METALAXYL-M (212)

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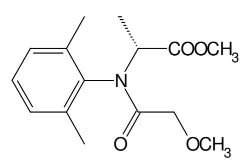
EXPLANATION

The toxicology of metalaxyl-M was evaluated by the 2002 JMPR, which established a group ADI of 0–0.08 mg/kg bw for metalaxyl and metalaxyl-M. Residue and analytical aspects were considered for the first time by the present Meeting. Metalaxyl-M is the biologically active enantiomer (R-enantiomer) of the racemic compound metalaxyl. Metalaxyl was first evaluated by the JMPR in 1982, and Codex MRLs for metalaxyl have been established.

IDENTITY

ISO common name	metalaxyl-M
Synonyms	Mefenoxam® CGA 329351
Chemical name	
IUPAC name	methyl *N*-(methoxyacetyl)-*N*-(2,6-xylyl-D-alaninate
CAS	methyl *N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)-D-alaninate
CAS Number	70630-17-0
CIPAC Number	580
Molecular formula	$C_{15}H_{21}NO_4$
Molecular mass	279.3
Structural formula	



PHYSICAL AND CHEMICAL PROPERTIES

<u>Pure active ingredient.</u> Purity 99.4% (including S-enantiomer), 97.2% R-enantiomer.

		Ref
Appearance	Pale yellow, clear viscous liquid	26171
Odour	Weak	26171
Boiling point	Thermal decomp ~ 270°C (below bp)	26165
Relative density	1.125 at 20°C	26166
Vapour pressure:	3.3×10^{-3} Pa at 25°C (extrapolated from measurements between 41.4 and 91.4°C)	PP-94/45P.VPC
Henry's law constant	3.5×10^{-5} $Pa.m^3/mol$ (calc from vp and water sol)	
Solubility in water	26 g/l at 25°C	26169
Solubility in organic solvents at 25°C:	See technical material	26833

Dissociation constant in water	No dissociation	PP-94/45P.DCW
Octanol/water partition coefficient:	log P_{OW} = 1.71±0.04 at 25°C	26168
Hydrolysis (sterile soln)	Stable to hydrolysis up to pH 7 even at 50°C. At pH 9 Half-life 116 days at 25°C 7.7 days at 50°C 2.7 days at 60°C	95EH05
Photolysis in water	Not degraded by light (2.2 ppm solution in pH 7 buffer, irradiated for 240 h). Degradation of metalaxyl-M by direct photolysis in surface waters is not expected because metalaxyl-M does not absorb sunlight wavelengths (above 290 nm).	95EH04

Technical material (97.1% ai)

Appearance:	Light brown, clear viscous liquid.	26831
Odour	Weak	26831
Minimum purity	Metalaxyl-M: no FAO specification . Metalaxyl, technical: FAO specification: 950 g/kg minimum, impurity 2,6-dimethylaniline maximum 1 g/kg.	FAO, 1992
Solubility in organic solvents at 25°C:	Completely miscible at 25°C in toluene, dichloromethane, ethanol, ethyl acetate, acetone, n-octanol. Hexane at 25°C: 59 g/l.	26833

FORMULATIONS

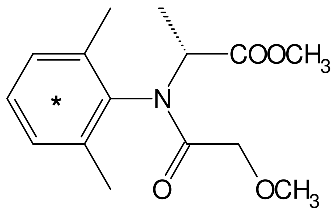
Metalaxyl-M is available in the following formulations:

EC	metalaxyl-M only and in combination with fluazinam
FS	combination with fludioxonil
GR	metalaxyl-M only
KL	combination with chlorothalonil
LS	metalaxyl-M only
SC	metalaxyl-M in combination with chlorothalonil
WG	combination with folpet, mancozeb
WP	combination with chlorothalonil, copper, folpet, mancozeb, zineb

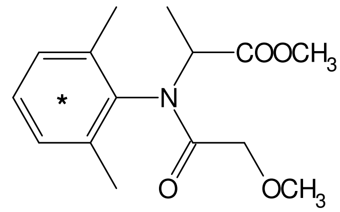
Metalaxyl-M is the biologically active R-enantiomer in the racemic compound metalaxyl. Metalaxyl was first evaluated by the JMPR in 1982 and Codex MRLs were recommended. In recent years it has become possible to manufacture metalaxyl-M industrially and to register products based on the active R-enantiomer only. However as metalaxyl-M constitutes 50% of metalaxyl-M investigations into the metabolism and fate of metalaxyl can legitimately be accepted as representative of the metabolism and fate of metalaxyl-M.

METABOLISM

Animal and plant metabolism and environmental fate studies were with metalaxyl or metalaxyl-M uniformly ^{14}C-labelled in the aromatic ring.



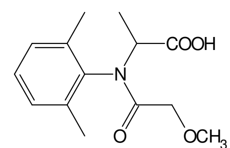
* 14C label position
metalaxyl-M



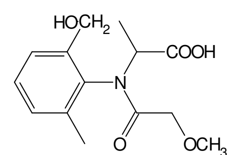
* 14C label position
metalaxyl

Structures, names and codes for metabolites are summarised below. The designations Metabolite 1 to Metabolite 14 were used in the toxicological evaluation of metalaxyl and metalaxyl-M (WHO, 2003) and are also used here. Metabolites are further identified by CAS numbers where available. Chemical names do not necessarily follow IUPAC or CAS practice.

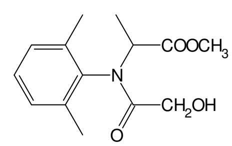
Metabolite 1 (CGA 62826. Enantiomer from metalaxyl-M is NOA 409045)
N-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)alanine
CAS 75596-99-5



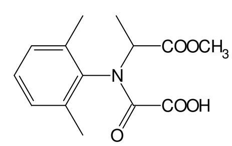
Metabolite 2 (Metab M9 or metab P0)
N-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine



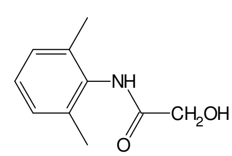
Metabolite 3 (CGA 67869)
N-(2,6-dimethylphenyl)-*N*-(hydroxyacetyl)alanine methyl ester
CAS 66637-79-4



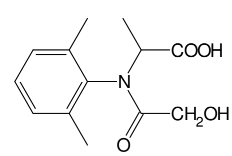
Metabolite 4 (CGA 79353)
N-(carboxycarbonyl)-*N*-(2,6-dimethylphenyl)alanine methyl ester



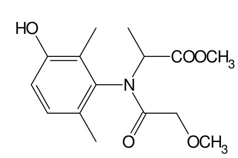
Metabolite 5 (CGA 37734)
N-hydroxyacetyl-2,6-dimethyl-aniline
CAS 29183-14-0



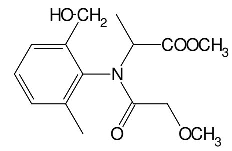
Metabolite 6 (CGA 107955)
N-(2,6-dimethylphenyl)-*N*-(hydroxyacetyl)alanine
CAS 104390-55-8



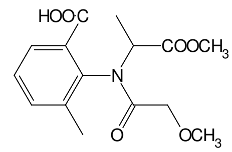
Metabolite 7 (CGA 100255)
N-(2,6-dimethyl- 5-hydroxyphenyl)-*N*-(methoxyacetyl)alanine methyl ester
CAS 96258-85-4



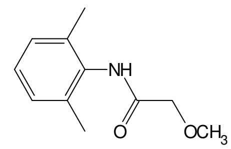
Metabolite 8 (CGA 94689)
N-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester (occurs as 2 isomers)
CAS 85933-49-9



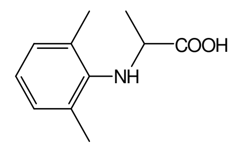
Metabolite 9 (CGA 108905)
N-(2-carboxy-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester



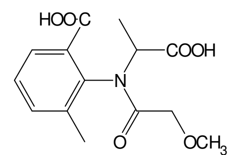
Metabolite 10 (CGA 67868)
N-methoxyacetyl-2,6-dimethyl-aniline
CAS 53823-88-4



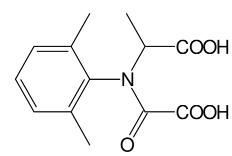
Metabolite 11 (CGA 67867)
N-(2,6-dimethylphenyl) alanine



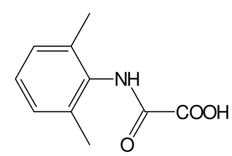
Metabolite 12 (CGA 108906)
N-(2-carboxy-6-methylphenyl)-*N*-(methoxyacetyl)alanine
CAS 104390-56-9



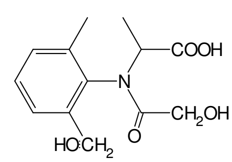
Metabolite 13 (CGA 78532)
N-(carboxycarbonyl)-*N*-(2,6-dimethylphenyl)alanine



Metabolite 14 (CGA 68124)
2,6-dimethylanilinoxoacetic acid
[(2,6-dimethylphenyl)-amino]oxoacetic acid
CAS 2903-48-2

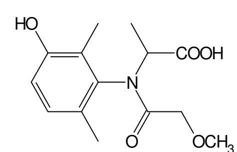


Metab P2
N-(2-hydroxymethyl)-6-methylphenyl]-*N*-(hydroxyacetyl)alanine



Metab P1 (St
N-(2-hydroxymethyl)-6-methylphenyl]-*N*-(hydroxyacetyl)alanine
(Sterioisomer of P2)

CGA 119857
N-(3-hydroxy-2,6-dimethylphenyl)-*N*-(methoxyacetyl)alanine



Animal metabolism

Studies on the use of metalaxyl on rats, lactating goats and laying hens were reported to the Meeting. (The metabolism of metalaxyl and metalaxyl-M in rats, goats and hens had already been evaluated for toxicology by the 2002 JMPR (WHO, 2003).)

When animals were dosed orally with radiolabelled metalaxyl, in a short time most of the radioactivity was excreted in the urine and a small amount in the faeces. In a goat study, metalaxyl was not detected in the residues in the tissues or milk. In a laying hen study, low levels were present in liver and eggs.

Numerous metabolites formed by hydrolysis, oxidation and demethylation of metalaxyl and subsequent conjugation were identified.

Rats

Rats dosed orally with a single treatment (27.9 mg/kg bw) of ring-labelled [^{14}C]metalaxyl excreted 63% and 33% of the administered ^{14}C within 48 h in the urine and faeces respectively (Hamböck, 1978, study 26/78). Metabolite 1, Metabolite 10, Metabolite 5 and Metabolite 8 were identified in the urine as free metabolites or glucuronic acid conjugates.

Four groups of rats were dosed with [^{14}C]metalaxyl at 1.1 mg/kg bw (intravenous), 1.1 mg/kg bw (oral), 1.1 mg/kg bw (oral, after 14 daily doses of unlabelled metalaxyl) and 203 mg/kg bw (oral) (Itterly and Eberle, 1990, report ABR-90079). Nine metabolites (2, 5, 1, 11, 4, 8, 7, 6 and 9) were identified in the excreta as free compounds, or as glucuronide or sulfate conjugates.

Muller (1997, report 19/97) showed that the absorption, distribution, metabolism and excretion of radiolabel from metalaxyl and metalaxyl-M dosing were similar in rats.

Goats

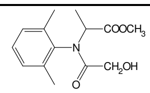
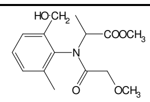
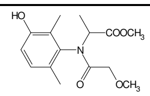
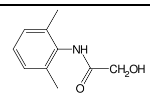
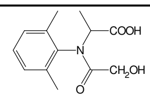
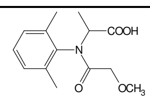
Fisher *et al.* (1978, report ABR-78046) orally dosed a lactating goat by capsule with [^{14}C]metalaxyl at the equivalent of 7 ppm in the feed for 10 consecutive days. Most of the radiolabel was excreted in the urine (93%) and faeces (11.6%), with total recovery of radiolabel of 107%. Very little ^{14}C was found in the milk (0.003 mg/kg) or tissues (0.019 and 0.057 mg/kg in kidney and liver respectively). TLC showed similar patterns of metabolites in rat and goat urine.

In another trial two lactating dairy goats weighing 37.4 and 38.5 kg were dosed orally once daily for 4 consecutive days by gelatin capsule with 150 mg/day of [^{14}C]metalaxyl, equivalent to 77 ppm metalaxyl in the diet (Emrani and Meadows, 1990, report ABR-90078). Milk was collected twice a day and the animals slaughtered 6 and 7 h respectively after the last dose. Recovery of administered ^{14}C was 80%.

Within 24 h of administration 67%, 9% and 0.1% of the daily dose was found in the urine, faeces and milk respectively. Six metabolites (5, 1, 3, 8, 7 and 6), mostly present as glucuronic acid conjugates, were identified in the urine. Tissues and milk were treated with glucuronidase to hydrolyse conjugates before analysis and identification (Table 1). Metalaxyl was not detected as a component of the residue. The metabolic pathways for metalaxyl in goats were similar to those in hens and rats.

Emrani and Meadows (1991, report ABR-91075) identified the main metabolites (66% of the radioactivity) in the milk as C_{10} and C_8 fatty acid conjugates through the hydroxyacetyl group of Metabolite 3.

Table 1. Metabolites in the tissues and milk of goats dosed orally by gelatin capsule for 4 consecutive days with 150 mg/day of [^{14}C]metalaxyl, equivalent to 77 ppm metalaxyl in the diet (Emrani and Meadows, 1990, 1991, reports ABR-90078, ABR-91075).

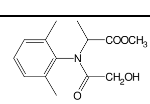
Metabolites	^{14}C, mg/kg as metalaxyl					
	Milk, goat 2, day 2	Liver, goat 2	Kidney, goat 2	Leg muscle, goat 2	Tenderloin, goat 2	Perirenal fat, mean of 2 goats
^{14}C as % of dose	0.10%	0.17%	0.02%	0.19%	0.16%	<0.01%
^{14}C conc	0.089	1.37	1.06	0.074	0.065	0.25
Metabolite 3 	0.004	0.025	0.036	0.006	0.004	0.029
Metabolite 3 fatty acid conj	0.058[1]					
Metabolite 8 	0.005	0.11	0.36	0.009	0.007	0.034
Metabolite 7 	0.008	0.070	0.029	0.004	0.011	0.007
Metabolite 5 	<0.001	[2]	0.007	0.006	[2]	0.014
Metabolite 6 	0.004	0.19	0.335	0.014	0.011	0.065
Metabolite 1 	<0.001	0.022	0.007	0.008	0.006	0.006

[1] Major metabolite in milk C_8 and C_{10} fatty acid conjugates of Metabolite 3.
[2] Metabolite 5 included in Metabolite 7 value.

Hens

Five laying hens weighing 1.3 to 1.7 kg were dosed orally once daily for 4 consecutive days by gelatin capsule with 10 mg/day of [^{14}C]metalaxyl, equivalent to approximately 100 ppm metalaxyl in the diet (Kennedy *et al.*, 1990, report ABR-90077). Eggs were collected once a day and the hens killed 6 h after the last dose. Recovery of administered ^{14}C was 92%, with 0.97% in edible tissues and eggs and the remainder in the excreta. Metabolites in eggs, liver, thigh muscle and peritoneal fat are shown in Table 2. Recoveries from other tissues were breast muscle 0.25%, skin + fat 0.05%, gizzard 0.08% and kidney 0.04%.

Table 2. Metabolites in the tissues and eggs of hens dosed orally for 4 consecutive days by gelatin capsule with 10 mg/day of [^{14}C]metalaxyl, equivalent to approximately 100 ppm metalaxyl in the diet (Kennedy *et al.*, 1990, report ABR-90077; 1991, report ABR-91077).

Metalaxyl, metabolites	^{14}C, mg/kg as metalaxyl (includes conjugates except where separately listed)				
	Egg white	Egg yolk	Liver	Thigh muscle	Fat
^{14}C as % of dose	0.01%	0.01%	0.14%	0.31%	0.02%
^{14}C conc	0.18	0.21	1.4	0.67	0.25
Metalaxyl	0.013	0.010	0.018	<0.001	<0.001
Metabolite 3 	<0.001		0.009	<0.001	
P3a (glucuronide of Metabolite 3)	<0.001	0.006		<0.001	0.002

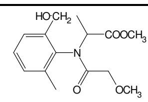
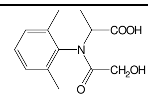
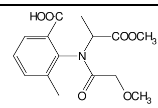
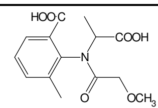
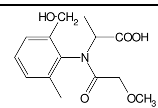
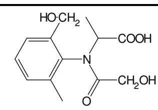
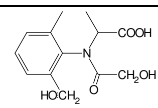
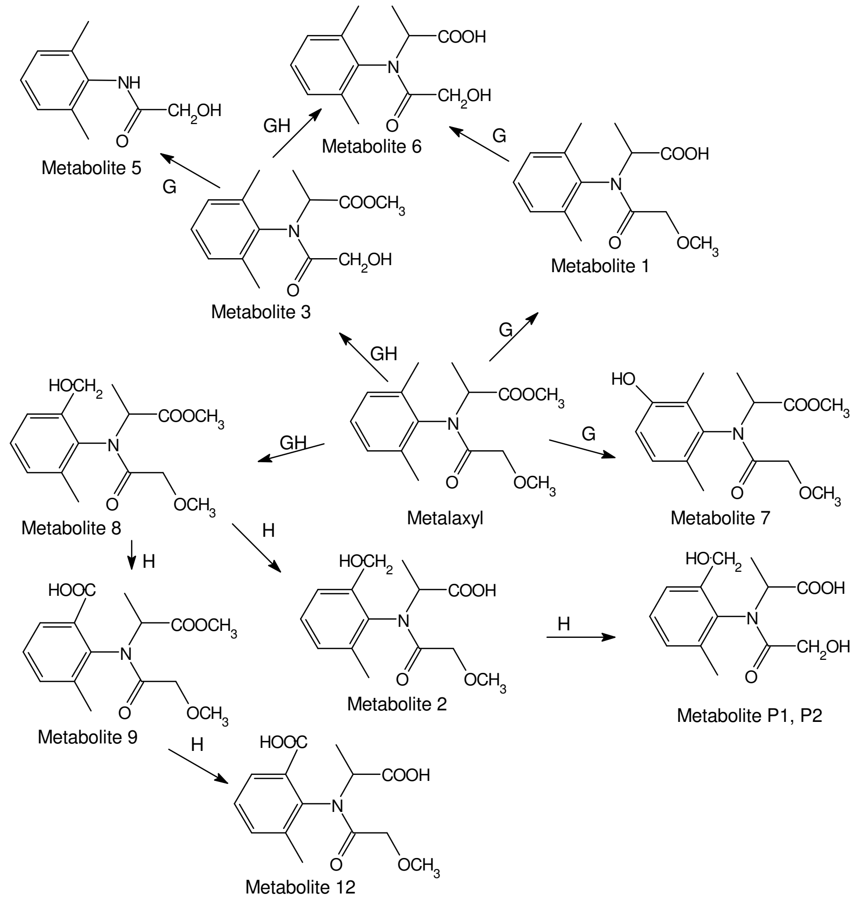
Metalaxyl, metabolites	^{14}C, mg/kg as metalaxyl (includes conjugates except where separately listed)				
	Egg white	Egg yolk	Liver	Thigh muscle	Fat
P4 (sulfate of Metabolite 3)	0.014	0.015		0.20	0.021
Metabolite 13 + Metabolite 14 + Metabolite 4			0.049		
Metabolite 8 	0.017	0.016	0.013	<0.001	<0.001
Metabolite 6 	<0.001	0.052	0.24	<0.001	0.10
Metabolite 9 	<0.001	0.007		<0.001	<0.001
Metabolite 12 			0.17		
Metabolite 2 	0.011	0.005		<0.001	<0.001
P1 	0.032	0.038		0.25	0.013
P2 	0.024	0.034		0.062	0.005

Figure 1. Metabolic pathways of metalaxyl in goats and hens. Metabolites may occur as conjugates in tissues, milk and eggs.



Plant metabolism

Studies on the metabolism of metalaxyl in grapes, lettuce and potatoes and of metalaxyl-M in lettuce were reported to the Meeting. The plant metabolites had previously been identified as animal metabolites.

The parent compound was the main component of the residue in grapes and grape juice when metalaxyl was applied to vines. In treated lettuce, metalaxyl and metabolite 8 were each present at approximately 20% of the total residue. Metabolite 8 was the main residue in both cases when metalaxyl and metalaxyl-M were applied to lettuce.

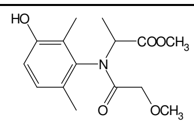
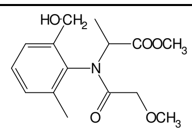
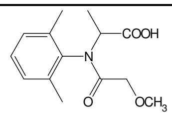
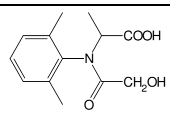
When metalaxyl was applied to potato plants, the main residue in the tubers was the parent compound.

Grapes

In a field trial in Switzerland Riesling and Sylvaner grapevines were sprayed to run-off seven times at 14-day intervals at a [^{14}C]metalaxyl concentration of 0.050 kg ai/hl. Although a severe hailstorm occurred sufficient ripe grapes and leaves were harvested 52 days after the seventh and last application for analysis (Gross, 1978, 11/78). Levels of ^{14}C (as metalaxyl) were 3.1 mg/kg in grapes, 1.04 mg/kg in juice, 7.3 mg/kg in presscake and 30 mg/kg in leaves. Metalaxyl constituted 64% and 22% of the total residues in grapes and leaves respectively.

