ANNEX B

Original version January 1997, revised in March 2010

Kresoxim-methyl

B.9 Ecotoxicology

Added in March 2010:

Kresoxim-methyl (BAS 490 F) is included in Annex I of the Directive 91/414/EEC, effective as from February 1, 1999 (see Official Journal of the European Union, Commission Directive 1999/1/EC). Expiry date of the inclusion is January 31, 2009. Annex I Renewal of Kresoxim-methyl is intended with the submission of the following evaluation.

Introductory note on the formulations :

Formulation CANDIT – BAS 490 02 F containing 50 % kresoxim-methyl

Formulation ALLEGRO – BAS 494 04 F or BAS 494 02 F containing 125 g/L kresoxim-methyl and 125 g/L epoxiconazole
ALLEGRO in its old formulation BAS 494 **02** F (see original DAR) was one of the representative formulations for first inclusion of kresoxim-methyl into Annex I of Council Directive 91/414/EEC. However, the formulation recipe of ALLEGRO was modified, resulting in a formulation coded as BAS 494 **04** F, which is now proposed as representative formulation for Annex I Renewal of kresoxim-methyl. It concerns a minor change in composition between both formulations, as explained in detail in Vol.4, C.1.3b.

Formulation MENTOR – BAS 490 01 F is no longer supported in the resubmission dossier
Information related to the plant protection product MENTOR is still included in the revised DAR. However, the risk assessment has not been based on the ecotox endpoints, since MENTOR is no longer proposed as the representative formulation in the framework of the Annex I Renewal of kresoxim-methyl.

The intended uses of kresoxim-methyl are summarized below :

Table B.9.0-1 : Proposed use pattern of the formulation CANDIT

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate (kg a.s./ha) [1)]	Application rate (kg product/ha) [1)]
Pome fruit (apple, pear)	1 - 4	7	53 - 79	0.100 - 0.125	0.200 - 0.250
Grapevine	1 - 3	8	19 - 81	0.100 - 0.150	0.200 - 0.300

[1)] application rate increases with plant growth stage

Table B.9.0-2 : Proposed use pattern of the formulation ALLEGRO

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate		
				BAS 494 04 F [L/ha]	Kresoxim-methyl (BAS 490 F) [kg a.s./ha]	Epoxiconazole (BAS 480 F) [kg a.s./ha]
Cereals	2	21	25 - 69	1.0	0.125	0.125

The risk assessments performed in the DAR are dealing mainly with the effects of the a.s. kresoxim-methyl. For the evaluation of effects of the a.s. epoxiconazole RMS refers to the DAR, addenda, List of Endpoints and EFSA conclusion of epoxiconazole.

B.9.1 Effects on birds (Annex IIA 8.1; Annex IIIA 10.1)

B.9.1.1 Acute oral toxicity (Annex IIA 8.1.1)

Avian single-dose oral LD_{50} of Reg. No. 242 009 on the bobwhite quail (*Colinus virginianus*). (Munk R., 1993a).

Guidelines :
US EPA, Subdivision E, § 71-1 (1982), acceptable
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N 27 (III a1)
Test species : bobwhite quails (*Colinus virginianus*)
Sex, weight, age : 5 male and 5 female birds per concentration, 153.7 - 202.8 g, ± 6 month old
Applied concentrations : untreated control; 464, 681, 1000, 1470, 2150 mg a.s. /kg body weight
Type of application : Dispersion of the a.s. in 0.5 % aqueous solution of carboxymethylcellulose. The test compound was administered into the crop by gavage.
Time of exposure : one single application, monitoring during 14 days
Findings :
Mortality : No mortality was observed.
Body weight : No statistically significant differences between control and treatments. The body weigth of the male birds at the 1000 mg a.s./kg bw dose was significantly different from the control. It is considered as accidental.
Clinical signs : No signs of sickness or toxicity were observed.
Feed consumption : Same order of magnitude between control and treatments.
Conclusion :
The study is acceptable.
Kresoxim-methyl is not toxic to bobwhite quails up to 2150 mg/kg bw.
Endpoints :
LD_{50} (*Colinus virginianus*) > 2150 mg a.s./kg bw (highest concentration tested)
NOEL (*Colinus virginianus*) = 2150 mg a.s./kg bw

B.9.1.2 Avian dietary toxicity (5day) (Annex IIA 8.1.2)

Avian dietary LC_{50} test of Reg. No. 242 009 in chicks of the bobwhite quail (*Colinus virginianus*). (Munk R., 1993d).

Guidelines :
US EPA, Subdivision E, § 71-2 (1982); Similar to guideline OECD 207
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 93.7 %, batch: N 36 (III C1)
Test species : bobwhite quails (*Colinus virginianus*)
Sex, weight, age : 10 chicks/concentration, unknown sex ratio since sex determination is uncertain at this age, 16.7 - 33.7 g, 13 day old
Applied concentrations : untreated control; 313, 625, 1250, 2500, 5000 mg a.s./kg feed
Type of application : 'Ssniff' experimental diet 'ad libitum' before and during the test. Stability (98.6 % recovery after 35 days) and homogeneity (98.5 - 98.9 % recovery) of test substance in the diet was determined analytically.
Time of exposure : short-term feeding test (5 days with exposure by the feed + 3 days observations)
Findings :
Mortality : No compound-related mortality. Mortalities caused by mutual face picking. More than 10 % mortality in control; due to the absence of mortality in the 2 highest concentrations the test is accepted.
Body weight : No significant impairment of the development of body weight.
Clinical signs : Apathy of one chick at dose 1250 mg a.s./kg feed (day 5), not treatment-related.
Feed consumption : No significant compound-related reduction of consumption.
Conclusion :
The study is acceptable.
Kresoxim-methyl administered in the feed caused no sign of toxicity to birds.
Endpoints :
LC_{50} (*Colinus virginianus*, 5 d) > 5000 mg a.s./kg feed = 1051 mg a.s./kg bw/d (based on a mean body weight of 31.4 g and a mean food consumption of 6.6 g/bird/d) (highest concentration tested)
NOEC (*Colinus virgininianus*, 5 d) = 5000 mg a.s./kg feed = 1051 mg a.s./kg bw/d

Avian dietary LC_{50} test of Reg. No. 242 009 in chicks of the mallard duck (*Anas platyrhynchos*). (Munk R., 1993i).

Guidelines :
US EPA, Subdivision E, § 71-2 (1982); Similar to guideline OECD 207
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N27 (III a1)
Test species : mallard ducks (*Anas platyrhynchos*)
Sex, weight, age : 10 chicks/concnetration, unknown sex ratio since sex determination is uncertain at this age, 31.1 - 94.1 g, 8 days old
Applied concentrations : untreated control; 625, 1250, 2500, 5000 mg a.s./kg feed
Type of application : 'Ssniff' experimental diet 'ad libitum' before and during the test. Homogeneity (98.2 - 109.4 % recovery) of test substance in the diet was determined analytically.
Time of exposure : short-term feeding test (5 days with exposure by the feed + 3 days observations)
Findings :
Mortality : No compound-related mortalities in neither test group.
Body weight : No significant impairment of the development of the body weight.
Clinical signs : No symptoms were detected.
Feed consumption : No compound-related differences in feed consumption in neither test group.

Conclusion :
The study is acceptable.
Kresoxim-methyl administered in the feed caused no sign of toxity to birds.
Endpoints :
LC_{50} (*Anas platyrhynchos*, 5 d) > 5000 mg a.s./kg feed = 2195 mg a.s./kg bw/d (based on a mean body weight of 91.1 g and a mean food consumption of 40 g/bird/d) (highest concentration tested)
NOEC (*Anas platyrhynchos*, 5 d) = 5000 mg a.s./kg feed = 2195 mg a.s./kg bw/d

B.9.1.3 Subchronic and reproductive toxicity (Annex IIA 8.1.3)

1-Generation reproduction study with Reg. No. 242 009 on the bobwhite quail (*Colinus virginianus*) by administration in the diet. (Munk R., 1994b).

Guidelines :
US EPA, subdivision E, § 71-4 (1982); study is conform to guideline OECD 206.
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 93.7 %, batch: 36 (III c-1)
Test species : bobwhite quails (*Colinus virginianus*)
Sex, weight, age : bobwhite quails (about 9 months old) approaching the first laying season were randomly allocated to cages with 1 male and 1 female each per replicate, 16 replicates X 4 concentrations
Applied concentrations : untreated control; 50, 500, 1000 mg a.s./kg feed
Type of application : 'Ssniff' experimental diet 'ad libitum' before and during the test. Homogeneity (93.45 - 93.88 % recovery) of test substance in the diet was determined analytically.
Time of exposure :
10 weeks : pre-egg production period
16 weeks : egg production period

Findings :

Table B.9.1.3-1 : Major effects of kresoxim-methyl observed during the reproduction study of bobwhite quails

Endpoints	**Doses (mg a.s./kg feed)**			
	0	**50**	**500**	**1000**
Adults				
Mortality	no effect			
Clinical symptoms	no effect			
Body weight	no effect			
Food consumption	no effect			
Reproduction Parameters				
No. of eggs laid	844	915	758	746
No. of eggs laid/female bird	52.8	57.2	47.4	46.6
No. of cracked and broken eggs	32	32	29	87
Mean egg weight (g)	10.3	9.6	10.2	9.6
Mean egg shell thickness (mm)	0.20	0.20	0.21	0.20
No. of eggs incubated	755	821	681	610
No. of fertile eggs	655	763	626	495
No. of infertile eggs	100	58	55	115
No. of early embryonic mortalities	11	29	40	22
No. of viable 11-day old embryos	644	734	586	473
No. of late embryonic mortalities	4	11	10	5
No. of viable 18-day old embryos	640	723	576	468
No. of total embryonic deaths	15	40	50	27
No. of "dead-in-shell"	66	163	68	57
No. of chicks hatched	574	560	508	411
No. of 14-day surviving chicks	516	489	450	363
No. of chicks hatched/female bird	35.9	35.0	31.0	25.7
No. of 14-day surviving chicks/female bird	32.3	30.6	28.1	22.7
Mean body weight of chicks at hatching (g)	6.6	6.3	6.6	6.5
Mean body weight of chicks 14 days after hatching (g)	24.6	24.2	24.3	23.7

Palability : No rejection of feed containing the test compound could be observed.

Parameters showing biologically significant differences between treatments and control are :
- Number of cracked eggs : 11.7 % at 1000 mg a.s./kg feed - 3.8 % in control
- Number of fertile eggs
- Viability of embryos (day 18)
- Number of surviving chicks/ female bird

Conclusion :
The study is acceptable.
At the highest concentration of 1000 mg a.s./kg feed effects on some evaluation parameters are observed.
NOEC (*Colinus virginianus*, 26 weeks) = 500 mg a.s./kg feed = 51.7 mg a.s./kg bw/d (based on a mean body weight of 191.4 g and a mean food consumption of 19.8 g/bird/d)

B.9.1.4 Acute oral toxicity of the preparations (Annex IIIA 10.1.1)

According to Directive 91/414, CD 96/12 and Working Document SANCO/10329/2002, rev. 2 (17.10.02) no acute test with the formulation is required since :

- All acute TERs are favourable, hence there is no indication of a risk based on the tests performed with the active substance kresoxim-methyl.
- The formulated products CANDIT (BAS 490 02 F) and ALLEGRO (BAS 494 04 F) will be applied exclusively in spray treatments. Thus exposure is better determined in terms of active substance than of the formulation.

B.9.1.5 Supervised cage or field trials (Annex IIIA 10.1.2)

According to Directive 91/414, amended by CD 96/12, no further test is required since all TERs are favourable and there is no evidence of risk based on the tests performed with the active substance kresoxim-methyl.

B.9.1.6 Acceptance of bait, granules or treated seeds by birds (palatability test) (Annex IIIA 10.1.3)

No testing is required since the formulated products CANDIT (BAS 490 02 F) and ALLEGRO (BAS 494 04 F) will be applied exclusively in spray treatments. Acceptance of baits, granules or treated seed is not applicable.

B.9.1.7 Effects of secondary poisoning (Annex IIIA 10.1.4)

No study required.
The secondary poisoning is discussed under point B.9.1.8.

B.9.1.8 Summary of effects on birds - exposure and hazard assessment for birds (Annex IIIA 10.1)

The endpoints for birds expressed as mg a.s./kg feed were recalculated in mg a.s./kg bw/d, based on food consumption and body weight.

Table B.9.1.8-1 : Effects of kresoxim-methyl on birds

Test species	Test System	Duration of exposure	Endpoints	References
Colinus virginianus	acute oral toxicity	single-dose application	LD_{50} **> 2150 mg a.s./kg bw**	Munk R., 1993a
Colinus virginianus	short-term dietary toxicity	5 days	LC_{50} > 5000 mg a.s./kg feed **> 1051 mg a.s./kg bw/d**	Munk R., 1993d
Anas platyrhynchos	short-term dietary toxicity	5 days	LC_{50} > 5000 mg a.s./kg feed > 2195 mg a.s./kg bw/d	Munk R., 1993e
Colinus virginianus	sub-chronic and reproductive toxicity	26 weeks	NOEC = 500 mg a.s./kg feed **= 51.7 mg a.s./kg bw/d**	Munk R., 1994b

First tier risk assessment for birds :

The risk assessment for birds is based on the Guidance Document for birds and mammals under Council Directive 91/414/EEC of September 2002 (SANCO/4145/2000). As a worst case it was assumed that the birds obtained 100 % of their diet in the treated area.

1- Formulation CANDIT

The formulation CANDIT (BAS 490 02 F) is a fungicidal product, which contains the active substance kresoxim-methyl with a nominal content of 50 % w/w.

Table B.9.1.8-2 : Proposed use pattern of the formulation CANDIT

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate (kg a.s./ha) [1)]	Application rate (kg product/ha) [1)]
Pome fruit (apple, pear)	1 - 4	7	53 - 79	0.100 - 0.125	0.200 - 0.250
Grapevine	1 - 3	8	19 - 81	0.100 - 0.150	0.200 - 0.300

[1)] application rate increases with plant growth stage

For simplification reasons, the risk assessment is only conducted for the higher application rates. This covers the increase in application rate during season.

2- Formulation ALLEGRO

The formulation ALLEGRO (BAS 494 04 F) is a fungicidal product, which contains the active substances
- kresoxim-methyl (BAS 490 F) with a nominal content of 125 g a.s./L
- epoxiconazole (BAS 480 F) with a nominal content of 125 g a.s./L

Table B.9.1.8-3 : Proposed use pattern of the formulation ALLEGRO

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate		
				BAS 494 04 F [L/ha]	Kresoxim-methyl (BAS 490 F) [kg a.s./ha]	Epoxiconazole (BAS 480 F) [kg a.s./ha]
Cereals	2	21	25 - 69	1.0	0.125	0.125

1.1 – Dietary exposure :

Table B.9.1.8-4 : Estimated oral uptake of kresoxim-methyl by insectivorous birds and first tier Toxicity Exposure Ratios (TERs) for use in pome fruit (apple, pear) at 1-4 applications x 0.100-0.125 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Bird type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.125	orchard early/ late	insecti-vorous	acute	1.04	52	n.a.	n.a.	6.76	> 318	10
			short-term	1.04	29	n.a.	n.a.	3.77	> 279	10
			long-term	1.04	29	n.a.	n.a.	3.77	13.7	5

Table B.9.1.8-5 : Estimated oral uptake of kresoxim-methyl by insectivorous birds and first tier Toxicity Exposure Ratios (TERs) for use in grapevines at 1-3 applications x 0.100-0.150 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Bird type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.150	grape-vines early/ late	insecti-vorous	acute	1.04	52	n.a.	n.a.	8.11	> 265	10
			short-term	1.04	29	n.a.	n.a.	4.52	> 232	10
			long-term	1.04	29	n.a.	n.a.	4.52	11.4	5

The acute, short-term and long-term risk of kresoxim-methyl is acceptable for the intended uses in pome fruit and grapevines.

Table B.9.1.8-6 : Estimated oral uptake of kresoxim-methyl by herbivorous and insectivorous birds and first tier Toxicity Exposure Ratios (TERs) for use in cereals at 2 applications x 0.125 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Bird type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.125	cereals early	herbivorous	acute	0.44	142	1.2[(1)]	n.a.	9.37	> 229	10
			short-term	0.44	76	1.23[(2)]	n.a.	5.14	> 204	10
			long-term	0.44	76	1.23[(2)]	0.53	2.72	19.0	5
	cereals early/ late	insecti-vorous	acute	1.04	52	n.a.	n.a.	6.76	> 318	10
			short-term	1.04	29	n.a.	n.a.	3.77	> 279	10
			long-term	1.04	29	n.a.	n.a.	3.77	13.7	5

(1) MAF based on 2 applications and 14 days spray interval because SANCO/4145/2000 does not provide respective value for 21 days spray interval (overestimation of the actual risk)
(2) MAF calculated for short-term and long-term exposure according to
$MAF = (1 - e^{-0.069ni}) / (1 - e^{-0.069i})$ with i = interval and n = number of applications
for 2 applications and 21 days spray interval, assuming default DT_{50} on plant of 10 days
MAF = 1.23

The acute, short-term and long-term risk of kresoxim-methyl is acceptable for the intended use in cereals.
For the risk assessment of epoxiconazole, RMS refers to the DAR, addenda, List of Endpoints and the EFSA conclusion on epoxiconazole.

1.2 - Secondary poisoning : Risk to earthworm-eating and fish-eating birds :

Since the log P_{OW} of kresoxim-methyl is higher than 3 (log P_{OW} = 3.4), there might be a potential for bioaccumulation.
The 21-day PEC values in soil and surface water are obtained from the section on fate and behaviour :

Apple : PECsoil (twa, 21 d) = 0.015 mg a.s./kg
Grapevine : PECsoil (twa, 21 d) = 0.022 mg a.s./kg
Cereals : PECsoil (twa, 21 d) = 0.010 mg a.s./kg

Apple : PECsw (twa, 21 d, step 2) = 6.684 µg a.s./L
Grapevine : PECsw (twa, 21 d, step 2, late application) = 2.102 µg a.s./L
Cereals : PECsw (twa, 21 d, step 2) = 0.471 µg a.s./L

The BCF in earthworms is calculated as :
$BCF = (0.84 + 0.01 \times P_{OW})/(f_{OC} \times K_{OC}) = (0.84 + 0.01 \times 2512)/(0.02 \times 308) = 4.2$
with the following values obtained from the section on fate and behaviour :
P_{OW} = 2512 for kresoxim-methyl
mean K_{OC} = 308 mL/g for kresoxim-methyl
From the study on bioaccumulation potential in *Oncorhynchus mykiss* with kresoxim-methyl a BCF of 220 was obtained for the whole fish.

Table B.9.1.8-7 : The long-term risk of kresoxim-methyl for birds eating contaminated earthworms and fish for the use in pome fruit

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
earthworm	0.015 mg a.s./kg	4.2	0.063	1.1	0.069	746	5
fish	6.684 µg a.s./L	220	1.470	0.21	0.309	167	5

Table B.9.1.8-7 : The long-term risk of kresoxim-methyl for birds eating contaminated earthworms and fish for the use in grapevine

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
earthworm	0.022 mg a.s./kg	4.2	0.092	1.1	0.102	509	5
fish	2.102 µg a.s./L	220	0.462	0.21	0.097	532	5

Table B.9.1.8-7 : The long-term risk of kresoxim-methyl for birds eating contaminated earthworms and fish for the use in cereals

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
earthworm	0.010 mg a.s./kg	4.2	0.042	1.1	0.046	1119	5
fish	0.471 µg a.s./L	220	0.104	0.21	0.022	2376	5

The long-term risk of kresoxim-methyl for birds eating contaminated earthworms and fish is acceptable for the intended uses in pome fruit, grapevine and cereals.

1.3- Plant metabolites :

In the plant metabolism and rotational crop studies with kresoxim-methyl, the metabolites BF 490-1 (B490M1), BF 490-2 (B490M2) and BF 490-9 (B490M9) were the main metabolites, which in one case approached or exceeded 10 % TRR (major metabolites) in green plant material (carrot forage), a potential feeding matrix of herbivorous birds.
Due to their significant relative quantities, the aforementioned metabolites would be potentially relevant for the avian risk assessment. However, the identified major metabolites were also found in laying hens.

Therefore, for the metabolites approaching or exceeding 10 % TRR in the plant metabolism and rotational crop studies, the following can be concluded:

- The identified major metabolites were also found in laying hens, hence would have been tested in the avian toxicity studies conducted with kresoxim-methyl.
- The risk assessment for the parent molecule kresoxim-methyl is thus assumed to cover the potential risk from the plant metabolites.

1.4- Drinking water : spray application

The Guidance Document on the Risk Assessment for Birds and Mammals SANCO 4145/2000 proposes that birds and wild mammals may obtain their water demand from two potential sources.

The major source of contaminated drinking water is surface water containing residues of the active substance for example via spray drift from adjacent treated fields. As a conservative measure the water concentration may be considered equivalent to the initial PEC calculated for surface water as obtained from the environmental fate section of the DAR (Vol. 3, B.8.6).

Puddles of spray liquid held in leaf axils may be relevant for certain crop types giving rise to leaf whorls after foliar spray application, e.g. vegetables with head-like structure such as cabbage or cauliflower. In this case the concentration of the active substance in the spray solution as obtained from the application data section of the DAR (Vol. 3, 3.2.3) would need to be taken into account. A field experiment after foliar spray application in white cabbage (Hommes *et al*. 1990)[1] showed that the initial concentration of the active substance in leaf puddles is in the range of 5 – 20 % of the spray concentration. Therefore, EPPO (1994)[2] and SANCO/4145/2000 recommend using a conservative dilution factor of 5.

For the representative uses of kresoxim-methyl in pome fruit orchards and vineyards (BAS 490 02 F), and in cereals (BAS 494 04 F) a leaf puddle scenario event is unlikely to occur for the following reasons:

– The flat morphology of the crop leaves does not provide reservoirs for collecting spray solution.
– In orchards and vineyards the morphology of the regularly mulched ground vegetation (if present) is not comparable to leafy vegetables with forming heads.
– The water volume typically used in the proposed uses of kresoxim-methyl is obtained form the application data section of the DAR (Vol. 3, 3.2.3). The water volume for the uses in pome fruit orchards and vineyards (BAS 490 02 F), and in cereals (BAS 494 04 F) ranges from 150 to 1 800 L/ha. This calculates to 15 to 180 mL/m^2 which, together with the leaf morphology of crops and undergrowth noted earlier, illustrate that orchard trees, grapes, their undergrowth, and cereals are unlikely to give rise to leaf puddles.

Therefore, the potential exposure of birds / mammals via spray solution puddles is considered negligible and deemed not relevant for this assessment. Nevertheless, exposure via spray drift to water bodies, although assumed being the exception under good agricultural practice, might be considered a potential source of exposure and thus will be evaluated in the following.

The daily water intake of a 10 g bird is calculated allometrically as follows (Calder and Braun, 1983) :

Total water ingestion rate (L/day) = $0.059 \times W^{0.67}$ where W is the body weight in kg

Total water ingestion rate (L/day) for a 10 g bird = $0.059 \times (0.010)^{0.67} = 0.0027$ L/day

The daily dose of active substance is calculated as

(PECsw * total water ingestion rate) / W

The PEC values for surface water in Step 1 and 2 represent ‘worst-case loadings’ (Step 1) and ‘loadings based on sequential application patterns’ (Step 2), as detailed in FOCUS (2001). In Step 1 inputs of spray drift, run-off, erosion and / or drainage are cumulated as a single loading (sum of individual applications) to surface water calculating into most conservative water concentrations. In Step 2 the loadings are refined to occur as successive individual applications, each resulting in drift to the water body, followed by a run-off / erosion / drainage event occurring four days after the last application, and additionally taking into account region of use (Northern or Southern Europe), season of application, and crop interception.

[1] Hommes, V.M., Buchs, W., Joermann, G., and Siebers, J. (1990). Vogelgefährdung durch Pflanzen-schutzmittelrückstände in Blattpfützen von Gemüsekohl (Poisoning risk of birds by residues of pesticides in leaf puddles of colre crops). Nachrichtenbl. Deut. Pflanzenschutzd. 42. 113-117.

