

APPENDIX 3

LISTING OF ENDPOINTS

Chapter 2.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

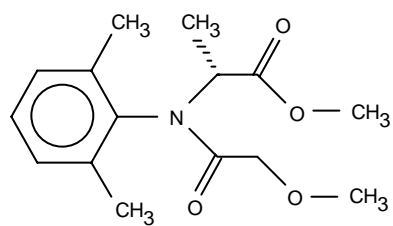
Active substance (ISO Common Name)	Metalaxyl-M (ISO-approved); Mefenoxam (unofficial)
Function (<i>e.g.</i> fungicide)	Fungicide
Rapporteur Member State	Belgium

Identity (Annex IIA, point 1)

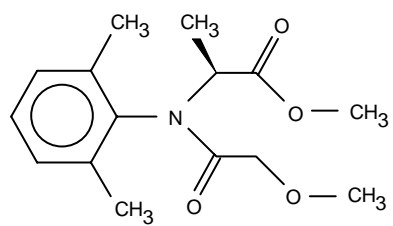
Chemical name (IUPAC)	mixture of (R)-2-[(2,6-dimethyl-phenyl)-methoxyacetyl-amino]- propionic acid methyl ester (min. 97 %) (S)-2-[(2,6-dimethyl-phenyl)-methoxyacetyl-amino]- propionic acid methyl ester (max. 3 %)
Chemical name (CA)	mixture of N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-D-alanine methyl ester (min. 97 %) N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-L-alanine methyl ester (max. 3 %)
CIPAC No	580
CAS No	70630-17-0 (R) 69516-34-3 (S)
EEC No (EINECS or ELINCS)	not available
FAO Specification (including year of publication)	-
Minimum purity of the active substance as manufactured (g/kg)	940 g/kg (R+S) 910 g/kg (R)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	2,6-dimethylaniline (max. 0.5 g/kg)
Molecular formula	C ₁₅ H ₂₁ NO ₄
Molecular mass	279.3

Structural formula

R-Isomer (CGA 329351)



S-isomer (CGA 351920)



Physical-chemical properties (Annex IIA, point 2)

Freezing point (state purity)	- 38.7°C (glass transition temperature) (99.4% pure)
Boiling point (state purity)	not determinable due to thermal decomposition
Temperature of decomposition	approx. 270°C
Appearance (state purity)	clear, pale yellow, viscous liquid with weak odour (99.4% pure) clear, light brown, viscous liquid with weak odour (97.1% pure)
Relative density (state purity)	1.125 at 20°C (99.4% pure)
Surface tension	$\sigma = 57.6 - 57.8$ mN/m (1 g/l) at 20°C (97.1% pure)
Vapour pressure (in Pa, state temperature)	$3.3 \cdot 10^{-3}$ Pa at 25°C (99.4% pure)
Henry's law constant ($\text{Pa m}^3 \text{mol}^{-1}$)	$3.5 \cdot 10^{-5}$ Pa.m ³ /mol at 25°C (99.4% pure)
Solubility in water (g/l or mg/l, state temperature)	pure water : 26 g/l at 25°C (99.4% pure) no effect of pH
Solubility in organic solvents (in g/l or mg/l, state temperature)	at 25°C (97.1% pure) : n-hexane : 59 g/l toluene : completely miscible dichloromethane : completely miscible methanol : completely miscible n-octanol : completely miscible acetone : completely miscible ethyl acetate : completely miscible
Partition co-efficient ($\log P_{OW}$) (state pH and temperature)	pH 7.6 : 1.71 at 25°C (99.4% pure) no effect of pH
Hydrolytic stability (DT_{50}) (state pH and temperature)	hydrolytical stability up to pH 7 pH 9 : 216 d at 20°C
Dissociation constant	no pK_a in an accessible pH-range
UV/VIS absorption (max.) (if absorption > 290 nm state ϵ at wavelength)	266 nm ($512 \text{ l.mol}^{-1}.\text{cm}^{-1}$) 274 nm ($477 \text{ l.mol}^{-1}.\text{cm}^{-1}$) no absorption between 290 and 750 nm
Photostability (DT_{50}) (aqueous, sunlight, state pH)	direct phototransformation at 25°C : not significant
Quantum yield of direct phototransformation in water at $\Sigma > 290$ nm	not determined ($\epsilon < 1 \text{ l.mol}^{-1}.\text{cm}^{-1}$ at 290 nm)
Flammability	flash point : 179°C (1013 mbar) auto-ignition temperature : 410°C
Explosive properties	not explosive

