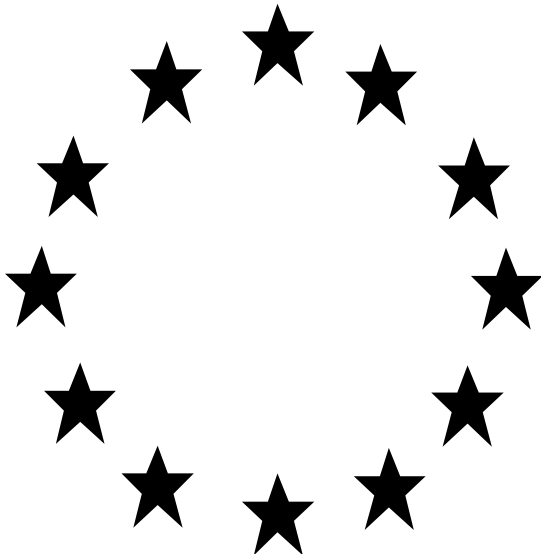

Draft Assessment Report (DAR)

- public version -

Initial risk assessment provided by the rapporteur Member State The Netherlands for the existing active substance

ETRIDIAZOLE

of the third stage (part B) of the review programme referred to in Article 8(2) of Council Directive 91/414/EEC

Volume 1

August 2007

European Commission

ETRIDIAZOLE

VOLUME 1

Rapporteur Member State: The Netherlands

April 2007

Draft Assessment Report and Proposed Decision of the Netherlands prepared in the context of the possible inclusion of etridiazole in Annex I of Council Directive 91/414/EEC

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LEVEL 1

Etridiazole

STATEMENT OF THE SUBJECT MATTER AND PURPOSE OF THE MONOGRAPH

1 Statement of subject matter and purpose for which the monograph was prepared

1.1 Purpose for which the monograph was prepared (dossier Document A)

This monograph on the active substance etridiazole has been prepared to support the inclusion of the active substance etridiazole in Annex I of the Directive 91/414/EEC.

1.2 Summary and assessment of information relating to the collective provision of dossiers (Dossier Document B)

Crompton Europe B.V. –now Chemtura Netherlands B.V.- is the sole notifier for etridiazole. The question of steps taken to collectively present the dossier does not therefore arise.

1.3 Identity of the active substance (Annex IIA 1) (Dossier Documents J, K-II and L-II)

1.3.1 Name and address of applicant(s) for inclusion of the active in Annex I (Annex IIA 1.1)

Applicant (name, address, etc.)

Address: **Chemtura Netherlands B.V.**
Ankerweg 18
1041 AT Amsterdam
The Netherlands

Contact person: [redacted]
Tel.no.: [redacted]
Fax no.: [redacted]
[redacted]

1.3.2 Common name and synonyms (Annex IIA 1.3)

Etridiazole (ISO); eclomezole (JMAF)
TERRAZOLE

1.3.3 Chemical name (Annex IIA 1.4)

IUPAC: ethyl-3-trichloromethyl-1,2,4-thiazol-5-yl ether
CA: 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole

1.3.4 Manufacturer's development code number (Annex IIA 1.5)

Olin-2424, OM 2424 (not any longer in use)

1.3.5 CAS, EEC and CIPAC numbers (Annex IIA.1.6)

CAS no.: 2593-15-9

EEC no.: 219-991-8

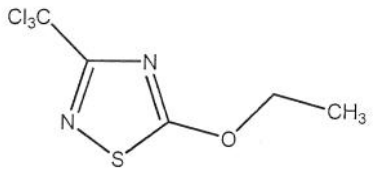
CIPAC no.: 518

1.3.6 Molecular and structural formulae, molecular mass (Annex IIA 1.7)

Molecular formula: $C_5H_5Cl_3N_2OS$

Molecular mass: 247.5

Structural formula:



1.3.7 Manufacturer or manufacturers of the active substance (Annex IIA 1.2)

Name Factory: Crompton Corporation

Address: Benson Road

Middlebury CT 06749

U.S.A.

Contact person: [redacted]

Tel.no.: [redacted]

Fax no.: [redacted]

Email: [redacted]

Location of plant See Volume 4, Annex C (Confidential Information).

1.3.8 Method or methods of manufacture (Annex IIA 1.8)

See Volume 4, Annex C (Confidential Information).

1.3.9 Specification of purity of the active substance (Annex IIA 1.9)

Specified as minimal 960 g/kg, based on pilot production. Notifier is asked to raise the minimal specification for the active substance to e.g. 975 g/kg as this appears to be technical possible.

1.3.10 Identity of isomers, impurities and additives (Annex IIA 1.10)

See Volume 4, Annex C (Confidential Information).

1.3.11 Analytical profile of batches (Annex IIA 1.11)

See Volume 4, Annex C (Confidential Information).

1.4 Identity of the plant protection products (Annex IIA 3.1; IIIA 1) (Dossier Documents J, K-II, L-II, K-III and L-III)

1.4.1 Current, former and proposed trade names and development code numbers (Annex IIIA 1.3)

Trade names: AATERRA ME, TERRAZOLE

Code names: ---

1.4.2 Manufacturer or manufacturers of the plant protection product (Annex IIIA 1.2)

Name Factory:	Chemtura Netherlands B.V.
Address:	Ankerweg 18
	1041 AT Amsterdam
	The Netherlands
Contact person:	[redacted]
	Tel.no.: [redacted]
	Fax no.: [redacted]
	Email: [redacted]
Location of plant	See Volume 4, Annex C (Confidential Information).

1.4.3 Type of the preparation and code (Annex IIIA 1.5)

ME: Micro-Emulsion

GIFAP code: ME

1.4.4. Function (Annex IIA 3.1; Annex IIIA 1.6)

Fungicide

1.4.5 Composition of the preparation (Annex III 1.4)

See Volume 4, Annex C (Confidential Information).

1.5 Use of the plant protection product (Annex IIA 3.2 to 3.4; Annex IIIA 3.1 to 3.7, 3.9 and 12.1) (Dossier Documents C, D and E)

1.5.1 Field of use (Annex IIA 3.3; Annex IIIA 3.1)

Glasshouse grown fruiting vegetables and cut flowers.

1.5.2 Effects on harmful organisms (Annex IIA 3.2; Annex IIIA 3.2)

Etridiazole is a contact fungicide with protective and curative action. Its protective action is restricted to the plant root zones in the soil or growth substrate. Etridiazole is a strong growth inhibitor of *Phytophthora* and *Pythium spp*.

1.5.3 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 to 3.7, 3.9)

See Table 1.5.3.

1.5.4 Information on authorization in EU Member States (Annex IIIA 12.1)

Etridiazole as a fungicide is authorised in Greece, Italy, The Netherlands, Spain and United Kingdom.

Table 1.5.3 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 - 3.7, 3.9)

Summary of intended uses

Crop and/ or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc of as	method kind	growth stage & season	number min max	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Non-soil bound glasshouse ornamental crops	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	n.a.	1-2	2 weeks	-	1000 min	0.7 g/m^2 substrate (7 kg/ha)	n.a.	
Substrate grown tomatoes	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28-0.56 kg/ha	3	
Substrate grown peppers	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28-0.56 kg/ha	7	
Substrate grown cucumbers	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28 kg/ha	14	

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval

(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench

(m) Remarks may include: Extent of use/economic importance/restrictions

LEVEL 2

Etridiazole

OVERALL CONCLUSIONS

2 Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

2.1.1 Identity

Refer to Volume 4/Confidential document.

2.1.2 Physical and chemical properties

Etridiazole pure is a clear and colourless liquid at 25°C with a freezing temperature of 22°C, a boiling temperature of 113°C (at reduced pressure; 0.53 kPa) and a vapour pressure of 1.43 Pa at 25°C. Up to a temperature of 318°C no decomposition was observed. Etridiazole Technical is a yellow liquid with low viscosity. The (technical) substance has a flash point of 111°C, an auto-ignition temperature of 342°C and has neither explosive properties nor oxidizing properties. Its water solubility at 25°C is 117.1 mg/L (85.8, 88.9 and 89.7 mg/L at pH 4, 7 and 10, respectively). The log Pow is 3.37 and the pKa is 2.77 at 25°C. The hydrolysis half-life of Etridiazole at 25°C in buffered solutions of pH 5.2, 7.1, 8.9 and distilled water is 88 to 98 days. Etridiazole does not appreciably absorb light in wavelengths relevant to natural sunlight (maximum ε over the range 290 to 800 nm: 2.13 L/(molxcm) at 290 nm). Consequently, photochemical degradation was not determined.

AATERRA ME (700 g/L Etridiazole) is a clear, yellow/light brown mobile liquid. The product has a flash point >100°C, an auto-ignition temperature of 382°C and has neither explosive nor oxidizing properties. The pH of a 1% dilution is 3.6 to 4.0. An accelerated storage test of 14 days at 54°C and 2 months at 40°C, a shelf-life study of 2 years at ambient and a low temperature stability test of 7 days at 0°C have determined the physico-chemical stability of the product.

2.1.3 Details of uses

Etridiazole is a contact fungicide with protective and curative action. Its protective action is restricted to the plant root zones in the soil or growth substrate. Etridiazole is basically regarded as a non-systemic product. Etridiazole is a fungicide to be used in agriculture against *Phytophthora* and *Pythium spp* (glasshouse: substrate grown tomatoes, peppers and cucumbers, and non-soil bound glasshouse ornamental crops).

Details of further information

Information supplied addresses methods for handling and storage of the active substance and plant protection product.

2.1.4 Classification and labelling

Active substance

Physical and chemical properties

No classification and labelling is needed based on the physical and chemical properties of the active substance Etridiazole.

Human health effects

Justified proposals for classification and labelling of the active substance, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	:	Xn (optional Xi)
Indications of danger	:	Harmful (optional Irritant)
Risk phrases	:	R22; Harmful if swallowed.
		R43; May cause sensitisation by skin contact.
		R40; Limited evidence of a carcinogenic effect.
Safety phrases	:	S36; Wear suitable protective clothing.
		S37; Wear suitable gloves.

Justification for the proposal

R22 Based on the results of the acute oral toxicity study.

R43 Based on the results of the skin sensitisation study.

R40 Based on the results of the carcinogenicity studies and mechanistic studies.

S36 Obligatory for substances labelled with R40 and/or R43.

S37 Obligatory for substances labelled with R40 and/or R43.

Ecotoxicological effects

In acute toxicity tests with technical etridiazole in fish, *Daphnia magna* and algae, the lowest LC/EC50 values were 2.4, 3.1 and 0.30 mg/L, respectively. Etridiazole has a log Pow value of >3.0, and the experimentally determined BCF is >100. It is proposed therefore, that on the basis of its acute toxicity etridiazole should be categorised as “Dangerous for the environment” (N), “Very toxic to aquatic organisms” (R50) and "May cause long-term adverse effects in the aquatic environment" (R53).

It is recommended that the active substance also carries the following ‘S’ safety phrases:

S57 Use appropriate containment to avoid environmental contamination

S60 This material and its container must be disposed of as hazardous waste

S61 Avoid release to the environment. Refer to special instructions/Safety data sheet

Justification for the proposal:

N, R50, R53	Based on the acute toxicity and the BCF
S57	Recommended for preparations labelled with R50
S60, S61	Recommended for preparations labelled with R50/R53

Formulation

Physical and chemical properties

No classification and labelling is needed based on the physical and chemical properties of AATERRA ME.

Human health effects

Justified proposals for classification and labelling of the preparation AATERRA ME, relating to human health effects, according to Directive 2001/59/EC are listed below.

Hazard symbol	:	Xn (optional Xi)
Indications of danger	:	Harmful (optional Irritant)
Risk phrases	:	R36; Irritating to eyes.
		R38; Irritating to skin.
		R43; May cause sensitisation by skin contact.
		R40; Limited evidence of a carcinogenic effect.
Safety phrases	:	S36; Wear suitable protective clothing.
		S37; Wear suitable gloves.

Justification for the proposal

R36	Based on the results of the eye irritation study.
R38	Based on the results of the skin irritation study.
R43	Based on the results of the skin sensitisation study.
R40	Since the product contains 700 g/L etridiazole, and etridiazole is labelled with R40.
S36	Obligatory for formulations labelled with R40 and/or R43.
S37	Obligatory for formulations labelled with R40 and/or R43.

Ecotoxicological effects

Tests with Aaterra were not submitted. Since the formulated product contains >25% of the active substance, the hazard classification and labelling of the plant protection product is identical to that of the active substance, in agreement with the recommendations in Dangerous Preparation Directive 99/45/EC and the 28th adaptation of the Dangerous Substance Directive 67/548/EC.

2.2 Methods of analysis

2.2.1 Analytical methods for analysis of the active substance as manufactured

A GC-FID method was submitted for the determination of etridiazole in technical material. The identity of etridiazole in technical material was confirmed by GC-MS. The validation results fulfilled all criteria.

2.2.2 Analytical methods for formulation analysis

A HPLC-UV method was submitted for the determination of etridiazole in the plant protection product EVO-50028-176 (identical to Aaterra ME). The validation results fulfilled all criteria.

2.2.3 Analytical methods for residue analysis

Treated plants, plant products, foodstuffs, feeding stuffs

A GC-MS method (AC-3012A) was submitted for the determination of etridiazole in green peppers (LOQ 0.01 mg/kg). The study contained fully acceptable validation results. An ILV for green peppers was submitted and deemed acceptable. The method is considered applicable for tomatoes and cucumbers (crops with high water content).

No multi-residue methods were investigated, whilst several multi-residue methods may be suitable for the determination of etridiazole in plant products (e.g. DFG multi-residue method S19-E1). The results from two studies indicate that the S19 method is probably suitable for the determination of etridiazole, but not for the metabolites.

Additional methodology for the metabolites 3-hydroxymethyl etridiazole and 5-hydroxyethoxy etridiazole acid included in the residue definition for plant products should be submitted unless non-inclusion of the metabolites in the residue definition is accepted by the RMS (provisional data gap).

Residues in body fluids and tissues

Etridiazole is not classified as toxic (T). An analytical method for body fluids and tissues is therefore not required.

Soil, water and air

Analytical methods were submitted for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in soil and water (surface water) and of etridiazole in air.

One GC-TSD method (AC-6003) was submitted for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in soil. The method was fully validated and confirmed by GC-MS. Method AC-6003 is

considered suitable for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in soil with an LOQ of 0.01 mg/kg. In addition, one GC-MS method was submitted for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in soil. The study was not accepted for post-registration monitoring purposes because of the use of diazomethane as derivatising agent.

One GC-NPD method (AC-7001) was submitted for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in surface water. The method was fully validated and confirmed by GC-MS. Method AC-7001 is considered suitable for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in surface water (LOQ 0.1 µg/L). The method is also suitable for drinking and groundwater (because surface water is considered the more difficult matrix). The LOQ of 0.1 µg/L for surface water is below the level of the lowest appropriate toxicity value for aquatic organisms (in this case the NOEC for rainbow trout (0.12 mg/L) (See B.9.2.2)). The established LOQ is also <NOEC/10 (i.e. including the risk assessment safety factor of 10). In addition, one GC-MS method was submitted for the determination of etridiazole, dichloro-etridiazole and etridiazole acid in groundwater. The study was not accepted for post-registration monitoring purposes because of the use of diazomethane as derivatising agent.

One GC-MS method was submitted for the determination of etridiazole in air. The method was fully validated and confirmed by GC-MS. The method is considered suitable for the analysis of etridiazole in air with an LOQ of 0.9 µg/m^3 (~25°C, ~26% rH and ~35°C, ≥80% rH; 1.7L/min during 6 hours). The method is considered suitable for post-registration monitoring because the LOQ (0.9 µg/m^3) is below the limit of 9 µg/m^3 calculated as: limit = AOEL*0.1*60/20 (AOEL = 0.03 mg/kg bw/day).

Additional methodology for the metabolites included in the residue definition for air should be submitted unless non-inclusion of the metabolites in the residue definition is accepted (provisional data gap).

2.3 Impact on human and animal health

2.3.1 Effects having relevance to human and animal health arising from exposure to the active substance or impurities contained in the active substance or to their transformation products

This toxicological dossier contains studies with the test substance etridiazole, which is also known under the name Terrazole.

2.3.1.1 Toxicokinetics

Absorption

In one study, at 168 hours after a single oral dose of 5 and 150 mg/kg bw, or repeated oral dosing at 5 mg/kg bw, 58-73% AR, 14-16% AR and 4.2-7.4% AR, respectively, was excreted with urine, faces and expired air, whilst 2.4-3.9% AR was retained in tissues. Excretion and retention after single intravenous dose administration was comparable to that for oral dosing. Radioactivity excreted with faeces following oral dosing may therefore be assumed to represent absorbed radioactivity, excreted via the biliary pathway. From the results of this study, oral absorption is estimated to be 100%.

In another study, peak ^{14}C-concentrations in blood were observed after 4 hours in both sexes after a single oral dose of 5 mg/kg bw, but only after 8 and 21 hours in males and females, respectively, that received a single oral dose of 150 mg/kg bw.

Elimination

In one study, at 168 hours after a single oral dose of 5 and 150 mg/kg bw, or repeated oral dosing at 5 mg/kg bw, the majority of administered radioactivity was excreted in urine (58-73% AR), whilst radioactivity in faeces accounted for 14-16% AR and in expired air for 4.2-7.4% AR. Pre-treatment for 14 days did not affect the pattern of excretion and retention.

In another study, the elimination half-life in blood after a single oral dose of 5 mg/kg bw (14 hours for both sexes) was much shorter than after a single oral dose of 150 mg/kg bw (36 and 60 hours in males and females, respectively). At 168 hours after a single oral dose of 5 and 150 mg/kg bw, the majority of administered radioactivity was excreted in urine (62-78% AR), whilst radioactivity in faeces accounted for 14-21% AR. At the high dose, the rate of excretion in urine was slower in females than in males (33% and 50% AR after 24 hours, respectively).

Distribution

In one study, at 168 hours after a single oral dose of 5 mg/kg bw, the highest radioactivity concentrations were found in liver (0.83-0.97 mg eq./kg), kidney (0.77-0.86 mg eq./kg) and lung (0.45-0.47 mg eq./kg), and the lowest in brain (0.08-0.09 mg eq./kg) and fat (0.05-0.06 mg eq./kg). Comparable concentrations were found in tissues and organs of rats after multiple oral dosing with 5 mg/kg bw. After a single oral dose of 150 mg/kg bw, the pattern of distribution was comparable to that after a single oral dose of 5 mg/kg bw, but the

concentrations in high dose male and female rats were on average a factor of 39 and 32, respectively, higher than in low dose rats (hence roughly proportional to the dose).

In another study, radioactivity in tissues (including the residual carcass) at 168 hours post a single oral dose of 5 or 150 mg/kg bw represented 3.2-4.7% AR. At the low dose, at ½ tmax and 168 hours post-dose, respectively, radioactivity concentrations in tissues with quantifiable residues were on average 41-54% and 8-9%, and at the high dose 34-43% and 12-15%, of those at tmax. At tmax, ½ tmax and 168 hours post-dose, respectively, the concentrations in tissues with quantifiable residues in rats receiving the high dose were on average a factor of 28-29, 14-18 and 30-34, respectively, higher than in low dose rats (hence roughly proportional to the dose). There were no remarkable differences between tissue levels and depletion rates of male and female rats.