[2] EPPO (1994): Decision-making scheme for the environmental risk assessment of plant protection products, Chapter 11 Terrestrial vertebrates. EPPO Bull 24, 37-87.

Assuming a reasonable worst-case scenario, the surface water concentration is considered equivalent to the PEC calculated for multiple applications according FOCUS Step 2. Referring to the environmental fate section of the DAR (Vol. 3, B.8.6) the related PEC values are as follows:

Pome fruit orchards	0.018393 mg kresoxim-methyl/L
Vineyards	0.005690 mg kresoxim-methyl/L
Cereals	0.001158 mg kresoxim-methyl/L

For kresoxim-methyl the relevant time scale for potential exposure of birds or mammals through contaminated surface water is acute. In water / sediment systems the active substance proved to have short DT_{50} values of 1.26 and 1.36 days (van Beinum and Beulke, 2008). Therefore, the following risk assessments focus on the acute route of exposure.

The exposure and TER calculations for the proposed uses of the representative formulations BAS 490 02 F (pomefruit orchards, vineyards) and BAS 494 04 F (cereals) are presented in table B.9.1.8-8 below.

Table B.9.1.8-8 : Acute Toxicity Exposure Ratios (TERa) for the most conservative small insectivorous bird indicator species (10 g b.w.) exposed through surface water

Crop	Body weight [kg]	Total water ingestion rate [L/day]	PEC_{sw} (Step 2) [mg a.s./L]	Daily intake of a.s. [mg a.s./kg b.w./day]	LD_{50} [mg a.s./kg b.w.]	TER_a --
Orchards	0.010	0.003	0.01893	0.006	> 2 150 [1]	> 358 333
Vineyards	0.010	0.003	0.00569	0.002	> 2 150 [1]	> 1 075 000
Cereals	0.010	0.003	0.001158	0.00035	> 2 150 [1]	> 6 142 857

[1] Acute oral toxicity study in the bobwhite quail (Munk R. 1993a, see Table B.9.1.8-1)

The risk for birds drinking contaminated surface water is acceptable for all intended uses.

In conclusion, the risk of kresoxim-methyl and its metabolites is acceptable for birds for the intended uses in pome fruit, grapevine and cereals.

B.9.2 Effects on aquatic organisms (fish, aquatic invertebrates, algae) (Annex IIA 8.2; Annex IIIA 10.2)

B.9.2.1 Acute toxicity of the active substance and metabolites, degradation or reactions products to fish (Annex IIA 8.2.1)

Acute toxicity of Reg. No. 242 009 on the rainbow trout *(Oncorhynchus mykiss* WALBAUM 1792). (Munk R., 1992).
Addendum to the study report: Acute toxicity on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of Reg. No. 242 009 of January 28, 1992. (Munk R., 1993h).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
EEC Directive 84/449 (updated 1989)
OECD 203 (1989)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N 27 (III a1)
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 7 cm (range: 6.0 - 7.6 cm), 4.2 g (range: 2.8 - 5.0 g), 0.42 g fish/L water
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : control; 0.046, 0.068, 0.1, 0.147, 0.215, 0.316, 0.464, 0.681, 1.0 mg a.s./L
measured concentrations ranging from 34.4 to 18.7 % of the nominal concentrations
Test conditions :
temperature : 12 ± 1 °C
pH : 8.5 - 8.7
oxygen content : about 10 mg O_2/L on day 1 and 8.5 - 8.8 mg O_2/L on day 4
total hardness : about 2.5 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Mortality : Occurred only in the top concentration of 1.0 mg/L with 20 %, 80 % and 100 % dead fish after 48, 72 and 96 hours, respectively.
Behavioral observations : Discolorations, convulsions and tumbling at the dose of 1mg/L (nominal).
Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 0.681 < 1.0 mg a.s./L (nominal)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.681 mg a.s./L (nominal)
Due to the low solubility of the a.s. in water the actual toxicity values are :
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 0.15 < 0.19 mg a.s./L (measured)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.15 mg a.s./L (measured)
Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 0.15 < 0.19 mg a.s./L (measured)
Kresoxim-methyl is very toxic to rainbow trout.

Added in March 2010:

A new study has been submitted to meet the requirements of the current regulations. This study has been conducted under flow-through conditions and is submitted due to the poor analytical recoveries in the original study with rainbow trout (Munk R., 1993b). This new study is used in the risk assessment.

BAS 490F: A 96-hour flow-through acute toxicity test with the rainbow trout *(Oncorhynchus mykiss* W.) (Graves W.C *et al*., 1995a).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
EEC Directive 84/449 (updated 1989)
OECD 203 (1989)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 % (re-analysed on 08/03/1995: 93.6 %, batch: N 36
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 2 replicates/treatment, 38 mm (range: 32 - 45 mm), 0.64 g (range: 0.4 - 1.1 g), 0.43 g fish/L water
Type of test : flow-through system (96 hours) receiving approximately 6 volume additions of test water every 24 hours
Applied and measured concentrations :
nominal : control; solvent control; 0.065, 0.108, 0.180, 0.300, 0.500 mg a.s./L
measured concentrations:
-at the beginning of test: ranging from 83 to 122 % of the nominal concentrations
-at 48 h: ranging from 71 to 139 % of the nominal concentrations
-at 96 h: ranging from 89 to 115 % of the nominal concentrations
mean measured concentrations (0 h, 48 h, 96 h): 0.063, 0.104, 0.190, 0.314, 0.475 mg a.s./L
Test conditions :
temperature : 11.3 - 12 °C
pH : 8.3 - 8.4
oxygen content : 9.2 - 9.9 mg O_2/L throughout the test (> 6.5 mg/L, thus > 60 % saturation at 12 °C)
total hardness : 128 - 132 mg/L (as $CaCO_3$) (stated as 'moderately hard')
photoperiod : 16/8 hours light/dark cycle
Analytical methods : GC with electron capture detection
Findings :
Mortality : Occurred at the mean measured concentrations of 0.190 (55 %), 0.314 (95 %) and 0.475 mg/L (100 %) at 96 h exposure.
Behavioral observations : Lethargy was observed at 0.190 mg/L and above. Onset time was 2 h (314 mg/L).
Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 0.190 mg a.s./L (measured)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.104 mg a.s./L (measured)
Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 0.190 mg a.s./L (measured)
Kresoxim-methyl is very toxic to rainbow trout.

Acute toxicity study on the bluegill (*Lepomis macrochirus* RAF.) of Reg. No. 242 009 in a static system (96 hours). (Munk R., 1993c).
Addendum to the report project No. 14F0180/915079: Acute toxicity on the bluegill (*Lepomis macrochirus* RAF.) of Reg. No. 242 009 of May 14, 1993. (Munk R., 1993f).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
EEC Directive 84/449 (updated 1989)
OECD 203 (adopted 1992)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N 27 (III a1)
Test species : bluegill fish (*Lepomis macrochirus*)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 5.49 cm (range: 4.9 - 6.0 cm), 1.9 g (range: 1.2 - 2.7 g), 0.19 g fish/L water
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : water control; solvent control; 0.316, 0.464, 0.681, 1.0, 1.47, 2.15, 3.16, 4.64 mg a.s./L
measured : The recovery rates of the active substance were in the ranges of 25.8 % to 58.4 % (day 0) and 13.6 % to 48.6 % (day 4), respectively.
Test conditions :
temperature : 21 ± 1 °C
pH : 8.2 - 8.6
oxygen content : about 8.8 mg O_2/L (1 hour) to about 7.0 mg O_2/L (96 hours)
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Mortality : Mortality occurred in the doses of 3.16 mg/L and 4.64 mg/L.
Behavioral observations : Apathy, narcotic-like state and tumbling at 3.16 and 4.64 mg/L.
Endpoints :
LC_{50} (*Lepomis macrochirus*, 96 h) = 3.2 mg a.s./L (nominal)
NOEC (*Lepomis macrochirus*, 96 h) = 2.15 mg a.s./L (nominal)
Due to the low solubility of the a.s. in water the actual toxicity values are :
LC_{50} (*Lepomis macrochirus*, 96 h) = 0.62 mg a.s./L (measured)
NOEC (*Lepomis macrochirus*, 96 h) = 0.5 mg a.s./L (measured)
Conclusion :
The study is acceptable.
LC_{50} (*Lepomis macrochirus*, 96 h) = 0.62 mg a.s./L (measured)
Kresoxim-methyl is very toxic to bluegill fish.

Acute toxicity study on the common carp (*Cyprinus carpio* L.) of Reg. No. 242 009 in a static system (96 hours). (Munk R., 1993b).
Addendum to the report project No. 11F0180/915083: Acute toxicity on the common carp (*Cyprinus carpio* L.) of Reg. No. 242 009 of May 12, 1993. (Munk R., 1993g).

Guidelines :
OECD 203 (updated 1992)
EEC Directive 84/449 (updated 1989)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N 27 (III a1)
Test species : common carp (*Cyprinus carpio* L.)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 5 - 8 cm
Type of test : static system (96 hours)

Applied and measured concentrations : ,
nominal : water control; solvent control (tween 0.1 g/L); 0.1, 0.215, 0.464, 1.0, 2.15, 4.64 mg a.s./L
measured : The recovery rates of the active substance were in the ranges of 31.4 % to 64.6 % (day 0) and 13.9 % to 112.9 % (day 4), respectively.
Test conditions :
temperature : 23 °C
pH : 8.1 - 8.6
oxygen content : about 7.5 mg O_2/L (1 h) to about 6 mg O_2/L (96 h)
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Mortality : Mortality occurred in the doses 2.15 mg/L and 4.64 mg/L.
Behavioral observations : Narcotic-like state, apathy and tumbling at 2.15 and 4.64 mg/L.
Endpoints :
LC_{50} (*Cyprinus carpio*, 96 h) > 1.0 < 2.2 mg a.s./L (nominal)
NOEC (*Cyprinus carpio*, 96 h) = 1.0 mg a.s./L (nominal)
Due to the low solubility of the a.s. in water the actual toxicity values are :
LC_{50} (*Cyprinus carpio*, 96 h) > 0.247 < 0.326 mg a.s./L (measured)
NOEC (*Cyprinus carpio*, 96 h) = 0.25 mg a.s./L (measured)
Conclusion :
The study is acceptable.
LC_{50} (*Cyprinus carpio*, 96 h) > 0.247 < 0.326 mg a.s./L (measured)
Kresoxim-methyl is very toxic to common carp.

Added in March 2010:

A new study has been submitted to meet the requirements of the current regulations. This study has been conducted under flow-through conditions and is submitted due to the poor analytical recoveries in the original study with bluegill (Munk R., 1993).

BAS 490F: A 96-hour flow-through acute toxicity test with the bluegill *(Lepomis macrochirus* RAF.). (Graves W.C *et al*., 1995b).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
Test method C.1 EEC Directive 84/449 (updated 1989)
OECD 203 (adopted 1992)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 % (93.6 % reanalysis in 1997), batch: N36
Test species : bluegill fish (*Lepomis macrochirus*)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 2 replicates/treatment, 18 mm (range: 17 - 21 mm), 0.15 g (range: 0.11 - 0.25 g), 0.098 g fish/L water
Type of test : flow-through system (96 hours)
Applied and measured concentrations :
nominal : water control; solvent (dimethylformamide) control; 0.162, 0.270, 0.450, 0.750, 1.250 mg a.s./L
measured : water control; solvent (dimethylformamide) control; 0.148, 0.265, 0.338, 0.642, 0.924 mg a.s./L
The recovery rates of the active substance were in the ranges of 76 % to 95 % (day 0) and 88 % to 114 % (day 4), respectively.
Test conditions :
temperature : 21.7 - 22.0 °C
pH : 8.2 - 8.4
oxygen content : about 8.2 - 8.7 mg O_2/L throughout the experiment
total hardness : 129 mg/L (as $CaCO_3$)
photoperiod : 16/8 hours light/dark cycle
Analytical methods : GC with electron capture detection

Findings :
Mortality : Mortality occurred at the dose of 0.642 mg/L and above.
Behavioral observations : Lethargy at 0.642 mg/L and above; onset of effects at 2 h after start of application.
Endpoints :
LC_{50} (*Lepomis macrochirus*, 96 h) = 0.499 mg a.s./L (mean measured concentration)
NOEC (*Lepomis macrochirus*, 96 h) = 0.388 mg a.s./L (mean measured concentration)
Conclusion :
The study is acceptable.
LC_{50} (*Lepomis macrochirus*, 96 h) = 0.499 mg a.s./L (mean measured concentration)
Kresoxim-methyl is very toxic to bluegill fish.

Acute toxicity test of Reg. No. 242 009 with common carp (semi-static procedure). (Nozaka T., 1991a).

Guidelines :
"Toxicity test with fish", Annex of Agricultural Chemicals Regulation Law of Japan
GLP :
No
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N 27
Test species : common carp (*Cyprinus carpio* L.)
Number of organisms, weight, length, age : 10 fish in one aquarium/concentration, 4.89 cm ± 0.20, 1.28 g ± 0.17
Type of test : semi-static system (96 hours), renewal after 48 hours
Applied and measured concentrations :
nominal : water control; solvent control (a.s. dissolved in dimethylsulfoxide); 0.0953, 0.171, 0.309, 0.556, 1.0 mg a.s./L
No information about the measured concentrations.
Test conditions :
temperature : 25 ± 2 °C
pH : 7.5
oxygen content : about 6 mg O_2/L
total hardness : 1.07 mmol/L
photoperiod : 14/10 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Mortality : Mortality occurred in the doses 0.556 and 1.00 mg/L.
Behavioral observations : Symptoms appear at doses 0.309, 0.556 and 1.00 mg/L. Fishes began to show hyper activity, swimming at the surface; then loss of equilibrum followed. Affected fishes became immobile and died.
Endpoints :
LC_{50} (*Cyprinus carpio*, 96 h) = 0.414 mg a.s./L (nominal)
LC_0 (*Cyprinus carpio*, 96 h) = 0.309 mg a.s./L (nominal)
NOEC (*Cyprinus carpio*, 96 h) = 0.171 mg a.s./L (nominal)
Conclusion :
The study is not GLP, main deviation is the lack of water analysis.
Due to the low solubility of a.s. in the other studies, the LC_{50} value is underestimated.
LC_{50} (*Cyprinus carpio*, 96 h) = 0.414 mg a.s./L (nominal)
Kresoxim-methyl is very toxic to common carp.

Acute toxicity study on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of Reg. No. 262 451 in a static system (96 hours). (Munk R., 1994a).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
EEC Directive 84/449 (1992)
OECD 203 updated version (adopted 1992)
GLP :
Yes
Material and Methods :
Test substance : BF 490-1, free acid metabolite of kresoxim-methyl (Reg. No. 262 451), chemical purity: 99.3 %
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fish/replicate, 1 replicate for control, 1 replicate for 50 mg/L, 3 replicates for 100 mg/L, 5.42 cm (range: 4.7 - 6.5 cm), 1.42 g (range: 0.9 - 2.5 g), about 4 months, 0.14 g fish/L
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : water control; 50, 100 mg BF 490-1/L
measured : Recovery rates of 98.5 % to 103.9 % after 1 hour and 96 hours respectively.
Test conditions :
temperature : 11 ± 1°C
pH : 8.1 - 8.6
total hardness : 2.5 mmol/L
oxygen content : 9.3 - 11 mg O_2/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : Reversed phase HPLC with UV detection
Findings :
Mortality : No mortality in the concentration 100 mg/L.
Behavioral observations : No symptoms of toxicity in the entire experiment.
Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 100 mg BF 490-1/L (nominal) (highest concentration tested)
LC_0 (*Oncorhynchus mykiss*, 96 h) = 100 mg BF 490-1/L (nominal)
NOEC (*Oncorhynchus mykiss*, 96 h) = 100 mg BF 490-1/L (nominal)
Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 100 mg BF 490-1/L (nominal) (highest concentration tested)
Kresoxim-methyl metabolite (free acid) is not toxic to rainbow trout.

B.9.2.2 Fish juvenile growth test (Annex IIA 8.2.2.1)

Sublethal toxic effects on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of Reg. No. 242 009 in a flow-through system (28 days). (Munk R., 1994c).

Guidelines :
OECD 204 (updated version 1984)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 %, batch: N36 (III c)
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 20 fish in one aquarium/concentration, 5.6 cm (range: 5.0 - 6.2 cm), 1.5 g (range: 1.2 - 1.9 g)
Type of test : flow-through system (28 days)
Applied and measured concentrations :
nominal : water control; solvent control; 0.004, 0.02, 0.1, 0.5 mg a.s./L
measured : The concentration control analyses in the water revealed individual recovery rates of the parent substance (and metabolite) in the range of 54 % to 92.8 % of the nominal values.
Test conditions :
temperature : 14 ± 1 °C
pH : 7.5 - 8.4
oxygen content : 7.8 mg - 10.4 mg O_2/L
total hardness : 2.3 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :

Table 9.2.3-1 : Effects in rainbow trouts exposed to kresoxim-methyl in a flow-through system over 28 days

-	**Concentration (mg a.s./L) (nominal)**					
	0 (water control)	**0 (solvent control)**	**0.004**	**0.02**	**0.1**	**0.5**
Mortality (day 1)	0	0	0	0	0	100
Mortality (day 20)	0	0	0	0	20	100
Mortality (day 28)	0	0	0	0	35	100
Weight gain (w day 28 /w day 0)	3.4	3.4	3.3	3.2	**2.1** [1)]	-
Length gain (l day 28 /l day 0)	1.4	1.4	1.4	1.4	**1.2** [2)]	-
Symptoms	-	-	-	-	apathy reduced or no food uptake discoloration	-

[1)] - 38.4 % deviation from control group ($p \leq 0.01$)
[2)] -12.5 % deviation from the control group ($p \leq 0.01$)

NOEC is equal to 0.02 mg/L since impairment of the weight gain, length gain and toxic symptoms appear at the 0.1 mg/L dose.
Endpoints:
LC_{50} (*Oncorhynchus mykiss*, 28 d) > 0.1 mg a.s./L (nominal)
LC_0 (*Oncorhynchus mykiss*, 28 d) = 0.02 mg a.s./L (nominal)
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.02 mg a.s./L (nominal)
Related to the lowest mean of analytically measured values (66.4 % at the 0.1 mg/L level):
LC_{50} (*Oncorhynchus mykiss*, 28 d) > 0.0665 mg a.s./L (measured)
LC_0 (*Oncorhynchus mykiss*, 28 d) = 0.013 mg a.s./L (measured)
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.013 mg a.s./L (measured)
Conclusion :
The study is acceptable.
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.013 mg a.s./L (measured)
This study confirms the toxicity values obtained in the previous studies on fishes.

B.9.2.3 Fish early life stage toxicity (Annex IIA 8.2.2.2)

Not required since fish juvenile growth test and mesocosm study were submitted.

Added in March 2010:

Following study has been performed after writing the original dossier. It has been conducted for the USA asking for an ELS-study (US specific requirement based on standard triggers and despite the rapid degradation of the active substance). The study is included here for completeness.

BAS 490 F: An early life-stage toxicity test with the fathead minnow (*Pimephales promelas*). (Graves W.C. *et al.*, 1996b).

Guidelines :
EPA 72-4 (a)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 % (93.6 % reanalysis in 1995), batch: N 36
Test species : fathaed minnow (*Pimephales promelas*)
Number of organisms, age : 20 embryos/incubation cup, 2 incubation cups/replicate, 2 replicates/treatment, eggs less than 24 hours old at test initiation, biomass loading at the end of the test: 0.26 g fish/L water
Type of test : flow-through test with 13 volume additions of test water every 24 hours;
32 days (4-day embryo hatching period and 28-day post-hatch juvenile growth period)
Applied and measured concentrations :
nominal : control (water); solvent control (0.10 mL/L dimethylformamide); 0.010, 0.020, 0.040, 0.080, 0.160 mg a.s./L
mean measured : control (water); solvent control (dimethylformamide); 0.0097, 0.020, 0.040, 0.087, 0.160 mg a.s./L (97, 100, 100, 109, 100 % of nominal concentrations)
Test conditions :
temperature : 24.4 – 25.3 °C
pH : 8.1 -8.4
oxygen content : 6.5 – 8.4 mg O_2/L
total hardness : 128 m/L (as $CaCO_3$)
photoperiod : 16/8 hours light/dark cycle
light intensity : 340 lux
Feeding : live brine shrimp nauplii (*Artemia* sp.)
Assessments : Daily assessment of survival (twice during the first 24 h), daily assessment of signs of toxicity and abnormal behavior during the post-hatch period, determination of weight and length of fish at test termination.
Analytical methods : GC using electron capture detector

Findings :

Table B.9.2.3-1 : Chronic toxicity (ELS, 32 d) of kresoxim-methyl on fathead minnow (*Pimephales promelas*)

Concentration [µg a.s./L] nominal	**Control [1)]**	**10**	**20**	**40**	**80**	**160**
Concentration [µg a.s./L] mean measured	**Control [1)]**	**9.7**	**20**	**40**	**87**	**160**
Hatching success [%]	85	80	86	80	84	80
Mean larvae survival (32 d) [%]	93	95	90	92	93	22*
Symptoms	none	none	none	none	none	lethargy
Mean wet weight (32 d) [mg]	57.1	60.8	59.0	59.1	52.1	42.2 [2)]
Mean body length (32 d) [mm]	20.6	20.8	21.0	20.3	19.8	17.5 [2)]
Endpoints [µg a.s./L] (mean measured)						
NOEC (overall)	**87**					
LOEC / MATC	**160 / 118**					

1: pooled data from negative and solvent control, as no statistically significant differences were observed between these two groups in any of the results
2: The 160 µg a.s./L treatment group was not analyzed statistically because of a significant effect on survival.
* statistically significant differences compared to the pooled control group (3x2 contingency tables, $p < 0.05$)

No statistical significant results were observed for hatching success at any of the treatment levels. Survival was statistically significantly reduced in the highest test concentration of 0.160 mg a.s./L. Adverse behavioral effects, i.e. lethargic behavior, were observed in the 0.160 mg a.s./L treatment group soon after hatching. There were no treatment related statistically significant differences in fish growth up to a concentration of 0.087 mg a.s./L when compared to the pooled controls. Total length, wet weight and dry weight were reduced in the 0.160 mg a.s./L treatment group when compared to control.

Conclusion :

The study is acceptable.

NOEC (*Pimephales promelas*, 32 d) = 0.087 mg a.s./L (mean measured) based on hatchability, post-hatch survival and growth parameters

B.9.2.4 Fish life cycle test (Annex IIA 8.2.2.3)

Study is not required due to the rapid degradation of kresoxim-methyl in water, in additions a mesocosm study was submitted.

B.9.2.5 Bioaccumulation potential in fish (Annex IIA 8.2.3)

14C-BAS 490 F (14C-Reg. No. 242 009) - the bioaccumulation and metabolism in rainbow trout. (Mayo B.C., 1994).

