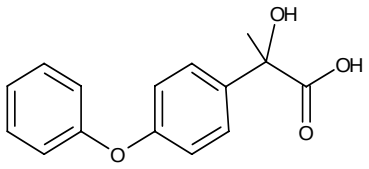
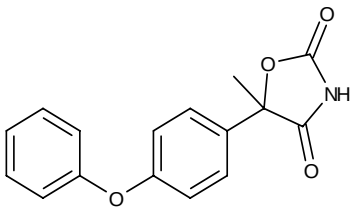
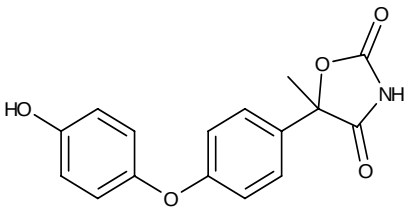
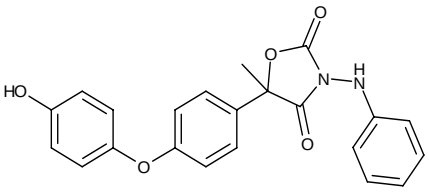
Soil samples taken from a supervised trial on potatoes, conducted in Italy, at 14 days after the last of 8 applications of famoxadone at 0.18 kg ai/ha, representing 2 times the GAP rate (Jernberg and Dubey, 1997a), showed average levels of famoxadone residues in soil of 0.09 mg/kg. Levels of the likely residues in succeeding crops were calculated by applying the crop:soil accumulation ratio values found in Table 9 to the average field soil residue level. Table 10 indicates the predicted residues of famoxadone in lettuce, sugar beet or wheat, following application to a preceding crop of potatoes.

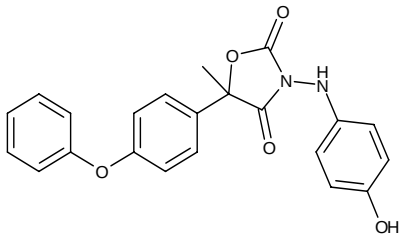
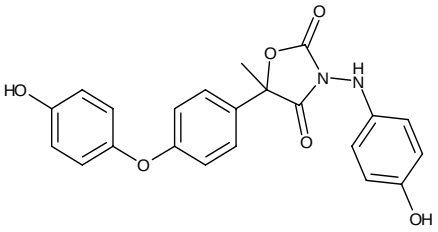
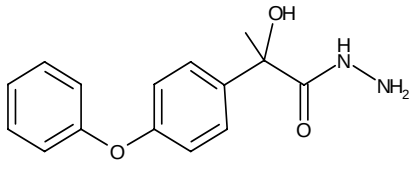
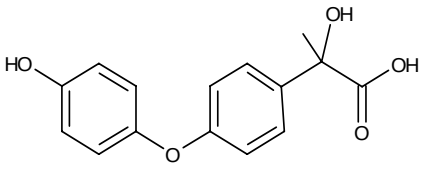
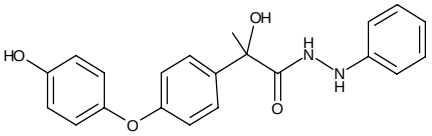
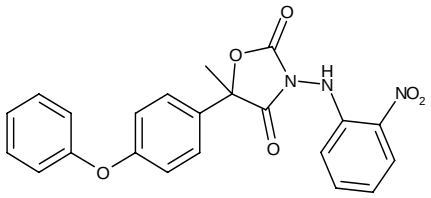
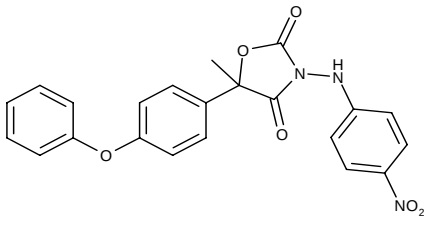
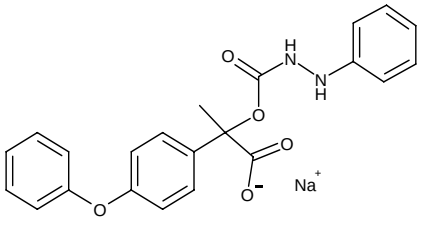
Table 10. Estimation of famoxadone residues in succeeding crops (Jernberg and Dubey, 1997a).

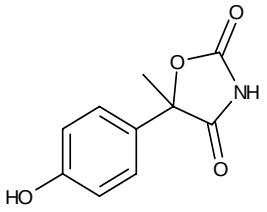
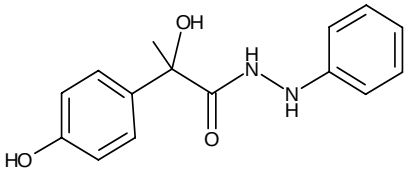
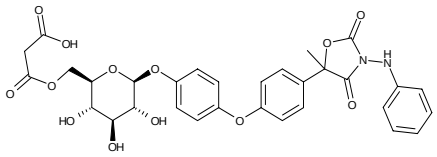
Crop	Average ratio famoxadone, crop:soil (B)	Estimated famoxadone in crop (mg/kg), following treatment to potatoes (0.09*B)
Lettuce	0.11	0.01
Sugar beet tops	-	<<0.01
Sugar beet roots	0.19	0.02
Wheat foliage	0.10	0.009
Wheat straw	0.58	0.05
Wheat grain	-	<<0.01

Table 11 summarizes the metabolites and degradation products of famoxadone found in studies of animal and plant metabolism and of environmental fate.

Table 11. Metabolites and degradation products of famoxadone.

Code	CAS name, number, MW	Structure	Observed in:
IN-00915	*N*-(4-hydroxyphenyl)acetamide 103-90-2 MW=151.17		hen
IN-BY759	4-aminophenyl acetate 13871-68-6 MW = 151.17		rat
IN-CH490	4-aminophenol 123-30-8 MW = 109.13		hen, goat
IN-E0933	benzenamine (aniline) 62-53-3 MW = 93.13		hen
IN-H3310	1-(4-phenoxyphenyl)ethanone 5031-78-7 MW=212.25		hydrolysis, rat, grapes, potatoes
IN-JL856	alpha-hydroxy-alpha-methyl-4-phenoxy benzeneacetic acid 2-phenylhydrazide MW = 348.41		Hydrolysis, rat
IN-JS940	alpha-hydroxy-alpha-methyl-4-phenoxybenzene acetic acid 157874-97-0 MW = 258.28		hydrolysis, hen, wheat
IN-KF015	5-methyl-5-(4-phenoxyphenyl)-2,4-oxazolidinedione MW = 283.29		hen, wheat
IN-KZ000	5-[4-(4-hydroxyphenoxy)phenyl]-5-methyl-2,4-oxazolidinedione MW = 299.29		Rat, goat, hen
IN-KZ007	5-[4-(4-hydroxyphenoxy)phenyl]-5-methyl-3-(phenylamino)-2,4-oxazolidinedione MW=390.40		rat, goat, hen, wheat, aerobic soil

Code	CAS name, number, MW	Structure	Observed in:
IN-KZ532	3-[(4-hydroxyphenyl)amino]-5-methyl-5-(4-phenoxyphenyl)-2,4-oxazolidinedione MW = 390.40		Goat, hen, wheat
IN-KZ534	5-[4-(4-hydroxyphenoxy)phenyl]-3-[(4-hydroxyphenyl)amino]-5-methyl-2,4-oxazolidinedione MW=406.40		rat, goat, hen, wheat
IN-ME338	alpha-hydroxy-alpha-methyl-4-phenoxybenzeneacetic acid hydrazide MW = 272.31		hen
IN-ML436	alpha-hydroxy-alpha-methyl-4-(4-hydroxyphenoxy)-4-phenoxy benzeneacetic acid MW = 274.28		hen
IN-ML815	alpha-hydroxy-alpha-methyl-4-(4-hydroxyphenoxy) benzeneacetic acid 2-phenylhydrazide MW=364.40		wheat
IN-MN467	5-methyl-3-[(2-nitrophenyl)amino]-5-(4-phenoxyphenyl)-2,4-oxazolidinedione MW=419.40		aerobic soil
IN-MN468	5-methyl-3-[(4-nitrophenyl)amino]-5-(4-phenoxyphenyl)-2,4-oxazolidinedione MW=419.40		aerobic soil
IN-MN968	1-carboxy-1-(4-phenoxyphenyl)ethyl 2-phenylhydrazinecarboxylate sodium salt MW = 414.40		hydrolysis

Code	CAS name, number, MW	Structure	Observed in:
IN-MP821	5-(4-hydroxyphenyl)-5-methyl-2,4-oxazolidinedione MW = 207.19		hen, wheat
IN-MQ609	alpha, 4-dihydroxy-alpha-methylbenzeneacetic acid phenylhydrazide MW = 272.31		hen
IN-MQ613	[4-[4-[5-methyl-2,4-dioxo-3-(phenylamino)-5-oxazolidinyl]phenoxy]phenyl]-β-D-glucopyranoside 6-(hydrogen propanedioate) MW = 638.59		wheat

METHODS OF RESIDUE ANALYSIS

Plant materials

Famoxadone was extracted from crop matrices with acetonitrile, the fat removed by partition with hexane and the famoxadone quantified by reversed-phase HPLC (phenyl column), under isocratic conditions with ultra-violet (228 nm) absorption detection. The limit of quantification (LOQ) was 0.020 mg/kg, based on 25 g samples (Cicotti *et al*., 1994). Alternatively, following the same extraction procedure, famoxadone was quantified by reversed-phase (C-8) HPLC-MS (positive thermospray, monitoring the *m/z* 392.2 ion, $[M + NH_4]^+$) (Cicotti *et al*., 1995). The LOQ for cereal straw and forage was 0.050 mg/kg, based on a 5 g sample. The LOQ for grapes and cereal grain was 0.020 mg/kg, based on a 10 g sample.

In a third method, the crop was extracted with acetonitrile/water, the extract was partitioned against hexane, then the acetonitrile extract was passed through a chromatography column packed with sodium sulfate and Florisil. The column was initially eluted with 10% ethyl ether in hexane, then the famoxadone was selectively eluted with 20% ethyl acetate in hexane and determined by column-switching HPLC using a phenyl/C-18 system and UV detection at 245 nm (Nathan et al., 1998; Holt et al., 1999). Column-switching liquid chromatography was found to give the best separation of famoxadone from matrix co-extractives. The LOQ was 0.020 mg/kg, based on a 20 g sample. This method was independently validated by Lucas (1999a) for the analysis of raw tomato and tomato paste and can be used for enforcement purposes. Comparative analysis of tomato samples containing incurred residues showed that acetonitrile/water had an average extraction efficiency of 110%, compared with that of the method used in a radio-labelled metabolism study (Holt and McClory, 1999).

In another method, samples were extracted with acetone/water, the extracts filtered through sodium sulfate, evaporated, then diluted with ethyl acetate. Sodium sulfate and sodium chloride were added, followed by cyclohexane. The mixture was filtered and the filtrate was subjected to gel permeation chromatography (GPC) clean-up on Bio Beads S-X3 polystyrene gel, using a mixture of ethyl acetate/cyclohexane (1:1) as the eluent. Concentrated GPC fractions were additionally cleaned up on a small silica gel column, to obtain extracts ready for GC-ECD determination and GC-MSD as a confirmation technique. Limits of quantification were: 0.05 mg/kg for raisins and tobacco; 0.02 mg/kg for grapes and cucumbers; and 0.010 mg/kg for wine, potatoes and wheat grain (Linkerhägner, 1999).

The performance of methods used for the determination of famoxadone residues in crops is summarized in Table 12.

Table 12. Overview of analytical methods for the determination of famoxadone in crops.

Matrix	Fortification level (mg/kg)	Mean recovery, (%)	Relative standard deviation (%)	Range of recoveries (%)		Reference
				low	high	
Grapes	0.02	78	7.4 (n=3)	75	85	Cicotti et al., 1994
	0.10	79	3.9 (n=3)	76	82	Study AMR 2802-93
	0.50	80	3.6 (n=3)	77	82	
Wheat straw	0.05	74	2.7 (n=3)	72	76	
	0.10	79	6.3 (n=3)	74	84	
	0.50	76	6.2 (n=3)	71	80	
Wheat grain	0.05	86	9.3 (n=3)	78	94	
	0.10	83	3.7 (n=3)	80	86	
	0.50	76	6.2 (n=3)	71	80	
Grapes	0.02	106	2.4 (n=3)	103	108	Cicotti et al., 1995
	0.10	98	13 (n=3)	87	112	Study AMR 2801-93
	0.50	94	11 (n=3)	84	105	
Wheat straw	0.05	109	1.1 (n=3)	108	110	
	0.10	101	14 (n=3)	86	114	
	0.50	85	18 (n=3)	70	100	
Wheat forage	0.05	101	8.0 (n=3)	92	108	
	0.10	99	9.6 (n=3)	92	110	
	0.50	85	2.5 (n=3)	83	87	
Wheat grain	0.02	94	21 (n=3)	72	112	
	0.10	90	16 (n=3)	79	106	
	0.50	94	11 (n=3)	86	105	
Tomato	0.02-0.12	93	2 (n=3)	86	106	Holt, et al., 1999
Tomato puree	0.02-0.12	82	11 (n=3)	73	90	Study DuPont-1651
Tomato paste	0.02-0.12	89	21(n=3)	74	110	
Tomato	0.02	113	- (n=2)	111	115	Lucas (1999a)
	1.0	118	- (n=2)	117	118	Study DuPont-2031
Tomato paste	0.02	122	- (n=2)	116	127	
	1.0	112	- (n=2)	111	113	
Potato	0.01	98	5.5 (n=5)	93	107	Linkerhägner, M. 1999
	0.10	95	6.1 (n=5)	88	102	.Study DuPont-3253
Cucumber	0.02	102	4.8 (n=5)	97	109	inkerhägner, M. 2000.
	0.20	100	5.0 (n=5)	94	105	Study DuPont-3253 Supplement No. 1
Grape	0.02	106	4.9 (n=5)	97	110	
	0.20	98	6.0 (n=5)	88	103	
Wine	0.01	91	1.8 (n=5)	89	93	
	0.10	91	2.5 (n=5)	87	93	
Raisin	0.05	94	2.7 (n=5)	92	98	
	0.50	95	1.2 (n=5)	93	96	
Grain	0.01	76	6.0 (n=5)	71	82	
	0.10	88	2.4 (n=5)	85	90	
Tobacco	0.05	100	9.5 (n=5)	91	114	
	0.50	106	5.1 (n=5)	98	112	

Animal materials

In a method described by Powley and de Bernard (1999), the animal tissue sample was mixed with 6 g of C-18 packing and allowed to air-dry. The mixture was packed into an SPE reservoir, eluted firstly with hexane and then the famoxadone was eluted with acetonitrile. The eluate was filtered through a bed of basic alumina and the extract was then passed through a graphitized-carbon SPE cartridge. The acetonitrile solution that passed through the cartridge was collected and the cartridge then eluted

with methanol/dichloromethane (10:90, v/v). The two eluates were combined and evaporated to dryness. A final clean-up was made by means of a silica cartridge, to remove additional lipid material. The final extract was analyzed by column-switching HPLC (phenyl and C18 columns) and UV detection at 245 nm. Limits of quantification (LOQ) were: 0.010 mg/kg for whole milk, skimmed milk, cream and whole egg; and 0.050 mg/kg for bovine liver. Recoveries were 70-105% at 0.010-2.0 mg/kg fortification levels. The method was proposed for regulatory use.