In a further field trial in Switzerland two vines were sprayed to run-off 6 times at approximately 14-day intervals with a [^{14}C]metalaxyl spray concentration of 0.030 kg ai/hl. Ripe grapes and leaves were harvested 68 days after the last application (Gross, 1979, 06/79). The grapes were separated into juice and presscake. The results are shown in Table 3.

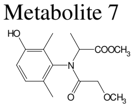
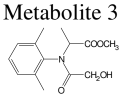
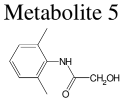
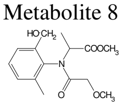
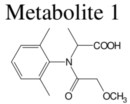
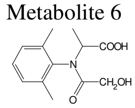
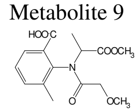
Table 3. Metalaxyl and its metabolites in grapes and leaves 68 days after spraying the vines with [^{14}C]metalaxyl (Gross, 1979, 06/79).

Component	Concentration, mg/kg, as metalaxyl			
	Grapes	Juice	Presscake	Leaves
^{14}C, % of total applied	0.18	0.06	0.12	2.4
^{14}C concentration, mg/kg as metalaxyl	1.4	0.9	1.7	19.8
Metalaxyl concentration, mg/kg	0.83	0.56	0.96	2.9
Compound including conjugates	% of ^{14}C in grapes			% of ^{14}C in leaves
Metalaxyl	64.1	7.8	56.3	22.4
Metabolite 7 	4.3	1.7	2.6	13
Metabolite 8 	20.4	7.0	13.4	55.4
Metabolite 1 + Metabolite 6  	1.8	1.0	0.8	5.0

Lettuce

Lettuce seedlings (variety Suzanne) in a greenhouse were sprayed twice with a 2-week interval with [^{14}C]metalaxyl at a rate equivalent to 0.25 kg ai/ha and harvested 2 weeks after the second application (Gross, 1979, 38/79). The total ^{14}C residue in the lettuce constituted 17.6% of the applied dose. Table 4 shows the identified components of the residues (Gross, 1980, 38/80).

Table 4. Percentages of residues identified in lettuce harvested 2 weeks after the second application of [^{14}C]metalaxyl at a rate equivalent to 0.25 kg ai/ha (Gross 1980, 38/80). Glucose conjugates are included in the metabolite concentrations.

Metalaxyl	Metabolite 7	Metabolite 3	Metabolite 5	Metabolite 8	Metabolite 1	Metabolite 6	Metabolite 9
							
18.6	6.2	8.9	2.9	22.1	6.0	10.1	1.2

Stingelin (2000, 98JS30) compared the metabolism of metalaxyl and metalaxyl-M in Sunny lettuce plants, in a field trial in Switzerland. The plants were treated 3 times (at 10-day intervals) with the labelled compound and samples taken 1 h and 14 and 21 days after the third treatment (Table 5).

Levels of total residue and proportions of parent compounds in the residue were generally comparable. Metabolite 8, free + conjugated, was the main identified component of the residue in the 14- and 21-days samples, accounting for approximately 60% and 35% of the total residue for the metalaxyl-M and metalaxyl treatments respectively. Enantiomeric ratio measurements suggested similar degradation rates for both isomers and very little interconversion.

Table 5. Comparison of identified components of the residue in lettuce after treatments with [^{14}C]metalaxyl-M and [^{14}C]metalaxyl (Stingelin 2000, 98JS30).

Component	^{14}C, mg/kg, as parent compound					
	Metalaxyl-M			Metalaxyl		
	1 h	14 days	21 days	1 h	14 days	21 days
Total ^{14}C	8.7	2.4	0.62	7.2	1.8	1.1
Parent	6.8	0.30	0.037	6.2	0.36	0.13
II_3 O-malonyl glycoside of Metabolite 8	0.83	1.0	0.20	0.35	0.27	0.16
II_8 O-glucoside of Metabolite 8	0.20	0.31	0.090	0.097	0.26	0.17
Metabolite 8	0.15	0.083	0.085	0.074	0.10	0.088
Metabolite 1	0.015	0.035	0.015	0.013	0.025	0.023
	Enantiomeric ratio (S/R)					
Parent compound, enantiomeric ratios	0.5/99.5	1.0/99.0	2.3/97.7	51.4/48.6	61.0/39.0	53.8/46.2

Potatoes

In a field trial in Switzerland Bintje plants were treated 5 times with [^{14}C]metalaxyl at a rate of 0.2 kg ai/ha at 10-day intervals and harvested at maturity 5 weeks after the last treatment (Gross 1977, 30/77).

Of the radiolabel applied to the plants 1.5% was present in the plants at harvest (90% in the leaves and 7.4% in the tubers, ^{14}C as metalaxyl 0.02 mg/kg) demonstrating that little of the residue was translocated to the tubers. The ^{14}C in the tubers was polar material; no ^{14}C was detected in the organic extract so no parent was detectable in tubers.

In a second experiment the level of ^{14}C as metalaxyl in tubers was below 0.0001 mg/kg after [^{14}C]metalaxyl was applied to the soil at 4.1 kg ai/ha (residues in soil approximately 0.5 mg/kg), demonstrating that metalaxyl is not taken up by the tubers directly from the soil.

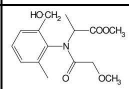
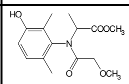
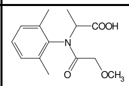
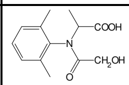
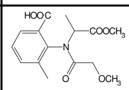
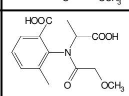
Gross (1979, 39/79) identified the components of the residue in potato leaves, showing percentages of ^{14}C found in the plants, metalaxyl 2.7; Metabolite 9, 43; Metabolite 1, 13.5; Metabolite 8, 5.7; and Metabolite 12, 4.5.

In an experiment in New York, USA, field-growing potato plants were treated 3 times with [^{14}C]metalaxyl at a rate of 1.2 kg ai/ha at 28-day intervals (Marco 1978, ABR-78001). Plant and soil samples were taken just before the second and third treatments and at maturity 4 weeks after the last treatment. Tubers were cut into pieces and immersed in a bucket of water that removed most of the soil but left a fine coating of soil particles on exposed surfaces. The level of ^{14}C in the mature tubers was 0.14 mg/kg as metalaxyl. The level of ^{14}C in the 0-7.5 cm soil layer at the same time was 2.6 mg/kg, most of which was identified as parent metalaxyl with a small amount of Metabolite 1. The composition of the residue in stalks and foliage was similar to that in the trial in Switzerland.

In a further trial two plots of field growing potato plants, variety Green Mountain, in New York, USA were treated 6 times, at about 2-week intervals, with [^{14}C]metalaxyl at rates of 0.43 (1×) and 1.3 (3×) kg ai/ha (Marco 1981, ABR-81037). Samples of tubers, foliage and soil were taken 24 h after the first treatment and at maturity 1 week after the last treatment. Total residues in the tubers were 0.14 mg/kg (peel 0.22 and flesh 0.11 mg/kg) and 0.5 mg/kg (peel 0.9 and flesh 0.4 mg/kg) for the 1× and 3× treatments respectively. The composition of the residue in tubers and foliage from the

3× treatment is summarised in Table 6. Metalaxyl was the major component of the residue in the tubers.

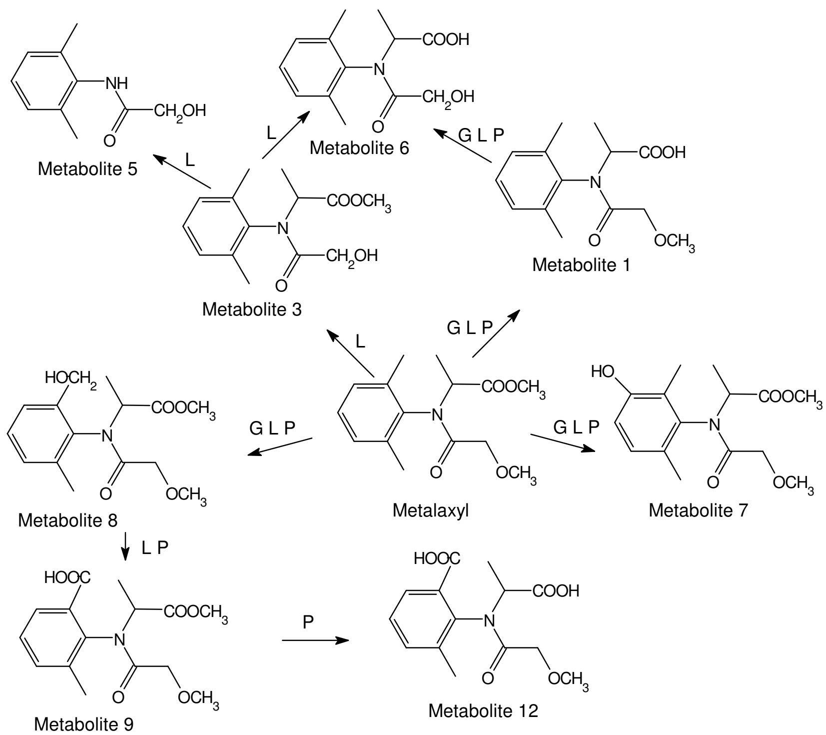
Table 6. Composition of the residue in tubers and foliage of potato plants treated three times with [^{14}C]metalaxyl at 1.3 kg ai/ha (Marco 1981, ABR-81037).

Component		^{14}C in compound as % of total ^{14}C			
		Tubers, ext A [1]	Tubers, ext B [1]	Foliage, early	Foliage, maturity
Total ^{14}C, mg/kg		0.5 mg/kg	0.5 mg/kg	3.7 mg/kg	32 mg/kg
Metalaxyl		51	57	20	2.2
Metabolite 8		5.6	1.6	8.5	20
Metabolite 7			4.0		
Metabolite 1			2.8		
Metabolite 6		1.0	1.4	1.8	1.0
Metabolite 9			0.6		<0.2
Metabolite 12			0.6		
Glucose conjugate of Metabolite 8		5.6	2.5	19	30
Glucose conjugate of Metabolite 7		1.4	0.4	8.9	2.7
Glucose conjugate of Metabolite 6		1.0	0.6	0.8	0.9

[1] A and B are different extraction procedures.

Metabolic pathways in grapes, lettuce and potatoes are shown in Figure 2.

Figure 2. Metabolism of metalaxyl in grapes, lettuce and potatoes. Some metabolites occur as glucose conjugates.



Environmental fate in soil

The Meeting received information on the aerobic degradation of [^{14}C]metalaxyl and [^{14}C]metalaxyl-M in a number of soils.

The rate of degradation is strongly influenced by the properties of the soil, including biological activity, its temperature and % moisture, and concentration of the residue. In direct comparisons of metalaxyl and metalaxyl-M, the latter was more persistent in one case and less persistent in two others. The main degradation product was Metabolite 1 or, in the case of metalaxyl-M, the specific enantiomer of Metabolite 1 (NOA 409045).

The details of one anaerobic and the aerobic studies (including one study with Metabolite 1 in chronological order are summarized below. The maximum concentration of each metabolite as the percentage of the dose plus the day it occurred are given.

Aerobic Ref: Ellgehausen, 08/78, 1978

Test material: [^{14}C-phenyl]metalaxyl		Dose rate: 10 mg/kg dry soil
Duration: 360 days	Temp: 25°C	Moisture: 75% water-holding capacity
Clay loam	pH: 6.5	Organic carbon: 2.2%
Half-life of metalaxyl: approx 40 days		
metalaxyl remaining, day 360 <2%		mineralization, day 360 = 25%

Products	Max (% of dose)	Day
Metabolite 1	54	66
Unextractable ^{14}C	38	360

Anaerobic (30 days aerobic, then flooded) Ref: Ellgehausen, 08/78, 1978

Test material: [^{14}C-phenyl]metalaxyl Dose rate: 10 mg/kg dry soil
Duration: 89 days Temp: 25°C
Clay loam pH: 6.5 Organic carbon: 2.2%
Half-life of metalaxyl: approx 40 days
metalaxyl remaining, day 89 = 33%

Products	Max (% of dose)	Day
Metabolite 1	52	89
Unextractable ^{14}C	9	66

Aerobic Ref: Guth, 19/85, 1985

Test material: [^{14}C-phenyl]metalaxyl Dose rate: 10 mg/kg dry soil
Duration: 252 days Temp: 15°C Moisture: 70% water-holding capacity
Soil: silt loam pH: 8.1 Organic carbon: 1.4%
Half-life of metalaxyl: approx 100 days. Initial (0-56 days) half-life approx 42 days
metalaxyl remaining, day 252 = 12% mineralization, day 252 = 16%

Products	Max (% of dose)	Day
Metabolite 1	34	84
Unextractable ^{14}C	37	252

Aerobic Ref: Guth, 19/85, 1985

Test material: [^{14}C-phenyl]metalaxyl Dose rate: 10 mg/kg dry soil
Duration: 252 days Temp: 15°C Moisture: 70% water-holding capacity
Soil: sand pH: 7.7 Organic carbon: 0.6%
Half-life of metalaxyl: approx 50 days
metalaxyl remaining, day 252 = 1.9% mineralization, day 252 = 20%

Products	Max (% of dose)	Day
Metabolite 1	34	84
Unextractable ^{14}C	44	252

Aerobic Ref: Schanné, 262315, 1991

Test material: [^{14}C-phenyl]metalaxyl Duration 167-246 days
Soil: silt loam pH: 6.1 Organic carbon: 1.4%

(1) Dose rate: 1.3 mg/kg dry soil Temp: 20°C Moisture: 60% water-holding capacity
Metalaxyl half-life (0-70 d): approx 14 days. Day 167, 2.3% metalaxyl remaining. 35% mineralization.
Metabolite 1 reached 22% (max) of dose on day 14.

(2) Dose rate: 1.3 mg/kg dry soil Temp: 20°C Moisture: 30% water-holding capacity
Metalaxyl half-life (0-113 d): approx 26 days. Day 246, 1.1% metalaxyl remaining: 32% mineralization.
Metabolite 1 reached 34% (max) of dose on day 28.

(3) Dose rate: 1.3 mg/kg dry soil Temp: 10°C Moisture: 60% water-holding capacity
Metalaxyl half-life (0-113 d): approx 45 days. Day 422, 1.9% metalaxyl remaining: 23% mineralization.
Metabolite 1 reached 34% (max) of dose on day 49.

(4) Dose rate: 0.13 mg/kg dry soil Temp: 20°C Moisture: 60% water-holding capacity
Metalaxyl half-life (0-70 d): approx 7-15 days. Day 167, 3.9% metalaxyl remaining: 33% mineralization.
Metabolite 1 reached 26% (max) of dose on day 7

Aerobic Ref: Ellgehausen, 35/94, 1994

Test material: [^{14}C-phenyl]metalaxyl and metalaxyl-M Dose rate: 0.5 mg/kg dry soil
Duration: 21 days Temp: 20°C Moisture: 40% water-holding capacity
Soil: silt loam pH: 7.3 Organic carbon: 2.1%
Half-life: metalaxyl approx 13 days; metalaxyl-M approx 6 days
% remaining, day 21: metalaxyl 32%; metalaxyl-M 8%

Aerobic Ref: Ellgehausen, 95EH03 1995

Test material: [^{14}C-phenyl]metalaxyl and metalaxyl-M | Dose rate: 0.5 mg/kg dry soil
Duration: 29days | Temp: 20°C | Moisture: 40% water-holding capacity
Soil: sand | pH: 7.4 | Organic carbon: 1.6%
Half-life: metalaxyl approx 15days; metalaxyl-M approx 8 days
% remaining, day 29 metalaxyl 29%; metalaxyl-M 8.7%

Aerobic Ref: Ellgehausen, 95EH06 1996

Test material: [^{14}C-phenyl]metalaxyl-M | Dose rate: 0.2 mg/kg dry soil
Duration: 120 days | Temp: 20°C | Moisture: 40% water-holding capacity
Soil: sandy loam | pH: 7.3 | Organic carbon: 2.2%
Half-life metalaxyl-M (0-28d): approx 5 days
% remaining, day 28; 1.9% | mineralization, day 120 = 34%

Products	Max (% of dose)	Day
Metabolite 1	26	7
Metabolite 10	6.2	7

Aerobic Ref: Ellgehausen, 95EH06 1996

Test material: [^{14}C-phenyl]metalaxyl-M | Dose rate: 2 mg/kg dry soil
Duration: 120 days | Temp: 20°C | Moisture: 40% water-holding capacity
Soil: sandy loam | pH: 7.3 | Organic carbon: 2.2%
Half-life metalaxyl-M (0-28d): approx 8 days
% remaining, day 56; 0.95%% | mineralization, day 120 = 24%

Products	Max (% of dose)	Day
Metabolite 1	40	14
Metabolite 10	3.7	14

Aerobic Ref: Ellgehausen, 95EH06 1996

Test material: [^{14}C-phenyl]metalaxyl-M | Dose rate: 0.2 mg/kg dry soil
Duration: 120 days | Temp: 20°C | Moisture: 40% water-holding capacity
Soil: sandy loam | pH: 7.3 | Organic carbon: 0.8%
Half-life metalaxyl-M: approx 80-180 days
% remaining, day 120; 56% | mineralization, day 120 = 2.6%

Products	Max (% of dose)	Day
Metabolite 1	23	120
Metabolite 10	1.3	120

Aerobic Ref: Ellgehausen, 95EH06 1996

Test material: [^{14}C-phenyl]metalaxyl | Dose rate: 0.2 mg/kg dry soil
Duration: 120 days | Temp: 20°C | Moisture: 40% water-holding capacity
Soil: sandy loam | pH: 7.3 | Organic carbon: 0.8%
Half-life metalaxyl: approx 70-140 days
% remaining, day 120; 50% | mineralization, day 120 = 1.6%

Products	Max (% of dose)	Day
Metabolite 1	30	120
Metabolite 10	2.4	120

Aerobic Ref: Fathulla HWI 6117-280, 1996

Test material: [^{14}Cphenyl]metalaxyl-M and [^{14}C]-metalaxyl Dose rate: 1.5 mg/kg dry soil
Duration: 160 days Temp: 25°C Moisture: 75% water-holding capacity
Soil: sandy loam pH: 7.0 Organic matter: 0.8%
Half-life: metalaxyl-M: approx 50-80 days; metalaxyl 35-40 days
% remaining day 160: metalaxyl-M 4%. metalaxyl 3% mineralization, day 160: metalaxyl-M 2.5% metalaxyl 2.8%

Metabolites from metalaxyl-M	Max (% of dose)	Day
Metabolite 1	67	160
Unextractable ^{14}C	7	130-160
Metabolites from metalaxyl	Max (% of dose)	Day
Metabolite 1	61	130-160
Unextractable ^{14}C	8	160

Aerobic Ref: Dorn, NOV11, 2001

Test material: [^{14}C-phenyl]metalaxyl Dose rate: 0.3 mg/kg dry soil
Duration: 118 days Temp: 20°C Moisture: 40% water-holding capacity
Soil: sandy loam pH: 5.6 Organic matter: 1.4%
Half-life of metalaxyl: approx 12 days (days 2 to 21), approx 35 days (days 42 to 118)
metalaxyl remaining, day 118 = 3.4% mineralization, day 118 = 16%

Products	Max (% of dose)	Day
Metabolite 1	53	28
Metabolite 10	3.8	21
Metabolite 12	3.0	118
Unextractable ^{14}C	37	118

Aerobic Ref: Dorn and Hein, NOV07, 2003

Test material: [^{14}C-phenyl]metalaxyl-M Dose rate: 0.3 mg/kg dry soil
Duration: 119 days Temp: 20°C Moisture: 40% water-holding capacity
Soil: sandy loam pH: 5.6 Organic matter: 1.4%
Half-life of metalaxyl-M: approx 27 days
metalaxyl-M remaining, day 119= 5.1% mineralization, day 119 = 16%

Products	Max (% of dose)	Day
NOA 409045	38	63
Metabolite 10	4.1	28
Metabolite 12	4.1	119
Unextractable ^{14}C	32	119

Aerobic Ref: Dorn and Hein, NOV06, 2003

Test material: [^{14}C-phenyl]-Metabolite 1 Dose rate: 0.18 mg/kg dry soil
Duration: 118 days Temp: 20°C Moisture: 40% water-holding capacity
Soil: sandy loam pH: 5.6 Organic matter: 1.4%
Half-life of Metabolite 1 : approx 50-60 days
% Metabolite 1 remaining, day 118 = 25% mineralization, day 118 = 22%

Products	Max (% of dose)	Day
Metabolite 12	2.8	84
Unextractable ^{14}C	43	118

Field dissipation

Field dissipation studies on metalaxyl-M were reported from Switzerland, France, Italy and Spain. Also, soils from the previously described metabolism studies on lettuce and potatoes were examined for their content of parent compound and metabolites.

Metalaxyl-M residues disappeared from the soil with half-lives ranging from 5 to 35 days. The residues occurred mostly in the top 10 cm of soil. Metabolite NOA 409045 (enantiomer of Metabolite 1) was produced in all cases and on some occasions its level exceeded that of the parent.

A comparison of enantiomeric ratios in metalaxyl residues in soil suggested that the R-enantiomer (i.e. the metalaxyl-M enantiomer) was degraded more quickly than the S-enantiomer as there was a preponderance of S-enantiomer in the metalaxyl residue and of R-enantiomer in Metabolite 1.

The soil degradation studies suggested that when metalaxyl-M is used as a seed treatment or at the time of sowing, very little or none should remain as a residue in the soil at harvest.

