

ANNEX B

Metalaxyl-M

B.8 Ecotoxicology

B.8.1 Effects on birds (Annex IIA 8.1; Annex IIIA 10.1)

B.8.1.1 Acute oral toxicity (Annex IIA 8.1.1)

CGA 329351 - Acute oral toxicity (LD₅₀) to the Bobwhite quail (Johnson, 1995)

Guidelines :

USEPA Guidelines, Subdivision E, Series § 71-1 (1982-1988)

GLP :

Yes

Material and Methods :

Test Substance: metalaxyl-M, chemical purity : 97.1%

Test species : Bobwhite quails, *Colinus virginianus*

Sex, weight, age : 5_ and 5_ birds/concentration, 192-229 g, 15-month old

Applied concentrations : 0, 521, 729, 1020, 1429, 2000 mg a.s. /kg bw;

Type of application : single oral dose, by intubation in corn oil

Time of exposure : one single application, monitoring during 14 days

Findings :

Mortality : Eight mortalities occurred at 2000 mg/kg and four at each of 1020 and 1429 mg/kg.

Clinical signs of toxicity, including subdued behaviour, unsteadiness, convulsions and inability to stand, were observed at all dose levels.

Body weight : Slight bodyweight losses occurred at 2000 mg/kg.

Food consumption : Food consumption remained unaffected by treatment with metalaxyl-M.

Autopsy : No abnormalities were observed in any birds examined *post mortem*.

Conclusions :

The study is acceptable. LD₅₀ (metalaxyl-M) = 1419 mg a.s./kg bw (95% Conf. limits : 1172-1827)

NOEL < 521 mg a.s. /kg bw

An acute oral toxicity test with the northern bobwhite (Palmer et al. , 1995a)

Guidelines :

USEPA Guidelines, Subdivision E, Series § 71-1 (1982-1988)

GLP :

Yes

Material and Methods :

Test Substance: metalaxyl-M, chemical purity : 96.6%

Test species : Bobwhite quails, *Colinus virginianus*

Sex, weight, age : 5_ and 5_ birds/concentration, 169-227 g, 29-week old

Applied concentrations : 0, 93 - 156 - 259 - 432 - 720 - 1200 - 2000 mg a.s. /kg bw;

Type of application : single oral dose, by intubation in corn oil

Time of exposure : one single application, monitoring during 14 days

Findings :

Mortality : There were no mortalities in the control group and in the 93, 156, 259, 432 and 720 mg a.s. /kg bw dosage groups. There was, however 90% mortality (9 of 10) at the 1200 mg ai/kg bw test dosage, and 100% (10 of 10) at the 2000 mg a.s./kg bw test dosage.

Clinical symptoms : At the 93, 156, and 259 mg a.s./kg bw test dosages, there were no over signs of toxicity observed during the test period.

At the 432 mg a.s./kg and higher test dosages, symptoms of toxicity were observed. These signs of toxicity were: reduced reaction to external stimuli (sound and movement), wing droop, loss of coordination, lethargy, depression, a ruffled appearance, lower limb weakness, panting, loss of righting reflex, prostrate posture, shallow and rapid respiration and coma. The accentuation of these symptoms correlated clearly with increased doses. At the lower dose levels (93 to 720 mg/kg) they disappeared one day after application.

Bodyweight losses and reduction in *feed consumption* occurred at 432 mg/kg bw dosage groups and above. *Post mortem* observations were not performed.

Conclusions :

Study is acceptable. LD₅₀ (metalaxyl-M) = 981 mg a.s./kg bw, (95% confidence limits 720-1200)

NOEL = 156 mg a.s. /kg bw

Two additional studies on the acute toxicity of metalaxyl were submitted.

Acute oral LD₅₀ Mallard duck CGA 48988 technical (Beavers, 1977a)

Guidelines :

Not specified.

GLP :

No

Material and Methods :

Test Substance: metalaxyl, chemical purity : 96.9%

Test species : Mallard ducklings (*Anas platyrhynchos*)

Sex, weight, age : 10 birds/concentration, 200 g, 14-day old

Applied concentrations : 0, 215, 464, 1000, 2150 and 4640 mg/kg; (the description of the dosage procedure is confuse) test with 5 concentrations of dieldrin were used as positive control

Type of application : single oral dose, by intubation in corn oil

Time of exposure : one single application, monitoring during 8 days

Findings :

Mortality : Dead animals were found at 1000 mg/kg dosage and above.

Clinical symptoms : Symptoms were observed at all dose levels : lethargy, convulsions, lower limb rigidity or weakness, loss of righting reflex, prostrate posture, loss of coordination, depression, reduced reaction to external stimuli.

Bodyweight and feed consumption : There was a dose related reduction in total food consumption and body weight gain at all dose levels.

Post mortem observations were not performed.

Conclusion :

The study is generally in accordance with the SETAC recommendations. The study is considered as additional information not strictly necessary to the evaluation of the a.s. metalaxyl-M.

LD₅₀ (Metalaxyl) = 1466 mg a.s. /kg bw (confidence limits 1128-1906 mg/kg).

NOEL (Metalaxyl) < 215 mg a.s. /kg bw

Acute oral LD₅₀ in the Japanese quail of technical CGA 48988 (Ullmann, 1976)

The study presents numerous shortcomings : no purity of the a.s., no description of the bird characteristics, no body weight, food consumption and health report.

The acute oral LD₅₀ for the Japanese quail (both sexes) observed over a period of 7 days is 923 mg metalaxyl / kg (798-1069); NOEL (Metalaxyl) < 600 mg a.s. /kg bw

B.8.1.2 Avian dietary toxicity (5day) (Annex IIA 8.1.2)

A dietary LC₅₀ study with the northern bobwhite (Palmer et al., 1995b)

Guidelines :

OECD Guideline 205; USEPA Guidelines, Subdivision E, Subsection § 71-2; ASTM Standard E857-87

GLP :

Yes

Material and Methods :

Test Substance: metalaxyl-M, chemical purity : 96.6%

Test species : Bobwhite quails, *Colinus virginianus*

Sex, weight, age : 10 chicks/group, 19 g, 10-day old

Applied concentrations : untreated control, 316 - 562 - 1000 - 1780 - 3610 - 5620 mg/kg diet.;

Type of application : Samples of the test diet were collected to verify test concentration (81-96% of nominal concentration) , homogeneity (91-98% at 316 ppm, 85-88% at 5620 ppm) and stability (92-112% of the nominal concentration in samples collected from the feeders on day 5) of the test substance.

Time of exposure : Short-term feeding test (5 days with exposition by the feed + 3 days observations)

Findings :

Mortality : No mortality in the control and in any test concentrations.

Body weight - feed consumption: food consumption and body weight gain are similar in control and all test groups.

Clinical signs : no overt signs of toxicity in any concentrations. Normal behaviour in all test groups.

Conclusions :

Study is acceptable. LC_{50} (5d- metalaxyl-M) > 5620 mg a.s./kg feed

NOEC = 5620 mg a.s./kg feed

“8-day-feeding toxicity” in the Japanese quail of technical CGA-48988 (Ullmann, 1976)

Guidelines :

“Procedure for Evaluation of Acute Toxicity of Pesticides to Fish and Wildlife”, United States Department of the Interior Fish and Wildlife Service, December 14 1964

GLP :

No

Material and Methods :

Test Substance : metalaxyl

Test species : Japanese quail (*Coturnix coturnix japonica*)

Sex, weight, age : 3 _ and 7 _ birds/concentration, 127 g, 50-60-day old

Applied concentrations : untreated control, 1000, 6000, 10000 mg/kg feed. The experiment was performed in parallel with 4 dieldrin concentrations as positive control.

Type of application : dietary application, no a.s. analysis of the food is reported.

Time of exposure : Short-term feeding test (5 days with exposition by the feed + 3 days observations)

Findings :

Mortality : One animal died accidentally in group 1000 ppm.

Body weight and feed consumption : food consumption and body weight gain are similar in control and all test groups.

Clinical signs : No substance-related toxic symptoms

Egg production : Eggs were counted daily during the whole study period (pre and post exposure)

A slight decrease of the egg production is observed in the test groups as compared to control. The phenomenon has to be checked in the reproductive studies.

Conclusions :

Although the report is not written according to the up-to-date standards, it gives all the information necessary to evaluate the experiment. The study is acceptable.

LC_{50} (5d- metalaxyl) > 10000 mg a.s./kg feed

NOEC = 10000 mg a.s./kg feed

Eight-day dietary LC_{50} - Bobwhite quail CGA-48988 technical final report (Beavers, 1977b)

Guidelines :

Not specified.

GLP :

No

Material and Methods :

Test Substance: metalaxyl, (purity : 96.6%)

Test species : Bobwhite quail (*Colinus virginianus*)

Sex, weight, age : 10 birds/group, 28 g, 14-day old

Applied concentrations : untreated control, 464, 1000, 2150, 4640, 10000 mg/kg feed; The experiment was performed in parallel with 5 dieldrin concentrations as positive control.

Type of application : dietary application, no a.s. analysis of the food is reported.

Time of exposure : Short-term feeding test (5 days with exposition by the feed + 3 days observations)

Findings :

Mortality : Cases of cannibalism occur in one control group (2/10 dead) and in the 2150 ppm test group (2/10 dead).

These test groups present lower body weight gain.

Body weight and feed consumption : food consumption is similar in control and all test groups.

A reduction of body weight gain is observed in the highest concentration group (10000 ppm).

Clinical signs : No symptoms of toxicity. The behaviour is normal.

Conclusions :

The study is acceptable.

LC_{50} (5d, metalaxyl) > 10000 mg a.s./kg feed;

NOEC = 4640 mg a.s./kg feed

Eight-day dietary LC₅₀ - Mallard duck CGA-48988 technical (Beavers, 1977c)

Guidelines :

Not specified.

GLP :

No

Material and Methods :

Test Substance: metalaxyl, purity : 96.9%

Test species : Mallard ducklings (*Anas platyrhynchos*)

Sex, weight, age : 10 birds/ group, 219 g, 14-day old

Applied concentrations : untreated control, 464, 1000, 2150, 4640 and 10000 mg/kg feed; The experiment was performed in parallel with 5 dieldrin concentrations as positive control.

Type of application : dietary application, no a.s. analysis of the food is reported.

Time of exposure : Short-term feeding test (5 days with exposition by the feed + 3 days)

Findings :

Mortality : No mortality in control and all test concentration groups.

Body weight : A reduction of body weight gain occurred at all dose levels but was more pronounced at the 4640 and 10000 ppm dose levels

Feed consumption : There was a reduction in feed consumption at 4640 and 10000 ppm dose levels.

Clinical signs : No symptoms of toxicity. The behaviour is normal.

Conclusions :

The study is acceptable.

LC₅₀ (5d, metalaxyl) > 10000 mg a.s./kg feed

NOEC < 464 mg a.s./kg feed

B.8.1.3 Subchronic and reproductive toxicity (Annex IIA 8.1.3)

Two reproductive studies performed with metalaxyl were submitted by the notifier. A study evaluating the reproductive toxicity of the R-enantiomer (metalaxyl-M) is not required because the acute and dietary toxicity studies performed with metalaxyl and metalaxyl-M reveal that both compounds present a similar low toxicity to birds

One-generation reproduction study - Bobwhite quail CGA-48988 technical. (Beavers, 1980a)

Guidelines :

Not specified in the report. The study was performed according to the recommendations of the OECD 206 guideline.

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : not given

Test species : Bobwhite quail (*Colinus virginianus*)

Sex, weight, age : 12 pens of 1 _ and 2 _ birds/treatment group, 197 g, 5-month old

Applied concentrations : untreated control, 100, 300, 900 mg a.s./kg in the feed

Type of application : dietary application

Time of exposure : Test birds were fed treated diet *ad libitum* for 10 weeks during the pre-egg laying period and for the 8-week egg production period. Control birds were fed untreated basal diet throughout.

Findings :

Table B.8.1.3-1 : Major effects of metalaxyl observed during the reproduction study of Bobwhite quail

Endpoints	Concentrations (mg a.s. /kg feed)
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	0	100	300	900
Adults				
Mortality	no compound related mortality			
Clinical symptoms	no compound related symptoms			
Body weight		Statistically significant lower body weight in comparison with control. Nevertheless, the actual mean difference was only 8 g		
Food consumption	no compound related difference in food consumption			
Reproduction Parameters				
Number of eggs laid	814	803	834	834
Mean egg weight	9.9	9.8	9.8	10.0
Eggs cracked	35	74	84	52
Eggs cracked of eggs laid (%)	4	9	10	6
Mean egg shell thickness (mm)	0.220	0.211	0.217	0.215
Eggs set	734	684	704	734
Viable embryos	635	607	492	633
Viable embryos of eggs set (%)	87	89	70	86
Live 3-week embryos	621	596	490	623
Live 3-week embryos of viable embryos (%)	98	98	99.6	98
Normal hatchlings	386	424	343	429
Normal hatchlings of live 3-week embryos (%)	62	71	70	69
14-day old survivors	286	286	258	271
14-day old survivors of hatchlings reared (%)	94	89	90	84*
14-day old survivors per female	15	16	13	15
Mean chick body weights at hatching (g)	6.6	6.3**	6.3**	6.3*
Mean chick body weights at 14 days (g)	19	20	19	19

* : significant ($p < 0.05$); ** : highly significant ($p < 0.01$)

Conclusions :

The study is acceptable. No reproduction parameter showed compound related differences which are biologically relevant. The NOEC (18 weeks, metalaxyl) = 900 mg a.s./kg feed.

One-generation reproduction study - Mallard duck CGA-48988 technical. (Beavers, 1980b)

Guidelines :

Not specified in the report. The study was performed according to the recommendations of the OECD 206 guideline.

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : not given

Test species : Mallard duck (*Anas platyrhynchos*)

Sex, weight, age : 5 pens of 2 _ and 5 _ birds/treatment group, 1165 g, 6-month old

Applied concentrations : untreated control, 100, 300, 900 mg a.s./kg in the feed

Type of application : dietary application

Time of exposure : Test birds were fed treated diet *ad libitum* for 10 weeks during the pre-egg laying period and for the 8-week egg production period. Control birds were fed untreated basal diet throughout.

Findings :

Table B.8.1.3-1 : Major effects of metalaxyl observed during the reproduction study of Mallard duck

Endpoints	Concentrations (mg a.s./kg feed)			
	0	100	300	900
Adults				
Mortality	no compound related mortality			
Clinical symptoms	no compound related symptoms			
Body weight, at termination (g)	1223	1206*	1287	1220
Food consumption	no compound related difference in food consumption			
Reproduction Parameters				
Number of eggs laid	666	786	818	705
Mean egg weight	59.5	60.6	61.7	59.0
Eggs cracked	27	18	39	47
Eggs cracked of eggs laid (%)	4	2	5	7
Mean egg shell thickness (mm)	0.365	0.372	0.362	0.346*
Eggs set	591	722	731	616
Viable embryos	544	662	660	570
Viable embryos of eggs set (%)	92	92	90	93
Live 3-week embryos	537	651	649	546
Live 3-week embryos of viable embryos (%)	99	98	98	96**
Normal hatchlings	379	473	387	319
Normal hatchlings of live 3-week embryos (%)	71	73	60	58*
14-day old survivors	292	300	313	255
14-day old survivors of hatchlings reared (%)	97	98	98	98
14-day old survivors per female	15	19	15	13
Mean chick body weights at hatching (g)	35	35	34*	33**
Mean chick body weights at 14 days (g)	213	215	211	207

* : significant ($p < 0.05$); ** : highly significant ($p < 0.01$)

The NOEC is 300 mg a.s./kg due to the presence of effects at 900 mg a.s./kg for the following reproduction parameters live 3-week embryos of viable embryos (%), normal hatchlings of live 3-week embryos (%)

Conclusions :

The study is acceptable. The NOEC (18 weeks, metalaxyl) = 300 mg a.s./kg feed.