Independent validation of this proposed method was conducted by Lucas (1999b). The average recovery and RSD (n=4) of famoxadone at 0.01 and 0.05 mg/kg was 98 ± 15% from muscle, 87 ± 8.0% from fat and 94 ± 4.0% from milk. From liver, the average recovery was 90 ± 4.3% at 0.05 and 0.25 mg/kg.

The efficiency of extraction of incurred radiolabelled famoxadone residues in animal tissues was tested using a matrix solid-phase dispersion method (Anderson and Swain, 1999). Tissues and milk samples obtained from a lactating goat that received a nominal 5 mg/kg (dietary) dose of ^{14}C-famoxadone were analyzed. The extraction efficiency of this residue extraction technique, compared with the extraction method used in the goat metabolism study for milk, liver and fat was 107%, 110%, and 87.4%, respectively. The method used in the metabolism study involved extraction with acetonitrile and clean-up with C-18 SPE.

A GC-NPD method was developed for milk, eggs and animal tissues (McClory, 1996). Samples were extracted with acetonitrile/water, the extract was salted out with sodium chloride, partitioned with hexane and cleaned-up on Florisil SPE column. Average recoveries at 0.02 and 0.5 mg/kg levels were 85-107%, with RSD 4-12% (n=3 at each level), from beef muscle and fat, milk, poultry muscle and eggs.

Stability of residues in stored analytical samples

Storage stability studies on famoxadone residues were conducted on samples of grapes, potatoes, wheat forage, straw, grain and soil (Dubey and Verdelet, 1996). The samples were fortified with famoxadone at 1 mg/kg and stored at -20°C for up to 18 months. At each sampling interval, two fortified and two control samples of each matrix were analyzed by the method of Cicotti *et al*. (1995). One control was freshly fortified, to determine method recovery, which was 80-110%. The results are shown in Table 13.

Table 13. Storage stability of famoxadone in crops fortified at 1 mg/kg (Dubey and Verdelet, 1996).

Matrix	Storage interval (months)	Average % Remaining (n=2)
Grapes	0	99
	6	105
	12	100
	18	99
Potatoes	0	97
	3	49
	6	73
	7	54
	12	65
	18	68
Wheat forage	0	87
	6	88
	12	87
	18	77
Wheat straw	0	80
	6	72
	7	82
	12	83
	18	70
Wheat grain	0	96
	6	98
	12	79
	18	70

Matrix	Storage interval (months)	Average % Remaining (n=2)
Soil	0	99
	6	99
	12	95
	18	94

Storage stability studies were also conducted on tomatoes and peppers (McClory, 1999; Report AMR 3740-96), cucumbers (Nathan, 1999a, Report AMR 4340-97) and potatoes (Nathan and McClory, 1998, Report AMR 4337-97), which were fortified with 0.3 mg/kg famoxadone and stored at -20°C for up to 18 months (Table 14).

Table 14. Storage stability study of famoxadone at 0.3 mg/kg in crops stored at -20 °C (Nathan and McClory, 1998; McClory, 1999; Nathan, 1999a,).

Matrix	Storage interval (months)	Average remaining, % (n=2)
Tomatoes	0	110
	1	113
	3	83
	6	100
	12	100
	18	110
Peppers	0	107
	1	110
	3	90
	6	123
	12	110
	18	107
Cucumbers	0	104
	3	102
	6	96
	10	94.5
Potatoes	0	80
	7 days	100
	14 days	107
	1	90
	2	100
	9.4	90
	10.5	102

A study was conducted into the storage stability of famoxadone residues in tomato paste, fortified at 1 mg/kg, and in tomato purée, fortified at 0.30 mg/kg, and stored at -10°C for up to 18 months (Grant, 2001). At intervals, 2 stored samples, 2 freshly fortified samples and one control sample were analyzed. Average procedural recoveries (fresh samples) were 74-98% from the two commodities at all storage intervals. The results are shown in Table 15.

Table 15. Storage stability study of famoxadone in tomato paste and tomato puree stored at -10°C (Grant, 2001).

Matrix	Storage interval (months)	Average remaining, % (n=2)
Tomato paste 1 mg/kg	0	74
	3	78
	6	88
	9	86
	12	88
	15	85
	18	93
Tomato puree 0.3 mg/kg	0	86
	3	85
	6	90
	9	87
	12	98
	15	90
	18	89

The storage stability of famoxadone was evaluated in whole milk, fortified with 0.1 mg/l, and in muscle and liver containing incurred residues at 9.0 mg/kg, when stored at -20ºC (Nathan, 1999b, Report 1219- Rev 1; Lee *et al*., 2000). The average remaining in milk was 90% at 0 day and 87% after 30 and 117 days (n=2). Residues in muscle did not change from day 21 (0.072 ± 0.019 mg/kg, n=3) to day 138 (0.073 ± 0.019 mg/kg, n=3). In liver, residues were 0.069 ± 0.010 mg/kg at day 21 and 0.065 ± 0.023 mg/kg at day 139.

USE PATTERN

Famoxadone is registered for use against a large number of plant diseases in a wide range of crops, in many countries. Table 16 contains a summary of registered uses of famoxadone in Europe on crops which were evaluated by the Meeting. Only data on trials conducted in Europe were submitted.

Table 16. Registered uses of famoxadone on crops.

Crop	Country	F/G	Form	Content of a.i(s).	Application				PHI
					Method	Rate, kg ai/ha	Spray conc., kg ai/hl	No.	
Barley	Belgium	F	EC	100 g/l famoxadone + 107 g/l flusilazole	foliar	0.15 + 0.16	not applicable	1	28
Barley	France	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	foliar	0.15 + 0.16	not applicable	2	49
Barley	Ireland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.150 + 0.160	not applicable	2	GS49
Barley	Switzerland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.15 + 0.16	0.04-0.075 + 0.04-0.08	1	not set
Barley	UK	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.150 + 0.160	0.075 + 0.08	2	GS53
Barley	Germany	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	spraying	0.15 + 0.16	0.04-0.08	2	42
Cucumber	Italy	F/G	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.1125 + 0.15	0.01125 + 0.015	3	10
Grape	France	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	foliar	0.05 + 0.5	0.005 + 0.05	3	28
		F	WG	225g/kg famoxadone + 300 g/kg cymoxanil	foliar	0.09 + 0.12	0.009 + 0.012	3	28
Grape	Germany	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	medium volume spray	0.036-0.144 + 0.048-0.192	0.009 + 0.012	8	28
Grape	Greece	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.07-0.09 + 0.09-0.12	0.14-0.18 l/ha + 0.9-0.24 l/ha	6	28
Grape	Greece	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	spray	0.05 + 0.5	0.005-0.00625 + 0.05-0.0625	4	28
Grape	Italy	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	low volume atomizer	0.09 + 0.12	0.009 + 0.12	3	28
Grape	Italy	F	WG	62.5g /kg famoxadone + 625 g/kg mancozeb	< 10hl/ha	0.05 + 0.5	0.005 + 0.05	3	28
Grape	Spain	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.09 + 0.12	-	6	28
Grape	Italy	F	WG	4% famoxadone + 60% fosetyl aluminium	low volume atomizer	0.100 + 1.5	0.033-0.067 + 0.5-1.0	3	40
Grape	Italy	F	WG	2% famoxadone + 20% copper	low volume atomizer	0.05 + 0..5	0.01 + 0.1	3	28
Grape	France	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	foliar	0.05 + 0.5	0.005 + 0.05	NA	28
Grape	Italy	F	WG	4% famoxadone + 60% fosetyl aluminium	high volume spray	0.100 + 1.5	0.01 + 0.15	3	40
Grape	Italy	F	WG	2% famoxadone + 20% copper	high volume spray	0.05 + 0.5	0.005 + 0.05	3	28
Melon	Italy	F/G	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.1125 + 0.15	0.01125 + 0.015	3	10
Potato	Belgium	F	WG	250 g/kg famoxadone + 250 g/kg cymoxanil	foliar	0.15 + 0.15	-	6	14

Crop	Country	F/G	Form	Content of a.i(s).	Application				PHI
					Method	Rate, kg ai/ha	Spray conc., kg ai/hl	No.	
Potato	Germany	F	WG	250 g/kg famoxadone + 250 g/kg cymoxanil	medium volume spray	0.175 + 0.175	-	6	14
Potato	Greece	F	WG	250 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.07-0.09 + 0.09-0.12	0.09-0.18 l/ha + 0.12-0.24 l/ha	8	14
Potato	Ireland	F	WG	250 g/kg famoxadone + 250 g/kg cymoxanil	medium volume spray	0.175 + 0.175	not applicable	12	14
Potato	Italy	F	WG	250 g/kg famoxadone + 300 g/kg cymoxanil	high volume spray	0.09 + 0.12	0.009 + 0.012	6	14
Potato	Netherlands	F	WG	250 g/kg famoxadone + 250 g/kg cymoxanil	spraying	0.15		3	-
Potato	Spain	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	medium volume spray	0.09 + 0.12	-	4	14
Potato	UK	F	WG	250 g/kg famoxadone + 250 g/kg cymoxanil	medium volume spray	0.125-0.175 + 0.125.175	0.035-0.058 + 0.035-0.058	12	14
Rye	Germany	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	spraying	0.15 + 0.16	0.04-0.08	2	42
Rye	Switzerland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.15 + 0.16	0.04-0.075 + 0.04-0.08	1	not set
Tomato	France	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	foliar	0.09 + 0.12	-	4	3
Tomato	France	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	foliar	0.05 + 0.5	-	4	3
Tomato	Italy	F/G	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.1125 + 0.15	0.01125 + 0.015	3	10
Tomato	Italy	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	low volume atomizer	0.05 + 0.5	0.005 + 0.05	6	3
Tomato	Spain	F/G	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.09 + 0.12	-	4	3
Tomato	Greece	F	WG	62.5 g/kg famoxadone + 625 g/kg mancozeb	spray	0.05 + 0.5	0.0031-0.00625 + 0.031-0.0625	4	3
Tomato	Greece	F	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	spray	0.07-0.09 + 0.09-0.12	0.09-0.18 l/ha + 0.12-0.24 l/ha	8	3
Triticale	Germany	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	spraying	0.15 + 0.16	0.04-0.08	2	42
Wheat	Belgium	F	EC	100 g/l famoxadone + 107 g/l flusilazole	foliar	0.15 + 0.16	NA	1	28
Wheat	France	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	foliar	0.15 + 0.16	NA	2	36
Wheat	Germany	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	spraying	0.15 + 0.16	0.04-0.08	2	42
Wheat	Switzerland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.28 + 0.30	0.014-0.075 + 0.075-0.15	1	not set
Wheat	Switzerland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.15 + 0.16	0.04-0.075 + 0.04-0.08	1	not set
Winter wheat	Ireland	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.150 + 0.160	not applicable	3	GS59
Winter wheat	UK	F	EC	100 g/l famoxadone + 106.7 g/l flusilazole	medium volume spray	0.150 + 0.160	0.075 + 0.08	3	GS60
Zucchini	Italy	F/G	WG	225 g/kg famoxadone + 300 g/kg cymoxanil	high volume spray	0.1125 + 0.15	0.01125-0.0450 + 0.015-0.060	3	10

F/G Foliar or ground application.
PHI Days or expressed as the latest growth stage (GS) permitted for application. NA: Information not available.
GS53 Apply before one quarter ear emergence; G60 = apply before flowering.

RESIDUES RESULTING FROM SUPERVISED TRIALS

Tables 17 to 25 summarize the data from supervised trials conducted in crops in Europe. When residues were not detected they are shown as below the LOQ (e.g. <0.02 mg/kg). Residue data were

rounded to two significant figures or, for values near the LOQ, to one significant figure. Values double underlined are within maximum GAP (+/- 30%) and were considered for the estimation of maximum residue levels, STMRs and HRs.

Studies were conducted according to GLP requirements and the data included method validation, dates of analysis of samples, sprayers used and their calibration, plot size, residue sample size and sampling method. Unless otherwise specified, all trials were conducted in the field, with foliar application. In each trial, two or three treated samples and one control sample were collected at sampling time and analyzed within 5 months after harvested. The average residue levels found in treated samples are shown. Data were not corrected for % recovery of the method.