In trials in Switzerland, France and Italy, metalaxyl-M was applied at a rate of approximately 1 kg ai/ha to plots of bare soil and soil cores (0-30 cm) were taken at intervals for 6-7 months for analysis by method REM 7/77, which is not enantio-selective, for residues of metalaxyl-M and NOA 409045 (the corresponding enantiomer of Metabolite 1). The results are shown in Table 7.

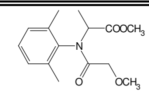
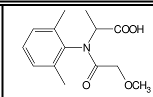
In one trial in Switzerland (Kühne, 2028/99, 2003), residues were detected in the 20-30 cm soil horizon on day 0 suggesting rapid movement (Table 7). Metalaxyl-M in the soil had a half-life of approximately 4-5 days. Residues of NOA 409045 reached a maximum 7 days after treatment and then also decreased rapidly. In the second trial in Switzerland (Kühne (2029/99, 2003), residues were again detected in the 20-30 cm soil horizon on day 0 suggesting rapid movement of a small part of the residue. Metalaxyl-M had a half-life of approximately 10 days, and residues of NOA 409045 reached a maximum 21 days after treatment and then decreased to a low level by day 56.

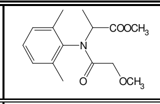
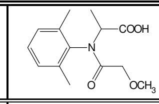
In a trial in France (Kühne, 2036/98, 2000), residues mostly remained in the top 10 cm of the soil (Table 7). Metalaxyl-M had a half-life of approximately 14 days. Residues of the metabolite NOA 409045 reached a maximum 21 days after treatment and then declined to a low level by day 56. In a second trial in France (Kühne, 2030/99, 2003), residues also mostly remained in the top 10 cm. Metalaxyl-M had a half-life of approximately 20-35 days. Residues of the metabolite NOA 409045 reached a maximum 28 days after treatment and always remained below those of metalaxyl-M.

In a trial in Italy (Kühne, 2383/97, 1998), residues were again mostly in the top 10 cm, with more product than parent appearing in the 10-20 cm horizon (Table 7). Metalaxyl-M had a half-life of approximately 10-12 days. Residues of NOA 409045 reached a maximum 14 days after treatment and exceeded those of the parent compound on days 28 and 57. In a second trial in Italy (Kühne, 2027/99, 2003), most of the residue remained in the top 10 cm. Metalaxyl-M had a half-life of about 10-20 days and residues of NOA 409045 reached a maximum 28 days after treatment and exceeded those of the parent on days 28 and 56.

In a trial in Spain with a loamy sand (Kühne, 2057/99, 2003), residues were mainly in the top 10 cm, with little product or parent in the 10-20 cm layer (Table 7). Metalaxyl-M had a half-life of about 10-16 days. Residues of NOA 409045 reached a maximum 21 days after treatment and never exceeded those of the parent compound.

Table 7. Residues of metalaxyl-M and NOA 409045 in soils after direct treatment with metalaxyl-M at 1 kg ai/ha.

Period after treatment	Metalaxyl-M, mg/kg			NOA 409045, mg/kg		
Kühne (2028/99, 2003)						
Switzerland, plot area 180 sq m. Loam soil - core 0-30 cm: pH 7.4, organic carbon 1.6%, sand 52%, silt 38%, clay 9%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.65	0.02	0.037	0.056	<0.01	<0.01
2	0.54	0.027	0.040	0.054	<0.01	0.016
4	0.48	0.011	0.012	0.17	0.013	0.015
7	0.22	<0.01	<0.01	0.33	<0.01	<0.01
14	0.038	<0.01	<0.01	0.087	0.10	0.010
21	0.013	<0.01	<0.01	0.011	0.052	0.013
28	<0.01	<0.01	<0.01	<0.01	0.052	<0.01
56	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
128	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
203	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2029/99, 2003)						
Switzerland, plot area 240 sq m. Silty clay soil - core 0-30 cm: pH 7.2, organic carbon 5.4%, sand 0.4%, silt 56%, clay 43%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.68	0.017	0.039	0.015	<0.01	<0.01
2	0.75	0.017	0.043	0.028	<0.01	0.017
4	0.80	0.01	0.012	0.026	<0.01	0.016
7	0.60	<0.01	<0.01	0.12	<0.01	<0.01
14	0.33	0.011	<0.01	0.18	0.01	0.014
21	0.21	<0.01	<0.01	0.22	0.01	0.014
28	0.097	<0.01	<0.01	0.036	0.01	<0.01
56	0.023	<0.01	<0.01	0.020	<0.01	<0.01
128	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
203	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2036/98, 2000)						
France, plot area 200 sq m. Silty clay loam - core 0-30 cm: pH 7.4, organic carbon 0.99%, sand 9.6%, silt 59%, clay 32%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.79	<0.01	<0.01	0.033	<0.01	<0.01
2	0.89	0.037	<0.01	0.026	<0.01	<0.01
4	0.36	<0.01	<0.01	0.056	<0.01	<0.01
7	0.81	<0.01	<0.01	0.11	<0.01	<0.01
14	0.34	<0.01	<0.01	0.098	<0.01	<0.01
21	0.32	<0.01	<0.01	0.17	<0.01	<0.01
28	0.20	<0.01	<0.01	0.15	<0.01	<0.01
56	0.041	<0.01	<0.01	0.050	0.032	0.012
127	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
198	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2030/99, 2003)						
France, plot area 200 sq m. Loam soil - core 0-30 cm: pH 7.6, organic carbon 0.75%, sand 30%, silt 51%, clay 19%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.51	0.015	0.020	0.010	<0.01	<0.01
2	0.41	<0.01	0.011	<0.01	<0.01	<0.01
4	0.39	0.010	0.028	0.013	<0.01	<0.01
7	0.36	<0.01	0.013	0.015	<0.01	<0.01
14	0.29	<0.01	0.027	0.025	<0.01	<0.01
21	0.36	<0.01	0.012	0.032	<0.01	<0.01
28	0.45	<0.01	<0.01	0.054	<0.01	<0.01

Period after treatment	Metalaxyl-M, mg/kg			NOA 409045, mg/kg		
55	0.091	0.030	<0.01	0.022	0.010	<0.01
125	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
200	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2383/97, 1998)						
Italy, plot area 114 sq m. Sandy loam - core 0-10 cm: pH 7.5, organic carbon 0.57%, sand 58%, silt 28%, clay 14%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.76	0.017	0.01	0.020	<0.01	<0.01
2	0.85	<0.01	<0.01	0.026	<0.01	<0.01
7	0.47	<0.01	<0.01	0.074	<0.01	<0.01
14	0.54	0.024	<0.01	0.20	0.038	<0.01
21	0.17	0.01	<0.01	0.13	0.067	<0.01
28	0.11	<0.01	<0.01	0.18	0.033	<0.01
57	<0.01	<0.01	<0.01	0.014	0.040	0.01
128	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
203	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2027/99, 2003)						
Italy, plot area 500 sq m. Silty clay loam - core 0-30 cm: pH 7.3, organic carbon 1.0%, sand 19%, silt 50%, clay 31%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.61	0.02	0.02	0.039	<0.01	<0.01
2	0.62	<0.01	0.024	0.028	<0.01	<0.01
4	0.58	0.01	0.017	0.042	<0.01	<0.01
7	0.62	<0.01	0.018	0.038	<0.01	<0.01
14	0.65	<0.01	<0.01	0.091	<0.01	<0.01
21	0.28	0.01	0.01	0.25	0.029	0.013
28	0.21	<0.01	<0.01	0.26	0.01	<0.01
56	0.012	<0.01	<0.01	0.025	<0.01	<0.01
128	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
200	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Kühne (2057/99, 2003)						
Spain, plot area 200 sq m. Loamy sand - core 0-30 cm: pH 7.8, organic carbon 0.68%, sand 82%, silt 5.2%, clay 13%						
Days	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm	soil 0-10 cm	soil 10-20 cm	soil 20-30 cm
0	0.522	0.023	0.025	<0.01	<0.01	<0.01
2	0.487	<0.01	0.014	0.01	<0.01	<0.01
4	0.43	<0.01	0.01	0.01	<0.01	<0.01
7	0.409	<0.01	<0.01	0.029	<0.01	<0.01
14	0.279	<0.01	0.01	0.029	<0.01	<0.01
21	0.254	<0.01	<0.01	0.046	<0.01	<0.01
28	0.056	0.017	0.01	0.016	0.026	0.017
56	0.012	<0.01	<0.01	<0.01	<0.01	<0.01
128	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
200	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

Soil (44.7% sand, 31.5% silt, 23.8% clay, 3.1% organic carbon, pH 7.6) from the previously described lettuce metabolism study (Stingelin 2000, 98JS30) was examined for residue composition, including enantiomeric ratios of parent and the major product Metabolite 1 (Table 8). Little of the residue moved below the 10 cm layer. The R-isomer of metalaxyl disappeared more quickly than the S-isomer, leading to a preponderance of R-isomer in Metabolite 1.

Table 8. Comparison of identified components of the residue in soil after treatment of lettuce with [^{14}C]metalaxyl-M and [^{14}C]metalaxyl (Stingelin 2000, 98JS30). Soil samples were taken 1 h and 21 days after the last of 3 treatments at 0.02 kg ai/ha.

Component	Residues in 0-10 cm soil layer, mg/kg. Enantiomeric ratio (S/R).			
	Metalaxyl-M		Metalaxyl	
	1 h	21 d	1 h	21 d
Total ^{14}C, mg/kg	0.34	0.16	0.41	0.14
Parent	0.062 mg/kg (5.5/94.5)	0.058 mg/kg (7.0/93.0)	0.18 mg/kg (83.6/16.4)	0.081 mg/kg (86.0/14.0)
Metabolite 1	0.16 mg/kg (3.2/96.8)	0.073 mg/kg (3.3/96.7)	0.13 mg/kg (28.4/71.6)	0.044 mg/kg (36.0/64.0)

Soil (31.2% sand, 46.4% silt, 22.4% clay, 2.7% organic matter, pH 6.5) from the previously described potato metabolism study in the USA (Marco 1981, ABR-81037) was similarly examined. Some residue, including parent metalaxyl, moved below the 0-7.5 cm layer.

Table 9. Comparison of identified components of the residue in soil after treatment of potatoes with [^{14}C]metalaxyl (Marco 1981, ABR-81037). Soil samples were taken after the first application and at harvest.

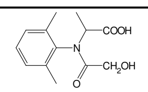
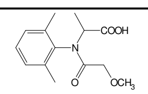
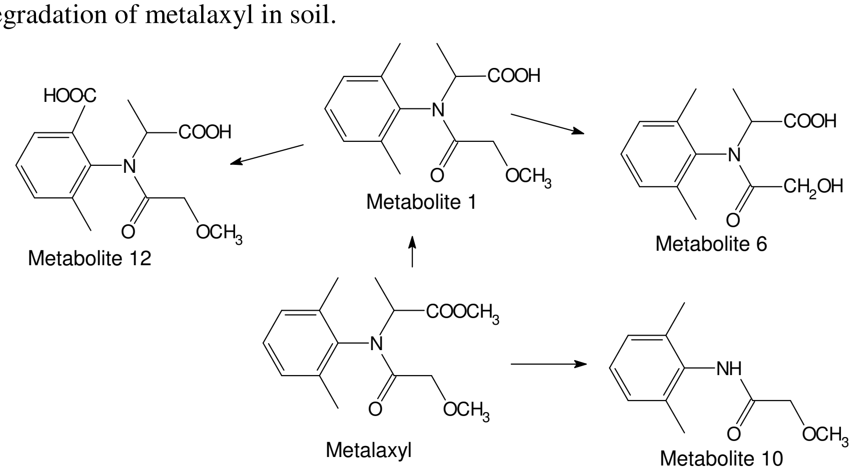
Component		Residues in soil		
		After 1st application	Harvest	
		0-7.5 cm	0-7.5 cm	7.5-15 cm
Total ^{14}C, mg/kg as metalaxyl		0.33	1.7	0.58
Unextractable, % of total ^{14}C		13	37	40
Metalaxyl, % as metalaxyl		87	48	31
Metabolite 6, % as metalaxyl		-	1.6	2.5
Metabolite 1, % as metalaxyl		-	3.3	4.5

Figure 3. Degradation of metalaxyl in soil.



Crop rotation studies

Information on the fate of radiolabelled metalaxyl in confined rotational crops and unlabelled metalaxyl-M in field rotational crops was reported to the Meeting.

The radiolabel studies showed that parent metalaxyl was usually a very minor part of the residue that reached the rotational crop. Identifiable metabolites were also usually very low, but Metabolite 8 was detected as glucose conjugates in spring wheat stalks at 2.3 mg/kg. Metalaxyl-M residues were not detected in the unconfined rotational crops in Switzerland or the UK, but residues of 0.11 mg/kg were present in broccoli and 0.03 mg/kg in lettuce leaves from crops sown 29 days after treatment of the first crop. The short interval was designed to simulate the ploughing in of a failed crop and the sowing of a new one.

The Meeting was provided with residue data from confined crop rotation trials using [^{14}C]metalaxyl (Table 10). In the earlier trials (1977) only the level of radiolabel was measured in the rotational crops. In the later trials (1989) the residue components were identified (Table 11) as well.

The highest levels of ^{14}C in the tissue of a rotational crop occurred in the stalks and hulls of spring wheat (ABR-91084). Parent metalaxyl constituted only 0.1% of the ^{14}C in the stalks, with the glucose conjugates of Metabolite 8 being the major identified component at 32% of the ^{14}C. Metalaxyl constituted 3.35 and 15% of the radiolabel in sugar beet roots and lettuce foliage respectively.

Table 10. Confined rotational crop studies in the USA.

First crop (state), year, ref.	Application		PHI, days[1]	Crop	TSI[2] days	THI[3] days	Sample	^{14}C, mg/kg as metalaxyl	Residues, metalaxyl, mg/kg
	Compound	kg ai/ha							
Potatoes (NC), 1977, ABR-78013	[^{14}C]metalaxyl	0.55 n=6	1 14 14				tuber tuber soil[5]	0.090 0.094 <0.003	na na
ABR-78013, ABR-78077				winter wheat	15	50 257 286 313 313	plant plant plant grain straw	4.0 0.36 0.35 0.11 0.56	na na na na na
ABR-78013, ABR-79005				sugar beet	246	292 333 372 372 413 413	plant plant tops roots tops roots	0.16 0.07 0.06 0.03 0.02 0.02	na na na na na na
ABR-78013, ABR-79004				maize	257	295 326 363 413 413 413	plant plant plant stalks cobs grain	0.05 0.06 0.05 0.06 0.02 0.03	na na na na na na
ABR-78013, ABR-79003				soya beans	270	314 341 363 413 413	plant plant plant leaves/ stems beans	0.40 0.81 0.74 0.59 0.17	na na na na na na

First crop (state), year, ref.	Application: Compound	Application: kg ai/ha	PHI, days[1]	Crop	TSI[2] days	THI[3] days	Sample	^{14}C, mg/kg as metalaxyl	Residues, metalaxyl, mg/kg
ABR-78013, ABR-79002				spring oats	246	277	plant	0.33	na
						294	plant	0.17	na
						323	plant	0.21	na
						343	grain	0.09	na
						343	straw	0.19	na
ABR-78013, ABR-78078				lettuce	246	292	leaves	0.11	na
						313	leaves	0.06	na
						326	leaves	0.05	na
Tobacco, USA (NC), 1989, BIOL-90017 *greenhouse*	[^{14}C-phenyl]metalaxyl	3.4 on soil	226				soil[6]	1.1	0.18
							soil[7]	0.59	0.089
BIOL-90017, ABR-91084				lettuce	232	261	foliage	0.88	0.13
						292	foliage	0.56	na
BIOL-90017, ABR-91084				spring wheat	232	254	stalks	5.1	na
						279	stalks	2.6	na
						323	stalks	7.2	0.007
						323	grain	0.59	na
						323	hulls	7.8	na
BIOL-90017, ABR-91084				soya beans	232	261	stalks	2.4	na
						292	stalks	2.7	na
						432	stalks	3.6	na
						432	pods	1.1	na
						432	beans	0.40	na
BIOL-90017, ABR-91084				sugar beet	232	271	foliage	1.1	na
						307	foliage	0.86	na
						307	roots	0.29	na
						411	foliage	1.1	na
						411	roots	0.28	0.009

na: not analysed.

[1] Pre-harvest interval of first crop.

[2] Interval between last treatment on first crop and sowing of rotation crop.

[3] Interval between last treatment on target crop and sampling or harvest of rotation crop.

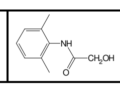
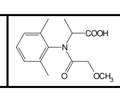
[4] Concentrations appear to be expressed on fresh weight.

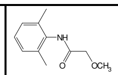
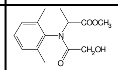
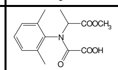
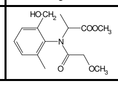
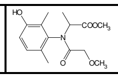
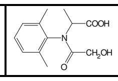
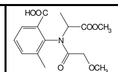
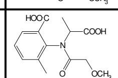
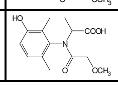
[5] ^{14}c in soil, expressed as metalaxyl 14 days after last treatment: 1.8, 0.31 and 0.05 mg/kg for 0-7.5 cm, 7.5-15 cm and 15-22.5 cm respectively.

[6] 0-7.5 cm.

[7] 15-20 cm.

Table 11. Compounds identified in tissues of rotation crops sown 232 days after soil treatment with [^{14}C-phenyl]metalaxyl at 3.4 kg ai/ha for a first crop of tobacco (McFarland 1992, BIOL-9016, BIOL-90017, ABR-91084).

Compound		Sugar beet roots: metalaxyl, mg/kg	Sugar beet roots: % of ^{14}C residue	Lettuce foliage: metalaxyl, mg/kg	Lettuce foliage: % of ^{14}C residue	Spring wheat stalks: metalaxyl, mg/kg	Spring wheat stalks: % of ^{14}C residue
Metalaxyl		0.009	3.3	0.13	15	0.007	0.1
Metabolite 5						0.086	1.2
Metabolite 5, gluc conj				0.015	1.7	0.31	4.3
Metabolite 1		0.017	6.2			0.086	1.2
Metabolite 1, complex conj		0.053	19				

Compound		Sugar beet roots		Lettuce foliage		Spring wheat stalks	
		metalaxyl, mg/kg	% of ^{14}C residue	metalaxyl, mg/kg	% of ^{14}C residue	metalaxyl, mg/kg	% of ^{14}C residue
Metabolite 1, gluc conjs				0.013	1.5	0.14	2.0
Metabolite 10		Included with Met 1		0.008	0.9	0.014	0.2
Metabolite 3						0.007	0.1
Metabolite 4		0.022	7.9				
Metabolite 8		0.003	1.1	0.004	0.5	0.40	5.6
Metabolite 8, gluc conjs				0.019	2.1	2.3	32
Metabolite 7				Included with Met 10		0.036	0.5
Metabolite 7, gluc conj				0.097	11	0.093	1.3
Metabolite 6		Included with Met 8		0.011	1.3	0.079	1.1
Metabolite 6, gluc conj		0.003	1.0	0.016	1.8	0.11	1.5
Metabolite 9		0.008	3.0	0.008	0.9	0.14	2.0
Metabolite 12		0.006	2.1				
CGA-119857						0.029	0.4
Total		0.28 mg/kg equiv to 100%		0.88 mg/kg equiv to 100%		7.2 mg/kg equiv to 100%	

Simoneaux (1994, ABR-91084 A1) showed that extracts of tissue samples from the 1989 crop rotation study (McFarland 1992, BIOL-9016, BIOL-90017, ABR-91084) were stable stored at approximately -20ºC. HPLC profiles of extracts after 3-4 years were similar to those of extracts analysed within 8 months. The stability of parent and metabolites in homogenates of lettuce foliage, wheat stalks and sugar beet roots stored at approximately -20ºC for 4.5 to 11.5 months was also indicated, since the HPLC profiles of their extracts were shown to be comparable with profiles from earlier samplings.

Table 12. Residues in unlabelled metalaxyl-M rotational crop studies.

First crop, country, year, ref.	Application				PHI[1] days	Rotational crop	TSI[2] days	THI[3] days	Sample	Residue, metalaxyl-M mg/kg
	Compound	Form	No	kg ai/ha						
Potato (Désirée), Switzerland, 1998 208/98	metalaxyl-M	EC	1	0.70	12[4]	barley	29	63 79 93	plant plant plant	<0.02 <0.02 <0.02
						carrots	29	71 82 93	leaves roots roots	<0.02 <0.02 <0.02
						lettuce	30	51 58 65	lettuce leaves leaves	<0.02 <0.02 <0.02

First crop, country, year, ref.	Application				PHI[1] days	Rotational crop	TSI[2] days	THI[3] days	Sample	Residue, metalaxyl-M mg/kg
	Compound	Form	No	kg ai/ha						
						cauliflower	27	51 75 82	plant flower head flower head	<0.02 <0.02 <0.02
Potato (Saxon), UK, 1998 209/98	metalaxyl-M	EC	1	0.70	12[4]	carrots	29	86 99	plant roots	<0.02 <0.02
						lettuce	29	99	plant	<0.02
						cauliflower	29	59 99	plant leaves	<0.02 <0.02
						wheat	29	86 99	plant plant	<0.02 <0.02
Potato (Primura), Italy, 1998 210/98	metalaxyl-M	EC	1	1.0	8[4]	lettuce	29	50 56 71	plant leaves leaves	0.04 0.03 <0.02
						broccoli	29	53 89 98	plant flower head flower head	0.11 <0.02 <0.02
						barley	29	89 124 141	plant plant plant	<0.02 <0.02 <0.02
						carrots	29	89 98 124	plant roots roots	<0.02 <0.02 <0.02

[1] Pre-harvest interval of first crop.