B.8.1.4 Acute oral toxicity of the preparations (Annex IIIA 10.1.1)

A study with the formulation RIDOMIL GOLD MZ 68 WP, containing mancozeb and metalaxyl-M, was performed. The results are shown in the table B.8.1.8-3

B.8.1.5 Supervised cage or field trials (Annex IIIA 10.1.2)

Not required.

B.8.1.6 Acceptance of bait, granules or treated seeds by birds (palatability test) (Annex IIIA 10.1.3)

Not required. Although seed treatment formulations containing metalaxyl are existing, the notifier did not submit annex III dossier for this use in the original dossier. The evaluation of this type of formulation should be done at Member State level.

B.8.1.7 Effects of secondary poisoning (Annex IIIA 10.1.4)

This study is not required because

- TER for birds consuming contaminated food are favourable.
- Bioaccumulation potential of the a.s. is limited

B.8.1.8 Summary of effects to birds - exposure and risk assessment for birds (Annex IIIA 10.1)

Table B.8.1.8-1 : Summary of effects of metalaxyl-M to birds.

Test species	Test System	Results	References
<i>Colinus virginianus</i>	Acute oral toxicity	LD ₅₀ = 1419 mg a.s./kg bw	Johnson, 1995
<i>Colinus virginianus</i>	Acute oral toxicity	LD ₅₀ = 981 mg a.s./kg bw	Palmer et al., 1995a
<i>Colinus virginianus</i>	5 day dietary toxicity	LC ₅₀ > 5620 mg a.s./kg feed	Palmer et al., 1995b

Table B.8.1.8-2 : Summary of effects of metalaxyl to birds.

Test species	Test System	Results	References
<i>Anas platyrhynchos</i>	Acute oral toxicity	LD ₅₀ = 1466 mg a.s./kg bw	Beavers, 1977a
<i>Coturnix coturnix japonica</i>	5 day dietary toxicity	LC ₅₀ > 10000 mg a.s./kg feed	Ullmann, 1976
<i>Colinus virginianus</i>	5 day dietary toxicity	LC ₅₀ > 10000 mg a.s./kg feed	Beavers, 1977b
<i>Anas platyrhynchos</i>	5 day dietary toxicity	LC ₅₀ > 10000 mg a.s./kg feed	Beavers, 1977c
<i>Colinus virginianus</i>	18-week reproduction study	NOEC = 900 mg a.s./kg feed	Beavers, 1980a
<i>Anas platyrhynchos</i>	18-week reproduction study	NOEC = 300 mg a.s./kg feed	Beavers, 1980b

Table B.8.1.8-3 : Summary of effects of RIDOMIL GOLD MZ 68 WP to birds. (*)

Test species	Test System	Results	References
<i>Colinus virginianus</i>	Acute oral toxicity	LD ₅₀ > 2000 mg a.s./kg bw	Johnson, 1995

(*) : No detailed description in the monograph; study performed with a formulation containing 64% mancozeb and 4% metalaxyl-M.

The risk assessment for birds is based on the following assumptions :

- small birds (< 100 g) with a food consumption of 30% bw
- the contamination of the food is estimated according to Hoerger and Kenaga (1972)

- the uses of metalaxyl-M susceptible to contaminate the food of birds are :

1 - The foliar spray to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP). Grapes and potatoes are the main crops treated with this type of formulation.

is 2 - The soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC). The formulation
was applied on the soil at sowing or (pre)-planting or at the base of the trees. The application rate of 1000 g/ha taken into account in the evaluation of the risk to birds.

to - The application of the a.s. in the root zone of orchard trees (1 g/m²) was not considered as a route leading a high contamination of the bird food.

The risk to leaf-eating and insectivorous birds resulting from the exposure to the a.s. in crops treated with foliar spray formulation is negligible (TER acute = 1272-15930; TER short term = 264-3303; TER long term = 81-1010). The evaluation of the risk resulting from mancozeb should be evaluated at Member State level.

The risk to leaf-eating, insectivorous birds resulting from the exposure to the a.s. in crops treated with soil treatment formulation is negligible (TER acute = 153-3638; TER short term = 32-363; TER long term = 10-111)

Table B.8.1.8-3 : TER birds for the metalaxyl-M

Application rate (g a.s./ha)	Crop	Organism	Time scale	TER	Annex VI trigger
Foliar spray to control airborne diseases					
120 g metalaxyl-M/ha 2-4 appl./season	grapes	small bird (< 100g) eating leaves and leafy crops	acute	1419/1.116 = 1272	10
		small bird (< 100 g) eating small seeds and small insects	acute	1419/1.044 = 1359	10
		small bird (< 100 g) eating big seeds and big insects	acute	1419/0.0972 = 14600	10
		small bird (< 100g) eating leaves and leafy crops	short term	981/3.72 = 264	10
		small bird (< 100 g) eating small seeds and small insects	short term	981/3.48 = 282	10
		small bird (< 100 g eating big seeds and big insects	short term	981/0.324 = 3028	10
		small bird (< 100g) eating leaves and leafy crops	long term (*)	300/3.72 = 81	5
		small bird (< 100 g) eating small seeds and small insects	long term (*)	300/3.48 = 86	5
		small bird (< 100 g) eating big seeds and big insects	long term (*)	300/0.324 = 926	5
110 g metalaxyl-M/ha 2-5 appl./season	potatoes	small bird (< 100g) eating leaves and leafy crops	acute	1419/1.023 = 1387	10
		small bird (< 100 g) eating small seeds and small insects	acute	1419/0.957 = 1483	10
		small bird (< 100 g) eating big seeds and big insects	acute	1419/0.0891 = 15930	10
		small bird (< 100g) eating leaves and leafy crops	short term	981/3.41 = 288	10

Application rate (g a.s./ha)	Crop	Organism	Time scale	TER	Annex VI trigger
		small bird (< 100 g) eating small seeds and small insects	short term	981/3.19 = 308	10
		small bird (< 100 g) eating big seeds and big insects	short term	981/0.297 = 3303	10
		small bird (< 100g) eating leaves and leafy crops	long term (*)	300/3.41 = 88	5
		small bird (< 100 g) eating small seeds and small insects	long term (*)	300/3.19 = 94	5
		small bird (< 100 g) eating big seeds and big insects	long term (*)	300/0.297 = 1010	5
		Soil treatment against soilborne diseases			
1000 g a.s./ha (typical high dose rate) 1 appl./season	wide variety of field crops, ornamental and orchard crops	small bird (< 100g) eating leaves and leafy crops	acute	1419/9.3 = 153	10
		small bird (< 100 g) eating small seeds and small insects	acute	1419/8.7 = 163	10
		small bird (< 100 g) eating big seeds and big insects	acute	1419/0.39 = 3638	10
		small bird (< 100g) eating leaves and leafy crops	short term	981/31 = 32	10
		small bird (< 100 g) eating small seeds and small insects	short term	981/29 = 34	10
		small bird (< 100 g eating big seeds and big insects	short term	981/2.7= 363	10
		small bird (< 100g) eating leaves and leafy crops	long term (*)	300/31 = 10	5
		small bird (< 100 g) eating small seeds and small insects	long term (*)	300/29 = 10	5
		small bird (< 100 g) eating big seeds and big insects	long term (*)	300/2.7 = 111	5

(*) : Data derived from the metalaxyl dossier

B.8.2 Effects on aquatic organisms (fish, aquatic invertebrates, algae) (Annex IIA 8.2; Annex IIIA 10.2)

B.8.2.1 Acute toxicity of the active substance and metabolites, degradation or reactions products to fish (Annex IIA 8.2.1)

The notifier submitted the following studies to assess the acute toxicity of the a.s. to fish :

- two 96-hour static studies evaluating the acute toxicity of metalaxyl-M to the rainbow trout;
- two studies evaluating the acute toxicity of metalaxyl to several warm and cold water fish studies
- three studies evaluating the acute toxicity of major metabolites (CGA 62826, CGA 67868, CGA 108906) to rainbow trout.

Acute toxicity of metalaxyl-M to fish

Report on the acute toxicity test of CGA 329351 tech. (enantiomer of CGA 48988) to Rainbow trout (*Oncorhynchus mykiss*) (Rufli, 1994b)

Guidelines :

OECD guideline 203

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M; chemical purity : 97.3%

Test species : Rainbow trout (*Oncorhynchus mykiss*)

Number of organisms, weight, length, loading :

7 fish/concentration, 1.70 g (1.41-1.94); 59 mm (55-61); 0.40 g/l

Type of test : static acute toxicity test (96 hours)

Applied and measured concentrations :

Nominal test concentrations were 0 and 100 mg a.s./l (limit test)

The concentrations as determined by HPLC analyses were found to be 94% of the nominal concentration at the beginning and end of the exposure period. The results are therefore presented using the nominal concentration.

Test conditions :

Oxygen content was between 87 - 100% of saturation value.

pH was in the range 7.7 - 8.2 for the duration of the study.

Temperature was 15°C throughout the study.

Total hardness was 182 mg CaCO₃/l .

Photoperiod was 16 hours daily

Analytical methods : HPLC analysis

Findings :

Mortality and behavioral observations : No mortality cases nor behavioral observations were reported.

Conclusions :

The study is acceptable.

LC₅₀ (96h, metalaxyl-M) > 100 mg a.s./l

NOEC (96h, metalaxyl-M) = 100 mg a.s./l

A 96-hour static acute toxicity test with the rainbow trout, *Oncorhynchus mykiss* (Drottar et al., 1995a)

Guidelines :

USEPA Guidelines Acute toxicity for freshwater fish; ASTM Standard E729-88a

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 96.6%

Test species : Rainbow trout, *Oncorhynchus mykiss*

Number of organisms, weight, length, loading : 2 replicates of 10 fish/concentration and control, 0.15-0.20 g, 22-25 mm, -

Type of test : Static system (96 hours)

Applied and measured concentrations :

The following nominal concentrations were tested : 0, 16, 26, 43, 72, 121 mg a.s./l

The concentrations in test media ranged on day 0 from 94 to 102% and after 96 h from 94 to 100%.

Test conditions :

temperature : $12^{\circ}\text{C} \pm 1^{\circ}\text{C}$,

pH : 8.4-8.5

oxygen content : The dissolved oxygen concentration exceeded 60% of saturation.

total hardness : 133 mg/l CaCO_3

Photoperiod : 16 hours light/day

Analytical methods : HPLC analysis

Findings :

Mortality : No mortality at any concentration.

Behavioral observations : Rainbow trouts (18/20) exposed to 121 mg a.s./l appeared darker than the control fish.

Loss of equilibrium, lethargy and erratic swimming were observed transiently on a few fish at 121 mg a.s./l

Conclusions :

LC_{50} (96h, metalaxyl-M) > 121 mg a.s./l

NOEC (96h, metalaxyl-M) = 72 mg a.s./l

Acute toxicity of metalaxyl to fish

Acute toxicity to rainbow trout, carp, catfish, bluegill and guppy of technical CGA 48988 (Sachsse, 1976)

Guidelines :

The method is a modification of the procedure then proposed by the United States Department of the Interior Fish and Wildlife Service, reported in "Procedure for Evaluation of Acute Toxicity of Pesticides to Fish and Wildlife" (14 December 1964).

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : not given

Test species : Several fish species (see table)

Number of organisms : 12 fish/test concentration

Type of test : static system (96 hours)

pH : 7.1-7.8

oxygen content : determination of the O₂ concentration was performed.

total hardness : -

Photoperiod : -

Analytical methods : not performed

Findings :

TableB.8.2.1-1 : Test description and main findings

Fish species	Weight, length	Metalaxyl concentrations	Temperature	Endpoints
<i>Oncorhynchus mykiss</i>	3.1 g; 62 mm	65, 87, 100 mg/l	14 ± 2°C	LC ₅₀ > 100 mg a.s./l
<i>Cyprinus carpio</i>	3.3 g; 57 mm	49, 87, 100 g/l	14 ± 2°C	LC ₅₀ > 100 mg a.s./l
<i>Ictalurus melas</i>	2.8 g; 68 mm	87, 100 g/l	14 ± 2°C	LC ₅₀ > 100 mg a.s./l
<i>Lepomis macrochirus</i>	2.5 g; 43 mm	87, 100 g/l	22 ± 2°C	LC ₅₀ > 100 mg a.s./l
<i>Lebistes reticulatus</i>	-; -	10, 65, 87, 100 mg/l	22 ± 2°C	LC ₅₀ > 100 mg a.s./l

Behavioral observations : Toxic signs and symptoms were observed. The distribution of these symptoms by dosage and by fish species is not reported

Conclusions :

This study showed the low toxicity of metalaxyl to several fish species. This study presents some shortcomings : no purity of the a.s., no report of the toxic signs....

Acute toxicity of CGA-48988 technical to Bluegill (*Lepomis macrochirus*) (Buccafusco, 1978)

Guidelines :

U.S. EPA (1975) Methods for acute toxicity tests with fish, macroinvertebrates and amphibians. Ecological Research Series (EPA-660/3-75-009), 61 pp

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : 94.4%

Test species : Bluegill (*Lepomis macrochirus*)

Number of organisms, weight, length, loading : 10 fish/concentration, 0.99 g (0.23-1.7), 44 mm (30-59), 0.51 g/l

Type of test : 96-hour static test

Applied and measured concentrations :

The following nominal concentrations were tested : 0, 90, 130, 170, 180, 180, 195, 220 mg a.s./l

The concentrations in test media were not determined.

Test conditions :

temperature : 22 ± 1°C

pH : 6.7-7.4

oxygen content : 9.1 to 0.3-4.1mg/l at the termination of the study. Oxygen saturation is very low after 48 h and 96 h (3.4-17% in the test concentrations)

total hardness : 28-44 mg/l CaCO₃

Photoperiod : -

Analytical methods : Not performed

Findings :

Mortality : Mortality of 100% at the concentrations of 170 mg/l and above. No mortality at concentrations 90 and 130 mg a.s./l. Mortality is correlated with the oxygen saturation figures.

Behavioral observations : dark coloration, fish at surface and fish respiring rapidly were recorded at concentrations 90 and 130 mg a.s./l. Similar symptoms also appeared before dead in the upper concentrations.

Conclusions :

The quality of the study is questionable.

LC₅₀ (96h, metalaxyl) = 150 mg a.s./l

NOEC (96h, metalaxyl) < 90 mg a.s./l

Acute toxicity of the metabolites to fish

Acute toxicity of CGA 62826 to Rainbow trout (*Oncorhynchus mykiss*) in a semi-static test (96 hours) (Memmert et al., 1991a)

Guidelines :

OECD guideline 203

GLP :

Yes

Material and Methods :

Test substance : acid metabolite CGA 62826, chemical purity : 99.6% \pm 2%

Test species : Rainbow trout (*Oncorhynchus mykiss*)

Number of organisms, weight, length, loading :

10 fish/concentration, 1.4 \pm 0.2 g, 4.9 \pm 0.4 cm, 0.35 g/l

Type of test : 96-hour semi-static test ;

Test substance was stored at 0-5°C in the dark in absence of stability information. Since the stability of the test substance in water was unknown at the start of the test, a semi-static test procedure was chosen with test medium renewal every 24 hours.

Applied and measured concentrations :

The nominal concentrations tested were 0, 9.5, 17.0, 31.0, 56.0, 100.0 mg/l

The measured concentrations were in the range 95.3-99.0 % of the nominal concentrations

Test conditions :

temperature : 13.0-15.3 °C,

pH : 7.2-8.6

oxygen content : 7.8-9.9 mg/l

total hardness : 180 mg/l CaCO₃

Photoperiod : 16 hours daily

Analytical methods : HPLC analysis

Findings :

Mortality and behavioral observations : No mortality cases nor behavioral observations were reported.

Conclusions :

The study is acceptable.