Metabolism

In 0-24 hour urine of rats treated with 14C-etridiazole (single oral dose of 5 and 150 mg/kg bw, or repeated oral dosing at 5 mg/kg bw), which contained 28-60% AR, the metabolite pattern was essentially the same for sexes and dosing regimes. Parent compound was not identified in urine. The main metabolite in urine was etridiazole carboxylic acid (20-36% AR, 53-71% TRR), which was also the main (and only identified) component in faeces. Other metabolites identified in urine were N-carbethoxy oxamic acid (4.1-12% AR, 14-20% TRR), ethyl (aminocarbamyl) carbamate (0.5-4.3% AR, 1.0-7.2% TRR), N-acetyl cysteinyl conjugate of etridiazole (0.3-2.0% AR, 0.9-3.6% TRR) and, tentatively, oxalic acid, at low levels (presumably <1% AR, <2% TRR). A multitude of unidentified polar components, each present at low levels, eluted close to natural urinary compounds such as uric acid, urea, hippuric acid etc. Metabolite identification in urine is acceptable for the major fractions only (metabolite 1, multi-component mixture of polar fractions; etridiazole carboxylic acid (20-36% AR, 53-71% TRR), and N-carbethoxy oxamic acid (4.1-12% AR, 14-20% TRR). It is uncertain whether the minor fractions (<7% AR) in urine are the result of metabolism, or that they were already present in the test material used for treating the rats, which was of low radiochemical purity (93-97%).

Dermal absorption data

The dermal absorption of etridiazole in rats *in vivo* from a 25 EC formulation (exposure periods of 4 or 10 hours) was 30% after a single application of test material at low dose (0.1 µg/cm^2), 19% at medium dose (1 µg/cm^2) and 18% at high dose (10 µg/cm^2). Since this was an EC formulation with a high content of organic solvent, the dermal absorption values based on the results of this study can be regarded as worst-case estimates for the formulation AATERRA ME.

2.3.1.2 Toxicodynamics

Acute toxicity

Etridiazole needs to be classified as harmful if swallowed (Xn, R22) on the basis of its acute oral toxicity in rats. Etridiazole does not need to be classified on the basis of its acute dermal and inhalation toxicity and is considered not irritating to the skin and eyes. Etridiazole needs to be classified as a skin sensitizer (Xi, R43).

Short-term and semi-chronic toxicity

Four weeks of dermal exposure of rats to 0, 20, 400 and 1000 mg/kg bw/day resulted in increased liver weights and concomitant centrilobular hypertrophy at 400 mg/kg bw/day and above. The NOAEL for systemic effects was set at 20 mg/kg bw/day. As no local effects were observed the NOAEL for local effects was established at 1000 mg/kg bw/day.

After subacute inhalation exposure of rats to 0, 15, 75 and 200 mg/m^3, a reduced body weight gain and an increased potassium concentration, of which the toxicological relevance was unclear, were observed at 75 mg/m^3 and above. Based on these effects a NOAEL of 15 mg/m^3 was established for systemic effects. For local effects no NOAEL could be derived, because squamous metaplasia of the larynx mucosa was observed at all dose levels.

Dietary exposure of rats to 0, 50, 600 and 1250 mg/kg food/day of etridiazole (equal to 0, 2.7, 29.5 and 64.7 mg/kg bw/day for males and 0, 3.3, 35.2 and 73.6 mg/kg bw/day for females) for 13 weeks caused decreased body weight at 600 mg/kg food in females and 1250 mg/kg food in both sexes. Food consumption was decreased at 1250 mg/kg food. Reticulocytes and platelet count were increased at 1250 mg/kg food. Prothrombin time and APTT were decreased at 600 and 1250 mg/kg food in males. Sodium and chloride were slightly reduced and potassium was increased in males at 1250 mg/kg food. Glucose was decreased at 1250 mg/kg food in both sexes. Bilirubin was increased at 1250 mg/kg food in males. T_3 levels were decreased at 1250 mg/kg food in females. Cholesterol was increased in males and liver weights were increased in both sexes with concomitant centrilobular hypertrophy at 600 and 1250 mg/kg food. The changes in sodium, chloride and potassium correlate with hyaline droplets observed in the kidneys of male animals. The incidence was slightly increased at 600 and 1250 mg/kg food, which is considered to be due to α2μglobulin (see mechanistic data). The NOAEL was established at 50 mg/kg food/d (equal to 2.7 mg/kg bw/d for males and 3.3 mg/kg bw/d for females), based on effects on liver and kidneys.

Dietary exposure of dogs to 0, 160, 500 and 1000 mg/kg food/d of etridiazole technical (equal to 0, 3.11, 8.07 and 22.4 mg/kg bw/d for males and 0, 4.27, 9.33 and 24.0 mg/kg bw/d for females) for 12 months resulted in reduced body weight gain at 1000 mg/kg food. An increased platelet count (males only) and APTT was noted at 1000 mg/kg food. Urea nitrogen and creatinine were decreased at 1000 mg/kg food.

Total protein, albumin and A/G ratio were decreased at 1000 mg/kg food. Alkaline phosphatase was increased at 500 and 1000 mg/kg food. Cholesterol was increased at 1000 mg/kg food. Increased alkaline phosphatase and cholesterol, and decreased protein parameters indicate a disturbed functioning of the liver. Concomitantly, liver weights were increased at 500 and 1000 mg/kg food. No macroscopic or microscopic findings were noted. Therefore, the NOAEL is set at 160 mg/kg food/d (equal to 3.1 mg/kg bw/d for males and 4.3 mg/kg bw/d for females).

Genotoxicity

Etridiazole did not induce point mutations in *S. typhimurium* tester strains TA98, TA100, TA1535 and TA1537, both with and without metabolic activation. Etridiazole was positive in a chromosome aberration test with Chinese hamster ovary cell line CHO. However these results were obtained at very toxic dose levels and the results could not be compared to the historical control data, therefore this study was not acceptable. Etridiazole was positive in two SCE studies (one study was considered not acceptable). In both studies statistically significant increases were observed, however if the results are judged for biological relevancy these increases are considered not relevant, since no more than a two-fold increase has been observed. Etridiazole was negative in a gene mutation test using CHO hamster cells. In addition, etridiazole was negative in an *in vivo*/*in vitro* DNA repair study using male rat hepatocytes, etridiazole was also negative in an *in vivo* mouse micronucleus test and in an *in vivo* rat chromosome aberration test. Etridiazole was positive an *in vivo*-*in vitro* replicative DNA synthesis test.

Based on the *in vivo*-*in vitro* replicative DNA synthesis test in combination with the results of the studies summarized at the mechanistic data it can be concluded that etridiazole possesses promotor activity, with a threshold level.

Based on the three well performed *in vivo* studies, in which etridiazole showed negative responses, etridiazole is considered to be non-genotoxic.

Long-term toxicity

In a 2-year chronic toxicity and carcinogenicity study in rats, administration of etridiazole (dietary administration of 0, 100, 640 and 1280 mg/kg food) resulted in reduced body weight and food consumption at 640 and 1280 mg/kg food. Treatment at 640 and 1280 mg/kg food resulted, in females, in a mild increase in leucocyte count, with increased neutrophils and decreased lymphocytes, and in a mild decrease in erythrocyte count and haematocrit. At post mortem necropsy, abnormalities were noted in liver and liver weights were increased at 640 and 1280 mg/kg food. Neoplastic lesions were observed in liver (hepatocellular adenoma and/or carcinoma at 1280 mg/kg food and cholangiosarcoma at 1280 mg/kg food), thyroid (follicular adenoma and/or carcinoma at 640 and 1280 mg/kg food, testis (interstitial cell tumours at 1280 mg/kg food) and kidney (tubular cell tumours at 640 ppm). A variety of non-neoplastic lesions were noted in liver (at 640 and 1280 mg/kg food) and kidney (at all dose levels).

Based on the non-neoplastic lesions in the low dose group (tubular cell karyomegaly in kidney), a NOAEL could not be established. The test substance had an oncogenic effect on rat liver, thyroid, kidney and testis.

In a 79-week carcinogenicity study in mice, etridiazole was administered via the diet at 0, 50, 900/1300 and 1800/2000/1600 mg/kg food. For the first week, dose levels in the diet were 0, 50, 900 and 1800 mg/kg food. After the first week of dosing the dietary concentration for the mid and high dose levels were increased to 1300 and 2000 mg/kg food, in Week 43, high dose level was decreased to 1600 mg/kg food due to excessive mortality in this group. Treatment at 900/1300 and 1800/2000/1600 mg/kg food resulted in reduced survival. A variety of clinical signs (a.o. decreased activity, tremors, inappetance, hunched posture, discoloured skin and/or breathing difficulties) were recorded in the high dose group. High dose males had lower body weights than controls from week 3 of treatment onwards. In addition, mid and high dose males, and high dose females showed lower food consumption than controls. Liver weights were increased, kidney and uterus weights reduced in mid and high dose groups. At post-mortem necropsy, abnormalities were noted in liver, kidney and spleen of mid and high dose groups.

Histopathological findings were recorded in mid and high dose groups and comprised findings in liver, kidneys and spleen. Neoplastic lesions (hepatocellular adenoma and carcinoma) were noted in liver of mid and high dose groups. A variety of non-neoplastic lesions were also noted in mid and high dose animals. These lesions were recorded in liver (hepatocellular necrosis, bile duct- and regenerative hyperplasia, hypertrophy and/or hyperplasia of hepatocytes and Kupffer cells, increased cellular pigment, and vacuolation), kidney (infarct), spleen (increased extramedullary haematopoiesis) and heart (myofiber mineralization and thrombi).

Based on abovementioned changes in mid and high dose groups, the NOAEL was set at 50 mg/kg food (equal to 7.5 and 9.1 mg/kg body weight/day for males and females, respectively). The test substance had an oncogenic effect on mouse liver, at dose levels clearly exceeding the MTD.

Mechanistic data

Based on chronic toxicity and carcinogenicity data in rats, it was concluded that etridiazole has an oncogenic effect on rat liver, thyroid, kidney and testis. Furthermore, based on the carcinogenicity data in mice, it was concluded that etridiazole has an oncogenic effect on mouse liver.

To further evaluate the carcinogenic mechanism of action a number of *in vivo* mechanistic studies were conducted that investigated whether etridiazole possessed promotor and/or initiator activity.

The first 2 studies by Tanaka (1995) were comparable in study design. Rats were treated for up to 28 days with etridiazole and various parameters indicative for promotor activity were evaluated. These parameters comprised metabolizing liver enzymes and connexin 32 levels in liver. In the first study, dose levels of etridiazole were 0, 640 and 1280 mg/kg food and in the second study dose levels were 0, 100, 200 and 400 mg/kg food. In the first study, a positive control (phenobarbital) was included.

Both etridiazole treatment (at 400, 640 and 1280 mg/kg food) and phenobarbital treatment for 28 days resulted in induction of liver enzymes and a reduction of connexin 32 levels in liver.

A discrepancy between the positive control group and etridiazole treated group(s) was recorded with regard to phase I metabolizing enzymes, whereas the induction of phase II enzymes was similar for etridiazole and

phenobarbital treatment. These differences indicate etridiazole has a different biochemical profile than the known tumour promotor phenobarbital.
Connexin 32 is a protein of the gap junction, involved in intercellular communication. A reduction in gap junctions lead to reduced intercellular communication, and is known to be related to (the promotion stage of) carcinogenesis. Both etridiazole treatment (at 400 and 1280 mg/kg food) and phenobarbital treatment resulted in reduced connexin 32 levels in liver. Etridiazole treatment at 400 mg/kg food led to a reduction of approximately 20%, phenobarbital treatment led to a reduction of approximately 40% and etridiazole treatment at 1280 mg/kg food resulted in a reduction of approximately 80%. No connexin effect was noted at 640 mg/kg food.
This all suggests that etridiazole may act as a tumour promotor, comparable to phenobarbital. However, based on the differences in induction of metabolizing enzymes, it is concluded that if etridiazole can act as promotor, it has another profile than phenobarbital. These effects were not noted at 100 or 200 mg/kg food, indicating that etridiazole has a threshold level for promotor activity.

The third study was designed to investigate whether etridiazole had promotor and/or initiator activity in liver tumour development. Animals were pretreated once, intraperitoneally, with N-nitrosodiethylamine (DEN) as an initiator (or saline as control). Two weeks later test diets were provided at dose levels of 100, 640 and 1280 mg/kg food, a phenobarbital group was also included as positive control for tumour promotion. After 1 and 6 weeks sections of liver lobes were stained immunohistochemically for GST-P GST-P positive liver foci served as an endpoint marker for hepatocarcinogenicity. Etridiazole treatment at 640 and 1280 mg/kg food markedly increased both the number and size of GST-P positive liver foci. Treatment with the positive promotor control resulted in comparable effects, with the magnitude of changes between those seen at 640 or 1280 mg/kg food etridiazole. This third study confirmed that etridiazole possesses promoter activity at 640 and 1280 mg/kg food, but not at 100 mg/kg food for hepatocarcinogenicity. In addition, no initiation potential was noted with doses up to 1280 mg/kg food etridiazole.

In conclusion, etridiazole possesses promotor activity, with a threshold level for this promotor activity of 200 mg/kg food (18 mg/kg bw/day). No initiation potential was noted for doses up to 1280 mg/kg etridiazole (88 mg/kg bw/day).

The RMS discussed the possible mechanisms and relevance of the tumours observed in the 2-year rat study and 18-month mouse study, on the basis of the study results, the mechanistic studies and the evaluation by the notifier, for each tumour type.

Liver tumours rat

The liver tumours were observed at a dose level exceeding the MTD, which means that the toxicological relevance is equivocal. The mechanistic studies showed that etridiazole possesses promoter activity for hepatocarcinogenicity, and this probably played an important role in the observed increased incidence of liver tumours at the highest dose in the 2-year rat study. The mechanistic studies also showed that there is a threshold dose for the promoter activity of etridiazole.

Liver tumours mouse

Etridiazole had an oncogenic effect on mouse liver, at dose levels clearly exceeding the MTD, and the toxicological relevance is therefore equivocal. Furthermore, since etridiazole is an enzyme inducer (see mechanistic studies), liver tumours in mice can be expected.

Thyroid tumours rat

The fact that the increased incidence in thyroid tumours does not always reach a statistically significant level, does not automatically mean it is not biologically relevant. In the mechanistic studies, an increase in UDP-GT was observed, but there was no corresponding increase in TSH in blood or changes in T_3 or T_4 in blood. The mechanism of the thyroid tumour formation is therefore not known. It should be noted that humans are considerably less sensitive to the development of follicular thyroid tumours as a result of long-term stimulation than rodents (especially rats).

Testis tumours rat

The testis tumours were observed at a dose level exceeding the MTD, meaning that, here too, the toxicological relevance is equivocal (the observed tumours at the low and mid dose, without a dose-response relationship, were within the historical control range). The incidence of interstitial cell tumours (Leydig cell tumours) in humans is extremely rare, while these tumours occur frequently in rats. Depending on the underlying mechanism, these tumours may not be relevant for human risk assessment. However, since the mechanism is not known for etridiazole, it should be assumed that humans are potentially susceptible.

Kidney tumours rat

In the 2-year rat study, the kidney tumours were only observed in males. There was no dose-response relationship. In the 13-week rat study, hyaline droplets were found, only in males. Finally, kidney tumours were not observed in the mouse study. Based on these observations, the RMS agrees with the notifier that although the mode of action has not actually been proven (by determination of the presence of the alpha-2-microglobulin in the hyaline droplets and binding of etridiazole to alpha-2-microglobulin) it is reasonable to assume that the kidney tumours in the rat are alpha-2-microglobulin associated, and therefore not relevant for human risk assessment.

Conclusion

Based on the observations in the 2-year rat study (liver tumours, and the potentially relevant thyroid and testis tumours), the18-month mouse study, the mechanistic studies and the argumentation in B.6.8.2.2, it is concluded that classification of etridiazole as Carcinogen Category 3 should be considered (Xn, R40), in line with the current ECB classification.

Reproduction and developmental toxicity

In an oral 2-generation reproduction study in rats (0, 80, 320 and 800 mg/kg food for males and 0, 80, 320 and 640 mg/kg food for females), a decrease in body weight and food consumption was noted among males and females from the F_0-generation at 800/640 mg/kg food and for the F_1-generation at 320 and 800/640 mg/kg food. An increase in T_3 concentration in males and a decrease in females at 320 and 800/640 mg/kg food (F_0-generation measured only) was noted. In addition, decreased pituitary weight at 320 mg/kg in F_0-males food and at 800 mg/kg food F_0- and F_1-males, changes in kidney weight at 320 and 800/640 mg/kg food in F_0 and F_1-animals, increases in liver weight at 320 and 800/640 mg/kg food in F_0 and F_1-animals, and increased seminal vesicle weight at 320 and 800 mg/kg food in F_1-males were observed. There were no changes detected between parental animals of the treated and control groups in mating indices, pregnancy rates, fertility, oestrus cycle and macroscopic findings.

Examination of the F_0 and F_1-offspring revealed decreased body weights of pups at 320 (F_0 only) and 800/640 mg/kg food. In addition, changes in thyroid weight were noted at both levels in the F_0-generation and in the F_1- high dosed group. T_3 concentration was only measured the F_1-offspring and was decreased in males at 800 mg/kg food and females at 320 and 640 mg/kg food. No treatment-related changes were detected in litter size, sex ratio, litter survival or macroscopic observations of the F_0 and F_1-offspring. Based on the data presented in this study, the NOAEL for parental toxicity was 80 mg/kg food (equivalent to 5.3 mg/kg bw/day). The NOAEL for developmental toxicity was 80 mg/kg food (equivalent to 5.3 mg/kg bw/day). The NOAEL for reproductive toxicity was considered to exceed 800/640 mg/kg food (equivalent to ≥ 53.3 mg/kg bw/day for males and ≥42.7 mg/kg bw/day for females).

In a teratogenicity study in rats (0, 10, 30 or 75 mg/kg bw/day) the NOAEL for maternal effects was 30 mg/kg bw/day, based on an increased mortality, clinical signs, and decreased body weight. The NOAEL for developmental effects was set at 30 mg/kg bw/day, based on decreased mean foetal weight, anasarca in 2 foetuses, and retarded ossification of various bones. No treatment-related effects were observed on the number of corpora lutea or implantations, the number or percentage of live foetuses, and the sex ratio. There were no morphological changes observed in foetuses that could be attributed to treatment. Therefore, the NOAEL for teratogenicity was considered to exceed 75 mg/kg bw/day.

In a teratogenicity study in rabbits (0, 1.7, 5, 15 or 45 mg/kg bw/day), a NOAEL for maternal effects of 15 mg/kg bw/day was derived, based on mortality and decreased body weight. Potential critical effects (liver, kidneys, and thyroid) were not studied and therefore, the derived maternal NOAEL from this study might not be accurate. The NOAEL for developmental effects was set at 15 mg/kg bw/day, based on decreased mean foetal weight, a reduction of live foetuses per dam and an increase of dams with resorptions at 45 mg/kg bw. No treatment-related effects were observed on the number of corpora lutea or implantation sites, and sex ratio.

Skeletal examination revealed an increased incidence of missing sternebrae, tail defects and underdeveloped hind limbs. Soft tissue examination showed an increased incidence of crossed hind legs and open eyes. Therefore, the NOAEL for teratogenicity was set at 15 mg/kg bw/day.

Neurotoxicity

No acute or semichronic oral neurotoxicity studies with etridiazole were submitted. However, clinical observations, FOB and pathology results from the subacute and (semi)chronic toxicity studies with rats, mice and dogs gave no indication for neurotoxicity of the test substance.

Toxicological data with metabolites

Metabolite 5-Ethoxy-1,2,4-thiadiazole-3-carboxylic acid showed to be less toxic than etridiazole for acute and semichronic toxicity. Both etridiazole and 5-Ethoxy-1,2,4-thiadiazole-3-carboxylic acid are considered non-genotoxic.

Derek modeling of the metabolites dichloro-etridiazole, 5-hydroxy-ethoxyetridiazole acid and 3-hydroxymethyl etridiazole, is negative for human health hazard.