Guidelines :
US EPA, § 165-4; guideline is acceptable
GLP :
Yes
Material and Methods :
Test substance: kresoxim-methyl, radiolabelled: radiolabel in phenyl-position, specific activity: 30.2 m Ci/mmol adjusted to 10400 dpm/µg, radiochemical purity: 97 %
Test species : rainbow trout (*Oncorynchus mykiss*)
Number of organisms, weight, length, age : 50 fish/100 L water tank.
Fish about 1 year old with 5.1 ± 0.5 cm body length, loading: < 4 g fish/L
Type of test : continuous flow-through system (28 days exposure period and 14 days depuration period)
Applied and measured concentrations :
nominal : water control; 25 µg a.s./L
A.s. concentrations were measured daily:
27.4 ± 3.5 mg/L during the exposure periods; < 1.4 - 1.7 mg/L during the depuration period
Test conditions :
flow rate: 1440 L per tank per day
dechlorinated water, aerated
The 3 following parameters were daily recorded: oxygen content of 9.8 - 10.1 mg O_2/L, pH: 7.6 - 7.8, 14 °C
Analytical methods : HPLC and TLC after acetonitrile and hexane extraction
Findings :
Exposure : Mean concentrations of radioactivity in the total fish reached a plateau of 5 µg/g to 6 µg parent equivalents per gramme after 3 days exposure. Concentrations at all sampling times throughout the 28-day exposure period were in the range of 9 µg/g to 15 µg/g in the viscera and 1 µg/g to 2 µg/g in the fillet.
Depuration : Concentration of radioactivity in tank water after day 1 of depuration fell substantially to below the limit of reliable measurement, i.e. 1 µg/L to 2 µg/L.
During the first day of the depuration period, mean concentrations of radioactivity in total fish, viscera and fillet decreased rapidly by about 70 % to 90 %.
In total fish the concentration decreased from 5 µg/g (day 28, exposure) to about 1 µg/g (day 1, depuration). Concentration continued to decrease throughout the depuration period and was 0.03 µg/g after 10 to 14 days.
Radioactivity in the total fish declined in a biphasic manner with an initial rapid phase over the first three days, resulting in an elimination half-life of 0.37 days, followed by a slower, terminal elimination phase, resulting in a half-life of 3.4 days. The decline of radioactive residues in the viscera and fillet tissue could be described accordingly.
Identification of the radioactivity recovered in viscera and fillet on days 21 and 28 was performed.
The major radioactive component in viscera extract was the parent substance (kresoxim-methyl = BAS 490 F) and accounted for 41 % to 45 % of viscera radioactivity. Secondary components as BF 490-4 (hydroxylated 490-F), BF 490-1 (free acid) and other minor components could be identified.
The parent compound was present in the fillet extract and accounted for 72 % to 82 % of the fillet radioactivity.

Table B.9.2.5-1 : Mean concentrations of radioactivity in fish samples during the exposure and the depuration

	Viscera		Fillet		Total Fish	
Exposure						
Time (days)	**Mean ± SD) (mg /kg)**	**BCF**	**Mean ± SD) (mg /kg)**	**BCF**	**Mean ± SD) (mg /kg)**	**BCF**
0	< 0.02		< 0.02		<0.02	
3	13 ± 8	340	1.5 ± 0.2	39	6.0 ± 2.2	150
7	11 ± 10	440	1.3 ± 0.3	52	6.2 ± 6.3	250
14	9 ± 1.6	320	1.3 ± 0.4	47	4.6 ± 1.4	170
21	15 ± 1	590	1.3 ± 0.1	51	6.2 ± 1.6	240
28	9.3 ± 2.7	370	1.4 ± 0.3	56	5.0 ± 1.5	200
Depuration						
Time (days)	**Mean ± SD) (mg /kg)**		**Mean ± SD) (mg /kg)**		**Mean ± SD) (mg /kg)**	
1	2.6 ± 0.2	-	0.14 ± 0.03	-	1.1 ± 0.1	-
3	0.25 ± 0.15	-	0.07 ± 0.02	-	0.14 ± 0.06	-
7	0.09 ± 0.01	-	0.03 ± 0.01	-	0.06 ± 0.01	-
10	0.09 ± 0.02	-	0.02 ± 0.01	-	0.03 ± 0.01	-
14	0.05 ± 0.02	-	0.02 ± 0.01	-	0.03 ± 0.01	-

Table B.9.2.5-2 : Major endpoints of the bioaccumulation study in rainbow trout.

	Viscera	Fillet	Whole fish
mean BCF (days 7-28)	430	52	220
Depuration half-life 1 (days 0-3) (in days)	0.36	0.21	0.37
Depuration half-life 2 (days 3-10) (in days)	3.5	3.9	3.4

Conclusion :
The study is acceptable.
Kresoxim-methyl is characterized by an important bioconcentration but with rapid depuration.

Added in March 2010:

Bioconcentration potential of the metabolites, degradation and reaction products

The metabolites BF 490-1 (Reg. No. 262 451) and BF 490-5 (Reg. No. 286 404) have a log $P_{o/w}$ < 3. Therefore, bioconcentration of these metabolites is unlikely and such studies are not required.

Aquatic bioavailability / biomagnification / depuration

The bioconcentration potential is low and depuration is fast. Furthermore, kresoxim-methyl is not stable in aquatic systems (DT_{50} < 2 days). Thus, there is no risk of biomagnification and no further specific studies are required.

B.9.2.6 Acute toxicity to aquatic invertebrates (Annex IIA 8.2.4)

Determination of the acute toxicity of Reg. No. 242 009 techn. to the waterflea *Daphnia magna* STRAUS. (Jatzek H.-J., 1993).

Guidelines :
EEC Directive 79/831 (updated 1989)
GLP :
yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 93.7 %, batch: N36
Test species : waterfleas (*Daphnia magna*)
Number of organisms, weight, age : 5 waterfleas X 4 replicates/concentration, 2-24 hours
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; 0.004, 0.009, 0.017, 0.034, 0.069, 0.137, 0.274, 0.548, 1.096 mg a.s./L
The concentration control analyses resulted in recovery rates of 85 % to 93.6 % after 48 hours.
Test conditions :
temperature : 20 ± 0.5 °C
pH : 7.5 ± 0.5
oxygen content : 8.2 - 9.0 mg O_2/L
medium : synthetic medium (reconstituted water)
total hardness : 2.7 ± 0.5 mmol/L
conductivity : 600 - 700 µs/cm
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Endpoints :
EC_{50} (*Daphnia magna*, 24 h) = 0.428 mg a.s./L (nominal) (CL 95 % 0.346-0.529)
EC_{50} (*Daphnia magna*, 48 h) = 0.186 mg a.s./L (nominal) (CL 95 % 0.161-0.216)
EC_0 (*Daphnia magna*, 48 h) = 0.069 mg a.s./L (nominal)
Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 48 h) = 0.186 mg a.s./L (nominal) (CL 95 % 0.161-0.216)
Kresoxim-methyl is very toxic to *Daphnia magna*.

Added in March 2010:

A new study has been performed after writing the original dossier for submission in the USA. This study has been conducted under flow-through conditions. The endpoint from this study proved to be higher than in the original study with *Daphnia* (Jatzek H.-J., 1993), therefore the lower endpoint from the original study has been used in the risk assessment. Nevertheless, this new study has been included here for completeness.

BAS 490F: A 48-hour flow-through acute toxicity test with the Cladoceran (*Daphnia magna*). (Graves W.C. *et al.*, 1995c).

Guidelines :
EEC Test method C.2 of Dir 79/831 (updated 1989)
OECD guideline 202
EPA 72-2
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 %, batch: N 36
Test species : waterfleas (*Daphnia magna*)
Number of organisms : 10 waterfleas X 2 replicates/concentration, neonates
Type of test : flow-through test (48 hours)
Applied and measured concentrations :
nominal : water control; solvent (dimethylformamide) control; 0.058, 0.097, 0.162, 0.270, 0.450 mg a.s./L
measured : water control; solvent (dimethylformamide) control; 0.059, 0.095, 0.160, 0.260, 0.400 mg a.s./L
The concentration control analyses resulted in recovery rates of 95 -107 % at t=0h, and 78 – 106 % at t=48h.
Test conditions :
temperature : 19.3 - 19.8 °C
pH : 8.3 - 8.5 throughout the experiment
oxygen content : 8.1 - 8.9 mg O_2/L
medium : filtered well water
total hardness : 131 mg/L as $CaCO_3$
conductivity : 315 µS/cm
photoperiod : 16/8 hours light/dark cycle
light intensity : 220 lux
Analytical methods : GC with electron capture detection
Findings :
Mortality : No immobility was observed at concentrations up to 0.260 mg a.s./L, although 35 % and 40 % of the daphnids in this treatment group appeared lethargic at 24 and 48 hours, respectively. At the highest test concentration of 0.400 mg a.s./L 80 % of the daphnids were dead or immobile within 24 hours. After 48 h 95 % of the daphnids in this treatment group had died.
Behavioral observations : Daphnids appeared lethargic at 0.260 mg a.s./L and above. Onset time was 2 h.
Endpoints :
EC_{50} (*Daphnia magna*, 24 h) = 0.350 mg a.s./L (measured) (CL 95 % 0.260-0.400)
EC_{50} (*Daphnia magna*, 48 h) = 0.332 mg a.s./L (measured) (CL 95 % 0.260-0.400)
NOEC (*Daphnia magna*, 48 h) = 0.160 mg a.s./L (measured)
Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 48 h) = 0.332 mg a.s./L (measured) (CL 95 % 0.260-0.400)
Kresoxim-methyl is very toxic to *Daphnia magna*.

Acute toxicity test of Reg. No. 242 009 with *Daphnia similis* Claus. (Nozaka T., 1991b).

Guidelines :
Toxicity test with daphnia (Annex of Agricultural Chemicals Regulation Law of Japan)
GLP :
No
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N27

Test species : waterfleas (*Daphnia similis*)
Number of organisms, age : 10 waterfleas X 2 replicates/concentration, 4 days old
Type of test : static test (24 hours)
Applied and measured concentrations :
nominal : water control; solvent control; 0.156, 0.313, 0.625, 1.25, 2.5, 5.0 mg a.s./L
No analytical measurements.
Test conditions :
temperature : 25 ± 2 °C
pH : 7.7
oxygen content : 7.9 - 8.3 mg O_2/L
photoperiod : 14/10 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :
Endpoints :
EC_{50} (*Daphnia similis*, 24 h) = 1.51 mg a.s./L (nominal)
NOEC (*Daphnia similis*, 24 h) = 0.156 mg a.s./L (nominal)
Conclusion :
The study is acceptable; nevertheless some deviations as the duration of the test (24 hours) and the age of the organisms (4 days) were recorded.
EC_{50} (*Daphnia similis*, 24 h) = 1.51 mg a.s./L (nominal)

Effect of BF 490-1 on *Daphnia magna* STRAUS in an acute toxicity test. (Dohmen G.P., 1994b).

Guidelines :
EEC Directive 79/831 (updated 1989)
GLP :
Yes
Material and Methods :
Test substance : BF 490-1, free acid metabolite of kresoxim-methyl (Reg. No. 262 451), chemical purity: 99.3 %
Test species : waterfleas (*Daphnia magna*)
Number of organisms, age : 5 waterfleas X 4 replicates/concentration, not older than 24 hours
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; 5, 15, 30, 60, 100 mg BF 490-1/L
measured : Recovery rates in the range of 96.1 - 101.3 %
Test conditions :
temperature : 19 ± 0.5 °C
pH : 8.1 ± 0.1
oxygen content : 9.1 mg O_2/L
medium : synthetic medium (reconstituted water)
total hardness : 2.55 mmol/L
conductivity : 624 µs/cm
photoperiod : 16/8 hours light/dark cycle
light intensity : *ca*. 1000 lux
Analytical methods : reversed phase HPLC with UV detection
Findings :
Endpoints :
EC_{50} (*Daphnia magna*, 48 h) > 100 mg BF 490-1/L (nominal) (highest concentration tested)
EC_0 (*Daphnia magna*, 48 h) = 100 mg BF 490-1/L (nominal)
Conclusion :
The study is acceptable.
Kresoxim-methyl metabolite (free acid) is not toxic to *Daphnia magna*.

Added in March 2010:

Metabolite BF 490-5 has been detected in soil at levels above 5 % and has therefore been checked for its ecotoxicological potential. As daphnids have been shown to be of similar sensitivity as fish to the parent compound and the main metabolite BF 490-1 and in order to avoid unnecessary testing, a study on *Daphnia magna* only has been performed. The absence of toxic effects confirms the low ecotoxicological potential and does not warrant any further animal testing.

Acute toxicity of Reg. No. 286404 (Metabolite of BAS 490F) to *Daphnia magna* STRAUS in a 48h static test. (Janson G.-M, 2008).

Guidelines :
Test method C.2 EEC Directive 79/831 (updated 1989)
OECD 202
EPA 850.1010
GLP :
Yes
Material and Methods :
Test substance : BF 490-5, soil metabolite of kresoxim-methyl (Reg. No. 286404), chemical purity: 99.2 %, batch: L76-100
Test species : waterfleas (*Daphnia magna*)
Number of organisms : 5 waterfleas X 4 replicates/concentration, less than 24 hours old
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; solvent (Cremophor) control; 6.25, 12.5, 25.0, 50, 100 mg BF 490-5/L
measured : water control; solvent (Cremophor) control; 6.34, 12.6, 25.3, 50.1, 99.7 mg BF 490-5/L
The concentration control analyses resulted in recovery rates of 99 – 102 % at t=0h, and 100 – 102 % at t=48h.
The test item is stable over the whole experimental period.
Test conditions :
temperature : 20 - 21 °C
pH : 7.84 - 8.04 throughout the experiment
oxygen content : 8.2 - 8.6 mg O_2/L
medium : reconstituted water (M4 Elendt synthetic medium)
total hardness : 2.26 mmol/L (t=0h)
conductivity : 614 µS/cm
photoperiod : 16/8 hours light/dark cycle
light intensity : 295 – 785 lux
Analytical methods : reversed phase HPLC with MS detection
Findings :
Behavioral observations : No abnormal behaviour detected at any dose up to 48h exposure.
Endpoints :
EC_{50} (*Daphnia magna*, 24 – 48 h) > 100 mg BF 490-5/L (nominal)
NOEC (*Daphnia magna*, 48 h) > 100 mg BF 490-5/L (nominal)
Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 24 – 48 h) > 100 mg BF 490-5/L (nominal)
Soil metabolite BF 490-5 is not toxic to *Daphnia magna* up to 100 mg/L.

Acute studies with other aquatic invertebrates are not required, direct application to surface water is not foreseen. However, a mesocosm study is available covering aquatic insects, too, showing no impact on this group of organisms up to and including the highest treatment level.

B.9.2.7 Chronic toxicity to aquatic invertebrates (Annex IIA 8.2.5)

Determination of the chronic toxicity of Reg. No. 242 009 techn. to the waterflea *Daphnia magna* STRAUS. (Elendt-Schneider B., 1993).

Guidelines :
EEC Guideline XI/681/86, draft 4
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 93.7 %, batch: N36
Test species : waterfleas (*Daphnia magna*)
Number of organisms, age : 1 waterflea X 10 replicates/concentration, 2 - 24 hours
Type of test : semi-static test (21 days), renewal of test medium: three times a week
Applied and measured concentrations :
nominal : water control; 0.01, 0.03, 0.1, 0.3, 1.0, 3.2, 10, 32, 100, 320 µg a.s./L
After 48 hours or 72 hours of the static phase the recovery rates were determined to be in the ranges of 79.3 % to 94.6 % without daphnids and 70.7 % to 99.8 % with daphnids in the test solution, thus confirming the nominal values in general as well.
Test conditions :
temperature : 20 ± 1 °C
pH : 7.1 - 7.9
oxygen content : 7.5 - 9.0 mg O_2/L
Analytical methods : RP-HPLC with UV detection
Findings :

Table 9.2.7-1 : Effects on daphnids exposed to kresoxim-methyl in a semi-static system over 21 days

	Concentration (µg a.s./L) (nominal)										
	0	**0.01**	**0.03**	**0.1**	**0.32**	**1.0**	**3.2**	**10**	**32**	**100**	**320**
% Mortality adults (day 7)	-	-	-	-	-	-	-	-	-	-	100
% Mortality adults (day 14)	-	-	-	-	-	-	-	-	10	-	100
% Mortality adults (day 21)	-	-	-	-	-	-	-	-	10	-	100
Reproduction rate (offspring/adult)	186.2	165.4	174.7	163.7	154.9	161.2	179.8	176.4	165.7	112.8	0
Dead young	-	-	-	-	-	-	-	-	-	11.5	-
Aborted eggs per live parent animal	0.2	0.2	0.4	0.4	0.5	0.2	0.4	0.4	0.6	0.4	-

Endpoints :
LC_0 (*Daphnia magna*, 21 d) = 0.1 mg a.s./L (nominal), related to parent animals
NOEC (*Daphnia magna*, 21 d) = 0.032 mg a.s./L (nominal), related to offspring
Conclusion :
The study is acceptable.
NOEC (*Daphnia magna*, 21 d) = 0.032 mg a.s./L (nominal), related to offspring

Added in March 2010:

A new study has been performed after writing the original dossier for submission in the USA. This study has been conducted under flow-through conditions. The endpoint from this study proved to be higher than in the original study with *Daphnia* (Elendt-Schneider B., 1993), therefore the lower endpoint from the original study has been used in the risk assessment. Nevertheless, this new study has been included here for completeness.

BAS 490 F: A flow-through life-cycle toxicity test with the Cladoceran (*Daphnia magna*). (Graves W.C. *et al.*, 1996a).

Guidelines :
EPA 72-4(b)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.3 % (93.6 % reanalysis in 1995), batch: N 36
Test species : waterfleas (*Daphnia magna*)
Number of organisms, age : 2 replicates/treatment, 8 test compartments containing 1 daphnid and 4 test compartments containing 5 daphnids per treatment, neonates, less than 24 hours old
Type of test : 21-day flow-through test, 5 volume additions of test water every 24 hours
Applied and measured concentrations :
nominal : control; solvent control (0.08 mL/L dimethylformamide); 0.0075, 0.015, 0.030, 0.060, 0.120 mg a.s./L
mean measured : control; solvent control (0.08 mL/L dimethylformamide); 0.0066, 0.013, 0.027, 0.055, 0.107 mg a.s./L
The concentration control analyses resulted in recovery rates of 80 – 97 % at day 0, 77 – 87 % at day 7, 80 – 93 % at day 14 and 93 – 107 % at day 21.
Test conditions :
temperature : 19.2 – 20.1 °C
pH : 8.3 – 8.4
oxygen content : 7.1 – 8.9 mg O_2/L
total hardness : 124 – 140 mg/L as $CaCO_3$
photoperiod : 16/8 hours light/dark cycle
light intensity : 510 lux
Feeding : mixture of yeast, Cherophyll® and trout chow, as well as a suspension of the freshwater green alga *Selenestrum capricornutum*
Assessments : assessment of immobility and mortality on day 2, 5, 7, 9, 12, 14, 16, 19 and 21 after test initiation; assessment of growth parameters and reproduction at test termination (day 21)
Analytical methods : gas chromatography using electron capture detector
Findings :

Table B.9.2.7-2 : Effect of kresoxim-methyl on the reproduction and parent mortality of *Daphnia magna*

Concentration (nominal) [µg a.s./L]	**Control [1)]**	**7.5**	**15**	**30**	**60**	**120**
Concentration (mean measured) [µg a.S./L]	**Control [1)]**	**6.6**	**13**	**27**	**55**	**107**
Offspring/parent	121	128	111	133	131	3*
Parent mortality (21 d) [%]	2	4	7	4	7	7
Parent length [mm]	4.68	4.71	4.66	4.78	4.61	4.45*
Parent dry weight [mg]	0.92	0.89	0.88	0.91	0.88	0.81*
	Endpoints [µg/L] (mean measured)					
NOEC (21 d)	55					
MATC (21 d)	77 (> 55 < 107)					

1) pooled data from negative and solvent control, as no statistically significant differences were observed between these two groups in any of the results
* statistically significant difference compared to pooled controls (Student's t-test, $p < 0.05$)

No statistically significant effects on survival were found in any of the treatments when compared to the pooled control group (negative and solvent control) after 21 days. Daphnids in those groups appeared healthy and normal during test with the exception of one lethargic daphnid in the 13 µg a.s./L treatment group on day 16. The number of offspring was not significantly different from pooled controls in the 6.6, 13, 27 and 55 µg a.s./L treatment groups. A statistically significant reduction in reproduction occurred in the 107 µg a.s./L treatment. No statistically significant growth effects existed in the 6.6, 13, 27 and 55 µg a.s./L treatment groups. Similarly, lengths and dry weights of daphnids in the 107 µg a.s./L treatment only were statistically significantly reduced when compared to the pooled controls (Student's t-test, $p<0.05$).

Conclusion :
The study is acceptable.
NOEC (*Daphnia magna*, 21 d) = 0.055 mg a.s./L (mean measured)

B.9.2.8 Effects on algal growth (Annex IIA 8.2.6)

Effect of Reg. No. 242 009 on the growth of the green alga *Ankistrodesmus bibraianus*. (Dohmen G.P., 1992a).

Guidelines :
OECD 201 (1984)
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94 %, batch: N27
Test species : unicellular freshwater green alga (*Ankistrodesmus bibraianus,* syn. *Selenastrum capricornutum)*
Number of organisms : initially: 3 x 10^4 cells/mL, 5 replicates/concentration
Type of test : static system (72 hours)
Applied and measured concentrations :
nominal : water control; solvent control; 0.003, 0.01, 0.03, 0.1, 0.3, 1.0, 3.0 mg a.s./L
Recovery rates were in the range of 25.4 to 61.6 % of the nominal values.
Test conditions :
temperature : 22 ± 1 °C
pH : 8.0 - 8.9
photoperiod : continuous uniform illumination
light intensity : *ca*. 8000 lux
Analytical methods : reversed phase HPLC with UV detection
Findings :
Observations : The lowest test concentration of 0.003 mg a.s./L caused a growth inhibition of 8.5 %, the highest dose of 3.0 mg a.s./L an inhibition of 100 %. No morphological effects on the alga could be observed.
Endpoints :
Growth inhibition
E_bC_{50} (*Ankistrodesmus bibraianus* syn. *Selenastrum capricornutum*, 0 – 72 h) = 0.063 mg a.s./L (nominal)
E_bC_{10} (*Ankistrodesmus bibraianus* syn. *Selenastrum capricornutum*, 0 – 72 h) = 0.007 mg a.s./L (nominal)
Conclusion :
The study is acceptable.
E_bC_{50} (*Ankistrodesmus bibraianus* syn. *Selenastrum capricornutum*, 0 – 72 h) = 0.063 mg a.s./L (nominal)

Effect of BF 490-1 on the growth of the green alga *Pseudokirchneriella subcapitata*. (Dohmen G.P., 1994a).

Guidelines :
OECD 201 (1984)
GLP :
Yes
Material and Methods :
Test substance : BF 490-1, free acid metabolite of kresoxim-methyl (Reg. No. 262 451), chemical purity: 99.3 %
Test species : unicellular freshwater green alga (*Pseudokirchneriella subcapitata,* syn. *Selenastrum capricornutum*)
Number of organisms : initially: 3 x 10^4 cells/mL, 5 replicates/concentration, 10 replicates for control
Type of test : static system (72 hours)
Applied and measured concentrations :
nominal : water control; 1, 3, 10, 50, 150, 300, 500 mg BF 490-1/L
Recovery rates were in the range of 94.5 to 102 %.
Test conditions :
temperature : 22 ± 1 °C
pH : 7.9
photoperiod : continuous uniform illumination
light intensity : *ca*. 8000 lux
Analytical methods : reversed phase HPLC with UV detection
Findings :
Observations : At the two lowest test concentrations a slight stimulation of the growth (biomass) could be determined. At the highest dose tested, i.e. 500 mg/L, the inhibition rate was 41.9 %. No morphological effects on the alga could be observed.
Endpoints :
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) > 500 mg BF 490-1/L (nominal) (highest concentration tested)
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 - 72 h) = 51.5 mg BF 490-1/L (nominal) (95 %: 28 - 96 mg/L)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 - 72 h) > 500 mg BF 490-1/L (nominal)
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 - 72 h) = 382 mg BF 490-1/L (nominal) (95 %: 192 - 761 mg/L)
$NOEC_b$ (*Pseudokirchneriella subcapitata*, 0 - 72 h) = 50 mg BF 490-1/L (nominal)
Conclusion :
The study is acceptable.
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) > 500 mg BF 490-1/L (nominal) (highest concentration tested)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 - 72 h) > 500 mg BF 490-1/L (nominal)

Tier 1 Non target aquatic plant toxicity study on BAS 490 F (242009). (Hughes J. and Jackson S., 1994).