The Meeting received information on:

Crop	Table	Crop	Table
Grapes	17	Barley	22
Melons, except watermelons	18	Wheat	23
Cucumbers	19	Barley straw and forage	24
Tomatoes	20	Wheat straw and forage	25
Potatoes	21		

Grapes

Twenty-five trials were conducted on grapes in France, Greece, Italy, Spain and Germany, between 1995 and 1999, using 10 to 12 applications of 0.05 to 0.15 kg a.i./ha of famoxadone as a WG formulation, at 7-day intervals (Table 17). Initial application was at flowering stage (young vine shoots approximately 15 cm). Five trials were decline studies, with samples being collected up to 30 days after the last application.

Table 17. Residues of famoxadone in/on grapes after 10-12 applications of famoxadone (Cicotti *et al*., 1996a and 1996b; Françon and Lee, 1997a and 1997b; Linkerhägner and Jernberg, 2000;).

Location, year, variety, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water (l/ha)		
France, Crezancy, 1995. Pinot	12	0.1	435-596	36	0.25
AMR 3361-95	12	0.09-0.12	435-596	36	0.24
France, Merrey/Arce, 1995. Pinot	12	0.1	281-346	30	0.48
AMR 3361-95	12	0.09-012	281-346	30	0.48
France, Amboise, 1995. Sauvignon	12	0.089-0.097	39-933	1 [1/]	0.34
AMR 3362-95				7	0.32
				14	0.28
				21	0.26
				30	0.19
France, Loupes, 1995. Barbera	12	0.86-0.094	403-707	1 [1/]	1.3
AMR 3362-95				7	1.1
				14	1.4
				21	0.89
				31	0.98
France,Vernou s/Brenne, 1996. Chenin blanc	12	0.085-0.097	193-293	30	0.54
AMR 3763-96					
France, Villetelle, 1996. Carignan	12	0.088-0.091	293-304	31	0.74
AMR 3763-96					
France Essoyes, 1999. Chardonnay	10	0.1106-0.1447	1268-1348	28	0.37
DuPont-2712					

Location, year, variety, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water (l/ha)		
France Le Landreau, 1999. Muscadet DuPont-2712	10	0.072-0.146	826-1046	28	0.48
Germany, Kleinkarlbach, 1995. Riesling AMR 3361-95	12	0.1	800	29	0.66
	12	0.09-0.12	800	29	0.66
Germany, Steigra, 1995. Muller-Thurgan AMR 3361-95	12	0.1	1000	31	0.90
	12	0.09-0.12	1000	31	1.0
Germany, Steigra, 1995. Muller-Thurgan AMR 3362-95	12	0.090	1000	1 [1/] 7 14 21 31	2.6 2.2 2.1 1.6 1.5
Germany Höhnstedt, 1999. Domfelder DuPont-2712	10	0.087-0.140	1000-1600	28	0.62
Germany, Radebeul, 1999. Kerner DuPont-2712	10	0.087-0.140	1000	2 hrs 1 7 14 28	0.39 0.33 0.33 0.27 0.29
Germany Kleinkarlbach, 1996. Riesling AMR 3810-96	12	0.053-0.104	304-888	28	0.55
Greece, Noa Gonia, 1995. Victoria AMR 3361-95	10	0.1	500	29	0.46
	10	0.09-0.12	500	29	0.50
Italy Isola D'Asti, 1995. Barbera AMR 3362-95	12	0.09	944-944	1 [1/] 7 14 21 30	0.41 0.28 0.30 0.32 0.19
Italy, Beano di Codroipo, 1996. Chardonnay AMR 3763-96	12	0.09	1000	30	0.56
Spain, Umbrete, 1995. Garrido fino AMR 3361-95	12	0.1	791-1019	28	0.90
	12	0.09-0.12	755-1060	28	1.2
Spain, Villanueva, 1996. Garrido fino AMR 3763-96	12	0.084-0.092	938-1019	28	0.50

[1/] Average of 4 samples, 2 at 23 hours and 2 at 25 hours after the last application.

Cucumbers

Ten trials were conducted on glasshouse cucumbers in Italy, Greece and Spain in 2001, in which 5 applications of famoxadone were made at 0.065 to 0.12 kg a.i./ha (Table 18). Five trials were residue decline studies.

Table 18. Residues of famoxadone in protected cucumbers after 5 applications of WG formulation in Europe in 2001 (Steinhauer *et al*., 2002).

Location, report No.	Application		PHI, days	Residue, mg/kg
	kg a.i./ha	kg a.i./hl		
Greece, Thessaloniki DuPont-5518	0.103-0.113	0.011	3 7	0.07 0.03
	0.08-0.11	0.013	2 hours 1 3 5 7	0.12 0.11 0.10 0.08 0.05
Italy, Bologna DuPont-5518	0.065-0.118	0.012	2 hours 1 3 5 7	0.37 0.37 0.17 0.08 0.05
	0.065-0.11	0.011	2 hours 1 3 5 7	0.04 0.04 0.06 0.04 0.02

Location, report No.	Application		PHI, days	Residue, mg/kg
	kg a.i./ha	kg a.i./hl		
Italy, Vittorio DuPont-5518	0.11	0.011	3 7	0.03 0.02
	0.11	0.011	3 7	0.04 0.01
Spain, El Ejido DuPont-5518	0.077-0.117	0.011	3 7	0.05 0.02
Spain, Pastrana DuPont-5518	0.11	0.011	2 hours 1 3 5 7	0.02 0.14 0.12 0.14 0.10
Spain, Mazarrón DuPont-5518	0.112-0.117	0.011	3 7	0.09 0.03
Spain, Sevilla DuPont-5518	0.112	0.011	2 hours 1 3 5 7	0.07 0.07 0.03 0.01 0.01

Melons, except watermelon

Twenty trials were conducted on melons in Italy, Greece, France and Spain, either in the glasshouse or in the field in 1991, using 5 applications of famoxadone (Table 19). Pulp and peel were analyzed separately and decline studies were also conducted.

Table 19. Residues of famoxadone in protected (Steinhauer and Jernberg, 2002a, Report No 5520) and field-grown (Steinhauer and Jernberg, 2002b, Report No 5521) melons, except watermelons, after 5 applications of WG formulation in Europe in 2001

Location, conditions, report No.	Application		PHI, days	Matrix	Residues, mg/kg
	kg a.i./ha	kg a.i./hl			
Protected crops (Study 5520)					
France, Rognonas	0.114-0.119	0.011	3	Pulp Peel Whole fruit	<0.01 0.18 0.06
France, Sénas	0.112-0.113	0.016-0.019	2 hrs	Pulp Peel Whole fruit	<0.01 0.05 0.16
			1	Pulp Peel Whole fruit	<0.01 0.22 0.08
			3	Pulp Peel Whole fruit	<0.01 0.22 0.07
			5	Pulp Peel Whole fruit	<0.01 0.26 0.09
			7	Pulp Peel Whole fruit	<0.01 0.18 0.06
Greece, Angelochori,	0.109-0.117	0.011-0.012	3	Pulp Peel Whole fruit	<0.01 0.10 0.05

Location, conditions, report No.	Application		PHI, days	Matrix	Residues, mg/kg
	kg a.i./ha	kg a.i./hl			
Zapponeta (FG), Italy	0.110-0.112	0.011	1	Pulp	<0.01
				Peel	0.18
				Whole fruit	0.10
			3	Pulp	<0.01
				Peel	0.16
				Whole fruit	0.09
			5	Pulp	<0.01
				Peel	0.12
				Whole fruit	0.07
			7	Pulp	<0.01
				Peel	0.21
				Whole fruit	0.12
Italy, Rodigo	0.109-0.114	0.011	3	Pulp	<0.01
				Peel	0.04
				Whole fruit	0.02
Italy, Zapponeta	0.110-0.112	0.011	1	Pulp	<0.01
				Peel	0.29
				Whole fruit	0.16
			3	Pulp	<0.01
				Peel	0.35
				Whole fruit	0.18
			5	Pulp	<0.01
				Peel	0.39
				Whole fruit	0.21
			7	Pulp	<0.01
				Peel	0.37
				Whole fruit	0.22
Spain, Pozuelo	0.110-0.115	0.0125-0.015	3	Pulp	<0.01
				Peel	0.26
				Whole fruit	0.14
Spain, Adra	0.110-0.113	0.013-0.015	2 hrs	Pulp	0.24
				Peel	0.22
			1	Whole fruit	0.12
				Pulp	<0.01
				Peel	0.18
			3	Whole fruit	0.10
				Pulp	<0.01
				Peel	0.21
			5	Whole fruit	0.11
				Pulp	<0.01
				Peel	0.18
			7	Whole fruit	0.11
				Pulp	<0.01
				Peel	0.14
				Whole fruit	0.08
Spain, Vejer de la Frontera	0.112-0.116	0.01125	3	Pulp	0.04
				Peel	0.55
				Whole fruit	0.23
Spain, Sanlucar de Barrameda	0.113-0.116	0.011	2 hrs	Pulp	<0.01
				Pell	0.07
				Whole fruit	0.03
			1	Pulp	<0.01
				Peel	0.44
				Whole fruit	0.14
			3	Pulp	<0.01
				Peel	0.74
				Whole fruit	0.23
			5	Pulp	<0.01
				Peel	0.32
				Whole fruit	0.11
			7	Pulp	<0.01
				Peel	0.39
				Whole fruit	0.13

Location, conditions, report No.	Application		PHI, days	Matrix	Residues, mg/kg
	kg a.i./ha	kg a.i./hl			
Field crops (Study 5521)					
France, Pierrerue	0.113-0.120	0.012	3	Pulp	<0.01
				Peel	0.23
				Whole fruit	0.06
France, Sénas	0.112-0.120	0.022	2 hrs	Pulp	<0.01
				Peel	0.18
				Whole fruit	0.05
			1	Pulp	<0.01
				Peel	0.17
				Whole fruit	0.06
			3	Pulp	<0.01
				Peel	0.13
				Whole fruit	0.05
			5	Pulp	<0.01
				Peel	0.10
				Whole fruit	0.04
			7	Pulp	<0.01
				Peel	0.10
				Whole fruit	0.04
Greece, Prohoma	0.112-0.117	0.011-0.022	3	Pulp	<0.01
				Peel	<0.01
				Whole fruit	<0.01
Greece, Epanomi	0.110-0.120	0.016	2 hrs	Pulp	<0.01
				Peel	0.39
				Whole fruit	0.21
			1	Pulp	<0.01
				Peel	0.20
				Whole fruit	0.11
			3	Pulp	<0.01
				Peel	0.21
				Whole fruit	0.13
			5	Pulp	<0.01
				Peel	0.10
				Whole fruit	0.06
			7	Pulp	<0.01
				Peel	0.26
				Whole fruit	0.13
Italy, Volania	0.111-0.115	0.0114-0.019	3	Pulp	0.01
				Peel	0.02
				Whole fruit	0.01
Italy, San Bartolomeo in Bosco	0.111-0.117	0.014-0.019	2 hrs	Pulp	<0.01
				Peel	0.33
				Whole fruit	0.16
			1	Pulp	<0.01
				Peel	0.25
				Whole fruit	0.12
			3	Pulp	<0.01
				Peel	0.07
				Whole fruit	0.04
			5	Pulp	<0.01
				Peel	0.35
				Whole fruit	0.18
			7	Pulp	<0.01
				Peel	0.24
				Whole fruit	0.12
Italy, Ginosa	0.108-0.117	0.0141	3	Pulp	0.01
				Peel	1.2
				Whole fruit	0.63

Location, conditions, report No.	Application		PHI, days	Matrix	Residues, mg/kg
	kg a.i./ha	kg a.i./hl			
Spain, Tomelloso	0.110-0.114	0.011-0.015	2 hrs	Pulp	<0.01
				Peel	0.09
				Whole fruit	0.05
			1	Pulp	<0.01
				Peel	0.10
				Whole fruit	0.06
			3	Pulp	<0.01
				Peel	0.06
				Whole fruit	0.03
			5	Pulp	<0.01
				Peel	0.04
				Whole fruit	0.02
			7	Pulp	<0.01
				Peel	0.03
				Whole fruit	0.02
Spain, Villalba del Alcor	0.108-0.113	0.011	3	Pulp	0.01
				Peel	0.10
				Whole fruit	0.04
Spain, Lora del Rio	0.110-0.113	0.011	2 hrs	Pulp	0.01
				Peel	0.17
				Whole fruit	0.07
			1	Pulp	0.02
				Peel	0.22
				Whole fruit	0.09
			3	Pulp	0.01
				Peel	0.20
				Whole fruit	0.07
			5	Pulp	<0.01
				Peel	0.06
				Whole fruit	0.03
			7	Pulp	<0.01
				Peel	0.05
				Whole fruit	0.03

Tomatoes

Thirty-six trials were conducted on tomato in France, Spain, Greece and Italy, 22 being decline studies, days 0-7 or 0-14 (Table 20).

Table 20. Residues of famoxadone in tomato after application of WG formulations (Cicotti *et al*. 1996c; Steinhauer *et al.*, 2002; Françon and Lee, 1997c).