[2] Interval between treatment on first crop and sowing of rotation crop.

[3] Interval between treatment on first crop and sampling or harvest of rotation crop.

[4] In trials 208/98 and 209/98 potatoes were ploughed in 12 days after application simulating crop loss before replanting, and in trial 210/98 8 days after application.

RESIDUE ANALYSIS

Analytical methods

The Meeting received validation data and details of analytical methods used for the determination of residues of metalaxyl in plant material, animal tissues, milk and eggs.

Common moiety methods rely on determination of the 2,6-dimethylaniline moiety of metalaxyl and many of its metabolites, and in particular have been used for animal commodities. Typical LOQs are 0.05 and 0.01 mg/kg for tissues and milk respectively. Metabolite 8, containing the 2-hydroxymethyl-6-methylaniline moiety, is apparently partially converted to 2,6-dimethylaniline and produces low and variable recoveries.

GLC-NPD and HPLC-MSD procedures for metalaxyl or metalaxyl-M after a simple extraction and limited clean-up achieve LOQs of 0.02-0.04 mg/kg for many crop substrates. A modification with the introduction of an HPLC chiral separation before the determination allows analysis for specific enantiomers.

The methods used in the studies are summarized below in chronological order, and recoveries are shown in Table 13.

Method DFG S19 is a multi-residue regulatory method suitable for metalaxyl, and Method REM 181.06 although not multi-residue is enantioselective and suitable as a regulatory method for metalaxyl-M.

Animal tissues, milk and eggs (Balasubramanian 1980, AG-349).

Analyte:	2,6-dimethylaniline	GLC-AFID or GLC-MS	AG-349
LOQ:	milk 0.01 mg/kg; muscle, fat tissues, eggs 0.05 mg/kg; liver and kidney 0.1 mg/kg		
Description	Samples are extracted with acetonitrile or acetonitrile/water, except fat samples, which are extracted with hexane. The extract is cleaned up by solvent partitioning and, after solvent evaporation, is refluxed with phosphoric acid in the presence of cobalt chloride. The solution is made alkaline and the resulting 2,6-dimethylaniline is steam distilled and derivatised with trichloroacetyl chloride for GLC determination		

Poultry tissues (Eudy 1991, AG-576)

Analyte:	2,6-dimethylaniline	capillary GLC-NPD	AG-576
LOQ:	0.05 mg/kg as metalaxyl equivalents		
Description	Samples are extracted with acetonitrile or acetonitrile/water, except fat samples, which are extracted with hexane. The extract is cleaned up by solvent partitioning and, after solvent evaporation, is refluxed with aqueous methanesulfonic acid. The solution is made alkaline and the resulting 2,6-dimethylaniline is steam distilled and cleaned up with a silica clean-up cartridge for capillary GLC-NPD determination		

Plant material (Kühne 1995, REM 181.01)

Analyte:	metalaxyl-M or metalaxyl	GLC-NPD	REM 181.01
LOQ:	0.02 mg/kg		
Description	Homogenized samples are extracted with methanol, the extract is diluted with water and the residue is partitioned into dichloromethane. Clean-up is by normal-phase preparative HPLC. GLC with NPD is used for the final determination. GC-MS is needed for confirmation. Method REM 181.01 is not enantioselective.		

Grapes, grape juice, wine (Adams, 1998, 261B.00)

Analyte:	metalaxyl	GLC-NPD	261B.00
LOQ:	0.02 mg/kg		
Description	Homogenized samples of grapes are extracted with methanol. The extract is diluted with saturated sodium chloride + water and the residue is partitioned into dichloromethane. Juice or wine is diluted with water and extracted with ethyl acetate. Clean-up is on a small chromatography column. The eluate is evaporated and the residue taken up in ethyl acetate for GLC with NP detection. Method 261B.00 is not enantioselective.		

Onions (Kühne 1998, 2338/97)

Analyte:	metalaxyl-M	GLC-MSD	DFG S19
LOQ:	0.02 mg/kg		
Description	Samples are extracted with acetone. Water is added before extraction to maintain a water:acetone ratio of 2:1. The residue is partitioned into ethyl acetate + cyclohexane and cleaned up by gel permeation chromatography on a polystyrene gel. The relevant fraction is collected and analysed by capillary GLC with MSD. Selected ions: m/z 249 for quantification and m/z 206 and 192 for verification. Method DFG S19 is not enantioselective.		

Plant material (Kühne 1999, 517/99)

Analyte:	metalaxyl-M	LC-MS/MS	REM 181.01
LOQ:	0.02 mg/kg		
Description	Samples are thoroughly extracted with methanol. No clean-up is required. A 1 ml aliquot of filtered crude extract is diluted with HPLC water containing 0.2% formic acid ready for LC-MS/MS analysis. The HPLC is a 2-column switching system. For detection the diagnostic masses are the parent ion (M+H) at m/z 280 and a product ion at m/z 220. Method REM 181.01 is not enantioselective.		

Lettuce (Weber and Pelz 2000, NOV-0015)

Analyte:	metalaxyl-M	GLC-MSD	L 00.00-34
LOQ:	0.02 mg/kg		
Description	Method L 00.00-34 is almost the same as DFG S19, the only difference being that the selected ions are m/z 206 for quantification and m/z 192 and 249 for verification. The method is not enantioselective.		

Plant material, orange, potato, rape seed, tomato, wheat (Kühne 2001, REM 181.06)

Analyte:	metalaxyl-M	GLC-MSD	REM 181.06
LOQ:	0.02 mg/kg		
Description	Homogenized samples are extracted with methanol. An aliquot of the extract is evaporated to dryness and the residue taken up in water-methanol. Clean-up is by a C-18 cartridge and preparative HPLC. Chiral separation is on a preparative HPLC system before GLC-MSD determination (m/z 206, 220, 234, 249, 279) of the metalaxyl enantiomers from the relevant HPLC fractions.		

Yokley (1991, ABR-91008) tested the precision of method AG-576 by analysing quadruplicate samples of eight different goat or poultry commodities. The mean relative standard deviation was 0.18. Tissue, egg and milk samples from the metabolism studies were analysed for comparison with the ^{14}C measurements, but interpretation was difficult because the common moiety method would not have included metabolites where parts of the 2,6-dimethylaniline had been oxidised or hydroxylated. The results of these and other recovery experiments are shown in Table 13.

Table 13. Analytical recoveries of metalaxyl or metalaxyl-M in from various spiked substrates. Metalaxyl was used in testing the common moiety method in ABR-81014 and ABR-91008.

Commodity	Analyte	Spike conc, mg/kg	no.	Mean recov., %	Recov., % range	Method	Ref.
Fat	common moiety	0.05-0.5	4	69	50-87	AG-349	ABR-81014
Kidney	common moiety	0.1-0.5	4	56	44-61	AG-349	ABR-81014
Liver	common moiety	0.1-0.2	9	68	44-103	AG-349	ABR-81014
Milk	common moiety	0.01	4	64	52-71	AG-349	ABR-81014
Milk	common moiety	0.02	4	70	56-76	AG-349	ABR-81014
Milk	common moiety	0.105	2	63	60, 65	AG-349	ABR-81014
Muscle	common moiety	0.05-0.1	4	80	64-100	AG-349	ABR-81014
Eggs	common moiety	0.05, 0.3	3	90	87-93	AG-576	ABR-91008
Goat leg muscle	common moiety	0.05, 0.2	3	94	88-104	AG-576	ABR-91008
Goat liver	common moiety	0.05, 2.0	3	73	52-101	AG-576	ABR-91008
Goat milk	common moiety	0.01, 0.05	3	112	88-159	AG-576	ABR-91008
Goat omental fat	common moiety	0.05, 0.07	3	101	83-127	AG-576	ABR-91008
Poultry breast	common moiety	0.05, 0.5	3	93	75-115	AG-576	ABR-91008
Poultry liver	common moiety	0.05, 1.5	3	135	103-194	AG-576	ABR-91008
Poultry skin+fat	common moiety	0.05, 0.5	3	88	82-96	AG-576	ABR-91008
Beef liver	metabolite 1, common moiety	0.05-0.5	5	72	23-97	AG-576	ABR-96108
Eggs	metabolite 1, common moiety	0.05-0.5	5	56	52-59	AG-576	ABR-96108
Poultry muscle	metabolite 1, common moiety	0.05-0.5	5	97	80-116	AG-576	ABR-96108
Poultry skin + fat	metabolite 1, common moiety	0.05-0.5	5	0.2	0-1	AG-576[1]	ABR-96108
Beef liver	metabolite 8, common moiety	0.05-0.5	5	40	11-84	AG-576	ABR-96108
Eggs	metabolite 8, common moiety	0.05-0.5	5	54	21-109	AG-576	ABR-96108
Poultry muscle	metabolite 8, common moiety	0.05-0.5	5	56	45-66	AG-576	ABR-96108
Poultry skin + fat	metabolite 8, common moiety	0.05-0.5	5	8.4	7-11	AG-576[1]	ABR-96108
Grape juice, wine	metalaxyl	0.02-0.1	14	95	78-128	261B.00	261B.00
Grapes	metalaxyl	0.02-5	21	95	72-118	261B.00	261B.00
Lemon fruits, peel, pulp	metalaxyl	0.04-0.8	10	100	79-117	REM 16/76 [2]	517/99
Orange fruits, peel, pulp	metalaxyl	0.04-0.8	26	105	81-132	REM 16/76 [2]	517/99
Sunflower seeds	metalaxyl	0.04-0.4	2	96	92, 100	REM 16/76 [2]	519/99
Oranges	metalaxyl [3]	0.02-0.2	10	85	70-101	REM 181.06	212/00
Potatoes	metalaxyl [3]	0.02-0.2	10	94	76-104	REM 181.06	212/00

Commodity	Analyte	Spike conc, mg/kg	no.	Mean recov., %	Recov., % range	Method	Ref.
Rapeseed	metalaxyl [3]	0.02-0.2	10	90	81-94	REM 181.06	212/00
Tomatoes	metalaxyl [3]	0.02-0.2	10	89	65-105	REM 181.06	212/00
Wheat	metalaxyl [3]	0.02-0.2	10	100	90-109	REM 181.06	212/00
Lettuce	metalaxyl-M	0.02-4	10	98	84-114	L00.00-34	
Orange fruits, peel, pulp	metalaxyl-M	0.02-4	29	93	81-108	REM 181.01	517/99
Cotton seeds, hulls	metalaxyl-M	0.02-0.4	4	92	85-99	REM 181.01	518/99
Grapes	metalaxyl-M	0.02, 0.2	6	104	96-107	REM 181.01	REM 181.01
Potato tubers	metalaxyl-M	0.02, 0.2	6	101	84-112	REM 181.01	REM 181.01
Tomatoes	metalaxyl-M	0.02, 0.2	19	99	90-114	REM 181.01	REM 181.01
Mandarin fruits, peel, pulp	metalaxyl-M	0.02-0.4	24	98	85-111	REM 181.01 [4]	517/99
Orange fruits, peel, pulp	metalaxyl-M	0.02-0.4	12	94	83-106	REM 181.01 [4]	517/99
Cotton seeds, hulls	metalaxyl-M	0.02-0.4	8	99	89-107	REM 181.01 [4]	518/99
Sunflower seeds	metalaxyl-M	0.02-0.2	4	91	83-103	REM 181.01 [4]	519/99
Tomatoes	metalaxyl-M	0.02-0.2	6	93	90-98	REM 181.06	212/00
Oranges	metalaxyl-M [5]	0.02-0.2	10	81	64-107	REM 181.06	NOV/MET/00111
Rapeseed	metalaxyl-M [5]	0.02-0.2	10	82	70-91	REM 181.06	NOV/MET/00111
Tomatoes	metalaxyl-M [5]	0.02-0.2	10	103	86-114	REM 181.06	NOV/MET/00111

[1] The extraction solvent, hexane, does not extract the compound from fat.
[2] REM 16/76 is the same procedure as REM 181.01, but used for metalaxyl.
[3] Samples spiked with metalaxyl, analytical results for the R-isomer (metalaxyl-M). Analytical recoveries for the S-isomer were similar, but are not recorded here.
[4] REM 181.01 with LC-MS-MS finish.
[5] Parallel recoveries with the S-isomer gave similar results, but are not recorded here.

Stability of residues in stored analytical samples

The Meeting received information on the stability of metalaxyl-M residues in crop and animal commodities during storage of analytical samples (Tables 14 and 15).

Metalaxyl-M residues were stable in the substrates and under the conditions and period of storage. There was no evidence of epimerization during freezer storage. A common moiety method was used for the animal commodity samples, so the storage stability refers to the total residue rather than parent metalaxyl-M. The common moiety method is not suitable for Metabolite 8 (low and variable recoveries) so the stability of this metabolite during storage was not demonstrated.

Kühne (201/01, 2003) tested the storage stability of metalaxyl-M residues in wheat, tomatoes, rape seed, oranges and potatoes to represent respectively cereals and other dry crops, commodities with high water content, commodities with high fat content, fruits with high acid content and starch-containing commodities. The homogenised and fortified samples were stored in polyethylene containers or plastic bags at or below -18°C. Periodically, analytical subsamples were analysed by the enantioselective method REM 181.06 (

Table 14). Metalaxyl-M was stable in samples throughout the two years; it was neither degraded nor converted to the S-isomer.

Table 14. Freezer storage stability of metalaxyl-M in spiked oranges, potatoes, rape seed, tomatoes and wheat (Kühne, 201/01, 2003).

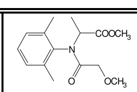
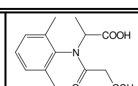
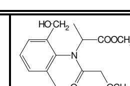
Months stored	Metalaxyl-M		S isomer		Metalaxyl-M		S isomer	
	Procedural recov %	Conc., mg/kg [1]	Procedural recov %	Conc., mg/kg [1]	Procedural recov %	Conc., mg/kg [1]	Procedural recov %	Conc., mg/kg [1]
	Oranges				Potatoes			
0	96 101	0.44	93 87	0.018	105 100	0.43	93 93	0.019
1	95 94	0.45	93 93	0.017	98 95	0.45	107 107	0.020
3	97 99	0.42	93 100	0.017	102 102	0.42	100 100	0.019
6	88 87	0.42	87 93	0.016	90 91	0.39	93 93	0.017
12	90 93	0.49	100 100	0.019	100 98	0.41	113 113	0.019
18	86 93	0.41	67 60	0.016	92 90	0.41	73 67	0.018
24	93 92	0.41	133 133	0.018	94 91	0.40	140 127	0.020
	Rape seed				Tomatoes			
0	105 93	0.43	93 87	0.020	108 103	0.47	93 93	0.019
1	88 93	0.43	93 83	0.018	102 101	0.56	100 100	0.023
3	102 103	0.46	100 100	0.020	100 102	0.43	93 100	0.017
6	87 85	0.41	87 87	0.017	87 96	0.52	93 93	0.021
12	92 93	0.47	93 93	0.018	105 97	0.51	113 113	0.023
18	96 91	0.43	67 67	0.018	91 92	0.46	73 73	0.022
24	86 83	0.38	93 93	0.014	101 95	0.48	133 120	0.019
	Wheat							
0	99 98	0.44	87 87	0.019				
1	96 94	0.45	93 100	0.019				
3	101 99	0.45	93 100	0.019				
6	92 91	0.40	93 93	0.017				
12	98 92	0.36	100 100	0.015				
18	92 88	0.39	73 73	0.018				
24	93 93	0.50	120 120	0.019				

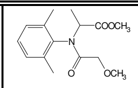
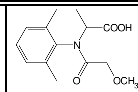
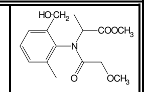
[1] Residue concentrations unadjusted for recoveries are means of triplicate analyses for storage periods of 1-24 months and of quintuplicate analyses at time zero.

Gruenwald (ABR-98053, 1998) tested the freezer storage stability of metalaxyl-M, Metabolite 1 and Metabolite 8 in beef muscle, beef liver, milk and eggs under frozen conditions at approximately -20°C for 2 years (Table 15). Samples were analysed by method AG-576, a common moiety method that determines the total residue of metalaxyl-M and metabolites containing the 2,6-dimethylaniline moiety.

Total residues of metalaxyl-M were stable in the animal commodities in freezer storage for 22 months. Residues of Metabolite 1 were also generally stable, but the results for eggs are questionable because of poor recoveries. The method mostly produced poor recoveries for Metabolite 8, so it is difficult to conclude whether the residues are stable or unstable.

Table 15. Freezer storage stability of metalaxyl-M and metabolites in animal commodities (Gruenwald, ABR-98053, 1998). Samples were analysed by common moiety method AG-576 (concentrations unadjusted for procedural recoveries).

Metalaxyl-M			Metabolite 1			Metabolite 8[2]		
Storage, days	Procedural recov %	Conc., mg/kg[1]	Storage, days	Procedural recov %	Conc., mg/kg[1]	Storage, days	Procedural recov %	Conc., mg/kg [1]
BEEF MUSCLE								
0	89 92 76	1.71	0	80 78 77	1.46	0	56 58 54	2.56
97	85 84	1.55	86	79 75	1.44	86	60 38	2.63

Metalaxyl-M			Metabolite 1			Metabolite 8[2]		
Storage, days	Procedural recov %	Conc., mg/kg[1]	Storage, days	Procedural recov %	Conc., mg/kg[1]	Storage, days	Procedural recov %	Conc., mg/kg [1]
180	80 85	1.68	183	77 80	1.32	183	56 58	2.77
382	90 86	1.67	360	84 85	1.66	360	52 51	2.50
543	87 77	1.74	546	86 79	1.57	567	33 41	2.80
657	81 76	1.44	701	88 83	1.58	701	30 35	1.53
BEEF LIVER								
0	81 92 86	1.84	0	56 57 77	1.43	0	21 20 29	1.36
96	84 85	1.80	89	75 71	1.44	89	28 23	1.18
181	85 86	1.66	187	74 76	1.47	187	20 28	1.27
382	96 96	1.87	365	79 80	1.64	365	24 26	1.23
545	99 85	1.77	550	86	1.72	550	22 22	1.03
656	80	1.44	705	89 86	1.64	705	19 23	0.72
MILK								
0	61 66 72	1.43	0	81 77 70	1.49	0	72 64 64	3.24
98	80 80	1.60	98	118 70	1.84	98	57 61	3.17
181	71 69	1.45	196	56 58	1.18	196	53 52	2.33
377	90 98	1.84	368	66 64	1.28	368	44 44	2.37
541	81 86	1.82	578	87 80	1.59	588	35 26	1.58
653	79 81	1.80	711	81 65	1.48	711	43 36	0.86
EGGS								
0	76 79 85	1.56	0	48 51 50	1.02	0	50 56 53	2.73
94	85 93	1.62	86	50 51	1.05	86	49 44	2.31
185	81 87	1.73	183	50 51	1.06	183	27 23	0.90
386	98 87	1.93	359	52 47	1.01	359	48 50	2.07
548	82 90	1.73	546	48	0.98	546	27 24	0.90
671	77 75	1.56	703	55 55	1.08	703	27 19	0.93

[1] Residues, unadjusted for recoveries, are means of triplicate analyses at time 0 and of duplicate analyses at other intervals.
[2] Yokley (ABR-91008, 1991) reported that Metabolite 8 is converted to 2,6-dimethylaniline during the refluxing step with aqueous methanesulfonic acid in Method AG-576.

USE PATTERN

Metalaxyl-M is registered for use on fruit, nut and vegetable crops for control of various fungal diseases such as Phytophthora and Pythium spp applied to foliage, soil or seed and as a post-harvest fruit treatment. The details are shown in Table 16.

Table 16. Registered uses of metalaxyl-M. Labels were provided for all listed uses.