Guidelines :
US EPA - FIFRA - Pesticide assessment guidelines - Subdivision J, Hazard evaluation: Non target-plants guidelines 122-2 Growth and reproduction of aquatic plants, Tier 1
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.68 %, batch: N33
Test species : see table below
Type of test : static system
Applied and measured concentrations :
One concentration equivalent to the highest application rate in the US (1Lb a.s./acre - overspray situation of a pond with a depth of 6 inches): 0.301 mg a.s./L
Analytical methods : GC with ECD detection
Test conditions : see table below

Table B.9.2.8-1 : Summary of study parameters - non-target aquatic plant toxicity study

Parameter	Measurement, setting or condition for each species				
Test organism	*Selenastrum capricornutum*	*Anabaena flos-aquae*	*Naviculosa pelliculosa*	*Skeletonema costatum*	*Lemna gibba*
Nominal concentration, µg a.s./L	301	301	301	301	301
Test duration	5 days	5 days	5 days	5 days	14 days
Medium	AAP	AAP	AAP/Si	MAA	20X-AAP
Temperature	24 ± 2 °C	24 ± 2 °C	24 ± 2 °C	20 ± 2 °C	25 ± 2 °C
Illumination	Continuous cool-white, 4306 ± 646 lumens/m²	Continuous cool-white, 2153 ± 323 lumens/m²	Continuous cool-white, 4306 ± 646 lumens/m²	Continuous cool-white, 4306 ± 646 lumens/m²	Continuous cool-white, 4198-5813 lumens/m²
Shaking	Continuous, 100 oscillations/min.	Manually, once per day	Continuous, 100 oscillations/min.	Manually, once per day	None
Inoculum size	3000 cells/mL	3000 cells/mL	3000 cells/mL	10000 cells/mL	12 fronds (4 3-frond plants)
Biomass monitoring	Days 3, 4 and 5	Days 3, 4 and 5	Days 3, 4 and 5	Days 3, 4 and 5	Days 2, 4, 7, 9, 11 and 14

Findings :

Table B.9.2.8-2 : Effects of kresoxim-methyl on several algal taxa and aquatic plant

	Selenastrum capricornutum	***Anabaena flos-aquae***	***Naviculosa pelliculosa***	***Skeletonema costatum***	***Lemna gibba***
concentration on day 0 (µg a.s./L)	258.67	233.33	274.67	282.67	231.33
a.s. concentration at the end of the test (µg/L)	167.67 (d 5)	n.d. (d 5)	226.0 (d 5)	87.33 (d 5)	n.d. (d 14)
BF 490-1 metabo-lite concentration at the end of the test (µg/L)	176.33 (d 5)	285.32 (d 5)	52.22 (d 5)	199.98 (d 5)	298.69 (d 14)
Percent inhibition biomass increase	98.1 % inhibition	7.92 % stimulation	63.7 % inhibition	61.8 % inhibition	10.2 % inhibition

n.d.: not detected

Conclusion:
This study is not required by the Directive 91/414/EEC.
Significant inhibition of the biomass increase was recorded for *Selenastrum capricornutum, Naviculosa pelliculosa, Skeletonema costatum.*
Effects lower than 50 % for *Lemna gibba* and *Anabaena flos-aquae* mean that further testing is not required (American rules).

Added in March 2010:

A new study has been performed after writing the original dossier for submission in the USA, where at that time longer duration studies had been required. This study has been included here for completeness. The endpoint from this study (59.4 µg a.s./L) is similar to the endpoint of the standard algal test (63 µg a.s./L from Dohmen G.P., 1992a) which is used in the risk assessment.

BAS 490 F: A Tier II 5-day toxicity test with the freshwater alga (*Selenastrum capricornutum*) (Thompson S.G. *et al*., 1995).

Guidelines :
EPA 123-2
GLP :
Yes
Material and Methods :
Test substance : kresoxim-methyl, chemical purity: 94.68 %, batch: N 33
Test species : unicellular freshwater green alga (*Pseudokirchneriella subcapitata*, syn. *Selenastrum capricornutum*)
Number of organisms : initially: 3 x 10^4 cells/mL, 3 replicates/concentration
Type of test : static test (5 days)
Applied and measured concentrations :
nominal : control; solvent control (25.8 µL/L dimethylformamide); 0.0161, 0.0323, 0.0645, 0.129, 0.258 mg a.s./L
measured at day 0 : control; solvent control; 0.0122, 0.0250, 0.0585, 0.144, 0.289 mg a.s./L
measured at day 5 : control; solvent control ; 0.0176, 0.0233, 0.0408, 0.125, 0.230 mg a.s./L
Test conditions :
temperature : 22.3 – 25.3 °C
pH : 7.4 – 7.5 (day 0) ; 7.8 – 8.6 (day 5)
photoperiod : continuous light
light intensity : 4310 – 4840 lux
Analytical methods : gas chromatograhy with electron capture detection
Findings :

Table B.9.2.8-3 : Effects of kresoxim-methyl on the growth of the green alga *Pseudokirchneriella subcapitata* (syn. *Selenastrum capricornutum*)

Concentration [µg/L] nominal	**16.1**	**32.3**	**64.5**	**129**	**289**
Concentration [µg/L] initially measured	**12.2**	**25.0**	**58.5**	**144**	**289**
Inhibition in biomass growth (72 h) [%]	5.5	18	57*	77*	94*
	Endpoints [µg/L] (initially measured)				
E_bC_{50} (0-72 h)	59.4				
NOEC (0-72 h)	12.2				

* Statistically significant compared to the pooled control replicates (Bonferroni t-test, $p < 0.05$)

No morphological effects on algae were observed. At test concentrations of 58.5 µg a.s./L and higher a statistically significant reduction of cell densities could be observed when compared to the pooled controls (Bonferroni t-test, $p < 0.05$).

Conclusion :
The study is acceptable.
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 - 72 h) = 0.0594 mg a.s./L (based on day 0 measured concentrations)
NOEC (*Pseudokirchneriella subcapitata*, 0 - 72 h) = 0.0122 mg a.s./L (based on day 0 measured concentrations)

B.9.2.9 Effects on the organisms of the sediments (Annex IIA 8.2.7)

No study is required. Effects on the organisms of the sediments are evaluated in the mesocosm study.

Added in March 2010:

Kresoxim-methyl is not stable in water (DT_{50} < 2 d) and does not adsorb to any significant extent to the sediment over a prolonged period of time. Thus, a test on sediment-dwelling organisms is not warranted. Furthermore, an outdoor mesocosm study (Dohmen, 1995) is available allowing to assess the risk to benthic species; it showed no impact up to and including the highest treatment level with several applications of 33.3 µg a.s./L.

B.9.2.10 Effects on aquatic plants (Annex IIA 8.2.8)

Effects on *Lemna gibba* were observed in the study of Hughes J. and Jackson S. (1994). See point B.8.2.8

Added in March 2010:

A test on aquatic plants is not needed for a fungicidal compound without indications of phytotoxicity. This is the case for kresoxim-methyl.

B.9.2.11 Acute toxicity of the preparations MENTOR, CANDIT and ALLEGRO (Annex IIIA 10.2.1)

Acute toxicity study on the rainbow trout (*Oncorhynchus mykiss* WaLBAUM 1792) of BAS 492 01 F in a static system (96 hours). (Munk R., 1994a).

Guidelines :
EPA, Parag. 72-1, 1982; guideline is acceptable.
GLP :
Yes
Material and Methods :
Test substance : BAS 492 01 F, SE containing 151.15 g/L kresoxim-methyl and 305.37 g/L fenpropimorph – formulation MENTOR
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fish/concentration/replicate, 1.7 g (range: 1.2 - 2.2 g), 5.6 cm (range: 4.9 - 6.3 cm), about 5 months old, loading: 0.17 g fish/L water
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : water control; 0.681, 1.0, 1.47, 2.15, 3.16, 4.64, 6.81 mg MENTOR/L
Recoveries for kresoxim-methyl varied between 84.0 - 95.3 % of the nominal concentration at t=0 to 49.3 -57.9 % after 48 hours (due to hydrolysis of the parent compound)
Test conditions :
3 first parameters measured daily
temperature : 11- 12 °C
pH : 8.3 - 8.6
oxygen content : 10.8 - 11.5 mg O_2/L at day 1 and 9.5 - 10.3 mg O_2/L at day 4
total hardness : about 2.5 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : HPLC with UV detection
Findings :
Mortality : Mortality occurred in the first hour of the test.
Behavioral observations : Apathy, narcotic-like state, discolorations and tumbling in all dose levels with surviving fish except the lowest one at 0.681 mg/L. No effects were monitored in the control group.

Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 1 – 4 - 24 h) = 1.848 mg MENTOR/L (95 % confid. limits: 1.592 - 2.142) (nominal)
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 1.470 mg MENTOR/L (10 % significance level)
LC_0 (*Oncorhynchus mykiss*, 96 h) = 1.0 mg MENTOR/L (nominal)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.681 mg MENTOR/L (nominal)
LC_{50} (*Oncorhynchus mykiss*, 96 h) > 0.81 < 1.2 mg MENTOR/L (significance level: 10 %; 1 %) (measured)
LC_0 (*Oncorhynchus mykiss*, 96 h) = 0.493 mg MENTOR/L (measured)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.366 mg MENTOR/L (measured)
Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 1.470 mg MENTOR/L (nominal concentration) is the most adequate due to the occurrence of the mortality during the first hour of the test and the hydrolysis of kresoxim-methyl at the end of the test.

Effect of BAS 492 01 F on *Daphnia magna* STRAUS in an acute toxicity test. (Dohmen G.P., 1994d).

Guidelines :
OECD 202, EEC Directive 79/831 (updated 1989)
GLP :
Yes
Material and Methods :
Test substance : BAS 492 01 F, SE containing 151.15 g/L kresoxim-methyl and 305.37 g/L fenpropimorph – formulation MENTOR
Test species : waterflea (*Daphnia magna*)
Number of organisms, age : 5 waterfleas X 4 replicates/concentration, 2 - 24 hours old
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; 0.25, 0.5, 0.75, 1.0, 1.5, 2.0, 3.0 mg MENTOR/L
Recovery of kresoxim-methyl and its acid metabolite between 88.6 - 92.2 % after 48 hours. This analysis confirms the hydrolysis of the parent compound.
Test conditions :
test medium : synthetic water (reconstituted, M4 according to Elendt)
temperature : 19 - 20 °C
pH : 7.92 - 8.24
oxygen content : 8.8 - 9.1 mg O_2/L
total hardness : 2.55 mmol/L
photoperiod : 16/8 hours light/dark cycle
light intensity : 900 - 1000 lux
Analytical methods : reversed phase HPLC with UV-detection
Findings :
Mortality : No mortality occurred up to 0.5 mg/L.
Behavioral observations : -
Endpoints :
EC_{50} (*Daphnia magna*, 48 h) = 1.2 mg MENTOR/L (nominal) (95 % limits: 1.06 - 1.37 mg/L)
EC_0 (*Daphnia magna*, 48 h) = 0.5 mg MENTOR/L (nominal)
Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 48 h) = 1.2 mg MENTOR/L (nominal) (95 % limits: 1.06 - 1.37 mg/L)

Effect of BAS 492 01 F on the growth of the green alga *Pseudokirchneriella subcapitata*. (Dohmen G.P., 1994e).

Guidelines :
OECD 201 (1984)
GLP :
Yes
Material and Methods :
Test substance : BAS 492 01 F, SE containing 151.15 g/L kresoxim-methyl and 305.37 g/L fenpropimorph - formulation MENTOR, batch: 93-2
Test species : unicellular freshwater green alga (*Pseudokirchneriella subcapitata* syn. *Selenastrum capricornutum*)
Number of organisms: initially : 1 x 10^4 cells/mL, 5 replicates/concentration
Type of test : static test (72 hours)
Applied and measured concentrations :
nominal : water control; 0.003, 0.01, 0.03, 0.1, 0.3, 1.0 mg MENTOR/L
measured concentrations ranging from 86.5 - 92.1 % of the nominal concentrations at day 0
Recoveries at the end of the test (parent compound + free acid metabolite): 90.7 % and 53.0 % of the nominal concentrations at doses 1 and 0.1 mg/L respectively (53.0 % due to values for the metabolite below the detection limit)
Test conditions :
temperature : 22 ± 1 °C
pH measured at the end of the test : 8.02 - 8.09
photoperiod : continuous uniform illumination
light intensity : 8000 lux
constant shaking at 125 rpm
Analytical methods : reversed phase HPLC with UV-detection
Findings :
Observations :
The lowest test concentration of 0.003 mg/L caused a biomass inhibition of 6.7 %, the highest dose of 1.0 mg/L an inhibition of 98.4 %.
The lowest test concentration of 0.003 mg/L caused a growth inhibition of 2.1 %, the highest dose of 1.0 mg/L an inhibition of 71.2 %.
Morphological effects on the alga could be observed, i.e. thickening and rounding, in few single cells at 0.01 mg/L and more frequently at higher concentrations (only mentioned in the abstract of the study).
Endpoints :
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.08 mg MENTOR/L (nominal) (95 % limits: 0.037 - 0.201 mg/L)
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.01 mg MENTOR/L (nominal) (95 % limits: 0.001 - 0.023 mg/L)
$NOEC_b$ (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.01 mg MENTOR/L (nominal)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.443 mg MENTOR/L (nominal) (95 % limits: 0.328 - 0.598 mg/L)
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.036 mg MENTOR/L (nominal) (95 % limits: 0.026 - 0.051 mg/L)
Conclusion :
The study is acceptable.
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.08 mg MENTOR/L (nominal) (95 % limits: 0.037 - 0.201 mg/L)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.443 mg MENTOR/L (nominal) (95 % limits: 0.328 - 0.598 mg/L)

Sublethal toxic effects on the rainbow trout (*Oncorhynchus mykiss* W.) of BAS 492 01 F in a flow-through system (28 days). (Munk R., 1995a).

Guidelines :
OECD 204 (updated version 1984)
Draft-OECD guideline "Proposal for: fish juvenile growth test - 28 days" of March 92 was also considered.
GLP :
Yes
Material and Methods :
Test substance : BAS 492 01 F, SE containing 151.15 g/L kresoxim-methyl and 305.37 g/L fenpropimorph - formulation MENTOR, batch 93-2
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 20 animals X 1 replicate/concentration, 1.03 g (range: 0.8 - 1.2 g), 4.64 cm (range: 4.2 - 5.3 cm), about 6 months old
Type of test : rlow-through system (28 days)
Applied and measured concentrations :
nominal : water control; 0.0004, 0.002, 0.01, 0.05, 0.25, 1.25 mg MENTOR/L
The two lowest concentrations (0.0004 and 0.002) were added during the course of the study since an impairment of body weight in the 0.01 mg/L dose was observed.
measured concentrations (sum of parent compound and its acid free metabolite) ranging from 56 - 188 % of the nominal concentrations.
Test conditions :
flow rate : 10 L/h per aquarium
The 3 following parameters were determined daily.
temperature : 13 ± 1 °C
pH : about 8.3
oxygen content : 8.5 - 11.2 mg O_2/L
total hardness weekly determined : 2.3 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : HPLC with UV detection
Findings :

Table 9.2.11-1 : Effects in rainbow trouts exposed to MENTOR in a flow-through system over 28 days

	Concentration (mg MENTOR/L) (nominal)						
	0 (water control)	**0.0004**	**0.002**	**0.01**	**0.05**	**0.25**	**1.25**
Mortality (day 28)	0	0	5 %	0	20 %	15 %	20 %
Body weight Length	-	-	smaller body weight and body length in the 0.002 group but not statistically significant	impairment of the mean body weight and length in these test groups at the $p \leq 0.01$ level			
Symptoms	-	-	apathy, discoloration/dark, reduced and/or no feed consumption, swimming near the bottom of the aquaria, tumbling, accelerated respiration, mucosis secretion from the anus, narcosis-like state				

Mortality : The mortality occurred during the second half of the test (days 13 - 28).
Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 28 d) > 1.25 mg MENTOR/L (nominal)
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.0004 mg MENTOR/L (nominal) is based on the mortality and clinical symptoms data

Conclusion :
The study is accepted as valid nevertheless some deviations of the recoveries.
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.0004 mg MENTOR/L (nominal) is based on the mortality and clinical symptoms data

Determination of the chronic toxicity of BAS 492 01 F to the waterflea *Daphnia magna* STRAUS. (Jatzek H.J., 1994).

Guidelines :
EEC Guideline XI/681/86, draft 4
GLP :
Yes
Material and Methods :
Test substance : BAS 492 01 F, SE containing 151.15 g/L kresoxim-methyl and 305.37 g/L fenpropimorph - formulation MENTOR, batch: 93-2
Test species : waterflea (*Daphnia magna*)
Number of organisms, age : 1 animal X 10 replicates/concentration, 2 - 24 hours old
Type of test : semi-static test (21 days)
Applied and measured concentrations :
nominal : water control; 0.002, 0.004, 0.008, 0.016, 0.031, 0.063, 0.125, 0.25, 0.5, 1.0 mg MENTOR/L
measured concentrations : 78.4 - 103.2 % of the nominal concentrations just after dilution.
Recoveries of 49.8 - 88.2 % after 48 hours due to hydrolysis of parent compound.
Test conditions :
Synthetic medium M4 was used for the culture and test. Renewal of the test solution three times a week.
temperature : 19.1 - 21.2 °C
pH : 7.6 - 8.4
oxygen content : 7.2 - 9.2 mg O_2/L
total hardness : 2.20 - 3.20 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : HPLC with UV detection
Findings :

Table 9.2.11-2 : Effects on daphnids exposed to MENTOR in a semi-static system over 21 days

	Concentration (mg MENTOR/L) (nominal)										
	0	**0.002**	**0.004**	**0.008**	**0.016**	**0.031**	**0.063**	**0.125**	**0.25**	**0.5**	**1.0**
% Mortality adults (day 7)	-	-	-	-	-	-	-	-	-	-	20 %
% Mortality adults (day 14)	-	-	-	-	-	-	-	-	-	-	60 %
% Mortality adults (day 21)	-	-	-	-	-	-	-	-	-	-	90 %
Reproduction rate (offspring/adult)	115.7	116.5	106.3	98.1	86.3	66.6	44.0	10.9	0	0	0
Dead young	0	2.1	5.5	4.4	6.5	2.1	0.5	1.1	0	0	0
Aborted eggs per live parent animal	0	0	0.2	0	0.1	2	0.4	0.4	0	0	0

Endpoints :
NOEC (*Daphnia magna*, 21 d) = 0.008 mg MENTOR/L (nominal), related to offspring
Conclusion :
The study is acceptable.

Added in March 2010:

Acute toxicity test on the rainbow trout *(Oncorhynchus mykiss* WALBAUM 1792) of BAS 490 02 F in a static system (96 hours). (Munk R., 1994a).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
Test method C.1 EEC Directive 84/449 (updated 1989)
OECD 203 (adopted 1992)
GLP :
Yes
Deviations:
-fishes were placed into the aquaria about 45' after the test article was added (deviation without major effect on the outcome of the test).
-the analysis of the water at study termination demonstrated that also the control samples were contaminated with an amount of test article (0.033 - 0.048 mg/L)
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) - formulation CANDIT, batch: 92-5
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fishes (5 months) in one aquarium/concentration, 54.2 mm (range: 47 - 65), 1.42 g (range: 0.9 - 2.5 g), charge 0.14 g fish/L water;
observations on 1, 4, 24, 48, 72 and 96 hours
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : control; 0.0464, 0.0681, 0.100, 0.147, 0.215, 0.316, 0.464, 0.681 mg CANDIT/L
measured concentrations (mean of 2 samples):
-at the beginning of test: ranging from 21 - 64 % of the nominal concentrations:
0.010, 0.019, 0.064, 0.046, 0.065, 0.086, 0.108, 0.192 mg CANDIT/L
-at 96 h: ranging from 38 - 148 % of the nominal concentrations:
0.069, 0.043, 0.136, 0.076, 0.098, 0.145, 0.175, 0.255 CANDIT/L

Remark of RMS: The measured concentrations at nominal levels of 0.147 mg CANDIT/L and above are >10% lower than intended. In the report, it was stated that the solubility was poor and irreproducible. It was observed that the granulate did not decompose immediately and homogeneous sampling was difficult under the study conditions. It was also stated that the *"generated hydrolysis product was taken into account but cannot explain the deficit in active ingredient"*. Contrarily to the opinion of the notifier, who took into account nominal dose-levels to express the relevant endpoints, RMS is of the opinion that the value should be corrected for the loss of a.s.. Based upon the loss of a.s. at the doses >NOEC, the average analytically detected concentrations (t = 1 h – 96 h) were used to express the endpoints.

Test conditions :
medium : active C filtered non aerated tap water
temperature : 11 - 12 °C
pH : 8.4 - 8.6
oxygen content : 9.6 - 11.3 mg O_2/L throughout the test (> 6.5 mg/L, thus > 60 % saturation at 12 °C)
total hardness : 250 mg/L (as $CaCO_3$), 2.5 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection

Findings :
Behavioral observations : Fishes exhibited symptoms like discoloration, apathy, convulsions, tumbling at 464 µg/L (nominal) and were in a narcotic-like state at the top dose (681 µg/L nominal). Onset time of signs was 4 h.
Mortality : 96 h-mortality was observed at 464 µg/L (3/10, onset time 48 h) and at the top dose (10/10, onset time 24 h).
Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 0.500 mg CANDIT/L (nominal)
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 0.150 mg CANDIT/L (analytical)

NOEC (*Oncorhynchus mykiss*, 96 h) = 0.316 mg CANDIT/L (nominal)
NOEC (*Oncorhynchus mykiss*, 96 h) = 0.095 mg CANDIT/L (analytical)

Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 0.150 mg CANDIT/L (analytical)
CANDIT is very toxic to rainbow trout.

Acute toxicity test on the common carp *(Cyprinus carpio* L.) of BAS 490 02 F in a static system (96 hours). (Munk R., 1994b).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
OECD guideline 203
EEC test method C.1 (Dir 84/449, update 12/1992)
Deviations: none
GLP :
Yes
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) – formulation CANDIT, batch: 92-5
Test species : common carp (*Cyprinus carpio* L.)
Number of organisms, weight, length, age : 10 fishes in one aquarium/concentration, 53.6 mm (range: 44 - 59), 2.75 g (range: 1.6 - 4.0 g), charge 0.28 g fish/L water;
observations on 1, 4, 24, 48, 72 and 96 hours
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : water control; 0.215, 0.464, 1.0, 2.15, 4.64, 10 mg CANDIT/L
measured concentrations (mean of 2 samples):
-at the beginning of test: ranging from 83 - 119 % of the nominal concentrations:
0.256, 0.472, 0.960, 1.951, 3.841, 8.499 mg CANDIT/L
-at 96 h: ranging from 72 - 105 % of the nominal concentrations:
0.225, 0.468, 0.966, 1.946, 3.626, 7.204 mg CANDIT/L

Remark of RMS: The measured concentrations at nominal levels of 2.15 mg CANDIT/L and above are >10% lower than intended. At 96 h, 72 – 91 % of nominal levels >NOEC were recovered. Therefore, the average analytical concentrations (t = 1 h – 96 h)were used to determine the endpoints.

Test conditions :
medium : active C filtered tap water, non aerated
temperature : 21 - 23 °C
pH : 8.3 - 8.6
oxygen content : 7.6 - 8.4 mg O_2/L throughout the test
total hardness : 250 mg/L (as $CaCO_3$), 2.5 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection

Findings :
Behavioral observations : Fishes exhibited symptoms like apathy, tumbling at 2.15 mg/L (nominal) and were in a narcotic-like state at 4.64 mg/L nominal and above. Onset time of signs was 1 h.
Mortality : 96 h-mortality was observed at 2.15 mg/L (6/10, onset time 24 h), 4.64 mg/L (9/10, onset time 4 h) and at the top dose (10/10, onset time 1 h).
Endpoints :
LC_{50} (*Cyprinus carpio*, 96 h) = 2.15 mg CANDIT/L (nominal)
LC_{50} (*Cyprinus carpio*, 96 h) = 1.946 mg CANDIT/L (analytical)

NOEC (*Cyprinus carpio*, 96 h) = 1 mg CANDIT/L (nominal)
NOEC (*Cyprinus carpio*, 96 h) = 0.96 mg CANDIT/L (analytical)

Conclusion :
The study is acceptable.
LC_{50} (*Cyprinus carpio*, 96 h) = 1.946 mg CANDIT/L (analytical)
CANDIT is toxic to common carp.