Location, year, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water, l/ha		
France Bouilhonnac, 1995 AMR 3363-95	7	0.10	280	1 hr	0.14
				3	0.15
				7	0.11
				14	0.08
	7	0.09-0.12	280	1 hr	0.09
				3	0.10
				7	0.08
				14	0.07
France, Sénas, Bouches du Rhône, 2001 DuPont-5519	5	0.062-0.092	691-1017	2 hrs	0.02
				1	0.01
				3	0.03
				5	0.01
				7	0.02
	5	0.0634-0.1361	706-1512	2 hrs	0.10
				1	0.09
				3	0.08
				5	0.04
				7	0.10
France, PierreLatte, Drôme, 2001	5	0.084-0.096	933-1067	3	0.12
DuPont-5519	5	0.09-0.132	100-1514	3	0.15

Location, year, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water, l/ha		
France, Sarrians, Vaucluse, 2001	5	0.0842-0.0898	936-1000	2 hrs	0.12
DuPont-5519				1	0.07
				3	0.10
				5	0.12
				7	0.10
	5	0.895-0.136	994-1512	2 hrs	0.12
				1	0.10
				3	0.10
				5	0.11
				7	0.11
France, Beaucaire, 1996	7	0.094-0.120	200-256	1 hr	0.08
AMR 3764-96				3	0.08
Greece, Epoxmani, 1995	7	0.1	300	1hr	0.25
AMR 3363-95				3	0.15
				7	0.10
				14	0.06
	7	0.09-0.12	300	1hr	0.14
				3	0.10
				7	0.08
				14	0.03
Greece, Metohi Eponomis, 1996	7	0.090	700	2 hrs	0.05
AMR 3764-96				3	0.04
Greece, Profitis, 2001	5	0.069-0.089	764-923	3	0.09
DuPont-5519	5	0.07-0.13	784-1472	3	0.11
Greece, Nea Magnisia, 2001	5	0.06-0.09	667-1008	2hrs	0.14
DuPont-5519				1	0.10
				3	0.11
				5	0.14
				7	0.12
	5	0.06-0.14	668-1574	2hrs	0.18
				1	0.25
				3	0.16
				5	0.12
				7	0.14
Italy, Emilia Romagna, 1995	7	0.097-0.105	680-722	1hr	0.02
AMR 3363-95				3	0.03
				7	0.04
				13	0.03
	7	0.09-0.12	701-780	2hr	0.04
				3	0.03
				7	0.03
				13	0.04
Italy, Puglia, 1995	7	0.10	600	1 hr	0.03
AMR 3363-95				3	0.02
				7	<0.02
				14	<0.02
	7	0.09-0.12	600	1 hr	0.02
				3	0.02
				7	0.02
				14	<0.02
Italy, Lombardi, 1996	7	0.087-0.093	194-207	1 hr	0.04
AMR 3764-96				3	0.03
Italy, Zapponeta (FG), 2001	5	0.070-0.091	775-1112	3	0.74
DuPont-5519	5	0.070-0.1369	779-1520	3	1.1

Location, year, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water, l/ha		
Italy, S. Bartolomeo al mare (IM), 2001 DuPont-5519	5	0.072-0.090	827-1000	2 hrs 1 3 5 7	0.18 0.16 0.04 0.02 0.03
	5	0.072-0.131	797-1458	2 hrs 1 3 5 7	0.21 0.10 0.05 0.05 0.04
Italy, Ceriale (SV), 2001	5	0.07-0.09	779-995	3	0.18
DuPont-5519	5	0.073-0.136	812-1512	3	0.33
Spain, Utrera, 1995 AMR 3363-95	7	0.10-0.11	513-800	2hrs 3 7 14	0.04 0.07 0.06 0.06
	7	0.09-0.12	503-775	2hrs 3 7 14	0.06 0.05 0.05 0.06
	7	0.099-0.104	493-780	1hr 3 7 14	0.05 0.05 0.05 0.04
	7	0.09-0.13	538-765	1hr 3 7 14	0.02 0.04 0.05 0.05
Spain, Utrera, 1996 AMR 3764-96	7	0.087-0.092	581-614	1 hr 3	0.06 0.02
Spain, Los Palacios y Villafranca, 2001 DuPont-5519	5	0.090-0.098	100-1048	2 hrs 1 3 5 7	0.07 0.06 0.10 0.07 0.08
	5	0.117-0.133	1402-1588	2 hrs 1 3 5 7	0.13 0.11 0.18 0.12 0.13
Spain, Vejer de la Frontera, 2001	5	0.091-0.108	1013-1096	3	0.12
DuPont-5519	5	0.131-0.137	1471-1517	3	0.20

Potatoes

Twelve trials which were conducted in Europe, using 6 to 12 applications of famoxadone as a WG formulation in each case, gave residues of <0.02 mg/kg in potato tubers (Table 21).

Table 21. Residues of famoxadone in potatoes after multiple applications of a WG formulation (Jernberg and Dubey, 1997a and 1997b).

Location, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water, l/ha		
Belgium, Saint-Amand. AMR 3788-96	12	0.194-0.224	185-224	14	<0.02
Denmark, Middelfart. AMR 3788-96	12	0.200	242-263	14	<0.02
France, Hameau de Pouilleux. AMR 3767-96	6	0.198-0.218	264-291	14	<0.02
France, Sernhac. AMR 3767-96	7	0.180-0.197	241-263	14	<0.02 (tuber) <0.02 (peel)
France, Somme. AMR 3788-96	11	0.176-0.211	216-260	14	<0.02
Germany, Sachsen. AMR 3788-96	12	0.200	300	14	<0.02
Greece, Chalkidiki. AMR 3767-96	8	0.180	500	14	<0.02
Italy, Caleppio di Settala (MI). AMR 3767-96	8	0.175-0.189	292-314	14	<0.02
Portugal, Torres Vedras. AMR 3767-96	8	0.180-0.191	430-502	14	<0.02

Location, report No.	Application			PHI, days	Residue, mg/kg
	No.	kg a.i./ha	Water, l/ha		
Spain, Utrera. AMR 3767-96	8	0.164-0.192	272-320	14	<0.02
The Netherlands Bemmel, Gelderland. AMR 3788-96	12	0.183-0.210	300	14	<0.02
UK, Melbourne, Derbyshire. AMR 3788-96	12	0.195-0.215	288-317	14	<0.02

Barley

Sixteen trials were conducted in Europe on winter or spring barley, which received two foliar applications of a famoxadone EC at 0.15 to 0.20 kg ai/ha (Table 22). Barley samples were collected at maturity, 32-78 days after the last application.

Table 22. Residues of famoxadone in barley grain after 2 applications of an EC formulation (Dubey and Jernberg, 1996a, 1996b, 1996c and 1997b).

Location, year, barley type, report No.	Application		PHI, days	Residue, mg/kg
	kg a.i./ha	Water, l/ha		
Belgium, Jauche, 1995, spring barley. AMR 3377-95	0.150	200	35	0.02
France, Marolles, 1995, winter barley. AMR 3367-95	0.20	229-282	62	0.02
	0.15	229-282	62	<0.02
France, Rouilly, 1995, winter barley. AMR 3367-95	0.15	167-194	53	<0.02
	0.20	167-194	53	<0.02
France, Frans, 1995, winter barley. AMR 3368-95	0.150	250	35	0.08
France, Marmeriville, 1995, spring barley. AMR 3377-95	0.150	214-272	32	0.11
France, Voves, 1996, winter barley. AMR 3766-96	0.133-0.142	192-218	56	0.04
Germany, Frankendorf, 1995, winter barley. AMR 3368-95	0.150	300	59	<0.02
Germany, Christinenthal, 1995, spring barley. AMR 3377-95	0.150	300	41	<0.02
Germany, Christinenthal, 1995, winter barley. AMR 3367-95	0.150	300	52	0.04
	0.2	300	52	0.18
UK, Long Whatton, 1995, winter barley. AMR 3367-95	0.150	200	78	<0.02
	0.20	200	78	<0.02
UK, Averham, 1995, spring barley. AMR 3377-95	0.150	200	56	<0.02
UK, Pinchbeck, 1996, winter barley. AMR 3766-96	0.151-0.172	199-210	68	<0.02

Wheat

Fifteen trials were conducted in Europe on winter wheat, using 3 applications of an EC formulation of famoxadone, with a total of 0.60 or 0.580 kg a.i./ha per trial (Table 23). Wheat grain samples were collected at maturity, 34 to 66 days PHI.

Table 23. Residues of famoxadone in winter wheat grain after 3 applications of an EC formulation in 1995-1996 (Dubey and Jernberg, 1996e, 1996d and 1997a).

Location, report No.	Application		PHI, days	Residue, mg/kg
	kg a.i./ha	kg a.i./ha		
Belgium, Saint-Amand. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	191-210	45	<0.02
	0.200	191-210	45	<0.02
France, Warmeriville. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	209-279	36	<0.02
	0.200	209-279	36	0.06
France, Corbarien. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	230-247	49	0.04
	0.200	230-247	49	<0.02
France, Provins. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	187-215	49	<0.02
France, Fouchères. AMR 3366-95	1st 0.280; 2nd & 3rd 0.150	242-282	34	<0.02
Gernany, Kötschau. AMR 3366-95	1st 0.280; 2nd & 3rd 0.150	300	51	<0.02
Germany, Christinenthal. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	300	50	<0.02
	0.200	300	50	<0.02
Germany, Christinenthal. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	250	52	<0.02
Germany, Borsum. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	250	55	<0.02
UK, Whatton. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	200	66	<0.02
	0.200	200	66	<0.02

Barley straw and forage

Sixteen trials were conducted on barley straw and 2 trials on barley forage, with two foliar applications of an EC formulation of famoxadone, at 0.150 or 0.20 kg ai/ha (Table 24). Straw samples were collected at grain maturity stage, whereas forage samples were collected 7 to 21 days after the last application.

Table 24. Residues of famoxadone in barley straw and forage, after 2 applications of an EC formulation in 1995-1996 (Dubey and Jernberg, 1996a, 1996b, 1996c and 1997b).

Location, report No.	Application		Crop	PHI, days	Residue, mg/kg
	kg a.i/ka	Water, l/ha			
Belgium, Jauche. AMR 3377-95	0.150	200	Straw	35	1.5
France, Marolles. AMR 3367-95	0.150	229-282	Straw	62	0.16
	0.200	229-282	Straw	62	0.35
France, Rouilly. AMR 3367-95	0.150	167-194	Straw	53	0.47
	0.200	167-194	Straw	53	3.9
France, Frans. AMR 3368-95	0.150	250	Straw	35	0.96
			Forage	7	1.4
				14	1.1
				21	0.84
France, Warmeriville. AMR 3377-95	0.150	214-272	Straw	32	3.8
France, Voves. AMR 3766-96	0.133-0.142	192-218	Straw	56	2.5
Germany, Frankendorf. AMR 3368-95	0.150	300	Straw	59	0.93
			Forage	7	1.8
				14	1.2
				23	0.38
Germany, Christinenthal. AMR 3377-95	0.150	300	Straw	41	1.4
Germany, Christinenthal. AMR 3367-95	0.150	300	Straw	52	0.85
	0.200	300	straw	52	3.7
UK, Long Whatton. AMR 3367-95	0.150	200	Straw	78	0.19
	0.200	200	Straw	78	0.67
UK, Averham. AMR 3377-95	0.150	200	Straw	56	0.34
UK, Pinchbeck. AMR 3766-96	0.151-0.172	199-210	Straw	68	0.86

Wheat straw and forage

Fifteen trials were conducted on straw and two on wheat straw and forage, in which three applications of an EC formulation of famoxadone were made to each trial. Straw samples were collected at grain maturity stage, whereas forage samples were collected 0-21 days after the last application (Table 25).

Table 25. Residues of famoxadone in wheat straw and forage after application of EC formulation (Dubey and Jernberg, 1996e, 1996d and 1997a).

Location, report No.	Application		Crop	PHI, days	Residue, mg/kg
	kg a.i./ha	Water, l/ha			
Belgium, Saint-Amand, 1995. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	191-210	Straw	45	1.2
	0.200	191-210	Straw	45	4.8
France, Warmeriville, 1995. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	209-279	Straw	36	2.0
	0.200	209-279	Straw	36	7.7
France, Corbarien, 1995. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	230-247	Straw	49	1.7
	0.200	230-247	Straw	49	4.8
France, Provins, 1996. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	250	Straw	49	2.5
France, Fouchères, 1995. AMR 3366-95	1st 0.280; 2nd & 3rd 0.150	242-282	Straw	34	2.1
			Forage	1 hr	4.2
				7	2.4
				14	1.8
				22	1.9
Gernany, Kötschau, 1995. AMR 3366-95	1st 0.280; 2nd & 3rd 0.150	300	Straw	51	4.3
			Forage	1 hr	5.8
				7	3.0
				14	2.0
				21	1.4
Germany, Christinenthal, 1995. AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	300	Straw	50	2.9
	0.200	300	Straw	50	11

Location, report No.	Application		Crop	PHI, days	Residue, mg/kg
	kg a.i./ha	Water, l/ha			
Germany, Christinenthal, 1996. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	250	Straw	52	2.7
Germany, Borsum, 1996. AMR 3765-96	1st 0.280; 2nd & 3rd 0.150	250	Straw	55	1.6
UK, Whatton, 1995, AMR 3365-95	1st 0.280; 2nd & 3rd 0.150	200	Straw	66	0.55
	0.200	200	Straw	66	3.4

Cow feeding study

Famoxadone was given in gelatin capsules to lactating Holstein dairy cows, twice daily for 28 days, at feeding levels of 9.0, 27 or 90 ppm, corresponding to 120-205, 374-569 or 1447-2070 mg/week, respectively(Nathan, 1999b report DuPont-1219, Rev. 1). Milk (a.m. and p.m. milkings) from cows given the same dosing level was composited. Ingestion of famoxadone had no apparent adverse effects on the animals and, at autopsy, no gross pathological lesions were found.

Twelve cows were sacrificed on day 29, after dosing had ceased (3 cows per dose level). Two cows given the highest dose during the 28 days of dosing, were sacrificed on day 42 and day 48. Famoxadone was determined in milk and tissues, using the matrix solid-phase dispersion HPLC method. Tables 26 and 27 show the residues of famoxadone found in milk and tissues, respectively, of dosed cows. Famoxadone residues were found at all doses in the tissues analyzed, with higher concentrations in liver and fat.