LC₅₀ (96h, CGA 62826) > 100 mg/l

NOEC (96h, CGA 62826) > 100 mg/l

Acute toxicity of CGA 67868 to Rainbow trout (*Oncorhynchus mykiss*) in a semi-static test (96 hours) (Memmert et al., 1992a)

Guidelines :

OECD guideline 203

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 67868, chemical purity : 98.9%

Test species : Rainbow trout (*Oncorhynchus mykiss*)

Number of organisms, weight, length, loading :

10 fish/concentration, 1.1 \pm 0.2 g, 5.0 \pm 0.2 cm, 0.275 g/l

Type of test : 96-hour semi-static test. Since the stability of the test substance in water was unknown at the start of the test, a semi-static test procedure was chosen with test medium renewal every 24 hours.

Applied and measured concentrations :

The nominal concentrations tested were 0, 9.4, 16.8, 30.7, 55.4, 98.9 mg/l

The measured concentrations were in the range 96.8-101.0 % of the nominal concentrations

Test conditions :

temperature : 14.6-15.5 °C,

pH : 7.8-8.5

oxygen content : 7.8-8.9 mg/l

total hardness : 210 mg/l CaCO₃

Photoperiod : 16 hours daily

Analytical methods : HPLC analysis

Findings :

Mortality : No mortality occurred at any concentration.

Behavioral observations : Symptoms of intoxication (changed body colour and slightly irregular swimming behaviour) were observed in a few of the fish at a range of test concentrations (9.4, 30.7, 55.4 and 98.9 mg/l).

However, these effects were not observed at 16.8 mg/l. The effects observed at 9.4 mg/l, only at 96 hours, were not considered as relevant when establishing the NOEC.

Conclusions :

The study is acceptable.

LC₅₀ (96h, CGA 67868) > 98.9 mg/l

NOEC (96h, CGA 7868) = 16.8 mg/l

Report on the acute toxicity test of CGA 108906 tech. (metabolite of CGA 48988) to Rainbow trout (*Oncorhynchus mykiss*) (Rulfi, 1994a)

Guidelines :

OECD guideline 203

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 108906, chemical purity : 99.9%

Test species : Rainbow trout (*Oncorhynchus mykiss*)

Number of organisms, weight, length, loading :

7 fish/concentration, 0.64 g (0.43-0.75); 41 mm (32-46); 0.30 g/l

Type of test : static acute toxicity test (96 hours)

Applied and measured concentrations :

Nominal test concentrations were 0 and 100 mg a.s./l (limit test)

The concentrations as determined by HPLC analyses were found to be 93.4-96.6 % of the nominal concentration at the beginning and end of the exposure period. The results are therefore presented using the nominal concentration.

Type of test : 96-hour static system

Test conditions :

temperature : 14°C,

pH : 7.2-8.2

oxygen content : 83-102% oxygen saturation

total hardness : 180 mg CaCO₃/l

Photoperiod : 16 hours light daily

Analytical methods : HPLC analysis

Findings :

Mortality and behavioral observations : No mortality cases nor behavioral observations were reported.

Conclusions :

The study is acceptable.

LC₅₀ (96h, CGA 108906) > 100 mg/l

NOEC (96h, CGA 108906) = 100 mg/l

B.8.2.2 Chronic toxicity to fish (Annex IIA 8.2.2)

The toxicity of CGA-48988 to Fathead minnow (*Pimephales promelas*) eggs and fry (LeBlanc et al., 1980)

Guidelines :

The study was performed prior the publication of OECD guideline 210.

GLP :

no

Material and Methods :

Test substance : metalaxyl, purity : 90.1%

Test species : Fathead minnow (*Pimephales promelas*)

Number of organisms, age :

The egg and fry exposure was initiated within 48 hours after egg fertilization and continued through 30 days post-hatch.

60 eggs/cup; 2 cups /concentration were used to evaluate the hatching percentage. To initiate the 30-day fry exposure, 40 fry were selected from each egg cup and transferred to the respective aquaria upon completion of hatching.

Type of test : flow-through test

Applied and measured concentrations :

The measured concentrations were 9.1, 4.6, 2.1, 1.1, 0.59 mg a.s./l.

During the test metalaxyl concentrations in test water were in the range of 78 - 104% of nominal (target) concentrations.

Test conditions :

temperature : 24-25°C,

pH : 7.1-7.6

oxygen content : 8.8-9.0 mg/l

total hardness : -

Photoperiod : Twelve hours per day of cool white fluorescent light

Analytical methods :

Gas chromatography

Findings :

Table B.8.2.2-1 : Hatchability of eggs and survival and growth of fry exposed to metalaxyl

Mean measured concentration	Percentage eggs hatched	Percentage survival over 30 days	Mean length after 30 days	Mean weight after 30 days
9.1	93	100	24	100
4.6	93	96	24	105
2.1	94	98	24	100
1.1	95	99	24	100
0.59	96	98	23	100
control	93	100	23	95

Behavioral observations : The daily observation of the appearance and behaviour did not reveal adverse effects.

Conclusions :

The study is acceptable. The study complies with the main recommendations of the OECD 210 guideline.

Hatchability of eggs and survival and growth of fry exposed to mean measured concentrations of metalaxyl as high as 9.1 mg/l were unaffected as compared to control eggs.

B.8.2.3 Bioaccumulation potential in fish (Annex IIA 8.2.3)

Two studies dealing with the bioaccumulation of metalaxyl in fish were provided.

Accumulation and elimination of ^{14}C -residues by Bluegill sunfish (*Lepomis macrochirus*) exposed to $\text{O-}^{14}\text{C}$ -CGA-48988 (Ladd et al., 1979a)

Guidelines :

Not specified.

GLP :

no

Material and Methods :

Test substance : metalaxyl, specific activity : 46.5 $\mu\text{Ci}/\text{mg}$

Test species : Bluegill sunfish (*Lepomis macrochirus*)

Number of organisms, weight, length : two sub-populations of fish (2 X 8 fish) were exposed to one metalaxyl concentration; mean weight : 5.6 ± 2.5 g; length 7.3 ± 0.9 cm

Type of test : Bioaccumulation test (29 days) in a flow through system

Measured concentrations : fish was exposed to 0.97 mg a.s./l

Test conditions :

temperature : - ; pH : 7.0-7.2; oxygen content : > 60 % saturation; total hardness : 31-35 mg CaCO_3/l

Analytical methods : Liquid Scintillation Counting for the water and fish. Due to the low concentrations recovered in the fish, no further TLC characterization of the recovered radioactivity was performed

Findings :

Table B.8.2.3-1 : Bioaccumulation potential of metalaxyl in fish

	water	Muscle (edible part)	Viscera, carcass (non-edible part)	Whole fish
mean residue concentration during the 29 day exposure period (mg/kg)	0.97	0.71	7.87	3.59
residue concentration after 3 days depuration (mg/kg)	0	0.24	1.38	0.70
residue concentration after 14 days depuration (mg/kg)	0	0.25	0.70	0.43
mean BCF (days 1-29)		0.73	8.11 (max BCF at day 14 = 15)	3.70 (max BCF at day 14 = 6)
depuration half-life		< 3 days	< 3 days	< 3 days

Determination of radioactivity made at day 7, 21 and 29 showed that the radioactivity is mainly recovered in the viscera.

The maximum BCF determined in non-edible part at day 14 is 15.

Significant elimination of ^{14}C residues was observed during the first 3 days of depuration . The depuration half-lives were between 1 and 3 days

Conclusions :

The main deviations from the OECD 305 guideline are : only one test concentration was used. Only 2 replicates were present and not 4. This study was not absolutely necessary for the evaluation of the dossier

The bioaccumulation potential of metalaxyl is low. This conclusion is confirming the results of the log Pow study (log Pow of metalaxyl-M = 1.71).

Kinetics of $\text{O-}^{14}\text{C}$ -CGA-48988 in a model aquatic ecosystem (Ladd, 1979b)

This study evaluated the bioaccumulation of metalaxyl in fish in presence of sediment. The study was not evaluated in detail because it does not answer to a specific requirement of the Directive. The study confirms results derived from other studies i.e. the fact that metalaxyl is distributed in both water and sediment phase, and the fact that the bioaccumulation potential is low, the main part of metalaxyl being found in the viscera.

B.8.2.4 Acute toxicity to invertebrates (Annex IIA 8.2.4)

Acute toxicity of metalaxyl-M to aquatic invertebrates

Report on the acute toxicity test of CGA 329351 tech. (enantiomer of CGA 48988) on *Daphnia* (*Daphnia magna* Straus 1820) (Grade, 1994b)

Guidelines :

OECD guideline n° 202

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 97.3%

Test species : *Daphnia magna* Straus

Number of organisms, weight, length, age : 20 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were in the range $100 \pm 20\%$ of the nominal concentrations.

The nominal concentrations were 0, 10, 18, 32, 58, 100 mg a.s./l

Test conditions :

Temperature : $20^{\circ}\text{C} \pm 1^{\circ}\text{C}$; pH : 7.9-8.0; oxygen content : Water aerated with clean air for at least 24 hours before use; total hardness : 240 mg CaCO_3/l ; Photoperiod : 16 hours light

Analytical methods : HPLC with UV detection.

Findings and conclusion:

EC_{50} (48h) > 100 mg a.s./l

NOEC (48h) = 100 mg a.s./l

A 48-hour static toxicity test with the cladoceran, *Daphnia magna* (Drott et al., 1995b)

Guidelines :

US EPA guideline (Acute toxicity test for freshwater invertebrates)

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 96.6%

Test species : *Daphnia magna* Straus

Number of organisms, weight, length, age : 20 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations ranged from 81 to 93% of the nominal concentrations.

The nominal concentrations were 0, 14, 23, 39, 65, 113 mg a.s./l

Test conditions :

Temperature : $20^{\circ}\text{C} \pm 1^{\circ}\text{C}$; pH : 8.1-8.4; oxygen content : 7.5-8.4 mg/l ; total hardness : 132 mg CaCO_3/l ;

Photoperiod : 16 hours light

Analytical methods : HPLC with UV detection.

Findings and conclusion:

EC_{50} (48h) > 113 mg a.s./l

NOEC (48h) = 39 mg a.s./l

A 96-hour shell deposition test with the eastern oyster, *Crassostrea virginica* (Drott et al., 1995)

Guidelines :

The test method is based on procedures outlined in Series 72 of Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms; and Standard Evaluation Procedure, Acute Toxicity Test for Estuarine and Marine Organisms.

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 97.1%

Test species : Eastern oyster (*Crassostrea virginica*)

Number of organisms, age : 1 replicate containing 20 oysters per concentration; animals in the range 31-44 mm length

Type of test : Flow through test (96 hours)

Nominal and measured concentrations :

The measured concentrations ranged from 103-115% of the nominal concentrations.

The nominal concentrations were 0, 5.4, 8.6, 14, 24, 37 mg a.s./l

Test conditions :

Temperature : 22 ± 1 °C; pH : 8.2-8.4; oxygen content : 5.8-7.4 ; Photoperiod : 16 hours light; Salinity : 2.1‰

Analytical methods : HPLC determination

Findings and conclusions :

Reduction of shell deposition was observed in all the treatments. The reduction was statistically significant at 14 mg a.s./l

EC₅₀ (96 hours) = 9.7 mg a.s./l (50% reduction of shell deposition)

NOEC (96 hours) = 8.6 mg a.s./l

Acute toxicity of metalaxyl to aquatic invertebrates

Acute toxicity of CGA-48988 to the water flea (*Daphnia magna*) (LeBlanc, 1978)

Guidelines :

Methods for acute toxicity tests with fish, macroinvertebrates and amphibians Ecological research series (US EPA, 1975). The procedure is quite similar to OECD guideline 202, nevertheless with some shortcomings.

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : 94.4%

Test species : *Daphnia magna* Straus

Number of organisms, weight, length, age : 15 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal concentrations :

The nominal concentrations were 0, 4.8, 8.2, 13, 22, 36, 61, 100, 170 mg a.s./l

Test conditions :

Temperature : $22 \pm 1^\circ\text{C}$; pH : 8.2-8.4 ; oxygen content : 8.2-8.5 mg/l; total hardness : 178 mg/l CaCO₃; Photoperiod : -

Analytical methods : not performed

Findings and conclusions :

Precipitate and surface film were observed in the 100 and 170 mg/l test vessels. The quality of this study is questionable.

EC₅₀ (48h) = 28 mg a.s./l

NOEC (48h) = 8.2 mg a.s./l

Metalaxyl technical: acute toxicity to Mysid shrimp (*Mysidopsis bahia*) under flow through conditions (Hoberg, 1989)

Guidelines :

The test protocol (Protocol # 100788/72.3 MYS-FA) closely followed FIFRA Guideline 72-3 and US EPA/OTS guideline - Federal Register (1985) Mysid shrimp acute toxicity test.

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 96.1%

Test species : mysid shrimp (*Mysidopsis bahia*)

Number of organisms, age : 2 replicates, each containing 10 organisms, per concentration; 1-2 days old

Type of test : Flow through test (96 hours)

Nominal and measured concentrations :

The measured concentrations averaged $87\% \pm 9$ of the nominal concentrations.

The measured concentrations were 0, 11, 12, 21, 34, 52 mg a.s./l

Test conditions :

Temperature : 23-25 °C; pH : 8.0-8.1 ; oxygen content : 5.5-6.9 mg/l; Photoperiod : 16 hours light; Salinity : 3.1‰

Analytical methods : GC determination

Findings and conclusions :

LC₅₀ (96h) = 25 mg a.s./l

NOEC (96) = 11 mg a.s./l

Metalaxyl technical: acute toxicity to Eastern oysters (*Crassostrea virginica*) under flow through conditions (Dionne, 1989)

Guidelines :

The test protocol (Protocol # 102787/72.3 OY-SD) meets the primary requirements of US EPA's Environmental

Effects Guidelines, as defined in the Standard Evaluation Procedure *Acute Toxicity Estuarine and Marine Organisms (Mollusc 96 Hour Flow-Through Shell Deposition Study)".

GLP:

Yes

Material and Methods:

Test substance : metalaxyl, chemical purity : 96.1%

Test species : Eastern oyster (*Crassostrea virginica*)

Number of organisms, age : 2 replicates, each containing 20 organisms, per concentration; immature animals <1 year old

Type of test : Flow through test (96 hours)

Nominal and measured concentrations :

The measured concentrations were ranging from 80.5-98.0% of the nominal concentrations.

The measured concentrations were 0, 1.4, 1.8, 3.1, 5.6, 9.4 mg a.s./l

Test conditions :

Temperature : 20-21 °C; pH : 7.7-8.0; oxygen content : 5.8-7.4 ; Photoperiod : 16 hours light; Salinity : 3.1-3.3‰

Analytical methods : GC determination

Findings and conclusions:

Only one mortality case was observed at the highest concentration treatment.

A dose related reduction of shell deposition was observed at the concentrations 1.8 to 9.4 mg/l.

EC₅₀ (96 hours) = 5.6 mg a.s./l (50% reduction of shell deposition)

NOEC (96 hours) = 1.4 mg a.s./l

Acute toxicity of metabolites to aquatic invertebrates

48-hour acute toxicity of CGA 62826 to *Daphnia magna* (OECD immobilisation test) (Memmert et al., 1991b)

Guidelines :

OECD guideline n° 202

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 62826, chemical purity : >95%

Test species : *Daphnia magna* Straus

Number of organisms, age : 20 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 89-104.5% of the nominal concentrations.

The nominal concentrations were 0, 62.5, 125, 250, 500, 1000 mg a.s./l

Test conditions :

Temperature : 19.9-21.5°C; pH : from 6.3 to 3.4, adjustment of pH was made at start of the experiment ; oxygen content : > 8.3 mg/l; total hardness : 250 mg/l CaCO₃; Photoperiod : 16 hours light

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EC₅₀ (48h, CGA 62826) = 852 mg/l

NOEC (48h, CGA 62826) = 125 mg/l

48-hour acute toxicity of CGA 67868 to *Daphnia magna* (OECD immobilisation test) (Memmert et al., 1991c)

Guidelines :

OECD guideline n° 202

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 67868 chemical purity : 98.9%

Test species : *Daphnia magna* Straus

Number of organisms, age : 20 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 97.5-105.0% of the nominal concentrations.