Crop	Country	Formulation	Method	Timing	Rate kg ai/ha	Spray conc ka ai/hl	No.	PHI, days
Citrus	Israel	EC 480	post-harvest			0.10	1	
Citrus	Italy	EC 480	drench		0.48-0.96 g ai/sq m at plant base		1	30
Cocoa	Côte d'Ivoire	WP 60 (+copper 600)	foliar		0.012	0.02-0.03	4	28
Grapes	Australia	WP 50 (+copper 390)	foliar		0.11	0.011	4	7
Grapes	Greece	WP 25 (+copper 400)	foliar		0.05-0.10		4	15

Crop	Country	Formulation	Method	Timing	Rate kg ai/ha	Spray conc ka ai/hl	No.	PHI, days
Grapes	Greece	WP 40 (+mancozeb 640)	foliar		0.05-0.10		4	15
Grapes	Uruguay	WP 40 (+mancozeb 640)	foliar		0.10	0.05	4	14
Lettuce	Israel	WG 40 (+mancozeb 640)	foliar		0.12		3	14
Lettuce	Germany	WG 50 (+folpet 400)	foliar		0.097		2	21
Lettuce	Spain	WP 40 (+mancozeb 640)	foliar		0.10		3	14
Onion	Ecuador	WP 40 (+mancozeb 640)	foliar		0.10-0.12		3	7
Onion	Germany	WG 50 (+folpet 400)	foliar		0.097		3	21
Onion	Israel	WG 40 (+mancozeb 640)	foliar		0.12		3	7
Onion	Uruguay	WP 40 (+mancozeb 640)	foliar		0.10	0.05	3	7
Peppers	Spain	GR 25	soil		0.75		3	15
Peppers, sweet	Australia	GR 25	soil	pre-transplant	1.0		1	7
Peppers, sweet	Italy	EC 480	soil		0.96		3	15
Peppers, sweet	Italy	GR 25	soil		1.00		3	15
Pome fruit	Italy	EC 480	drench		0.48-0.96 g ai/sq m at plant base		2	28
Pome fruit	Italy	GR 25	soil		approx 2-4 g ai/tree		1	30
Pome fruit	Spain	GR 25	soil		0.5 - 1 g ai/tree		2	15
Potato	Algeria	WP 40 (+mancozeb 640)	foliar		0.10		3	7
Potato	Australia	GR 25	soil	at sowing	0.50		1	
Potato	Australia	WP 40 (+mancozeb 640)	foliar		0.10		3	7
Potato	Austria	WG 40 (+mancozeb 640)	foliar		0.10		4	14
Potato	Chile	WP 40 (+mancozeb 640)	foliar		0.10		3	7
Potato	Ecuador	WP 40 (+mancozeb 640)	foliar		0.10-0.12		3	7
Potato	Greece	WP 25 (+copper 400)	foliar		0.10		3	28
Potato	Greece	WP 40 (+mancozeb 640)	foliar		0.10		3	28
Potato	Israel	WG 40 (+mancozeb 640)	foliar		0.12		3	7
Potato	Morocco	WG 40 (+mancozeb 640)	foliar		0.10		4	15
Potato	Uruguay	WP 40 (+mancozeb 640)	foliar			0.01	3	14
Spinach	Chile	WP 40 (+mancozeb 640)	foliar		0.10		3	10
Spinach	Italy	WP25 (+copper 400)	foliar		0.10		3	20
Spinach	Switzerland	WG 40 (+mancozeb 640)	foliar		0.10		6	14
Sunflower	China	ES 350	seed treatment		0.035-0.105 kg ai/100 kg seed			
Sunflower	Serbia and Montenegro	ES 350	seed treatment		0.105 kg ai/100 kg seed			
Tomato	Algeria	WP 40 (+mancozeb 640)	foliar		0.14		3	3
Tomato	Australia	GR 25	soil	pre-transplant	0.50-1.0		2	
Tomato	Chile	WP 40 (+mancozeb 640)	foliar		0.10		4	3
Tomato	Ecuador	WP 40 (+mancozeb 640)	foliar		0.10-0.12		3	3
Tomato	Greece	WP 25 (+copper 400)	foliar		0.05-0.14		3	3
Tomato	Greece	WP 40 (+mancozeb 640)	foliar		0.06-0.14		3	3
Tomato	Israel	WP 40 (+mancozeb 640)	foliar		0.12		3	5
Tomato	Morocco	WG 40 (+mancozeb 640)	foliar		0.14		4	3
Tomato	Uruguay	WP 40 (+mancozeb 640)	foliar			0.014	4	3

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised field trials with metalaxyl-M on the following crops.

Citrus fruits in Israel.	Table 18
Apples in France, Italy and Spain.	Table 19
Grapes in Australia, Germany, Italy, Portugal and Switzerland.	Table 20
Onions in Brazil, Italy, Spain and Switzerland.	Table 21
Tomatoes in France, Spain and Switzerland.	Table 22
Peppers in Italy and Spain.	Table 23
Lettuce in France, Germany, Italy, The Netherlands, Spain and Switzerland.	Table 24
Spinach in France, Germany and Switzerland.	Table 25
Potatoes in Brazil, Germany, Switzerland and the UK.	Table 26
Sunflowers in France and Spain.	Table 27
Cocoa in Côte d'Ivoire.	Table 28

Trials were well documented with laboratory and field reports. Laboratory reports included method validation, including procedural recoveries with spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Although trials included control plots, control data are only recorded in the Tables where residues exceeded the LOQ. Residues are unadjusted for recoveries.

When residues were undetected they are shown as below the LOQ (e.g. <0.02 mg/kg). Residues, application rates and spray concentrations have generally been rounded to two significant figures or, for residues near the LOQ, to one significant figure. Residues from the trials conducted according to maximum GAP have been used for the estimation of maximum levels. Residue trials at exaggerated application rates have also been included when residues did not exceed the LOQ. Those results included in the evaluation are double underlined.

Conditions of the supervised residue trials are shown in Table 17. In most trials unreplicated plots were used, and details of sprayers used, plot size, sample size and sampling dates are given when reported.

Periods of frozen storage between sampling and analysis were recorded for all trials and were covered by the conditions of the freezer storage stability studies.

In some trials, residues were measured on samples taken just before the last application as well as just after (the "zero day" samples). The samples taken just before the last application are listed in the Tables as having one fewer application and with a PHI equivalent to the interval between the penultimate and last applications. They provide information on carry-over from previous applications.

Table 17. Sprayers, plot and field sample sizes in the supervised trials. Almost all trials were with unreplicated single plots.

Crop	Country	Year	Application method	Plot	Sample
Apple	France	1997	manual application on soil	16-20 m^2	2 kg
Apple	Italy	2000	soil drench in root zone	50-140 m^2	12 fruits
Apple	Spain	1997	manual application on soil	20-50 m^2	2.1-3.4 kg
Cocoa	Côte d'Ivoire	2000, 2001	motorised knapsack	1000 m^2	12-68 kg pods
Grapes	Australia	1998	backpack CO_2, orchard pump sprayer	2-8 panels	0.5-1 kg

Crop	Country	Year	Application method	Plot	Sample
Grapes	Germany	1994, 1997	high-volume plot sprayer	250-300 m^2	1.3-2.8 kg
Grapes	Italy	1994, 1997	knapsack, motor sprayer	36-250 m^2	2.2-2.9 kg
Grapes	Portugal	1997	knapsack	250 m^2	12 bunches
Grapes	Switzerland	1997	knapsack with lance	151 m^2	0.9-1.2 kg
Lettuce	France	1997-2000	knapsack with boom	30-50 m^2	2.1-11 kg
Lettuce	Germany	1997-2000	mobile plot sprayer, boom sprayer	30-80 m^2	0.5-4.5 kg
Lettuce	Italy	1997-1999	knapsack with boom, knapsack sprayer	20-40 m^2	1-2.8 kg
Lettuce	Netherlands	1999	compressed air sprayer	45 m^2	0.34-5.8 kg
Lettuce	Spain	1999	motorised knapsack sprayer	50 m^2	1.5 kg
Lettuce	Switzerland	1999	knapsack with boom, knapsack sprayer	18 m^2	0.9-2.4 kg
Onion	Brazil	1997	CO_2 sprayer	20 m^2	2 kg
Onion	Italy	1997, 1998	knapsack sprayer	20-50 m^2	12 bulbs
Onion	Spain	1997	knapsack sprayer	20-50 m^2	1-3.9 kg
Onion	Switzerland	1997	knapsack with boom	24-31.5 m^2	0.4-2.5 kg
Orange	Spain	1999	motorised knapsack	12 trees	500 kg
Peppers, sweet	Italy	1997	manual on soil	20-86 m^2	1.6-3.5 kg
Peppers, sweet	Spain	1998-2000	manual on soil	25-45 m^2	1.3-3.5 kg
Potatoes	Brazil	1997	CO_2 sprayer	40 m^2	2 kg
Potatoes	Germany	1995, 1996	plot sprayer	30 m^2	2-3 kg
Potatoes	Switzerland	1998	knapsack with boom	22.5-60 m^2	3-4 kg
Potatoes	UK	1994, 1995	precision plot sprayer	40-60 m^2	6-24 tubers
Spinach	France	1997, 1999	knapsack with boom, hand-carried boom with flat fan	75-80 m^2	0.9-1.2 kg
Spinach	Germany	1998	boom sprayer	75 m^2	0.5-0.8 kg
Spinach	Switzerland	1999	knapsack with boom	24-30 m^2	0.6-2.5 kg
Sunflowers	France	1998, 1999	seed treatment	45-90 m^2	1-1.7 kg
Sunflowers	Spain	1998, 1999	seed treatment	53-54 m^2	1.1 kg
Tomatoes	France	1997-2001	knapsack with boom	20-30 m^2	1.9-4.4 kg
Tomatoes	Spain	1997, 1998	motorised knapsack	12-99 m^2	2-3 kg
Tomatoes	Switzerland	1997-2001	knapsack with lance	8-18 m^2	12 fruits

Table 18. Metalaxyl-M residues from oranges in supervised trials in Israel in 1997 with post-harvest uses of metalaxyl-M.

ORANGES[1] (variety)	Application			Commodity[2]	Metalaxyl-M, mg/kg			Ref.
	Form	kg ai/hl	spray l/100 kg fruit		Pulp	Peel	Whole fruit calc from pulp and peel	
(Valencia)	EC 480	0.096	0.22	large fruit (275 g) small fruit (125 g) large fruit (250 g) small fruit (125 g) large fruit (240 g) small fruit (160 g)	<0.02 <0.02 <0.02 <0.02 <0.02 <0.02	3.4 3.2 2.3 3.9 3.7 3.1	1.7 1.7 1.1 1.9 1.8 1.6 mean 1.6	2325/97
(Valencia)	EC 480	0.096	0.22	fruit (310 g) fruit (150 g) fruit (300 g) fruit (275 g) fruit (160 g) fruit (160 g)	<0.02 <0.02 <0.02 <0.02 <0.02 <0.02	2.2 2.4 2.0 2.2 2.8 2.5	1.0 1.2 0.94 1.1 1.4 1.3 mean 1.2	2326/97

ORANGES[1] (variety)	Application			Commodity[2]	Metalaxyl-M, mg/kg			Ref.
	Form	kg ai/hl	spray l/100 kg fruit		Pulp	Peel	Whole fruit calc from pulp and peel	
	EC	0.096	0.22	fruit (275 g)	<0.02	2.6	1.3	2327/97
	480			fruit (160 g)	<0.02	2.6	1.4	
				fruit (260 g)	<0.02	2.4	1.2	
				fruit (160 g)	<0.02	2.7	1.3	
				fruit (250 g)	<0.02	2.0	1.0	
				fruit (170 g)	<0.02	2.6	1.3	
							mean 1.3	

[1] 400 ml formulation was mixed with a commercial wax to produce 200 l of spray solution, sufficient for approximately 90 tonnes of fruit (theoretical concentration of residue 2.1 g/tonne). The solution was sprayed onto the fruit in a single layer on a conveyor belt with rotating brushes to distribute the wax evenly on the fruit surface. Six sequential samples were taken during the 30-min treatment, each consisting of 4, 8 or 12 fruits. The mean weight of a fruit is recorded.

[2] Mean weight of an orange in parentheses.

Table 19. Metalaxyl-M residues in apples from supervised trials in France, Italy and Spain.

APPLES country, year (variety)	Application			PHI days	Residues, mg/kg metalaxyl-M	Ref.
	Form	kg ai/ha	No.			
France, 1997 (Golden)	GR	10.0	1	31	<0.02	124/97
		soil treatment	2	0	<0.02	2139/97
				7	<0.02	
				14	<0.02	
				21	<0.02	
France, 1997 (Golden)	GR	10.0	1	30	<0.02	124/97
		soil treatment	2	0	<0.02	2140/97
				7	<0.02	
				14	<0.02	
				21	<0.02	
Italy, 2000 (Imperatore, Morgenduft)	EC	10 soil treatment	2	31	<0.02	2081/00
Italy, 2000 (Stark Spur Red)	EC	10 soil treatment	2	30	<0.02	2082/00
Spain, 1997 (Golden Delicious)	GR	0.78	1	124	<0.02	2015/97
		soil treatment	2	3	<0.02	
				7	<0.02	
				14	<0.02	
				21	<0.02	
					<0.02	
Spain, 1997 (Golden)	GR	1.9	1	113	<0.02	2016/97
		soil treatment	2	0	<0.02	
				3	<0.02	
				7	<0.02	
				14	<0.02	
				21	<0.02	

Table 20. Metalaxyl-M residues in grapes and grape commodities from supervised trials in Australia, Germany, Italy, Portugal and Switzerland.

GRAPES country, year (variety)	Application					PHI, days	Commodity	Residues, mg/kg metalaxyl-M [1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
Australia (NSW), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.11		900 -1100	5 6	8 0 1 3 7	grapes	0.04 0.44 0.16 0.15 0.06	98/7/1615
Australia (NSW), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.22		900 -1100	5 6	8 0 1 3 7	grapes	0.12 0.98 0.76 0.36 0.20	98/7/1615
Australia (SA), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.11	0.013	853	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.03 0.14 0.05 0.04 <0.02 <0.02 0.02	98/7/1615
Australia (SA), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.22	0.026	853	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.04 0.14 0.12 0.08 0.08 0.02 0.04	98/7/1615
Australia (SA), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.11	0.041	274	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.06 0.10 0.10 0.06 0.03 <0.02 0.03	98/7/1615
Australia (SA), 1998 (Cabernet Sauvignon)	WP includes copper hydroxide	0.22	0.082	274	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.05 0.14 0.08 0.10 0.10 0.03 0.05	98/7/1615
Australia (Vic), 1998 (Chardonnay)	WP includes copper hydroxide	0.11	0.012	947	5 6	7 0 1 3 7	grapes	0.11 0.30 0.18 0.16 0.14	98/7/1615
Australia (Vic), 1998 (Chardonnay)	WP includes copper hydroxide	0.22	0.024	947	5 6	7 0 1 3 7	grapes	0.18 0.41 0.41 0.34 0.28	98/7/1615

GRAPES country, year (variety)	Application Form	kg ai/ha	kg ai/hl	water, l/ha	No.	PHI, days	Commodity	Residues, mg/kg metalaxyl-M [1]	Ref.
Australia (Vic), 1998 (Riesling)	WP includes copper hydroxide	0.22	0.022	1050	5 6	7 0 1 3 7 7 7	grapes grape juice wine	3.5 5.7 1.5 1.4 1.1 0.51 0.72	98/7/1615
Australia (Vic), 1998 (Riesling)	WP includes copper hydroxide	0.11	0.044	253	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.68 2.0 1.2 1.0 0.52 0.19 0.20	98/7/1615
Australia (Vic), 1998 (Riesling)	WP includes copper hydroxide	0.22	0.088	253	5 6	7 0 1 3 7 7 7	grapes grape juice wine	1.4 8.5 1.9 3.7 3.6 0.61 0.57 [2]	98/7/1615
Australia (Vic), 1998 (Riesling) [3]	WP includes copper hydroxide	0.11	0.011	1050	5 6	7 0 1 3 7 7 7	grapes grape juice wine	0.34 1.4 0.71 0.62 0.48 0.28 0.32	98/7/1615
Germany, 1994 (Dornfelder)	WP includes folpet	0.10		400 +600 +800 +800	3 4	18 0 14 29 34 43 34 34	grapes grapes grapes grapes grapes grapes young wine wine	0.27 0.43 0.19 0.14 0.12 0.11 0.08 0.08	gr 5194 gr 52994
Germany, 1994 (Kerner)	WP includes folpet	0.10		400 +600 +800 +800	3 4	18 0 14 29 34 43 34 34	grapes grapes grapes grapes grapes grapes young wine wine	0.30 0.45 0.33 0.24 0.18 0.23 0.11 0.12	gr 5194 gr 52894
Germany, 1997 (Riesling)	WP includes folpet	0.10 +0.10 +0.10 +0.12		400 +600 +800 +800	3 4	35 0 14 28 35 42 35	grapes grapes grapes grapes grapes grapes young wine	0.13 0.32 0.19 0.11 0.08 0.04 0.06	gr 50597

GRAPES country, year (variety)	Application Form	kg ai/ha	kg ai/hl	water, l/ha	No.	PHI, days	Commodity	Residues, mg/kg metalaxyl-M [1]	Ref.
Germany, 1997 (Riesling)	metalaxyl WP includes folpet	0.20 +0.20 +0.20 +0.24		400 +600 +800 +800	3 4	35 28 42 35	grapes grapes grapes young wine	0.41 metalaxyl 0.31 metalaxyl 0.13 metalaxyl 0.13 metalaxyl	gr 50597
Italy, 1994 (Moscato)	WP includes copper	0.10	0.02	500	4	0 7 14 21 28 44 85 85 85	grapes grapes grapes grapes grapes grapes grapes new wine wine	0.29 c 0.07 0.17 0.15 0.19 c 0.31 0.13 0.08 0.04 c 0.10 0.03 c 0.05 0.04 c 0.03	2124/94
Italy, 1994 (Schiava)	WP includes folpet	0.10	0.0094	1060	3	0 7 14 21 28 45 78 78 78	grapes grapes grapes grapes grapes grapes grapes new wine wine	0.10 0.07 0.04 0.03 0.02 0.02 <0.02 <0.02 <0.02	2123/94
Italy, 1994 (Tocai)	WP includes copper	0.10	0.09	1100	4	0 7 14 21 28 46 74 74 74	grapes grapes grapes grapes grapes grapes grapes new wine wine	0.71 c 0.16 0.26 0.21 0.19 0.17 c 0.10 0.07 0.04 c 0.02 <0.02 <0.02	2125/94
Italy, 1994 (Trebbiano Romagnolo)	WP includes folpet	0.10	0.01	1000	3	0 7 14 21 28 45 88 88 88	grapes grapes grapes grapes grapes grapes grapes new wine wine	1.2 c0.06 0.60 0.55 0.40 0.44 c 0.03 0.26 0.17 c 0.03 0.05 0.03	2122/94
Italy, 1997 (Merlot)	WP includes mancozeb	0.10	0.01	1000	3 4	12 0 14 21 28 42 42 42	grapes grapes grapes grapes grapes grapes young wine wine	0.04 0.10 0.06 0.03 0.03 0.02 <0.02 <0.02	2035/97

GRAPES country, year (variety)	Application Form	kg ai/ha	kg ai/hl	water, l/ha	No.	PHI, days	Commodity	Residues, mg/kg metalaxyl-M [1]	Ref.
Portugal, 1997 (Periquita)	WP includes mancozeb	0.10	0.01	1000	3 4	14 0 14 21 28 42 42 42	grapes grapes grapes grapes grapes grapes young wine wine	0.09 0.16 0.18 0.10 0.10 0.07 0.18 0.08	2030/97
Switzerland, 1997 (Pinot Noir)	WP includes folpet	0.10	0.083	1200	3 4	14 0 14 21 28 42 42 42	grapes grapes grapes grapes grapes grapes young wine wine	0.41 0.96 0.43 0.49 0.52 0.24 0.24 0.27	2332/97

[1] c: control sample from untreated plot

[2] Fermented only until 25 g/l residual sugar.

[3] Suffered drought damage: berries small and matured 1 month earlier than expected, vines defoliated with bird damage to the berries, which were left on the vines too long. The trial was described as atypical and should be disregarded.

Table 21. Metalaxyl-M residues in onion bulbs from supervised trials in Brazil, Italy, Spain and Switzerland.

Country, year (variety)	Application Form	kg ai/ha	kg ai/hl	water, l/ha	No.	PHI, days	Residues, mg/kg metalaxyl-M	Ref.
Brazil (SP), 1997 (Cerrana)	WP includes mancozeb	0.10			4	0 3 7 10 14	<0.02 <0.02 <0.02 <0.02 <0.02	FR 033/96
Brazil (SP), 1997 (Cerrana)	WP includes mancozeb	0.20			4	0 3 7 10 14	<0.02 <0.02 <0.02 <0.02 <0.02	FR 034/96
Brazil (SP), 1997 (Granex 33)	WP includes chlorothalonil	0.10			4	7 14	0.02 <0.02	RFFA 09/97
Brazil (SP), 1997 (Granex 33)	WP includes chlorothalonil	0.20			4	7 14	0.03 0.03	RFFA 09/97
Brazil (SP), 1997 (Serrana)	WP includes chlorothalonil	0.10			4	0 3 7 10 14	<0.02 <0.02 <0.02 <0.02 <0.02	RFZO 09/97
Brazil (SP), 1997 (Serrana)	WP includes chlorothalonil	0.20			4	0	<0.02	RFZO 09/97

Country, year (variety)	Application					PHI, days	Residues, mg/kg metalaxyl-M	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.			
Italy, 1997 (Density)	WP includes copper oxychloride	0.15	0.025	600	2 3	11 0 7 14 21	<0.02 0.02 <0.02 <0.02 <0.02	2032/97
Italy, 1997 (Density)	SC includes chlorothalonil	0.10	0.017	600	2 3	11 0 7 14 21	<0.02 <0.02 <0.02 <0.02 <0.02	2033/97
Italy, 1998 (Musona)	WP includes copper oxychloride	0.15	0.021	700	3	0 3 7 21	0.05 <0.02 <0.02 <0.02	2025/98
Italy, 1998 (Musona)	SC includes chlorothalonil	0.10	0.014	700	3	0 3 7 21	0.03 <0.02 <0.02 <0.02	2025/98
Spain, 1997 (Liria)	WP includes mancozeb	0.15	0.030	500	2 3	7 0 4 7 14 21	<0.02 0.06 0.02 <0.02 <0.02 <0.02	2013/97
Spain, 1997 (Llopis)	WP includes mancozeb	0.15	0.038	400	2 3	8 0 3 7 14 21	<0.02 0.07 <0.02 0.02 <0.02 <0.02	2014/97
Switzerland, 1997 (Burgos F1)	WP includes mancozeb	0.15	0.019	800	2 3	9 0 7 14 21	<0.02 0.04 <0.02 <0.02 <0.02	2338/97
Switzerland, 1997 (Burgos F1)	SC includes chlorothalonil	0.10	0.013	800	2 3	9 0 7 14 21	<0.02 0.03 <0.02 <0.02 <0.02	2339/97
Switzerland, 1997 (Copra F1)	WP includes mancozeb	0.15	0.019	800	2 3	8 0 7 14 21	<0.02 <0.02 <0.02 <0.02 <0.02	2340/97
Switzerland, 1997 (Copra F1)	SC includes chlorothalonil	0.10	0.013	800	2 3	8 0 7 14 21	<0.02 <0.02 <0.02 <0.02 <0.02	2341/97

Table 22. Metalaxyl-M residues in tomatoes from supervised trials in France, Spain and Switzerland.