Table 26. Famoxadone residues (mg/kg) in milk and milk fractions, following dosing of cows with famoxadone (Nathan, 1999b report DuPont-1219, Rev. 1).

Food commodity	Day	Dosing level, ppm in feed		
		9.0	27	90
		Residue, mg/kg		
Whole milk	1	0.03	0.08	0.30
	2	0.07	0.14	0.68
	3	0.09	0.23	0.82
	4	0.10	0.27	1.2
	7	0.11	0.35	1.3
	10	0.12	0.46	1.4
	14	0.12	0.41	1.4
	18	0.13	0.45	1.6
	21	0.13	0.43	1.7
	24	0.13	0.49	1.5
	25	0.19	--	--
	26	0.17	--	--
	28	0.14	0.36	1.5
	29	--	--	1.3 (1.0, 1.6)
	30	--	--	0.76 (0.54, 0.97)
	32	--	--	0.36 (0.21, 0.52)
	34	--	--	0.24 (0.15, 0.34)
	36	--	--	0.11 (0.04, 0.18)
	40	--	--	0.04 (0.02, 0.07)
	41	--	--	0.01
	42	--	--	0.04
	44	--	--	0.03
	47	--	--	0.02
	Average (days 1-28)	0.12	0.33	1.2
	Average (days 10-28)	0.14	0.43	1.5
Milk fat	14	1.4	4.5	14
	21	1.4	4.3	16
	28	1.3	4.1	16
Skimmed milk	14	0.07	0.18	0.43
	21	0.02	0.07	0.25
	28	0.06	0.05	0.25
	Average (days 14-28)	0.05	0.1	0.31

Table 27. Residues of famoxadone in the tissues of dosed cows, in mg/kg (mean in parenthesis) (Nathan, 1999b report DuPont-1219, Rev. 1).

Tissue	Day	Dosing level, ppm in feed		
		9.0	27	90
		Residue, mg/kg		
Liver	29	0.68, 0.70, 0.69 (0.69)	2.2, 2.0, 1.9 (2.0)	6.3, 6.6, 6.0 (6.3)
	42	--	--	0.03
	48	--	--	0.04
Kidney	29	0.12, 0.15, 0.18 (0.15)	0.59 (3) (0.59)	1.8, 1.5, 1.3 (1.5)
	42	--	--	<0.01
	48	--	--	0.02
Muscle	29	0.05, 0.08, 0.09 (0.07)	0.20, 0.23, 0.29 (0.24)	1.5, 1.1, 0.48 (1.0)
	42	--	--	<0.01
	48	--	--	0.01
Fat	29	0.81, 1.2, 1.1 (1.0)	3.7, 4.6, 3.9 (4.1)	20, 21, 8.5 (17)
	42	--	--	0.10
	48	--	--	0.19

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

Grape processing and wine fermentation studies were conducted in France and Italy during the 1994 growing season (Lee *et al*., 1996; report AMR 2973-94). Grapes vines were treated with 12 applications of a WG formulation of famoxadone, at 100 g a.i./ha, with 30 days PHI. Grapes were processed using traditional French wine-making techniques and the products analyzed. The processing factors (PF) are shown in Table 28.

Table 28. Grape processing studies (Lee *et al*., 1996).

Fractions	Famoxadone, mg/kg	Processing factor	Famoxadone, mg/kg	Processing factor
Grapes	1.4	-	1.6	-
Juice	<0.02	<0.01	<0.02	<0.01
Raisin	2.1	1.5	3.7	2.3
Must	0.87	0.62	1.4	1.0
Wet pomace	3.7	2.6	2.4	1.5
Dry pomace	5.6	4.0	5.2	3.2
Lees/must deposit	0.05	0.04	0.10	0.62
Wine (alcoholic fermentation)	<0.02	<0.01	0.02	0.01
Wine (malolactic fermentation)	<0.02	<0.01	<0.02	<0.01
Fresh wine	<0.02	<0.01	<0.02	<0.01

Tomato processing studies were conducted in France and Spain in 1994 (Cicotti *et al*., 1996d; report AMR 2974-94). Tomato plants were treated with 12 applications of a WG formulation of famoxadone, at 100 g a.i./ha and with 14 days PHI. Tomatoes were processed following industrial manufacturing procedures and the fractions were analyzed for the presence of famoxadone (Table 29). Another study was conducted in California, with 9 applications made at 1x and 5x the maximum GAP rate and with 3 days PHI (Rühl and Okeyo, 1999; report AMR 4355-97).

Table 29. Tomato processing studies (Cicotti *et al*., 1996d; Rühl and Okeyo, 1999).

Fractions	France		Spain		California			
	Famoxadone (mg/kg)	PF	Famoxadone (mg/kg)	PF	Famoxadone (mg/kg)	PF	Famoxadone (mg/kg)	PF
Tomato	0.13	-	0.09	-	0.86	-	0.17	-
Washed fruit	-	-	-	-	0.23	0.26	0.05	0.29
Juice	0.03	0.23	0.02	0.22	-	-	-	-
Paste	-	-	-	-	1.1	1.3	0.22	1.3
Catsup	0.14	1.1	0.09	1.0	-	-	-	-
Puree	0.05	0.38	0.05	0.56	0.34	0.40	0.07	0.41
Wet pomace	0.31	2.4	0.16	1.8	-	-	-	-
Dry pomace	3.1	24	0.62	6.7	-	-	-	-

PF = processing factor.

Samples of winter barley, from trials in France and Germany that had been treated with 2 applications of famoxadone at 0.2 kg a.i./ha and with a PHI of 55-59 days, were processed using traditional malting, brewing, milling and baking techniques and procedures (Dubey & Jernberg, 1996f report AMR 3599-95). The results are shown in Table 30.

Table 30. Processing studies on barley (Dubey & Jernberg, 1996f).

Sample	Saucergues, France		Seehausen, Germany	
	Famoxadone, mg/kg	Processing factor	Famoxadone, mg/kg	Processing factor
Grain	0.04	-	0.06	-
Malt	<0.02	<0.5	<0.02	<0.33
Malt germ	<0.02	<0.5	<0.02	<0.33
Spent grain	<0.02	<0.5	0.04	0.67
Trub	<0.02	<0.5	<0.02	<0.33
Yeast [1/]	<0.02	<0.5	<0.02	<0.33
Beer	<0.02	<0.5	<0.02	<0.33
Grits	<0.02	<0.5	-	-
Pearl barley	<0.02	<0.5	-	-
Pearling dust	0.07	1.8	-	-
Wholemeal bread	<0.02	<0.5	-	-

[1/] Remained at the bottom of the vessel after the fermentation process.

One processing study was conducted in France on winter wheat (Dubey & Jernberg, 1996g report AMR 3600-95). Grain from crops treated with 3 applications of 0.2 kg a.i./ha were processed in a milling and baking pilot plant, which simulated commercial practice. The famoxadone level in the grain was 0.04 mg/kg, whereas that in bran was 0.08 mg/kg, indicating a processing factor (PF) of 2. No residues (i.e. <0.02 mg/kg) were found in wholemeal flour and wholemeal bread.

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

No data were submitted.

NATIONAL MAXIMUM RESIDUE LIMITS

The information provided to the Meeting is summarized in Table 31.

Table 31. National MRLs for famoxadone.

Country	Commodity	MRL, mg/kg
Brazil	Grapes	0.5
	Potatoes	1.0
	Tomatoes	1.0
Bulgaria	Grapes	2
	Potatoes	0.02
	Tomatoes	0.2
Czech Republic	Barley grain	0.2
	Potatoes	0.02
	Wheat grain	0.2
Estonia	Potatoes	0.05
Japan	Cucumbers	0.5
	Potatoes	0.1
	Tomatoes	2
Korea	Cucumbers	0.3
	Grapes	1
	Oriental melons	0.5
	Potatoes	0.1
	Tomatoes	0.7
Latvia	Potatoes	0.05
Lithuania	Potatoes	0.05
Netherlands	Potatoes	0.02
Slovenia	Grapes	2
	Potatoes	0.05

Country	Commodity	MRL, mg/kg
Switzerland	Barley grain	0.2
	Grapes	2
	Rye	0.1
	Wheat grain	0.1
USA	Cattle, fat	0.02
	Cattle, liver	0.05
	Goat, fat	0.02
	Goat, liver	0.05
	Grapes [1/]	2.5
	Grapes, raisins [1/]	4.0
	Horse, fat	0.02
	Horse, liver	0.05
	Lettuce, head	10.0
	Milk, fat (reflecting negligible residues in whole milk)	0.06
	Potatoes	0.02
	Sheep, fat	0.02
	Sheep, liver	0.05
	Tomatoes	1.0
	Vegetables, cucurbits	0.30
	Vegetables, fruiting, except tomatoes	4.0
Yugoslavia	Grapes	2
	Potatoes	0.05
	Tomatoes	0.02

[1/] Import tolerance.

APPRAISAL

Famoxadone is a an oxazolidinedione fungicide belonging to the quinol inhibitor family, which inhibits mitochondrial respiration of fungi. The compound was scheduled at the 33rd Session of the CCPR (ALINORM 01/24A) for evaluation by the 2003 JMPR as a new compound. Data were provided on metabolism and environmental fate; methods of residue analysis; supervised trials on grapes, melons, cucumbers, tomatoes, potatoes, barley and wheat; a cow feeding study; and the fate of residues in processing. Information on GAP, national MRLs and residue data were reported by the governments Germany, the Netherlands and Poland.

Metabolism

In animals

Metabolism studies were conducted with ^{14}C famoxadone labelled in the phenoxyphenyl- and phenylamino moieties.

Rats given single or multiple oral doses of 5 and 100 mg/kg body weight of ^{14}C famoxadone excreted between 88.8 and 96% of the administered radioactivity in the faeces and from 3 to 12% in the urine, most within 24 h. Famoxadone was the major component in faeces, and the monohydroxy derivative in the phenoxyphenyl and the dihydroxy in the phenoxyphenyl and phenylamino moieties were the main metabolites, each representing up to 13% of the administered dose. In urine, only hydrolytic and cleavage products were detected, including 4-aminophenyl acetate (4-acetoxyaniline), at up to 7% of the administered dose. When [^{14}C]famoxadone was given to biliary-cannulated rats in a single oral dose of 5 mg/kg bw, excretion in bile ranged from 30 to 39% and in faeces from 56 to 65% of the administered dose. Famoxadone was the only labelled component in faeces and it was not detected in the bile. The main metabolites released in bile treated with β-glucuronidase/sulfatase were the mono-hydroxylated compound, the catechol 1,2-dihydroxybenzene and a hydrolysis cleavage product (α-hydroxy-4-(4-hydroxyphenoxy)-α -methylbenzeneacetic acid) but none was higher than 6% of the administered dose.

Lactating goats dosed orally for 7 days at the equivalent of 10 ppm in the diet excreted most of the radioactivity (>80%) in the faeces. Famoxadone was the major radioactive component in milk and tissues. Radioactive residues in milk reached a plateau at day 6–7, with up to 0.025 mg/kg ^{14}C famoxadone equivalents. On average, famoxadone was present in muscle at 0.009 mg/kg, in fat at

0.086 mg/kg, in liver at 0.025 mg/kg, in kidney at 0.011 mg/kg and in milk at 0.006 mg/kg, representing from 18.5 to 57.5% of the TRR in each matrix. Mono- and dihydroxylated metabolites were detected in either faeces or liver at up to 4.8% of the TRR. Individual components released by protease digestion and the remaining unextractable residues were <0.05 mg/kg.

Laying hens dosed for 7 consecutive days at a dietary level of 10 ppm excreted most of the radioactivity in faeces (>88%). Eggs accounted for <0.04% and tissues for <0.15% of the administered dose. Radioactive residues were equivalent to <0.01-0.067 mg/kg in the egg yolk and 0.06-0.3 mg/kg in liver. No residues (<0.01 mg/kg famoxadone equivalents) were detected in muscle, skin or egg white. Famoxadone was the major component in the excreta (up to 17.8% of the TRR), followed by the polar metabolite 5-(4-hydroxyphenyl)-5-methyloxazolidine-2,4-dione (15.4% of the TRR) The major radioactive compound in egg yolk and liver was the mono-hydroxylated compound (up to 0.08 mg/kg famoxadone equivalents). No radioactive famoxadone was detected in liver.

In summary, famoxadone accumulation in animals is low, with most of the administered radioactivity being excreted in faeces. The metabolism includes hydroxylation of the phenoxyphenyl and phenylamino rings, hydrolytic cleavage of the oxazolidinedione moiety, and cleavage of the hydrazine bond and the phenoxyphenyl ether linkage. Low levels of famoxadone or metabolites were found in goat and poultry tissues, milk and eggs.

In plants

When grape vines were treated with a simulated WG formulation of [^{14}C]famoxadone (three times at 0.3 kg ai/ha) most of the radioactivity was recovered from the surface of the leaves and fruits (79-98% of the TRR), with >95% of the residue identified as famoxadone. A minor metabolite, 1-(4-phenoxyphenyl)ethanone, was also observed (<2%). In the fruit, famoxadone residues reached a maximum of 0.03 mg/kg equivalents at day 14.

Tomatoes were treated twice with a simulated WG formulation of [^{14}C]famoxadone at a rate of 0.63 kg a.i./ha and most of the radioactivity could be extracted into acetone (~80% TRR). On average, >90% of the residue was famoxadone and no significant metabolites were identified (<10% of the TRR). At 14 days the residue of famoxadone in tomato fruits was 0.07 mg/kg.