The measured concentrations were 0, 8.0, 25.3, 80.0, 253, 800 mg a.s./l

Test conditions :

Temperature : 19.9-20°C; pH : 8.0-8.2 ; oxygen content : > 9.3 mg/l; total hardness : 250 mg/l CaCO₃; Photoperiod : 16 hours light

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EC₅₀ (48h, CGA 67868) = 158 mg/l

NOEC (48h, CGA 67868) = 25 mg/l

Report on the acute toxicity test of CGA 108906 tech. (Metabolite of CGA 48988) on *Daphnia* (*Daphnia magna* Straus 1820) (Grade, 1994a)

Guidelines :

OECD guideline n° 202

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 108906 chemical purity : 99.9%

Test species : *Daphnia magna* Straus

Number of organisms, age : 20 daphnids (0-24 h old)/concentration

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 97-100% of the nominal concentrations.

The nominal concentrations were 0, 10, 18, 32, 58, 100 mg a.s./l

Test conditions :

Temperature : 21-22°C; pH : 6.3-8.0 ; oxygen content : 103-100% saturation; total hardness : 250 mg/l CaCO₃;

Photoperiod : 16 hours light

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EC₅₀ (48h, CGA 108906) > 100 mg/l

NOEC (48h, CGA 108906) = 100 mg/l

B.8.2.5 Chronic toxicity to aquatic invertebrates (Annex IIA 8.2.5)

The chronic toxicity of CGA-48988 to the water flea (*Daphnia magna*) (LeBlanc, 1980)

Guidelines :

Not specified in the report

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 90.1%

Test species : *Daphnia magna* Straus

Number of organisms, age : 20 daphnids per treatment (0-24 h old)

Type of test : Flow through test - 2 generation study

Nominal and measured concentrations :

The measured concentrations averaged 98% of the nominal concentrations.

The measured concentrations were 0, 1.2, 2.7, 4.5, 10, 18 mg a.s./l

Test conditions :

Temperature : 22 ± 1°C; pH : 8.0-8.2 ; oxygen content : 8.5-8.7 mg/l; total hardness : 170 mg/l CaCO₃; Photoperiod : -

Analytical methods : GC determination

Findings :

Survival :

Table B.8.2.5-1 : Percentage survival of first and second generation water flea continuously exposed to metalaxyl

Concentration (mg a.s. /l)	First generation			Second generation		
Days	7	14	21	29	35	42
0	95	94	84	96	91	86
1.2	90	88	85	95	90	82
2.7	100	98	94	96	80	75
4.5	99	91	84	94	88	86
10.0	60	52	45	66	49	31
18.0	5	0	0	0	0	0

Reproduction parameters : Offsprings production of the first and second generations was significantly reduced at 2.7, 4.5, 10.0 and 18.0 mg/l.

Surviving daphnids exposed to 10 mg/l were obviously smaller than control daphnids throughout the exposure.

Conclusions :

The study is not performed according to the OECD guideline No 202. Some shortcomings in the report on reproduction parameters .

NOEC (42 days) = 1.2 mg a.s./l

B.8.2.6 Effects on algal growth (Annex IIA 8.2.6)

Effects of metalaxyl-M on algal growth

Report on the growth inhibition test of CGA 329351 tech. (enantiomer of CGA 48988) to green algae (*Scenedesmus subspicatus*) (Grade, 1994d)

Guidelines :

OECD guideline n° 201

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 97.3%

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 3 replicates/concentration; 10600 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 87-96% of the nominal concentrations.

The nominal concentrations were 0, 4.4, 9.6, 21, 46, 100 mg a.s./l

Test conditions :

Temperature : $22 \pm 1^\circ\text{C}$; pH : 7.7-8.2 ; Lighting : continuous illumination with fluorescent light, 8000 lux

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EbC_{50} (72h) = 36 mg a.s./l

NOEbC (72 h) = 9.6 mg a.s./l

Effects of metalaxyl on algal growth

Report on the growth inhibition test of CGA 48988 tech. to green algae (*Scenedesmus subspicatus*) (Grade, 1995)

Guidelines :

OECD guideline n° 201

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 96.1%

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 3 replicates/concentration; 11400 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 92-104% of the nominal concentrations.

The nominal concentrations were 0, 5.8, 10, 18, 32, 58, 100 mg/l

Test conditions :

Temperature : $23 \pm 1^\circ\text{C}$; pH : 8.0-8.8 ; Lighting : continuous illumination with fluorescent light, 8000 lux

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EbC_{50} (72h) = 46 mg a.s./l

NOEbC (72 h) < 5.8 mg a.s./l

Report on the growth inhibition test of algae (*Scenedesmus subspicatus*) by CGA 48 988 (Hitz, 1981)

Guidelines :

AFNOR-Norm T 90-304

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : -

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 4 replicates/concentration; 6×10^6 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 74-148 % of the nominal concentrations. Two outliers at 21-30%

The nominal concentrations were 0, 10, 18, 32, 58, 100 180, 320 mg/l

Test conditions :

Temperature : $24 \pm 3^\circ\text{C}$; pH: - ; Lighting : 16 hours light, 4000 lux

Analytical methods : GC with thermoionic detection

Findings and conclusions :

The study was not performed according to a recent guideline. The quality of the study is bad.

IC₅₀ (96 h) = 42.69 mg a.s./l

Effects of metabolites on algal growth

Toxicity of CGA 62826 to *Scenedesmus subspicatus* (algae growth inhibition test) (Memmert, 1991d)

Guidelines :

OECD guideline n° 201

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 62826, chemical purity : > 95%

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 3 replicates/concentration; 10000 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 95-100% of the nominal concentrations.

The nominal concentrations were 0, 10.0, 32.0, 100, 320, 1000 mg/l

Test conditions :

Temperature :22-23°C (deviates to 26°C at day 1); pH :7.8. The pH needs to be adjusted at the start of the experiment ; Lighting : continuous illumination with fluorescent light, 8000 lux

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EbC₅₀ (72h, CGA 62826) > 1000 mg/l

NOEbC (72 h, CGA 62826) = 100 mg/l

Toxicity of CGA 67868 to *Scenedesmus subspicatus* (algae growth inhibition test) (Memmert, 1992b)

Guidelines :

OECD guideline n° 201

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 67868, chemical purity : 98.9%

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 3 replicates/concentration; 10000 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 98-100% of the nominal concentrations.

The nominal concentrations were 0, 9.9, 31.6, 98.9, 316.5, 989 mg/l

Test conditions :

Temperature : 21.0-23.6; pH :7.8-7.9 at start, 8.1-11.0 at end. This increase is caused by the consumption of CO₂ by algae ; Lighting : continuous illumination with fluorescent light, 8000 lux

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EbC₅₀ (72h, CGA 67868) = 195.4 mg/l

NOEbC (72 h, CGA 67868) = 9.9 mg/l

Report on the growth inhibition test of CGA 108906 tech. (metabolite of CGA 48988) to green algae (*Scenedesmus subspicatus*) (Grade, 1994c)

Guidelines :

OECD guideline n° 201

GLP :

Yes

Material and Methods :

Test substance : metabolite CGA 108906, chemical purity : 99.9%

Test species : green algae (*Scenedesmus subspicatus*)

Number of organisms : 3 replicates/concentration; 12000 cells/ml at initiation

Type of test : Static test

Nominal and measured concentrations :

The measured concentrations were ranging from 96-102% of the nominal concentrations.

The nominal concentrations were 0, 4.4, 9.6, 21, 46, 100 mg/l

Test conditions :

Temperature : $23 \pm 1^{\circ}\text{C}$; pH :7.5-8.8 ; Lighting : continuous illumination with fluorescent light, 7500 lux

Analytical methods : HPLC with UV detection.

Findings and conclusions :

EbC_{50} (72h, CGA 108906) = 74 mg/l

NOEbC (72 h, CGA 108906) = 21 mg/l

B.8.2.7 Effects on sediment dwelling organisms (Annex IIA 8.2.7)

The results of the water/sediment study show that the active substance and its metabolites are distributed in both sediment and water phases. It is therefore not necessary to require specific study with sediment dwelling arthropods.

B.8.2.8 Effects on aquatic plants (Annex IIA 8.2.8)

Tests on aquatic plants are not required since metalaxyl-M is not an herbicide.

B.8.2.9 Acute toxicity of the preparations (Annex IIIA 10.2.1)

Studies were performed with the formulation RIDOMIL GOLD MZ 68 WP. See table B.8.2.13-5.

B.8.2.10 Microcosm and mesocosm study (Annex IIIA 10.2.2)

The study is not required since $\text{TERa} < 100$ or $\text{TER It} < 10$

B.8.2.11 Residue data in fish (Annex IIIA 10.2.3)

The study is not required. The bioaccumulation potential is low.

B.8.2.12 Supplementary studies of toxicity to fish and aquatic invertebrates (Annex IIIA 10.2.4)

Not required.

B.8.2.13 Summary of effects to water organisms (Annex IIA 8.2, Annex IIIA 10.2)*Acute toxicity to aquatic organisms*

Metalaxyl-M and the 3 tested metabolites are non-toxic to fish and daphnia.

Metalaxyl-M and metabolite CGA 108906 are harmful to algae. Metabolites CGA 62826 and CGA 67868 are non-toxic to algae

The acute toxicity studies performed with metalaxyl-M and with racemic metalaxyl reveal that both substances have a similar pattern of toxicity to aquatic organisms. Therefore the results of the chronic toxicity studies (fish and daphnia) performed with metalaxyl were extrapolated to metalaxyl-M.

Chronic toxicity to aquatic organisms

Chronic toxicity of metalaxyl was evaluated in two studies performed with fish and Daphnia. The NOEC were 9.1 mg/l and 1.2 mg/l respectively for fish and daphnia.

Bioaccumulation

The maximum BCF determined in non-edible part at day 14 is 15.

Significant elimination of ¹⁴C residues was observed during the first 3 days of depuration. The depuration half-lives were between 1 and 3 days.

The bioaccumulation potential of metalaxyl is low. This conclusion is confirming the results of the log Pow study (log Pow of metalaxyl-M = 1.71).

Table B.8.2.13-1 : Summary of effects of metalaxyl-M to water organisms

Test species	Test system	Duration of exposure	Results	References
<i>Oncorhynchus mykiss</i>	Static system	96 hours	LC ₅₀ > 100 mg a.s./l NOEC = 100 mg a.s./l	Rufli, 1994b
<i>Oncorhynchus mykiss</i>	Static system	96 hours	LC ₅₀ > 121 mg a.s./l NOEC = 72 mg a.s./l	Drottat, 1995a
<i>Daphnia magna</i>	Static system	48 hours	LC ₅₀ > 100 mg a.s./l NOEC = 100 mg a.s./l	Grade, 1994b
<i>Daphnia magna</i>	Static system	48 hours	EC ₅₀ > 113 a.s./l NOEC = 39 mg a.s./l	Drottat, 1995b
<i>Crassostrea virginica</i>	Flow-through system	96 hours	EC ₅₀ (shell deposition) = 9.7 mg a.s./l Effects observed at 5.4 and 8.6 mg/l	Drottat, 1995c
<i>Scenedesmus subspicatus</i>	Static system	72 hours	EbC ₅₀ = 36 mg/l NOEbC = 9.6 mg/l	Grade, 1994d

Table B.8.2.13-2 : Summary of effects of metalaxyl to water organisms

Test species	Test system	Duration of exposure	Results	References
<i>Oncorhynchus mykiss</i>	Static system	96 hours	LC ₅₀ > 100 mg a.s./l	Sachsse, 1976
<i>Cyprinus carpio</i>			LC ₅₀ > 100 mg a.s./l	
<i>Ictalurus melas</i>			LC ₅₀ > 100 mg a.s./l	
<i>Lepomis macrochirus</i>			LC ₅₀ > 100 mg a.s./l	
<i>Lebistes reticulatus</i>			LC ₅₀ > 100 mg a.s./l	
<i>Pimephales promelas</i>	Fish Early Life Stage	from 48 hours post-fertilization, up to 30 days post-hatch	No effect on hatchability of eggs, survival and growth of fry at 9.1 mg a.s./l	LeBlanc, 1980
<i>Lepomis macrochirus</i>	Bioaccumulation potential	29 days exposure/ 14 days depuration	max BCF = 15 depuration half-life < 3 days	Ladd, 1979a
<i>Daphnia magna</i>	Static system	48 hours	EC ₅₀ = 28 mg a.s./l NOEC = 8.2 mg a.s./l	LeBlanc, 1978
<i>Mysid shrimp</i> <i>Mysidiopsis bahia</i>	Flow-through system	96 hours	LC ₅₀ = 25 mg a.s./l NOEC = 11 mg a.s./l	Hoberg, 1989
<i>Crassostrea virginica</i>	Flow-through system	96 hours	EC ₅₀ (shell deposition) = 5.6 mg a.s./l NOEC = 1.4 mg a.s./l	Dionne, 1989
<i>Daphnia magna</i>	2 generations chronic toxicity test	42 days	NOEC = 1.2 mg a.s./l	LeBlanc, 1980
<i>Scenedesmus subspicatus</i>	Static system	120 hours	EC ₅₀ = 42.69 mg a.s./l (bad quality)	Hitz, 1981
<i>Scenedesmus subspicatus</i>	Static system	72 hours	EbC ₅₀ = 46 mg/l NOEbC < 5.8 mg/l	Grade, 1995

Table B.8.2.13-3 : Summary of effects of metabolites of metalaxyl/metalaxyl-M to water organisms

Test species	Test system	Duration of exposure	Results	References
<i>Oncorhynchus mykiss</i>	CGA 62826 Semi-static system	96 hours	LC ₅₀ > 100 mg a.s./l NOEC = 100 mg a.s./l	Memmert, 1991a
<i>Oncorhynchus mykiss</i>	CGA 67868 Semi-static system	96 hours	LC ₅₀ > 98.9 mg a.s./l NOEC = 16.8 mg a.s./l	Memmert, 1992a
<i>Oncorhynchus mykiss</i>	CGA 108906 Static system	96 hours	LC ₅₀ > 100 mg a.s./l NOEC = 100 mg a.s./l	Rufli, 1994a
<i>Daphnia magna</i>	CGA 62826 static system	48 hours	EC ₅₀ = 852 mg a.s./l NOEC = 125 mg a.s./l	Memmert, 1991b
<i>Daphnia magna</i>	CGA 67868 static system	48 hours	EC ₅₀ = 158 mg a.s./l NOEC = 25 mg a.s./l	Memmert, 1991c
<i>Daphnia magna</i>	CGA 108906 static system	48 hours	EC ₅₀ > 100 mg a.s./l NOEC = 100 mg a.s./l	Grade, 1994a
<i>Scenedesmus subspicatus</i>	CGA 62826 static system	72 hours	EC ₅₀ > 1000 mg/l NOEC = 100 mg/l	Memmert, 1991d
<i>Scenedesmus subspicatus</i>	CGA 67868 static system	72 hours	EbC ₅₀ = 195.4 mg/l NOEC = 9.9 mg/l	Memmert, 1992b
<i>Scenedesmus subspicatus</i>	CGA 108906 static system	72 hours	EbC ₅₀ = 74 mg/l NOEbC = 21 mg/l	Grade, 1994c

Table B.8.2.13-4 : Summary of effects of formulation RIDOMIL GOLD EC 480 to water organisms (EC containing 480g/l metalaxyl-M)

Test species	Test system	Duration of exposure	Results	References
<i>Selenastrum capricornutum</i>	Static system	96 hours	EbC ₅₀ = 54 mg /l NOEbC = 32 mg/l	Grade, 1995

Table B.8.2.13-5 : Summary of effects of formulation RIDOMIL GOLD MZ 68 WP to water organisms (WP containing 640 g/kg mancozeb and 40 g/kg metalaxyl-M)

Test species	Test system	Duration of exposure	Results	References
<i>Oncorhynchus mykiss</i>	Static system	96 hours	LC ₅₀ = 0.54 mg /l NOEC < 0.15 mg/l	Rufli, 1995
<i>Daphnia magna</i>	Static system	48 hours	EC ₅₀ = 1.2 mg /l NOEC = 0.58 mg/l	Neumann, 1995
<i>Daphnia magna</i>	Semi-static system - effects on the reproduction	21 days	EC ₅₀ = 0.64 mg /l NOEC = 0.2 mg/l	Neumann, 1996
<i>Selenastrum capricornutum</i>	Static system	72 hours	EbC ₅₀ = 0.13 mg/l NOEbC < 0.025 mg/l	Grade, 1995

B.8.2.14 Exposure and risk assessment for aquatic organisms (Annex IIIA 10.2)

The main uses of metalaxyl-M susceptible to lead to a contamination of surface waters are :

- The foliar spray treatment to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP) : grapes and potatoes
- The soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC) : orchard, ornamental and annual field crops

The details of the PEC calculations are presented on point B.7.6. The calculations presented in this monograph are only related to the active substance metalaxyl-M. The toxicity endpoints were compared to the maximum concentrations found just after the last application of the active substance.