Formulation data

AATERRA ME does not need to be classified on the basis of its acute oral and dermal toxicity in rats. AATERRA ME needs to be classified as a skin irritant (Xi R38) and an eye irritant (Xi R36) AATERRA ME also needs to be classified as a skin sensitizer (Xi R43).

2.3.2 ADI

The ADI has to be derived from the results of toxicity studies with experimental animals. The calculation of the ADI is based on the highest dose at which no adverse effect is observed in the most appropriate study in the most sensitive species. Etridiazole was tested in several subacute, semi-chronic and chronic studies in dogs, rats and mice, in a reproduction study in rats, and in teratogenicity studies in rats and rabbits. Furthermore, it was established in several *in vitro* and *in vivo* genotoxicity tests that etridiazole does not have genotoxic potential.

The critical effects of etridiazole were considered to be effects on liver and kidneys. Several repeated dose studies, including the 2-generation reproduction toxicity study and teratogenicity studies were considered for the establishment of the ADI (table 2.3.2.1).

Table 2.3.2.1 Studies considered for the establishment of the ADI

Study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Semichronic toxicity studies			
13-week, oral, rat (diet)	2.7	29.5	Richards, 1994
1-year, oral, dog (diet)	3.1	8.1	Goldenthal, 2002
Chronic toxicity studies			
2-year, oral, rat	< 5.0	5.0	Trutter, 1988
18-month, oral, mouse	7.5	185	Goldenthal, 2004
Reproduction and teratogenicity studies			

Study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
2-generation, oral, rat	Parental and developmental: 5.3	21.3	Turck, 2003
Teratogenicity, oral, rat	Maternal and developmental: 30	75	Wahlberg, 1982
Teratogenicity, oral, rabbit	Maternal and developmental: 15	45	Knicker-bocker, 1979

Unfortunately, no clear NOAEL was established in the chronic study in rats, in which non-neoplastic lesions (tubular cell karyomegaly in kidney) were noted at the lowest dose level of 5 mg/kg bw/day.

Based on the LOAEL of 5 mg/kg bw/day in the chronic study in rats, an ADI might be derived based on application of an additional safety factor 10 for extrapolation of a LOAEL to a NOAEL. Based on a overall safety factor of 1000 an ADI of 0.005 mg/kg bw/day can be derived. This provides a Margin of Safety of 6000 for tumour development, observed at 30 mg/kg bw/day (640 ppm) in the 2-year rat study.

2.3.3 ARfD (acute reference dose)

An ARfD was not allocated by the notifier.

According to the Guidance for the setting of an Acute Reference Dose (Document 7199/VI/99 rev. 5) an ARfD should not be allocated if:

- The pesticide has shown a very low acute oral toxicity (e.g. no adverse clinical sings and deaths have been observed at the limit dose for acute LD50 testing), and
- the toxicological profile was based only on e.g. mild effects, which are not relevant for acute intake (e.g. adaptive liver enlargement, chronic body weight reduction, reduced food intake), and
- the toxicological profile has not other alerts for acute toxicity.
- Furthermore, residue data should be taken into account to conclude on the necessity of an ARfD.

Based on the submitted data on etridiazole, the following considerations were made:

- The acute oral LD50 of etridiazole was found to be 1141 mg/kg bw in male rats and 945 mg/kg bw in females rats.
- In the acute, semichronic or chronic toxicity studies, no specific effects were observed relevant for acute intake.
- For etridiazole, there were no alerts observed for acute toxicity, e.g. acute neurotoxicity.
- In the teratogenicity study in rats and rabbits skeletal malformations/variations were noted in foetuses at maternal toxic levels.
- Because of insufficient residue data (see B.7), no conclusion on the necessity of an ARfD can be based on submitted residue data.

Based on the above data, it can be concluded that the criteria for not allocating an ARfD are not met, since the LD50 value <2000 mg/kg bw. Although there are no triggers from repeated dose toxicity studies

indicating acute toxic effects for etridiazole, based on the above considerations on the acute toxicity and residue data of etridiazole, it was concluded that allocation of an ARfD is considered justified.

The calculation of the acute reference dose is based on the highest dose at which no adverse effect is observed in the most appropriate acute toxicological endpoint of relevance to humans, derived from the most appropriate study in the most appropriate species.
The following studies were considered relevant for the establishment of the ARfD:

- The acute oral toxicity study in rats: a LOAEL of 700 mg/kg bw could be established. As clinical signs (decreased activity and decreased defecation) were noted at all dose levels, no NOAEL could be established.
- The subacute oral toxicity in rats (mechanistic study, 28 days): a NOAEL of 200 mg/kg food (18 mg/kg bw/d) was established (with a limited number of parameters).
- The 2-generation study in rats: a NOAEL of 5.3 mg/kg bw/day for parental and developmental effects.
- The teratogenicity study in rabbits: a NOAEL of 15 mg/kg bw/day was established for maternal and developmental effects.
- The teratogenicity study in rats: a NOAEL of 30 mg/kg bw/day was established for maternal and developmental effects.

The 2-generation reproduction study and the subacute oral toxicity study are considered less suitable for the establishment of an ARfD, due to the length of exposure, the limited number of investigated parameters, and since observed effects are more likely to be cause due to repeated exposure or due to indirect effects on the parental animals.
The latter can also not be excluded for the teratogenicity studies. However, considering the shorter exposure time of the teratogenicity studies, and the absence of a clear NOAEL for acute toxicity of etridiazole, the NOAEL of 15 mg/kg bw/day from the teratogenicity study in rabbits is considered to be most suitable NOAEL for the derivation of an ARfD.
Application of a safety factor of 100 for inter- and intraspecies differences, results in an ARfD of 0.15 mg/kg bw/day.

2.3.4 AOEL

AATERRA ME is used in glasshouses, on substrate grown cucumber, tomato and pepper, and on non-soil-bound ornamentals.
Application of AATERRA ME on cucumber, tomato and pepper takes place once or twice during growth stage BBCH 81. Application of AATERRA ME on ornamentals takes place before planting. Although multiple cultures might be produced within one year in glasshouses, the assumption of semi-chronic use of AATERRA ME is justified (only one or two applications per culture, and one culture takes at least 4 months).
Exposure of bystanders can be excluded, since AATERRA ME is used in glasshouses.
For the use of AATERRA ME, re-entry activities should be considered for inspection, binding and harvesting of cucumber, tomato, pepper and ornamentals. The exposure period will not exceed three months.

Etridiazole was tested in several subacute, semi-chronic and chronic oral studies in dogs, rats, and mice, in a reproduction study in rats and in teratogenicity studies in rats and rabbits (see table 2.3.4.1).

Table 2.3.4.1 Studies considered for the establishment of the AOEL

Study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Reference
Dermal and inhalation toxicity studies			
28-day, inhalation, rat	4 (15 mg/m^3)	20 (75 mg/m^3)	Hoffman, 2002
28-day, dermal, rat	20	400	Goldenthal, 2002
Semichronic toxicity studies			
13-week, oral, rat (diet)	2.7	29.5	Richards, 1994
1-year, oral, dog (diet)	3.1	8.1	Goldenthal, 2002
Chronic toxicity studies			
2-year, oral, rat	< 5.0	5.0	Trutter, 1988
18-month, oral, mouse	7.5	185	Goldenthal, 2004
Reproduction and teratogenicity studies			
2-generation, oral, rat	Parental and developmental: 5.3	21.3	Turck, 2003
Teratogenicity, oral, rat	Maternal and developmental: 30	75	Wahlberg, 1982
Teratogenicity, oral, rabbit	Maternal and developmental: 15	45	Knicker-bocker, 1979

As etridiazole is extensively metabolised, route-specific toxicity cannot be excluded. Therefore, if available, toxicity studies for the route concerned should be considered to calculate route-specific AOELs. In case of etridiazole subacute dermal and inhalation studies were available.

In a 28-day inhalation study, a NOAEL of 15 mg/m^3 (equivalent to 4 mg/kg bw/day) was established for systemic effects. The observed effects at the LOAEL of 75 mg/m^3 (20 mg/kg bw/day) were equivalent to the effects observed after oral exposure, mainly liver effects. The effect levels for both oral and respiratory route are in the same order of magnitude. Therefore, it is concluded that derivation of a specific AOEL for respiratory exposure is not considered necessary.

In a 28-day dermal toxicity study, a NOAEL of 20 mg/kg bw/day was derived, based on increased liver weights and concomitant centrilobular hypertrophy. At the NOAEL the estimated area concentration is 0.1 mg/cm^2 (assuming a body weight of 0.2 kg and a corresponding 400 cm^2 body surface, and using the reported 10% exposed body surface). For an area dose of 10 µg/cm^2, a dermal absorption value of 18% was derived (see B.6.12).This dermal absorption value can be considered a worst-case value for an area dose of 0.1 mg/cm^2. This means that a dermal dose of 20 mg/kg bw/day is comparable to a systemic dose of about 3.6 mg/kg bw/d. The observed effects at the LOAEL were equivalent to the effects observed after oral exposure, mainly liver effects. The NOAELs for both oral and dermal route are in the same order of magnitude. Therefore, it is concluded that derivation of a specific AOEL for dermal exposure is not considered necessary.

The semi-chronic AOEL for systemic exposure is set on the basis of the most relevant NOAEL from semi-chronic oral toxicity studies. The most relevant NOAELs (2.7 and 3.1 mg/kg bw/day) were obtained from a 13-week rat study and a 1-year dog study, respectively.

The most relevant NOAEL of 3.1 mg/kg bw/day in the 1-year dog study is used as a starting point for the establishment of the AOEL. Application of a safety factor of 100 for inter- and intraspecies differences, results in an ADI of 0.03 mg/kg bw/day. This provides a Margin of Safety of 1000 for tumour development, observed at 30 mg/kg bw/day (640 ppm) in the 2-year rat study.
Occupational risk assessments will be based on the AOEL of 0.03 mg/kg bw/day.

2.3.5 Drinking water limit

According to Council Directive 97/57/EC, exposure to etridiazole through the drinking water should account for not more than 10% of the ADI. If it is assumed that the average daily consumption of water amounts to 2 litre per person of 60 kilogram, a drinking water limit of (60x0.005)/10)/2 mg/l, i.e. 0.015 mg/l can be established.
According to Document 8064/VI/79 of the European Commission, the EU drinking water limit for pesticides of 0.1 µg/l is applicable for etridiazole.

2.3.6 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it

AATERRA ME is used as a fungicide in the treatment of substrate grown tomato, cucumber, pepper, and ornamentals (non-soil bound), and contains 700 g/L etridiazole. AATERRA ME is applied in glasshouses, by drip-irrigation. No exposure studies were submitted by the notifier. Exposure data were derived using models and estimated air concentrations of etridiazole and dichloro-etridiazole.

Operators

According to the notifier, exposure of the operator only occurs during mixing and loading since it is assumed that for application of AATERRA ME by drip-irrigation operators are not exposed. However, considering the volatility of etridiazole, occurrence of etridiazole in air cannot be excluded a priori. Significant losses of etridiazole through volatilisation were also observed in soil and water/sediment studies. Respiratory exposure of the operator to etridiazole during application (inspection during drip irrigation) cannot be excluded therefore.

Internal operator exposure values during mixing and loading, with and without personal protective equipment (PPE) were calculated using the UK and the German model. Since etridiazole is volatile, it is possible that the respiratory exposure during mixing/loading is underestimated by the German model (within the UK model, it is assumed that there is no inhalation exposure during mixing and loading). The notifier submitted estimations of concentrations of etridiazole in air due to volatilisation. Based on these estimates also, the respiratory exposure of the operator during mixing/loading and possible inspection activities during the drip-irrigation, was calculated, and compared with the exposure calculations based on the German model.

From the laboratory studies it can be concluded that also the soil/water metabolite dichloro-etridiazole may volatilise from soil and water, although at lower quantities compared to etridiazole. Therefore, respiratory exposure of the operator to dichloro-etridiazole during application (inspection during drip irrigation) cannot be excluded, and was calculated based on the submitted estimations of concentrations of dichloro-etridiazole in air due to volatilisation.

Bystanders

The presence of bystanders should be kept to a minimum. This can easily be achieved in a greenhouse, where no person should be allowed in who is not involved in the application process. Therefore, no estimation of bystander exposure for application of AATERRA ME in greenhouses is performed.

Workers

According to the notifier, AAATERRA ME is applied to substrates (as a root and substrate fungicide) and therefore no dislodgeable residues are anticipated and no exposure of workers when handling treated plants. This is acceptable and it is indeed assumed that dermal expsore of the workers is negligible. However, during and after treatment via the irrigation system, workers can be present in the glasshouses for re-entry activities.

Given the volatility of etridiazole and the soil/water metabolite dichloro-etridiazole, occurrence of etridiazole and dichloro-etridiazole in air cannot be excluded a priori. Based on the estimated air concentrations of etridiazole and dichloro-etridiazole (submitted by the notifier), the respiratory exposure of the workers during re-entry activities was calculated. Based on the molecular structure and the Derek analysis, it is assumed that the toxicity of dichloro-etridiazole is comparable to the toxicity of etridiazole. Therefore, the AOEL derived for etridiazole is also used for the risk assessment of dichloro-etridiazole.

Internal exposures and risk- assessments for the operator and worker are presented in Table 2.3.6.1 – Table 2.3.6.4.

Table 2.3.6.1 Operator internal exposure and risk assessment

Model	Route	Estimated internal exposure (mg a.s./day)		AOEL Systemic * (mg a.s/day)	% AOEL	
		without PPE	with PPE		without PPE	with PPE
Mixing/loading AATTERRA ME for application on cucumber via drip irrigation						
UK- 75th	Respiratory	-	-	1.8	-	-
	Dermal	2.52	0.13	1.8	140	7
	Total	**2.52**	**0.13**	**1.8**	**140**	**7**
DE- GM	Respiratory	0.0005**	0.0005**	2.1	0.02	0.02
	Dermal	0.3629	0.0036	2.1	17	0.2
	Total	**0.36**	**0.004**	**2.1**	**17**	**0.2**

Model	Route	Estimated internal exposure (mg a.s./day)		AOEL Systemic * (mg a.s/day)	% AOEL	
		without PPE	with PPE		without PPE	with PPE
Mixing/loading AATTERRA ME for application on tomato and pepper via drip irrigation						
UK- 75th	Respiratory	-	-	1.8	-	-
	Dermal	3.78	0.19	1.8	210	11
	Total	**3.78**	**0.19**	**1.8**	**210**	**11**
DE- GM	Respiratory	0.001**	0.001**	2.1	0.05	0.05
	Dermal	0.7258	0.007	2.1	35	0.3
	Total	**0.73**	**0.008**	**2.1**	**35**	**0.4**
Mixing/loading AATTERRA ME for application on ornamentals via drip irrigation						
UK- 75th	Respiratory	-	-	1.8	-	-
	Dermal	25.2	1.26	1.8	1400	70
	Total	**25.2**	**1.26**	**1.8**	**1400**	**70**
DE- GM	Respiratory	0.0084**	0.0084**	2.1	0.4	0.4
	Dermal	6.048	0.0605	2.1	288	3
	Total	**6.06**	**0.07**	**2.1**	**288**	**3**

* Assuming a body weight of 60 kg for UK-POEM and 70 kg for German model
\- No data available
** exposure might be an underestimation, because exposure to vapours is not considered in the German model, see also below for further calculations

Calculated data for respiratory exposure of the operators during mixing and loading might be underestimations, because exposure to vapours is not considered in the German model.
No data were available on the exposure of operators during application.

The notifier submitted estimations of concentrations of etridiazole and dichloro-etridiazole in air due to volatilisation. Based on these estimates, the respiratory exposure of the operator was calculated.

Table 2.3.6.2 Estimated respiratory exposure of the operator

	Estimated respiratory exposure of the operator to etridiazole (mg/day)	Estimated respiratory exposure of the operator to dichloro-etridiazole (mg/day)
Vegetable crops	0.013 (= 0.6% of the AOEL)	0.0015 (= 0.07% of the AOEL)
Ornamentals	0.168 (= 8% of the AOEL)	0.019 (= 0.9% of the AOEL)

The calculations in Table 2.3.6.2 illustrate that the respiratory exposure of the operator was indeed underestimated by the German model. However, the additional calculations of the respiratory exposure

based on estimated air concentrations, do not change the conclusions drawn based on calculations with UK-POEM and the German model.

Table 2.3.6.3 Worker internal exposure and risk assessment for etridiazole

Model *	Route	Estimated internal exposure (mg a.s./day)		AOEL systemic ** (mg a.s/day)	% AOEL	
		without PPE	with PPE		without PPE	with PPE
Re-entry exposure during and after application of AATERRA ME via drip irrigation in vegetables						
	Respiratory	0.067	n.a.	2.1	3	n.a.
	Dermal	-	-	-	-	-
	Total	**0.067**	**n.a.**	**2.1**	**3**	**n.a.**
Re-entry exposure during and after application of AATERRA ME via drip irrigation in ornamentals						
	Respiratory	0.840	n.a.	2.1	40	n.a.
	Dermal	-	-	-	-	-
	Total	**0.840**	**n.a.**	**2.1**	**40**	**n.a.**

* No model available. Respiratory exposure of the worker was calculated based on estimated air concentrations.
* * Assuming a body weight of 70 kg
n.a. Not applicable
- The dermal exposure is not quantifiable.

Table 2.3.6.4 Worker internal exposure and risk assessment for dichloro-etridiazole

Model *	Route	Estimated internal exposure (mg a.s./day)		AOEL systemic ** (mg a.s/day)	% AOEL	
		without PPE	with PPE		without PPE	with PPE
Re-entry exposure during and after application of AATERRA ME via drip irrigation in vegetables						
	Respiratory	0.0076	n.a.	2.1	0.4	n.a.
	Dermal	-	-	-	-	-
	Total	**0.0076**	**n.a.**	**2.1**	**0.4**	**n.a.**
Re-entry exposure during and after application of AATERRA ME via drip irrigation in ornamentals						
	Respiratory	0.094	n.a.	2.1	4.5	n.a.
	Dermal	-	-	-	-	-
	Total	**0.094**	**n.a.**	**2.1**	**4.5**	**n.a.**

* No model available. Respiratory exposure of the worker was calculated based on estimated air concentrations.
* * Assuming a body weight of 70 kg
n.a. Not applicable
- The dermal exposure is not quantifiable.

Based on the available data from the exposure models and the additional calculations of the respiratory exposure, the following conclusions can be drawn:

- Safe uses for operators without PPE were identified for substrate grown cucumber, tomato and pepper, using the German model. Safe uses for operators with PPE were identified for substrate grown cucumber, tomato and pepper, and non-soil bound ornamentals using the German model and UK-POEM.
- No bystanders should be allowed in greenhouses during the application of AATERRA ME.
- Safe uses for workers without PPE were identified for substrate grown cucumber, tomato and pepper, and non-soil bound ornamentals, based on estimated air concentrations of etridiazole and dichloro-etridiazole.

2.4 Residues

2.4.1 Definition of the residues relevant to MRLs

Plant products

The residue definition for post-registration monitoring is proposed as etridiazole.

Animal products

Peppers, cucumbers and tomatoes are not constituents of animal feed. Therefore, use of etridiazole on substrate grown peppers, cucumbers and tomatoes will not lead to residues in animal products. No definition of the residue in animal products is required.

2.4.2 Residues relevant to consumer safety

Residues in products of plant origin

For tomatoes, 10 supervised residue trials are available. A sufficient number of residue trials is available.

For cucumber, 3 supervised residue trials are available. Five more trials are needed. One trial performed in The Netherlands (Ooltgensplaat) may be suitable provided storage stability is demonstrated.

For peppers, 2 supervised residue trials are available. Six more trials are needed.

Due to insufficient residue data, no MRLs for pepper and cucumber can be set at this moment.
An MRL of 0.02* mg/kg is proposed for tomato.