Country, year (variety)	Application					PHI	Residues, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.	days		
France, 1997 (4369) *greenhouse*	WP includes mancozeb	0.15	0.038	400	4	3	0.08	2349/97
France, 1997 (Kalimba) *greenhouse*	WP includes mancozeb	0.15	0.038	400	4	3	<0.02	2350/97
France, 1997 (Le Trepier) *greenhouse*	WP includes mancozeb	0.15	0.037	400	3 4	7 0 3 7 14 22	<0.02 <0.02 <0.02 <0.02 <0.02 <0.02 c 0.02[1]	2347/97
France, 1997 (Roncoula) *greenhouse*	WP includes mancozeb	0.15	0.038	400	3 4	7 0 3 7 14 21	<0.02 0.05 0.02 <0.02 <0.02 <0.02	2348/97
France, 2001 (Brenda) *greenhouse*	WG includes mancozeb	0.15	0.015	1000	4	3	0.03	0111301
France, 2001 (Granitio) *greenhouse*	WG includes mancozeb	0.15	0.015	1000	4	0 1 3 7 10	0.05 0.02 0.04 <0.02 <0.02	0111401
Spain, 1997 (Genaro)	WP includes mancozeb	0.15	0.0088	1700	3 4	11 0 7 14 21 28	<0.02 0.06 <0.02 <0.02 <0.02 <0.02	2011/97
Spain, 1997 (Royestra)	WP includes mancozeb	0.15	0.015	1000	3 4	12 0 7 14 21 28	<0.02 0.02 <0.02 <0.02 <0.02 <0.02	2012/97
Spain, 1998 (Daniella) *greenhouse*	WP includes mancozeb	0.15	0.015	1000	4	0 3 7 14 20	0.23 0.18 0.07 0.06 0.03	2048/98

Country, year (variety)	Application					PHI	Residues, mg/kg[1]	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.	days		
Spain, 1998 (Genaro) *greenhouse*	WP includes mancozeb	0.15	0.012	1300	4	0 3 7 14 21	0.17 0.05 <0.02 <0.02 <0.02	2049/98
Switzerland, 1997 (Cristal)	WP includes mancozeb	0.15	0.0075	2000	4	3	0.02	2334/97
Switzerland, 1997 (Cristal)	WP includes copper	0.15	0.0075	2000	4	3	<0.02	2335/97
Switzerland, 1997 (Selhardy)	WP includes copper	0.15	0.0075	2000	3 4	7 0 3 7 14	<0.02 0.04 <0.02 <0.02 <0.02	2337/97
Switzerland, 1997 (Selhardy)	WP includes mancozeb	0.15	0.0075	2000	3 4	7 0 3 7 14	<0.02 0.03 <0.02 <0.02 <0.02	2336/97
Switzerland, 1998 (Paola) *greenhouse*	WG includes mancozeb	0.15	0.0075	2000	4	0 3 7 14 21	0.18 0.09 0.06 0.03 <0.02	2071/98
Switzerland, 1998 (Paola) *greenhouse*	WG includes mancozeb	0.15	0.0075	2000	4	0 3 7 14 21	0.07 0.04 0.02 <0.02 <0.02	2072/98
Switzerland, 2001 (Paola) *greenhouse*	WG includes mancozeb	0.15	0.0083	1800	4	3	0.12	2011/01
Switzerland, 2001 (Paola) *greenhouse*	WG includes mancozeb	0.15	0.015	1000	4	0 1 3	0.12 0.08 0.05	2012/01

[1] c: sample from control plot.

Table 23. Metalaxyl-M residues in sweet peppers from supervised trials in Italy and Spain with a granular formulation used in soil treatments.

Country, year (variety)	Application			PHI	Residues, mg/kg	Ref.
	Form	kg ai/ha	No.	days		
Italy, 1997 (Benrico) *greenhouse*	GR	1.0 soil treatment	3	10	<0.02	121/97 2130/97

Country, year (variety)	Application			PHI	Residues, mg/kg	Ref.
	Form	kg ai/ha	No.	days		
Italy, 1997 (Campor) *greenhouse*	GR	1.0 soil treatment	2 3	20 0 5 10 20	<0.02 0.02 <0.02 <0.02 <0.02	121/97 2129/97
Italy, 1997 (Friariello)	GR	1.0 soil treatment	3	30	<0.02	2045/97
Italy, 1997 (Magister)	GR	1.0 soil treatment	2 3	20 0 5 9 20	<0.02 <0.02 <0.02 0.02 0.02	121/97 2127/97
Italy, 1997 (Osir)	GR	1.0 soil treatment	3	9	<0.02	121/97 2128/97
Italy, 1997 (Peto)	GR	1.0 soil treatment	2 3	39 0 5 10 20	<0.02 <0.02 <0.02 <0.02 <0.02	2044/97
Spain, 1997 (Diamante) *greenhouse*	GR	1.0 soil treatment	2 3	40 0 5 10 15 20	0.04 0.03 0.02 0.02 0.02 0.02	2008/97
Spain, 1997 (Italico) *greenhouse*	GR	1.0 soil treatment	2 3	46 0 5 10 15 20	0.08 0.07 0.25 0.40 0.35 0.36	2007/97
Spain, 1998 (Estar) *greenhouse*	GR	1.0 soil treatment	3	0 5 10 15 20	0.12 0.08 0.09 0.08 0.03	2046/98
Spain, 1998 (Italico) *greenhouse*	GR	1.0 soil treatment	3	10	0.24	2047/98
Spain, 2000 (Cadia) *greenhouse*	GR	1.0 soil treatment	3	0 3 7 15 21	0.06 0.05 0.07 0.10 0.07	2024/00
Spain, 2000 (Roxi) *greenhouse*	GR	1.0 soil treatment	3	0 3 7 15 21	0.04 0.05 0.06 0.03 0.02	2023/00

Table 24. Metalaxyl-M residues in lettuce from supervised trials in France, Germany, Italy, The Netherlands, Spain and Switzerland.

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
France, 1997 (head lettuce, Christine)	WP includes mancozeb	0.10	0.025	400	3	14	heads	0.03	2262/97
France, 1997 (head lettuce, Flandria)	WP includes mancozeb	0.10[1]	0.030	330	3	14	heads	<0.02	2263/97
France, 1997 (head lettuce, Floreal)	WP includes mancozeb	0.10	0.025	400	3	14	heads	<0.02	2260/97
France, 1997 (head lettuce, Newton)	WP includes mancozeb	0.10	0.025	400	3	10 0 7 15 21	heads heads heads heads heads	0.03 1.5 0.06 0.02 0.03	2261/97
France, 1999 (head lettuce, Angie) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.035	400	3	0 3 7 10 14	heads heads heads heads heads	3.0 1.6 1.0 0.64 0.43	2169/99
France, 1999 (head lettuce, Angie) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.035	400	3	0 3 7 10 14	heads heads heads heads heads	4.5 2.6 1.5 1.1 0.43	2170/99
France, 1999 (head lettuce, Augié) *greenhouse*	WG includes acibenzolar-S-methyl	0.14 +0.14 +0.13	0.035	400 +410 +370	3	11	heads	0.86	2000/00
France, 1999 (head lettuce, Nalis) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.035	400	4	0 3 7 10 14	heads heads heads heads heads	8.1 4.0 1.8 1.0 0.50	2171/99
France, 1999 (head lettuce, Norma) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.035	400	3	0 3 7 10 14	heads heads heads heads heads	7.3 3.0 1.8 1.7 1.1	2172/99
France, 2000 (head lettuce, Manita) *greenhouse*	WG includes acibenzolar-S-methyl	0.14 +0.15 +0.16	0.035	410 +430 +440	3	10	heads	0.17	2001/00
France, 2000 (head lettuce, Perlane) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.028	500	3	10	heads	0.15	2002/00

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
Germany, 1997 (head lettuce, Rapsodi)	WP includes folpet	0.10	0.017	600	2 3	8 0 6 14 21	heads heads heads heads heads	0.07 3.6 0.56 0.04 0.02	2255/97
Germany, 1997 (head lettuce, Rapsodi) *greenhouse*	WP includes folpet	0.10	0.017	600	2 3	7 0 7 14 21	heads heads heads heads heads	0.40 10 0.72 0.07 <0.02	2254/97
Germany, 1997 (head lettuce, Rosali)	WP includes folpet	0.10	0.017	600	2 3	12 0 7 14 21	heads heads heads heads heads	<0.02 3.5 0.04 0.03 <0.02	2252/97
Germany, 1997 (head lettuce, Rosali)	WP includes folpet	0.10	0.017	600	2 3	9 0 7 14 21	heads heads heads heads heads	<0.02 2.6 0.04 0.03 0.03	2253/97
Germany, 1998 (head lettuce, Macarena)	WP includes folpet	0.10		610	2	0 7 10 14 21	plants plants heads heads heads	1.6 0.06 <0.02 <0.02 <0.02	gr 22998
Germany, 1998 (head lettuce, Troubadur) *greenhouse*	WP includes folpet	0.10		630	2	0 7 10 14 21	whole plant whole plant heads heads heads	3.4 1.7 0.94 0.59 0.41	gr 23998
Germany, 2000 (head lettuce, Fiorella)	WP includes folpet	0.10		610	3	0 14	plants heads	1.1 0.02	gr 52700
Germany, 2000 (head lettuce, Nadine)	WP includes folpet	0.10		610	3	0 14	plants heads	2.1 0.02	gr 51900
Germany, 2000 (head lettuce, Nadine)	WP includes folpet	0.10		630	3	0 7 10 13 20	plants plants heads heads heads	1.2 0.09 0.02 <0.02 <0.02	gr 50800
Germany, 2000 (lettuce, Pullmann)	WP includes folpet	0.10		600	3	0 7 10 14 20	plants plants plants heads heads	2.6 0.03 0.02 <0.02 <0.02	gr 49500

Country, year (variety)	Application Form	kg ai/ha	kg ai/hl	water, l/ha	No.	PHI, days	Sample	Residues, mg/kg	Ref.
Italy, 1997 (head lettuce, Justine)	WP includes copper oxychloride	0.10	0.016	600	2 3	10 0 7 14 21	heads heads heads heads heads	<0.02 2.1 0.02 <0.02 <0.02	2062/97
Italy, 1998 (head lettuce, Martina)	WG includes acibenzolar-S-methyl	0.14	0.023	600	3	0 3 7 10 14	heads heads heads heads heads	2.4 0.31 0.04 0.02 0.02	2028/98
Italy, 1999 (head lettuce, Martina)	WG includes acibenzolar-S-methyl	0.14	0.014	1000	3	0 3 7 10 14	heads heads heads heads heads	1.8 <0.02 0.02 0.02 <0.02	2035/99
Italy, 1999 (head lettuce, Musette ez)	WG includes acibenzolar-S-methyl	0.14	0.014	1000	3	0 3 7 10 14	heads heads heads heads heads	2.3 1.7 0.26 0.07 0.02	2036/99
Netherlands, 1999 (head lettuce, Ardeola)	WP includes mancozeb	0.11 + 0.12	0.012	900 + 1040	2	0 7 14 21	heads heads heads heads	0.84 <0.02 <0.02 <0.02	2131/99
Netherlands, 1999 (head lettuce, Einstein)	WP includes mancozeb	0.12 + 0.13	0.012	970 + 1060	2	0 7 14 21	heads heads heads heads	1.2 <0.02 <0.02 <0.02	2132/99
Spain, 1999 (head lettuce, Iceberg)	WG includes acibenzolar-S-methyl	0.14	0.020	700	3	0 3 7 10 14	heads heads heads heads heads	0.11 0.07 0.02 <0.02 <0.02	2009/99[2]
Spain, 1999 (head lettuce, Iceberg)	WG includes acibenzolar-S-methyl	0.14	0.020	700	3	0 3 7 10 14	heads heads heads heads heads	0.10 0.07 0.02 <0.02 <0.02	2010/99[2]
Switzerland, 1999 (head lettuce, Levis) *greenhouse*	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	0 3 7 11 14	heads heads heads heads heads	5.2 3.7 1.8 0.96 0.68	2052/99
Switzerland, 1999 (head lettuce, Reskia NL)	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	0 3 7 10 14	heads heads heads heads heads	1.0 0.13 0.04 0.02 <0.02	2050/99

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
Switzerland, 1999 (head lettuce, Reskia NL)	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	0 3 7 10 14	heads heads heads heads heads	1.6 0.07 <0.02 <0.02 <0.02	2051/99

[1] Outdoor foliar under protective covering.

[2] Trials 2009/99 and 2010/99 appear to be replicate plots with same treatment rather than separate trials.

Table 25. Metalaxyl-M residues in spinach resulting from supervised trials in France, Germany and Switzerland.

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
France (Beaucaire), 1997 (Kerdion)	WP includes copper	0.10	0.029	360	1 2	10 0 5 10 21	leaf leaf leaf leaf leaf	0.03 3.5 0.09 0.02 <0.02	125/97 2142/97
France (Beaucaire), 1997 (Kerdion)	ES				ST	105	leaf	<0.02	125/97 2141/97
France (Beaucaire), 1997 (Kerdion)	ES + WP includes copper	0.10	0.029	360	ST 1 2	10 0 5 10 21	leaf leaf leaf leaf leaf	0.05 2.8 0.07 0.02 <0.02	125/97 2143/97
France (Senas), 1997 (Kerdion)	WP includes copper	0.10	0.029	360	1 2	10 0 5 10 20	leaf leaf leaf leaf leaf	0.02 2.7 0.18 0.05 0.03	125/97 2148/97
France (Senas), 1997 (Kerdion)	ES				ST	108	leaf	<0.02	125/97 2147/97
France (Senas), 1997 (Kerdion)	ES + WP includes copper	0.10	0.029	360	ST 1 2	10 0 5 10 20	leaf leaf leaf leaf leaf	0.03 3.3 0.19 0.04 0.03	125/97 2149/97
France (Tarascon), 1997 (Kerdion)	WP includes copper	0.10	0.029	360	1 2	10 0 5 10 21	leaf leaf leaf leaf leaf	0.03 2.1 0.07 0.02 <0.02	125/97 2145/97

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
France (Tarascon), 1997 (Kerdion)	WP includes copper	0.10	0.029	360	1 2	10 0 5 10 20	leaf leaf leaf leaf leaf	0.03 3.3 0.10 0.04 0.02	125/97 2151/97
France (Tarascon), 1997 (Kerdion)	ES				ST	105	leaf	<0.02	125/97 2144/97
France (Tarascon), 1997 (Kerdion)	ES				ST	103	leaf	<0.02	125/97 2150/97
France (Tarascon), 1997 (Kerdion)	ES + WP includes copper	0.10	0.029	360	ST 1 2	10 0 5 10 21	leaf leaf leaf leaf leaf	0.03 2.2 0.05 0.02 <0.02	125/97 2146/97
France (Tarascon), 1997 (Kerdion)	ES + WP includes copper	0.10	0.029	360	ST 1 2	10 0 5 10 20	leaf leaf leaf leaf leaf	0.03 2.9 0.07 0.03 <0.02	125/97 2152/97
France, 1999 (Santana)	WG includes acibenzolar-S-methyl	0.10[1]	0.025	380	3	10	leaf	<0.02	2062/99
France, 1999 (Santana)	WG includes acibenzolar-S-methyl	0.14[1]	0.035	390	3	10	leaf	<0.02	2062/99
Germany, 1998 (Bolero)	WP includes folpet	0.10		580	2	0 7 10 14 21	leaf leaf leaf leaf leaf	5.1 <0.02 <0.02 <0.02 <0.02	gr 24998
Germany, 1998 (Laska)	WP includes folpet	0.10		600	2	0 7 10 14 21	leaf leaf leaf leaf leaf	4.3 0.13 0.02 <0.02 <0.02	gr 25998
Switzerland, 1999 (Chica F1)	WG includes acibenzolar-S-methyl	0.10	0.013	800	3	0 3 7 10 14	leaves leaves leaves leaves leaves	2.6 <0.02 <0.02 <0.02 <0.02	2045/99
Switzerland, 1999 (Chica F1)	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	0 3 7 10 14	leaves leaves leaves leaves leaves	5.2 0.02 <0.02 <0.02 <0.02	2045/99

Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
Switzerland, 1999 (Monnopa)	WG includes acibenzolar-S-methyl	0.10	0.013	800	3	10	whole plant	<0.02	2046/99
Switzerland, 1999 (Monnopa)	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	10	whole plant	<0.02	2046/99
Switzerland, 1999 (Monnopa)	WG includes acibenzolar-S-methyl	0.10	0.013	800	3	0 3 7 10 14	whole plant whole plant whole plant whole plant whole plant	2.0 <0.02 <0.02 <0.02 <0.02	2044/99
Switzerland, 1999 (Monnopa)	WG includes acibenzolar-S-methyl	0.14	0.018	800	3	0 3 7 10 14	whole plant whole plant whole plant whole plant whole plant	3.0 0.02 <0.02 <0.02 <0.02	2044/99

ST: seed treatment 0.088 kg ai/100 kg seed.

[1] seeds treated by the seller with metalaxyl before sowing.

Table 26. Metalaxyl-M residues in potato tubers from supervised trials in Brazil, Germany, Switzerland and the UK.

Country, year (variety)	Application					PHI, days	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.			
Brazil (SP), 1997 (Achat)	WP includes mancozeb	0.10			4	7 14	<0.02 <0.02	FR 017/96
Brazil (SP), 1997 (Achat)	WP includes mancozeb	0.20			4	7 14	<0.02 <0.02	FR 018/96
Brazil (SP), 1997 (Achat)	WP includes chlorothalonil	0.10			4	0 7	<0.02 <0.02	RFFA 06/97
Brazil (SP), 1997 (Achat)	WP includes chlorothalonil	0.20			4	7	<0.02	RFFA 06/97
Brazil (SP), 1997 (Monalisa)	WP includes chlorothalonil	0.20			4	7	<0.02	RFLU 06/97
Brazil (SP), 1997 (Monalisa)	WP includes chlorothalonil	0.10			4	0 3 7 14 21	<0.02 <0.02 <0.02 <0.02 <0.02	RFLU 06/97
Germany, 1995 (Agria)	WP includes mancozeb	0.10		400	4	0 14	<0.02 <0.02	gr 4795 gr 41395
Germany, 1995 (Agria)	EC includes fluazinam	0.10		400	5	0 7	<0.02 <0.02	gr 4895 gr 41495

Country, year (variety)	Application					PHI, days	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.			
Germany, 1995 (Linda)	WP includes mancozeb	0.10		400	4	0 15	<0.02 <0.02	gr 4795 gr 31395
Germany, 1995 (Linda)	EC includes fluazinam	0.10		400	5	0 7	<0.02 <0.02	gr 4895 gr 31495
Germany, 1996 (Hansa)	EC includes fluazinam	0.10		400	5	0 7	<0.02 <0.02	gr 46696
Germany, 1996 (Panda)	EC includes fluazinam	0.10		400	5	0 7	<0.02 <0.02	gr 45396
Switzerland, 1998 (Agria)	WP includes mancozeb	0.075	0.015	500	5	0 1 3 7 14	<0.02 <0.02 <0.02 <0.02 <0.02	2068/98
Switzerland, 1998 (Désirée)	WP includes mancozeb	0.075	0.015	500	5	7	<0.02	2070/98
Switzerland, 1998 (Sirtema)	WP includes mancozeb	0.075	0.015	500	5	0 1 3 7 14	<0.02 <0.02 <0.02 <0.02 <0.02	2069/98
UK, 1994 (Estima)	WP includes mancozeb	0.1		250	5	0 28	<0.02 <0.02	02/95
UK, 1994 (Pentland Squire)	WP includes mancozeb	0.1		250	5	0 28 29	<0.02 <0.02 <0.02	01/95
UK, 1995 (Anna)	EC includes fluazinam	0.10	0.05	200	5	1 7	<0.02 <0.02	FR0595BR
UK, 1995 (Kerrs Pink)	EC includes fluazinam	0.10	0.05	200	5	1 7	<0.02 <0.02	FR0595AR

Table 27. Metalaxyl-M residues in sunflower seed resulting from supervised trials in France and Spain.