Summary of intended uses

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Grapes	Austria France Greece Italy Portugal Spain	RidomilR Gold MZ 68 WP	F	Plasmopara viticola Peronospora viticola	WP	40 M 329 640 MZB	Foliar spray	Pre and post flowering (Preventative)	2-4	10-14 days		100-1200	0.04-0.12	15-56	
Onion	Austria France Germany Italy Spain UK	RidomilR Gold MZ 68 WP	F	Peronospora destructor	WP	40 M 329 640 MZB	Foliar spray	First sign of disease	2-3	8-21 days		200-1000	0.075-0.15	14-21-28	
Tomato	France Greece Italy Portugal Spain	RidomilR Gold MZ 68 WP	F	Phytophthora infestans Alternaria solani Phomides Septoria lycopersici	WP	40 M 329 640 MZB	Foliar spray	From start of first disease Preventative	2-4	10-14 days		500-1500	0.04-0.15	3-28	
Cucumber	Austria France Greece Portugal Spain	RidomilR Gold MZ 68 WP	F	Pseudoperonospora cubensis Phytophthora infestans	WP	40 M 329 640 MZB	Foliar spray	First applic. : before infection	3-4	10-14 days		500-1500	0.04-0.15	3,14	
Melon	France Italy Portugal	RidomilR Gold MZ 68 WP	F	Pseudoperonospora cubensis	WP	40 M 329 640 MZB	Foliar spray	After 3-4 leaves	3	10-14 days		600-1000	0.094-0.12	14,20	
Broccoli	Italy	RidomilR Gold Plus 42.5 WP	F	-	WP	-	Foliar spray	-	3	7-10 days		600-1200	0.1	21	
Lettuce	Belgium Luxembourg Netherlands Portugal Spain	RidomilR Gold MZ 68 WP	F/G	Bremia lactucae	WP	40 M 329 640 MZB	Foliar spray	After 3-4 leaves	1-3	10-14 days		400-1000	0.1-0.125	14, 28-42	

Rapporteur Member State Month and year

Active Substance (Name)

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Appendix 6

Format For The Listing Of End Points to be Included in the Reasoned Statement of the Overall Conclusions Drawn by the Rapporteur Member State (Level 2)

Spinach	Italy	RidomilR Gold Plus 42.5 WP	F	-	WP	-	Foliar spray	-	2	7-10 days		600-1200	0.1	20	
Artichoke	Italy	RidomilR Gold Plus 42.5 WP	F	-	WP	-	Foliar spray	-	3	10-14 days		600-1200	0.1	20	
Potato	Austria Belgium Finland France Germany Ireland Italy Luxemburg Netherlands Portugal Spain Sweden, UK	RidomilR Gold MZ 68 WP	F	Phytophthora infestans, Alternaria solani	WP	40 M 329 640 MZB	Foliar spray	From start of disease development until before desiccation	2-5	7-14 days		100-1000	0.075- 0.113	7-28	
Tobacco	Austria France Greece Italy Portugal Spain	RidomilR Gold MZ 68 WP	F	Peronospora tabacina	WP	40 M 329 640 MZB	Foliar spray	Active growth stage	2-6	7-14 days		400-1250	0.0024- 0.15	7,21,28	

- (a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
- (b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
- (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
- (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
- (f) All abbreviations used must be explained
- (g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
- (i) g/kg or g/l
- (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (k) Indicate the minimum and maximum number of application possible under practical conditions of use
- (l) PHI - minimum pre-harvest interval
- (m) Remarks may include: Extent of use/economic importance/restrictions

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	-
with regard to toxicological data	Xn, R22, Xi, R41
with regard to fate and behaviour data	R53
with regard to ecotoxicological data	R52

Chapter 2.2: Methods of Analysis**Analytical methods for the active substance** (Annex IIA, point 4.1)

Technical as (principle of method)	GC with FID (sum of 2 enantiomers) HPLC (chiral) with UV detection (separate enantiomers)
Impurities in technical as (principle of method)	GC with FID (organic by-products)
Plant protection product (principle of method)	GC with FID (sum of 2 enantiomers)

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	<u>parent compound :</u> GC with NPD LOQ = 0.02 mg/kg for tomatoes, grapes, potatoes, wine, must 0.1 mg/kg for tobacco (green leaves) 0.2 mg/kg for tobacco (dried leaves) <u>total residues as DMA (parent + metabolites) :</u> GC with NPD LOQ = 0.05 mg/kg for all tested matrices or HPLC (2-column switch) with electrochemical detection LOQ = 0.04 mg/kg for all tested matrices, except for peas (haulms & empty pods) and broad beans (whole plant) where LOQ is 0.08 mg/kg and grapes where LOQ is 0.2 mg/kg
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	<u>total residues as DMA (parent + metabolites) :</u> GC with NPD LOQ = 0.05 mg/kg for eggs, fat/skin, muscle tissue 0.1 mg/kg for liver 0.01 mg/kg for milk (provisional)
Soil (principle of method and LOQ)	GC with AFID or CECD or HECD LOQ = 0.05 mg/kg for parent and acid metabolite CGA 62826 (provisional)
Water (principle of method and LOQ)	<u>parent and metabolite CGA 62826 (single compounds)</u> HPLC with UV detection LOQ = 0.1 µg/l <u>parent and metabolite CGA 62826 (sum of both)</u> HPLC (2-column switch) with UV detection LOQ = 0.1 µg/l
Air (principle of method and LOQ)	GC with NPD

Body fluids and tissues (principle of method and LOQ)

LOQ = 10 µg/m ³ (provisional)
not required as mefenoxam is not classified as toxic or highly toxic

Chapter 2.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of absorption:	100% , within 24 h
Distribution:	large
Potential for accumulation:	no accumulation
Rate and extent of excretion:	73-80% within 24 h
Metabolism in animals	ether demethylation, aromatic methyl oxidation, ester demethylation, hydroxylation on meta position of phenyl ring
Toxicologically significant compounds (animals, plants and environment)	parent compound for animals CGA 62826 and CGA 108906 : soil metabolites

Acute toxicity (Annex IIA, point 5.2)