Substrate-grown tomatoes, peppers and cucumbers in glasshouses are high added value crops which are not intended for industrial processing. Household processing (e.g. washing) may be performed on these commodities. Processing studies may be asked when the intake of residues through a commodity uses >10% of the ADI. The evaluation of the need for processing studies is postponed pending submission of additional data (residue trials) allowing a risk assessment to be made.

Residues in products of animal origin

Peppers, cucumbers and tomatoes are not constituents of animal feed. Therefore, use of etridiazole on substrate grown peppers, cucumbers and tomatoes will not lead to residues in animal products. No definition of the residue in animal products is required.

Residue intakes by livestock animals and humans

Intakes by livestock animals

Not applicable.

Intake by humans

Consumer chronic risk assessment shows acceptable risks for the WHO-EU consumer diet (0.4% ADI) and the UK adult (0.006% ADI) and UK-toddler diet (0.01% ADI). Consumer acute intake shows acceptable risks for all consumer groups with the UK-toddler giving the highest risk (0.6% ARfD for tomato).

The RMS cannot judge at this moment whether the use of etridiazole according to the intended use for cucumbers and sweet peppers will or will not result in an unacceptable risk of adverse effects due to exposure to residues in these food products.

2.4.3 Residues relevant to worker safety

See toxicology section.

2.4.4 Proposed EU MRLs and compliance with existing MRLs

Community MRLs are proposed for tomato (0.02* mg/kg). Before MRLs can be calculated for cucumber and sweet pepper, a complete data base for sweet peppers and cucumbers should be available for each crop.

2.4.5 Proposed EU import tolerances and compliance with existing MRLs

Not applicable, since no non-EU applications are proposed in the intended use pattern.

2.4.6 Basis for differences, if any, in conclusions reached having regard to established or proposed CAC MRLs

Not applicable, since no Codex MRLs have been established or proposed yet.

2.5 Fate and behaviour in the environment

2.5.1 Definition of the residues relevant to the environment

Detailed guidance to define the environmental residue is not available. Provisionally therefore, the active substance and major metabolites are listed in the definition. The metabolites etridiazole acid and dichloro-etridiazole were formed at >10% AR under aerobic laboratory conditions in soil treated with etridiazole. The metabolite etridiazole acid was formed at >10% AR in the water phase and at >5% AR at two consecutive timepoints in the sediment of water/sediment systems treated with etridiazole. The metabolite dichloro-etridiazole was <10% AR at any time and never >5% AR at two consecutive timepoints in any compartment of water/sediment systems and therefore not included in the residue definition for water. No additional major photolysis or hydrolysis degradation products were observed. Dichloro-etridiazole and etridiazole are provisionally included in the residue definition for air (pending on the outcome of additional data requirements listed under B.8.8).

The major components of the environmental residue are therefore as follows:

Soil:	- (no exposure of soil)
Surface Water:	etridiazole, etridiazole acid
Sediment:	etridiazole, etridiazole acid
Ground water:	- (no exposure of groundwater)
Air:	etridiazole, dichloro-etridiazole, etridiazole acid (provisional)

2.5.2 Fate and behaviour in soil

Aerobic degradation

In laboratory studies on aerobic incubation of etridiazole at 20°C (two soils) and 25°C (one soil) (pH 6.0-7.4, 2.1-3.1% oc), etridiazole degraded with DT50 and DT90 values (recalculated to 20°C) of 2.22-67.9 days (mean 25.0 days) and 7.37-289 days (mean 104 days). The DT50 and DT90 values were derived from the best fit model (FOMC for the soil at 25°C and SFO for the soils at 20°C) and were corrected for volatilisation of etridiazole from soil. Hence, they represent half-lives for degradation and can be used as worst case endpoints to assess persistence (under practical use conditions volatilisation of etridiazole may contribute to its dissipation from treated soil).

Major metabolites (exceeding 10% AR at any time point or 5% AR at 2 consecutive time points) were etridiazole acid (maximum 31% AR on day 32) and dichloro-etridiazole (maximum 13.3% AR on day 4, including 1.3% AR volatilised dichloro-etridiazole). No other metabolite fractions >5% AR were observed.

DT50/DT90 values for dichloro-etridiazole were obtained from studies with etridiazole and were 4.66-178/33.3-590 days at 20°C with a mean of 63.5/224 days (3 soils). The DT50 and DT90 values were derived from the best fit model (SFO for the soil at 25°C and FOMC for the soils at 20°C). These values should be

considered worst case values for dissipation (degradation and volatilisation), as dissipation and formation may have occurred simultaneously. Since no correction for volatile losses of dichloro-etridiazole could be made, no DT50 values for degradation of this metabolite are available. DT50/90 values for etridiazole acid were obtained from studies with the metabolite and were (at 20°C) 7.64-36.5/25.4-121 days with a mean of 26.7/88.8 days (3 soils). The DT50 and DT90 values were derived from the best fit model (SFO for all soils). These values represent degradation of etridiazole acid.

Table 2.5.2-1 presents a summary of the available DT50 and DT90 values of etridiazole and major metabolites (to be used as persistence endpoints). Persistence endpoints can be used for modelling when obtained from SFO kinetics and when describing "degradation" (not dissipation). Modelling endpoints (for PECgw and STEP 3/4 PECsw) are given in Table 2.5.2-2.

Table 2.5.2-1 Laboratory DT_{50} and DT_{90} values (persistence) for the aerobic degradation or dissipation of etridiazole and major metabolites in soil, at 20°C (SFO unless indicated differently)

substance	soil	pH	% oc	mois-ture	dose (mg/kg)	temp. (°C)	DT_{50} (d)	DT_{90} (d)	**DT_{50} (20°C, d)**	**DT_{90} (20°C, d)**
Etridiazole	sandy loam	6.6	2.4	75% FC	5.0	25	45.5[1]	194[1]	67.9	289
	loam	7.4	3.1	pF 2.5	3.6	20	2.22	7.37	2.22	7.37
	sandy loam	6.0	2.1	pF 2.5	3.7	20	4.80	16.0	4.80	16.0
	mean								**25.0**	**104**
Dichloro-etridiazole	sandy loam	6.6	2.4	75% FC	5.0[2]	25	119[3]	395	178	590
	loam	7.4	3.1	pF 2.5	3.6[2]	20	7.76[1,3]	47.7[1]	7.76	47.7
	sandy loam	6.0	2.1	pF 2.5	3.7[2]	20	4.66[1,3]	33.3[1]	4.66	33.3
	mean								**63.5**	**224**
Etridiazole acid	sandy loam	6.0	2.1	45% MWHC	0.86	20	36.0	120	36.0	120
	loam	7.4	3.1	45% MWHC	0.86	20	36.5	121	36.5	121
	sandy loam	5.1	3.6	45% MWHC	0.86	20	7.64	25.4	7.64	25.4
	mean								**26.7**	**88.8**

[1] based on first order multicompartment model (FOMC)
[2] this represents the dose of the parent compound etridiazole
[3] half-life for dissipation (degradation plus volatilisation)

Table 2.5.2-2 Laboratory DT_{50} values (modelling) for the aerobic degradation or dissipation of etridiazole and major metabolites in soil, at 20°C (SFO unless indicated differently)

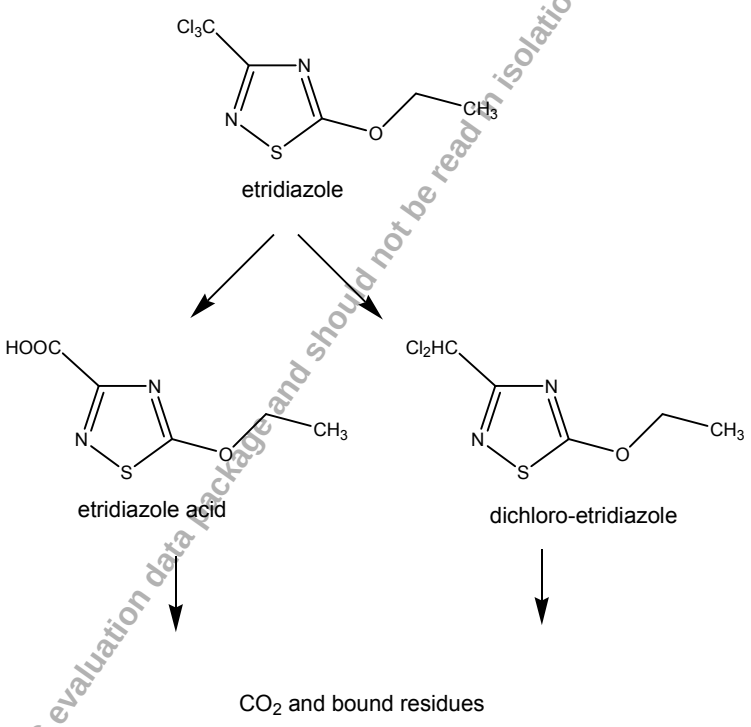
substance	soil	pH	% oc	mois-ture	dose (mg/kg)	temp. (°C)	DT_{50} (d)	**DT_{50} (20°C, d), pF 2/10 kPa**
Etridiazole	sandy loam	6.6	2.4	75% FC	5.0	25	58.4[1]	71.2
	loam	7.4	3.1	pF 2.5	3.6	20	2.22	2.22
	sandy loam	6.0	2.1	pF 2.5	3.7	20	4.80	4.80
	geometric mean							**9.12**
Dichloro-etridiazole	sandy loam	6.6	2.4	75% FC	5.0[2]	25	-[3]	-
	loam	7.4	3.1	pF 2.5	3.6[2]	20	-[3]	-
	sandy loam	6.0	2.1	pF 2.5	3.7[2]	20	-[3]	-
	geometric mean							**-**
Etridiazole acid	sandy loam	6.0	2.1	45% MWHC	0.86	20	36.0	30.4
	loam	7.4	3.1	45% MWHC	0.86	20	36.5	29.3
	sandy loam	5.1	3.6	45% MWHC	0.86	20	7.64	7.64
	geometric mean							**19.0**

[1] based on first order multicompartment model (FOMC)
[2] this represents the dose of the parent compound etridiazole
[3] no half-life for degradation is available

Mineralisation of etridiazole was observed in all soils: 8.2-22% AR on day 90-120 (25°C), maximum 8.7% on day 64, 4.8% AR on day 100 (soil 1, 20°C) and maximum 4.7% AR on day 100 (soil 2, 20°C). Non-extractable residues were also formed but never exceeded 70% AR: for etridiazole incubated at 25°C maximum 6.0% AR after 90 days and for etridiazole incubated at 20°C, maximum 40% and 33% AR after 100 and 32 days.

Aerobic metabolism of etridiazole proceeds due to microbial processes by simultaneous hydrolysis to etridiazole acid or dechlorination to dichloro-etridiazole. The ultimate breakdown products are CO_2 and non-extractable residues. Figure 2.5.2-1 shows the proposed metabolic pathway.

Figure 2.5.2-1 Aerobic metabolic pathway of Etridiazole in soil



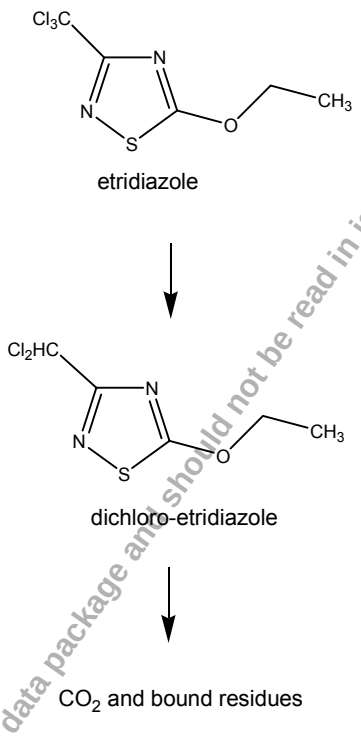
Anaerobic degradation

Data on anaerobic degradation of etridiazole in soil are not required because anaerobic conditions in soil treated with etridiazole are not anticipated, considering the proposed use pattern (greenhouse applications).

Etridiazole degraded under anaerobic conditions in a soil/water system with a (persistence) DT_{50}/DT_{90} of 0.59/1.97 (25°C) days (0.88/2.92 days at 20°C). The DT_{50} and DT_{90} values were derived from the best fit model (SFO) and were corrected for volatilisation of etridiazole from the soil. Hence, they represent the half-

life for degradation and can be used as endpoint to assess persistence. CO_2 production was 5.1% AR after 179 days (2.7% AR after 91 days) and unextractables were maximum 58% AR (day 91). Dichloro-etridiazole was the most important metabolite (maximum 41% AR on day 2) and dissipated with a (persistence) DT_{50}/DT_{90} (25°C) of 11.5/38.2 days (17.2/57.0 days at 20°C). The DT_{50} and DT_{90} values were derived from the best fit model (SFO) and should be considered worst case values for dissipation (degradation and volatilisation), as dissipation and formation may have occurred simultaneously. No other metabolites >10% AR or 2 x >5% AR were observed. Figure 2.5.2-2 shows the proposed metabolic pathway. The above mentioned DT_{50} values for etridiazole and dichloro-etridiazole can also be used as modelling endpoints.

Figure 2.5.2-2 Anaerobic metabolic pathway of Etridiazole in soil



Soil photolysis

The half-life of etridiazole in irradiated soil (330-800 nm: 151.7 W/m^2, 12 hour dark-light cycles) was 12.6 days. No significant degradation was observed in dark soil. Etridiazole acid was the most important metabolite in irradiated soil: maximum 32% AR (6.6% AR in dark soil). No other metabolites exceeded 10% AR. The degradation of etridiazole was accelerated under irradiated conditions but no specific photodegradation products (i.e. not occurring in dark samples) were observed.

Field dissipation trials

Field studies were not submitted. The laboratory DT_{50} of etridiazole and the major soil metabolite etridiazole acid at 20°C is <60 days. The DT_{50} (lab, 20°C) of the major soil metabolite dichloro-etridiazole (4.66-178 days, mean 63.5 days) however is >60 days. Therefore field studies (or more reliable laboratory studies

clearly indicating half-lives for degradation) are required for this metabolite when exposure of the soil compartment becomes relevant.

PECsoil estimations

Exposure of soil is not relevant for the intended uses (glasshouse, application through (drip-) irrigation system to non-soil bound ornamentals and substrate grown peppers, tomatoes and cucumbers).

Batch sorption

Table 2.5.2-3 presents a summary of the adsorption coefficients of etridiazole and the metabolites dichloro-etridiazole and etridiazole acid determined in batch sorption studies at 25°C and a soil:water ratios of 1:5.

Table 2.5.2-3 Adsorption coefficients of etridiazole and metabolites from batch sorption studies

substance	Soil	pH	% oc	CEC (meq/100 g)	% clay	K_F (L/kg)	1/n	Koc (L/kg)
Etridiazole	Sandy loam	6.6	2.4	8.9	8	8.21	0.86	349
	Clay	7.4	4.2	27	41	8.24	0.92	195
	Silt loam	7.3	1.6	17	23	5.06	0.84	323
	Mean					**7.17**	**0.87**	**289**
Dichloro-etridiazole	Sandy loam	6.6	2.4	8.9	8	2.77	0.81	118
	Clay	7.4	4.2	27	41	2.11	0.89	50
	Silt loam	7.3	1.6	17	23	1.99	0.83	128
	Mean					**2.29**	**0.84**	**99**
Etridiazole acid	Sandy loam	6.6	2.4	8.9	8	0.459	0.95	20
	Clay	7.4	4.2	27	41	0.547	0.84	13
	Silt loam	7.3	1.6	17	23	0.344	0.75	22
	Mean					**0.45**	**0.85**	**18**

No pH dependency of adsorption at the environmental relevant pH range is expected (based on pKa values of 2.77 for etridiazole and dichloro-etridiazole (set equal to parent) and 2.44 for etridiazole acid, charge transitions will only be significant outside of the environmental relevant pH range).

Non-aged column leaching

Reliable data were not submitted and are not required.

Aged column leaching

No studies submitted and not required.

PECgw estimations

Exposure of groundwater is not relevant for the intended uses (glasshouse, application through (drip-) irrigation system to non-soil bound ornamentals and substrate grown peppers/tomatoes/cucumbers).

Data requirements

Because exposure of soil is negligible for the representative uses included in the Annex I dossier, no further data on soil degradation are required.

2.5.3 Fate and behaviour in water

Hydrolysis

The hydrolysis half-lives at 25°C in distilled water, 0.01M phosphate buffered solutions of pH 5.2, 7.1 and 8.9 in the dark were 98, 92, 98 and 88 days, respectively. Etridiazole-acid was the only product of hydrolysis (65-72% AR). In additional experiments (start concentration ~6 mg/L) half-lives of 96, 98 and 97 days were obtained at pH 3, 6 and 9 at 25°C; 32, 31 and 24 days at 35°C and 11, 12 and 5.9 days at 45°C. Similar half-lives were observed at startconcentrations of ~45 mg/L. At pH 9 and 45°C (conditions giving highest hydrolysis rate), oxalic acid (<5% AR) was identified in addition to etridiazole acid.

Photolysis

No study was submitted. A study is not required because the molar absorption coefficient of etridiazole was <10 L mol^{-1} cm^{-1}

Biodegradability

Ready biodegradability

Etridiazole was not readily biodegradable in a closed bottle test.

Aerobic water/sediment studies

In two water/sediment systems, treated with [3-^{14}C]-etridiazole at a concentration of 839 µg/L and incubated at 20°C in the dark, etridiazole *degraded* in the total water/sediment system with (persistence & modelling) half-lives of 1.78 and 1.92 d. No half-life for the sediment could be calculated. The (persistence) half-lives for *dissipation* from the water layer were 1.33 and 1.29 d. CO_2 production was low (≤3.1% after 104 days). Significant amount of volatiles were trapped (up to 36-46% AR on day 104), containing mostly etridiazole. Unextractables were maximum 21 and 26% AR (day 14) and were 16-24% AR on day 104. Etridiazole acid was the most important metabolite in both water/sediment systems: maximum 13/8.3/<0.1% AR in water/sediment/volatiles on day 62/30/104. Other metabolites exceeding 5% AR in any compartment or total system were dichloro-etridiazole (maximum 9.5/1.4/3.2% AR in water/sediment/volatiles on day 2/2/104) and unidentified M5 (maximum 4.8/2.9/1.6% AR in water/sediment/volatiles on day 7/7-14/14). Other identified metabolites never exceeding 5% AR in any compartment were 3-OHM-T and 3-MCM-T. No other unidentified fractions exceeded 4.8% AR (total system). Dichloro-etridiazole dissipated in the total water/sediment system with (persistence & modelling) half-lives of 1.55 and 2.99 d. M5 dissipated in the total water/sediment system of one system with a (persistence) half-life of 17.2 d (no value could be calculated for the other system). For dichloro-etridiazole and M5, no half-life for the sediment could be calculated.

In two water/sediment systems, treated with [3-^{14}C]-etridiazole acid at a concentration of 167 µg/L and incubated at 20°C in the dark, etridiazole acid degraded in the total water/sediment system with (persistence & modelling) half-lives of 427 and 517 days. The (persistence) half-life in sediment (one system) was 291 days. The (persistence) half-lives for dissipation from the water layer were 320 and 189 days. CO_2

production was 15% AR after 180 days. Unextractables were maximum 3.3 and 4.3% AR (day 64 and 180, respectively).

The (persistence) half-lives of etridiazole and of the relevant (>10% AR in water) water/sediment metabolite etridiazole acid are listed in Table 2.5.3-1. DT_{50} values for modelling are listed in Table 2.5.3-2.