When potato plants were treated in a greenhouse three times at 0.3 kg ai/ha with a WG of [^{14}C]famoxadone, most of the applied radioactivity was recovered in the acetone wash of the foliage surface (means of 86.5 and 61.8% at days 37 and 51) and 76-95% of the residue was characterized as famoxadone. Two minor hydrolytic metabolites were observed, 1-(4-phenoxyphenyl)ethanone and α-hydroxy-α-methyl-4-phenoxybenzeneacetic acid 2-phenylhydrazide, accounting for <5% of the total radioactivity. Negligible systemic translocation of radiolabelled residues to the tubers was found (<0.01 mg/kg famoxadone equivalent).

In mature wheat plants from a field harvested 50 days after the last of three applications at 0.2 kg ai/ha of an EC containing [^{14}C]famoxadone, low levels of ^{14}C residues were detected in the grain (0.01-0.02 mg/kg equivalents). Most of the radiolabelled residue (>98%) was found in the straw (average 3.4 mg/kg). Famoxadone was the main component (average 0.36 mg/kg ^{14}C equivalents) of the extractable residues in the foliage and mature straw. The main metabolites were monohydroxy-famoxadone (0.24 mg/kg famoxadone equivalents in straw at day 72), dihydroxy-famoxadone (0.30 mg/kg famoxadone equivalents in foliage at day 29) and a conjugation product (0.26 mg/kg famoxadone equivalents in foliage at day 29).

In summary, famoxadone was the main compound found in treated grapes, tomatoes and potatoes. Little translocation of the radioactivity to potato tubers was found and residues in wheat grain were low. Metabolism in wheat plants was significant, mainly through hydroxylation and conjugation.

Environmental fate

The degradation of famoxadone in soils under aerobic conditions showed half-lives varying from 2 days in silt loam to 11 days in sandy loam (DT_{90} was 134 days). Famoxadone was not detected in the unextractable fraction of residues subjected to strong acidic treatments. Approximately 79.4-93.3% of

the parent compound remained after 90 days in sterile soil, indicating that famoxadone is mainly subject to microbial degradation. The major degradation products were phenoxyphenyl-hydroxylated famoxadone (IN-KZ007), with a peak level of 7 to 16% of the applied dose occurring within 4 days, and the hydrolysis cleavage product α-hydroxy-4-(4-hydroxyphenoxy)-α-methyl-4-phenoxy benzeneacetic acid (IN-JS940), which reached a peak of 11% of the applied radioactivity. The half-lives of IN-KZ007 and IN-JS940 in soils were 3.2-15 days and 6-23 hours, respectively.

Under field conditions in the USA and Canada, unquantifiable or low residues of famoxadone were found below the 15 cm depth, showing low mobility in soil. The half-life in various soils was 5 to 28 days.

One rotation crop study was reported to the Meeting. Soils treated once or three times with famoxadone at 0.4 kg ai/ha were aged under greenhouse conditions for 30, 120 and 365 days before planting different crops. Famoxadone residues were detected in lettuce, sugar beet roots, wheat forage and straw (0.02 to 0.06 mg/kg equivalents) but not in sugar beet tops or wheat grain (<0.01 mg/kg eq). Average residues in treated soils were 0.26 and 0.04 mg/kg famoxadone equivalents at days 30 and 120, respectively. No famoxadone was detected in crops or soil after 365 days. On average, crop:soil residue ratios were 0.11 in lettuce, 0.19 in sugar beet, 0.10 in wheat foliage and 0.58 in wheat straw. When these ratios were applied to an average field soil famoxadone residue level of 0.09 mg/kg, found 14 days after the last of 8 applications at 0.18 kg ai/ha (twice GAP) in a supervised trial on potatoes in Italy, the calculated residues of famoxadone in lettuce, sugar beet and wheat, after application to a previous crop of potatoes, ranged from 0.01 mg/kg in lettuce and wheat foliage to 0.05 mg/kg in wheat straw.

In summary, famoxadone is degraded in soil by microbial activity, mainly through hydroxylation, with a half-life up to 28 days in the field. The compound has low mobility in soil and only a low level of translocation into crops grown in soils containing aged residues.

Methods of residue analysis

Famoxadone can be extracted from plants with acetonitrile/water, the extract being cleaned-up by partition against hexane and the famoxadone quantified by reversed-phase HPLC-UV or HPLC-MS (positive-ion thermospray). The LOQ was 0.02 mg/kg for grapes and cereal grain or 0.05 mg/kg for cereal straw and forage. Average recoveries of famoxadone at levels from 0.02 to 0.5 mg/kg were 74-109%, with a maximum RSD of 21% (n=3 at each level). Where required, clean-up with a Florisil/sodium sulfate SPE column followed extraction, before quantification by column-switching HPLC-UV, with initial chromatographic separation on a phenyl column, followed by a C-18 column. The LOQ was 0.02 mg/kg. Average recoveries from tomato fruit, purée and paste, at 0.02 and 0.12 mg/kg, were 82-93%, with a maximum RSD (n=3) of 21%. Extraction of incurred residues from tomato samples with acetonitrile/water showed an average extraction efficiency of 110%, compared with the values obtained with the method used for determination in the metabolism study described above. In another method, samples were extracted with acetone/water, the extract cleaned-up by GPC and silica gel columns and famoxadone determined by GC-ECD. The LOQs were: 0.05 mg/kg for raisins and tobacco; 0.02 mg/kg for grapes and cucumbers; and 0.01 mg/kg for wine, potatoes and wheat grain. Average recoveries at 0.01-0.5 mg/kg were 76-106%, with maximum RSD of 9.5% (n=5 at each level).

Samples of milk, eggs and animal tissues were extracted with acetonitrile/water, the extracts partitioned against hexane, cleaned-up on a Florisil SPE column and the famoxadone determined by GC-NPD. Average recovery at 0.02 and 0.5 mg/kg was 85-107%, with an RSD of 4-12% (n=3 at each level), from beef muscle and fat, milk, poultry muscle and eggs. In another method to determine famoxadone residues in animal tissues, the sample was mixed with C-18 packing, the mixture was washed with hexane and the famoxadone then eluted with acetonitrile. The eluate was filtered through a bed of basic alumina and the extract then passed through a graphitized carbon and silica SPE columns. Famoxadone was determined by column-switching (phenyl and C-18 columns) HPLC-UV. The LOQ was 0.01 mg/kg for whole milk, skimmed milk, cream and whole egg and 0.05 mg/kg for bovine liver. Recoveries were 70-105% at 0.01-2.0 mg/kg fortification levels. This particular method was proposed as suitable for regulatory purposes. The efficiency of extraction of incurred

radio-labelled famoxadone residues in animal tissues by this method, compared with the extraction method (extraction with acetonitrile and clean-up with C-18 SPE) used in the goat metabolism study, was ≥87.4% from milk, liver and fat.

Stability of residues in stored analytical samples

Storage stability studies of residues in samples fortified with famoxadone at 1 mg/kg, were conducted in grapes, potatoes, wheat forage, straw, grain and soil, stored at -20°C. After 18 months, 70% (wheat grain and straw) to 99 % (grapes) of famoxadone residues remained in the samples. Famoxadone at 0.3 mg/kg was stable in tomatoes and peppers for 18 months (110 and 107% remained, respectively) and in cucumbers for 10 months (102% remaining). Famoxadone was also stable in tomato paste (at 1mg/kg) and tomato purée (0.3 mg/kg) stored at -10°C, with 93 and 89%, respectively, remaining after 18 months. Two studies conducted in potato showed different results for the stability of famoxadone in this crop. In one study, the residue level in samples fortified at 1 mg/kg declined to half after 3 months. In another study, conducted in conjunction with the supervised trials on potatoes, residues were stable up to 10.5 months (0.3 mg/kg fortification level). Procedural recoveries in both studies were acceptable.

The storage stability of famoxadone was evaluated in whole milk samples fortified with 0.1 mg/l and in muscle and liver samples containing incurred residues from a feeding trial. The average percentage of famoxadone remaining in milk after 117 days was 87% and residues in muscle (0.072 mg/kg) did not change significantly from day 21 to day 138. In liver, residues were 0.069 ± 0.010 mg/kg at day 21 and 0.065 ± 0.023 mg/kg at day 139.

Definition of the residue

Metabolism studies showed that famoxadone was the main radiolabelled residue in vegetable crops, milk and cow tissues. In egg yolk and hen liver, a monohydroxylated metabolite was the major residue, but present at low concentration. Famoxadone concentrates in the fat of treated goats and in egg yolk. In a cow feeding study, to be described later, residues also concentrated in fat and cream. Famoxadone has a log K_{OW} of 4.65.

The Meeting agreed that the definition of the famoxadone residue for compliance with MRLs and for dietary intake estimations in plant and animal commodities should be famoxadone. The compound is fat-soluble.

Results of supervised trials

Grapes. Famoxadone can be used on grapes in Europe at a maximum application rate of 0.05 kg ai/ha (France and Greece), 0.09 kg ai/ha (Italy and Spain) or 0.144 kg ai/ha (Germany). Spain and Greece allow a maximum of 6 applications per season and the other countries a maximum of 3 applications, except Germany (8). The PHI in all countries is 28 days (40 days in Italy for formulations with fosestyl-Al).

A total of 25 trials using 10 to 12 applications, with a 7-day interval, were conducted in these countries between 1995 and 1999, at 0.05 to 0.146 kg ai/ha. The initial application was at flowering. The varieties used in the trials were mainly for the production of wine. In five decline studies residues decreased by 61.8%, on average, from days 1 to 30 after the last application.

Residues within about 28 days PHI were (in rank order, median underlined) 0.19 (2), 0.24, 0.25, 0.29, 0.37, 0.46, 0.48 (3), 0.50 (2), 0.54, 0.55, 0.56, 0.62, 0.66 (2), 0.74, 0.90 (2), 0.98, 1.0, 1.2 and 1.5 mg/kg.

The Meeting agreed that, with applications starting at flowering, it is unlikely that the first applications would influence the residue levels and that all trials conducted at the GAP rate and PHI in Europe should be considered for the estimations.

The Meeting estimated a maximum residue level of 2 mg/kg, an STMR of 0.54 mg/kg and an HR of 1.5 mg/kg for famoxadone in grapes.

Cucumbers and summer squash. The current Italian label indicates that famoxadone may be applied to cucumbers at 0.112 kg ai/ha at flowering, followed by 2 applications at the same rate (maximum of 3 applications) with a minimum 1-week interval, with a 10-day PHI. This label applies also to zucchini (summer squash) and melons. The label does not give any explicit restrictions for use under protected conditions. There is no GAP for famoxadone in Greece or Spain.

Ten trials were conducted on protected cucumbers using 5 applications at 0.065 to 0.118 kg ai/ha (1 week interval) in Italy, Greece and Spain in 2001. Decline studies showed residues decreasing by 39%, on average, from days 1 to 7 after the last application. Residues at 7 days PHI were (in rank order, median underlined) 0.01 (2), 0.02 (3), 0.03 (2), 0.05 (2) and 0.10 mg/kg.

The Meeting agreed that, as cucumbers under protected conditions grow quickly, it is unlikely that the higher number of applications used in the trials would influence the residue within a 10-day PHI. The Meeting also agreed to evaluate the trials conducted in Greece and Spain against Italian GAP and to extrapolate the recommendations to summer squash.

The Meeting estimated a maximum residue level of 0.2 mg/kg, an STMR of 0.025 mg/kg and an HR of 0.10 mg/kg for famoxadone in cucumbers and summer squash.

Melons. In Italy, GAP for use of famoxadone on cucumbers also applies to melons. There is no GAP for famoxadone use on melons in Greece, France or Spain. Twenty trials were conducted on melons using 5 applications at about the Italian GAP rate in Italy, Greece, France and Spain, either in the glasshouse or in the field in 1991. No significant difference in residue levels was found between the glasshouse and field trials. Residues 7 days after the last application were 0.02-0.22 mg/kg in whole fruit. Residues in pulp were <0.01 or 0.01 mg/kg from day 1 to 7 and, in one sample, the residue 2 h after the last application was 0.22 mg/kg.

As the trials were not according to GAP (too many applications), the Meeting agreed not to recommend an MRL of famoxadone in melons.

Tomatoes. Thirty-six trials were conducted in Europe on tomatoes, where the maximum GAP is 0.09 kg ai/ha in France, Spain and Greece and 0.11 kg ai/ha in Italy. France and Spain allow up to 4 applications and a PHI of 3 days. Italy allows 3 applications and 10 days PHI or 6 applications at a lower rate (0.005 kg ai/ha) and 3 days PHI. Greece allows 8 applications and 3 days PHI. Trials were conducted using 5 or 7 applications at 0.07 to 0.137 kg ai/ha, with a PHI of 3 days or decline studies from 0 to 7 or 14 days.

Six trials conducted in the south of France according to French GAP gave residues at 3 days PHI of 0.03, 0.08, 0.10 (2), 0.12 and 0.15 mg/kg. Three trials of 7 applications complying with GAP in Greece showed residues of 0.08, 0.10 and 0.15 mg/kg.

In Greece, 3 trials according to Greek GAP (7 applications) and 4 trials according to Italian GAP (5 applications) gave residues at 3 days PHI of 0.04, 0.09, 0.10, 0.11(2), 0.15 and 0.16 mg/kg.

In Italy, eleven trials with 5 or 7 applications matching either Greek or Italian GAP gave residues at 3 days PHI of 0.02 (2), 0.03 (3), 0.04, 0.05, 0.18, 0.33, 0.74 and 1.1 mg/kg.

In Spain, 5 trials with 7 applications which matched Greek GAP and 3 trials according to Spanish GAP gave residues at 3 days PHI of 0.02, 0.04, 0.05 (2) 0.07, 0.10, 0.12 and 0.18 mg/kg. One trial conducted at 0.131-0.137 kg ai/ha gave a residue level of 0.20 mg/kg.