Rat LD ₅₀ oral	Male = 953 mg/kg bw ; Female = 375 mg/kg bw combined = 667 mg/kg bw
Rat LD ₅₀ dermal	> 2000 mg/kg bw
Rat LC ₅₀ inhalation	> 2.29 mg/m ³ (192 mg/kg bw)
Skin irritation	not irritating
Eye irritation	not irritating
Skin sensitization (test method used and result)	M&K = not sensitizer Buelher = not sensitizer

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	liver / small necrotic effects
Lowest relevant oral NOAEL / NOEL	7.25 mg/kg bw/day ; dog , 90 day and 6 month
Lowest relevant dermal NOAEL / NOEL	1000 mg/kg bw/day, rat, 21 day
Lowest relevant inhalation NOAEL / NOEL	no data

Genotoxicity (Annex IIA, point 5.4)

<i>In vitro</i> gene mutation test	negative
<i>In vitro</i> chromosome assay	negative but weak cell cycle arresting activity in CHO cells without S9
<i>In vitro</i> DNA repair assays	negative in human fibroblasts and rat hepatocytes
<i>In vivo</i> genotoxicity tests	negative in micronuclei, nucleus anomalies in bone marrow cells and dominant lethal assay

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target / critical effect	liver / liver hypertrophy and periportal hepatocytic vacuolation
Lowest relevant NOAEL / NOEL	50 ppm = 2 mg/kg bw/day
Carcinogenicity	not carcinogenic

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect	liver / hepatomegaly in F2B females
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Lowest relevant reproductive NOAEL / NOEL	>1250 ppm = 58 mg/kg bw/day
Developmental target / critical effect	maternal body weight reduction
Lowest relevant developmental NOAEL / NOEL	50 mg/kg bw/day

Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7)

.....	No data, not necessary
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Other toxicological studies (Annex IIA, point 5.8)

Enzyme induction in rat liver	increased level of cyt P450 ; induction of PNOD and UDP glucuronyl transferase activities
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Other toxicological studies on metabolites (Annex IIA, point 5.8)

Rat LD ₅₀ oral CGA 108906	combined >2000 mg/kg bw
Rat LD ₅₀ oral CGA 62826	combined >1000 mg/kg bw
Rat LD ₅₀ oral CGA 107'955	combined > 3000 mg/kg bw
Oral NOAEL 28 day, rat CGA 108906	200 mg/kg bw/d
Oral NOAEL 28 day, rat CGA 62826	1000 mg/kg bw/d
In vitro bacterial genotoxicity test CGA 108906	negative
In vitro bacterial genotoxicity test CGA 62826	negative

Medical data (Annex IIA, point 5.9)

No findings

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI	2 mg/kg bw/day	rat, 2 year, oral	100
AOEL	7.5 mg/kg bw/day	90 day, 6 month dog , oral	100
Drinking water limit	0.07 mg/l		
ARfD (acute reference dose)	-	-	-

Dermal absorption (Annex IIIA, point 7.3)

<i>In vivo</i> rat study and <i>in vitro</i> comparative study with rat and human skin	7% low dose ; 8% for high dose For operator exposure a value of 10% is used
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Acceptable exposure scenarios for RIDOMIL GOLD 480 EC (soil application) (including method of calculation)

Operator	E = 0.4 for field crops, ornamentals E = 0.561 for root zones of trees , German model
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Workers	applied onto or into soil , low vapor pressure, not necessary to define re-entry period
Bystanders	due to application technique, no exposure is anticipated

Acceptable exposure scenarios for RIDOMIL GOLD MZ 68 WP (foliar application) (including method of calculation)

Operator	with PPE, vehicle mounted air assisted / orchard (UK model) with PPE vehicle mounted with cab, hydraulic nozzles / field crop (UK model) with PPE hand held hydraulic nozzles, low level (UK model)
Workers	acceptable with PPE (German re-entry model approach)
Bystanders	based on dermal exposure during application (UK model)

Chapter 2.4: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	grapevine, lettuce, potato, tobacco
Rotational crops	winter and spring wheat, lettuce, spring oat, soybeans, corn, sugar beet
Plant residue definition for monitoring	Metalaxyl
Plant residue definition for risk assessment	Metalaxyl
Conversion factor (monitoring to risk assessment)	-grapes : 2 -lettuce : 4 -potato tuber : 1

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	goats, hens
Animal residue definition for monitoring	Total metalaxyl including all the metabolites forming the 2,6-dimethylaniline moiety upon hydrolysis and expressed as metalaxyl equivalents.
Animal residue definition for risk assessment	Total metalaxyl including all the metabolites forming the 2,6-dimethylaniline.
Conversion factor (monitoring to risk assessment)	for commodities of animal origin : 1
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

.....	Residue values in rotational plant parts, at time of harvesting, ranged from 0.275 to up to 7 mg/kg of total metalaxyl with elapse time from the soil treatment of 323 to 432 days. Regarding the important levels of residues found back, further informations about the agricultural practices are required from the notifier.
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Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

.....	Total residues of metalaxyl determined as 2,6-dimethylaniline are stable in several crops stored for up to 3 years when the crops are stored under freezer conditions.
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Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Intakes by livestock ≥ 0.1 mg/kg diet/day: (Residues of total metalaxyl expressed as metalaxyl equiv./kg)	Ruminant: yes/no	Poultry: yes/no	Pig: yes/no
Muscle	0.08-0.17	<0.05-0.13	
Liver	<0.1-1.1	<0.05-0.16	
Kidney	0.11-5.5	-	
Fat	<0.05	*Peritoneal : <0.05-0.34 *skin+attached fat : <0.05-0.40	
Milk	0.02		
Eggs		<0.05	

Intakes by livestock ≥ 0.1 mg/kg diet/day:
(Residues of total metalaxyl expressed as metalaxyl
equiv./kg)

In absence of intake calculations for livestock, no dose
group can be chosen as representative of the likely
highest residue level that may occur in the feedingstuff of
chicken.