Table 2.5.3-1 Persistence DT_{50} and DT_{90} values (20°C) of etridiazole and etridiazole acid in water-sediment systems.

compound	System	DT_{50}			DT_{90}		
		water[1]	sediment[1]	total[2]	water	sediment	Total
Etridiazole	Espel	1.33[3]	-[5]	1.78[3]	4.41	-	5.91
	Rohrspitz	1.29[3]	-	1.92[3]	4.29	-	6.38
	mean	**1.31**		**1.85**	**4.35**		**6.15**
Etridiazole acid	River	320[4]	291[3]	427[3]	1547	968	1417
	Pond	189[4]	-	517[3]	1649	-	1718
	mean	**255**	**291**	**472**	**1598**	**968**	**1568**

[1] half-lives for dissipation
[2] half-lives for degradation
[3] based on SFO model
[4] based on DFOP model
[5] - : could not be calculated

Table 2.5.3-2 Modelling DT_{50} values (20°C) of etridiazole and etridiazole acid in water-sediment systems.

compound	System	DT_{50}		
		water	sediment	total
Etridiazole	Espel	1.78[1]	1.78[1]	1.78
	Rohrspitz	1.92[1]	1.92[1]	1.92
	mean	**1.85**	**1.85**	**1.85**
Etridiazole acid	River	427[1]	427[1]	427
	Pond	517[1]	517[1]	517
	mean	**472**	**472**	**472**

[1] values for total system are used for water and sediment

Anaerobic water/sediment studies
No study submitted (and not required).

The main transformations of etridiazole in the aquatic environment are shown in Figure 2.5.3-1.

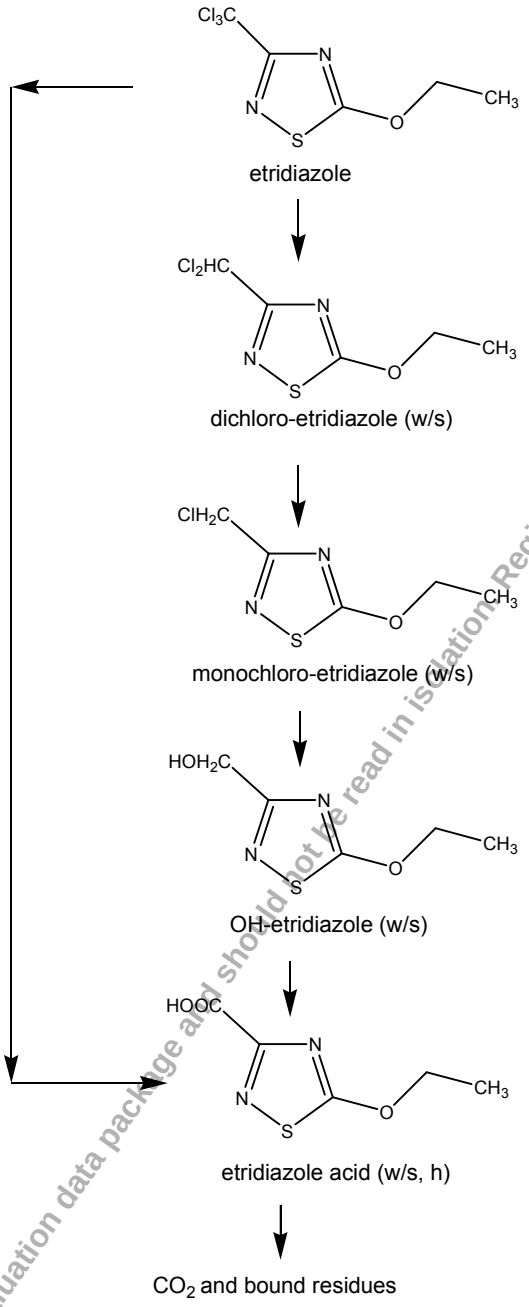


Figure 2.5.3-1 Metabolic pathway of etridiazole in water (h = hydrolysis, w/s = water/sediment)

PECsw estimations

Predicted environmental concentrations in surface water (PECsw) of etridiazole and the major (>10%) water/sediment metabolite etridiazole acid were calculated according STEP 2 procedures outlined in Sanco/4802/2001 rev.2 final (May 2003) “FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC” using FOCUS 1-2 software, version 1.1. Calculations for dichloro-etridiazole were also performed, although this metabolite is not a major water/sediment metabolite (<10%). STEP 1 calculations

were not performed because the STEP 1 default scenario is not applicable for greenhouse applications. In order to mimic a greenhouse application, inputs through runoff and drainage were set equal to zero. For soil, the mean (persistence) soil $DT_{50,lab}$ and the mean K_{om} was used in agreement with the guidance. For water and sediment, no individual DT_{50} values for degradation are available. Therefore the mean of the available (persistence) DT_{50} values for the whole water/sediment system was used for water and sediment.

All of the proposed uses on ornamentals, tomatoes, peppers and cucumbers involve greenhouse applications with limited exposure of surface water. An accepted EU sneario for emission from greenhouses to surface water is not available. In The Netherlands, an emission rate to surface water of 0.1% of the applied dose is used for greenhouse applications. The calculation was based on this surface water loading of 0.1% of the dose. STEP 2 calculations have a default drift value of 2.438% (2 applications). Therefore, the STEP 2 results were divided by a factor of 24.38 to obtain PECsw and PECsed concentrations relevant for a total assumed loading of 0.1% of the dose for greenhouse applications.

Under the above assumptions, application of etridiazole formulated as Aaterra ME 700 g/L according to to cGAP will lead to PEC_{SW} values of etridiazole, etridiazole acid and dichloro-etridiazole listed in Table 2.5.3-3 to -11.

Table 2.5.3-3 Calculated etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on ornamentals (2 x 7 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	2.343	-	2.244	-
1	1.313	1.828	1.685	1.965
2	0.884	1.464	1.168	1.695
4	0.417	1.046	0.552	1.263
7	0.135	0.706	0.179	0.866
14	0.010	0.377	0.013	0.465
21	0.001	0.253	0.001	0.312
28	0.000	0.190	0.000	0.234
42	0.000	0.126	0.000	0.156
50	0.000	0.106	0.000	0.131
100	0.000	0.053	0.000	0.065

Table 2.5.3-4 Calculated etridiazole acid concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on ornamentals (2 x 7 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.419	-	0.050	-
1	0.415	0.417	0.050	0.050
2	0.415	0.416	0.050	0.050
4	0.414	0.415	0.049	0.050
7	0.412	0.414	0.049	0.050
14	0.408	0.412	0.049	0.049
21	0.403	0.410	0.048	0.049
28	0.399	0.408	0.048	0.049
42	0.391	0.403	0.047	0.048

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
50	0.387	0.401	0.046	0.048
100	0.359	0.387	0.043	0.046

Table 2.5.3-5 Calculated dichloro-etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on ornamentals (2 x 7 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.193	-	0.083	-
1	0.132	0.162	0.064	0.073
2	0.097	0.138	0.047	0.064
4	0.052	0.106	0.026	0.050
7	0.021	0.075	0.010	0.036
14	0.002	0.042	0.001	0.020
21	0.000	0.028	0.000	0.013
28	0.000	0.021	0.000	0.010
42	0.000	0.014	0.000	0.007
50	0.000	0.012	0.000	0.006
100	0.000	0.006	0.000	0.003

Table 2.5.3-6 Calculated etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on tomatoes/peppers (2 x 0.56 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.187	-	0.180	-
1	0.105	0.146	0.135	0.157
2	0.071	0.117	0.093	0.136
4	0.033	0.084	0.044	0.101
7	0.011	0.057	0.014	0.069
14	0.001	0.030	0.001	0.037
21	0.000	0.020	0.000	0.025
28	0.000	0.015	0.000	0.019
42	0.000	0.010	0.000	0.012
50	0.000	0.008	0.000	0.010
100	0.000	0.004	0.000	0.005

Table 2.5.3-7 Calculated etridiazole acid concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on tomatoes/peppers (2 x 0.56 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.034	-	0.004	-
1	0.033	0.033	0.004	0.004
2	0.033	0.033	0.004	0.004
4	0.033	0.033	0.004	0.004
7	0.033	0.033	0.004	0.004
14	0.033	0.033	0.004	0.004
21	0.032	0.033	0.004	0.004
28	0.032	0.033	0.004	0.004
42	0.031	0.032	0.004	0.004
50	0.031	0.032	0.004	0.004
100	0.029	0.031	0.003	0.004

Table 2.5.3-8 Calculated dichloro-etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on tomatoes/peppers (2 x 0.56 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.015	-	0.007	-
1	0.011	0.013	0.005	0.006
2	0.008	0.011	0.004	0.005
4	0.004	0.008	0.002	0.004
7	0.002	0.006	0.001	0.003
14	0.000	0.003	0.000	0.002
21	0.000	0.002	0.000	0.001
28	0.000	0.002	0.000	0.001
42	0.000	0.001	0.000	0.001
50	0.000	0.001	0.000	0.000
100	0.000	0.000	0.000	0.000

Table 2.5.3-9 Calculated etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on cucumbers (2 x 0.28 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.094	-	0.090	-
1	0.053	0.073	0.067	0.079
2	0.035	0.059	0.047	0.068
4	0.017	0.042	0.022	0.051
7	0.005	0.028	0.007	0.035
14	0.000	0.015	0.001	0.019
21	0.000	0.010	0.000	0.012
28	0.000	0.008	0.000	0.009
42	0.000	0.005	0.000	0.006
50	0.000	0.004	0.000	0.005
100	0.000	0.002	0.000	0.003

Table 2.5.3-10 Calculated etridiazole acid concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on cucumbers (2 x 0.28 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.017	-	0.002	-
1	0.017	0.017	0.002	0.002
2	0.017	0.017	0.002	0.002
4	0.017	0.017	0.002	0.002
7	0.016	0.017	0.002	0.002
14	0.016	0.016	0.002	0.002
21	0.016	0.016	0.002	0.002
28	0.016	0.016	0.002	0.002
42	0.016	0.016	0.002	0.002
50	0.015	0.016	0.002	0.002
100	0.014	0.015	0.002	0.002

Table 2.5.3-11 Calculated dichloro-etridiazole concentrations in the water body (STEP 2) for greenhouse application (0.1% drift emission) on cucumbers (2 x 0.28 kg a.s./ha; cGAP)

Time (d)	PECsw (µg/L)		PECsed(µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
0	0.008	-	0.003	-
1	0.005	0.006	0.003	0.003
2	0.004	0.006	0.002	0.003
4	0.002	0.004	0.001	0.002
7	0.001	0.003	0.000	0.001
14	0.000	0.002	0.000	0.001
21	0.000	0.001	0.000	0.001
28	0.000	0.001	0.000	0.000
42	0.000	0.001	0.000	0.000
50	0.000	0.000	0.000	0.000
100	0.000	0.000	0.000	0.000

PECsed estimations

For calculations of sediment concentrations of etridiazole and etridiazole acid after application of etridiazole formulated as Aaterra ME 700 g/L in ornamentals, tomatoes, peppers and cucumbers, see Table 2.5.3-3 to -11.

Data requirements

No additional data requirements are identified to fulfil the data requirements of Annex II, point 7.2.

2.5.4 Fate and behaviour in air

Given the high volatility of etridiazole (as indicated by the high vapour pressure and high Henry's law constant), and the atmospheric DT_{50} of 1.556 days, occurrence of etridiazole in air and subsequent deposition cannot be excluded *a priori*. Significant losses of etridiazole through volatilisation were also observed in soil and water/sediment studies. The notifier is therefore requested to submit a risk assessment for the air compartment. The RMS realises that currently no final "FOCUS air" guidance is available. However, EPPO guidance is currently available for air (EPPO Bulletin 33, 115-129).

From the laboratory studies it can be concluded that also dichloro-etridiazole may volatilise from soil and water, although at lower quantities compared to etridiazole. The notifier is requested to submit a risk assessment for the air compartment for dichloro-etridiazole.

Concentrations of etridiazole and its major metabolite 3-DCM-T in air resulting from volatilisation and concentrations in soil and surface water based on successive deposition of parent and metabolite were calculated based on the models EVA 1.1 and EVA 2.0 (Exposure via Air) developed by the German Federal Environmental Agency (UBA) for registration purposes in Germany. Due to the intended application regime,

etridiazole may enter the different compartments only via volatilisation and deposition, whereas 3-DCM-T may additionally be formed in soils and surface waters following deposition of the parent substance.
Estimated concentrations of etridiazole in the air of glasshouses reached maximum values of 134.48 μg ai/m^3 for the intended use in ornamental crops and of 10.76 ug ai/m^3 for application to vegetables (tomatoes, peppers, cucumbers). For 3-DCM-T, maximum concentrations of 15.06 μg ai/m^3 (ornamental crops) and 1.21 μg ai/m^3 (vegetable crops) are encountered.
The initial predicted environmental concentrations of etridiazole in soil following application to ornamental crops at a rate of 7 kg ai/ha were estimated to be < 52.7 μg ai/kg soil. For application to vegetables at a rate of 0.56 kg ai/ha, initial values of < 4.21 μg ai/kg were encountered. Time weighted average PECS (based on the assumption that dissipation of etridiazole follows a first-order kinetic with a DT50 in soil of 8.98 days) ranged from 5.9 to 6.8 μg/kg after 100 days for application to ornamental crops and from 0.47 to 0.55 μg/kg for application to vegetable crops. Initial PEC_S of the metabolite 3-DCM-T resulting from both deposition of 3-DCM-T and on formation of 3-DCM-T outside the application area following deposition of etridiazole amounted to ≤ 11.80 and ≤ 0.95 μg/kg for the different application scenarios.
The initial predicted environmental concentrations of etridiazole in surface water following application to ornamental crops and vegetables were estimated to be ≤ 13.17 μg ai/L and ≤ 1.05 μg ai/L, respectively. Based on the assumption that dissipation of etridiazole follows a first-order kinetic with a DT50 of 1.85 days actual PECSw values were determined to be ≤ 0.01 μg/L after 21 and 14 days in the different application scenarios. Total initial PECSw of the metabolite 3-DCM-T were estimated to be ≤ 2.712 and ≤ 0.218 μg/L for application to ornamental crops and vegetables, respectively.

According to the RMS the FOCUS Air approach is not final therefore this approach should be discussed in an expert meeting.
Moreover because this approach was taken for the calculation of PEC_S and PEC_{SW} concentrations, The impact on the environmental risk assessment needs to be discussed.

2.6 Effects on non-target species

2.6.1 Effects on terrestrial vertebrates

For the application in ornamentals, tomatoes/peppers and cucumbers, (glass house), the routes of exposure for birds and mammals are considered to be limited to consumption of surface water and fish containing residues of etridiazole.

2.6.1.1 Birds

Avian toxicity data

Less reliable acute oral toxicity studies with etridiazole were submitted, from which the lowest LD50 was 560 mg a.s./kg bw (bobwhite quail).

Less reliable short-term dietary toxicity studies with etridiazole were supplied, from which the lowest LC50 was 286 mg a.s./kg bw/d (mallard duck).

Reproductive toxicity studies with etridiazole in mallard duck and bobwhite quail were submitted, in which there were no effects on reproductive parameters at 50 mg/kg diet, equivalent to 4.1 mg a.s./kg bw/day (males) and 4.2 and 3.7 mg a.s./kg bw/day (females), respectively.

Acute/short term risk assessment (active substance)

The acute/short term risk for birds as a result of consumption of water containing residues is performed based on the lowest acute/short term endpoint, the LC50 of 286 mg a.s./kg bw/d. The total water ingestion rate is based on a small bird of 10 g body weight. This leads to a total water ingestion rate of $0.059 \times 0.010^{0.67} = 2.7 \times 10^{-3}$ L water/d. The daily dose of the active substance etridiazole is based on the highest actual PECsw of 2.343 µg a.s./L (ornamentals) and is calculated to be $(2.343 \times 2.7 \times 10^{-3})/0.010 = 0.63$ µg a.s./kg bw/d. Thus, the TER for a small bird drinking contaminated surface water amounts 286000/0.63 = 452095. This TER is far above the trigger value of 10, which addresses the possible uncertainty associated with the lesser reliability of the endpoint.

Based on the above, the acute and short term risk for birds as a result of drinking contaminated surface water is considered acceptable.

Long-term risk assessment (bioaccumulation and food chain behaviour)

Long-term risk assessment is based on a fish-eating bird weighing 1000 g with a daily food intake (DFI) of 206 g fish/day.

Residue values in fish, ETE and TER values are presented in Table 2.6.1.1.1.

Table 2.6.1.1-1. Long-term toxicity Exposure Ratios for exposure of birds to etridiazole due to consumption of contaminated fish

appln. kg a.s./ha	Dose (kg as/ha)	NOEC (mg/kg bw/d)	PEC_{FEED} (mg/kg wwt)	ETE (mg/kg bw/d)	TERlt
Ornamentals	2 x 7.0	3.7	0.04	0.01	430
Tomatoes/peppers	2 x 0.56	3.7	3E-03	7E-04	5443
Cucumbers	2 x 0.28	3.7	2E-03	3E-04	10886

The long-term risk to birds as a result of bioaccumulation in fish is considered to be acceptable (TERlt above 5).

Conclusion:

Both the acute, short- and long-term risk is considered to be acceptable.

Bio-magnification in terrestrial food chains

The bioaccumulation potential reported in the List of Endpoints of the Toxicology section is stated to be low. Hence, according to the guidance provided in SANCO/4145/2000 – final (25 September 2002), the risk for biomagnification in terrestrial food chains is low.

Risk of metabolites for birds

Etridiazole acid

Etridiazole acid was the only major (>10%) metabolite in water (maximum in water 13%), which was also found in rat (20-36% AR in 0-24 h urine), orally dosed with parent etridiazole. Based on the low toxicity of this metabolite as compared to the parent for aquatic organisms (factor 100 less toxic) and earthworms (factor > 5 less toxic) and in view of the large margin of safety that was calculated for the parent in both the short- and long-term risk assessment, the risk for birds from etridiazole acid is considered as low. In addition, the experimental logPow of etridiazole acid is 0.7 (section B.2.1), and hence <3, therefore long-term risk to birds due to consumption of fish contaminated with etridiazole acid is considered to be acceptable.

MINOR METABOLITES

Dichloro-etridiazole

Dichloro-etridiazole was a minor metabolite in a water-sediment study (max. 9.5% AR in water, see section B.8.4), which was not found in rat (section B.6.1) orally dosed with etridiazole. The acute toxicity of this metabolite to fish and daphnia was a factor of about 3 higher than that of parent etridiazole (LC50 trout 0.77 mg/L *versus* 2.4 mg/L; EC50 daphnia 1.1 mg/L *versus* 3.1 mg/L), whilst its toxicity to algae was a factor of about 2 lower (EbC50 algae 0.62 mg/L *versus* 0.30 mg/L). On the basis of this information dichloro-etridiazole still possesses the active moiety.

However, in the acute risk assessment for the parent, a TER-value of 452095 was calculated, which means that the metabolite dichloro-etridiazole should be over a factor 45000 more toxic than the parent to show a risk (TER below 10). This is considered unlikely. For the long term risk assessment this factor should be over 86, which is also considered unlikely, and in addition the estimated logPow of dichloro-etridiazole is 2.7 (Table B.9.1), indicating a low potential for bioaccumulation.

Therefore, the risk for birds as a result of exposure to dichloro-etridiazole is considered acceptable.

Monochloro-etridiazole

Monochloro-etridiazole was a minor (<10%) metabolite in a water-sediment study (≤4.0% AR in any compartment, see section B.8.4), which was not found in rat (section B.6.1), orally dosed with parent etridiazole. No data are available on its occurrence in birds dosed with etridiazole. Data on the toxicity of this metabolite to birds, mammals and other aquatic or terrestrial organisms was not submitted. Monochloro-etridiazole may still possess the active moiety.

For this metabolite the same line of reasoning can be followed as for dichloro-etrididazole (large margin of safety calculated for the parent). In addition the estimated logPow of monochloro-etridiazole is 2.5 (Table B.9.1), indicating a low potential for bioaccumulation. The risk is considered acceptable.