Effect of BAS 490 02 F on *Daphnia magna* STRAUS in an acute toxicity test. (Dohmen G.P., 1994b).

Guidelines :
Test method C.2 EEC Directive 79/831 (updated 1989)
OECD 202
GLP :
Yes
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) – formulation CANDIT, batch: 92-5
Test species : waterfleas (*Daphnia magna*)
Number of organisms : 5 waterfleas X 4 replicates/concentration, 24 and 48 hours observation
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; 0.01, 0.025, 0.050, 0.075, 0.1, 0.25, 0.5, 0.75 mg CANDIT/L
measured : only the nominal doses of 0.1, 0.5 and 0.75 mg/L were analysed
at t = 0 h, the level of a.s. was 0.073, 0.442 and 0.662 mg a.s./L, corresponding with 72.9 %, 88.4 % and 88.2 % of nominal
at t = 48 h, the level of a.s. was 0.0558, 0.383 and 0.588 mg a.s./L (average value of 4 samples), corresponding with 56 %, 77 % and 78 % of nominal

Remark of RMS: The notifier also analysed the content of the acid metabolite (Reg No. 262451=BF 490-1), and the concentration was added to the content of active ingredient; the total level amounted to 0.078, 0.454 and 0.721 mg/L, accounting for respectively 78 %, 91 % and 96 % of nominal.
However, it has been demonstrated in earlier tests that this metabolite was not acutely toxic to water organisms (LC_{50} > 100 mg/L), and therefore only the concentration of the a.s. itself should be taken into account. RMS proposes to correct the obtained value of the LC_{50} value and the NOEC with the mean recovery at the nearest nominal level, i.e. 64.4 % and 82.5 %, respectively.

Test conditions :
medium : reconstituted water (M4 Elendt synthetic medium)
temperature : 19.3 - 19.8 °C
pH : 8.1 - 8.2 throughout the experiment
oxygen content : 8.1 – 8.6 mg O_2/L
total hardness : 2.34 mmol/L
conductivity : 600 µS/cm
photoperiod : 16/8 hours light/dark cycle
light intensity : 900 – 1000 lux
Analytical methods : reversed phase HPLC with UV detection
Findings :
Behavioral observations : Daphnids appeared impaired at 0.75 mg/L (nominal).
Endpoints :
EC_{50} (*Daphnia magna*, 48 h) = 0.350 mg CANDIT/L (nominal)
EC_{50} (*Daphnia magna*, 48 h) = 0.289 mg CANDIT/L (corrected for a mean recovery of a.s. of 82.5 %)
NOEC (*Daphnia magna*, 48 h) = 0.1 mg CANDIT/L (nominal)
NOEC (*Daphnia magna*, 48 h) = 0.064 mg CANDIT/L (corrected for a mean recovery of a.s. of 64.4 %)
Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 48 h) = 0.289 mg CANDIT/L (corrected for a mean recovery of a.s. of 82.5 %)
CANDIT is very toxic to *Daphnia magna*.

Effect of BAS 490 02 F on the growth of the green alga *Pseudokirchneriella subcapitata*. (Dohmen G.P., 1994a).

Guidelines :
Test method C.3 EEC Directive 79/831 (updated 1989)
OECD 201 (1984)
GLP :
Yes
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) – formulation CANDIT, batch: 92-5
Test species : unicellular freshwater green alga (*Pseudokirchneriella subcapitata*, syn. *Selenastrum capricornutum*)
Number of organisms : initially (t = 0 h) : 1 x 10^4 cells/mL, 5 replicates/concentration, 10 replicates for control
Type of test : static system (72 hours)
Applied and measured concentrations :
nominal : water control; 0.003, 0.01, 0.03, 0.1, 0.3, 1, 3 mg CANDIT/L
measured : only the nominal doses of 0.1 and 3 mg/L were analysed at start of the test and at 72 h. The level of a.s. (average value of 2 samples)
at t = 0 h was 0.062 and 2.88 mg a.s./L corresponding with 62 % and 96 % of nominal;
at t = 72 h was 0.051 and 2.44 mg a.s./L corresponding with 51 % and 81 % of nominal.

Remark of RMS: The notifier also analysed the content of the acid metabolite of kresoxim-methyl (Reg No. 262451=BF 490-1) at t = 72 h and the concentration was added to the content of active ingredient; the total level amounted to 0.082 and 3.28 mg/L, accounting for respectively 82 % and 109 % of nominal.
However, it has been demonstrated in earlier tests that this metabolite was not acutely toxic to water organisms (EC_{50} >100 mg/L), and therefore only the concentration of the a.s. itself should be taken into account. RMS proposes to correct the obtained value of the EC_x value with the recovery at the nearest nominal (in this case the lowest) level, mean measured, i.e. 57 %.

Test conditions :
temperature : 21 ± 1 °C
pH : 7.92 - 8.12
photoperiod : continuous uniform illumination
light intensity : *ca.* 8000 lux
Analytical methods : reversed phase HPLC with UV detection
Findings :
Observations : No morphological effects on algae were observed.

Table B.9.2.11-3 : Effect of CANDIT on the growth of the green alga *Pseudokirchneriella subcapitata*

	Concentration (mg CANDIT/L) (nominal)						
Endpoint 0 – 72 h	**0.003**	**0.01**	**0.03**	**0.10**	**0.30**	**1.0**	**3.0**
Growth rate inhibition (%)	-3.2	2.0	23.2	68.2	93.2	97.8	98.3
Biomass inhibition (%)	-0.8	0.5	5.4	23.1	53.3	65.3	69.3

- Negative values indicated stimulated growth

Endpoints :
Expressed in nominal concentrations:
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.071 mg CANDIT/L (95%: 0.059 – 0.083)
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.015 mg CANDIT/L (95%: 0.011 – 0.019)

E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.532 mg CANDIT/L (95%: 0.405 – 0.714)
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.033 mg CANDIT/L (95%: 0.019 – 0.051)

Expressed in analytically measured concentrations (correction for 57 % recovery):
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.040 mg CANDIT/L
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.0086 mg CANDIT/L

E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.303 mg CANDIT/L
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.019 mg CANDIT/L

Conclusion :
The study is acceptable.
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.040 mg CANDIT/L (correction for 57 % recovery)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.303 mg CANDIT/L (correction for 57 % recovery)
CANDIT is very toxic to algae.

The acute toxicity for fish, aquatic invertebrates and algae was tested with the formulation BAS 494 02 F. As BAS 494 02 F is a minor change to BAS 494 04 F (details are given in document JM3), this study is considered relevant to assess the potential risk arising from uses of BAS 494 04 F.

Acute toxicity study on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of BAS 494 02 F in a static system (96 hours). (Munk R., 1994).

Guidelines :
US EPA, Subdivision E, § 72-1 (1982)
OECD guideline 203
EEC test method C.1 (Dir 84/449, update 12/1992)
GLP :
Yes
Material and Methods :
Test substance : BAS 494 02 F, SE containing 126.25 g/L (nominal 125.0 g/L) kresoxim-methyl and 126.22 g/L (nominal 125.0 g/L) epoxiconazole – formulation ALLEGRO, batch: 93-1
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 10 fish/concentration/replicate, 1.8 g (range: 1.2 - 3.6 g), 4.87 cm (range: 4.0 - 6.0 cm), about 4 months old, loading: 0.18 g fish/L water
Type of test : static system (96 hours)
Applied and measured concentrations :
nominal : water control; 1.0, 1.47, 2.15, 3.16, 4.64, 6.81 mg ALLEGRO/L
measured concentrations of kresoxim-methyl (mean of 2 samples):
-at the beginning of test: ranging from 93 - 98 % of the nominal concentrations:
0.972, 1.42, 2.02, 2.98, -, 6.70 mg ALLEGRO/L (no meaningful degradation)
-at 96 h: only nominal levels of 1, 1.47 and 2.15 mg ALLEGRO/L were analysed, and measurements amounted to 0.502, 0.699 and 1.17 mg ALLEGRO/L, representing 50 %, 48 % and 55 % of the nominal concentrations, respectively (at t = 1 h, the values at these levels were 97 %, 97 % and 94 % respectively). The time-weighed average (1 – 96 h) is 74 %, 73 % and 75 %.

Remark of RMS: The notifier also analysed the content of the acid metabolite of kresoxim-methyl (Reg No. 262451=BF 490-1) and the concentration of this hydrolysis product was added to the content of active ingredient measured at t = 96 h (average of 2 samples only for the levels 1, 1.47 and 2.15 mg/L). The total level amounted to 0.792, 1.15 and 1.82 mg/L, accounting for respectively 79 %, 78 % and 85 % of the nominal value.
However, it has been demonstrated in earlier tests that this metabolite was not acutely toxic to water organisms (LC_{50} > 100 mg/L), and therefore only the concentration of the a.s. itself should be taken into account.

In conclusion, the measured concentrations of kresoxim-methyl at all levels was > 10 % lower than intended at 96 h. RMS proposed to correct the obtained endpoints for an overall recovery of 74 % of kresoxim-methyl for the whole duration of the test (1 – 96 h).

The recovery of epoxiconazole in the preparation was 100 – 109 % (t = 0 h) and 93 – 98 % (t = 96 h), thus no correction is necessary.

Test conditions :
temperature : 13 - 14 °C
pH : 8.4 - 8.9
oxygen content : 8.6 - 11.55 mg O_2/L throughout the experiment
total hardness : about 2.5 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : HPLC with UV detection

Findings :
Mortality : Mortality occurred in the first hour of the test (3/10) at the top-concentration; from t= 4 h onwards, mortalities were observed at 2.15 mg/L and above, and 100 % mortality occurred at 24 – 48 h at ≥ 2.15 mg/L.

Table 9.2.11-4 : Effect of ALLEGRO on the growth of the rainbow trout (*Oncorhynchus mykiss*)

Concentration (mg/L) nominal	**1.00**	**1.47**	**2.15**	**3.16**	**4.64**	**6.81**
Concentration (mg/L) analytical[1]	**0.74**	**1.09**	**1.59**	**2.34**	**3.43**	**5.04**
Mortality (/10) 1 h	0	0	0	0	0	3
4 h	0	0	3	8	10	10
24 – 96 h	0	0	10	10	10	10

[1] corrected for 74 % recovery throughout the study (1 – 72 h)

Behavioral observations : Tumbling was observed at 2.15 mg/L; convulsions and lethargic state were observed at 3.16 mg/L onwards.

Endpoints :
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 1.8 mg ALLEGRO/L (nominal)
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 1.33 mg ALLEGRO/L (analytical)

NOEC (*Oncorhynchus mykiss*, 96 h) = 1.47 mg ALLEGRO/L (nominal)
NOEC (*Oncorhynchus mykiss*, 96 h) = 1.09 mg ALLEGRO/L (analytical)

Conclusion :
The study is acceptable.
LC_{50} (*Oncorhynchus mykiss*, 96 h) = 1.8 mg ALLEGRO/L (nominal)
ALLEGRO is toxic to rainbow trout.

Effect of BAS 494 02 F on *Daphnia magna* STRAUS in an acute toxicity test. (Dohmen G.P., 1995a)

Guidelines :
Test method C.2 EEC Directive 79/831 (updated 1989)
OECD 202
GLP :
Yes
Material and Methods :
Test substance : BAS 494 02 F, SE containing 126.25 g/L (nominal 125.0 g/L) kresoxim-methyl and 126.22 g/L (nominal 125.0 g/L) epoxiconazole – formulation ALLEGRO, batch: 93-1
Test species : waterfleas (*Daphnia magna*)
Number of organisms : 5 waterfleas X 4 replicates/concentration, neonates, less than 24 hours old; 24 and 48 hours observation
Type of test : static test (48 hours)
Applied and measured concentrations :
nominal : water control; 0.2, 0.3, 0.45, 0.6, 0.8, 1.0 mg ALLEGRO/L
measured concentrations of kresoxim-methyl (mean of 2 samples, only nominal levels of 0.2, 0.45 and 1.0 mg/L and additionally the stock solution, 125 mg/L, were analysed):
-at the beginning of test: 0.180, 0.372 and 0.933 mg ALLEGRO/L (no meaningful degradation, as recovery was 90 %, 83 % and 93 % of nominal)

-at 48 h: (i) without daphniae: 0.153, 0.338 and 0.776 mg ALLEGRO/L, representing 76 %, 75 % and 78 % of the nominal concentrations, respectively,
and (ii) with daphniae: 0.163, 0.342 and 0.756 mg ALLEGRO/L, representing 82 %, 76 % and 76 % of the nominal concentrations, respectively

Based upon these overall recoveries throughout the experiment (82 %, 80 %, 89 %), a correction was not deemed necessary.

Test conditions :
medium : reconstituted water (M4 Elendt synthetic medium)
temperature : 20.3 - 21.3 °C
pH : 7.95 - 8.13 throughout the experiment
oxygen content : 8.7 - 8.9 mg O_2/L
total hardness : 2.49 mmol/L
conductivity : 673 µS/cm
photoperiod : constant artificial light
Analytical methods : reversed phase HPLC with UV detection

Findings :
Behavioral observations : Daphnids appeared impaired at 0.6 mg/L (nominal) and above.

Table 9.2.11-5 : Effect of ALLEGRO on the immobility of the *Daphnia magna*

	Concentration (mg ALLEGRO/L) (nominal)					
Endpoint 24 – 48 h	**0.2**	**0.3**	**0.45**	**0.6**	**0.8**	**1.0**
Immobile (%) 24 h	0	0	0	0	15	80
48 h	0	0	0	15	70	100

Endpoints :
EC_{50} (*Daphnia magna*, 48 h) = 0.73 mg ALLEGRO/L (nominal)
NOEC (*Daphnia magna*, 48 h) = 0.45 mg ALLEGRO/L (nominal)

Conclusion :
The study is acceptable.
EC_{50} (*Daphnia magna*, 48 h) = 0.73 mg ALLEGRO/L (nominal)
ALLEGRO is very toxic to *Daphnia magna*.

Effect of BAS 494 02 F on the growth of the green alga *Pseudokirchneriella subcapitata*. (Dohmen G.P., 1995c).

Guidelines :
Test method C.2 EEC Directive 79/831 (updated 1989)
OECD 201 (1984)
GLP :
Yes
Material and Methods :
Test substance : BAS 494 02 F, SE containing 126.25 g/L (nominal 125.0 g/L) kresoxim-methyl and 126.22 g/L (nominal 125.0 g/L) epoxiconazole – formulation ALLEGRO, batch: 93-1
Test species : unicellular freshwater green alga (*Pseudokirchneriella subcapitata,* syn. *Selenastrum capricornutum*)
Number of organisms : initially (t = 0 h) : 1 x 10^4 cells/mL, 5 replicates/concentration, 10 replicates for control
Type of test : static system (72 hours)
Applied and measured concentrations :
nominal : water control; 0.003, 0.01, 0.03, 0.1, 0.3, 1, 3 mg ALLEGRO/L
measured : only the nominal doses of 0.03, 0.3 and 3 mg/L (start and end), and in addition the stock solution 10 mg/L (only start) were analysed. The level of a.s. (average value of 2 samples)
at t = 0 h was 0.032, 0.316 and 2.811 mg a.s./L corresponding with 94 – 106 % of nominal
at t = 72 h was 0.013, 0.269 and 2.289 mg a.s./L corresponding with 44 %, 90 % and 76 % of nominal.

Remark of RMS: However, at 72 h, notifier took into account both the a.s. kresoxim-methyl and its hydrolic degradate (acid metabolite Reg No. 262451=BF 490-1) to calculate the recovery.
However, it has been demonstrated in earlier tests that this metabolite was not acutely toxic to water organisms (EC_{50} > 100 mg/L), and therefore only the concentration of the a.s. itself should be taken into account. Unfortunately, the separate concentrations were not reported in this experiment.

Therefore, RMS would propose to correct the obtained value of the EC_x value with the recovery at the nearest nominal (in this case the lowest) level at, mean measured, i.e. 75 %

Test conditions :
temperature : 22 ± 1 °C
pH : 7.9
photoperiod : continuous uniform illumination
light intensity : *ca*. 8000 lux
Analytical methods : reversed phase HPLC with UV detection

Findings :
Observations : At the lowest dose, few scattered cells showed morphological changes. At 0.03 mg/L up to 50 % and at the top-dose up to 80 % of the algae showed morphological changes (smaller and rounder).

Table 9.2.11-6 : Effect of ALLEGRO on the growth of the green alga *Pseudokirchneriella subcapitata*

	Concentration (mg ALLEGRO/L) (nominal)						
Endpoint 0 – 72 h	**0.003**	**0.01**	**0.03**	**0.10**	**0.30**	**1.0**	**3.0**
Growth rate inhibition (%)	-5.2	1.4	6.9	2.9	12.2	25.2	40.7
Biomass inhibition (%)	-8.9	14.5	23.9	17.9	41.5	66.6	79.5

- Negative values indicated stimulated growth

Endpoints :
Expressed in nominal concentrations:
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.398 mg ALLEGRO/L (95%: 0.166 – 1.320)
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.010 mg ALLEGRO/L (95%: 0.0004 – 0.034)

E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) > 3 mg ALLEGRO/L
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.161 mg ALLEGRO/L (95%: 0.099 – 0.262)

Expressed in analytically measured concentrations (correction for 75 % recovery):
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.299 mg ALLEGRO/L
E_bC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.0075 mg ALLEGRO/L

E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) > 2.25 mg ALLEGRO/L
E_rC_{10} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.121 mg ALLEGRO/L

Conclusion :
The study is acceptable.
E_bC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) = 0.299 mg ALLEGRO/L (correction for 75 % recovery)
E_rC_{50} (*Pseudokirchneriella subcapitata*, 0 – 72 h) > 2.25 mg ALLEGRO/L (correction for 75 % recovery)
ALLEGRO is very toxic to algae.

B.9.2.12 Mesocosm study (Annex IIIA 10.2.2)

The effects of BAS 490 02 F in an aquatic ecosystem - an outdoor microcosm study. (Dohmen G.P., 1995).

Guidelines :
"Guidance document on testing procedures for pesticides in fresh-water mesocosms" SETAC Europe (1992)
"Proceedings of a workshop on aquatic microcosm for ecological assessment of pesticides" SETAC RESOLVE (1992)
"Freshwater field tests for hazard assessment of chemicals" Hill *et al*. (1994)
GLP :
Yes
Material and methods :
Test substance : kresoxim-methyl, as contained in BAS 490 02 F, WG containing 500 g a.s./kg - formulation CANDIT, batch: 93-4
Scenarios :
The study performed simulates the 'worst case' exposure scenarios resulting from applications in orchards at 0.2 kg product/ha (100 g a.s./ha). 6 applications have been made at intervals of about 2 weeks, the first one on 19-04-95 and the last one on 28-06-95. 3 drift patterns were investigated (4 %, 20 %, 100 % - 30 cm water depth).
Experimental design :
[3 replicates (tanks) + 1 tank with fishes (*Cyprinus carpio*)] for each concentration and the control
The mesocosm site located in BASF research station of Limburgerhof (south-west Germany) consists of 16 single round tanks (diameter: 2.84 m; height: 1.5 m). They are embedded in the soil, about 10 cm protruding. They are constructed in black polyethylene high density to avoid adsorpion of test substance.
They contain from bottom to edge :
- 15 cm of sand
- 5 cm of clay
- 10 cm of natural sediment coming from lake 'Neuhofener Altrhein': the sediment was taken at a water depth of 50 - 100 cm at 1 - 5 m from the shore. It has a high sand content (85 % particles > 200 µm), little organic matter (0.2 % OC), low CEC (0.9 meq/100g), (pH = 8.1).
- 100 cm water (6335 L water/tank) coming from lake 'Neuhofener Altrhein'. Absence of eventual pesticides in water was assessed.
- 20 cm free at the top of the tank
Findings :

Physico-chemical parameters in water
Oxygen content (average %; diurnal cycle), pH (mean values; diurnal changes), conductivity, organic content, hardness, nutrients : no effect related to treatments

Phytoplankton (80 taxa)
- Cyanophyta : No effect related to treatments; important variability between samples
- Euglenophyta : No effect related to treatments; important variability between samples
- Cryptophyta (*Chroomonas nordstedti*, *Cryptomonas erosa*) : The population development of *C. erosa* differed from the *Chroomonas* curve; **statistically significant higher densities of *C. erosa* in the highest treatment as compared to control**
- Dinophyta : No dose-related effects; these algae were found only sporadically during the course of the experiment.
- Chlorophyta : No dose-related effect; *Ankistrodesmus* and *Scenedesmus* populations densities were similar in treatments and control during the course of the experiment
- Chrysophyta (Diatomeae as dominant group, Chrysophyceae, Xantophyceae) : No dose-related effect
- Total diversity (Simpson's diversity index) : No dose-related effect; diversity curves of treatments and control are parallel during the course of the experiment
- Chlorophylls ('a' found in eukaryotic algae, 'b' found in Chlorophyta, 'c' found in Cryptophyta, Dinophyta, Chrysophyta) : No dose-related effect; the evolution of chlorophylls content during the course of the experiment is similar in the different treatments and control.
- Periphyton : non-pelagic species growing on glass plates (biomass, chlorophyll amount) : No dose-related effect; due to the important variability between replicates it was impossible to detect differences between the treatments.

Macrophytes
(*Chara fragilis*, *Elodea nuttallii*, *Myriophyllum spicatum*, *Najas marina*, *Potamogeton* sp. : No effect recorded; visual assessement of macrophytes communities.

Zooplankton (50 taxa)
- Cladocera : **Highest concentration of a.s. caused some transient reduction in population levels;** two weeks after the last application the cladocera populations had recovered.
Effect of the a.s. on *Daphnia longispina* at the highest dose - recoveries occurred between the applications.
- Copepoda : **Detrimental effects on *Eudiaptomus gracilis* (Calanoida) at the highest dose.**
Numbers of Cyclopidea is slightly higher in treatment than in control (difference is not significant).
- Rotatoria : Only one species showed increased numbers in the highest concentration as compared to control. This may be due to reduced competition of Cladocera and Calanoida
- Testacea, Heliozoa, Ostracoda, Acari : No effect due to treatment.

Sediment species
-Tricladia, Gastropoda, Bivalvia, Oligocheta, Hirudinea, Crustacea (*Aselus aquaticus*), Acari (Hydrachnellae), Ephemeroptera, Odonata (Zygoptera), Heteroptera, Coleoptera, Trichoptera, Diptera : No negative impact in the benthic community; the overall number of organisms in the high treatment are greater than in control but the difference is not statistically significant.

Emerging insects (25 taxa identified)
- Trichoptera, Ephemeroptera, Odonata, Coleoptera, Diptera : No negative impact on the insects populations due to treatment; the average total number of emerged insects and the average number of taxa in control and treatments are quite similar during the course of the experiment

Fishes
Carp (*Cyprinus carpio*) :
- (mortality in the control and the lowest concentration)
- no effect on fish growth (length, weight)
- no effects on behaviour; fishes were in good condition
- dissection (treat. III) reveals no pathological abnormalities (all organs, gills, intestines in good conditions)

B.9.2.12-1 : Concentrations of kresoxim-methyl and its acid metabolite (BF 490-1) when applied to a mesocosm-system

	C	I	II	III
Scenario	**Control**	**100 g a.s./ha in orchard; 20 m buffer zone 4 % drift**	**100 g a.s./ha in orchard; 5 m buffer zone 20 % drift**	**100 g a.s./ha in orchard; overspray 100 % ente-ring water**
applied concentration	**0 µg a.s./L**	**1.33 µg a.s./L**	**6.65 µg a.s./L**	**33.3 µg a.s./L**
Concentration of a.s. and metabolite in water				
theorical cumulative level of a.s. at the last application (to be compared with metabolite + a.s. level - 28.6.94)	0 µg/L	7.98 µg/L	39.9 µg/L	199.8 µg/L
metabolite + a.s. at the last application (28.6.94) (*)	-	5.4 µg/L	21.0 µg/L	111.9 µg/L
kresoxim-methyl level at the last application (28-06-94)	-	1.3 µg/L	1.9 µg/L	4.3 µg/L
metabolite level at the last application (28.6.94)	-	4.1 µg/L	19.1 µg/L	107.6 µg/L
kresoxim-methyl level before winter (4.10. 94) (*)	-	0.2 µg/L	0.07 µg/L	0.9 µg/L
metabolite level before winter (4.10. 94) (*)	-	1.4 µg/L	2.5 µg/L	44.0 µg/L
kresoxim-methyl level after winter (4.4.95) (*)	-	0 µg/L	0 µg/L	0 µg/L
metabolite level after winter (4.4.95) (*)	-	0.7 µg/L	3.2 µg/L	27.2 µg/L
Concentrations of a.s. and metabolite in sediment (analysis were performed at 3 dates 3 to 13 days after the applications)				
kresoxim-methyl level	No accumulation of a.s. in the sediment (n.d. or sporadically found)			
metabolite level	The metabolite is easily soluble in water and absent of the sediment (n.d. or sporadically found)			

(*) : average of the 3 tanks which do not contain fishes

Conclusion :
This study shows that the effects of the a.s. in a mesocosm are less important than in laboratory studies with single test species.
- Nevertheless effects on some zooplankton species were observed at the highest dose (unrealistic situation of overspray)
- Kresoxim-methyl degraded rapidly between the applications; there was never accumulation of the a.s. in water
The degradation of metabolite BF 490-1 is less rapid and there was a steady increase of this substance in water up to the last application. The degradation was rapid during mid-summer but slowed down during autumn and winter
- There was no accumulation of a.s and its free acid metabolite in the sediment.