- The TER was also evaluated taking into account the figures from a drain discharge study where 2 kg a.s./ha was applied on bare soil. The maximum concentration found in the drain water was 87 µg/l.

The toxicity of the 3 metabolites is similar/lower than the toxicity of metalaxyl-M. Therefore, the TER calculations for the a.s. cover the risk resulting from the presence of the metabolites.

For both types of formulation the acute and long term risk to aquatic organisms are negligible. See table B.8.2-14-1

The evaluation of the risk resulting from mancozeb should be evaluated at Member State level.

Table B.8.2.14-1 : TER aquatic organisms

Application rate (g a.s./ha)	Crop	Organism	Time scale	Distance (m)	TER	Annex VI trigger
Foliar spray to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP).						
120 g metalaxyl-M/ha 2-4 appl./season just after 4th application	grapes	<i>Oncorhynchus mykiss</i>	Acute	5	100 /0.0069 = 14493	100
		<i>Daphnia magna</i>	Acute		100 /0.0069 = 14493	100
		<i>Selenastrum capricornutum</i>	Acute		36/0.0069 = 5217	10
		<i>Lepomis macrochirus</i> (*)	Chronic		9.1/0.0069 = 1319	10
		<i>Daphnia magna</i> (*)	Chronic		1.2/0.0069 = 174	10
110 g metalaxyl-M/ha 2-5 appl./season just after 5th application	potatoes	<i>Oncorhynchus mykiss</i>	Acute	1	100 /0.0076 = 13158	100
		<i>Daphnia magna</i>	Acute		100 /0.0076 = 13158	100
		<i>Selenastrum capricornutum</i>	Acute		36/0.0076 = 4737	10
		<i>Lepomis macrochirus</i> (*)	Chronic		9.1/0.0076 = 1197	10
		<i>Daphnia magna</i> (*)	Chronic		1.2/0.0076 = 158	10

Application rate (g a.s./ha)	Crop	Organism	Time scale	Distance (m)	TER	Annex VI trigger
Soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC)						
1000 g a.s./ha (typical high dose rate) 1 appl./season 5% drift, at 1st application	orchard and ornamental crops	<i>Oncorhynchus mykiss</i>	Acute	1	$100 / 0.01 = 10000$	100
		<i>Daphnia magna</i>	Acute		$100 / 0.017 = 5882$	100
		<i>Selenastrum capricornutum</i>	Acute		$36 / 0.017 = 2118$	10
		<i>Lepomis macrochirus</i> (*)	Chronic		$9.1 / 0.014 = 650$	10
		<i>Daphnia magna</i> (*)	Chronic		$1.2 / 0.012 = 100$	10
2000 g a.s./ha 1 appl./season maximum concentration in drain water = 87 µg/l	bare soil	<i>Oncorhynchus mykiss</i>	Acute	-	$100 / 0.087 = 1149$	100
		<i>Daphnia magna</i>	Acute		$100 / 0.087 = 1149$	100
		<i>Selenastrum capricornutum</i>	Acute		$36 / 0.087 = 414$	10
		<i>Lepomis macrochirus</i> (*)	Chronic		$9.1 / 0.087 = 105$	10
		<i>Daphnia magna</i> (*)	Chronic		$1.2 / 0.087 = 14$	10

(*) : Data derived from the metalaxyl dossier

B.8.3 Effects on other terrestrial vertebrates (Annex IIIA 10.3.1)

The risk assessment for small mammals is based on the following assumptions :

- LD₅₀ (oral, _ rat) = 375 mg a.s./kg bw
- NOEC (oral, rat, 90 days) = 250 mg a.s./kg food
- small mammals (< 100 g) with a food consumption of 30% bw
- the contamination of the food is estimated according to Hoerger and Kenaga (1972)
- the uses of metalaxyl-M susceptible to contaminate the food of small mammals are :

1 - The foliar spray to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP). Grapes and potatoes are the main crops treated with this type of formulation.

2 - The soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC). The formulation is applied on the soil at sowing or (pre)-planting or at the base of the trees. The application rate of 1000 g/ha taken into account in the evaluation of the risk to small mammals.

- The application of the a.s. in the root zone of orchard trees (1 g/m²) was not considered as a route leading to a high contamination of the mammals food.

The risk to leaf-eating and insectivorous mammals resulting from the exposure to the a.s. in crops treated with foliar spray formulation is negligible (TER acute = 336-4209 ; TER short term = 67-842)

The evaluation of the risk resulting from mancozeb should be evaluated at Member State level.

The risk to leaf-eating, insectivorous mammals resulting from the exposure to the a.s. in crops treated with soil treatment formulation is negligible (TER acute = 40-463; TER short term = 8-93) The TER short term is slightly

below the trigger value of 10. We can nevertheless accept that the risk is low because the NOEC is derived from a 90-day study and because the food concentration is expressed as an initial residue.

Table B.8.3-1 : TER mammals for the metalaxyl-M

Application rate (g a.s./ha)	Crop	Organism	Time scale	TER	Annex VI trigger
Foliar spray to control airborne diseases					
120 g metalaxyl-M/ha 2-4 appl./season	grapes	small mammal (< 100g) eating leaves and leafy crops	acute	375/1.116 = 336	10
		small mammal (< 100 g) eating small seeds and small insects	acute	375/1.044 = 359	10
		small mammal (< 100 g) eating big seeds and big insects	acute	375/0.072 = 3858	10
		small mammal (< 100g) eating leaves and leafy crops	short term	250/3.72 = 67	10
		small mammal (< 100 g) eating small seeds and small insects	short term	250/3.48 = 72	10
		small mammal (< 100 g eating big seeds and big insects	short term	250/0.324 = 772	10
110 g metalaxyl-M/ha 2-5 appl./season	potatoes	small mammal (< 100g) eating leaves and leafy crops	acute	375/1.023 = 367	10
		small mammal (< 100 g) eating small seeds and small insects	acute	375/0.957 = 392	10
		small mammal (< 100 g) eating big seeds and big insects	acute	375/0.0891 = 4209	10
		small mammal (< 100g) eating leaves and leafy crops	short term	250/3.41 = 73	10
		small mammal (< 100 g) eating small seeds and small insects	short term	250/3.19 = 78	10
		small mammal (< 100 g) eating big seeds and big insects	short term	250/0.297 = 842	10
Soil treatment against soilborne diseases					
1000 g a.s./ha (typical high dose rate) 1 appl./season	wide variety of field crops, ornamental and orchard crops	small mammal (< 100g) eating leaves and leafy crops	acute	375/9.3 = 40	10
		small mammal (< 100 g) eating small seeds and small insects	acute	375/8.7 = 43	10
		small mammal (< 100 g) eating big seeds and big insects	acute	375/0.81 = 463	10
		small mammal (< 100g) eating leaves and leafy crops	short term	250/31 = 8	10
		small mammal (< 100 g) eating small seeds and small insects	short term	250/29= 9	10
		small mammal (< 100 g eating big seeds and big insects	short term	250/2.7 = 93	10

(*) : Data derived from the metalaxyl dossier

B.8.4 Effects on bees (Annex IIA 8.3.1; Annex IIIA 10.3.2)

B.8.4.1 Acute toxicity to bees (Annex IIA 8.3.1.1)

An acute contact toxicity study with the honey bee (Palmer, et al., 1995)

Guidelines :

US EPA FIFRA guideline 141-1

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 98.2%

Test species : Honeybees (*Apis mellifera* L.); worker bees

Number of organisms : 25 bees X 2 replicates/ concentration

Type of test : acute contact toxicity test (48 hours)

Applied concentrations : 1.56, 3.13, 6.25, 12.5, 25.0 µg a.s./bee (nominal); solvent control; positive control :

Exposure route :

Honey bees were exposed to metalaxyl-M solution, administered topically in a droplet to the abdomen and/or thorax of each bee.

Test conditions :

Temperature of approximately 26 to 30°C, with relative humidity above approximately 40%.

Findings and conclusion:

LD₅₀ (48h, metalaxyl-M) contact > 25.0 µg a.s./bee (nominal) (highest concentration tested)

NOEL (48h, metalaxyl-M) contact = 25.0 µg a.s./bee (nominal)

Testing toxicity to honeybee - *Apis mellifera* L. (Laboratory) according to EPPO guideline No. 170 - CGA 48988 tech. (Kleiner, 1994)

Guidelines :

EPPO guideline No. 170

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 96.1%

Test species : Honeybees (*Apis mellifera* L.); worker bees

Number of organisms : 10 bees X 3 replicates/ concentration

Type of test : acute oral and contact toxicity test (48 hours)

Applied concentrations :

oral administration : 100, 160, 200, 300 µg a.s./bee (nominal); solvent control; positive control : dimethoate

topical administration : 50, 100, 200 µg a.s./bee (nominal); solvent control; positive control : dimethoate

Exposure route :

Honey bees were exposed to metalaxyl solution, administered topically in a droplet to the abdomen and/or thorax of each bee.

Oral administration to 10 bees of 0.2 ml sucrose solution containing 0.5 to 1.5 % metalaxyl.

Test conditions :

Temperature of approximately 25 to 27°C, with relative humidity above approximately 54-76%.

Findings and conclusion:

LD₅₀ (48h, metalaxyl) contact > 200 µg a.s./bee (nominal)

NOEL (48h, metalaxyl) contact = 200 µg a.s./bee (nominal)

LD₅₀ (48h, metalaxyl) oral = 269 µg a.s./bee (nominal)

NOEL (48h, metalaxyl) oral = 100 µg a.s./bee (nominal)

B.8.4.2 Bee brood feeding test (Annex IIA 8.3.1.2)

The study is not required since metalaxyl-M does not act as an insect growth regulator.

B.8.4.3 Acute toxicity of the preparations to bees (Annex IIIA 10.4.1)

CGA 329351 EC 480 (A-9048B): Laboratory oral and contact test with the honeybee, *Apis mellifera*, based on the EPPO guideline 170 (1992) (Candolfi, 1995)

Guidelines :

EPPO guideline No. 170

GLP :

Yes

Material and Methods :

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

Test species : Honeybees (*Apis mellifera* L.); worker bees

Number of organisms : 10 bees X 3 replicates/ concentration

Type of test : acute oral and contact toxicity test (72 hours)

Applied concentrations :

oral administration : 12.5, 25, 50, 100, 200 µg a.s./bee (nominal); solvent control; positive control : dimethoate

topical administration : 200 µg a.s./bee (nominal); solvent control; positive control : dimethoate

Exposure route :

Honey bees were exposed to a 200 µg formulation/µl solution, administered topically in a droplet to the thorax of each bee.

Oral administration to 10 bees of 0.1 ml sucrose solution containing 1.25 to 10 µg formulation /µl.

Test conditions :

Temperature of 23.5-25.5 °C, with relative humidity of 59-63%

Findings and conclusion:

LD₅₀ (48h, EC 480) contact > 200 µg a.s./bee (nominal)

NOEL (48h, EC 480) contact = 200 µg a.s./bee (nominal)

LD₅₀ (48h, EC 480) oral > 127 µg a.s./bee (nominal)

NOEL (48h, EC 480) oral = 59 µg a.s./bee (nominal)

B.8.4.4 effects on bees of residues on crops (Annex IIIA 10.4.2)

B.8.4.5 Cage tests (Annex IIIA 10.4.3)

B.8.4.6 Field tests to investigate special effects (Annex IIIA 10.4.4)

B.8.4.7 Tunnel testing to investigate effects of feeding on contaminated honey (Annex IIIA 10.4.5)

These studies are not required since the hazard quotients show that the risk to bees is negligible (HQ = 10-17).

B.8.4.8 Exposure and risk assessment for bees (Annex IIIA 10.4)

Table B.8.4.8-1 : Honeybees toxicity studies

Test species	Test system	Results	References
Honeybee (<i>Apis mellifera</i> L)	Acute contact toxicity test	LD ₅₀ (48h, metalaxyl-M) contact > 25.0 µg a.s./bee	Palmer et al., 1995
Honeybee (<i>Apis mellifera</i> L)	Acute oral and contact toxicity test	LD ₅₀ (48h, metalaxyl) contact > 200 µg a.s./bee NOEL (48h, metalaxyl) contact = 200 µg a.s./bee LD ₅₀ (48h, metalaxyl) oral = 269 µg a.s./bee NOEL (48h, metalaxyl) oral = 100 µg a.s./bee	Kleiner, 1994
Honeybee (<i>Apis mellifera</i> L)	Acute oral and contact toxicity test	LD ₅₀ (72 h, EC 480) contact > 200 µg a.s./bee NOEL (72 h, EC 480) contact = 200 µg a.s./bee LD ₅₀ (72 h, EC 480) oral > 127 µg a.s./bee NOEL (72 h, EC 480) oral = 59 µg a.s./bee	Candolfi, 1995
(*) Honeybee (<i>Apis mellifera</i> L)	Acute oral and contact toxicity test	LD ₅₀ (72 h, WP 4% metalaxyl-M + 64% mancozeb) contact > 200 µg a.s./bee NOEL (72 h, WP 4% metalaxyl-M + 64% mancozeb) contact = 200 µg a.s./bee LD ₅₀ (72 h, WP 4% metalaxyl-M + 64% mancozeb) oral > 200 µg a.s./bee NOEL (72 h, WP 4% metalaxyl-M + 64% mancozeb) oral = 200 µg a.s./bee	Candolfi, 1995

(*) : No detailed description in the monograph; study performed with a formulation containing 64% mancozeb and 4% metalaxyl-M.

The applications of RIDOMIL GOLD MZ 68 WP in grape and potatoes were chosen as representative scenarios for the foliar spray.

Application of RIDOMIL GOLD 480 EC is made essentially at sowing and pre-planting, or at the base of the trees. The exposure of bees resulting from this use pattern is negligible. Nevertheless we calculate the hazard quotient taking into account an application rate of 1000 g a.s./ha (typical high dose rate in a wide variety of orchard, ornamental and field crops)

The hazard ratios calculated for both use types (10-17) indicate that risk of metalaxyl-M to bees is negligible.