3-Hydroxymethyl-etridiazole

3-Hydroxymethyl-etridiazole was a minor metabolite in a water-sediment study (≤3.4% AR in any compartment, see section B.8.4), which was not found in rat (section B.6.1), orally dosed with parent etridiazole. No data are available on its occurrence in birds dosed with etridiazole. Data on the toxicity of this metabolite to birds, mammals and other aquatic or terrestrial organisms was not submitted. This metabolite has lost the last chlorine atom, and is structurally more closely related to etridiazole acid than to parent etridiazole. Its toxicity profile is therefore likely to resemble that of etridiazole acid, rather than that of parent etridiazole.

For this metabolite the same line of reasoning can be followed as for etrididazole-acid (large margin of safety calculated for the parent). In addition the estimated logPow of 3-Hydroxymethyl-etridiazole is 0.78 (Table B.9.1), indicating a low potential for bioaccumulation. The risk is considered acceptable.

Conclusion:

The acute and long-term risk resulting from exposure of birds to the metabolites of etridiazole is low for all applications.

Mammals

Risk assessment (active substance)

The acute risk assessment is based on a small mammal weighing 10 g, with a daily water intake (DWI) of 1.6 mL/day.

The risk of bio-accumulation was considered for the route fish. The assessment was based on a fish-eating mammal weighing 3000 g with a daily food intake (DFI) of 390 g fish/day.

Residue levels in food and water, and ETE and TER values are presented in Table 2.6.1.2-1.

Table 2.6.1.2-1 Toxicity Exposure Ratios for exposure of mammals to etridiazole due to consumption of contaminated drinking water and fish

appln. (kg as/ha)	Time scale	Toxicity endpoint (mg a.s./kg bw or mg a.s./kg bw/day)	Route	PEC_{FEED} or PEC_{WATER} (mg/kg wwt or mg/L)	ETE (mg/kg bw/d)	TER
Ornamentals (2 x 7.0)	Acute	945	Water	2E-03	4E-04	3E+06
	Long-term	5.3	Fish	0.04	0.01	977
Tomatoes/peppers (2 x 0.56)	Acute	945	Water	2E-04	3E-05	3E+07
	Long-term	5.3	Fish	3E-03	4E-04	1E+04
Cucumbers (2 x 0.28)	Acute	945	Water	9E-05	1E-05	6E+07
	Long-term	5.3	Fish	2E-03	2E-04	2E+04

The acute and long-term risk to mammals is considered to be acceptable (TER above 10 and 5 for acute and long-term exposure).

Conclusion:

The acute and long-term risk is considered to be acceptable.

Risk of metabolites for mammals

Etridiazole acid was the only major (>10%) metabolite in water (maximum in water 13%), which was also found in rat (20-36% AR in 0-24 h urine), orally dosed with parent etridiazole. This metabolite is of low acute toxicity to rat (acute oral LD50 >2000 mg/kg bw).

Since the acute risk of etridiazole to mammals was considered acceptable (TERa ≥3E+06), the initial PECsw of etridiazole acid is 6 times lower than that of etridiazole, and the acute toxicity of this metabolite is 2 times lower than that of etridiazole, the acute risk of this metabolite to mammals is considered to be acceptable.

Since the experimental logPow of etridiazole acid is 0.7, and hence <3, the long-term risk to mammals due to consumption of fish contaminated with etridiazole acid is considered to be acceptable.

MINOR METABOLITES

Dichloro-etridiazole

Since no toxicity data are available for this metabolite, the LD50 needed to reach TERa<10 is calculated from the initial PECsw. Residue levels in water and ETE values are presented in Table 2.6.1.2-2, together with the LD50 that would result in TERa<10.

Table 2.6.1.2-2 PECwater and ETE values for exposure of mammals to dichloro-etridiazole due to consumption of contaminated drinking water, and LD50 values needed to reach TER<10

appln.	Dose (kg as/ha)	PEC_{WATER} (mg/L)	ETE (mg/kg bw/d)	LD50 (mg/kg bw/d)	Factor more toxic than etridiazole
Ornamentals	2 x 7.0	2E-04	3E-05	3E-04	3E+06
Tomatoes/peppers	2 x 0.56	2E-05	2E-06	2E-05	4E+07
Cucumbers	2 x 0.28	8E-06	1E-06	1E-05	8E+07

The TERa of the metabolite would only be below the trigger of 10 if the acute toxicity would exceed that of parent etridiazole by a factor of at least 3E+06. This is considered unlikely, and the risk is considered to be low for these applications.

Since the estimated logPow of dichloro-etridiazole is 2.7, and hence <3, the long-term risk to mammals due to consumption of fish contaminated with dichloro-etridiazole is considered to be acceptable.

Monochloro-etridiazole

The TERa of the metabolite would only be below the trigger value of 10 if the acute toxicity would exceed that of parent etridiazole by a factor of at least 9E+06. This is considered unlikely, and the acute risk is considered to be low.

Since the estimated logPow of monochloro-etridiazole is 2.5, and hence <3, the long-term risk to mammals due to consumption of fish contaminated with monochloro-etridiazole is considered to be acceptable.

3-Hydroxymethyl-etridiazole

The TERa of the metabolite would only be below the trigger value of 10 if the acute toxicity would exceed that of parent etridiazole by a factor of at least 1E+07. This is considered unlikely, and the acute risk is considered to be low.

Since the estimated logPow of 3-hydroxymethyl-etridiazole is 0.78 and hence <3, the long-term risk to mammals due to consumption of fish contaminated with 3-hydroxymethyl-etridiazole is considered to be acceptable.

Conclusion:

The acute and long-term risk resulting from exposure of mammals to the metabolites of etridiazole is low for all applications.

2.6.2 Effects on aquatic species

Summary of acute toxicity data

Results of studies on the acute toxicity of etridiazole and the metabolites etridiazole acid and dichloro-etridiazole to aquatic life are summarised in Table 2.6.2-1 to 2.6.2-3.

Table 2.6.2-1. The acute toxicity of etridiazole to aquatic life

Species	Test type	LC/EC_{50} (mg a.s./L) (95% CL)	NOEC (mg a.s./L)
Fish			
Oncorhynchus mykiss	Flow-through	2.4(A)	1.3(A)
Cyprinodon variegatus	Flow-through	4.0(A)	0.91(A)
Invertebrates			
Daphnia magna	Flow-through	3.1(A)	2.0(A)
Mysidopsis bahia	Flow-through	2.5(A)	0.61(A)
Crassostrea virginica	Flow-through	3.0(A)	0.94(A)
Algae			
Selenastrum capricornutum	Static	EbC50 0.30(B) ErC50 >1.0(B)	NOEbC & NOErC 0.027(B)
Anabaena flos-aquae	Static	EbC50 0.42(B) ErC50 >1.0(B)	NOEbC & NOErC 0.063(B)
Aquatic plants			
Lemna gibba	Static	EbC50 7.3(C) ErC50 14(C)	NOEbC 2.9(C) NOErC 5.7(C)

(A) Based on mean measured concentrations.
(B) Based on nominal concentrations (analytically confirmed for initial concentrations).
(C) Based on initial measured concentrations

Table 2.6.2-2. The acute toxicity of etridiazole acid to aquatic life

Species	Test type	LC/EC_{50} (mg a.s./L) (95% CL)	NOEC (mg a.s./L)
Fish			
Oncorhynchus mykiss	Static	>100(A)	100(A)
Invertebrates			
Daphnia magna	Static	350(B)	130(B)
Algae			
Selenastrum capricornutum	Static	EbC50 27(B) ErC50 29(B)	NOEbC & NOErC 12(B)

(A) Based on analytically confirmed nominal concentrations.
(B) Based on mean measured concentrations

Table 2.6.2-3. The acute toxicity of dichloro-etridiazole to aquatic life

Species	Test type	LC/EC_{50} (mg a.s./L) (95% CL)	NOEC (mg a.s./L)
Fish *Oncorhynchus mykiss*	Flow-through	0.77(A)	0.24(A)
Invertebrates *Daphnia magna*	Flow-through	1.1(A)	<0.39(A)
Algae *Selenastrum capricornutum*	Static	EbC50 0.62(A) ErC50 >0.98(A)	NOEbC 0.069(A) NOErC 0.15(A)

(A) Based on mean measured concentrations.

Summary of chronic toxicity data

Studies on the chronic toxicity of etridiazole are summarised in Table 2.6.2-4.

Table 2.6.2-4 The chronic toxicity of etridiazole to aquatic life

Species	Type of test	NOEC (µg a.s./L)
Oncorhynchus mykiss	90-day fish early life stage test	120(A)
Daphnia magna	21-day study	370(A)

(A) Based on mean measured concentrations.

Risk assessment (active substance)

Acute risk assessment will be based on the results of the studies with the active substance for fish, *Daphnia*, shrimp, algae and *Lemna.*

The acute TERs, based on the lowest of the available LC/EC50 values and initial PECsw values (calculated by FOCUS Step 2) for fish, *Daphnia magna*, shrimp, algae and *Lemna* are shown in Table 2.6.2-5.

Table 2.6.2-5 Acute TERs for etridiazole for fish, *Daphnia,* shrimp, algae and *Lemna*

Crop	Dose (kg a.s./ha)	LC/EC50 (µg as/L)					PECsw (µg as/L)	TER				
		Fish	*Daphnia*	Shrimp	Algae	*Lemna*		Fish	*Daphnia*	Shrimp	Algae	*Lemna*
O	2 x 7	2400	3100	2500	300	7300	2.343	1024	1323	1067	128	3116
T	2 x 0.56	2400	3100	2500	300	7300	0.187	1E+04	2E+04	1E+04	1604	4E+04
C	2 x 0.28	2400	3100	2500	300	7300	0.094	1E+04	3E+04	3E+04	3191	8E+04

O: ornamentals; T: tomatoes/peppers; C: cucumbers

The acute risk from the proposed use should be low for fish, *Daphnia*, shrimp, algae and aquatic plants (TER above 100 for fish, *Daphnia magna* and shrimp and above 10 for algae and *Lemna*).

The long-term TERs based on the initial PECsw are shown in Table 2.6.2-6.

Table 2.6.2-6 Long-term TERs for etridiazole assuming constant exposure to the initial PECs

Crop	dose (kg a.s./ha)	NOEC (µg as/L)		PECsw (µg a.s./L)	TER	
		Fish	*Daphnia*		Fish	*Daphnia*
Ornamentals	2 x 7.0	120	370	2.343	51	158
Tomatoes/peppers	2 x 0.56	120	370	0.187	642	1979
Cucumbers	2 x 0.28	120	370	0.094	1277	3936

The long-term TER for fish and *Daphnia* are all below the Annex VI trigger of 10. Therefore, the long-term risk is considered to be acceptable.

Bioaccumulation

In a bio-concentration study with 14C-etridiazole under flow-through conditions, the BCFs for etridiazole was 256 L/kg wet weight for whole fish. The Annex VI trigger factor is 100 L/kg for non-readily biodegradable substances. Etridiazole was not readily biodegradable in a closed bottle test. However, etridiazole does not exceed the triggers for a fish ELS or FLC test (EC50 >0.1 mg/L), nor that for evaluation of biomagnification in aquatic food chains (DT90 in water/sediment system 5.9-6.4 days, hence <10 days). In addition, the risk of poisoning of birds and mammals due to intake of contaminated fish was evaluated and found to be low. The risk for bioaccumulation is therefore considered to be of no concern.

Conclusion:

The acute and chronic risk of etridiazole is considered to be low. The risk for bioaccumulation is considered to be low.

Risk assessment of metabolites

Acute risk

Etridiazole acid

The worst-case TERs for this metabolite are summarised in Table 2.6.2-7.

Table 2.6.2-7 Acute TERs for etridiazole acid

	LC/EC50 (µg/L)			PECsw (µg/L)	TER		
Crop	Fish	*Daphnia*	Algae		Fish	*Daphnia*	Algae
Ornamentals	>100000	350000	27000	0.419	>2E+05	8E+05	6E+04
Tomatoes/peppers	>100000	350000	27000	0.034	>3E+06	1E+07	8E+05
Cucumbers	>100000	350000	27000	0.017	>6E+06	2E+07	2E+06

The acute TERs of etridiazole for fish, *Daphnia* and algae are all far above the relevant Annex VI triggers (100, 100 and 10, respectively). Hence the acute risk from the proposed use should be low.

Dichloro-etridiazole

The worst-case TERs for this metabolite are summarised in Table B.2.6.2-8.

Table 2.6.2-8 Acute TERs for dichloro-etridiazole

	LC/EC50 (µg/L)			PECsw	TER		
Crop	Fish	*Daphnia*	Algae	(µg/L)	Fish	*Daphnia*	Algae
Ornamentals	770	1100	620	0.193	3990	5699	3212
Tomatoes/peppers	770	1100	620	0.015	5E+04	7E+04	4E+04
Cucumbers	770	1100	620	0.008	1E+05	1E+05	8E+04

The acute risk from the proposed use should be low (TER for fish, *Daphnia* and algae above 100, 100 and 10, respectively).

Monochloro-etridiazole and 3-hydroxymethyl etridiazole

High safety margins were calculated for the acute risk for parent etridiazole (TERa ≥1024 for fish, daphnia and shrimp and ≥128 for algae and aquatic plants) and for the metabolites etridiazole acid and dichloro-etridiazole (TERa ≥3990 for fish and daphnia and ≥3212 for algae and aquatic plants). Given this fact, together with the low levels of the metabolites monochloro-etridiazole and 3-hydroxymethyl etridiazole, and the structural similarity between these two metabolites and those for which a very low risk was calculated, the acute risk of these minor metabolites is considered to be low.

Long-term risk

Etridiazole acid

Etridiazole acid is acutely not more toxic than parent etridiazole. Therefore, chronic testing is not required for this metabolite. Etridiazole acid was a minor metabolite in sediment (max. 8.3% AR). Therefore, testing with sediment-dwelling organisms is not required.

Dichloro-etridiazole

The safety margins for chronic exposure to parent etridiazole were large, (TERlt ≥51) and the initial concentrations of dichloro-etridiazole are much lower than those of the parent etridiazole (0.193, 0.015 and 0.008 µg/L as opposed to 2.343, 0.187 and 0.094 µg/L). Taking this into consideration, as well as the fact that the DT50 for dissipation from the water column is only slightly higher than 2 days, it is not expected that exposure to dichloro-etridiazole will lead to an unacceptable long-term risk. Therefore the chronic risk of this metabolite should be low. Dichloro-etridiazole was a minor metabolite in sediment (max. 1.4% AR). Therefore, testing with sediment-dwelling organisms is not required.

Monochloro-hydroxymethyl etridiazole

Monochloro-etridiazole was a minor metabolite in water and sediment (max. 4% AR). Therefore, testing with sediment-dwelling organisms is not required. Considering the close similarity between the molecular structures of monochloro-etridiazole, etridiazole and dichloro-etridiazole, the low chronic risk expected for etridiazole and dichloro-etridiazole, and the lower initial concentrations of monochloro-etridiazole compared to those of etridiazole and dichloro-etridiazole, it is not considered likely that the long-term risk due to exposure to monochloro-etridiazole will be higher than that of etridiazole or dichloro-etridiazole. The chronic risk of this metabolite to aquatic organisms should therefore be low.

3-Hydroxymethyl-etridiazole

3-Hydroxymethyl etridiazole was a minor metabolite in water and sediment (max. 3.4% AR). Therefore, testing with sediment-dwelling organisms is not required. Considering the close similarity between the molecular structures of 3-hydroxymethyl etridiazole and etridiazole acid, the large safety margin for the chronic risk of etridiazole acid and the lower initial concentrations of 3-hydroxymethyl etridiazole compared to those of etridiazole acid, it is not considered likely that the long-term risk due to exposure to 3-hydroxymethyl etridiazole will be higher than that of etridiazole acid. The chronic risk of this metabolite to aquatic organisms should therefore be low.

Bioaccumulation

No experimentally determined BCF values in fish are available for etridiazole acid, dichloro-etridiazole, monochloro-etridiazole and 3-hydroxymethyl etridiazole. An experimentally determined logPow value is available for etridiazole acid. LogPow values for dichloro-etridiazole, monochloro-etridiazole and 3-hydroxymethyl etridiazole were estimated by the RMS using EPA EPI Suite software. The BCF for fish can be estimated according to the formula logBCF=0.85*logPow-0.7 (USES 2.0). The logPow values and estimated BCF values are presented in Table 2.6.2-9.

Table 2.6.2-9 LogPow and BCF-values for metabolites of etridiazole

Metabolite	LogPow	BCF (L/kg)
Etridiazole acid	0.7	0.79
Dichloro-etridiazole	2.7(A)	39
Monochloro-etridiazole	2.5 (A)	27
3-Hydroxymethyl etridiazole	0.78 (A)	0.92

(A) Estimated by RMS using EPA EPI Suite software

The estimated BCF values are all below the Annex VI trigger of 100 and the risk of the above metabolites for bioaccumulation should be low.

Conclusion:

Acute and chronic exposure to metabolites of etridiazole is considered to be of no concern.

2.6.3 Effects on bees and other arthropod species

2.6.3.1 Bees

The risk for honey bees in the proposed uses in cucumber and peppers is considered acceptable, since normally honey bees are not used as pollinators in these uses. In tomatoes however, pollination always takes place by the use of bumblebees. RMS considers this as general practice in all member states. Therefore, the risk to bumblebees for the use in tomatoes should be addressed.

If etridiazole can be considered as non-systemic, exposure of bumblebees is considered not to take place. But etridiazole was found in tomatoes in a supervised residue trial (see section B.7.6.2). And etridiazole was also found in cucumbers after treatment with etridiazole in a hydroponic growth system (see section B.7.1.1, study 2). Although amounts found were low (max 23% TRR / 0.1 mg/kg and 0.034 – 0.023 mg/kg in cucumber and tomatoe respectively), and the amounts in flowers/pollen/nectar are unknown, this shows that etridiazole is absorbed by the roots of the plant and translocates to the fruits. Thus, etridiazole seems to have some systemic activity. Therefore it cannot be excluded that bumblebees used as pollinators in glasshouses will be exposed to etridiazole. Also, it cannot be excluded that bumblebees enter glasshouses, unless measures are taken to avoid entry of pollinators into glasshouses (e.g. by placing bee mesh in front of the openings). For the proposed use in glasshouse in tomatoes, bumblebees may therefore be exposed to etridiazole or its metabolites. No toxicity studies with honey bees or bumblebees were submitted, therefore the risk cannot be evaluated. Therefore, the notifier is requested to provide an acute oral toxicity study with bumblebees with the a.s. etridiazole, in order to enable a (first tier) risk assessment for the use in tomatoes.
(Reference for a bumblebee test could be for example: Steen JJM, Gretenkord C & Schaefer H (1996): Method to determine the acute oral LD50 and acute contact LD50 of pesticides for bumble bees (*Bombus terrestris* L.). Proc. 6th Int. Symp. on the hazard of pesticides for bumble bees (ICPBR), September 17-19, Braunschweig, Germany, appendix 28.)

2.6.3.2 Other arthropod species

Etridiazole was systemic in cucumber after treatment of the hydroponic culture (see section B.7.1.1). For the proposed uses in glasshouses (application through (drip-) irrigation system to non-soil bound ornamentals and substrate grown peppers, tomatoes and cucumbers), non-target arthropods may therefore be exposed to etridiazole or its metabolites. Exposure of soil is not relevant for the intended non-soil bound uses. A risk assessment is provided below.

The maximum recommended dose for glass substrate during dose-response laboratory tests for parasitiods and predatory mites will be 11900 g a.s./ha (applying a MAF of 1.7). Table 2.6.3.2-1 below summarises the results of laboratory testing with non-target arthropod species.