Ruminant: yes/no	Poultry: yes/no	Pig: yes/no

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Table and wine grapes	N	Metalaxyl-M : <0.02, 0.04, 0.07, 0.19, 0.30, 0.33 mg/kg for berries	Results from 6 trials carried out in the North of France and Germany. These trials were made following 4 foliar spray applications at the rate of 0.10 kg a.s./ha; PHI : 14 to 31 days. Commodities which were analysed were the berries, must and wine.	1	0.1
	S	Metalaxyl-M : 0.03, 0.04, 0.05, 0.05, 0.06, 0.09, 0.13, 0.15, 0.21, 0.55 mg/kg for berries	Results from 10 trials carried out in the South of France and Italy. These trials were made following 4 foliar spray applications at the rate of 0.10 kg a.s./ha; PHI : 14 to 39 days. Commodities which were analysed were the berries, must and wine.		
Onion	N	Metalaxyl-M : 9 x <0.02 mg/kg for bulb	Results from 9 trials carried out in Switzerland, UK and France. These trials were made following 3 foliar applications at rates of 0.1 and 0.15 kg a.s./ha with 7 to 12 days between applications; PHI : 14 days. Decay curves are given with last sampling 21 days after last application. All the residue values were below the LOD.	0.02*	0.02*

	S	Metalaxyl-M : 7 x <0.02 mg/kg for bulb	Results from 7 trials carried out in Spain, Italy and France. These trials were made following 3 foliar applications at rates of 0.1 and 0.15 kg a.s./ha with 7 to 12 days between applications; PHI : 13,14 days. Decay curves are given with last sampling 21 days after last application. All the residue values were below the LOD.		
Tomato	N	<u>Outdoor</u> : Metalaxyl-M : 5 x <0.02, 0.02 mg/kg	Results from 6 trials carried out in Switzerland and in France. These trials were made following 4 applications at rates of 0.1 and 0.15 kg a.s./ha with 6 to 11 days between applications; PHI : 3 and 7 days. Decay curves are given with last sampling 28 days after last application.	0.1	0.02*
	S	<u>Outdoor</u> : Metalaxyl-M : 9 x <0.02, 0.02 mg/kg	Results from 10 trials carried out in Italy, France and Spain. These trials were made following 4 applications at rates of 0.09 and 0.1 kg a.s./ha with 6 to 11 days between applications; PHI : 3-10 days. Decay curves are given with last sampling 28 days after last application.		
	N+S	<u>Indoor</u> : Metalaxyl-M : 6 x <0.02, 0.02, 0.04, 0.08 mg/kg	Results from 9 trials conducted in France, Italy and Spain. These trials were made following 4 foliar applications at rates between 0.094 and 0.15 kg a.s./ha; PHI of 3 and 7 days.		

Cucumber	N	<u>Indoor</u> : Metalaxyl-M : 0.12, 0.13, 0.15, 0.18, 0.19, 0.32 mg/kg	Results from 6 trials carried out in France. These trials were made following 4 foliar applications at a rate of 0.15 kg a.s/ha with 3 and 10 days between applications; PHI 7 days. Decay curves were given with last sampling 21 days after last application.	0.5	0.15
	S	<u>Outdoor</u> : Metalaxyl-M : 0.10, 0.12, 0.14, 0.15, 0.15, 0.17, 0.18, 0.19, 0.19 mg/kg	Results from 9 trials carried out in Italy and Spain. These trials were made following 4 foliar applications at a rate of 0.15 kg a.s/ha with 3 and 10 days between applications; PHI 6 days. Decay curves were given with last sampling 21 days after last application.		
		<u>Indoor</u> : Metalaxyl-M : 0.11, 0.13, 0.21 mg/kg	Results from 3 trials carried out in Italy and Spain. These trials were made following 4 foliar applications at a rate of 0.15 kg a.s/ha with 3 and 10 days between applications; PHI 3,7 days. Decay curves were given with last sampling 21 days after last application.		
Melon	S	<u>Outdoor</u> : Metalaxyl-M : 5 x <0.02, 0.02, 0.03 mg/kg	Results from 7 trials carried out in France and Italy. These trials were made following 3 foliar applications at rates of 0.113 and 0.125 kg a.s./ha, with 9 to 12 days between applications; PHI of 3 days. Decay curves were given with last sampling 21 days after last application.	0.05	0.02*
		<u>Indoor</u> : Metalaxyl-M : <0.02, 0.02 mg/kg	Results from 2 trials carried out in the South of France. These trials were made following 3 foliar applications at a rate of 0.113 kg a.s/ha, PHI of 3 days.		
Broccoli	S	<u>Outdoor</u> : Metalaxyl-M : <0.02, <0.02, 0.02 mg/kg for flower head <u>Indoor</u> : Metalaxyl-M : 0.02 mg/kg	Results from 4 trials conducted in Spain. These trials were made following 3 foliar applications at a rate of 0.1 kg	0.02*	0.02*