Table B.8.4.8-2 : Hazard quotients for honeybees

Application rate (g a.s./ha)	Crop	Route	Hazard quotient	Annex VI trigger
3000 g/ha formulation RIDOMIL GOLD MZ 68 WP (corresponding to 120 g metalaxyl-M and 1920 g mancozeb /ha)	grapes	contact	$3000/200 = 15$	50
		oral	$3000/200 = 15$	50
2750 g/ha formulation RIDOMIL GOLD MZ 68 WP (corresponding to 110 g metalaxyl-M and 1705 g mancozeb /ha)	potatoes	contact	$2750/200 = 14$	50
		oral	$2750/200 = 14$	50
2100 g/ha formulation RIDOMIL GOLD 480 EC (corresponding to 1000 g metalaxyl-M /ha)	orchard, ornamental and field crops	contact	$2100/200 = 10$	50
		oral	$2100/127 = 17$	50

B.8.5 Effects on other arthropods species (Annex IIA 8.3.2; Annex IIIA 10.5)**B.8.5.1 Effects of the active substance and formulations on non-target terrestrial arthropods**

Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the predatory ground beetle *Poecilus cupreus* L. (Reber, 1995)

Guidelines :

IOBC guideline, Heimbach (1992) and Hassan (1992)

GLP :

yes

Material and Methods :

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

Test species : *Poecilus cupreus* (ground dwelling predators), adults

Number of organisms : 5 replicates per treatment each with 3 _ and 3 _

Type of test : Lab test

Applied concentrations :

The formulation was applied at the field rate of 1 kg a.s./ha in 400 l/ha water control, methyl-parathion as positive control

Exposure route :

14 days exposure in containers filled with sand.

Test conditions :

Temperature 20 ± 2 °C; relative humidity : $80 \pm 20\%$; light regime : 16 hours light, 12000-16000 lux; beetles fed with fly pupae.

Findings :

Evaluation criteria	Control	Treatment	Endpoints
mortality	0	0	
feeding rate (number of pupae/beetle)	2.04	2.01	No difference in mortality and feeding rate

Conclusion :

Study is acceptable. The formulation EC 480 is harmless to *Poecilus cupreus* at the application rate of 1 kg a.s./ha.

Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the predaceous mite *Typhlodromus pyri* Scheuten. (Reber, 1995)

Guidelines :

IOBC guideline, Bakker et al. (1992) and Hassan (1992)

GLP :

yes

Material and Methods :

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

Test species : *Typhlodromus pyri*, protonymphs 3-4 days old

Number of organisms :

20 replicates per treatment, each with 5 protonymphs (nymphal mortality).

20 replicates, each containing surviving females and males in the sex ratio of approximately of 1/1 (reproduction)

Type of test : Lab test

Applied concentrations :

The formulation was applied at the field rate of 1 kg a.s./ha in 200 l/ha water control, dimethoate as positive control

Exposure route :

14 days exposure on bean leaf discs placed in Petri dishes.

Test conditions :

Temperature 25 ± 2 °C; relative humidity : $80 \pm 10\%$; light regime : 16 hours light, 12000-16000 lux;

Findings :

Evaluation criteria	Control	Treatment	Endpoints
mortality	15%	92%	corrected mortality : 90.6%
reproduction rate (number of eggs/female)	2.15	2.00	
			E(combined effects) = 91.26%

Conclusion :

Study is acceptable. The formulation EC 480 is moderately harmful to *Typhlodromus pyri* at the application rate of 1 kg a.s./ha.

Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the parasitic wasp *Aphidius colemani* Viereck (Hymenoptera: Aphidiidae) (Wesiak et al., 1995)

Guidelines :

IOBC guideline, Polgar (1988) and Hassan (1992)

GLP :

yes

Material and Methods :

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

Test species : *Aphidius colemani*, young adults (up to 24 hours)

Number of organisms :

4 replicates per treatment, each with 10 female adults (mortality assessment).

10 replicates, each with 1 adult female (reproduction assessment - was not performed)

Type of test : Lab test

Applied concentrations :

The formulation was applied at the field rate of 1 kg a.s./ha in 200 l/ha

water control, dimethoate as positive control

Exposure route :

2 days exposure followed by 15 days observation period for parasitisation.

Test conditions :

Temperature 20 ± 2 °C; relative humidity : $80 \pm 10\%$; light regime : 16 hours light, 2000 lux;

Findings :

Evaluation criteria	Control	Treatment	Endpoints
mortality	0%	100%	

Conclusion :

Study is acceptable. The formulation EC 480 is harmful to *Aphidius colemani* at the application rate of 1 kg a.s./ha.

Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the aphid predator *Orius insidiosus* (Wesiak et al., 1995)

Guidelines :

IOBC guideline, Bakker et al. (1992) and Hassan (1992)

GLP :

yes

Material and Methods :

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

Test species : *Orius insidiosus*, nymphs, stage 2 (5 days old)

Number of organisms :

20 replicates per treatment, each with 5 nymphs (mortality assessment).

5 replicates, each with 6 bugs (3 _ and 3_) (reproduction assessment)

Type of test : Lab test

Applied concentrations :

The formulation was applied at the field rate of 1 kg a.s./ha in 200 l/ha; water control, dimethoate as positive control

Exposure route :

10 days exposure followed by 10 days observation period for production of eggs.

Test conditions :

Temperature 25 ± 2 °C; relative humidity : $80 \pm 10\%$; light regime : 16 hours light, 2000 lux;

Findings :

Evaluation criteria	Control	Treatment	Endpoints
mortality	7%	15.8%	corrected mortality : 9.5%
reproduction rate (number of eggs/female)	14.0	13.0	
			E(combined effects) = 15.8%

Conclusion :

Study is acceptable. The formulation EC 480 is harmless to *Orius insidiosus* at the application rate of 1 kg a.s./ha.

Extended laboratory test to evaluate the side effects of CGA 329351 EC 480 (A-9408 B) applied to plants on adult *Aphidius rhopalosiphi* (Hymenoptera: Aphidiidae) (Candolfi, 1997)

Guidelines :

IOBC (1992), ESCORT (1994) and Mead-Briggs (1994)

GLP :

Yes

Material and Methods :

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

Test species : *Aphidius rhopalosiphi*, adult females, less than 48 hours old

Number of organisms :

6 replicates per treatment, each with 6 wasps (mortality assessment).

6 replicates, each with 3 wasps (parasitization assessment)

Type of test : extended lab test

Applied and measured concentrations :

The formulation was applied at the field rate of 1 kg a.s./ha in 200 l/ha

water control, dimethoate as positive control

Exposure route :

Survival and behaviour of adult *Aphidius* was assessed during a period of 48 hours to the test substance sprayed on plant material. Subsequently, the surviving wasps were allowed to parasitize aphids over 24 hours, and after 12 days their fecundity was assessed.

Test conditions :

Temperature 20 ± 2 °C; relative humidity : $70 \pm 20\%$; light regime : 16 hours light, 1000-2000 lux;

Findings :

Evaluation criteria	Control	Treatment	Endpoints
mortality	0%	0%	
parasitization (mean number of mummies per female)	18.8 ± 3.4	25.3 ± 9.2	
Reduction of beneficial capacity = -34.2%			

Conclusion :

Study is acceptable. The formulation EC 480 is harmless to *Aphidius rhopalosiphi* at the application rate of 1 kg a.s./ha. (Under extended lab test conditions)

B.8.5.2 Summary of effects, exposure and risk assessment for non-target terrestrial arthropods

The studies which were performed showed that the formulations RIDOMIL GOLD EC 480 and RIDOMIL GOLD MZ 68 WP present low risk to the different groups of non-target arthropods.

Table B.8.5.2-1 : Summary of effects of Metalaxyl-M formulations to non-target terrestrial arthropods

Test species	Test system	Duration of exposure	Results	Risk Assessment	References
RIDOMIL GOLD EC 480 (EC containing 480 g/l metalaxyl-M)					
<i>Poecilus cupreus</i>	lab test	14 days	E (mortality) = 0% (Dose : 1 kg a.s./ha in 400 l water)	harmless	Reber, 1995
<i>Typhlodromus pyri</i>	lab test	14 days	E (mortality and reproduction) = 91.26% (Dose : 1 kg a.s./ha in 200 l water)	moderately harmful	Reber, 1995
<i>Aphidius colemani</i>	lab test	2 days	E (mortality) = 100% (Dose : 1 kg a.s./ha in 200 l water)	harmful	Wesiak et al., 1995
<i>Orius insidiosus</i>	lab test	20 days	E (mortality and reproduction) = 15.8% (Dose : 1 kg a.s./ha in 200 l water)	harmless	Wesiak et al., 1995
<i>Aphidius rhopalosiphii</i>	extended lab test	15 days	E (mortality and reproduction) = -34.2% (Dose : 1 kg a.s./ha in 200 l water)	harmless	Candolfi, 1997
(*) RIDOMIL GOLD MZ 68 WP (WP containing 640 g/kg mancozeb and 40 g/kg metalaxyl-M)					
<i>Poecilus cupreus</i>	lab test	14 days	E (mortality) = 0% (Dose : 3.5 kg formulation/ ha in 400 l water)	harmless	Reber, 1995
<i>Orius insidiosus</i>	lab test	20 days	E(mortality and reproduction) = 18.3% (Dose : 3.5 kg formulation/ ha in 200 l water)	harmless	Wesiak et al., 1995
<i>Aphidius colemani</i>	lab test	17 days	E(mortality and reproduction) = 94.6% (Dose : 3.5 kg formulation/ ha in 200 l water)	moderately harmful	Wesiak et al., 1995
<i>Aphidius rhopalosiphii</i>	extended lab test	15 days	E(mortality and reproduction) = -14.5% (Dose : 3.5 kg formulation/ ha in 200 l water)	harmless	Candolfi, 1997
<i>Typhlodromus pyri</i>	grapes, 5 applications (2-week interval) 2.5 kg formulation/ ha (0.1 kg/ha metalaxyl-M + 1.6 kg mancozeb/ha) 1000 l water/ha		E(7 days after the applications) = 11.8%	harmless	Reber, 1995

(*) : No detailed description in the monograph; study performed with a formulation containing 64% mancozeb and 4% metalaxyl-M.

B.8.6 Effects on earthworms (Annex IIA 8.4; Annex IIIA 10.3.6)

B.8.6.1 Acute toxicity to earthworms (Annex IIA 8.4.1)

Acute toxicity test of CGA 329351 (Enantiomer of CGA 48988) to the earthworm (*Eisenia foetida*) (Rufli, 1997)

Guidelines :

OECD guideline No 207

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 97.1%

Test species : Earthworms (*Eisenia foetida*);

Number of organisms, weight : 10 worms X 4 replicates / concentration; 330-360 mg weight at start

Type of test : acute toxicity test (14 days)

Applied concentrations : 12.3, 37, 111, 333, 1000 mg a.s./kg (nominal); water control, positive control : chloracetamide

Soil type and test conditions :

Test substrate : 10% sphagnum peat, 20% kaolin clay, 69% sand, 1% CaCO₃,

water content : 60% dry weight

Temperature : 22-23°C

Light regime : continuous fluorescent light of 400-800 lux.

Findings :

Mortality : 93% mortality at the highest dose; no mortality in the other treatments

Observations : the decrease of the average live weight was statistically significant at concentrations 333 and 1000 mg/kg

Conclusion :

Study is acceptable.

LC₅₀ (14d) = 830 mg a.s./kg substrate

NOEC (14d) = 111 mg a.s./kg substrate

Report on the acute toxicity test of CGA 48988 technical to earthworm (*Eisenia foetida foetida*) (Vial, 1990)

Guidelines :

OECD guideline No 207

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 96.1%

Test species : Earthworms (*Eisenia foetida*)

Number of organisms, weight, age : 10 worms X 4 replicates / concentration; 182-221 mg weight at start, adult mature (> 2 month of age)

Type of test : acute toxicity test (14 days)

Applied concentrations : 12.3, 37, 111, 333, 1000 mg a.s./kg (nominal); water control, positive control : -

Soil type and test conditions :

Test substrate : 'according to the guideline', 8% CaCO₃ to correct soil pH.

water content : 36-37% dry weight

Temperature : 20 ± 1°C

Light regime : continuous fluorescent light of 400-800 lux.

Findings :

Mortality - observations : No treatment related mortality, nor treatment related weight decrease

Conclusion :

Study is acceptable.

LC₅₀ (14d) > 1000 mg a.s./kg substrate

NOEC (14d) = 1000 mg a.s./kg substrate

B.8.6.2 Sublethal effects on earthworms (Annex IIA 8.4.2)

The evaluation of the sublethal effects on earthworms was not required because the calculation of the TER acute show favourable results even in the case of orchard soil disinfection with very high application rate (1 g a.s./m²)

B.8.6.3 Acute toxicity of the formulations to earthworms (Annex IIIA 10.6.1.1)

A study with the formulation RIDOMIL GOLD MZ 68 WP, containing mancozeb and metalaxyl-M, was performed. The results are shown in the table B.8.6.6-1

B.8.6.4 Sublethal effects of the formulation on earthworms (Annex IIIA 10.6.1.2)**B.8.6.5 Field tests - residue content of earthworms (Annex IIIA 10.6.1.3)**

These studies are not required.

B.8.6.6 Summary and risk assessment for earthworms (Annex III, 10.6.1.1)

Table B.8.6.6-1 : Summary of effects of metalaxyl-M and metalaxyl to earthworms

Test species	Test system	Duration of exposure	Results (mg/kg soil)	References
<i>Eisenia foetida</i>	metalaxyl-M acute toxicity test	14 days	LC ₅₀ = 830 mg a.s./kg substrate NOEC = 111 mg a.s./kg substrate	Rufli, 1997
<i>Eisenia foetida</i>	metalaxyl acute toxicity test	14 days	LC ₅₀ > 1000 mg a.s./kg substrate NOEC = 1000 mg a.s./kg substrate	Vial, 1990
(*) <i>Eisenia foetida</i>	WP containing 640 g/kg mancozeb and 40 g/kg metalaxyl-M acute toxicity test	14 days	LC ₅₀ > 1000 mg/kg substrate NOEC = 1000 mg/kg substrate	König, 1995

(*) : No detailed description in the monograph; study performed with a formulation containing 64% mancozeb and 4% metalaxyl-M.

The main uses of metalaxyl-M susceptible to lead to a contamination of soil are :

- The foliar spray to control airborne diseases (formulation RIDOMIL GOLD MZ 68 WP)
- The soil treatment against soilborne diseases (formulation RIDOMIL GOLD 480EC)

The details of the PEC calculations are presented on point B.7.3. The calculations presented in this monograph are only related to the active substance metalaxyl-M. The toxicity endpoints were compared to the maximum concentrations found just after the last applications of the active substance.

The acute risk to earthworms is negligible.

The calculation of the TER acute show very favourable results even in the case of orchard soil disinfection with very high application rate (1 g a.s./m²). Therefore, specific studies to determine the long term risk seem not appropriate.

The evaluation of the risk resulting from mancozeb should be evaluated at Member State level.

Table B.8.6.6-2 : Toxicity/exposure ratios for earthworms

Application rate	Crop	Time scale	TER	Annex VI trigger
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(g a.s./ha)				
Foliar spray to control airborne diseases				
120 g a.s./ha 2-4 appl./season just after 4th appl.	grapes	acute	$830/0.374 = 2219$	10
110 g a.s./ha 2-5 appl./season just after 5th appl.	potatoes	acute	$830/0.290 = 2862$	10
Soil treatment against soilborne diseases				
1 g a.s./m ² 1 appl./season	root zones in orchards	acute	$830/13.33 = 62$	10
1000 g a.s./ha 1 appl./season	orchard and ornamental crops	acute	$830/1.33 = 624$	10

B.8.7 Effects on other soil non-target macro-organisms (Annex IIIA 10.6.2)

Not required. No effects were observed on the earthworms and the soil microflora.

B.8.8 Effects on soil non-target micro-organisms (Annex IIA 8.5; Annex IIIA 10.7)**B.8.8.1 Impact of the active substance on soil microbial activity (Annex IIA 8.5)**

The effects of CGA 48988- metalaxyl on soil respiration and nitrification (Völkl, 1992)

Guidelines :

BBA Richtlinien Teil VI 1-1 (1990)

GLP :

Yes

Material and methods :

Test Substance: metalaxyl, chemical purity : 96.1%

Soils : The tests were realized with the Speyer 2.1 (sand) and Speyer F3 (sandy silty loam).