Table 2.6.3.2-1 Summary of effects of Aaterra ME on non-target arthropod species during laboratory testing

Species	Test type, Substrate	Max. recommended test dose (g a.s./ha)	Actual dose tested (g a.s./ha)	Effect (%) at respective dose in test and LR50 and ER50 (reproduction) values
Aphidius rhopalosiphi	Laboratory, glass	11900	720; 1980; 3240; 4500; 5760	10; 59; 100; 100; 100 (% mortality) 24; n.a. (A); n.a. (A); n.a. (A); n.a. (A) (% reduction of reproduction) LR50 (g a.s./ha): 1494 ER50 (g a.s./ha): >720
Typhlodromus pyri	Laboratory, glass	11900	72; 360; 720; 1440; 1440 (D); 2880 (D); 2880; 4320; 5760; 7200	0; 14; 20; 4; 12; 24; 18; 60; 23; 51(% mortality) 1; 7; -3 (B); 16; 22; 45; 18; n.a. (A); 65; n.a. (A) (% reduction of reproduction) LR50 (g a.s./ha): 5003 ER50 (g a.s./ha): 4200
Aphidius rhopalosiphi	Extended laboratory, barley seedlings	11900	360; 2520; 5040; 7200; 14400	0; 16; 12; 20; 96 (% mortality) n.a. (C); 29; 30; 41; n.a. (A) (% reduction of reproduction) LR50 (g a.s./ha): 8280 ER50 (g a.s./ha): >7200
Typhlodromus pyri	Extended laboratory, plant leafs	11900	72; 360; 720; 3600; 7200; 14400	4; 0; 0; 0; 59; 96 (% mortality) 4; -25 (B); -16 (B); 12; n.a. (A); n.a. (A) (% reduction of reproduction) LR50 (g a.s./ha): 6292 ER50 (g a.s./ha): >3600
Chrysoperla carnea	Extended laboratory, plant leaves	11900	5112; 8208; 11304; 14400	0; 0; 3; 0 (% mortality) n.a. (C); n.a. (C); -19 (B); 16 (% reduction of reproduction) LR50 & ER50 (g a.s./ha): >14400

(A) n.a. = not applicable (insufficient survivors from initial phase to assess reproduction).
(B) Note: negative effect %, hence no adverse effect.
(C) n.a. = not applicable (not tested)
(D) This dose was tested twice.

A Tier I assessment (HQ-approach) is performed using the data from the laboratory studies with *T. pyri* and *A. rhopalosiphi*. Table 2.6.3.2-2 below summarizes the results.

Table 2.6.3.2-2 Risk to *Typhlodromus pyri* and *Aphidius rhopalosiphi* as a result of in-field (0 m) exposure of the proposed Aaterra ME formulation in ornamentals, tomatoes/peppers and cucumbers (Hazard Quotient Approach), **based on LR50 values from inert substrate**

Crop / species	Dose g as/ha	Distance (m)	% drift	Exposure (g a.s./ha)	LR50 (g a.s./ha)	HQ Lethal	Trigger value
Typhlodromus pyri							
Ornamentals	2 x 7000	0	-	11900	5003	**2.4**	2
Tomatoes/ peppers	2 x 560	0	-	952	5003	0.2	2
Cucumbers	2 x 280	0	-	476	5003	0.1	2
Aphidius rhopalosiphi							
Ornamentals	2 x 7000	0	-	11900	1494	**8.0**	2
Tomatoes/ peppers	2 x 560	0	-	952	1494	0.6	2
Cucumbers	2 x 280	0	-	476	1494	0.3	2

The HQs for application in tomatoes/peppers and cucumbers were all below 2, and an in-field risk is not present for these applications. Since the HQs for in-field exposure for *T. pyri* and *A. rhopalosiphi* for application in ornamentals are above 2, an in-field risk is assumed to be present.

Data from the extended laboratory studies with *T. pyri*, *A. rhopalosiphi* and *C. carnea* are used for a higher tier risk assessment. In the extended laboratory study with *C. carnea* exposed to laboratory-sprayed leaves, no effects on survival and reproduction were noted at the highest test dose of 14400 g a.s./ha, hence effects on this species should be negligible.
Table 2.6.3.2-3 below summarises the results.

Table 2.6.3.2-3 Risk to *Typhlodromus pyri* and *Aphidius rhopalosiphi* as a result of in-field (0 m) exposure of the proposed Aaterra ME formulation in ornamentals (Hazard Quotient Approach), **based on LR50 and ER50 values on plant leaves**

Crop / species	Dose g as/ha	Distance (m)	% drift	Exposure (g a.s./ha)	LR50 (g a.s./ha)	ER50	HQ Lethal	HQ Sublethal	Trigger value
Typhlodromus pyri									
Ornamentals	2 x 7000	0	-	11900	6292	>3600	**1.9**	**3.3**	1
Aphidius rhopalosiphi									
Ornamentals	2 x 7000	0	-	11900	8280	>7200	**1.4**	**1.7**	1

The HQs for in-field exposure are above the trigger of 1 for *A. rhopalosiphi* and *T. pyri*. On the basis of this assessment there is still a risk.

However, all of the above calculations assume that the arthropods are exposed to the entire dose as if the product was sprayed on the leaves. This is not the case, since the product is applied by dripping onto the substrate. The relevant exposure route for non-target arthropods will therefore

be, due to the systemic behaviour of etridiazole, exposure of insects parasitizing or predating on 'sap sucking' insects that are contaminated with etridiazole.

The worst case application rate is 7 kg a.s./ha for ornamentals. For the risk assessment it is assumed that the concentration of etridiazole in the sap sucking insects is equal to that in the plants. However, assuming that the total dose added to the water is absorbed by the plants is an unrealistic worst case assumption. Data for refinement can be found in study 2 of section B.7.1, which describes the fate of etridiazole in cucumbers after treatment of the water in a hydroponic growth system. The lowest test dose of 2x21.3 mg per plant was in agreement with that of the proposed GAP. The maximum TRR in harvested cucumber was 0.911 mg eq./kg at 21 days after treatment. Data on plant and cucumber weight were not provided in the study report, but assuming that (1) each plant contains in total 8 kg of cucumbers (likely to be an unrealistic worst-case), (2) the remaining weight of the cucumber plant is 2 kg, (3) the residues are evenly distributed over the whole plant; the total residue in the entire plant with fruits is 10 X 0.911 = 9.11 mg eq.. This would suggest that the absorbed dose represents about (9.11/(2x21.3)=) 20% of the amount dosed into the water. Further, parent etridiazole represented at the most 23% of the TRR, 3 days after the first treatment, when the TRR (0.442 mg eq./kg) was much lower than the maximum TRR.

After correction of the exposure by the absorption rate of 20%, all HQ values would be below the trigger of 1 (lowered by factor 5), and they would be lower when degradation is taken into consideration. Although there are uncertainties associated with the above refinement (e.g. extrapolation from cucumber to ornamentals, even distribution of residues in whole plant), it should also be taken into account that both ER50 values were lower limit values, where no effect on reproduction was noted at the stated highest tested dose. Higher doses were not tested for effects on reproduction because of the high mortality. This suggests that the LR50 provides a good estimate to test effects on reproduction, and the trigger value of 1 was only slightly exceeded for evaluation using lethal effects.

It is reasonable to assume therefore, that the risk to non-target arthropods from the proposed applications will be acceptable.

Risk of metabolites

Major metabolites in cucumbers treated with etridiazole were 5-hydroxyethoxy etridiazole acid (max. 33% TRR), 3-hydroxymethyl etridiazole (max. 12% TRR), etridiazole acid (max. 18% TRR) and the glucose conjugate of 3-hydroxymethyl etridiazole (max. 17% TRR), while dichloro-etridiazole was a minor metabolite (max. 3.9% TRR). These major metabolites were present at 2.8-18%% TRR 3 days after application, and all non-conjugated metabolites had reached levels >10% TRR within 11 days, implicating that these metabolites were covered in the extended studies. Given the low risk for parent etridiazole, the risk of metabolites is considered low for the application through (drip) irrigation in the glasshouses.

2.6.4 Effects on earthworms and other soil macro-organisms

2.6.4.1 Effects on earthworms

Acute toxicity studies with Aaterra ME (LC50 198 mg a.s./kg dry soil) and etridiazole acid (LC50 >1000 mg/kg dry soil) were submitted. However, since the proposed uses are non-soil bound and in glasshouses, it is unlikely that earthworms will be exposed to etridiazole or its metabolites. Therefore the risk to earthworms is acceptable for these uses.

2.6.4.2 Effects on other soil macro-organisms

Since the proposed uses are non-soil bound and in glasshouses, it is unlikely that soil non-target macro-organisms will be exposed to etridiazole or its metabolites. Therefore the risk to soil non-target macro-organisms is acceptable for these uses.

2.6.5 Effects on soil micro-organisms

A study on the respiration and nitrification processes in soil treated with Aaterra ME was submitted (NOEC 3.36 and 3.49 mg a.s./kg soil for loamy sand and sandy loam, respectively). However, since the proposed uses are non-soil bound and in glasshouses, it is unlikely that soil non-target micro-organisms will be exposed to etridiazole or its metabolites. Therefore the risk to soil non-target micro-organisms is acceptable for these uses.

2.6.6 Effects on other non-target organisms (flora and fauna)

Since the proposed uses are non-soil bound and in glasshouses, it is unlikely that terrestrial non-target organisms will be exposed to etridiazole or its metabolites. Therefore the risk to terrestrial non-target organisms is acceptable for these uses.

For the tadpole, a non-target aquatic species, the exposure is negligible compared to the effect concentration (highest initial PECsw 2.343 µg/L as opposed to a median tolerance limit of 12 mg/L). Therefore the risk to this non-target organism is acceptable.

2.6.7 Effects on biological methods of sewage treatment

Given the nature of the proposed uses, it is unlikely that etridiazole will reach sewage treatment works in significant levels to have an impact on water treatment procedures (taking into consideration 30 min and 3 hour EC50 values for bacterial respiration of 105 and 32 mg a.s./L). Discharge of contaminated water from greenhouses may vary within the EU. This issue should be further addressed at MS level.

APPENDIX 1 STANDARD TERMS AND ABBREVIATIONS

Part 1 Technical Terms

A	ampere
ACh	acetylcholine
AChE	acetylcholinesterase
ADI	acceptable daily intake
ADP	adenosine diphosphate
AE	acid equivalent
AFID	alkali flame-ionization detector or detection
A/G	albumin/globulin ratio
ai	active ingredient
ALD_{50}	approximate median lethal dose, 50%
ALT	alanine aminotransferase (SGPT)
AOEL	acceptable operator exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
ARC	anticipated residue contribution
ARfD	acute reference dose
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BSAF	biota-sediment accumulation factor
BSE	bovine spongiform encephalopathie
BSP	bromosulfophthalein
Bt	Bacillus thuringiensis
Bti	Bacillus thuringiensis israelensis
Btk	Bacillus thuringiensis kurstaki
Btt	Bacillus thuringiensis tenebrionis
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
°C	degree Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CADDY	computer aided dossier and data supply (an electronic dossier interchange and archiving format)
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DNA
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre

CNS	central nervous system
COD	chemical oxygen demand
CPK	creatinine phosphatase
cv	coefficient of variation
Cv	ceiling value
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DES	diethylstilboestrol
DFR	dislodgeable foliar residue
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic Acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days pot inoculation
DRES	dietary risk evaluation system
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
&	decadic molar extinction coefficient
EC_{50}	median effective concentration
ECD	electron capture detector
ECU	European currency unit
ED_{50}	median effective dose
EDI	estimated daily intake
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EPMA	electron probe micro analysis
ERC	environmentally relevant concentration
ERL	extraneous residue limit
F	field
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FIA	fluorescence immuno assay
FID	flame ionization detector
FOB	functional observation battery
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
g	gram
G	glasshouse
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionization detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract

GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMO	genetically modified organism
GMM	genetically modified micro-organism
GPC	gel-permeation chromatography
GPPP	good plant protection practice
GPS	global positioning system
GSH	glutathion
GV	granulosevirus
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare
Hb	haemoglobin
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
hL	hectolitre
HEED	high energy electron diffraction
HID	helium ionization detector
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography - mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H_S	Shannon-Weaver index
Ht	haematocrit
I	indoor
I_{50}	inhibitory dose, 50%
IC_{50}	median immobilization concentration or median inhibitory concentration
ICM	integrated crop management
ID	ionization detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
inh	inhalation
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
iv	intravenous
IVF	*in vitro* fertilization
k	kilo
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole) (see also H) [1]
K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
kg	kilogram
L	litre
LAN	local area network

LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC_{Lo}	lethal concentration low
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LD_{Lo}	lethal dose low
LDH	lactate dehydrogenase
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometer (micron)
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
µg	microgram
mg	milligram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
MLT	median lethal time
MLD	minimum lethal dose
mm	millimetre
mo	month(s)
mol	Mole(s)
MOS	margin of safety
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level or limit
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
n	normal (defining isomeric configuration) or number of observations [1]
NAEL	no adverse effect level
nd	not detected
NEDI	national estimated daily intake
NEL	no effect level
NERL	no effect residue level
ng	nanogram
nm	nanometer

NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported
NTE	neurotoxic target esterase
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OM	organic matter content
op	organophosphorous pesticide
Pa	pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PC	personal computer
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIC	prior informed consent
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the dissociation constant)
PNEC	predicted no effect concentration
po	by mouth
P_{OW}	partition coefficient between n-octanol and water
POP	persistent organic pollutants
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
ppq	parts per quadrillion (10^{-24})
ppt	parts per trillion (10^{-12})
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	prothrombin time
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r	correlation coefficient

r^2	coefficient of determination
RBC	red blood cell
REI	restricted entry interval
Rf	retardation factor
RfD	reference dose
RH	relative humidity
RL_{50}	median residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	rotations per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
s	second
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SD	standard deviation
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
sq	square
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STMR	supervised trials median residue
t	tonne (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
TADI	temporary acceptable daily intake
TBC	tightly bound capacity
TCD	thermal conductivity detector
TC_{Lo}	toxic concentration, low
TID	thermionic detector, alkali flame detector
TD_{Lo}	toxic dose low
TDR	time domain reflectrometry
TER	toxicity exposure ration
TER_I	toxicity exposure ration for initial exposure
TER_{ST}	toxicity exposure ration following repeated exposure
TER_{LT}	toxicity exposure ration following chronic exposure
tert	tertiary (in a chemical name)
TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TIFF	tag image file format

TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TOC	total organic carbon
Tremcard	Transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UV	ultraviolet
v/v	volume ratio (volume per volume)
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
XRFA	X-ray fluorescence analysis
yr	year

<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

Part 2 Organisations and Publications

ACPA	American Crop Protection Association
ASTM	American Society for Testing and Materials
BA	Biological Abstracts (Philadelphia)
BART	Beneficial Arthropod Registration Testing Group
CA	Chemical Abstracts
CAB	Centre for Agriculture and Biosciences International
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCGP	Codex Committee on General Principles
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Food
CE	Council of Europe
CIPAC	Collaborative International Pesticides Analytical Council Ltd
COREPER	Comite des Representants Permanents
EC	European Commission
ECB	European Chemical Bureau
ECCA	European Crop Care Association
ECDIN	Environmental Chemicals Data and Information Network of the European Communities
ECDIS	European Environmental Chemicals Data and Information System
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
ECLO	Emergency Centre for Locust Operations
ECMWF	European Centre for Medium Range Weather Forecasting
ECPA	European Crop Protection Association
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EHC (number)	Environmental Health Criteria (number)
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMIC	Environmental Mutagens Information Centre
EPA	Environmental Protection Agency
EPO	European Patent Office
EPPO	European and Mediterranean Plant Protection Organization
ESCORT	European Standard Characteristics of Beneficials Regulatory Testing
EU	European Union
EUPHIDS	European Pesticide Hazard Information and Decision Support System
EUROPOEM	European Predictive Operator Exposure Model
FAO	Food and Agriculture Organization of the UN
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FRAC	Fungicide Resistance Action Committee
GATT	General Agreement on Tariffs and Trade
GAW	Global Atmosphere Watch
GIFAP	Groupement International des Associations Nationales de Fabricants de Produits Agrochimiques (now known as GCPF)
GCOS	Global Climate Observing System
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEDD	Global Environmental Data Directory
GEMS	Global Environmental Monitoring System
GIEWS	Global Information and Early Warning System for Food and Agriculture

GRIN	Germplasm Resources Information Network
HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IATS	International Academy of Toxicological Science
IBT	Industrial Bio-Test Laboratories
ICBB	International Commission of Bee Botany
ICBP	International Council for Bird Preservation
ICES	International Council for the Exploration of the Seas
ICPBR	International Commission for Plant-Bee Relationships
ILO	International Labour Organization
IMO	International Maritime Organisation
IOBC	International Organization for Biological Control of Noxious Animals and Plants
IPCS	International Programme on Chemical Safety
IRAC	Insecticide Resistance Action Committee
IRC	International Rice Commission
ISCO	International Soil Conservation Organization
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JECFA	FAO/WHO Joint Expert Committee on Food Additives
JFCMP	Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme
JMP	Joint Meeting on Pesticides (WHO/FAO)
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
NATO	North Atlantic Treaty Organisation
NAFTA	North American Free Trade Agreement
NCI	National Cancer Institute (USA)
NCTR	National Centre for Toxicological Research (USA)
NGO	non-governmental organization
NTP	National Toxicology Programme (USA)
OECD	Organization for Economic Co-operation and Development
OLIS	On-line Information Service of OECD
PAN	Pesticide Action Network
RNN	Re-registration Notification Network
RTECS	Registry of Toxic Effects of Chemical Substances (USA)
SCPH	Standing Committee on Plant Health
SETAC	Society of Environmental Toxicology and Chemistry
SI	Systeme International d'Unites
SITC	Standard International Trade Classification
TOXLINE	Toxicology Information On-line
UN	United Nations
UNEP	United Nations Environment Programme
WCDP	World Climate Data Programme
WCP	World Climate Programme
WCRP	World Climate Research Programme
WFP	World Food Programme
WHO	World Health Organization
WTO	World Trade Organization
WWF	World Wildlife Fund

Part 3

PREPARATION (FORMULATION) TYPES AND CODES*

Code	Description	Definition
AB	Grain bait	Special forms of bait.
AE	Aerosol dispenser	A container-held preparation which is dispersed generally by a propellant as fine droplets/particles upon actuation of a valve.
AL	Other liquids to be applied undiluted	Self defining.
BB	Block baits	Special forms of bait.
BR	Briquette	Solid block designed for controlled release of active ingredient into water.
CB	Bait concentrate	A solid or liquid intended for dilution before use as a bait.
CG	Encapsulated granule	A granule with a protective or release controlling coating.
CS	Capsule suspension	A stable suspension of capsules in a fluid normally intended for dilution with water before use.
DC	Dispersible concentrate	A liquid homogeneous preparation to be applied as a solid dispersion after dilution in water.
DP	Dustable powder	A free-flowing powder suitable for dusting.
DS	Powder for dry seed treatment	A powder for application in the dry state directly to seed.
EC	Emulsifiable concentrate	A liquid, homogenous preparation to be applied as an emulsion after dilution in water.
ED	Electrochargeable liquid	Special liquid preparation for electrostatic (electrodynamic) spraying.
EO	Emulsion, water in oil	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in water in a continuous organic liquid phase.
ES	Emulsion for seed treatment	A stable emulsion for application to the seed either directly or after dilution.
EW	Emulsion, oil in water	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in an organic liquid in a continuous water phase.
FD	Smoke tin	Special form of smoke generator.
FG	Fine granule	A granule in the particle size range from 300 to 2500 m.
FK	Smoke candle	A smoke generator in the form of a candle.
FP	Smoke cartridge	Special form of smoke generator.
FR	Smoke rodlet	Special form of smoke generator.