			a.s/ha with 10 days between applications; PHI of 14 and 21 days. Decay curves were given with last sampling 21 days after last application.		
Lettuce	N	<u>Outdoor</u> : Metalaxyl-M : 0.02, 0.02, 0.03, 0.03 mg/kg <u>Indoor</u> : Metalaxyl-M : 0.04, 0.07 mg/kg	Results from 6 trials conducted in the North of France and Germany. These trials were carried out following 3 foliar applications at a rate of 0.1 kg a.s/ha with 8 to 13 days between applications; PHI of 14, 15 days. Decay curves were given with last sampling 21 days after last application.	0.05	0.02
	S	<u>Outdoor</u> : Metalaxyl-M : 4 x <0.02, 0.03 mg/kg	Results from 6 trials carried out in the South of France, Italy and Spain. These trials were carried out following 3 foliar applications at rates of 0.75 and 0.1 kg a.s/ha with 8 to 13 days between applications; PHI of 14 days. Decay curves were given with last sampling 21 days after last application. One trial couldn't be taken into account as the residue value (0.16) was considered as an "outlier" according to the Dixon Q-test.		
Spinach	S	<u>Seed treatment</u> : Metalaxyl-M : 3 x <0.02 mg/kg <u>Foliar treatment</u> : Metalaxyl-M : 4 x <0.02, 0.03, 0.03 mg/kg	<u>Foliar treatment</u> : results from 6 trials conducted in the South of France. These trials were carried out following 2 foliar applications at a rate of 0.1 kg a.s/ha, PHI of 20 and 21 days. Decay curves were given with last sampling 21 days after the last application.	0.05	0.02*
Globe artichoke	S	Metalaxyl-M : 4 x <0.02 mg/kg for flower head.	Results from 4 outdoor trials carried out in Italy and Spain. These trials were conducted following 3 foliar sprays at a rate of 0.1 kg a.s/ha, with 8 to 12 days between applications; PHI of 20 days.	0.02*	0.02*

			All the residues of metalaxyl-M were below the LOD.		
Potato	N	Metalaxyl-M : 11 x <0.02 mg/kg for tuber	Results from 11 trials carried out in Switzerland, Germany and UK. These trials were made following 4 to 5 foliar spray applications at rates of 0.075 and 0.1 kg a.s/ha; PHI of 7, 14 and 28 days. All the residues of metalaxyl-M were below the LOD.	0.02*	0.02*
	S	Metalaxyl-M : 5 x <0.02 mg/kg for tuber	Results from 5 trials conducted in Italy, Spain and France. These trials were made following 3 to 4 foliar spray applications at rates of 0.075 and 0.1 kg a.s/ha; PHI of 17, 20, 25 and 35 days. All the residues of metalaxyl-M were below the LOD.		

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the critical GAP

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.2 mg/kg b.w./day
TMDI (European Diet) (% ADI)	-for the WHO European diet : 0.29% of ADI -for the German diet for a 4-6 years old girl : 0.214% of ADI -for the Pesticides Safety Directorate Consumer Exposure Model : 0.19% and 0.033 % of ADI respectively for children and infants from UK.
NEDI (% ADI)	-
Factors included in NEDI	-
ARfD	-
Acute exposure (% ARfD)	-

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Studies on the effects of industrial processing on the metalaxyl-M residues are not required since the TMDI is below 10 % of the ADI. 4 processing studies are proposed and concern the identification and characterization of metabolites of metalaxyl in cigarettes containing tobacco treated with metalaxyl. These studies are out of interest.			

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Table and wine grapes	1
Onion	0.02*
Tomato	0.1
Cucumber	0.5
Melon.	0.05
Broccoli	0.02*
Lettuce	0.05
Spinach	0.05
Globe Artichoke	0.02*
Potato	0.02*

Chapter 2.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1) (metalaxyl-M)

Mineralization after 100 days	Up to 22-33% after 84 d
Non-extractable residues after 100 days	63-73% after 84 d
Relevant metabolites - name and/or code, % of applied (range and maximum)	CGA 62826 : Max 22.91-40.36%

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation	(Metalaxyl) Degradation pathway similar to the pathway under aerobic conditions, however at lower rate
Soil photolysis	(Metalaxyl-M) No photodegradation was observed