Added in March 2010:

There is low risk from kresoxim-methyl under realistic worst case conditions with maximum peak concentration of 33 µg a.s./L.
NOEC = 0.0067 mg a.s./L
NOAEC = 0.0333 mg a.s./L

B.9.2.13 Residue data in fish (Annex IIIA 10.2.3)

Not required : bioaccumulation study was provided

Added in March 2010:

The log P_{ow} of the active substance kresoxim-methyl was determined to be 3.4. A bioaccumulation study in fish was performed. The bioconcentration factor for whole fish was 220 and elimination was very rapid. Due to the fast degradation of kresoxim-methyl in water and the rapid excretion of the active substance from fish it is concluded that there is no risk of bioaccumulation in food chains.
Thus residues of the active substance of BAS 490 02 F in fish are of no concern and no accumulation in the food chain is to be expected.

B.9.2.14 Supplementary studies of toxicity to fish and aquatic invertebrates (Annex IIIA 10.2.4)

No study required.

Added in March 2010:

Sublethal toxic effects on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of BAS 490 02 F in a flow-through system (28 days). (Munk R., 1994c).

Guidelines :
OECD 204: Fish, Prolonged Toxicity Test: 14-Day Study
Draft OECD Guideline: Proposal for: Fish, Juvenile Growth Test – 28 days
GLP :
Yes
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) - formulation CANDIT, batch: 92-5
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 20 fish in one aquarium/concentration, 4.7 cm (range: 4.3 – 5.1 cm), 1.01 g (range: 0.8 - 1.2 g), approximately 5 months old
Type of test : flow-through system (28 days), 10 L/hour/aquarium, aquarium volume 60 L
Applied and measured concentrations :
nominal : control; 0.019, 0.056, 0.167, 0.50 mg CANDIT/L
measured : only the nominal doses of 0.056, 0.167, 0.50 mg/L were analysed at weekly intervals. From the lowest test concentration (0.019 mg/L) the stock dilution was analysed instead due to the detection limit.
at test initiation : 85.8 – 92.5 % of nominal
at test termination : 77.6 – 97.6 % of nominal
mean over complete range of the study : 76.7 – 102.2 % of nominal

Remark of RMS: The notifier also analysed the content of the acid metabolite (Reg No. 262451=BF 490-1), and the concentration was added to the content of active ingredient.
However, it has been demonstrated in earlier tests that this metabolite was not acutely toxic to water organisms (LC_{50} > 100 mg/L), and therefore only the concentration of the a.s. itself should be taken into account. However, since in the study report only the sum of a.s. and metabolite BF 490-1 is reported as measured concentration, it is not possible to calculate measured concentrations for a.s. only.

Test conditions :
temperature : 13 - 15 °C
pH : 8.2 - 8.4
oxygen content : 10.2 mg – 11.5 mg O_2/L
total hardness : 2.2 – 2.4 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : reversed phase HPLC with UV detection
Findings :

Table B.9.2.14-1 : Chronic toxicity (28 day) of CANDIT on rainbow trout (*Oncorhynchus mykiss*)

Concentration [mg/L] nominal	**Control**	**0.019**	**0.056**	**0.167**	**0.5**
Mortality [%]	0	0	0	0	100
Symptoms	none	none	none	none	--
Mean weight [g]	3.31	3.43	3.41	3.38	--
Mean length [cm]	6.69	6.77	6.86	6.86	--
	Endpoints [mg/L]				
LC_{50} (28 d)	0.29 (> 0.167 < 0.5)[1]				
NOEC (28 d)	0.167				

-- = not applicable, all animals dead
[1] LC_{50} estimated as geometric mean between LC_0 and LC_{100}

Kresoxim-methyl caused no mortality up to a concentration of 0.167 mg/L. 100 % mortality was observed at the highest test concentration of 0.5 mg/L. No toxic symptoms were seen in the remaining treatment groups after 28 days. No significant effects of kresoxim-methyl on weight and length gain were detected.

Conclusion :
The study is acceptable.
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.167 mg CANDIT/L (nominal)

Effect of BAS 490 02 F on the reproduction of *Daphnia magna* STRAUS in a chronic toxicity test. (Dohmen G.P., 1994c).

Guidelines :
EC Guideline XI/681/86 (draft 4), OECD 202
GLP :
Yes
Material and Methods :
Test substance : BAS 490 02 F, kresoxim-methyl 50 % granulate (actual: 48.37 %) - formulation CANDIT, batch: 92-5
Test species : waterfleas (*Daphnia magna*)
Number of organisms, age : 1 waterflea/replicate, 10 replicates/treatment, neonates, 2 - 24 hours old
Type of test : 21-day semi-static test, changing of test solution 2-3 times a week

Applied and measured concentrations :
nominal : control; 0.020, 0.040, 0.060, 0.090, 0.150, 0.250 mg CANDIT/L
mean measured :
t = 0 h : 86.2 – 92.7 % of nominal (only a.s. measurements)
t = 48 – 72 h : 52.8 – 67.5 % of nominal (only a.s. measurements)
RMS calculated mean recovery rate : 74.8 %

Test conditions :
temperature : 20 – 21 °C
pH : 8.1 – 8.8
oxygen content : 9.0 – 9.5 mg O_2/L
total hardness : 2.51 – 2.78 mmol/L
photoperiod : 16/8 hours light/dark cycle
light intensity : 1000 lux
Feeding : mixture of green alga *Pseuokirchneriella subcapitata* and *Scenedesmus subspicatus*
Assessments : assessment of immobility and mortality on day 2, 4, 5, 7, 8, 9, 11, 12, 14, 16, 18, 19, 20 and 21 after test initiation; assessment of reproduction at test termination (day 21)
Analytical methods : HPLC with UV detection

Findings :

Table B.9.2.14-2 : Effect of CANDIT on the reproduction and parent mortality of *Daphnia magna*

Concentration (nominal) [µg/L]	**Control**	**20.0**	**40.0**	**60.0**	**90.0**	**150.0**	**250.0**
Offspring/parent	166.6	159.5	162.8	145.5	166.0	156.5	21.6*
Parent-mortality [%]	0	0	0	0	0	0	0
Endpoints [µg/L]							
NOEC (21 d)	150						
LC_0 (21 d)	250						

* statistically significant difference compared to control (Dunnett´s multiple comparison test, $\alpha = 0.05$)

No mortality of parent animals was observed in any of the treatment groups after 21 days. The number of offspring was significantly reduced compared to the control only at the highest test concentration of 250 µg BAS 490 02 F/L.

Conclusion :
The study is acceptable.
NOEC (*Daphnia magna*, 21 d) = 0.150 mg CANDIT/L (nominal)
NOEC (*Daphnia magna*, 21 d) = 0.112 mg CANDIT/L (nominal) (based on mean recovery rate 74.8 %)

The chronic toxicity for fish and aquatic invertebrates was tested with the formulation BAS 494 02 F. As BAS 494 02 F is a minor change to BAS 494 04 F (details are given in document JM3), this study is considered relevant to assess the potential risk arising from uses of BAS 494 04 F.

Sublethal toxic effects on the rainbow trout (*Oncorhynchus mykiss* WALBAUM 1792) of BAS 494 02 F in a flow-through (28 days). (Munk R., 1995).

Guidelines :
OECD 204: Fish, Prolonged Toxicity Test: 14-Day Study
Draft OECD Guideline: Proposal for: Fish, Juvenile Growth Test – 28 days
GLP :
Yes
Material and Methods :
Test substance : BAS 494 02 F, SE containing 126.25 g/L (nominal 125.0 g/L) kresoxim-methyl and 126.22 g/L (nominal 125.0 g/L) epoxiconazole – formulation ALLEGRO, batch: 93-1
Test species : rainbow trout (*Oncorhynchus mykiss*)
Number of organisms, weight, length, age : 20 fish in one aquarium/concentration, 5.23 cm (range: 4.8 – 5.6 cm), 1.32 g (range: 1.1 - 1.5 g), approximately 4 months old
Type of test : flow-through system (28 days), 10 L/hour/aquarium, aquarium volume 60 L
Applied and measured concentrations :
nominal : control; 0.012, 0.06, 0.3, 1.5 mg ALLEGRO/L
mean measured :
0.06 mg/L : 73.1 – 101.1 % of nominal
0.3 and 1.5 mg/L : 84.0 – 118.2 % of nominal
Test conditions :
temperature : 13 - 15 °C
pH : 8.2 - 8.5
oxygen content : 9.8 mg – 10.9 mg O_2/L
total hardness : 2.3 – 2.4 mmol/L
photoperiod : 16/8 hours light/dark cycle
Analytical methods : HPLC with UV detection

Findings :

Table B.9.2.14-3 : Chronic toxicity (28 day) of ALLEGRO on rainbow trout (*Oncorhynchus mykiss*)

Concentration [mg/L] nominal	**Control**	**0.012**	**0.06**	**0.3**	**1.5**
Mortality [%]	0	0	0	0	90
Symptoms	none	none	none	Slightly reduced feed consumption	Apathy, discoloration, reduced/no feed uptake, tumbling, narcosis-like state
Mean weight [g]	4.3	4.4	4.3	3.1*	2.1*
Mean length [cm]	7.2	7.3	7.1	6.6*	6.2*
Endpoints [mg/L]					
LC_{50} (28 d)	> 0.3 < 1.5				
NOEC (28 d)	0.06				

* statistically significant difference compared to control (Dunnett´s test, $p \leq 0.01$)

ALLEGRO caused no mortality up to a concentration of 0.3 mg/L. At the highest tested concentration of 1.5 mg/L 90 % mortality occurred. Toxic symptoms were observed in the 0.3 mg/L treatment group (slightly reduced food consumption) and in the 1.5 mg/L treatment group (apathy, discoloration, reduced/no feed consumption, tumbling and narcosis-like state), respectively. A significant reduction of body weight and length occurred in the two highest treatment groups.

Conclusion :
The study is acceptable.
NOEC (*Oncorhynchus mykiss*, 28 d) = 0.06 mg ALLEGRO/L (nominal)

Determination of the chronic toxicity of BAS 494 02 F to the water flea *Daphnia magna* STRAUS. (Jatzek J., 1995).

Guidelines :
EC Guideline XI/681/86 (draft 4), OECD 202
GLP :
Yes
Material and Methods :
Test substance : BAS 494 02 F, SE containing 126.25 g/L (nominal 125.0 g/L) kresoxim-methyl and 126.22 g/L (nominal 125.0 g/L) epoxiconazole – formulation ALLEGRO, batch: 93-1
Test species : waterfleas (*Daphnia magna*)
Number of organisms, age : 1 waterflea/replicate, 10 replicates/treatment, neonates, 2 - 24 hours old
Type of test : 21-day semi-static test, changing of test solution 3 times a week
Applied and measured concentrations :
nominal : control; 0.0039, 0.0078, 0.0156, 0.0313, 0.0625, 0.125, 0.25, 0.5, 1 mg ALLEGRO/L
mean measured :
t = 0 h : 74.6 – 103.6 % of nominal
t = 48 h : 74.9 – 107.8 % of nominal
Test conditions :
temperature : 19.1 – 21.3 °C
pH : 7.3 – 8.8
oxygen content : 8.8 – 13.8 mg O_2/L
total hardness : 2.20 – 3.20 mmol/L
photoperiod : 16/8 hours light/dark cycle
light intensity : 5 – 6 µE/m²*s
Feeding : green alga *Scenedesmus subspicatus*
Assessments : daily assessment of reproduction and survival
Analytical methods : HPLC with UV detection

Findings :

Table B.9.2.14-4 : Effect of ALLEGRO on the reproduction and parent mortality of *Daphnia magna* after 21 days exposure

Concentration (nominal) [mg/L]	**Control**	**0.0039**	**0.0078**	**0.0156**	**0.0313**	**0.0625**	**0.125**	**0.25**	**0.5**	**1**
Offspring/parent	116.6	128.9	127.8	115.5	122.3	113.1	101.3	73.4	29.9	--
Parent-mortality [%]	0	10	0	0	0	20	10	0	0	100
Endpoints [mg/L]										
NOEC (21 d)	0.125									

After 21 days no treatment related mortality of parent animals was observed at test concentrations of 0.5 mg/L and below. The number of offspring was significantly reduced compared to the control at test rates of 0.25 mg ALLEGRO/L and higher.

Conclusion :
The study is acceptable.
NOEC (*Daphnia magna*, 21 d) = 0.125 mg ALLEGRO/L (nominal)

B.9.2.15 Summary of effects to water organisms

Revised in March 2010:

Aquatic toxicity tests were performed with the a.s. kresoxim-methyl, metabolites BF 490-1 and BF 490-5 and the formulations CANDIT and ALLEGRO.

Kresoxim-methyl, metabolites BF 490-1 and BF 490-5

Table B.9.2.15-1 : Summary of effects of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 on aquatic organisms

Test species	Test system	Test conc.	Result [µg a.s./L]		Effect parameter	Reference
			LC_{50}/EC_{50}	NOEC		
Kresoxim-methyl						
Oncorhynchus mykiss	Static 96 h	Measured at test termination	> 150 < 190	150	Mortality	Munk, 1992/10211, amended by 1993/11444
Oncorhynchus mykiss	Flow-through 96 h	Mean measured	**190** [9)]	104	Mortality	Graves et al., 1995/5167
Lepomis macrochirus	Static 96 h	Measured at test termination	620	500	Mortality	Munk, 1993/10483 amended by 1993/11442
Lepomis macrochirus	Flow-through 96 h	Mean measured	499	388	Mortality	Graves et al., 1995/5168
Cyprinus carpio	Static 96 h	Mean measured	> 247 < 326	250	Mortality	Munk, 1993/10457 amended by 1993/11443
*(Cyprinodon variegatus)**	Flow-through 96 h	Mean measured	1173	397	Mortality	Graves et al., 1996/5153
Oncorhynchus mykiss	Flow-through 28 d	Mean Measured	--	**13**	Survival/ growth	Munk, 1994/10921
Pimephales promelas (ELS)	Flow-through 32 d	Mean measured	--	87	Survival/ growth	Graves et al. 1996/5155
Daphnia magna	Static 48 h	Nominal	**186**	69	Immobilization	Jatzek, 1993/10497
Daphnia magna	Flow-through 48 h	Mean measured	332	160	Immobilization	Graves et al., 1995/5169
*(Daphnia similis)**	Static 24 h	Nominal	1 990[1)] 1 510[2)]	156	Mortality / immobilization	Nozaka, 1991/10710
Daphnia magna	Semi-static 21 d	Nominal	--	**32**	Reproduction	Elendt-Schneider, 1993/10335
Daphnia magna	Flow-through 21 d	Mean measured	--	55	Reproduction	Graves et al., 1996/5154
*(Mysidopsis bahia)**	Flow-through 96 h	Mean measured	59	39	Mortality	Graves et al., 1996/5151
*(Crassostrea virginica)**	Flow-through 96 h	Mean measured	> 19[1)] 15[3)]	4.2	Mortality/ shell deposition	Graves et al., 1996/5152

Table B.9.2.15-1 : Summary of effects of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 on aquatic organisms

Test species	Test system	Test conc.	Result [µg a.s./L]		Effect parameter	Reference
			LC_{50}/EC_{50}	NOEC		
Ankistrodesmus bibraianus	Static 72 h	Nominal	**63**[4)]	7[7)]	Biomass	Dohmen, 1992/11598
*(Navicula pelliculosa)**	Static 5 d	Initially measured	29.2[#]	12	Biomass	Thompson et al., 1995/5048
Selenastrum capricornutum	Static 5 d	Initially measured	59.4	12.2	Biomass	Thompson et al., 1995/5051
*(Anabaena flos-aquae)**	Static 5 d	Initially measured	> 295	295	Biomass	Thompson et al., 1995/5050
*(Skeletonema costatum)**	Static 5 d	Initially measured	> 293	293	Biomass	Thompson et al., 1995/5054
Mesocosm (conducted with CANDIT)	Multiple applications ca. 6 months	Nominal	-	NOEC = 6.6 NOEAEC = 33	Populations, communities, functions	Dohmen, 1995/11150
BF 490-1						
Oncorhynchus mykiss	Static 96 h	Nominal	> 100 000	100 000	Mortality	Munk, 1994/10621
Daphnia magna	Static 48 h	Nominal	> 100 000	100 000	Immobilization	Dohmen, 1994/10622
Pseudokirchneriella. subcapitata	Static 72 h	Nominal	≥500 000[5)] ≥500 000[6)]	51 000[7)] 382 000[8)]	Biomass Growth rate	Dohmen, 1994/10616
BF 490-5						
Daphnia magna	Static 48 h	Nominal	> 100 000	100 000	Immobilization	Janson 2008/1037017

1) Mortality 2) Immobilization 3) Shell deposition 4) graphically determined
5) E_bC_{50} 6) E_rC_{50} 7) E_bC_{10} 8) E_rC_{10}
9) This study is used for TER-calculations as it provides more reliable analytical measurements
* US (Japan) specific studies, not required for registration in the EU; furthermore, a mesocosm study with a multitude of fresh water species is available
# Not reliable due to high variability within and between controls and treatments
Bold letters: Values are used for TER-calculations

Kresoxim-methyl degrades rapidly to very rapidly in water due to hydrolysis, photolysis and biotic degradation with DT_{50} < 1.5 day. As a result, several of the studies showed analytical deficiencies, particularly in static studies when samples have been stored and not analysed immediately after sampling. Some of the results based on analytical measurements have thus to be taken with care; several of the studies have been repeated under flow-through conditions with appropriate sampling and measurements. Due to the very rapid degradation of kresoxim-methyl in water with half lives shorter than the study duration, flow-through conditions in such studies represents a worst-case with respect to actual acute toxicity resulting from realistic exposure events.

Formulation CANDIT - BAS 490 02 F

Studies on the acute and chronic toxicity of the formulated product BAS 490 02 F have been performed with fish, *Daphnia* and algae.
The results obtained with the formulated product BAS 490 02 F are in good agreement with the results expected from the data with the active substances, demonstrating that the formulation does not cause significant unexpected (additional) toxicity. Therefore, no specific TER calculations have been conducted with the formulation; instead the information derived for the active substances is appropriate for the risk assessment. Furthermore, a mesocosm study has been performed with kresoxim-methyl applied as formulated product BAS 490 02 F supporting the statement made above.

Table B.9.2.15-2 : Summary of effects of the formulation CANDIT (50 % kresoxim-methyl)

Test species	**Test system**	**EC_{50}/LC_{50} [mg/L]**	**NOEC [mg/L]**	**Reference**
Oncorhynchus mykiss	Acute (96 h), static	0.5 (nom) 0.150 (analytic)	0.316 (nom) 0.095 (analytic)	Munk, 1994/10532
Cyprinus carpio	Acute (96 h), static	2.2 (nom) 1.946 (analytic)	1.0 (nom) 0.96 (analytic)	Munk, 1994/10620
Oncorhynchus mykiss	Chronic (28 d), flow-through	0.29 (> 0.167 < 0.5) (nom)	0.167 (nom)	Munk, 1994/11123
Daphnia magna	Acute (48 h), static	≈ 0.35 (> 0.25 < 5) (nom) 0.289 (recovery 82.5 %)	0.1 (nom) 0.064 (recovery 64.4 %)	Dohmen, 1994/10479
Daphnia magna	Reproduction (21 d), semi-static	--	0.150 (nom) 0.112 (recovery 74.8 %)	Dohmen, 1994/10604
Pseudokirchneriella subcapitata	Static, 72 h	0.532 [1)] (nom) 0.303 (recovery 57 %) 0.071 [2)] (nom) 0.040 (recovery 57 %)	0.033 [3)] (nom) 0.019 (recovery 57 %) 0.015 [4)] (nom) 0.0086 (recovery 57 %)	Dohmen, 1994/10472

1) E_rC_{50} 2) E_bC_{50} 3) E_rC_{10} 4) E_bC_{10}

Formulation ALLEGRO - BAS 494 04 F

Studies on the acute and chronic toxicity of the formulated product BAS 494 02 F (minor change to BAS 494 04 F) have been performed with fish, *Daphnia* and algae.

Table B.9.2.15-3 : Effects of BAS 494 02 F on aquatic organisms

Test species	Test system	EC_{50}/LC_{50} [mg/L]	NOEC [mg/L]	Reference
Oncorhynchus mykiss	Acute (96 h), static	1.8 (> 1.5 < 2.2) (nom) 1.33 (analytical)	1.47 (nom) 1.09 (analytical)	Munk, 1994/11213
Oncorhynchus mykiss	Chronic (28 d), flow-through	> 0.3 < 1.5 (nom)	0.06 (nom)	Munk, 1995/10267
Daphnia magna	Acute (48 h), static	0.73 (nom)	0.45 [1] (nom)	Dohmen, 1995/10269
Daphnia magna	Reproduction (21 d), semi-static	--	0.125 (nom)	Jatzek, 1995/10234
Pseudokirchneriella subcapitata	Static, 72 h	> 3 [2] (nom) > 2.25 (recovery 75 %) 0.398 [3] (nom) 0.299 (recovery 75 %)	0.161 [4] (nom) 0.121 (recovery 75 %) 0.010 [5] (nom) 0.0075 (recovery 75 %)	Dohmen, 1995/10291

1) EC_0 2) E_rC_{50} 3) E_bC_{50} 4) E_rC_{10} 5) E_bC_{10}

The results obtained with the formulated product BAS 494 02 F are within a factor of two (both, higher and lower) to the results expected from the data with the active substances, indicating that there are no significant unexpected toxic or synergistic effects from the combination of the two substances in the formulation BAS 494 04 F. Therefore, no specific TER calculations have been conducted with the formulation; instead the information derived for the active substances is appropriate for the risk assessment.

B.9.2.16 Risk assessment for aquatic organisms (Annex IIIA 10.2)

Revised in March 2010:

The risk assessment for aquatic organisms is based on the Guidance Document on Aquatic Ecotoxicology under Council Directive 91/414/EEC of October 2002.

1- Formulation CANDIT

The formulation CANDIT (BAS 490 02 F) is a fungicidal product, which contains the active substance kresoxim-methyl with a nominal content of 50 % w/w.

Table B.9.2.16-1 : Proposed use pattern of the formulation CANDIT

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate (kg a.s./ha) [1)]	Application rate (kg product/ha) [1)]
Pome fruit (apple, pear)	1 - 4	7	53 - 79	0.100 - 0.125	0.200 - 0.250
Grapevine	1 - 3	8	19 - 81	0.100 - 0.150	0.200 - 0.300

[1)] application rate increases with plant growth stage

For simplification reasons, the risk assessment is only conducted for the higher application rates. This covers the increase in application rate during season.