Country, year (variety)	Application			Days after sowing	Residues, mg/kg	Ref.
	Form	g ai/100 kg seed	No.			
France, 1998 (Albena)	ES	83 (nominal 105)	1	125	<0.02	2118/98
France, 1998 (Albena)	ES	80 (nominal 105)	1	139	<0.02	2120/98
France, 1998 (Autan)	ES	75 (nominal 105)	1	126	<0.02	2121/98

Country, year (variety)	Application			Days	Residues, mg/kg	Ref.
	Form	g ai/100 kg seed	No.	after sowing		
France, 1998 (Cliosol)	ES	70 (nominal 105)	1	151	<0.02	2119/98
France, 1999 (Cliosol)	ES	61 (nominal 105)	1	144	<0.01	4013/99
France, 1999 (Cliosol)	ES	61 (nominal 105)	1	134	<0.01	4014/99
Spain, 1998 (Tornasol)	ES	67 (nominal 105)	1	138	<0.02	2116/98
Spain, 1999 (Coban)	ES	71 (nominal 105)	1	146	<0.02	4012/99

Table 28. Metalaxyl-M residues in cacao beans resulting from supervised trials in Côte d'Ivoire. [1,2]

Year (variety)	Application					PHI	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.	days		
2000 (Selectioné)	WP includes copper	0.09	0.09	100	4	29	<0.02	2148/00
2000 (Tout Venant)	WP includes copper	0.09	0.09	100	4	30	0.02	2149/00
2000 (Selectioné)	WP includes copper	0.09	0.09	100	4	30	<0.02	2150/00
2000 (Tout Venant)	WP includes copper	0.09	0.09	100	4	29	0.02	2151/00
2001 (Various local varieties)	WP includes copper	0.09	0.020	450	4	30	0.02	2102/01
2001 (Various local varieties)	WP includes copper	0.09	0.020	450	4	30	0.02	2103/01
2001 (Various local varieties)	WP includes copper	0.09	0.020	450	4	30	<0.02	2104/01
2001 (Selectioné)	WP includes copper	0.09	0.020	450	4	30	<0.02	2105/01

[1] Pods harvested, and fermented and dried beans analysed.

[2] Kühne (2148/00, 2002) described the fermentation and drying of cacao beans after harvest and before analysis in supervised trials on cocoa. The pods were cut open and beans and pulp were removed from the shell, placed inside black plastic and sealed. Every 48 h the plastic was opened and the contents stirred. Fermentation lasted 6 days. The fermented beans were then placed in a thin layer on black plastic under the open sky and stirred 2-3 times per day for 5 days, and overnight were protected with a layer of plastic. Samples of fermented and dried beans were deep-frozen for despatch to the analytical laboratory.

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

The Meeting received information on the fate of metalaxyl-M residues during the production of fruit juices and wine, and on its fate under hydrolysis conditions simulating commercial food processing.

Adam (00.DAOS, 2000) hydrolysed [^{14}C]metalaxyl-M as in food provessing. The HPLC analytical method was not enantiomer-selective, so epimerisation, if it occurred, would not have been observed. Metalaxyl-M was stable under these conditions (Table 29).

Table 29. Effect of food processing conditions on the hydrolysis of metalaxyl-M (Adam, 00DA05, 2000).

pH	Temperature, °C	Incubation , min	% of applied metalaxyl-M remaining	Process represented
4	90	20	96, 101	pasteurisation
5	100°C	60	96, 106	baking, brewing, boiling
6	120°C	20	97, 102	sterilisation

In a study on orange processing (Kühne, 2186/99, 2000), 163 kg of fruit were used for juice production, while 44 kg were used for marmalade. Subsamples of peel (1 kg) and pulp (6 kg) were used to produce 10 kg of marmalade.

Table 30. Fate of metalaxyl-M residues in oranges during orange processing.

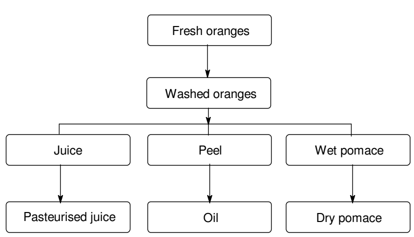
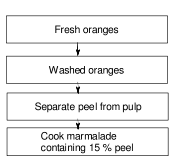
Country, year (variety)	Application					PHI, days	Sample	Residues, mg/kg	Ref.
	Form	kg ai/ha	kg ai/hl	water, l/ha	No.				
Spain, 2000 (Valencia)	WP includes mancozeb	0.20 +0.60	0.02 +0.06	1000 +980	2	0 14	fruit fruit peel pulp	1.0 0.11 0.11 0.23 0.24 <0.01 <0.01	2186/99
						14	fruit fruit washed juice, raw juice, pasteurised oil pomace, wet pomace, dry	0.13 0.15 <0.01 <0.01 <0.01 0.01 0.01 1.3 0.98 1.2 1.2 0.13 0.11 0.15 0.17 0.51 0.51 0.61 0.48	
						14	fruit fruit, washed peel pulp marmalade	0.11 0.086 0.34 0.01 0.043 0.042 0.040 0.048	

Table 31. Calculated processing factors for metalaxyl-M residues in orange products (2186/99).

Residue in RAC, mg/kg	Sample	Residues, mg/kg	Processing factors (PF)	Mean PF
0.13	Fruit, washed	0.15	1.2	

Residue in RAC, mg/kg	Sample	Residues, mg/kg	Processing factors (PF)	Mean PF
0.11	Fruit, washed	0.086	0.78	0.97
0.13	Juice, raw	<0.01	<0.08	<0.08
0.13	Juice, pasteurised	0.007 0.006 0.009 0.009	0.054 0.046 0.069 0.069	0.060
0.13	Oil	1.3 0.98 1.2 1.2	10.0 7.5 9.2 9.2	9.0
0.13	Pomace, wet	0.13 0.11 0.15 0.17	1.0 0.8 1.2 1.3	1.1
0.13	Pomace, dry	0.51 0.51 0.61 0.48	3.9 3.9 4.7 3.7	4.1
0.11	Peel	0.34 0.23 0.24	3.09 2.09 2.18	2.5
0.11	Pulp	0.01	0.09	0.09
0.11	Marmalade	0.043 0.042 0.040 0.048	0.39 0.38 0.36 0.44	0.39

Table 32. Processing factors calculated from the metalaxyl-M residues in grapes and their processed commodities shown in Table 20.

Residues, mg/kg				Processing factors			Ref.
Grapes	Grape juice	Young wine	Wine	Juice	Young wine	Wine	
<0.02	<0.02		0.02				98/7/1615
0.08	0.02		0.04	*0.25*		*0.50*	98/7/1615
0.03	<0.02		0.03			*1.00*	98/7/1615
0.1	0.03		0.05	*0.30*		*0.50*	98/7/1615
1.1	0.51		0.72	*0.46*		*0.65*	98/7/1615
0.52	0.19		0.2	*0.37*		*0.38*	98/7/1615
3.6	0.61		0.57	*0.17*		*0.16*	98/7/1615
0.48	0.28		0.32	*0.58*		*0.67*	98/7/1615
0.12		0.08	0.08		*0.67*	*0.67*	gr 5194
0.18		0.11	0.12		*0.61*	*0.67*	gr 5194
0.08		0.06			*0.75*		gr 50597
0.41		0.13			*0.32*		gr 50597
0.04		0.03	0.04		*0.75*	*1.00*	2124/94
<0.02		<0.02	<0.02				2123/94
0.04		<0.02	<0.02				2125/94
0.17		0.05	0.03		*0.29*	*0.18*	2122/94
0.02		<0.02	<0.02				2035/97
0.07		0.18	0.08		*2.57*	*1.14*	2030/97
0.24		0.24	0.27		*1.00*	*1.13*	2332/97
			Mean	*0.36*	*0.87*	*0.66*	

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

A lactating dairy cow feeding study and a laying hen study with metalaxyl, which provided information on likely residues in tissues, milk and eggs from residues in animal feeds, were reported to the Meeting.

In the first study 3 lactating Holstein cows weighing 445-698 kg each were dosed daily at a rate of 1.5 g metalaxyl per cow per day, equivalent to 75 ppm in the diet (Kahrs, ABR-82052, 1982). The dose was mixed with 1 kg of untreated commercial dairy ration. Milk was collected twice daily and a cow was slaughtered on days 14, 21 and 28. Animals consumed approximately 20 kg of dairy ration and hay each per day. Samples of liver, kidney, fat and muscle were analysed by the dimethylaniline common moiety method AG-349.

Residues did not accumulate and were transitory, with the interval between the last dose and slaughter influencing the levels more than the duration of dosing (Table 33). Residues 4 h after dosing in the cow slaughtered on day 14 were higher than in the cows that were dosed for the last time 23.5 h before slaughter. Residues in the blood were higher 1.5-2 h after dosing (0.32 mg/kg on day 13) than after 19-20 h (<0.05 mg/kg on days 21 and 28).

Table 33. Residues in the tissues and milk of dairy cows dosed with metalaxyl at 1.5 g metalaxyl per cow per day, equivalent to 75 ppm in the diet (Kahrs, ABR-82052, 1982).

<table>
<tr><th rowspan="2">Tissue</th><th colspan="4">Total residues, mg/kg. Method AG-349</th></tr>
<tr><th>Day 14 (4 h post-dosing)</th><th colspan="2">Day 21 (23.5 h post-dosing)</th><th>Day 28 (23.5 h post-dosing)</th></tr>
<tr><td>Tenderloin muscle</td><td>0.09</td><td colspan="2"><0.05</td><td>0.06</td></tr>
<tr><td>Round muscle</td><td>0.15</td><td colspan="2">0.07</td><td>0.08</td></tr>
<tr><td>Round muscle (control)</td><td>0.06</td><td colspan="2"></td><td>0.07</td></tr>
<tr><td>Omental fat</td><td><0.05</td><td colspan="2"><0.05</td><td><0.05</td></tr>
<tr><td>Perirenal fat</td><td><0.05</td><td colspan="2"><0.05</td><td><0.05</td></tr>
<tr><td>Liver</td><td>0.96</td><td colspan="2">0.14</td><td>0.12</td></tr>
<tr><td>Kidney</td><td>5.4</td><td colspan="2">0.12</td><td>0.11</td></tr>
<tr><td>Milk</td><td>Day 1</td><td>Day 14</td><td>Day 20</td><td>Day 27</td></tr>
<tr><td>Cow A</td><td>0.02</td><td>0.02</td><td></td><td></td></tr>
<tr><td>Cow B</td><td>0.02</td><td>0.02</td><td>0.02</td><td></td></tr>
<tr><td>Cow C</td><td>0.02</td><td>0.02</td><td>0.02</td><td>0.02</td></tr>
</table>

In the second study three groups of 15 laying White Leghorn hens, were dosed daily for 28 days with metalaxyl mixed with untreated poultry feed at levels equivalent to 10 ppm, 30 ppm and 100 ppm in the feed, fed *ad libitum* (Eudy, ABR-91047, 1991). Average consumption was 0.133-0.153 kg/bird/day. Eggs were collected for analysis. Birds were slaughtered on days 7, 14, 21 and 28 days after the first dose, and samples analysed by the dimethylaniline common moiety method AG-576.

There were no detectable residues in the eggs (<0.05 mg/kg) at any dose level (Table 34). In the tissues, residues were higher at higher doses. In the 10 ppm group, residues in the tissues were generally below the LOQ (<0.05 mg/kg) or, in a few cases, slightly above. Highest residues occurred in the skin + attached fat. In the 100 ppm feeding group, residues at 14, 21 and 28 days were generally similar, suggesting no continued accumulation in the tissues.

Table 34. Residues in tissues and eggs of laying hens dosed daily for 28 days with metalaxyl at levels equivalent to 10 ppm, 30 ppm and 100 ppm in the feed (Eudy, ABR-91047, 1991).

Sample	Total residues, mg/kg. Method AG-576			
	Days of dosing			
	7	14	21	28
10 ppm group				
Muscle, breast plus thigh	<0.05	0.06	<0.05	<0.05
Skin + attached fat	<0.05	<0.05	<0.05	<0.05
Fat, peritoneal	<0.05	<0.05	<0.05	<0.05
Liver	<0.05	<0.05	0.10 c 0.08	0.05
30 ppm group				
Muscle, breast plus thigh	0.06	0.10	<0.05	<0.05
Skin + attached fat	<0.05	0.07	0.10	0.08
Fat, peritoneal	<0.05	0.07	0.08	0.07
Liver	0.07	0.07	0.09 c 0.08	0.10
100 ppm group				
Muscle, breast plus thigh	0.13	0.13	<0.05	0.12
Skin + attached fat	0.12	0.32	0.40	0.34
Fat, peritoneal	0.09	0.27	0.34	0.17
Liver	0.16	0.10	0.09 c 0.08	0.11

Eggs	Day 1	Day 3	Day 7	Day 14	Day 21	Day 28
10 ppm group	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
30 ppm group	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
100 ppm group	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

c: control group sample

RESIDUES IN FOOD IN COMMERCE OR AT CONSUMPTION

No information was reported for metalaxyl-M.

NATIONAL MAXIMUM RESIDUE LIMITS

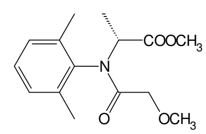
The Meeting was aware of the following national MRLs. Only MRLs that have been set solely for metalaxyl-M uses on crops that have residue data provided for this residue evaluation are included. (MRLs or tolerances based on metalaxyl data covering the use of metalaxyl-M and metalaxyl are not included.)

Country	Crop	MRL, mg/kg
Brazil	Grape	1
	Onion	0.5
	Potato	0.05
	Tomato	0.05
EU	Citrus fruit	0.5
	Grape	1
	Lettuce	2
	Onion	0.02
	Pepper	0.5
	Pome fruit	0.02
	Potato	0.02
	Spinach	0.05
	Sunflower seeds	0.05
	Tomato	0.2

APPRAISAL

The toxicology of metalaxyl-M was evaluated by the 2002 JMPR, which established a group ADI of 0–0.08 mg/kg bw for metalaxyl and metalaxyl-M. Residue and analytical aspects were considered for the first time by the present Meeting. Metalaxyl-M is the biologically active enantiomer (R-enantiomer) of the racemic compound metalaxyl. Metalaxyl was first evaluated by the JMPR in 1982, and Codex MRLs for metalaxyl have been established.

Metalaxyl-M is registered for use on fruit, nut and vegetable crops for the control of various fungal diseases such as those caused by *Phytophthora* and *Pythium* spp. It is applied to foliage, soil or seed and also as a post-harvest fruit treatment.



IUPAC name	(R)-2-[(2,6-dimethylphenyl)-methoxyacetylamino]-propionic acid methyl ester
Chemical Abstracts name	*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)-D-alanine methyl ester

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

As metalaxyl-M constitutes 50% of metalaxyl, investigations into the metabolism and fate of metalaxyl can legitimately be accepted as supporting the metabolism and fate of metalaxyl-M. When the metabolism of metalaxyl and metalaxyl-M was compared directly, it was found to be similar.

In the studies of animal and plant metabolism and environmental fate, metalaxyl or metalaxyl-M uniformly ^{14}C labelled in the aromatic ring was used.

Metabolism

In the list below, the numbering is preserved from the 2002 JMPR toxicology evaluation.

Metabolite 1: *N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl)alanine

Metabolite 3: *N*-(2,6-dimethylphenyl)-*N*-(hydroxyacetyl)alanine methyl ester

Metabolite 6: *N*-(2,6-dimethylphenyl)-*N*-(hydroxyacetyl)alanine

Metabolite 7: *N*-(2,6-dimethyl-5-hydroxyphenyl)-*N*-(methoxyacetyl)alanine methyl ester

Metabolite 8: *N*-(2-hydroxymethyl-6-methylphenyl)-*N*-(methoxyacetyl)alanine methyl ester (occurs as two isomers)

Metabolite P: *N*-[(2-hydroxymethyl)-6-methylphenyl]-*N*-(hydroxyacetyl)alanine (occurs as two isomers)

Animals

The Meeting received the results of studies on metabolism in rats, lactating goats and laying hens. When animals were dosed orally with radiolabelled metalaxyl, most of the radiolabel was excreted in the urine within a short time, with a small amount in the faeces. Numerous metabolites resulting from hydrolysis, oxidation and demethylation of metalaxyl and subsequent conjugate formation were identified. In a study in goats, metalaxyl itself was not detected as a component of the residue in tissues or milk. In a study in laying hens, low levels of metalaxyl were present in liver and eggs. The metabolic pathway for metalaxyl was similar in rats, goats and hens.

The absorption, distribution, metabolism and excretion of radiolabel were similar in *rats* dosed orally with ^{14}C-metalaxyl or ^{14}C-metalaxyl-M. Detailed information on metabolism in this species is reported in the 2002 JMPR toxicological evaluations.

Very little radiolabel was found in milk (0.003 mg/kg) or tissues (0.057 mg/kg in liver) from a *goat* dosed with ^{14}C-metalaxyl at the equivalent of 7 ppm in the feed for 10 days.

When two lactating dairy goats were dosed orally once daily for 4 consecutive days by gelatin capsule with ^{14}C-metalaxyl, equivalent to 77 ppm in the diet, the radiolabel was excreted rapidly: within 24 h of administration, 67% of the daily dose appeared in urine, 9% in faeces and 0.1% in milk. Metalaxyl was not detected as a component of the residue. Metabolite 6 was the main component of the residue in liver (0.19 mg/kg), leg muscle (0.014 mg/kg) and perirenal fat (0.065 mg/kg); metabolite 8 was the main residue component in kidney. The main metabolites in milk were C-10 and C-8 fatty acid conjugates of metabolite 3 (0.058 mg/kg). These fatty acids are conjugated through the hydroxyacetyl group of metabolite 3.

When five laying *hens* were dosed orally once daily for 4 consecutive days by gelatin capsule with ^{14}C-metalaxyl, equivalent to approximately 100 ppm metalaxyl in the diet, radiolabel recovered in edible tissues and eggs represented 0.97% of the administered dose; the remainder was recovered in excreta. Metabolite P (consisting of P1 and P2, steric isomers) was the main metabolite in egg white (0.056 mg/kg), egg yolk (0.072 mg/kg) and thigh muscle (0.31 mg/kg). Metalaxyl parent was identified in egg white (0.013 mg/kg), egg yolk (0.010 mg/kg) and liver (0.018 mg/kg), but not in thigh muscle or fat (< 0.001 mg/kg).

Plants

The Meeting received the results of studies on the metabolism of metalaxyl in grape, lettuce and potato and of metalaxyl-M in lettuce. No metabolites were identified in plants which had not already been identified in animals. Parent metalaxyl was the main component of the residue in grapes and in juice produced from the grapes when metalaxyl was used on grape vines. In treated lettuce, parent metalaxyl and metabolite 8 were each present at approximately 20% of the total residue. Metabolite 8 was the main residue component in lettuce in both cases in which metalaxyl and metalaxyl-M were compared. When metalaxyl was used on potato plants, some residue reached the tubers, where parent metalaxyl was the main residue component.

Grapevines in Switzerland were sprayed to runoff seven times at 14-day intervals with a ^{14}C-metalaxyl spray at a concentration of 0.050 kg ai/hl and were harvested 52 days after the last application. Parent metalaxyl (2.0 mg/kg) constituted 64% of the total residues in *grapes*.

When two grapevines in Switzerland were sprayed to runoff six times at approximately 14-day intervals with a ^{14}C-metalaxyl spray at a concentration of 0.030 kg ai/hl and harvested 68 days after the last application, parent metalaxyl (0.83 mg/kg) comprised 64% of total residues in the grapes. Metabolite 8 accounted for 20% of the residue, and metabolites 1, 6 and 7 were minor components (1.8–4.3%). When the grapes were separated into juice and presscake, metalaxyl was still the main part of the residue (62% and 57%, respectively).

Metalaxyl was the main identified component of the residue in *lettuce* (18.6% of the total ^{14}C residue) after seedlings in a greenhouse were sprayed twice, 2 weeks apart, with ^{14}C-metalaxyl at a rate equivalent to 0.25 kg ai/ha and harvested 2 weeks later. The identified metabolites (including glucose conjugates) were metabolite 8 (22% of the total ^{14}C residue), metabolite 6 (10%), metabolite 3 (8.9%), metabolite 7 (6.2%) and metabolite 1 (6.0%).

The metabolic pathways of metalaxyl-M and metalaxyl were compared in lettuce in a field in Switzerland treated three times at 10-day intervals with labelled compounds. The levels of total applied residue and parent compounds in the residue were generally comparable. Metabolite 8 (free and conjugated) was the main identified component of the residue in samples taken 14 and 21 days after treatment. Enantiomeric ratio measurements suggested similar disappearance rates for the two enantiomers and little interconversion.

Potato plants in the field in Switzerland received five foliar treatments of ^{14}C-metalaxyl at 0.2 kg ai/ha at 10-day intervals and were harvested at maturity 5 weeks after the last treatment. Little residue reached the tubers (0.02 mg/kg ^{14}C as metalaxyl). No parent metalaxyl was detected in tubers. In a second experiment, the level of ^{14}C as metalaxyl in tubers was < 0.0001 mg/kg after ^{14}C-metalaxyl was applied to the soil (residues in soil, approximately 0.5 mg/kg), indicating that metalaxyl is not taken up by the tubers directly from the soil.

Potato plants in the field in the USA received six foliar treatments, about 2 weeks apart, of ^{14}C-metalaxyl at 1.3 kg ai/ha. Tubers harvested at maturity, 1 week after the last treatment, contained 0.5 mg/kg ^{14}C as metalaxyl, of which 50–60% was parent metalaxyl. A number of metabolites were identified, but only the concentration of metabolite 8 exceeded 5% of the residue.

Environmental fate

Soil

The Meeting received information on the behaviour and fate of metalaxyl and metalaxyl-M during aerobic metabolism in a number of soils. The rate of degradation is strongly influenced by the properties of the soil, including its biological activity and the conditions of temperature, moisture and concentration of the residue, with recorded half-lives in the range of 5–180 days. In direct comparisons of metalaxyl and metalaxyl-M under aerobic conditions, metalaxyl-M was the more persistent in one case and less persistent in two others. The main soil metabolite is metabolite 1 or, in the case of metalaxyl-M, the specific enantiomer of metabolite 1.