Applied concentrations : 0.66 and 6.6 mg a.s./kg soil, equivalent to 500 and 5000 g a.s./ha, related to a soil depth of 5 cm and a soil density of 1.5 kg/dm³ and no crop interception. 3 replicates/concentration/soil for soil respiration and nitrification.

Type of test : respiration and nitrogen turnover tests

Test conditions :

Soil moisture : 40 % of its maximum water capacity

Soil samples were incubated at 20°C ± 2 °C in the dark.

Findings :

Table 8.8.1-1 : Influence of metalaxyl on soil respiration

Days	O ₂ - Consumption Rates (mg O ₂ /100 g dry soil) and % of Control				
	0 (mg a.s./kg dry soil)		0.66 (mg a.s./kg dry soil)		6.6 (mg a.s./kg dry soil)
	mg		mg	% (*)	mg
Speyer 2.1 (0.7 %OC, pH 6.1, CEC 4.9 meq/100g)					
0	0.281		0.259	-8	0.431
14	1.319		1.400	06	0.707
28	0.227		0.258	14	0.278
50	0.148		0.215	45	0.193
90	0.567		0.566	-	0.595
Speyer F3 (1.2 %OC, pH 7.3, CEC 13.0 meq/100g)					
0	1.641		1.719	5	1.326
14	2.217		2.378	7	2.238
28	1.808		1.655	-8	1.741

(*) : the percentages represent the variation of the treatment in respect to control.

Table 8.8.1-2 : Influence of metalaxyl on soil nitrification

Speyer 2.1 (0.7 %OC, pH 6.1, CEC 4.9 meq/100g)															
days	0 mg/kg			0.66 mg/kg						6.6 mg/kg					
	NH ₄	NO ₂	NO ₃	NH ₄		NO ₂		NO ₃		NH ₄		NO ₂		NO ₃	
	mg (*)	mg (*)	mg (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)
0	0.06	<0.01	0.04	0.07	14	<0.01	-	0.04	-	0.07	8.2	<0.01	-	0.04	-
14	0.09	<0.01	1.36	0.09	-2.3	<0.01	-	1.34	-1.1	0.09	-0.9	<0.01	-	1.48	9.0
28	0.03	<0.01	3.06	0.03	9.5	<0.01	-	3.43	12.1	0.03	5.2	<0.01	-	3.51	14.7
Speyer F3 (1.2 %OC, pH 7.3, CEC 13.0 meq/100g)															
days	0 mg/kg			0.66 mg/kg						6.6 mg/kg					
	NH ₄	NO ₂	NO ₃	NH ₄		NO ₂		NO ₃		NH ₄		NO ₂		NO ₃	
	mg (*)	mg (*)	mg (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)	mg (*)	% (*)
0	0.15	<0.01	0.97	0.03	-78.7	<0.01	73.3	0.91	-6.0	0.03	-79.8	<0.01	-	0.84	-13.9
14	0.01	<0.01	1.08	0.01	-	<0.01	-	1.12	3.5	0.01	-	<0.01	-	1.16	7.2
28	0.02	<0.01	2.56	0.02	-2.6	<0.01	-	2.33	-8.8	0.02	32.0	<0.01	-	2.58	0.7
56	0.01	<0.01	4.77	0.01	7.7	<0.01	-	4.37	-8.4	0.01	14.5	<0.01	-	4.40	-7.7
90	0.01	<0.01	4.81	0.01	-6.2	<0.01	-	4.42	-10.6	0.02	5.8	<0.01	-	4.08	-15.3

(*) : the percentages represent the variation of the treatment in respect to control.

Conclusions :

The modifications of soil respiration and nitrification were lower than 25% after 100 days (28 or 90 days in the test) for both soils at both concentrations.

The effects of N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester on soil microorganisms (Ercegovich, -)

A study was conducted to determine the response of a selection of micro-organisms including actinomycetes, bacteria, fungi and algae to 5, 25, 125 ppm metalaxyl in nutrient cultures. The study was not performed according to a known guideline. The study was not taken into account in the final evaluation.

B.8.8.2 Impact of the formulations on soil microbial activity (laboratory) (Annex IIIA 10.7.1)

B.8.8.3 Further laboratory, glasshouse or field testing to investigate impact on soil microbial activity (Annex IIIA 10.7.2)

Not required. Modifications observed in the studies performed with the a.s. were < 25% after 100 days

B.8.8.4 Summary of studies on non-target micro-organisms - exposure and risk assessment for non-target micro-organisms

The effects on soil respiration and nitrification were evaluated with the Speyer 2.1 (sand) and Speyer F3 (sandy silty loam) soils. The study was realized with metalaxyl at the concentrations of 0.66 and 6.6 mg a.s./kg soil equivalent to 500 and 5000 g a.s./ha, related to a soil depth of 5 cm and a soil density of 1.5 kg/dm³ and no crop interception. No process modification > 25% at the termination of the test was observed at both concentration levels.

The application rates of metalaxyl-M are covered by the study realized with metalaxyl at the maximum rate of 5000 g/ha (typical uses as foliar spray 100-150 g/ha; typical use as soil treatment up to 1000 g a.s./ha; application rate as root zone treatment : 10000 g/ha).

Other studies such as the aerobic soil degradation studies, the activated sludge respiration studies reveal that metalaxyl and metalaxyl-M have similar effects on the microflora. It is therefore possible to extrapolate from the racemic metalaxyl to metalaxyl-M.

B.8.9 Effects on other non-target organisms (flora and fauna) believed to be at risk (Annex IIA 8.6; Annex IIIA 10.8)

No specific information was submitted.

B.8.10 Effects on biological methods of sewage treatment (Annex IIA 8.7)

Report on the Test for Activated Sludge Respiration Inhibition of CGA 329351 (Enantiomer of CGA 48988) (Grade, 1996)

Guidelines :

OECD guideline No 209

GLP :

Yes

Material and Methods :

Test substance : metalaxyl-M, chemical purity : 97.1%

Test design :

The inhibitory effect of the metalaxyl-M on the oxygen consumption of activated sludge suspension (1.48 g sludge/l water) was determined. The applied a.s. concentrations were 100.0, 32.0, 10.0, 3.2, 1.0 mg a.s./l.

Incubation at 20 ± 2 °C for 3 hours

Findings and conclusions :

The 3-hour EC₂₀, EC₅₀ and EC₈₀ were all calculated to be >100 mg/l (nominal)

Report on the test for activated sludge respiration inhibition of CGA 48988 techn. (Weinstock, 1994)

Guidelines :

OECD guideline No 209

GLP :

Yes

Material and Methods :

Test substance : metalaxyl, chemical purity : 96.1%

Test design :

The inhibitory effect of the metalaxyl on the oxygen consumption of activated sludge suspension (1.68 g sludge/l water) was determined. The applied a.s. concentrations were 106, 61.0, 37.5, 23.0, 13.0 mg a.s./l.

Incubation at 20 ± 2 °C for 3 hours

Findings and conclusions :

The 3-hour EC_{20} , EC_{50} and EC_{80} were all calculated to be >100 mg/l (nominal)

Effects of CGA-48988 on the performance of the activated sludge process (Glinski, 1979)

Guidelines :

Not specified

GLP :

No

Material and Methods :

Test substance : metalaxyl, chemical purity : 95.4%

Test design :

The influence of metalaxyl on the the performance of activated sludge process was determined in a continuous flow activated sludge units. The parameters of total suspended solids concentration (TSS), total organic carbon concentrations (TOC), pH and turbidity were measured. Standard bacterial plates counts and macroscopic examination of the liquor were performed. The applied a.s. concentrations were 0.1, 1.0, 10.0, 50.0, 100.0 mg a.s./l in the continuous test (1 week) units and 0.1, 1.0, 10.0, 25.0, 50.0, 100.0 mg a.s./l in the shock test units (5 hours)

Findings and conclusions :

The results are considered as additional information.

- Results from the continuous dosing experiments showed that for concentrations of 0.1 to 10 mg a.s./l no adverse effects were observed. At the concentrations of 50 and 100 mg a.s./l effluent TOC were significantly higher than those in the control, indicating that the unit was not removing the TOC as well as the control unit.

- Results from the shock dosing experiments showed no adverse effects at 0.1, 1.0, 10.0 mg a.s./l At higher concentrations (25, 50, 100 mg a.s./l) significant increase of TOC was observed.

B.8.11 References relied on**Ecotoxicology of the active substance (Annex IIA 8)**

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
IIA 8.1.1	Beavers, J.B. 1977a. Acute oral LD ₅₀ - Mallard duck, CGA 48988 technical, Wildlife International Ltd., USA, Rep.Nr. 108-149, 30.11.1977 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 149	no	unpublished -
IIA 8.1.2	Beavers, J.B. 1977b. Eight-day dietary LC ₅₀ - bobwhite quail, CGA 48988 techn., Wildlife International Ltd., USA, Rep.Nr. 108-147, 01.12.1977 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 147	no	unpublished -
IIA 8.1.2	Beavers, J.B. 1977c. Eight-day dietary LC ₅₀ - Mallard duck, CGA 48988, technical, Wildlife International Ltd., USA, Rep.Nr. 108-148, 23.11.1977 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 1998	no	unpublished -
IIA 8.1.3	Beavers, J.B. 1980a. One-generation reproduction study - bobwhite quail, CGA 48988 technical, Wildlife International Ltd., USA, Rep.Nr. 108-175, 27.10.1980 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 151	no	unpublished -
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IIA 8.2.1	Buccafusco, R.J. 1978. Acute toxicity of CGA 48988 technical to Bluegill, Bionomics Aquatic Tox. Lab., Mass., USA, Rep.Nr. BW-78-12-381, 01.12.1978 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 156	yes	unpublished -
IIA 8.2.4	Dionne, E.Y. 1989. Acute toxicity to Eastern oysters under flow-through conditions, Springborn, Wareham, Mass., Rep.Nr. 89-9-3093, 26.10.1989 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 163	yes	unpublished -
IIA 8.2.1	Drottar K.R., Swigert J.P. 1995a. CGA 329351, A 96-hour static acute toxicity test with the rainbow trout, Oncorhynchus mykiss, Report N° 108A-164, Wildlife International Ltd., USA, September 15, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 299	yes	unpublished protected
IIA 8.2.4	Drottar, K.R., Swigert J.P. 1995b. A 48-hour static acute toxicity test with the cladoceran, Daphnia magna, Report N° 108A-166, Wildlife International Ltd., USA, August 21, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland	329351/ 298	yes	unpublished protected

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
	Submitted by Ciba-Geigy Ltd. Basle			
IIA 8.2.4	Drottar K.R., Swigert J.P. 1995c. A 96-hour shell deposition test with the eastern oyster, <i>Crassostrea virginica</i> , Report N° 108A-165, Wildlife International Ltd., USA, September 15, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 300	yes	unpublished protected
IIA 8.5	Ercegovich, C.D. The effects of N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester on soil microorganisms, Pesticide Research Laboratory, The Pennsylvania State University - Literature Reference Submitted by Ciba-Geigy Ltd., Basel, Switzerland	48988/ 166	no	published -
IIA 8.7	Glinski, D.J. 1979. Effects of CGA 48988 on the activated sludge process, Union carbide corporation Environmental services, Tarrytown, NY, USA, February 1979 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 3492	no	unpublished -
IIA 8.2.4	Grade, R. 1994a. Report on the acute toxicity test of CGA 108906 tech. (Metabolite of CGA 48988) on <i>Daphnia</i> , Project Report 943524, Ecotoxicology, Ciba-Geigy, Basel, 24.06.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	108906/ 2	yes	unpublished protected
IIA 8.2.4	Grade, R. 1994b. Report on the acute toxicity test of CGA 329351 tech. (Enantiomer of CGA 48988) on <i>Daphnia</i> (<i>Daphnia magna</i> Strauss), Project Report 933719, Ecotoxicology, Ciba-Geigy, Basel, 1.12.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 26	yes	unpublished protected
IIA 8.2.6	Grade, R. 1994c. Report on the growth inhibition test of CGA 108906 tech. (Metabolite of CGA 48988) to Green Algae, Project Report 943525, Ecotoxicology, Ciba-Geigy, Basel, 24.06.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	108906/ 1	yes	unpublished protected
IIA 8.2.6	Grade, R. 1994d. Report on the growth inhibition test of CGA 329351 tech. (Enantiomer of CGA 48988) to green alga (<i>Scenedesmus subspicatus</i>), Project Report 933720, Ecotoxicology, Ciba-Geigy, Basel, 1.12.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 27	yes	unpublished protected
IIA 8.2.6	Grade, R. 1995. Report on the growth inhibition test of CGA 48988 tech. to Green Algae (<i>Scenedesmus subspicatus</i>), Project Report 943628, Ecotoxicology, Ciba-Geigy, Basel, 24.03.1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 3737	yes	unpublished protected
IIA 8.7	Grade, R. 1996. Report on the test for activated sludge respiration inhibition of CGA 329351 (enantiomer of CGA 48988), Project Report 953610, Ecotoxicology, Ciba-Geigy Basel, January 10, 1996 Owned by Ciba-Geigy Ltd. Basle Switzerland	329351/ 324	yes	unpublished protected

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	Submitted by Ciba-Geigy Ltd. Basle			
IIA 8.2.6	Hitz, H.R. 1981. Growth-inhibition of algae (<i>Scenedesmus subspicatus</i>) by CGA 48988, Ciba-Geigy Ltd., Basle, Rep.Nr. 810761, 23.09.1981 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 164	no	unpublished -
IIA 8.2.4	Hoberg, J.R. 1989. Acute toxicity to Mysid shrimp under flow-through conditions, Springborn, Wareham, Mass., Rep.Nr. 89-10-3125, 26.10.1989 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 162	yes	unpublished -
IIA 8.1.1	Johnson, A. 1995. CGA 329351, Acute oral toxicity to bobwhite quail, Report N° CBG 749, Huntingdon Research Centre, UK, 21.12.1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 310	yes	unpublished protected
IIA 8.3.1.1	Kleiner, R. 1994. Testing to Honeybee- <i>Apis mellifera</i> L. (Laboratory) According to EPPO Guideline No. 170, Report No.:941048056, 05.12.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 3642	yes	unpublished protected
IIA 8.2.3	Ladd, S.A. and Wilson, W.G. 1979a. Accumulation and Elimination of ¹⁴ C-Residues by Bluegill sunfish (<i>Lepomis macrochirus</i>) exposed to phenyl labelled- ¹⁴ C-CGA-48988, BW-78-10328, EG&G, Bionomics, Wareham, Mass., USA, 01.04.1979 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 202	no	unpublished -
IIA 8.2.3	Ladd, S.A. and Enos, J. 1979b. Kinetics of phenyl labelled ¹⁴ C-CGA-48988 in a model aquatic ecosystem, BW-79-2-401, EG&G, Bionomics, Wareham, Mass., USA, 01.02.1979 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 203	no	unpublished -
IIA 8.2.4	LeBlanc, G.A. 1978. Acute toxicity of CGA 48988 to the water flea (<i>Daphnia magna</i>), Bionomics Aquatic Tox. Lab., Mass., USA, Rep.Nr. BW-78-12-364, 01.12.1978 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 159	yes	unpublished -
IIA 8.2.2.2	LeBlanc, G.A. 1980a. The toxicity of CGA 48988 to fathead minnow (<i>Pimephales promelas</i>) eggs and fry, Bionomics Aquatic Tox. Lab., Mass., USA, Rep.Nr. BW-80-4-642, 01.04.1980 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 157	yes	unpublished -
IIA 8.2.5	LeBlanc, G.A. 1980b. The chronic toxicity of CGA 48988 to the water flea (<i>Daphnia magna</i>), Bionomics Aquatic Tox. Lab., Mass., USA, Rep.Nr. BW-80-5-668, 01.05.1980 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 160	yes	unpublished -
IIA 8.2.1	Memmert, U. and Knoch, E. 1991a. Acute toxicity of CGA 62826 to Rainbow trout in a semi-static test (96h), Project Report 251054, RCC	62826/	yes	unpublished protected