Thirty six trials conducted according to GAP in Europe gave residues, in rank order (median underlined), of 0.02 (3), 0.03 (4), 0.04 (3), 0.05 (3), 0.07, 0.08 (2), 0.09, 0.10 (5), 0.11(2), 0.12 (2), 0.15 (3), 0.16, 0.18 (2), 0.20, 0.33, 0.74 and 1.1 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg, an HR of 1.1 mg/kg and an STMR of 0.10 mg/kg for famoxadone in tomato.

Potatoes. Famoxadone can be applied in Europe with a 14 days PHI. The application rate is 0.09 kg ai/ha in Greece, Italy and Spain (up to 8, 6 and 4 applications respectively), 0.175 kg ai/ha in the UK and Germany (12 and 6 applications respectively) and up to 6 application at 1.15 kg ai/ha in Belgium.

There is no approved GAP in Denmark or France. In 12 trials conducted in Europe at a higher rate (6 to 12 applications at 0.164 to 0.224 kg ai/ha), residues at 14 days PHI were <0.02 mg/kg.

A metabolism study on potatoes with 3 applications of 0.3 kg ai/ha showed <0.01 mg/kg famoxadone equivalents in tubers.

Data from supervised trials conducted at higher rates and from the metabolism study support the conclusion that no detectable residues are to be expected in potato tubers after the plants are treated with famoxadone according to good agricultural practice.

The Meeting agreed to recommend an MRL of 0.02* mg/kg and an HR and STMR of 0 mg/kg for famoxadone in potatoes.

Barley. The current UK label indicates that famoxadone may be applied once or twice to barley before quarter ear emergence, as a foliar spray at a maximum rate of 0.150 kg ai/ha. In Belgium, only 1 application is allowed, with a 28 days PHI. Sixteen trials using two foliar applications at 0.15 or 0.20 kg ai/ha were conducted in Belgium, France, Germany and the UK. Samples were collected at maturity, 32-78 days after the last application.

Twelve trials conducted with winter or spring barley, matching the UK GAP rate, gave residues in rank order (median underlined) of <u>≤0.02</u> (8), 0.04 (2), 0.08 and 0.11 mg/kg, 32 to 78 days after the last application. Four trials conducted at 0.2 kg ai/ha gave residues of <0.02 to 0.18 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.02 mg/kg for famoxadone in barley.

Wheat. The current UK label indicates that famoxadone may be applied to winter wheat before flowering as a foliar spray, up to 3 times at a maximum rate of 0.150 kg ai/ha, with a maximum of 0.45 kg ai/ha per season. In Belgium, GAP is one application of 0.15 kg ai/ha and 28 days PHI. Fifteen trials were conducted in Belgium, France, Germany and the UK. In 10 trials with 1 application of 0.28 kg ai/ha and 2 of 0.15 kg ai/ha, samples harvested at maturity, between 36 and 66 days after the last application, contained residues of <u>≤0.02</u> (9) and 0.04 mg/kg in grain. The Meeting agreed that it is unlikely that the higher rate in the first application would influence the residues in the grain at a mature stage therefore and evaluated these trials. In 5 trials with 3 sprays of 0.20 kg ai/ha, residues were in the same range (<0.02-0.06 mg/kg).

The Meeting estimated a maximum residue level of 0.1 mg/kg and an STMR of 0.02 mg/kg for famoxadone in wheat.

Barley straw and forage. In twelve trials within the GAP rate, residues in barley straw harvested at maturity (32-78-day PHI) were 0.16, 0.19, 0.34, 0.47, 0.85, <u>0.86</u>, <u>0.93</u>, 0.96, 1.4, 1.5, 2.5 and 3.8 mg/kg. Allowing for 88% DM (FAO Manual, 2002), the median and the highest residues in barley straw were calculated to be 0.99 (0.895/0.88) and 4.3 mg/kg (3.8/0.88), respectively. Trials at higher rates gave residues from 0.35 to 3.9 mg/kg. Forage samples were harvested in two trials at 7, 14 and 21 days after the last application. Residues after 7 days were 1.4 and 1.8 mg/kg.

The Meeting estimated a maximum residue level of 5 mg/kg and an STMR of 0.99 mg/kg for famoxadone in barley straw.

As too few trials were conducted, the Meeting agreed not to estimate a maximum residue level for famoxadone in barley forage.

Wheat straw and forage. In ten trials within the GAP rate, residues in wheat straw harvested at maturity (34-45 days PHI) were 0.55, 1.2, 1.6, 1.7, <u>2.0</u>, <u>2.1</u>, 2.5, 2.7, 2.9 and 4.3 mg/kg. Allowing for 89% DM (FAO Manual, 2002), the median and the highest residues in wheat straw were calculated to be 2.28 (2.05/0.89) and 4.8 mg/kg (4.3/0.89), respectively. Residues from 5 trials at a higher rate gave residues from 3.4 to 11 mg/kg. Wheat forage samples were harvested in two trials at 0, 7, 14 and 21 days after the last application. The residues at 0 days were 4.2 and 5.8 mg/kg.

The Meeting estimated a maximum residue level of 7 mg/kg and an STMR of 2.28 mg/kg for famoxadone in wheat straw.

There were too few trials to recommend a maximum residue level for famoxadone in wheat forage.

Fate of residues in processing

Grapes. Grapes from vines treated with famoxadone were processed using traditional French wine-making techniques, using alcoholic or malolactic fermentation. Residue levels in grapes were 1.4 and 1.6 mg/kg, decreasing in juice and wine, (processing factor, PF, of <0.01), in lees (PF 0.33) and in must (PF 0.81). Residue levels increased in raisins (PF 1.9), wet pomace (PF 2.0) and dry pomace (PF 3.6).

Tomatoes. In four studies conducted in France, Spain and the USA, treated tomatoes were processed according to industrial manufacturing procedures. Residues in the tomatoes were 0.09-0.86 mg/kg, decreasing after washing (PF 0.28, n=2), in juice (PF 0.22, n=2) and in purée (PF 0.44, n=4). Residue levels increased in tomato paste (PF 1.3, n=2), wet pomace (PF 2.1, n=2) and dry pomace (PF 15, n=2).

Barley. Samples of treated barley from France and Germany were processed using traditional malting, brewing, milling and baking procedures. Residues were detectable only in pearling dust (PF 1.8) and in spent grain (PF 0.67). No residues (<0.02 mg/kg) were found in barley grits, pearl barley, wholemeal bread, malt, malt germ, trub, yeast isolated after brewing (PF <0.5) or beer (PF <0.42, n=2).

Wheat. Treated wheat from one site in France contained a residue level of 0.04 mg/kg, which increased in bran (PF 2). No residues (<0.02 mg/kg) were found in wholemeal, flour or wholemeal bread, with processing factors <0.5.

Residues in processed commodities

Estimates of residues in processed commodities were derived after multiplying the highest residue and/or STMR found in supervised trials on the raw commodity conducted according to GAP by the appropriate processing factor (PF) calculated from the processing studies. Maximum residue levels were only estimated for commodities of human consumption with a PF >1 with a Codex classification number and for commodities of animal consumption which can be used to estimate dietary burdens. An HR-P was estimated only when its use was required for the calculation of short-term exposure.

On the basis of a highest residue of 1.5 mg/kg and an STMR of 0.54 mg/kg in grapes, the Meeting estimated an STMR-P of 0.005 mg/kg for famoxadone in wine and grape juice (PF 0.01), a maximum residue level of 5 mg/kg, an HR-P of 2.85 mg/kg and an STMR of 1.03 mg/kg for famoxadone in raisins (PF 1.9), and a maximum residue level of 7 mg/kg and an STMR of 1.94 mg/kg in dry pomace (PF 3.6).

On the basis of an STMR of 0.10 mg/kg for tomatoes, the Meeting estimated an STMR-P of 0.022 mg/kg for famoxadone in tomato juice (PF 0.22), an STMR-P of 0.044 mg/kg for famoxadone in tomato purée (PF 0.44), and an STMR-P of 0.13 mg/kg for famoxadone in tomato paste (PF 1.3).

On the basis of an STMR of 0.02 mg/kg in barley, the Meeting estimated an STMR-P of 0.008 mg/kg for famoxadone in beer (PF 0.42) and an STMR-P of 0.01 mg/kg for famoxadone in wholemeal barley bread (PF 0.5).

On the basis of an HR of 0.04 mg/kg and an STMR of 0.02 mg/kg in wheat, the Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR-P of 0.04 for famoxadone in wheat bran (PF 2), and an STMR-P of 0.01 mg/kg for famoxadone in wheat flour and wheat wholemeal (PF 0.5).

Animal dietary burdens

The Meeting estimated the dietary burdens of famoxadone in cattle and poultry, on the basis of the diets listed in Appendix IX of the FAO Manual (FAO, 2002) and the MRLs and STMRs estimated at this Meeting, and the results are presented in Tables 32 and 33.

Table 32. Estimated maximum farm animal dietary burden of famoxadone.

Commodity	Group	Residues, mg/kg	Basis	% dry matter	Residues, on dry basis, mg/kg	% of diet			Residue contribution, mg/kg		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	GC	0.2	MRL	88	0.23	50	40	75	0.12	0.09	0.17
Wheat grain	GC	0.1	MRL	89	0.11	50	40	80			
Barley straw	AS	5	MRL	100	5.0	10	60	-	-	3.0	-
Wheat straw	AS	7	MRL	100	7.0	10	10	-	0.70	-	-
					TOTAL	60	100	75	0.82	3.09	0.17

Table 33. Estimated STMR farm animal dietary burden of famoxadone.

Commodity	Group	Residues, mg/kg	Basis	% dry matter	Residues, on dry basis, mg/kg	% of diet			Residue contribution, mg/kg		
						Beef	Dairy	Poultry	Beef	Dairy	Poultry
Barley grain	GC	0.02	STMR	88	0.023	50	40	75	0.012	0.009	0.017
Wheat grain	GC	0.02	STMR	89	0.023	50	40	80			
Barley straw	AS	0.99	STMR	100	0.99	10	60	-	-	0.594	-
Wheat straw	AS	2.28	STMR	100	2.28	10	10	-	0.228	-	-
					TOTAL	60	100	75	0.24	0.603	0.017

Animal feeding studies

Famoxadone was given in gelatine capsules twice daily to lactating Holstein dairy cows, for 28 days at feeding levels of 9, 27 and 90 ppm. Three cows at each dose were slaughtered on day 29, and one at the higher feeding level was slaughtered on each of days 42 and 48.

In whole milk, residue levels of famoxadone reached a plateau by the tenth day of dosing, at all treatment levels. The mean plateau level (days 10-28) was 0.14, 0.43 and 1.5 mg/kg at feeding levels of 9, 27 and 90 ppm, respectively. The average residues from days 1-28 were 0.12, 0.33 and 1.2 mg/kg, respectively. Residues in milk from the cow killed on day 48 (highest feeding level) decreased from 1.5 mg/kg at day 28 to 0.02 mg/kg at day 47. Residues in milk fat from days 14-28 were 10 times higher than in whole milk (1.4, 4.3 and 15 mg/kg, respectively).

In tissues, famoxadone residues were detected at day 28 (sacrifice) in liver (averages of 0.69, 2.0 and 6.3 mg/kg at the low, medium and higher dose, respectively); kidney (0.15, 0.59 and 1.5 mg/kg); muscle (0.07, 0.24 and 1.0 mg/kg); and fat (1.0, 4.1 and 17 mg/kg, respectively). Tissues from the cow killed 20 days after the end of dosing had decreased to 0.04, 0.02, 0.01 and 0.19 mg/kg in liver, kidney, muscle and fat, respectively.

Residue levels in animal commodities

Cattle. The maximum dietary burdens of beef and dairy cattle estimated by the Meeting were 0.82 and 3.1 ppm, respectively, and the higher value of 3.1 ppm was used for calculation of the residues. The levels were derived by applying the transfer factor (residue level in milk or tissue ÷ residue level in diet) from the lowest feeding level (9 ppm) to the calculated maximum dietary burden. For the STMR estimate, the same procedure was applied to the STMR dietary burden for dairy cattle of 0.60 ppm.

As the residue levels of famoxadone reached a plateau rapidly in milk (<14 days), the maximum residue levels in tissues were derived from the maximum dietary burden by applying the transfer factor to the highest individual residue levels found in the feeding study (FAO Manual, 2002). The STMRs were derived from the STMR dietary burden and the mean residue levels. For milk, the mean residue at the plateau level from the 9 ppm feeding group was used to estimate both the maximum residue level and the STMR.

Table 34. Estimated residue levels in cattle consuming feed from crops treated with famoxadone.

Dose (ppm) *(extrapolated)* [actual]	Milk fat	Whole milk	Famoxadone concentration (mg/kg)							
			Liver		Kidney		Muscle		Fat	
	Mean	Mean	Highest	Mean	Highest	Mean	Highest	Mean	Highest	Mean
MRL *(3.1)* [9.0]	*(0.48)* [1.4]		*(0.24)* [0.70]		*(0.062)* [0.18]		*(0.031)* [0.09]		*(0.41)* [1.2]	
STMR *(0.60)* [9.0]		*(0.009)* [0.14]		*(0.046)* [0.69]		*(0.010)* [0.15]		*(0.005)* [0.07]		*(0.067)* [1.0]

Assuming milk to contain 4% fat, the estimated mean concentration of famoxadone in milk fat, expressed as whole milk, was 0.019 mg/kg (0.48 ÷ 25).

The Meeting estimated a maximum residue level of 0.03 mg/kg (F) and an STMR of 0.009 mg/kg (F) for famoxadone in milks, a maximum residue level of 0.5 mg/kg, an STMR of 0.046 mg/kg and an HR of 0.24 mg/kg for famoxadone in edible offal (mammalian), and a maximum residue level of 0.5 mg/kg for famoxadone in meat (fat) from mammals other than marine mammals.