Field dissipation studies for metalaxyl-M were provided from France, Italy, Spain and Switzerland. Metalaxyl-M residues disappeared from the soil with half-lives ranging from 5 to 35 days. The residues occurred mostly in the top 10 cm of soil, but some reached lower levels. The enantiomer of metabolite 1 was produced in all cases, and its level sometimes exceeded that of the parent metalaxyl-M. A comparison of enantiomeric ratios in metalaxyl residues in soil suggested that the R-enantiomer (i.e. the metalaxyl-M enantiomer) disappeared more quickly than the S-enantiomer. This resulted in a preponderance of S-enantiomer in the metalaxyl residue and a preponderance of R-enantiomer in metabolite 1.

The studies of dissipation in the field suggest that, after use of metalaxyl-M for seed treatment or at the time of sowing, little or none will remain as a soil residue when the crop is harvested.

Rotational crops

Information on the fate of radiolabelled metalaxyl in confined crop rotational studies and of unlabelled metalaxyl-M in field rotational crops was made available to the Meeting. The studies with radiolabel showed that parent metalaxyl was usually a minor part of the residue that reached the rotational crop. The identifiable metabolites were also usually minor, but metabolite 8 as glucose conjugates was detected in spring wheat stalks at 2.3 mg/kg. Metalaxyl-M residues were not detected in unconfined field rotational crops in Switzerland or the United Kingdom, but levels of 0.11 mg/kg were present in broccoli and 0.03 mg/kg in lettuce leaves from crops sown 29 days after treatment of the first crop in a study in Italy. The short interval was used in order to simulate the ploughing-in of a failed crop and the sowing of a new one.

Methods of analysis

The Meeting received descriptions and validation data for analytical methods for residues of metalaxyl in plant material, animal tissues, milk and eggs.

Common moiety methods rely on the 2,6-dimethylaniline moiety of metalaxyl and many of its metabolites, and these methods have been used to identify metalaxyl residues in animal commodities. The typical LOQs are 0.05 mg/kg for tissues and 0.01 mg/kg for milk. Metabolite 8, containing the 2-hydroxymethyl-6-methylaniline moiety, is apparently partially converted to 2,6-dimethylaniline, resulting in low and variable recoveries.

With gas–liquid chromatography and nitrogen–phosphorus detection and HPLC with mass spectrometry detection procedures for identifying metalaxyl or metalaxyl-M after a simple extraction and limited clean-up, the LOQs are 0.02–0.04 mg/kg for many crop substrates. A modification to the method (method REM 181.06), with the introduction of an HPLC chiral separation step before determination, allows for the analysis of specific enantiomers.

A multi-residue regulatory method (DFG S19) is available for metalaxyl.

Method REM 181.06 (gas–liquid chromatography with mass spectrometry detection) is not a multi-residue method, but it is enantioselective and suitable as a regulatory method for metalaxyl-M.

Stability of residues in stored analytical samples

The Meeting received information on the stability of residues of metalaxyl-M in crops (orange, potato, rape-seed, tomato, wheat) and animal commodities (beef muscle, beef liver, milk, eggs) during storage of analytical samples. Metalaxyl-M residues were stable in these substrates and under the conditions and intervals of storage (2 years). There was no evidence of epimerization during freezer storage. As a common moiety method was used for the animal commodity samples, storage stability refers to the total residue rather than to parent metalaxyl-M. As the common moiety method, which relies on the 2,6-dimethylaniline moiety, is less suitable for metabolite 8, the freezer stability of this metabolite during storage is not demonstrated.

Definition of the residue

Parent metalaxyl is the main identifiable component of the residue in crops resulting from use of metalaxyl, although metabolite 8 can occur at approximately the same levels. Metabolite 8 was not considered to be toxicologically significant.

The current residue definition of metalaxyl is metalaxyl. As metalaxyl-M is one enantiomer of metalaxyl, it is covered by the current residue definition. Non-enantioselective methods cannot distinguish metalaxyl-M from metalaxyl, but an enantioselective method is available. While metalaxyl-M and metalaxyl are both registered for crop uses, it is preferable, for enforcement purposes, to maintain a single residue definition. As the 2002 JMPR recommended a group ADI for metalaxyl and metalaxyl-M, the inclusive residue definition is also suitable for risk assessment purposes. The Meeting recommended that metalaxyl-M be contained within the metalaxyl residue definition and recommended amendment of the metalaxyl residue definition to provide definitions for enforcement and risk assessment purposes.

For plant commodities: Metalaxyl, including metalaxyl-M. Definition of the residue (for compliance with MRL and for estimation of dietary intake): metalaxyl. Note: Metalaxyl is a racemic mixture of an R-enantiomer and an S-enantiomer. Metalaxyl-M is the R-enantiomer.

In animals dosed with metalaxyl, parent metalaxyl was either a minor part of the residue or was not detected. Analytical methods for metalaxyl are based on a common moiety method, and residues in the farm animal feeding studies were measured by this method. Common moiety residues are acceptable for estimation of dietary intake when the parent compound is a minor part of the residue. The log P_{OW} for metalaxyl-M is 1.7, and the studies of animal metabolism confirm that metalaxyl is not fat-soluble.

For animal commodities: Metalaxyl including metalaxyl-M. Definition of the residue (for compliance with MRL and for estimation of dietary intake): metalaxyl and metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl.

Results of supervised trials on crops

The Meeting received data from supervised trials with metalaxyl-M used on citrus fruit, apple, grape, onion, tomato, pepper, lettuce, spinach, potato, sunflower and cacao. In some trials, residues were measured on samples taken just before and just after ('zero-day' residue) the last application. The residue level measured just before the last application, expressed as a percentage of zero-day residue, provides a measure of the contribution of previous applications to the final residue in the use pattern used in the trial. For grapes, the average carryover of residue was 32% in 12 trials in Australia, 57% in three trials in Germany and 46% in three trials in Italy. In lettuce, the average carryover was 1.7% in six trials in France, Germany and Italy. In spinach, the average carryover was 1.1% in eight trials in France.

Residue data were evaluated only when labels (or translations of labels) describing the relevant GAP were available to the Meeting.

Citrus fruit

Metalaxyl-M is registered for use as a post-harvest treatment on citrus in Israel. It is applied as a 0.1 kg ai/hl spray.

In the trials, the formulation of metalaxyl-M was mixed with a commercial wax to produce a spray solution, which was applied at a rate of 200 l /90 t of fruit (theoretical concentration of residue, 2.1 g/t). The residue levels in three trials on *oranges* were 1.2, 1.3 and 1.6 mg/kg in whole fruit and < 0.02 mg/kg in pulp. This method of post-harvest application includes control of the application rate in terms of the amount of metalaxyl-M per unit weight of fruit. The residue levels agreed substantially with expectations.

The Meeting noted that three supervised trials is generally an insufficient number for a major commodity such as oranges.

The residue levels of metalaxyl-M in the trials conducted in line with Israeli GAP did not exceed the current metalaxyl MRL of 5 mg/kg for citrus fruit.

Apple

Metalaxyl-M is registered in Spain for soil treatment around apple trees at 0.5–1.0 g ai/tree and in Italy at 0.5–4 g ai/tree. In two trials each in France, Italy and Spain at application rates of 0.78–10 kg ai/ha, no residues were detected in apples (< 0.02 mg/kg). For an assumed 500–1000 trees per ha, the rate of 10 kg ai/ha appears to be exaggerated.

The Meeting estimated a maximum residue level for metalaxyl-M in apples of 0.02* and an STMR value of 0 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.02* mg/kg would not exceed the current metalaxyl MRL of 1 mg/kg for pome fruits.

Grape

In Australia, metalaxyl-M is registered for a maximum four applications on grapes at 0.11 kg ai/ha, with a PHI of 7 days. The residue levels in grapes in five Australian trials matching GAP, but with six applications instead of four, were: < 0.02, 0.03, 0.06, 0.14 and 0.52 mg/kg. As the final residue level should not be influenced by earlier applications, residue levels after six applications are acceptable as equivalent to residues levels in GAP trials.

No GAP was available to evaluate the data for grapes treated in Germany and Switzerland.

In Greece, grapes may be treated four times with metalaxyl-M at 0.1 kg ai/ha, with harvest 15 days after the last application. The residue levels in grapes in six trials in Italy and Portugal, conducted substantially according to Greek GAP, were: 0.04, 0.06, 0.18, 0.19, 0.21 and 0.55 mg/kg.

The residue levels in the Australian and European trials appear to be similar and can be combined. In summary, the residue levels in the 11 trials, in ranked order, were: < 0.02, 0.03, 0.04, 0.06, 0.06, 0.14, 0.18, 0.19, 0.21, 0.52 and 0.55 mg/kg

The Meeting estimated a maximum residue level for metalaxyl-M in grapes of 1 mg/kg and an STMR value of 0.14 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 1 mg/kg would not exceed the current metalaxyl MRL of 1 mg/kg for grapes.

Onion

In Ecuador and Uruguay, metalaxyl-M is registered for a maximum of three applications on onions at 0.1 and 0.12 kg ai/ha, with a PHI of 7 days. Metalaxyl-M residue levels in bulb onions in three Brazilian trials matching Uruguayan GAP, but with four applications instead of three, were < 0.02 (two) and 0.02 mg/kg.

Metalaxyl-M is registered in Germany for a maximum of three applications on onions at 0.097 kg ai/ha, with a PHI of 21 days. In four trials in Switzerland with conditions matching German GAP, the residue levels were all below the LOQ (0.02 mg/kg).

Data on residues in trials in onions in Italy and Spain could not be evaluated because no relevant GAP was available.

In summary, the residue levels in the seven trials, in ranked order, were < 0.02 (six) and 0.02 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in onions of 0.03 mg/kg and an STMR value of 0.02 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.02 mg/kg would not exceed the current metalaxyl MRL of 2 mg/kg for bulb onions.

Tomato

Metalaxyl-M is registered for foliar application on tomatoes in Algeria, Chile, Ecuador, Greece, Israel and Morocco at 0.10–-0.14 kg ai/ha, with a PHI of 3 days and a maximum of three or four treatments.

Residue levels in tomatoes in six greenhouse trials in France, two in Spain and four in Switzerland at 0.15 kg ai/ha, with harvest 3 days after treatment (equivalent to the stated GAP) were: 0.02 (two), 0.02, 0.03, 0.04, 0.04, 0.05, 0.05, 0.08, 0.09, 0.12 and 0.18 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in tomatoes of 0.2 mg/kg and an STMR value of 0.045 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.2 mg/kg would not exceed the current metalaxyl MRL of 0.5 mg/kg for tomatoes.

Pepper

GAP for use of metalaxyl-M in Italy allows three soil applications of 1 kg ai/ha with a 15-day PHI. Data on residues from Italian and Spanish trials approximating Italian GAP were provided. In some of the trials, residues were measured 10 and 20 days after the last application instead of 15 days, but these trials were considered valid because the residue levels were relatively unchanged. The residue levels in the seven greenhouse trials were: < 0.02 (two), 0.02, 0.03, 0.08, 0.10 and 0.36 mg/kg; and those in the three outdoor trials in Italy were: < 0.02 (two) and 0.02 mg/kg.

The Meeting decided to use the data from the greenhouse trials: < 0.02 (two), 0.02, 0.03, 0.08, 0.10 and 0.36 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in sweet peppers of 0.5 mg/kg and an STMR value of 0.03 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.5 mg/kg would not exceed the current metalaxyl MRL of 1 mg/kg for peppers.

Lettuce

Metalaxyl-M is registered in Spain for use on lettuce at 0.10 kg ai/ha with a PHI of 14 days. The residue levels in lettuce were < 0.02 mg/kg in an Italian trial matching Spanish GAP. The residue levels in lettuce in four French trials matching Spanish GAP were: < 0.02 (two), 0.02 and 0.03 mg/kg.

Metalaxyl-M is registered in Germany for a maximum of two applications on lettuce at 0.097 kg ai/ha, with a PHI of 21 days. In six trials on head lettuce in Germany under conditions matching GAP, but with three applications instead of two, the residue levels were: < 0.02 (four), 0.02 and 0.03 mg/kg. In two German greenhouse trials at 0.10 kg ai/ha with harvest 21 days after the second application, the residue levels were < 0.02 and 0.41 mg/kg.

In two trials in The Netherlands matching German GAP, the residue levels were < 0.02 mg/kg.

Trials in Spain and Switzerland could not be evaluated because there was no matching GAP.

In summary, the residue levels in lettuce in the 15 trials, in ranked order, were: < 0.02 (10), 0.02 (two), 0.03 (two) and 0.41 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in head lettuce of 0.5 mg/kg and an STMR value of 0.02 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.5 mg/kg would not exceed the current metalaxyl MRL of 2 mg/kg for head lettuce.

Spinach

Metalaxyl-M is registered in Switzerland for a maximum of six applications on spinach at 0.10 kg ai/ha with a PHI of 14 days. In three trials on spinach in Switzerland at 0.10 kg ai/ha and three at 0.14 kg ai/ha, with intervals before harvest of 10 or 14 days, the residue levels were all < 0.02 kg/ha. The levels were also < 0.02 mg/kg in two trials in Germany matching the conditions of GAP in Switzerland.

In a number of trials in France in which the application rate was 0.10 or 0.14 kg ai/ha, spinach was sampled for analysis 10 and 20 days after treatment. The Meeting noted that the residue levels generally changed slowly between 10 and 20 days post-treatment and decided to accept the residue levels at 10 days as sufficiently close to those expected at 14 days. The residue levels in the 10 French trials were: < 0.02 (two), 0.02 (four), 0.03, 0.04 (two) and 0.05 mg/kg.

In summary, metalaxyl-M residue levels in the 18 trials were < 0.02 (10), 0.02 (four), 0.03, 0.04 (two) and 0.05 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in spinach of 0.1 mg/kg and an STMR value of 0.02 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.1 mg/kg would not exceed the current metalaxyl MRL of 2 mg/kg for spinach.

Potato

Labels were available from Algeria, Australia, Austria, Chile, Ecuador, Greece, Israel and Morocco from formulations for foliar application of metalaxyl-M to potatoes at 0.1–0.12 kg ai/ha. The information on GAP suggests that the recommended foliar application rate on potatoes is 0.1 kg ai/ha in many situations.

The results of supervised trials were available from Brazil (three at 0.1 kg ai/ha and three at 0.2 kg ai/ha), Germany (six at 0.1 kg ai/ha), Switzerland (three at 0.075 kg ai/ha) and the United Kingdom (four at 0.1 kg ai/ha). The residue levels in all 19 trials, measured at intervals of 0–28 days after the last treatment, were below the LOQ (0.02 mg/kg).

As residues were found in potato tubers in the metabolism studies after high application rates, the median residue values cannot be assumed to be nil. The Meeting estimated a maximum residue level for metalaxyl-M in potato of 0.02* mg/kg and an STMR value of 0.02 mg/kg. Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.02* mg/kg would not exceed the current metalaxyl MRL of 0.05* mg/kg for potato.

Sunflower seed

Metalaxyl-M is registered in China and Serbia and Montenegro for use as a seed treatment at 0.105 kg ai/100 kg sunflower seed. The Meeting agreed that the results of trials from other countries could be evaluated with respect to this seed treatment GAP.

In six trials in France and two in Spain, metalaxyl-M was used as seed treatment at a nominal rate of 105 g ai/100 kg seed (measured, 61–80 g ai/100 kg seed). The residue levels in harvested sunflower seed 125–151 days after sowing were all below the LOQ (0.01 and 0.02 mg/kg). Because of the long interval between sowing and harvest and the solubility of metalaxyl-M, residues would not be expected in harvested sunflower seed.

The Meeting estimated a maximum residue level for metalaxyl-M in sunflower seed of 0.02* mg/kg and an STMR value of 0 mg/kg. Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.02* mg/kg would not exceed the current metalaxyl MRL of 0.05* mg/kg for sunflower seed.

Cacao beans

Metalaxyl-M is registered in Côte d'Ivoire for use on cacao at 0.012 kg ai/ha. In eight trials in Côte d'Ivoire in which metalaxyl-M was applied as foliar treatment four times at 0.09 kg ai/ha (an exaggerated rate), with harvest 29–30 days after the last treatment, the residue levels in the cacao beans were: < 0.02 (four) and 0.02 (four) mg/kg. The cacao beans were fermented and dried before analysis. The Meeting agreed that the residue levels after application at the label rate would not exceed 0.02 mg/kg.

The Meeting estimated a maximum residue level for metalaxyl-M in cacao beans of 0.02 mg/kg and an STMR value of 0.02 mg/kg.

Metalaxyl-M residue levels complying with the estimated maximum residue level of 0.02 mg/kg would not exceed the current metalaxyl MRL of 0.2 mg/kg for cacao beans.

Fate of residues during processing

The Meeting received information on the fate of metalaxyl-M residues during the production of fruit juices and vinification. The Meeting also received information that metalaxyl-M is hydrolytically stable under hydrolysis conditions that simulate those occurring during food processing.

The following processing factors were calculated from the data from the trials. The factors are mean values, excluding those calculated in cases of undetectable residues.

Commodity	Processed product	Processing factor	No. of trials
Orange	Washed fruit	0.97	2
	Juice, pasteurized	0.060	4

	Oil	9.0	4
	Pomace, wet	1.1	4
	Pomace, dry	4.1	4
	Peel	2.5	3
	Pulp	0.091	1
	Marmalade	0.39	4
Grapes	Juice	0.36	6
	Young wine	0.87	8
	Wine	0.66	13

The Meeting used the processing factors to estimate STMR-Ps for processed commodities. The processing factor for wine (0.66) was applied to the grape STMR (0.14 mg/kg) to calculate an STMR-P of 0.092 mg/kg for wine. The processing factor for grape juice (0.36) was applied to the grape STMR (0.14 mg/kg) to calculate an STMR-P of 0.050 mg/kg for grape juice

Residues in animal commodities

Feeding studies

The Meeting received the results of studies of feeding metalaxyl to lactating dairy cows and laying hens, which provided information on probable residue levels in tissues, milk and eggs from residues in animal feeds.

A group of three lactating dairy cows were dosed daily with metalaxyl, equivalent to 75 ppm in their diet, and were slaughtered for tissue collection on days 14, 21 and 28. Liver, kidney, fat and muscle were analysed by a dimethylaniline common moiety method. The residues were transitory and did not accumulate, and the interval between last dose and slaughter (4 and 23.5 h) influenced the residue levels more than the duration of dosing. The level of residue in milk was 0.02 mg/kg. The residue levels in the tissues collected on day 28 from the animal slaughtered 23.5 h after the last dose were 0.11 mg/kg in kidney, 0.12 mg/kg in liver, < 0.05 mg/kg in fat and 0.06–0.08 mg/kg in muscle.

Groups of 15 laying hens were dosed daily for 28 days with metalaxyl at levels equivalent to 10, 30 and 100 ppm in the feed. Tissue and egg samples were analysed by a dimethylaniline common moiety method. No residues appeared in the eggs (< 0.05 mg/kg) at any dose. The residue levels in the tissues of hens fed 10 ppm were generally below the LOQ (< 0.05 mg/kg) or, in a few cases, just above the LOQ.

Maximum residue levels

The farm animal feeding studies suggest that residues would generally be undetected or transitory in meat, milk and eggs if metalaxyl was present in animal feeds.

Farm animals are therefore not exposed to residues in their feed from commodities in this evaluation, and no MRLs have been established for metalaxyl in animal commodities. Consequently, the Meeting agreed not to recommend animal commodity maximum residue levels.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the metalaxyl-M residue levels listed below are already covered by existing metalaxyl MRLs.

Definition of the residue

For plant commodities.

Metalaxyl including metalaxyl-M: for compliance with MRL and for estimation of dietary intake: metalaxyl.

For animal commodities. (Note that no metalaxyl MRLs are currently recommended for animal commodities).

Metalaxyl including metalaxyl-M: for compliance with MRL and for estimation of dietary intake: metalaxyl and metabolites containing the 2,6-dimethylaniline moiety, expressed as metalaxyl.

Note: Metalaxyl is a racemic mixture of an R-enantiomer and an S-enantiomer. Metalaxyl-M is the R-enantiomer.

CCN	Commodity Name	Metalaxyl-M		Metalaxyl
		Estimated maximum residue level, mg/kg	STMR or STMR-P mg/kg	Existing MRL mg/kg
FP 0009	Apple	0.02(*)	0	Pome fruits 1
FB 0269	Grapes	1	0.14	1
VL 0482	Lettuce, Head	0.5	0.02	2
VA 0385	Onion, Bulb	0.03	0.02	2
VO 0445	Peppers, Sweet	0.5	0.03	Peppers 1
VO 0448	Tomato	0.2	0.045	0.5
VR 0589	Potato	0.02(*)	0.02	0.05(*)
VL 0502	Spinach	0.1	0.02	2
SO 0702	Sunflower seed	0.02(*)	0	0.05(*)
SB 0715	Cacao beans	0.02	0.02	0.2
	Grape juice		0.050	
	Wine		0.092	

* at or about the LOQ

DIETARY RISK ASSESSMENT

Long-term intake

Estimated Theoretical Maximum Daily Intakes for the five GEMS/Food regional diets, based on recommended MRLs for metalaxyl, were in the range of 2-10% of the ADI (Annex 3 of the Report). The Meeting concluded that the long-term intake of residues of metalaxyl and metalaxyl-M resulting from their uses that have been considered by JMPR is unlikely to present a public health concern.

Short-term intake

The 2002 JMPR decided that an ARfD is unnecessary. The Meeting therefore concluded that the short-term intake of metalaxyl and metalaxyl-M residues is unlikely to present a public health concern.

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