2- Formulation ALLEGRO

The formulation ALLEGRO (BAS 494 04 F) is a fungicidal product, which contains the active substances
- kresoxim-methyl (BAS 490 F) with a nominal content of 125 g a.s./L
- epoxiconazole (BAS 480 F) with a nominal content of 125 g a.s./L

Table B.9.2.16-2 : Proposed use pattern of the formulation ALLEGRO

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate		
				BAS 494 04 F [L/ha]	Kresoxim-methyl (BAS 490 F) [kg a.s./ha]	Epoxiconazole (BAS 480 F) [kg a.s./ha]
Cereals	2	21	25 - 69	1.0	0.125	0.125

PECsw values were calculated in the section on fate and behaviour.

Table B.9.2.16-3 : $PEC_{sw,ini}$ values (Focus, Step 1 and 2) of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 following application of BAS 490 02 F to pomefruit

FOCUS Step		$PEC_{sw,ini}$ [µg/L]		
		Kresoxim-methyl	**BF 490-1**	**BF 490-5**
Step 1		**41.702**	**167.495**	**7.505**
Step 2*	Europe North	**18.393**	25.963	0.052
	Europe South	**18.393**	**28.945**	**0.101**

* Multiple application scenario representing worst-case
Bold letters: worst-case PEC values used for TER calculations

Table B.9.2.16-4 : $PEC_{sw,ini}$ values (Focus, Step 1 and 2) of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 following application of BAS 490 02 F to grapevine

FOCUS Step		$PEC_{sw,ini}$ [µg/L]		
		Kresoxim-methyl	**BF 490-1**	**BF 490-5**
Step 1		**39.458**[2)]	**126.114**[2)]	**6.751**[2)]
Step 2*	Europe North	**5.690**[2)]	9.411[2)]	0.093[1)]
	Europe South	**5.690**[2)]	12.648[1)]	0.185[1)]

* Multiple application scenario representing worst-case
1) worst-case PEC values resulting from early application
2) worst-case PEC values resulting from late application
Bold letters: worst-case PEC values used for TER calculations

Table B.9.2.16-5 : $PEC_{sw,ini}$, 2 and 7 day PEC_{twa} values (Step 3 and 4 level) of kresoxim-methyl following application of BAS 490 02 F to pomefruit (early application)

$PEC_{sw,ini}$ [µg/L]								
Scenario			**Step 3** edge of field	**Step 4** 5 m buffer#	**Step 4** 10 m buffer#	**Step 4** 15 m buffer#	**Step 4** 20 m buffer#	**Step 4** 30 m buffer#
D3	ditch	ini	9.699[1)]	7.621[1)]	4.680[1)]	2.105[1)]	1.070[1)]	0.409[1)]
		twa (2 d)	5.019[2)]	3.876[1)]	2.380[1)]	1.206[2)]	--	--
		twa (7 d)	1.950[1)]*	1.315[1)]*	0.717[2)]	--	--	--
D4	pond	ini	1.296[2)]	1.459[2)]	0.815[2)]	0.419[2)]	0.236[2)]	0.057[1)]
		twa (2 d)	--	--	--	--	--	--
		twa (7 d)	1.236[2)]	1.391[2)]	0.778[2)]	--	--	--
	stream	ini	9.393[1)]	8.071[1)]	4.956[1)]	2.230[1)]	1.133[1)]	0.434[1)]
		twa (2 d)	0.551[1)]	--	--	--	--	--
		twa (7 d)	0.194[1)]*	0.151[1)]*	0.078[2)]	--	--	--
D5	pond	ini	1.325[2)]	1.491[2)]	0.833[2)]	0.428[2)]	0.242[2)]	0.057[1)]
		twa (2 d)	0.677*	--	--	--	--	--
		twa (7 d)	1.266[2)]	1.425[2)]	0.796[2)]	--	--	--
	stream	ini	9.403[1)]	8.079[1)]	4.962[1)]	2.232[1)]	1.135[1)]	0.434[1)]
		twa (2 d)	0.969[1)]	--	--	--	--	--
		twa (7 d)	0.277[1)]*	0.216[1)]*	0.097[2)]	--	--	--
R1	pond	ini	1.298[2)]	1.461[2)]	0.817[2)]	0.420[2)]	0.237[2)]	0.057[1)]
		twa (2 d)	--	--	--	--	--	--
		twa (7 d)	1.228[2)]	1.382[2)]	0.773[2)]	--	--	--
	stream	ini	7.847[1)]	6.743[1)]	4.141[1)]	1.863[1)]	0.947[1)]	0.362[1)]
		twa (2 d)	0.681[1)]					
		twa (7 d)	0.195[1)]	0.167[1)]	0.064[2)]	--	--	--
R2	stream	ini	10.396[1)]	8.933[1)]	5.486[1)]	2.468[1)]	1.254[1)]	0.480[1)]
		twa (2 d)	0.443[1)]					
		twa (7 d)	0.127[1)]	0.109[1)]	0.050[2)]	--	--	--
R3	stream	ini	11.102[1)]	9.540[1)]	5.858[1)]	2.635[1)]	1.340[1)]	0.512[1)]
		twa (2 d)	1.809[1)]					
		twa (7 d)	0.518[1)]	0.445[1)]	0.216[2)]	--	--	--
R4	stream	ini	7.849[1)]	6.745[1)]	4.142[1)]	1.863[1)]	0.947[1)]	0.362[1)]
		twa (2 d)	0.685[1)]					
		twa (7 d)	0.196[2)]	0.191[2)]	0.120[2)]	--	--	--

1) Worst-case PEC values resulting from single application
2) Worst-case PEC values resulting from four applications
drift and if possible runoff mitigation
* worst-case PEC values resulting from late application in pomefruit
-- not needed for TER calculations

Table B.9.2.16-6 : $PEC_{sw,ini}$, 2 and 7 day PEC_{twa} values (Step 3 and 4 level) of kresoxim-methyl following application of BAS 490 02 F to grapevine (late application)

Scenario			**$PEC_{sw,ini}$ [µg/L]**		
			Step 3 - edge of field	**Step 4** - 5 m buffer[#]	**Step 4** - 10 m buffer[#]
D6	ditch	Ini	2.954[2)]	1.774[2)]	0.634[2)]
		twa (2 d)	--	--	--
		twa (7 d)	2.001[1)]	1.209[1)]	--
R1	pond	Ini	0.186[2)]	0.217[2)]	0.118[2)]
		twa (2 d)	--	--	--
		twa (7 d)	0.176[2)]	0.205[2)]	--
	stream	Ini	1.888[1)]	1.375[1)]	0.498[1)]
		twa (2 d)	--	--	--
		twa (7 d)	0.058[1)]	0.042[1)]	--
R2	stream	Ini	2.530[1)]	1.844[1)]	0.668[1)]
		twa (2 d)	0.141[1)]	--	--
		twa (7 d)	0.040[1)]	0.029[1)]	--
R3	stream	Ini	2.661[1)]	1.939[1)]	0.702[1)]
		twa (2 d)	--	--	--
		twa (7 d)	0.248[1)]	0.208[1)]	--
R4	stream	Ini	1.888[1)]	1.375[1)]	0.498[1)]
		twa (2 d)	--	--	--
		twa (7 d)	0.135[2)]	0.135[2)]	--

1) Worst-case PEC values resulting from single application
2) Worst-case PEC values resulting from three applications
[#] drift and if possible runoff mitigation
-- not needed for TER calculations

Table B.9.2.16-7 : $PEC_{sw,ini}$ values (Focus, Step 1 and 2) of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 following application of BAS 494 04 F to winter and spring cereals

FOCUS Step		**$PEC_{sw,ini}$ [µg/L]**		
		Kresoxim-methyl	**BF 490-1**	**BF 490-5**
Step 1		**30.686**	**66.657**	**3.750**
Step 2*	Europe North	**1.158**	4.017	0.068
	Europe South	**1.158**	**6.837**	**0.134**

* Multiple application scenario representing worst case # single application scenario represents worst case
Bold letters: worst-case PEC values used for TER calculations

B.9.2.16.1 Aquatic risk assessment for use in pome fruit (1-4 applications of max 0.125 kg a.s./ha)

TER calculations were not performed with FOCUS step 1 and 2 since at first view it is clear that the TER values do not pass the triggers. Therefore, TER calculations were directly performed with FOCUS step 3 and 4.

As kresoxim-methyl degrades very rapidly in aquatic systems with half lives much shorter (< 1.5 day) than the study duration of toxicity tests, TER calculations based on PEC_{ini} should be considered worst-case. Therefore, additionally TER calculations were performed based on time weighted average PEC-values over 2 days for the acute fish TERs (i.e. half the study duration) and over 7 days for the chronic TERs as a more realistic worst-case.

The acute TER for fish is based on an endpoint determined in a study under flow-through conditions to account for the rapid degradation of kresoxim-methyl in aquatic systems. Accordingly, this endpoint (LC_{50} = 190 µg a.s./L) is expressed as mean measured concentration. In this case it is appropriate to use the PEC_{TWA} values to calculate the acute TER values.

Table B.9.2.16-8 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in pome fruit (1-4 x 0.125 kg a.s./ha) based on FOCUS step 3 calculations ($PEC_{max\ ini}$ and PEC_{TWA} over 2 days for acute and PEC_{TWA} over 7 days for chronic)

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch (PEC_{ini})	*Oncorhynchus mykiss*	Acute	LC_{50} = 190 µg/L	9.699	20	100
	Ditch (PEC_{TWA})				5.019	38	100
D4	Pond (PEC_{ini})				1.296	**147**	100
	Stream (PEC_{ini})				9.393	20	100
	Stream (PEC_{TWA})				0.551	**345**	100
D5	Pond (PEC_{ini})				1.325	**143**	100
	Stream (PEC_{ini})				9.403	20	100
	Stream (PEC_{TWA})				0.969	**196**	100
R1	Pond (PEC_{ini})				1.298	**146**	100
	Stream (PEC_{ini})				7.847	24	100
	Stream (PEC_{TWA})				0.681	**279**	100
R2	Stream (PEC_{ini})				10.396	18	100
	Stream (PEC_{TWA})				0.443	**429**	100
R3	Stream (PEC_{ini})				11.102	17	100
	Stream (PEC_{TWA})				1.809	**105**	100
R4	Stream (PEC_{ini})				7.849	24	100
	Stream (PEC_{TWA})				0.685	**277**	100
D3	Ditch (PEC_{ini})	*Oncorhynchus mykiss*	Long-term	NOEC = 13 µg/L	9.699	1.3	10
	Ditch (PEC_{TWA})				1.950	6.7	10
D4	Pond (PEC_{ini})				1.296	**10**	10
	Pond (PEC_{TWA})				1.236	**11**	10
	Stream (PEC_{ini})				9.393	1.4	10
	Stream (PEC_{TWA})				0.194	**67**	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
D5	Pond (PEC_{ini})				1.325	9.8	10
	Pond (PEC_{TWA})				1.266	**10**	10
	Stream (PEC_{ini})				9.403	1.4	10
	Stream (PEC_{TWA})				0.277	**47**	10
R1	Pond (PEC_{ini})				1.298	**10**	10
	Pond (PEC_{TWA})				1.228	**11**	10
	Stream (PEC_{ini})				7.847	1.7	10
	Stream (PEC_{TWA})				0.195	**67**	10
R2	Stream (PEC_{ini})				10.396	1.3	10
	Stream (PEC_{TWA})				0.127	**102**	10
R3	Stream (PEC_{ini})				11.102	1.2	10
	Stream (PEC_{TWA})				0.518	**25**	10
R4	Stream (PEC_{ini})				7.849	1.7	10
	Stream (PEC_{TWA})				0.196	**66**	10
D3	Ditch (PEC_{ini})	*Daphnia magna*	Acute	EC_{50} = 186 µg/L	9.699	19	100
D4	Pond (PEC_{ini})				1.296	**144**	100
	Stream (PEC_{ini})				9.393	20	100
D5	Pond (PEC_{ini})				1.325	**140**	100
	Stream (PEC_{ini})				9.403	20	100
R1	Pond (PEC_{ini})				1.298	**143**	100
	Stream (PEC_{ini})				7.847	24	100
R2	Stream (PEC_{ini})				10.396	18	100
R3	Stream (PEC_{ini})				11.102	17	100
R4	Stream (PEC_{ini})				7.849	24	100
D3	Ditch (PEC_{ini})	*Daphnia magna*	Long-term	NOEC = 32 µg/L	9.699	3.3	10
	Ditch (PEC_{TWA})				1.950	**16**	10
D4	Pond (PEC_{ini})				1.296	**25**	10
	Stream (PEC_{ini})				9.393	3.4	10
	Stream (PEC_{TWA})				0.194	**165**	10
D5	Pond (PEC_{ini})				1.325	**24**	10
	Stream (PEC_{ini})				9.403	3.4	10
	Stream (PEC_{TWA})				0.277	**115**	10
R1	Pond (PEC_{ini})				1.298	**25**	10
	Stream (PEC_{ini})				7.847	4.1	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
	Stream (PEC_{TWA})				0.195	**164**	10
R2	Stream (PEC_{ini})				10.396	3.1	10
	Stream (PEC_{TWA})				0.127	**252**	10
R3	Stream (PEC_{ini})				11.102	2.9	10
	Stream (PEC_{TWA})				0.518	**62**	10
R4	Stream (PEC_{ini})				7.849	4.1	10
	Stream (PEC_{TWA})				0.196	**163**	10
D3	Ditch (PEC_{ini})				9.699	6.5	10
D4	Pond (PEC_{ini})				1.296	**49**	10
	Stream (PEC_{ini})				9.393	6.7	10
D5	Pond (PEC_{ini})				1.325	**48**	10
	Stream (PEC_{ini})	*Ankistrodermus bibraianus*	Acute	EC_{50} = 63 µg/L	9.403	6.7	10
R1	Pond (PEC_{ini})				1.298	**49**	10
	Stream (PEC_{ini})				7.847	8.0	10
R2	Stream (PEC_{ini})				10.396	6.1	10
R3	Stream (PEC_{ini})				11.102	5.7	10
R4	Stream (PEC_{ini})				7.849	8.0	10

Based on the worst-case assumption (use of PEC_{ini}), the aquatic risk assessment needs refinement, using FOCUS step 4.

Table B.9.2.16-9 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in pome fruit (1-4 x 0.125 kg a.s./ha) based on FOCUS step 4 calculations ($PEC_{max\ ini}$ and PEC_{TWA} over 2 days for acute and PEC_{TWA} over 7 days for chronic)

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch (PEC_{ini})	*Oncorhynchus mykiss*	Acute	LC_{50} = 190 µg/L	10 15 20	4.680 2.105 1.070	41 90 **178**	100
	Ditch (PEC_{TWA})				15	1.206	**158**	100
D4	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.956 2.230 1.133	38 85 **168**	100
	Stream (PEC_{TWA})							
D5	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.962 2.232 1.135	38 85 **167**	100

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
	Stream (PEC_{TWA})							
R1	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15	4.141 1.863	46 **102**	100
	Stream (PEC_{TWA})							
R2	Stream (PEC_{ini})				10 15 20	5.486 2.468 1.254	35 77 **152**	100
	Stream (PEC_{TWA})							
R3	Stream (PEC_{ini})				10 15 20	5.858 2.635 1.340	32 72 **142**	100
	Stream (PEC_{TWA})							
R4	Stream (PEC_{ini})				10 15	4.142 1.863	46 **102**	100
	Stream (PEC_{TWA})							
D3	Ditch (PEC_{ini})	*Oncorhynchus mykiss*	Long-term	NOEC = 43 µg/L	10 15 20	4.680 2.105 1.070	2.8 6.2 **12**	10
	Ditch (PEC_{TWA})				5	1.315	**10**	10
D4	Pond (PEC_{ini})				--	--	--	
	Pond (PEC_{TWA})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.956 2.230 1.133	2.6 5.8 **11**	10
	Stream (PEC_{TWA})				--	--	--	
D5	Pond (PEC_{ini})				5 10	1.491 0.833	8.7 **16**	10
	Pond (PEC_{TWA})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.962 2.232 1.135	2.6 5.8 **11**	10
	Stream (PEC_{TWA})				--	--	--	
R1	Pond (PEC_{ini})				--	--	--	
	Pond (PEC_{TWA})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.141 1.863 0.947	3.1 7.0 **14**	10
	Stream (PEC_{TWA})				--	--	--	
R2	Stream (PEC_{ini})				10 15 20	5.486 2.468 1.254	2.4 5.3 **10**	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
R2	Stream (PEC_{TWA})				--	--	--	
R3	Stream (PEC_{ini})				10 15 20	5.858 2.635 1.340	2.2 4.9 **10**	10
	Stream (PEC_{TWA})				--	--	--	
R4	Stream (PEC_{ini})				10 15 20	4.142 1.863 0.947	3.1 7.0 **14**	10
	Stream (PEC_{TWA})				--	--	--	
D3	Ditch (PEC_{ini})	*Daphnia magna*	Acute	EC_{50} = 186 µg/L	10 15 20	4.680 2.105 1.070	40 88 **174**	100
D4	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.956 2.230 1.133	38 83 **164**	100
D5	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15 20	4.962 2.232 1.135	37 83 **164**	100
R1	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				10 15	4.141 1.863	45 **100**	100
R2	Stream (PEC_{ini})				10 15 20	5.486 2.468 1.254	34 75 **148**	100
R3	Stream (PEC_{ini})				10 15 20	5.858 2.635 1.340	32 71 **139**	100
R4	Stream (PEC_{ini})				10 15	4.142 1.863	45 **100**	100
D3	Ditch (PEC_{ini})	*Daphnia magna*	Long-term	NOEC = 32 µg/L	5 10 15	7.621 4.680 2.105	4.2 6.8 **15**	10
	Ditch (PEC_{TWA})				--	--	--	
D4	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				5 10 15	8.071 4.956 2.230	4.0 6.5 **14**	10
	Stream (PEC_{TWA})				--	--	--	
D5	Pond (PEC_{ini})				--	--	--	

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
	Stream (PEC_{ini})				5 10 15	8.079 4.962 2.232	4.0 6.4 **14**	10
	Stream (PEC_{TWA})				--	--	--	
R1	Pond (PEC_{ini})				--	--	--	
	Stream (PEC_{ini})				5 10 15	6.743 4.141 1.863	4.7 7.7 **17**	10
	Stream (PEC_{TWA})				--	--	--	
R2	Stream (PEC_{ini})				5 10 15	8.933 5.486 2.468	3.6 5.8 **13**	10
	Stream (PEC_{TWA})				--	--	--	
R3	Stream (PEC_{ini})				5 10 15	9.540 5.858 2.635	3.4 5.5 **12**	10
	Stream (PEC_{TWA})				--	--	--	
R4	Stream (PEC_{ini})				5 10 15	6.745 4.142 1.863	4.7 7.7 **17**	10
	Stream (PEC_{TWA})				--	--	--	
D3	Ditch (PEC_{ini})	*Ankistrodermus bibraianus*	Acute	EC_{50} = 63 µg/L	5 10	7.621 4.680	8.3 **13**	10
D4	Pond (PEC_{ini})				--	--	--	10
	Stream (PEC_{ini})				5 10	8.071 4.956	7.8 **13**	10
D5	Pond (PEC_{ini})				--	--	--	10
	Stream (PEC_{ini})				5 10	8.079 4.962	7.8 **13**	10
R1	Pond (PEC_{ini})				--	--	--	10
	Stream (PEC_{ini})				5 10	6.743 4.141	9.3 **15**	10
R2	Stream (PEC_{ini})				5 10	8.933 5.486	7.1 **11**	10
R3	Stream (PEC_{ini})				5 10	9.540 5.858	6.6 **11**	10
R4	Stream (PEC_{ini})				5 10	6.745 4.142	9.3 **15**	10

Based on the worst-case assumption (use of PEC_{ini} step 4), the risk of kresoxim-methyl for use in pomefruit is acceptable with a buffer zone of 20 m to protect the most sensitive species (fish and aquatic invertebrates) for all FOCUS scenarios.

Table B.9.2.16-10 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in pome fruit (1-4 x 0.125 kg a.s./ha) based on FOCUS step 3 calculations ($PEC_{max\ ini}$) and mesocosm endpoint

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Trigger
D3	Ditch (PECini)	Mesocosm study	Long-term	NOEAEC = 33 µg a.s./L	9.699	3.4	3
D4	Pond (PECini)				1.296	25.5	3
	Stream (PECini)				9.393	3.5	3
D5	Pond (PECini)				1.325	24.9	3
	Stream (PECini)				9.403	3.5	3
R1	Pond (PECini)				1.298	25.4	3
	Stream (PECini)				7.847	4.2	3
R2	Stream (PECini)				10.396	3.2	3
R3	Stream (PECini)				11.102	3.0	3
R4	Stream (PECini)				7.849	4.2	3

The aquatic risk assessment is also based on the mesocosm endpoint. Applying an assessment factor of 3 is justified (well performed mesocosm study, different taxa tested, multiple applications, …).
Based on the worst-case assumption (use of PEC_{ini} step 3), the risk of kresoxim-methyl for use in pomefruit is acceptable without buffer zone to protect aquatic invertebrates and algae for all FOCUS scenarios.

Table B.9.2.16-11 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to metabolites BF 490-1 and BF 490-5 in surface water for use in pome fruit (1-4 x 0.125 kg a.s./ha) based on FOCUS step 1 calculations (PEC_{ini})

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{ini} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
BF 490-1	*Oncorhynchus mykiss*	LC_{50} > 100 mg/L	Acute	167.495	-	> 597	100
	Daphnia magna	EC_{50} > 100 mg/L	Acute	167.495	-	> 597	100
	Pseudokirchneriella subcapitata	EC_{50} > 500 mg/L	Acute	167.495	-	> 2985	10
BF 490-5	*Daphnia magna*	EC_{50} > 100 mg/L	Acute	7.505	-	> 13324	100

The risk of the metabolites BF 490-1 and BF 490-5 for use in pomefruit is acceptable based on FOCUS step 1 calculations, indicating low risk.

B.9.2.16.2 Aquatic risk assessment for use in grapevine (1-3 applications of max 0.150 kg a.s./ha)

Table B.9.2.16-12 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in grapevine (1-3 x 0.150 kg a.s./ha) based on FOCUS step 3 calculations ($PEC_{max\ ini}$ and PEC_{TWA} over 2 days for acute and PEC_{TWA} over 7 days for chronic)

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
D6	Ditch (PEC_{ini})	*Oncorhyn-chus mykiss*	Acute	LC_{50} = 190 µg/L	2.954	64	100
R1	Pond (PEC_{ini})				0.186	**1022**	100
	Stream (PEC_{ini})				1.888	**101**	100
R2	Stream (PEC_{ini})				2.530	75	100
	Stream (PEC_{TWA})				0.141	**> 1 000**	100
R3	Stream (PEC_{ini})				2.661	71	100
	Stream (PEC_{TWA})				0.504	**377**	100
R4	Stream (PEC_{ini})				1.888	**101**	100
D6	Ditch (PEC_{ini})	*Oncorhyn-chus mykiss*	Long-term	NOEC = 13 µg/L	2.954	4.4	10
	Ditch (PEC_{TWA})				2.001	6.5	10
R1	Pond (PEC_{ini})				0.186	**70**	10
	Pond (PEC_{TWA})				0.176	**74**	10
	Stream (PEC_{ini})				1.888	6.9	10
	Stream (PEC_{TWA})				0.058	**224**	10
R2	Stream (PEC_{ini})				2.530	5.1	10
	Stream (PEC_{TWA})				0.040	**325**	10
R3	Stream (PEC_{ini})				2.661	4.9	10
	Stream (PEC_{TWA})				0.248	**52**	10
R4	Stream (PEC_{ini})				1.888	6.9	10
	Stream (PEC_{TWA})				0.135	**96**	10
D6	Ditch (PEC_{ini})	*Daphnia magna*	Acute	EC_{50} = 186 µg/L	2.954	63	100
R1	Pond (PEC_{ini})				0.186	**1 000**	100
	Stream (PEC_{ini})				1.888	99	100
R2	Stream (PEC_{ini})				2.530	74	100
R3	Stream (PEC_{ini})				2.661	70	100
R4	Stream (PEC_{ini})				1.888	99	100
D6	Ditch (PEC_{ini})	*Daphnia magna*	Long-term	NOEC = 32 µg/L	2.954	**11**	10
R1	Pond (PEC_{ini})				0.186	**172**	10
	Stream (PEC_{ini})				1.888	**17**	10
R2	Stream (PEC_{ini})				2.530	**13**	10
R3	Stream (PEC_{ini})				2.661	**12**	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
R4	Stream (PEC_{ini})				1.888	**17**	10
D6	Ditch (PEC_{ini})	*Ankistro-dermus bibraianus*	Acute	EC_{50} = 63 µg/L	2.954	**21**	10
R1	Pond (PEC_{ini})				0.186	**339**	10
	Stream (PEC_{ini})				1.888	**33**	10
R2	Stream (PEC_{ini})				2.530	**25**	10
R3	Stream (PEC_{ini})				2.661	**24**	10
R4	Stream (PEC_{ini})				1.888	**33**	10

Based on the worst-case assumption (use of PEC_{ini}), the aquatic risk assessment needs refinement, using FOCUS step 4.