For the purpose of dietary intake calculations, the Meeting recommended an STMR of 0.067 mg/kg and a HR of 0.41 mg/kg in fat from mammals other than marine mammals and an STMR of 0.005 mg/kg and an HR of 0.031 mg/kg for famoxadone in muscle from mammals other than marine mammals.

Poultry. The metabolism study conducted with laying hens at 10 ppm in the feed (7 days dosing) showed no radioactive residues in muscle, fat, skin or egg white (<0.01 mg/kg). Radioactive residues were detected only in egg yolk and liver, with a maximum of 0.003 mg/kg famoxadone found in yolk. The feeding level in this study is almost 60 times the calculated maximum dietary burden for poultry (0.17 mg/kg feed).

The Meeting agreed that it is unlikely that famoxadone residues would remain in poultry tissues and eggs after feeding with commodities containing residues of the fungicide. The Meeting estimated a maximum residue level of 0.01* mg/kg for famoxadone in poultry meat, poultry edible offal and eggs, and an HR and an STMR of 0 for famoxadone in poultry edible offal and eggs.

For the purpose of dietary intake calculations, the Meeting estimated an HR and an STMR of 0 for famoxadone in poultry muscle and fat.

RECOMMENDATIONS

On the basis of the data from supervised trials, the Meeting concluded that the residue levels shown in Table 35 are suitable for establishing maximum residue limits and for dietary intake assessment.

Definition of the residue for compliance with MRL and for estimation of dietary intake in plant and animal commodities: *famoxadone*.

The compound is fat soluble.

Table 35. Summary of recommendations.

Commodity		MRL, mg/kg		STMR or STMR-P mg/kg	HR or HR-P, mg/kg
CCN	Name	New	Previous		
GC 0640	Barley	0.2		0.02	
	Barley bread, wholemeal			0.01	
	Beer			0.008	
AS 0640	Barley straw and fodder (dry)	5		0.99	
VC 424	Cucumbers	0.2		0.025	0.10
FB 0269	Grapes	2		0.54	1.5
JF 269	Grape juice			0.005	
	Wine			0.005	
AB 269	Grape pomace, dry	7		1.94	
DF 269	Dried grapes (raisins)	5		1.03	2.85
MO 105	Edible offal (mammalian)	0.5		0.046	0.24
PE 0112	Eggs	0.01* (note)		0	0
MM 0095	Meat (from mammals other than marine mammals)	0.5 fat		Muscle: 0.005 Fat: 0.07	Muscle: 0.031 Fat: 0.41
ML 0106	Milks	0.03 (F)		0.009	
VR 0589	Potatoes	0.02*		0	0
PM 0110	Poultry meat	0.01* (note)		Muscle: 0 Fat: 0	Muscle: 0 Fat: 0
PM 0111	Poultry, edible offal of	0.01* (note)		0	0
VC 431	Squash, summer	0.2		0.025	0.10
VO 0448	Tomatoes	2		0.10	1.1
VJ 0448	Tomato juice			0.022	
	Tomato paste			0.13	
	Tomato puree			0.044	
GC 0654	Wheat	0.1		0.02	
CM 0654	Wheat bran, unprocessed	0.2		0.04	
CF 1211	Wheat flour			0.01	
CF 1212	Wheat wholemeal			0.01	
AS 0654	Wheat straw and fodder, dry	7		2.28	

Note. No residues expected from consumption of feed commodities with famoxadone residues, as evaluated by JMPR.

DIETARY RISK ASSESSMENT

Long-term intake

The ADI for famoxadone is 0-0.006 mg/kg body weight/day. International estimated daily intakes (IEDIs) were calculated for the commodities of human consumption for which STMRs were estimated by the Meeting. The results are shown in Table 36.

IEDIs for the five GEMS/Food regional diets, based on estimated STMRs, were 1-7% of the maximum ADI. The Meeting concluded that the intake of residues of famoxadone, resulting from uses that have been considered by the JMPR, is unlikely to present a public heath concern.

Table 36. Assessment of risks from the long-term dietary intake of residues of famoxadone (ADI = 0-0.006 mg/kg bw/day).

Code	Commodity	STMR/ STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
GC 0640	Barley (fresh)	0.02	1.0	0.0	3.5	0.0	1.8	0.0	6.5	0.1	19.8	0.2
GC 0640	Barley (beer only)	0.008	-	-	-	-	-	-	-	-	-	-
VC 0424	Cucumber	0.025	2.4	0.1	2.3	0.1	0.0	0.0	4.2	0.1	4.5	0.1
MO 0105	Edible offal (mammalian)	0.046	4.2	0.2	1.4	0.1	2.8	0.1	6.1	0.3	12.4	0.6
PE 0112	Eggs	0	14.6	0.0	13.1	0.0	3.7	0.0	11.9	0.0	37.6	0.0
FB 0269	Grapes (fresh, wine, dried)	0.54	16.1	8.7	1.0	0.5	0.0	0.0	1.6	0.9	16.1	8.7
DF 0269	Grapes, dried (= currants, raisins and sultanas)	1.03	0.3	0.3	0.0	0.0	0.0	0.0	0.3	0.3	2.3	2.4

Code	Commodity	STMR/ STMR-P mg/kg	Diets: g/person/day. Intake = daily intake: µg/person									
			Mid-East		Far-East		African		Latin American		European	
			diet	intake	diet	intake	diet	intake	diet	intake	diet	intake
MM 0095	Meat from mammals other than marine mammals: 20% as fat	0.067	7.4	0.5	6.6	0.4	4.8	0.3	9.4	0.6	31.1	2.1
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	0.005	29.6	0.1	26.2	0.1	19.0	0.1	37.6	0.2	124.4	0.6
ML 0106	Milks	0.009	116.9	1.1	32.1	0.3	41.8	0.4	160.1	1.4	289.3	2.6
VR 0589	Potato	0	59.0	0.0	19.2	0.0	20.6	0.0	40.8	0.0	240.8	0.0
PM 0110	Poultry meat: 10% as fat	0	3.1	0.0	1.3	0.0	0.6	0.0	2.5	0.0	5.3	0.0
PM 0110	Poultry meat: 90% as muscle	0	27.9	0.0	11.9	0.0	5.0	0.0	22.8	0.0	47.7	0.0
PO 0111	Poultry, edible offal of	0	0.1	0.0	0.1	0.0	0.1	0.0	0.4	0.0	0.4	0.0
VC 0431	Squash, summer	0.025	10.5	0.3	2.2	0.1	0.0	0.0	14.0	0.4	3.5	0.1
VO 0448	Tomato (fresh)	0.1	44.1	4.4	5.7	0.6	14.6	1.5	25.5	2.6	34.9	3.5
JF 0448	Tomato juice	0.022	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.0	0.0
	Tomato paste	0.13	5.8	0.8	0.2	0.0	0.3	0.0	0.0	0.0	4.0	0.5
GC 0654	Wheat	0.02										
CM 0654	Wheat bran, unprocessed	0.04	-	-	-	-	-	-	-	-	-	-
CF 1211	Wheat flour	0.01	323.0	3.2	114.0	1.1	28.3	0.3	112.0	1.1	175.8	1.8
CF 1212	Wheat wholemeal	0.01	-	-	-	-	-	-	-	-	-	-
	Wine only	0.005	0.5	0.0	0.0	0.0	0.8	0.0	19.8	0.1	97.8	0.5
Total intake (µg/person)=				19.6		3.3		2.7		8.0		23.6
Bodyweight per region (kg bw) =				60		55		60		60		60
ADI (µg/person)=				360		330		360		360		360
%ADI=				5.5		1.0		0.8		2.2		6.6
Rounded %ADI=				5		1		1		2		7

Short-term intake

The International estimated short-term intakes (IESTIs) for famoxadone were calculated for commodities for which STMR and HR values were estimated by the Meeting and for which data on consumption (large portion and unit weight) were available. The results for the general population are shown in Table 37 and those for children up to 6 years of age are shown in Table 38.

The acute RfD for famoxadone is 0.6 mg/kg bw. The IESTI represented 0-8 % of acute RfD for children and 0-3 % acute RfD for the general population. The Meeting concluded that the short-term intake of residues of famoxadone, from uses on the commodities that have been considered by the JMPR, is unlikely to present a public health concern.

Table 37. Assessment of risk to the general population from the short-term dietary intake of residues of famoxadone (acute RfD = 0.6 mg/kg bw or 600 µg/kg bw).

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion			Unit weigh			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	g	Country	Unit wt, g	Unit wt, edible part, g				
GC 0640	Barley (beer only)	0.008	-	AUS	67.0	528	-	-	-	-	3	0.06	0
GC 0640	Barley (fresh, flour, beer)	-	0.11	NLD	63.0	378	-	-	-	-	3	-	-
VC 0424	Cucumbers	-	0.1	NLD	63.0	313	FRA	400	360	3	2b	1.49	0
MO 0105	Edible offal (mammalian)	-	0.24	FRA	62.3	277	-	-	-	-	1	1.07	0
PE 0112	Eggs	-	0	FRA	17.8	134		-	-	-	1	0.0	0
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	67.0	513	FRA	125	118	3	2a	16.75	3
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.85	FRA	62.3	135	-	-	-	-	1	6.18	1
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.41	AUS	67.0	104	-	-	-	-	1	0.64	0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.031	AUS	67.0	417	-	-	-	-	1	0.19	0
ML 0106	Milks	0.009	-	USA	65.0	2466	-	-	-	-	3	0.34	0
VR 0589	Potatoes	-	0	NLD	63.0	687	FRA	200	160	3	2a	0.00	0
PM 0110	Poultry meat: 10% as fat	-	0	AUS	67.0	43	-	-	-	-	1	0.00	0
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	67.0	388	-	-	-	-	1	0.00	0
PO 0111	Poultry, edible offal of	-	0	USA	65.0	248	-	-	-	-	1	0.00	0
VC 0431	Squash, summer	-	0.1	FRA	62.3	343	FRA	300	270	3	2a	1.42	0
VO 0448	Tomatoes (fresh, juice, paste, peeled)	-	1.1	USA	65.0	391	FRA	105	102	3	2a	10.06	2
JF 0448	Tomato juice	0.022	-	-	-	-	-	-	-	-	3	-	-
	Tomato paste	0.13	-	-	-	-	-	-	-	-	-	-	-
GC 0654	Wheat	0.02	-	USA	65.0	383	-	-	-	-	3	0.12	0
CF 1211	Wheat flour	0.01	-	USA	65.0	365	-	-	-	-	3	0.06	0
CF 1212	Wheat wholemeal	0.01	-	USA	65.0	155	-	-	-	-	3	0.02	0
	Wine only	0.005	-	AUS	67.0	1131	-	-	-	-	3	0.08	0

Table 38. Assessment of risk to children up to 6 years old from the short-term dietary intake of residues of famoxadone (acute RfD = 0.6 mg/kg bw or 600 µg/kg bw).

Codex Code	Commodity	STMR or STMR-P mg/kg	HR or HR-P mg/kg	Large portion			Unit weigh			Variability factor	Case	IESTI µg/kg bw/day	% acute RfD rounded
				Country	Body wt (kg)	g	Country	Unit wt, g	Unit wt, edible part, g				
GC 0640	Barley (beer only)	0.008	-	AUS	19.0	12	-	-	-	-	3	0.00	0
GC 0640	Barley (fresh, flour, beer)	-	0.11	AUS	19.0	14	-	-	-	-	3	-	-
VC 0424	Cucumber	-	0.1	NLD	17.0	162	FRA	400	360	3	2b	2.86	0
MO 0105	Edible offal (mammalian)	-	0.24	FRA	17.8	203	-	-	-	-	1	2.73	0
PE 0112	Eggs	-	0	FRA	17.8	134	-	-	-	-	1	0.00	0
FB 0269	Grapes (fresh, dried, excluding wine)	-	1.5	AUS	19.0	342	FRA	125	118	3	2a	45.55	8
DF 0269	Grapes, dried (= currants, raisins and sultanas)	-	2.85	USA	15.0	59	-	-	-	-	1	11.26	2
MM 0095	Meat from mammals other than marine mammals: 20% as fat	-	0.41	AUS	19.0	52	-	-	-	-	1	1.12	0
MM 0095	Meat from mammals other than marine mammals: 80% as muscle	-	0.031	AUS	19.0	208	-	-	-	-	1	0.34	0
ML 0106	Milks	0.009	-	USA	15.0	1286	-	-	-	-	3	0.77	0
VR 0589	Potato	-	0	SAF	14.2	300	FRA	200	160	3	2a	0.00	0
PM 0110	Poultry meat: 10% as fat	-	0	AUS	19.0	22	-	-	-	-	1	0.00	0
PM 0110	Poultry meat: 90% as muscle	-	0	AUS	19.0	201	-	-	-	-	1	0.00	0
PO 0111	Poultry, edible offal of	-	0	USA	15.0	37	-	-	-	-	1	0.00	0
VC 0431	Squash, summer	-	0.1	AUS	19.0	219	FRA	300	270	3	2b	3.46	1
VO 0448	Tomato (fresh, juice, paste, peeled)	-	1.1	USA	15.0	159	FRA	105	102	3	2a	26.60	4
FJ 0448	Tomato juice	0.022	-	-	-	-	-	-	-	-	3	-	-
-d	Tomato paste	0.13	-	-	-	-	-	-	-	-	-	-	-
GC 0654	Wheat	0.02	-	USA	15.0	151	-	-	-	-	3	0.20	0
CF 1211	Wheat flour	0.01	-	AUS	19.0	194	-	-	-	-	3	0.10	0
CF 1212	Wheat wholemeal	0.01	-	USA	15.0	74	-	-	-	-	3	0.05	0
-	Wine only	0.005	-	AUS	19.0	4	-	-	-	-	3	0.00	0

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