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Method of calculation	First order kinetics
Laboratory studies (range or median, with n value, with r^2 value)	DT _{50lab} (20-25°C, aerobic, metalaxyl): 7-58.4 d, 9 values, median = 20 d DT _{50lab} (15°C, aerobic, metalaxyl): 33-42 d, 2 values, median = 38 d
	DT _{50lab} (20°C, aerobic, CGA62826): 4.2-102 d, 6 values, median = 14.9d
	DT _{90lab} (20-25°C, aerobic, metalaxyl): 35.7-140 d, 5 values, median = 45 d
	DT _{50lab} (10°C, aerobic, metalaxyl): 43 d, 1 value
	DT _{50lab} (10°C, aerobic, CGA62826): 62.1 d, 1 value
	DT _{50lab} (20°C, anaerobic): -
	degradation in the saturated zone: -
Field studies (state location, range or median with n value)	DT _{50f} : Germany, metalaxyl, 19.5-86.9 d, 4 values California, metalaxyl, 38.5-38.8 d, 2 values Minnesota, metalaxyl, 113 d, 1 value North Carolina, metalaxyl, 38.3-39.1 d, 2 values Median = 38.7 d; Realistic worst case : 39.4 d Germany, CGA62826, 10.4-36.4 d, 2 values California, CGA62826, 27.9-34.6 d, 2 values Minnesota, CGA62826, - North Carolina, CGA62826, 128-142 d, 2 values Median = 31.2 d
	DT _{90f} : Germany, metalaxyl, 64.7-288.7 d, 4 values California, metalaxyl, 127.8-128.8 d, 2 values Minnesota, metalaxyl, - North Carolina, metalaxyl, - Median = 128.3 d
	Canada, Switzerland, The Netherlands, 3-13 appl./season, 200-250 g a.s./ha/appl., metalaxyl, 8 trials maximum a.s. concentration in top soil : 0.13-0.44 mg a.s./kg soil
Soil accumulation and plateau concentration	

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K _f /K _{oc}	K _f (metalaxyl-M) 0.1-7.6 K _{oc} (metalaxyl-M) = 20-1299
K _d	K _d (metalaxyl-M) = 1.8-18.4

CEC dependence (yes / no) (if yes type of dependence)

Kf (CGA62826) = 0.02-0.9
Koc (CGA62826) = 3-72
Kd (CGA62826) = 1-11.4

Yes

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching

Metalaxyl, 200 mm rainfall, 2 days, 4 soils : 0.4-92% RR in the leachate

Aged residues leaching

Metalaxyl, 508 mm rainfall, 4 soils : 7.7-76.7% RR in the leachate
Metalaxyl-M, 508 mm rainfall, 4 soils : 12.1-61.4% RR in the leachate

Lysimeter/ field leaching studies

4 lysimeters, appl. rate: 330-365 g a.s./ha/season :
Concentration in the leachate of one year :
metalaxyl : <0.01 to 0.05 µg/l
CGA 62286 : 0.25-4.12 µg/l
CGA108906 : 0.48-1.11 µg/l

Field leaching studies received low weight in the final assessment

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation

First order kinetics, DT50 = 38.5 d

Application rate

0.120 kg a.s./ha, 4 appl. with 7 days interval, 70% a.s. reaching soil surface in grape (foliar use metalaxyl-M)

PEC_(s)

	Single application Actual	Single Application Time weighted average	Multiple Application Actual	Multiple application Time weighted average
Initial	0.112 mg a.s./kg soil	0.112	0.112	Max conc after the 4 th appl. : 0.374 mg a.s./kg soil
Short term 24h	0.110	0.111	0.110	
2d	0.108	0.110	0.108	
4d	0.104	0.108	0.104	
Long term 7d	0.099	0.105	0.210	
28d	0.068	0.088	0.330	
50d			0.222	
100d			0.090	

Method of calculation

First order kinetics, DT50 = 38.5 d

Application rate

1 kg a.s./ha, 1 appl., 100 % a.s. reaching soil surface in orchard, ornamental and field crops (soil use metalaxyl-M)

PEC_(s)

	Single Application Actual	Single Application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	1.33 mg a.s./kg soil	1.33	-	-
Short term 24h	1.31	1.32		
2d	1.29	1.31		
4d	1.24	1.29		
Long term 7d	1.18	1.25		
28d	0.81	1.05		
50d	0.54	0.88		
100d	0.22	0.62		

The PEC CGA 62826 are similar to the PEC a.s.

Route and rate of degradation in water (Annex IIA, point 7.2.1)Hydrolysis of active substance and relevant metabolites (DT₅₀) (state pH and temperature)

(Metalaxyl-M) No hydrolysis at any pH

Photolytic degradation of active substance and relevant metabolites

(Metalaxyl-M) No photolysis

Readily biodegradable (yes/no)

(Metalaxyl-M) No

Degradation in - DT₅₀ water- DT₅₀ and DT₉₀ water are similar to the corresponding

water/sediment - DT₉₀ water

- DT₅₀ whole system

- DT₉₀ whole system

Mineralization

Non-extractable residues

Distribution in water / sediment systems (active substance)

Distribution in water / sediment systems (metabolites)

DT whole system.
DT50 (metalaxyl) = 47.5 d; DT50 (CGA 62826) > 1 yr -
Max 3% after 112 d
max 8.8% after 112 d
Distributed in water and sediment phases (max 20.4% at day 7)
CGA62826 distributed in water (max 23.0% at day 56) and sediment phases (max 68.8% at day 112)

PEC (surface water) (Annex IIIA, point 9.2.3)

Method of calculation

Application rate

Main routes of entry

First order kinetics, DT50 = 47.5 d (whole sed/water system)
Grape, 120 g a.s./ha, 4 appl., 5 m buffer zone, 5% drift, metalaxyl-M
Spray drift

PEC_(sw)	Single application Actual	Single Application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.0020 mg a.s./l	0.0020	0.0020	Max conc after the 4 th appl : 0.0069
Short term 24h	0.0019	0.0020	0.0019	
2d	0.0019	0.0020	0.0019	
4d	0.0019	0.0019	0.0019	
Long term 7d	0.0018	0.0019	0.0038	
14d			0.0054	
21d			0.0069	
28d			0.0062	
42d			0.0051	