Table B.9.2.16-13 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in grapevine (1-3 x 0.150 kg a.s./ha) based on FOCUS step 4 calculations ($PEC_{max\ ini}$ and PEC_{TWA} over 2 days for acute and PEC_{TWA} over 7 days for chronic)

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
D6	Ditch (PEC_{ini})	*Oncorhyn-chus mykiss*	Acute	LC_{50} = 190 µg/L	5	1.774	**107**	100
R1	Pond (PEC_{ini})				--	--	--	100
	Stream (PEC_{ini})				--	--	--	100
R2	Stream (PEC_{ini})				5	1.844	**103**	100
	Stream (PEC_{TWA})							100
R3	Stream (PEC_{ini})				5	1.939	**98***	100
	Stream (PEC_{TWA})							100
R4	Stream (PEC_{ini})				--	--	--	100
D6	Ditch (PEC_{ini})	*Oncorhyn-chus mykiss*	Long-term	NOEC = 13 µg/L	5 10	1.774 0.634	7.3 **21**	10
	Ditch (PEC_{TWA})				5	1.209	**11**	10
R1	Pond (PEC_{ini})				--	--	--	10
	Pond (PEC_{TWA})				--	--	--	10
	Stream (PEC_{ini})				5 10	1.375 0.498	9.5 **26**	10
	Stream (PEC_{TWA})				--	--	--	10
R2	Stream (PEC_{ini})				5 10	1.844 0.668	7.0 **19**	10
	Stream (PEC_{TWA})				--	--	--	10
R3	Stream (PEC_{ini})				5 10	1.939 0.702	6.7 **19**	10
	Stream (PEC_{TWA})				--	--	--	10

Scenario	Water body type	Test organism	Time scale	Toxicity end point	Buffer zone distance	PECsw (µg/L)	TER	Annex VI trigger
R4	Stream (PEC_{ini})				5 10	1.375 0.498	9.5 **26**	10
	Stream (PEC_{TWA})				--	--	--	10
D6	Ditch (PEC_{ini})	*Daphnia magna*	Acute	EC_{50} = 186 µg/L	5	1.774	**105**	100
R1	Pond (PEC_{ini})				--	--	--	100
	Stream (PEC_{ini})				5	1.375	**135**	100
R2	Stream (PEC_{ini})				5	1.844	**100**	100
R3	Stream (PEC_{ini})				5 10	1.939 0.702	96 **265**	100
R4	Stream (PEC_{ini})				5	1.375	**135**	100

* Considering the fast degradation of kresoxim-methyl in water and the short exposure time in streams, the value of 98 appears sufficiently close to the required standard trigger to conclude low risk of unacceptable limits

Based on the worst-case assumption (use of PEC_{ini} step 4), the risk of kresoxim-methyl for use in grapevine is acceptable with a buffer zone of 10 m to protect the most sensitive species (fish and aquatic invertebrates) for all FOCUS scenarios.

Table B.9.2.16-14 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in grapevine (1-3 x 0.150 kg a.s./ha) based on FOCUS step 3 calculations ($PEC_{max\ ini}$) and mesocosm endpoint

Scenario	Water body type	Test organism	Time scale	Toxicity end point	PECsw (µg/L)	TER	Annex VI trigger
D6	Ditch (PECini)	Mesocosm study	Long-term	NOEAEC = 33 µg a.s./L	2.954	11	3
R1	Pond (PECini)				0.186	177	3
	Stream (PECini)				1.888	17	3
R2	Stream (PECini)				2.530	13	3
R3	Stream (PECini)				2.661	12	3
R4	Stream (PECini)				1.888	17	3

The aquatic risk assessment is also based on the mesocosm endpoint. Applying an assessment factor of 3 is justified (well performed mesocosm study, different taxa tested, multiple applications, …).
Based on the worst-case assumption (use of PEC_{ini} step 3), the risk of kresoxim-methyl for use in grapevine is acceptable without buffer zone to protect aquatic invertebrates and algae for all FOCUS scenarios.

Table B.9.2.16-15 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to metabolites BF 490-1 and BF 490-5 in surface water for use in grapevine (1-3 x 0.150 kg a.s./ha) based on FOCUS step 1 calculations (PEC_{ini})

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{ini} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
BF 490-1	*Oncorhynchus mykiss*	LC_{50} > 100 mg/L	Acute	126.114	-	> 793	100
	Daphnia magna	EC_{50} > 100 mg/L	Acute	126.114	-	> 793	100
	Pseudokirchneriella subcapitata	EC_{50} > 500 mg/L	Acute	126.114	-	> 3965	10
BF 490-5	*Daphnia magna*	EC_{50} > 100 mg/L	Acute	6.751	-	> 14813	100

The risk of the metabolites BF 490-1 and BF 490-5 for use in grapevine is acceptable based on FOCUS step 1 calculations, indicating low risk.

B.9.2.16.3 Aquatic risk assessment for use in cereals (2 applications of 0.125 kg kresoxim-methyl/ha)

Table B.9.2.16-16 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in cereals (2 x 0.125 kg a.s./ha) based on FOCUS step 1 calculations (PEC_{ini})

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC_{ini} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
kresoxim-methyl	*Oncorhynchus mykiss*	LC_{50} = 190 µg/L	Acute	30.686	-	6.19	100
		NOEC = 63 µg/L	Long-term	30.686	-	0.42	10
	Daphnia magna	EC_{50} = 186 µg/L	Acute	30.686	-	6.06	100
		NOEC = 32 µg/L	Long-term	30.686	-	1.04	10
	Ankistrodermus bibraianus	EC_{50} = 63 µg/L	Acute	30.686	-	2.05	10

Table B.9.2.16-17 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to kresoxim-methyl in surface water for use in cereals (2 x 0.125 kg a.s./ha) based on FOCUS step 2 calculations (PEC_{ini})

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC_{ini} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
kresoxim-methyl	*Oncorhynchus mykiss*	LC_{50} = 190 µg/L	Acute	1.158	-	164	100
		NOEC = 13 µg/L	Long-term	1.158	-	11	10
	Daphnia magna	EC_{50} = 186 µg/L	Acute	1.158	-	161	100
		NOEC = 32 µg/L	Long-term	1.158	-	28	10
	Ankistrodermus bibraianus	EC_{50} = 63 µg/L	Acute	1.158	-	54	10

The risk of kresoxim-methyl for use in cereals is acceptable based on FOCUS step 2 calculations, indicating low risk.

Table B.9.2.16-18 : Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to metabolites BF 490-1 and BF 490-5 in surface water for use in cereals (2 x 0.125 kg a.s./ha) based on FOCUS step 1 calculations (PEC_{ini})

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{ini} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
BF 490-1	*Oncorhynchus mykiss*	LC_{50} > 100 mg/L	Acute	66.657	-	> 1500	100
	Daphnia magna	EC_{50} > 100 mg/L	Acute	66.657	-	> 1500	100
	Pseudokirchneriella subcapitata	EC_{50} > 500 mg/L	Acute	66.657	-	> 7501	10
BF 490-5	*Daphnia magna*	EC_{50} > 100 mg/L	Acute	6.837	-	> 14626	100

The risk of the metabolites BF 490-1 and BF 490-5 for use in cereals is acceptable based on FOCUS step 1 calculations, indicating low risk.

In conclusion, the risk of kresoxim-methyl and its metabolites BF 490-1 and BF 490-5 is acceptable based on the worst-case PEC_{ini} values with risk mitigation to protect the most sensitive species (fish):
- buffer zone of 20 m for the use in pomefruit
- buffer zone of 10 m for the use in grapevine
- no risk mitigation for the use in cereals for the a.s. kresoxim-methyl

Using more realistic exposure scenarios (PEC_{TWA} values) will lead to reduced buffer zones. This is an option for refinement that can be considered at Member State level.
Also, the mesocosm study shows acceptable risk for aquatic invertebrates and algae without buffer zones, indicating low risk

B.9.3 Effects on other terrestrial vertebrates (Annex IIIA 10.3.1)

The ecotoxicologically-relevant endpoints for mammals were derived from the section on mammalian toxicology.

Table B.9.3-1 : Summary of effects of kresoxim-methyl on mammals

Test species	Test substance	Test system	Endpoints	References
rat	kresoxim-methyl	acute oral toxicity	LD_{50} > **5000 mg a.s./kg bw**	Kirsch et al., 1993
rat	kresoxim-methyl	2-generation reproduction toxicity	NOAEL = **100 mg a.s./kg bw/d**	Hellwig *et al*., 1994a

The choice of the long-term NOAEL is based on decreased body weight, increase in serum GGT and decrease in liver fat storing cells in the F0 generation, and on retarded morphological development in the F1b pup generation.

First tier risk assessment for mammals :

The risk assessment for mammals is based on the Guidance Document for birds and mammals under Council Directive 91/414/EEC of September 2002 (SANCO/4145/2000). As a worst case it was assumed that the mammals obtained 100 % of their diet in the treated area.

1- Formulation CANDIT

The formulation CANDIT (BAS 490 02 F) is a fungicidal product, which contains the active substance kresoxim-methyl with a nominal content of 50 % w/w.

Table B.9.3-2 : Proposed use pattern of the formulation CANDIT

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate (kg a.s./ha) [1)]	Application rate (kg product/ha) [1)]
Pome fruit (apple, pear)	1 - 4	7	53 - 79	0.100 - 0.125	0.200 - 0.250
Grapevine	1 - 3	8	19 - 81	0.100 - 0.150	0.200 - 0.300

[1)] application rate increases with plant growth stage

For simplification reasons, the risk assessment is only conducted for the higher application rates. This covers the increase in application rate during season.

2- Formulation ALLEGRO

The formulation ALLEGRO (BAS 494 04 F) is a fungicidal product, which contains the active substances
- kresoxim-methyl (BAS 490 F) with a nominal content of 125 g a.s./L
- epoxiconazole (BAS 480 F) with a nominal content of 125 g a.s./L

Table B.9.3-3 : Proposed use pattern of the formulation ALLEGRO

Crop	Number of applications	Minimum Interval (days)	Growth stage (BBCH)	Application rate		
				BAS 494 04 F [L/ha]	Kresoxim-methyl (BAS 490 F) [kg a.s./ha]	Epoxiconazole (BAS 480 F) [kg a.s./ha]
Cereals	2	21	25 - 69	1.0	0.125	0.125

1.1 – Dietary exposure :

The relevant indicator species for the use in orchards and grapevines is a small herbivorous mammal of 25 g like the vole.
For orchards a MAF of 1.8 for acute exposure (4 applications, 7 days spray interval) was used.
The MAF for the long-term exposure was calculated according to
$MAF = (1 - e^{-0.069ni}) / (1 - e^{-0.069i})$ with i = interval and n = number of applications
for 4 applications and 7 days spray interval, assuming default DT_{50} on plant of 10 days
MAF = 2.2
For the RUD values, a deposition factor of 0.6 was assumed.

Table B.9.3-4 : Estimated oral uptake of kresoxim-methyl by herbivorous mammals and first tier Toxicity Exposure Ratios (TERs) for use in pome fruit (apple, pear) at 1-4 applications x 0.100-0.125 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Mammal type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.125	orchard early/ late	herbivorous	acute	1.39	85	1.8	n.a.	26.6	> 188	10
			long-term	1.39	46	2.2	0.53	9.45	10.6	5

For grapevines a MAF of 1.7 (3 applications, 7 days spray interval as a worst-case, covering the 8 days spray interval) was used.
The MAF for the long-term exposure was calculated according to
$MAF = (1 - e^{-0.069ni}) / (1 - e^{-0.069i})$ with i = interval and n = number of applications
for 3 applications and 7 days spray interval as a worst-case (covering the 8 days spray interval), assuming default DT_{50} on plant of 10 days
MAF = 2.00
For the RUD values, a deposition factor of 0.6 was assumed.

Table B.9.3-5 : Estimated oral uptake of kresoxim-methyl by herbivorous mammals and first tier Toxicity Exposure Ratios (TERs) for use in grapevines at 1-3 applications x 0.100-0.150 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Mammal type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.150	grape-vines early/ late	herbivorous	acute	1.39	85	1.7	n.a.	30.1	> 166	10
			long-term	1.39	46	2.00	0.53	10.2	9.84	5

The acute and long-term risk of kresoxim-methyl is acceptable for the intended uses in pome fruit and grapevines.

Table B.9.3-6 : Estimated oral uptake of kresoxim-methyl by herbivorous and insectivorous mammals and first-tier Toxicity Exposure Ratios (TERs) for use in cereals at 2 applications x 0.125 kg a.s./ha

Application rate (kg a.s./ha)	Crop	Bird type	Time-scale	FIR/ bw	RUD	MAF	f_{twa}	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger value
0.125	cereals early	herbivorous	acute	1.39	142	1.2[(1)]	n.a.	29.61	> 168.9	10
			long-term	1.39	76	1.23[(2)]	0.53	8.61	41.6	5
	cereals early/ late	insecti-vorous	acute	0.63	14	n.a.	n.a.	1.1	> 4535	10
			long-term	0.63	5.1	n.a.	n.a.	0.40	249	5

(1) MAF based on 2 applications and 14 days spray interval because SANCO/4145/2000 does not provide respective value for 21 days spray interval (overestimation of the actual risk)
(2) MAF calculated for short-term and long-term exposure according to
$MAF = (1 - e^{-0.069ni}) / (1 - e^{-0.069i})$ with i = interval and n = number of applications
for 2 applications and 21 days spray interval, assuming default DT_{50} on plant of 10 days
MAF = 1.23

The acute and long-term risk of kresoxim-methyl is acceptable for the intended use in cereals.
For the risk assessment of epoxiconazole, RMS refers to the DAR addenda, List of Endpoints and the EFSA conclusion on epoxiconazole.

1.2 - Secondary poisoning : Risk to earthworm-eating and fish-eating mammals :

Since the log P_{OW} of kresoxim-methyl is higher than 3 (log P_{OW} = 3.4), there might be a potential for bioaccumulation.
The 21-day PEC values in soil and surface water are obtained from the section on fate and behaviour :

Apple : PECsoil (twa, 21 d) = 0.015 mg a.s./kg
Grapevine : PECsoil (twa, 21 d) = 0.022 mg a.s./kg
Cereals : PECsoil (twa, 21 d) = 0.010 mg a.s./kg

Apple : PECsw (twa, 21 d, step 2) = 6.684 µg a.s./L
Grapevine : PECsw (twa, 21 d, step 2, late application) = 2.102 µg a.s./L
Cereals : PECsw (twa, 21 d, step 2) = 0.471 µg a.s./L

The BCF in earthworms is calculated as :
$BCF = (0.84 + 0.01 \times P_{OW})/(f_{oc} \times K_{OC}) = (0.84 + 0.01 \times 2512)/(0.02 \times 308) = 4.2$
with the following values obtained from the section on fate and behaviour :
P_{OW} = 2512 for kresoxim-methyl
mean K_{OC} = 308 mL/g for kresoxim-methyl
From the study on bioaccumulation potential in *Oncorhynchus mykiss* with kresoxim-methyl a BCF of 220 was obtained for the whole fish.

Table B.9.3-7 : The long-term risk of kresoxim-methyl for mammals eating contaminated earthworms and fish for the use in pome fruit

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
earthworm	0.015 mg a.s./kg	4.2	0.063	1.4	0.088	1134	5
fish	6.684 µg a.s./L	220	1.470	0.13	0.191	523	5

Table B.9.3-8 : The long-term risk of kresoxim-methyl for mammals eating contaminated earthworms and fish for the use in grapevine

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
Earthworm	0.022 mg a.s./kg	4.2	0.092	1.4	0.129	773	5
Fish	2.102 µg a.s./L	220	0.462	0.13	0.060	1663	5

Table B.9.3-9 : The long-term risk of kresoxim-methyl for mammals eating contaminated earthworms and fish for the use in cereals

Food type	$PEC_{environment}$	BCF	PEC_{food} (mg a.s./kg)	Factor (1/day)	ETE (mg a.s./kg b.w./day)	TER	Annex VI Trigger value
earthworm	0.010 mg a.s./kg	4.2	0.042	1.4	0.059	1700	5
fish	0.471 µg a.s./L	220	0.140	0.13	0.013	7424	5

The long-term risk of kresoxim-methyl for mammals eating contaminated earthworms and fish is acceptable for the intended uses in pome fruit, grapevine and cereals.

1.3- Plant metabolites :

In the plant metabolism and rotational crop studies with kresoxim-methyl, the metabolites BF 490-1 (B490M1), BF 490-2 (B490M2) and BF 490-9 (B490M9) were the main metabolites, which in one case approached or exceeded 10 % TRR (major metabolites) in green plant material (carrot forage), a potential feeding matrix of herbivorous wild mammals.
Due to their significant relative quantities, the aforementioned metabolites would be potentially relevant for the mammalian risk assessment. However, the identified major metabolites were also found in rats and lactating goats.

Therefore, for the metabolites approaching or exceeding 10 % TRR in the plant metabolism and rotational crop studies, the following can be concluded:

- The identified major metabolites were also found in rats and lactating goats, hence would have been tested in the mammalian toxicity studies conducted with kresoxim-methyl.
- The risk assessment for the parent molecule kresoxim-methyl is thus assumed to cover the potential risk from the plant metabolites.

1.4- Drinking water : spray application

The Guidance Document on the Risk Assessment for Birds and Mammals SANCO 4145/2000 proposes that birds and wild mammals may obtain their water demand from two potential sources.

The major source of contaminated drinking water is surface water containing residues of the active substance for example via spray drift from adjacent treated fields. As a conservative measure the water concentration may be considered equivalent to the initial PEC calculated for surface water as obtained from the environmental fate section of the DAR (Vol. 3, B.8.6).

Puddles of spray liquid held in leaf axils may be relevant for certain crop types giving rise to leaf whorls after foliar spray application, e.g. vegetables with head-like structure such as cabbage or cauliflower. In this case the concentration of the active substance in the spray solution as obtained from the application data section of the DAR (Vol. 3, 3.2.3) would need to be taken into account. A field experiment after foliar spray application in white cabbage (Hommes *et al*. 1990)[3] showed that the initial concentration of the active substance in leaf puddles is in the range of 5 – 20 % of the spray concentration. Therefore, EPPO (1994)[4] and SANCO/4145/2000 recommend using a conservative dilution factor of 5.

For the representative uses of kresoxim-methyl in pome fruit orchards and vineyards (BAS 490 02 F), and in cereals (BAS 494 04 F) a leaf puddle scenario event is unlikely to occur for the following reasons:

– The flat morphology of the crop leaves does not provide reservoirs for collecting spray solution.
– In orchards and vineyards the morphology of the regularly mulched ground vegetation (if present) is not comparable to leafy vegetables with forming heads.
– The water volume typically used in the proposed uses of kresoxim-methyl is obtained form the application data section of the DAR (Vol. 3, 3.2.3). The water volume for the uses in pome fruit orchards and vineyards (BAS 490 02 F), and in cereals (BAS 494 04 F) ranges from 150 to 1 800 L/ha. This calculates to 15 to 180 mL/m^2 which, together with the leaf morphology of crops and undergrowth noted earlier, illustrate that orchard trees, grapes, their undergrowth, and cereals are unlikely to give rise to leaf puddles.

Therefore, the potential exposure of birds / mammals via spray solution puddles is considered negligible and deemed not relevant for this assessment. Nevertheless, exposure via spray drift to water bodies, although assumed being the exception under good agricultural practice, might be considered a potential source of exposure and thus will be evaluated in the following.

The daily water intake of a 10 g mammal is calculated allometrically as follows (Calder and Braun, 1983) :

Total water ingestion rate (L/day) = $0.099 \times W^{0.90}$ where W is the body weight in kg

Total water ingestion rate (L/day) for a 10 g mammal = $0.099 \times (0.010)^{0.90} = 0.0016$ L/day

The daily dose of active substance is calculated as

(PECsw * total water ingestion rate) / W

The PEC values for surface water in Step 1 and 2 represent ‘worst-case loadings’ (Step 1) and ‘loadings based on sequential application patterns’ (Step 2), as detailed in FOCUS (2001). In Step 1 inputs of spray drift, run-off, erosion and / or drainage are cumulated as a single loading (sum of individual applications) to surface water calculating into most conservative water concentrations. In Step 2 the loadings are refined to occur as successive individual applications, each resulting in drift to the water body, followed by a run-off / erosion / drainage event occurring four days after the last application, and additionally taking into account region of use (Northern or Southern Europe), season of application, and crop interception.

[3] Hommes, V.M., Buchs, W., Joermann, G., and Siebers, J. (1990). Vogelgefährdung durch Pflanzen-schutzmittelrückstände in Blattpfützen von Gemüsekohl (Poisoning risk of birds by residues of pesticides in leaf puddles of colre crops). Nachrichtenbl. Deut. Pflanzenschutzd. 42. 113-117.

[4] EPPO (1994): Decision-making scheme for the environmental risk assessment of plant protection products, Chapter 11 Terrestrial vertebrates. EPPO Bull 24, 37-87.

Assuming a reasonable worst-case scenario, the surface water concentration is considered equivalent to the PEC calculated for multiple applications according FOCUS Step 2. Referring to the environmental fate section of the DAR (Vol. 3, B.8.6) the related PEC values are as follows:

Pome fruit orchards	0.018393 mg kresoxim-methyl/L
Vineyards	0.005690 mg kresoxim-methyl/L
Cereals	0.001158 mg kresoxim-methyl/L

For kresoxim-methyl the relevant time scale for potential exposure of birds or mammals through contaminated surface water is acute. In water / sediment systems the active substance proved to have short DT_{50} values of 1.26 and 1.36 days (van Beinum and Beulke, 2008). Therefore, the following risk assessments focus on the acute route of exposure.

The exposure and TER calculations for the proposed uses of the representative formulations BAS 490 02 F (pomefruit orchards, vineyards) and BAS 494 04 F (cereals) are presented in table B.9.3-10 below.

Table B.9.3-10 : Acute Toxicity Exposure Ratios (TERa) for the most conservative small insectivorous mammal indicator species (10 g b.w.) exposed through surface water

Crop	Body weight [kg]	Total water ingestion rate [L/day]	PEC_{sw} (Step 2) [mg a.s./L]	Daily intake of a.s. [mg a.s./kg b.w./day]	LD_{50} [mg a.s./kg b.w.]	TER_a --
Orchards	0.010	0.002	0.01893	0.004	> 5 000 [1]	> 1 250 000
Vineyards	0.010	0.002	0.00569	0.001	> 5 000 [1]	> 5 000 000
Cereals	0.010	0.002	0.001158	0.00023	> 5 000 [1]	> 21 739 130

[1] Acute oral toxicity study in the rat (Kirsch *et al.*, 1993, see Table B.9.3-1)

The risk for mammals drinking contaminated surface water is acceptable for all intended uses.

In conclusion, the risk of kresoxim-methyl and its metabolites is acceptable for mammals for the intended uses in pome fruit, grapevine and cereals.