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
	GmbH, Rossdorf, Germany, 18.12, 1991 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	3		protected
IIA 8.2.4	Memmert, U. and Knoch, E. 1991b. 48-hour toxicity of CGA 62826 to <i>Daphnia magna</i> (OECD-Immobilization -Test), Project Report 251032, RCC GmbH, Rossdorf, Germany, 18.12.1991 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	62826/ 1	yes	unpublished protected
IIA 8.2.4	Memmert U. and Knoch, E. 1991c. 48-hour toxicity of CGA 67868 to <i>Daphnia magna</i> (OECD-Immobilization -Test), Project Report 257038, RCC GmbH, Rossdorf, Germany, 11.12.1991 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	67868/ 1	yes	unpublished protected
IIA 8.2.6	Memmert, U. and Knoch, E. 1991d. Toxicity of CGA 62826 to <i>Scenedesmus subspicatus</i> (Algae Growth Inhibition Test), Project Report 251010, RCC GmbH, Rossdorf, Germany, 18.12.1991 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	62826/ 2	yes	unpublished protected
IIA 8.2.1	Memmert, U. and Knoch, E. 1992a. Acute toxicity of CGA 67868 to Rainbow trout in a semi-static test (96h), Project Report 257051, RCC GmbH, Rossdorf, Germany, 13.01. 1992 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	67868/ 2	yes	unpublished protected
IIA 8.2.6	Memmert, U. and Knoch, E. 1992b. Toxicity of CGA 67868 to <i>Scenedesmus subspicatus</i> (Algae Growth Inhibition Test), Project Report 257016, RCC GmbH, Rossdorf, Germany, 13.01.1992 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	67868/ 3	yes	unpublished protected
IIA 8.1.1	Palmer S.J., Campbell S.M., Beavers J.B. 1995a. An acute oral toxicity test with the northern bobwhite, Report N° 108-375, Wildlife International Ltd., USA, August 21, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 301	yes	unpublished protected
IIA 8.1.2	Palmer S.J., Campbell S.M., Beavers J.B., 1995b. A dietary LC50 study with the northern bobwhite, Report N° 108-374, Wildlife International Ltd., USA, August 03, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Baslex	329351/ 302	yes	unpublished protected
IIA 8.3.1.1	Palmer S.J., Beavers J.B. 1995c. An acute contact toxicity with the honey bee, Report N° 108-376, Wildlife International Ltd., USA, August 21, 1995 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 303	yes	unpublished protected
IIA 8.2.1	Rufli, H. 1994a. Report on the acute toxicity test of CGA 108906 techn. (Metabolite of CGA 48988) to Rainbow Trout, Project Report 943542, Ecotoxicology, Ciba-Geigy, Basel, 11.07.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland	108906/ 3	yes	unpublished protected

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
	Submitted by Ciba-Geigy Ltd. Basle			
IIA 8.2.1	Rufli, H. 1994b. Report on the acute toxicity test of CGA 329351 techn. (Enantiomer of CGA 48988) to Rainbow Trout, Project Report 933718, Ecotoxicology, Ciba-Geigy, Basel, 1.12.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	329351/ 25	yes	unpublished protected
IIA 8.4.1	Rufli, H. Acute toxicity test of CGA 329351 (enantiomer of CGA 48988) to earthworm (<i>Eisenia foetida</i>). Report n° 973501, Novartis Crop Protection AG, Ecotoxicology Dept., Basel, Switzerland, July 28, 1997 Owned by Novartis Crop Protection AG Submitted by Novartis Crop Protection AG	329351/ 689	yes	unpublished protected
IIA 8.2.1	Sachsse, K. 1976. Acute toxicity to rainbow trout, carp, catfish, bluegill and guppy of technical CGA 48988, Ciba-Geigy Ltd., Basle, Rep.Nr. SISS-5388, 21.09.1976 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 155	no	unpublished -
IIA 8.1.1	Ullmann, L. 1976a. Acute oral LD ₅₀ in the Japanese quail of technical CGA 48988, Ciba-Geigy Ltd., Basle, Rep.Nr. SISS-5388, 18.08.1976 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 153	no	unpublished -
IIA 8.1.2	Ullmann, L. 1976b. Eight-day-feeding toxicity in the Japanese quail of CGA 48988 technical, Ciba-Geigy Ltd., Basle, Rep.Nr. SISS-5388, 08.09.1976 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 154	no	unpublished -
IIA 8.4.1	Vial, A. 1990. Acute toxicity test of CGA 48988 techn. to Earthworm (<i>Eisenia foetida foetida</i>), Ciba-Geigy Ltd., Basle, Rep.Nr. 901034, 27.04.1990 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 168	yes	unpublished protected
IIA 8.5	Völk, S. 1992. The effects of CGA 48988-Metalaxyl on soil respiration and nitrification, RCC AG, Itingen, Switzerland, Rep.Nr. 305785, 24.02.1992 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 3122	yes	unpublished protected
IIA 8.7	Weinstock, M. 1994. Report on the test for Activated Sludge Respiration Inhibition of CGA 48988 techn., Project Report 943512, Ecotoxicology, Ciba-Geigy Basel, 24.03.1994 Owned by Ciba-Geigy Ltd. Basle Switzerland Submitted by Ciba-Geigy Ltd. Basle	48988/ 3528	yes	unpublished protected

Ecotoxicology of the formulation **RIDOMIL GOLD 480 EC** (Annex IIIA 10)

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
IIIA 10.4.1	Candolfi, M.P. 1995. CGA 329351 EC 480 (A-9408 B) Laboratory oral and contact test with the honeybee, <i>Apis mellifera</i> , Springborn Lab., Horn, Switzerland, Rep. N° 95-061-1008, June 29, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/115	yes	unpublished protected
IIIA 10.5.1	Candolfi, M. 1997. Extended laboratory test to evaluate the side effects of CGA 329351 EC 480 (A 9408 B) applied to plants on adult <i>Aphidius rhopalosiphii</i> (Hymenoptera; Aphididae), Report n° 973550, Springborn Laboratories AG, Horn, Switzerland, June 5, 1997 Owned by Novartis Crop Protection AG Submitted by Novartis Crop Protection AG	329351/647	yes	unpublished protected
IIIA 10.2.1	Grade, R. 1995. Growth inhibition test of CGA 329351 EC 480 (A-9408 B) to green algae (<i>Selenastrum capricornutum</i>) in a static system, Ciba-Geigy Ltd., Basle, Switzerland, Rep. N° 95G022, August 02, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/156	yes	unpublished protected
IIIA10.2.1.4	Neumann, Ch. Effects of A-9407 A (CGA 329351/Mancozeb WP 68) on reproduction of the Cladoceran <i>Daphnia magna</i> STRAIS in a semi-static laboratory test. Report n° 95NO19, CIBA-GEIGY Limited, Crop Protection Division, Basel, Switzerland, May 27, 1997 Owned by Novartis Crop Protection AG Submitted by Novartis Crop Protection AG	329351/446	yes	unpublished protected
IIIA 10.5.1	Reber, B. 1995a. Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the predatory ground beetle <i>Poecilus cupreus</i> L., Ciba-Geigy Ltd., Basle, Switzerland, Rep. N° 95W001, September 15, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/224	yes	unpublished protected
IIIA 10.5.1	Reber, B. 1995b. Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the predaceous mite <i>Typhlodromus pyri</i> Scheuten, Ciba-Geigy Ltd., Basle, Switzerland, Rep. N° 953524, October 9, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351289	yes	unpublished protected
IIIA 10.5.1	Wesiak H., Neumann Ch. 1995a. Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the aphid predator <i>Orius insidiosus</i> , Report N° 953523, Ciba-Geigy Basel, Oekotoxikologie, November 20, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/305	yes	unpublished protected
IIIA 10.5.1	Wesiak, H., Neumann Ch. 1995b. Acute toxicity test of CGA 329351 EC 480 (A-9408 B) on the parasitic wasp <i>Aphidius colemani</i>	329351/304	yes	unpublished protected

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
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Viereck (Hymenoptera: Aphidiidae), Report N° 953522, Ciba-Geigy
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 Owned by: Ciba-Geigy Limited
 Submitted by: Ciba-Geigy Limited

Ecotoxicology of the formulation **RIDOMIL MZ 68 WP** (Annex IIIA 10)

Annex point(s) 91/414/EEC	Author, title, report number, test institute, date of report Owner of the report (company or organisation) Submitted by (company or organisation) For publications: reference	Ciba file N°	GLP GEP	Published Protected
IIIA 10.4.1	Candolfi, M.P. 1995. CGA 329351 + Mancozeb WP 68 (A-9407 A): Laboratory oral and contact test with the honeybee, <i>Apis mellifera</i> , Report N° 95-060-1008, Springborn Lab., Horn, Switzerland, June 29, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/114	yes	unpublished protected
IIIA 10.5.1	Candolfi, M. 1997. Extended laboratory test to evaluate the side effects of CGA 329351 + mancozeb (4 + 64) WP 68 (A 9407 A) applied to plants on adult <i>Aphidius rhopalosiphii</i> (Hymenoptera; Aphididae), Report n° 973550, Springborn Laboratories AG, Horn, Switzerland, May 27, 1997 Owned by Novartis Crop Protection AG Submitted by Novartis Crop Protection AG	329351/642	yes	unpublished protected
IIIA 10.2.1	Grade, R. 1995. Growth inhibition test of CGA 329351/mancozeb WP 68 (A-9407 A) to green algae (<i>Selenastrum capricornutum</i>) in a static system, Report N° 95G034, Ciba-Geigy Basel, Oekotoxikologie, July 27, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/136	yes	unpublished protected
IIIA 10.1.1	Johnson, A.J. 1995. Acute oral toxicity (LD50) to Bobwhite Quail of CGA 329351 + mancozeb WP 68 (A-9407 A), Report N° CBG 748, Huntingdon Research Centre, UK, 11 December 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/309	yes	unpublished protected
IIIA 10.6.1.1	König, B. 1995. Acute effects on earthworm <i>Eisenia fetida</i> (Savigny) of CGA 329351 + mancozeb WP 68 (A-9407 A, Report N° 950508CC, Dr. U. Noack Laboratorium, D-Hildesheim, July 14, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/129	yes	unpublished protected
IIIA 10.2.1	Neumann, Ch. 1995. Acute toxicity test of CGA 329351 + mancozeb (4+64) WP68 (A-9407 A) to the cladoceran <i>Daphnia magna</i> Straus under static conditions, Report N° 95N018, Ciba-Geigy Basel, Oekotoxikologie, November 14, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/296	yes	unpublished protected
IIIA 10.5.1	Reber, B. 1995a. Acute toxicity test of CGA 329351 + mancozeb (4+64) WP68 (A-9407 A) on the predatory ground beetle <i>Poecilus cupreus</i> L., Report N° 95W006, Ciba-Geigy Basel, Oekotoxikologie, September 15, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/223	yes	unpublished protected
IIIA 10.5.2	Reber, B. 1995b. Population development of the predatory mite <i>Typhlodromus pyri</i> Scheuten under field conditions on grapes after treatment with CGA 329351 + mancozeb (4+64) WP 68 (A-9407 A), Report N° 953529, Ciba-Geigy Basel, Oekotoxikologie,	329351/312	no	unpublished protected

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	November 28, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited			
IIIA10.2.1	Rufli, H. 1995. Acute toxicity test of CGA 329351/mancozeb WP 68 (A-9407 A) to rainbow trout (<i>Oncorhynchus mykiss</i>) in the static system, Report N° 95R024, Ciba-Geigy Basel, Oekotoxikologie, August 31, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/219	yes	unpublished protected
IIIA 10.5.1	Wesiak H., Neumann Ch. 1995a. Acute toxicity test of CGA 329351 + mancozeb (4+64) WP 68 (A-9407 A) on the aphid predator <i>Orius insidiosus</i> , Report N° 953531, Ciba-Geigy Basel, Oekotoxikologie, November 20, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/307	yes	unpublished protected
IIIA 10.5.1	Wesiak, H., Neumann Ch. 1995b. Acute toxicity test of CGA 329351 + mancozeb (4+64) WP 68 (A-9407 A) on the parasitic wasp <i>Aphidius colemani</i> Viereck (Hymenoptera: Aphidiidae), Report N° 953532, Ciba-Geigy Basel, Oekotoxikologie, November 20, 1995 Owned by: Ciba-Geigy Limited Submitted by: Ciba-Geigy Limited	329351/306	yes	unpublished protected

ANNEX B

Metalaxyl-M

B.9 Proposals for classification and labelling

B.9.1 Proposals for the classification and labelling of the active substance (Annex IIA 10)

Table B.9.1-1 : Classification and labelling of metalaxyl-M made by the Rapporteur

Classification	Xn, R22 Xi, R41, R52/53	
Labelling:		
Hazard symbol:	Xn, R22-41 , R52/53	
Indication of danger:	harmful	
Risk phrases:	R22	harmful
	R41	risk of serious damage to eyes
	R52/53	harmful to aquatic organisms, may cause long-term adverse effect in the aquatic environment
Safety phrases	S2	keep out of reach of the children
	S26	in case of contact with eyes, rinse immediately with plenty of water and seek medical advice
	S39	wear eye/face protection

Table B.9.1-2 : Justification for the proposal made by the Rapporteur concerning the classification and labelling of metalaxyl-M.

Proposed classification	Justification
Xn, R22	LD ₅₀ oral, rat : 669 mg/kg bw
Xi, R41	severe irritant to rabbit eyes
R52	Eb ₅₀ (<i>Scenedesmus subspicatus</i>) = 36 mg a.s./l
R53	the biodegradation of the a.s. is 0% in 29 days

B.9.2a Proposals for the classification and labelling of the formulations (Annex IIIA 12.3)

Table B.9.2a-1 : Classification and labelling of RIDOMIL GOLD 480 EC made by the Rapporteur

<i>Classification :</i>	Xn, R22 Xi, R36 R43, R52/53	
<i>Labelling :</i>		
Hazard symbols :	Xn	
Indication of danger :	harmful	
Risk phrases :	R22	harmful if swallowed
	R 36	irritant to eyes
	R43	may cause sensitization by skin contact
	R52/53	harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Safety phrases :	S2	keep out of reach of children
	S13	keep away from food, drink and animal feeding stuffs
	S20/21	when using, do not eat or drink or smoke
	S24/25	avoid contact with skin and eyes
	S37	wear suitable gloves
	S45	in case of accident or if you feel unwell, seek medical advice immediately

Table B.9.2a-2 : Justification for the proposal made by the Rapporteur concerning the classification and labelling RIDOMIL GOLD 480EC

Proposed classification	Justification
Xn, R22	LD ₅₀ oral rat female : <2000 and > 1000 mg/kg bw
Xi, R36	irritating to rabbit eyes
R43	skin sensitizer in the guinea pig
R52/53	derived from the a.s. data
R50	LC ₅₀ (rainbow trout) = 0.54 mg/l Eb (<i>Selenastum capricornutum</i>) = 0.13 mg/l

Table B.9.2a-3 : Classification and labelling of RIDOMIL GOLD 68 WP made by the Rapporteur

<i>Classification :</i>	N, R50	
<i>Labelling :</i>		
Hazard symbols :	N	
Indication of danger :	dangerous for the environment	
Risk phrases :	R50	very toxic to aquatic organisms
Safety phrases :		
	S2	keep out of reach of children
	S13	keep away from food, drink and animal feeding stuffs
	S20/21	when using, do not eat or drink or smoke
	S60	this material and its container must be disposed as hazardous waste
	S61	avoid release to the environment. Refer to special instruction instructions/safety data sheets

Table B.9.2a-4 : Justification for the proposal made by the Rapporteur concerning the classification and labelling of RIDOMIL GOLD 68 WP

Proposed classification	Justification
N, R50	LC ₅₀ (rainbow trout) = 0.54 mg/l Eb (<i>Selenastum capricornutum</i>) = 0.13 mg/l