Method of calculation

Application rate

Main routes of entry

First order kinetics, DT50 = 47.5 d (whole sed/water system)
Soil uses in orchard, ornamental and field crops, 1 appl., 1 kg a.s./ha, 1 m buffer zone, 4% drift, metalaxyl-M
Spray drift

PEC_(sw)	Single application Actual	Single Application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.013	0.013	-	-
Short term 24h	0.013	0.013		
2d	0.013	0.013		
4d	0.013	0.013		
Long term 7d	0.012	0.013		
14d	0.011	0.012		
21d	0.010	0.011		
28d	0.009	0.011		
42d	0.007	0.010		

PEC CGA62826 = initial PEC a.s.

PEC (sediment)

Method of calculation

Application rate

Max PEC
Soil uses in orchard, ornamental and field crops, 1 appl., 1 kg a.s./ha, 1 m buffer zone, 4% drift Sediment depth : 2 cm Max % AR in sediment : metalaxyl-M 20.4%; CGA 62826 58.8%

PEC _(sed)	Single application	Single Application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Max PEC a.s.	0.031 mg a.s./kg sed	-	-	-
Max PEC CGA 62826	0.106 mg a.s./kg sed	-	-	-

PEC (ground water) (Annex IIIA, point 9.2.1)Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)

Application rate

Modelling with LEACHP (Norway, Belgium, Italy) Modelling with PESTLA (The Netherlands)
Potatoes, 4 appl., 100 g a.s./ha DT50 (a.s.) 5-10 d; Koc (a.s.) 25-500 DT50 (CGA62826) 5-15 d; Koc (CGA62826) 25-200

PEC_(gw)

Maximum concentration

Average annual concentration

-
Norway : a.s. : 0 to 1.1 µg/l; CGA 62826 : 0 to 2.06 µg/l Belgium : a.s. : 0 to 0.205 µg/l; CGA 62826 : 0 to 0.437 µg/l Italy : a.s. : 0 to 0.196 µg/l; CGA 62826 : 0 to 0.59 µg/l The Netherlands : a.s. : 0 to 0.653 µg/l; CGA 62826 : 0 to 9.78 µg/l

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)

Application rate

Modelling with PESTLA
The Netherlands, potatoes, 3 appl., 100 g a.s./ha UK, potatoes, 5 appl., 76 g a.s./ha France, vines, 4 appl., 100 g a.s./ha Germany, vines, 3 appl., 120 g a.s./ha Italy, vines, 4 appl., 100 g a.s./ha

PEC_(gw)

Maximum concentration

Average annual concentration
(max/70th percentile)

-
<u>DT50 a.s.: 20 d and Koc a.s.:69</u> < 0.001 µg/l for 5 scenarios <u>DT50 a.s. :20 d and Koc a.s. :20</u> The Netherlands, potatoes : a.s. : 0.089/0.085 µg/l UK, potatoes : a.s. : 0.21/0.11 µg/l France, vines : a.s. : 0.043/0.010 µg/l Germany, vines : a.s. : 1.62 10 ⁻³ / 5.46 10 ⁻⁴ µg/l Italy, vines : a.s. : 0.14/0.065 µg/l

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air	-
Quantum yield of direct phototransformation	-
Photochemical oxidative degradation in air (metalaxyl-M)	Latitude: Season: DT ₅₀ = 4-6 h By the Atkinson method assuming 12h dark /12 h light
Volatilization (metalaxyl)	from plant surfaces: 35% volatilization (after 24 h, glasshouse conditions)
	From soil: 49% volatilization (35°C, 30l/h air flow)

PEC (air)

Method of calculation	Not required : a.s. slightly volatile, short half-life
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PEC_(a)

Maximum concentration	-
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Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil : active substance, CGA 62826, CGA 108906 Water : active substance and CGA 62826
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Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	-
Surface water (indicate location and type of study)	Europe : compilation of drinking water and surface water monitoring studies in several European countries. A few detections of metalaxyl were made at low level (generally below 0.1 µg/l)
Ground water (indicate location and type of study)	Europe : compilation of drinking water and surface water monitoring studies in several European countries. A few detections of metalaxyl were made at low level (generally below 0.1 µg/l) USA : wells monitoring in areas with high metalaxyl uses in citrus and tobacco Canada : monitoring in 2 areas where metalaxyl is used in potatoes (wells, piezometers, drainage water)
Air (indicate location and type of study)	-

Chapter 2.6: Effects on Non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals	LD50 = 375 mg a.s./kg bw
Acute toxicity to birds	LD50 = 1419 mg a.s./kg bw
Dietary toxicity to birds	LC50 = 981 mg a.s./kg food
Reproductive toxicity to birds	NOEC = 300 mg a.s./kg food

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Application rate (kg as/ha)	Crop	Category (e.g. insectivorous bird)	Time-scale	TER	Annex VI Trigger
Foliar spray to control airborne diseases					
0.120	grapes	small bird (< 100g) eating leaves and leafy crops	acute	1272	10
		small bird (< 100g) eating leaves and leafy crops	short term	264	10
		small bird (< 100g) eating leaves and leafy crops	long term	81	5
0.110	potatoes	small bird (< 100g) eating leaves and leafy crops	acute	1387	10
		small bird (< 100g) eating leaves and leafy crops	short term	288	10
		small bird (< 100g) eating leaves and leafy crops	long term	88	5
Soil treatment against soilborne diseases					
1	wide variety of field crops, ornamental and orchard crops	small bird (< 100g) eating leaves and leafy crops	acute	153	10
		small bird (< 100g) eating leaves and leafy crops	short term	32	10
		small bird (< 100g) eating leaves and leafy crops	long term	10	5
Foliar spray to control airborne diseases					
0.120	grapes	small mammal (< 100g) eating leaves and leafy crops	acute	336	10
		small mammal (< 100g) eating leaves and leafy crops	short term	67	10
0.110	potatoes	small mammal (< 100g) eating leaves and leafy crops	acute	367	10
		small mammal (< 100g) eating leaves and leafy crops	short term	73	10
Soil treatment against soilborne diseases					
1	wide variety of field crops, ornamental and orchard	small mammal (< 100g) eating leaves and leafy crops	acute	40	10

	crops	small mammal (< 100g) eating leaves and leafy crops	short term	8	10
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Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests				
fish	Metalaxyl-M	96 h	LC50	> 100
Daphnia	Metalaxyl-M	48 h	LC50	> 100
Algae	Metalaxyl-M	72 h	EC50	36
Fish	Metalaxyl	30 d	NOEC	9.1
Daphnia	Metalaxyl	42 d	NOEC	1.2
Microcosm or mesocosm tests				
Not required				

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Foliar spray to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP).						
0.120	grapes	Oncorhynchus mykiss	Acute	5	14493	100
		Daphnia magna	Acute		14493	100
		Selenastrum capricornutum	Acute		5217	10
		Lepomis macrochirus	Chronic		1319	10
		Daphnia magna	Chronic		174	10
0.110	potatoes	Oncorhynchus mykiss	Acute	1	13158	100
		Daphnia magna	Acute		13158	100
		Selenastrum capricornutum	Acute		4737	10
		Lepomis macrochirus	Chronic		1197	10
		Daphnia magna	Chronic		158	10
Soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC)						
1	orchard and ornamental crops	Oncorhynchus mykiss	Acute	1	10000	100
		Daphnia magna	Acute		5882	100
		Selenastrum capricornutum	Acute		2118	10
		Lepomis macrochirus	Chronic		650	10
		Daphnia magna	Chronic		100	10
2 max conc. in drain water = 87 µg/l	bare soil	Oncorhynchus mykiss	Acute	-	1149	100
		Daphnia magna	Acute		1149	100

Selenastrum capricornutum	Acute	414	10
Lepomis macrochirus	Chronic	105	10
Daphnia magna	Chronic	14	10

Bioconcentration

Bioconcentration factor (BCF)	15
Annex VI Trigger for the bioconcentration factor	100
Clearance time (CT ₅₀)	< 3 days
(CT ₉₀)	-
Level of residues (%) in organisms after the 14 day depuration phase	12%

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Acute oral toxicity	LD50 (72 h, EC480) > 127 µg a.s./bee
Acute contact toxicity	LD50 (72 h, EC480) > 200 µg a.s./bee

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.120	Grapes	Oral	15	50
		Contact	15	50
0.110	Potatoes	Oral	14	50
		Contact	14	50
1	Orchard, ornamental and field crops	Oral	17	50
		Contact	10	50

Field or semi-field tests
Not required

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Poecilus cupreus	Adults	EC 480	1 kg a.s./ha	Mortality	0%	30%
Typhlodromus pyri	Protonymph	EC 480	1 kg a.s./ha	Beneficial capacity	91.26%	30%
Aphidius colemani	Adults	EC 480	1 kg a.s./ha	Beneficial capacity	100%	30%
Orius insidiosus	Nymphs	EC 480	1 kg a.s./ha	Beneficial capacity	15.8%	30%
Aphidius rhopalosiphi	Adults	EC 480	1 kg a.s./ha	Beneficial capacity	-34.2%	30%
Poecilus cupreus	Adults	WP 64/4	3.5 kg form/ha	Mortality	0%	30%

Orius insidiosus	Nymphs	WP 64/4	3.5 kg form/ha	Beneficial capacity	18.3%	30%
Aphidius colemani	Adults	WP 64/44	3.5 kg form/ha	Beneficial capacity	94.6%	30%
Aphidius rhopalosiphi	Adults	WP 64/4	3.5 kg form/ha	Beneficial capacity	-14.5%	30%

EC 480 : EC containing 480 g/l metalaxyl-M

WP 64/4 : WP containing 640 g/kg mancozeb and 40 g/kg metalaxyl-M

Field or semi-field tests

Typhlodromus pyri (grape, 5 appl. of 2.5 kg/ha WP64/4) E = 118%

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity

LC50 = 830 mg a.s./kg soil

Reproductive toxicity

Not required

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
Foliar spray to control airborne diseases				
0.120	Grapes	acute	2219	10
0.110	Potatoes	acute	2862	10
Soil treatment against soilborne diseases				
10	Root zones in orchard	acute	62	10
1	Orchard and ornamentals	acute	624	10

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralization

< 25% after 100 days, at rates of 500 and 5000 g a.s./ha

Carbon mineralization

< 25% after 100 days, at rates of 500 and 5000 g a.s./ha