FS	Flowable concentrate for seed treatment	A stable suspension for application to the seed either directly or after dilution.
FT	Smoke tablet	Special form of smoke generator.
FU	Smoke generator	A combustible preparation generally solid, which upon ignition releases the active substances in the form of a smoke.
FW	Smoke pellet	Special form of smoke generator.
GA	Gas	A gas packed in pressure bottle or pressure tank.
GB	Granular bait	Special forms of bait.
GE	Gas generating product	A preparation which generates a gas by chemical reaction.
GG	Macrogranule	A granule in the particle size range from 2000 to 6000 m.
GP	Flo-dust	Very fine dustable powder for pneumatic application in glass-houses.
GR	Granule	A free-flowing solid preparation of a defined granule size range ready for use.
GS	Grease	Very viscous preparation based on oil or fat.
HN	Hot fogging concentrate	A preparation suitable for application by fogging equipment either directly or after dilution.
KN	Cold fogging concentrate	A preparation suitable for application by cold fogging equipment, either directly or after dilution.
LA	Lacquer	A solvent based film-forming preparation.
LS	Solution for seed treatment	A solution for application to the seed either directly or after dilution.
MG	Microgranule	A granule in the particle size range from 100 to 600 m.
OF	Oil miscible flowable (=oil active substances in a miscible suspension)	A stable suspension of concentrate fluid intended for dilution in an organic liquid before use.
OL	Oil miscible liquid	A liquid, homogenous preparation to be applied as a homogenous liquid after dilution in an organic liquid.
OP	Oil dispersible powder	A powder preparation to be applied as a suspension after dispersion in an organic liquid.
PA	Paste	A water based film forming preparation.
PB	Plate bait	Special forms of bait.
PC	Gel or paste concentrate	A solid preparation to be applied as a gel or a paste after dilution with water.
PR	Plant rodlet	A small rodlet, usually a few centimetres in length and a few millimetres in diameter containing active substance.
PS	Seed coated with a pesticide	Self defining.
RB	Bait (ready for use)	A preparation designed to attract and be eaten by the target species.

SB	Scrap bait	Special forms of bait.
SC	Suspension concentrate (= flowable concentrate)	A stable suspension of active substance(s) in a fluid intended for dilution with water before use.
SE	Suspo-emulsion	A fluid, heterogeneous preparation consisting of a stable dispersion of active substance(s) in the form of solid particles and of fine globules in a continuous water phase.
SG	Water soluble granules	A preparation consisting of granules to be applied as a true solution of active substance after dissolution in water but may contain insoluble inert ingredients.
SL	Soluble concentrate	A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.
SO	Spreading oil	A preparation designed to form a surface layer on application to water.
SP	Water soluble powder	A powder preparation to be applied as a true solution of the active substance after solution in water but which may contain insoluble inert ingredients.
SS	Water soluble powder for seed treatment	A powder to be dissolved in water before application to the seed.
SU	Ultra low volume (ULV) suspension	A suspension ready for use through ULV equipment.
TB	Tablet	Solid preparation in the form of small, flat plates for dissolution in water.
TP	Tracking powder	A rodenticidal contact preparation in powder form.
UL	Ultra low volume (ULV) liquid	A homogenous liquid ready for use through ULV equipment.
VP	Vapour releasing product	A preparation containing one or more volatile ingredients, the vapours of which are released into the air. Evaporation rate normally is controlled by using suitable preparations and/or dispensers.
WG	Water dispersible	A preparation granule consisting of granules to be applied after disintegration and dispersion in water.
WP	Wettable powder	A powder preparation to be applied as a suspension after dispersion in water.
WS	Water dispersible powder for slurry seed treatment	A powder to be dispersed at high concentration in water before application as a slurry to the seed.
XX	Others	

*based upon the catalogue of Pesticide Formulation types and International Coding Systems, developed by GIFAP in co-operation with the German working group on documentation questions. (Arbeitsgruppe EDV Pflanzenschutz Versuchswesen). GIFAP Technical Monograph No 2. 1989.

APPENDIX 2: SPECIFIC TERMS AND ABBREVIATIONS

a	absolute organ weight
AAP	Algal Assay Procedure medium
aerob	aerobic test conditions
a-GT	alpha-glutamyl-transferase
ALAT	alanine aminotransferase
ALP	alkaline phosphatase
amu	atomic mass units
anaer	anaerobic test conditions
AR	applied radioactivity in dermal studies, administered radioactivity in oral studies
ASAT	aspartate aminotransferase
ASTM	American Society for Testing and Materials
B	bacteria
biodeg	biodegradation
Chr. ab.	chromosome aberrations
CMC	carboxymethylcellulose
CoE	Council of Europe
crit.	criterion
d	decreased, but not statistically significantly
dc	statistically significantly decreased
DFI	Daily Food Intake
DMF	dimethylformamide
DO	Dissolved Oxygen
dr	dose-related
DWI	Daily Water Intake
E	total effect of mortality and fecundity/parasitic capacity, used in arthropod toxicity tests
E. coli	*Escherichia coli*
equal	used when the values given by the notifier are expressed in mg/kg bw/day.
equivalent	used when values given by the notifier are only expressed in mg/kg food, not in mg/kg bw/day, as species-dependent factor is used to translate these data to mg/kg bw/day.
ETE	Estimated Theoretical Exposure
GCP	good clinical practice
GIDH	glutamic-acid dehydrogenase

GOT	glutamic-oxalacetic transaminase
GPT	glutamic-pyruvic transaminase
HDL	high density lipoproteins
HPRT	hypoxanthine- guanine phosphoribosyl transferase
i	increased, but not statistically significantly
ic	statistically significantly increased
MC	moisture content in soil (v/v)
Mc	mammalian cells
MWHC	maximum water holding capacity (soils)
n/a	not applicable
n.d.	not detected
n.r.	not reported
ns	not significant
o.m.	organic matter
PEC	Predicted Environmental Concentration
PEG	polyethylene glycol
pF	moisture tension (soil) in [log $cm_{water\ column}$]
PIEC	Predicted Initial Environmental Concentration
pointmut.	pointmutations
r	relative organ weight
r.a.	radioactivity
res.	result
Ri	Reliability Index, referring to the intrinsic reliability of a test with respect to the quality of methodology and the description of the study. 1=reliable (can be used for risk assessment), 2=less reliable (can be used if reliable data are not available), 3=not reliable (can be used if reliable or less reliable data are not available), 4= no original data (reliable (can be used if reliable, less reliable, or unreliable data are not available).
S. typh.	*Salmonella typhimurium*
SPE	Solid Phase Extraction
Sub.	Substance
T	temperature

TWA	time weighted average
TWAEC	time weighted average environmental concentration
wat/sed	water/sediment systeem
w/w	weight per weight
-	negative
+	positive
-act.	without activation
+act.	with activation
%v/v	the percentage expressed by volume
%w/w	the percentage expressed by weight

APPENDIX 3

ETRIDIAZOLE

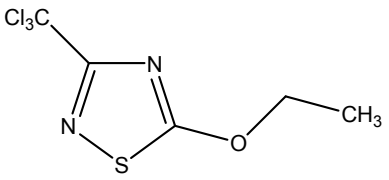
LIST OF END-POINTS

Chapter 2.1 Identity, Physical and Chemical Properties, Details of Uses, Further Information

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name)	Etridiazole
Function (*e.g.* fungicide)	Fungicide
Rapporteur Member State	The Netherlands

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	ethyl-3-trichloromethyl-1,2,4-thiazol-5-yl ether
Chemical name (CA)	5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole
CIPAC No	518
CAS No	2593-15-9
EEC No (EINECS or ELINCS)	219-991-8
FAO Specification (including year of publication)	Not available
Minimum purity of the active substance as manufactured (g/kg)	> 960 g/kg **To be discussed**
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	No relevant impurities
Molecular formula	$C_5H_5Cl_3N_2OS$
Molecular mass	247.5
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point	purity 99.7%: 22.0°C
Boiling point	purity 99.3%: 113°C (at reduced pressure; 0.53 kPa)
Temperature of decomposition	no decomposition up to a temperature of 113°C (boiling point at reduced pressure)
Appearance	pure material (99.7%) at 20°C: semisolid (mixture of a clear, colourless solid and a clear colourless liquid). pure material (99.7%) at 25°C: liquid with low viscosity and volatility. technical material (98.9%) at 20°C: semisolid (mixture of a clear, colourless solid and a yellow liquid). technical material (98.9%) at 25°C: liquid with low viscosity and volatility.
Relative density	purity 99.7%: 1.497 at 25°C
Surface tension	purity 99.8%: 71.9 mN/m (59.6 mg/L; 22°C; Ca 70% saturated solution)
Vapour pressure (in mBar and Pa, state temperature)	technical material: 0.01073 mm Hg at 25°C (equivalent to 1.43 Pa, calculated by RMS)
Henry's law constant (Pa m^3 mol^{-1})	3.02 Pa.m^3.mol^{-1} at 25°Csolids or liquids determined or calculated from water solubility and vp (units Pa m^3 mol^{-1})
Solubility in water (g/l or mg/l at 20 °C)	technical material at 25°C: 117.1 mg/L in water 85.8 mg/L in buffer pH 4 88.9 mg/L in buffer pH 7 89.7 mg/L in buffer pH 10
Solubility in organic solvents (in g/L or mg/L)	purity 99.5%, at 20°C: miscible in all proportions with n-Heptane, toluene, xylenes, dichloromethane, 1,2-dichloroethane, methanol, acetone, ethyl acetate and n-octanol.
Partition co-efficient (log P_{OW}) (state temperature)	purity 98.2%: Log P_{ow} (aqueous pH7 buffer/n-octanol) at 26°C to 27.5°C: 3.37. No effect of pH was required since there is no dissociation in the relevant pH range
Dissociation constant	purity 98.2%: pKa at 25°C: 2.77
UV/VIS absorption (max.) incl. ε (state purity, pH)	purity 99.7% acetonitrile solution: 0.2891x10^{-3} mol/L λmax (nm); ε (L.mol-1.cm-1) 220 5444 The maximum molar absorption coefficient of etridiazole (99.6%) over the range 290 to 800 nm was calculated to be 2.13 L.mol-1.cm-1 at 290 nm.
Flammability and auto-flammability	purity 99.8%: flammability (A.10): not applicable for liquids auto-ignition temperature (A.15): 342°C
Explosive properties	not explosive
Oxidising properties	not oxidizing

Classification and proposed labelling (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	No classification and labelling is needed based on the physical and chemical properties of the active substance etridiazole

Summary of representative uses evaluated (etridiazole)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
Non-soil bound glasshouse ornamental crops	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	n.a.	1-2	2 weeks	-	1000 min	0.7 g/m^2 substrate (7 kg/ha)	n.a.	
Substrate grown tomatoes	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28-0.56 kg/ha	3	
Substrate grown peppers	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28-0.56 kg/ha	7	
Substrate grown cucumbers	EU	AATERRA	G	Soil and root fungi (*Pythium & Phytophtera*)	ME	700 g/l	Application through drip-irrigation	ca. 81	1-2	2 weeks	-	1000 min	0.28 kg/ha	14	

* For uses where the column "Remarks" is marked in grey further consideration is necessary.
Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench

(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Chapter 2.2 Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	Dissolution in acetone containing internal standard (pentachlorobenzene) followed by GC-FID analysis.
Impurities in technical as (analytical technique)	Dissolution in solvent containing internal standard followed by GC-FID analysis.
Plant protection product (analytical technique)	Dissolution in acetonitrile:water containing internal standard (Di-n-amyl phtalate) followed by reversed phase HPLC-UV analysis.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Etridiazole, 3-hydroxymethyl etridiazole and 5-hydroxyethoxy etridiazole acid (provisional)
Food of animal origin		No residue definition required
Soil		Etridiazole, dichloro-etridiazole, etridiazole acid
Water	surface	Etridiazole, etridiazole acid
	drinking/ground	No residue definition required
Air		Etridiazole, dichloro-etridiazole, etridiazole acid (provisional)

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Single Method AC-3012A (etridiazole): GC-MS 0.01 mg/kg (peppers, crops with high water content) **Data requirement** for metabolites 3-hydroxymethyl etridiazole and 5-hydroxyethoxy etridiazole acid
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No methods required because no residue definition for animal products is proposed.
Soil (analytical technique and LOQ)	Method AC 6003: GC-TSD 0.01 mg/kg (etridiazole) 0.01 mg/kg (dichloro-etridiazole) 0.01 mg/kg (etridiazole acid) Confirmation with GC-MS
Water (analytical technique and LOQ)	Method AC 7001: GC-NPD 0.1 µg/L (etridiazole) 0.1 µg/L (dichloro-etridiazole) 0.1 µg/L (etridiazole acid) matrix: surface water (also applicable for drinking and groundwater) Confirmation with GC-MS

Air (analytical technique and LOQ)	Method: no method number specified GC-MS 0.9 µg/m³ **Data requirement** for dichloro-etridiazole and etridiazole acid
Body fluids and tissues (analytical technique and LOQ)	No method submitted. Not required because etridiazole is not a toxic substance.

Chapter 2.3 Impact on Human and Animal Health

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

Rate and extent of oral absorption	100 % (based on urinary (58-73%), faeces (assumed biliary) (14-16%) and expired air (4.2-7.2%), excretion within 168 h)
Distribution	Highest residues in skeletal muscle, liver, blood cells and bone at 168 h.
Potential for accumulation	No evidence for accumulation
Rate and extent of excretion	Rapid and extensive within 72 h: mainly via urine (51-67%), 13-16% via faeces, 4.2-7.2% via expired air (168 h)
Metabolism in animals	Extensively metabolised, main metabolite etridiazole carboxylic acid
Toxicologically relevant compounds (animals and plants)	Parent compound
Toxicologically relevant compounds (environment)	Parent compound and dichloro-etridiazole

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	> 945 mg/kg bw	**R22**
Rat LD_{50} dermal	> 5000 mg/kg bw	
Rat LC_{50} inhalation	> 5.7 mg/L air /4h (nose only)	
Skin irritation	Non-irritant	
Eye irritation	Non-irritant	
Skin sensitisation	Sensitising (M & K)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Liver (hypertrophy)	
Relevant oral NOAEL	13-week, rat, 2.7 mg/kg bw/day 1-year, dog, 3.1mg/kg bw/day	
Relevant dermal NOAEL	4-week, rat, 20 mg/kg bw/day	
Relevant inhalation NOAEL	4-week, rat, 15 mg/m^3	

Genotoxicity (Annex IIA, point 5.4)

Etridiazole is considered not genotoxic *in vivo*	

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

Target/critical effect	Kidney (tubular cell karyomegaly), liver (hepatotoxicity),	
Relevant NOAEL	< 5 mg/kg bw/day; 2-year, rat 7.5 mg/kg bw/day; 18-month, mouse	
Carcinogenicity	Tumours in liver, testes and thyroid	**R40**

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	Growth reduced and decreased thyroid weight at the parental toxic dose in the rat.	
Relevant parental NOAEL	5.3 mg/kg bw/day (organ weight changes, reduced bw and food consumptions)	
Relevant reproductive NOAEL	≥ 43 mg/kg bw/day (no fertility effects)	
Relevant offspring NOAEL	5.3 mg/kg bw/day (reduced bw, decreased thyroid weight)	

Developmental toxicity

Developmental target / critical effect	Developmental toxicity (e.g. foetus bw, retarded ossification, irreversible structural effecs) at maternally toxic dose	
Relevant maternal NOAEL	Rat: 30 mg/kg bw/day (mortality, reduced bw, critical effects not studied) Rabbit: 15 mg/kg bw/day (mortality, reduced bw, critical effects not studied)	
Relevant developmental NOAEL	Rat: 30 mg/kg bw/day (reduced bw, retarded ossification, no irreversible structural effects) Rabbit: 15 mg/kg bw/day (reduced bw, reduced lived foetuses, irreversible structural effects)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	No data-not required	
Repeated neurotoxicity	No data-not required	
Delayed neurotoxicity	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	Promotor activity detection test: etridiazole can act as a promotor, but with another profile than Phenobarbital. Promotor activity detection test: etridiazole at 400 mg/kg food can act as a promotor based on induction of phase II liver enzymes and reduction of connexin 32 protein in liver. Effects were not noted at 100 and 200 mg/kg food. Liver medium term Bioassay: etridiazole possesses promotor activity at 640 or 1280 mg/kg food, but not at 100 mg/kg food for hepatocarcinogenicity.
Studies performed on metabolites or impurities	Studies with 5-ethoxy-1,2,4-thiadiazol-3-carboxylic acid: LD_{50} oral> 2000 mg/kg bw, 13-week oral, NOAEL 39 mg/kg bw/day, non-genotoxic in Ames tes, Chromosome aberrations study and micronucleus test. Derek modeling of the metabolites dichloro-etridiazole, 5-hydroxy-ethoxyetridiazole acid and 3-hydroxymethyl etridiazole, is negative for human health hazard.

Medical data (Annex IIA, point 5.9)

Skin irritation/sensitisation in worker reported; no evidence of adverse effects in consumers.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI	0.005 mg/kg bw/day	rat, 2-year study	1000
AOEL	0.03 mg/kg bw/day	1-year dog study	100
ARfD	0.15 mg/kg bw	rabbit, developmental study	100

Dermal absorption (Annex IIIA, point 7.3)

Formulation (Terrazole 25 EC)	High dose (10 µg/cm^2): 18% Low dose (0.1 µg/cm^2): 30 %

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Safe uses calculated for mixing and loading according to the German model without PPE for substrate grown tomato and pepper (35% of

	AOEL),, and cucumber (17% of AOEL) Safe uses calculated for mixing and loading according to the German model with PPE for substrate grown tomato (0.4% of AOEL), pepper (0.4 of AOEL), cucumber (0.2% of AOEL) and ornamentals (3% of AOEL) Safe uses calculated for mixing and loading according to UK-POEM with PPE for substrate grown tomato and pepper (11% of AOEL), cucumber (7% of AOEL), and ornamentals (70% of AOEL)
Workers	Safe uses for workers without PPE were identified for substrate grown tomato, pepper and cucumber (3% of AOEL), and ornamentals (40% of AOEL), using estimated air concentrations of etridiazole
Bystanders	Bystanders should not be allowed in greenhouses.

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (etridiazole)	**Xn** "Harmful" **Xi** "Irritant" **R22** "Harmful if swallowed" **R43** "May cause sensitization by skin contact" **R40** "Limited evidence of a carcinogenic effect"

Chapter 2.4 Residues

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

Plant groups covered	Vegetables – fruits (cucumber) (substrate grown, drip application). Oilseeds (cotton) (soil treatment).
Rotational crops	No studies submitted. Not applicable.
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable.
Processed commodities	No studies submitted. A data requirement was identified in case dietary exposure exceeds 10% of the ADI.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No studies submitted.
Plant residue definition for monitoring	Etridiazole.
Plant residue definition for risk assessment	Etridiazole.
Conversion factor (monitoring to risk assessment)	None.

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

Animals covered	No studies submitted and not required.
Time needed to reach a plateau concentration in milk and eggs	Not applicable.
Animal residue definition for monitoring	No definition of the residue in animal products is required.
Animal residue definition for risk assessment	No definition of the residue in animal products is required.
Conversion factor (monitoring to risk assessment)	Not applicable.
Metabolism in rat and ruminant similar (yes/no)	Not applicable.
Fat soluble residue: (yes/no)	Not applicable.

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

No studies submitted. Not required for intended use.

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Etridiazole is stable for up to 13.8 months in tomato matrix during frozen storage (-20°C).

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Not applicable (no livestock feeding studies were submitted and not required)

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses	Recommendation/comments	MRL estimated from trials according to the representative use	HR	STMR
Tomatoes	Glasshouse	<0.01* (8x); <0.02* (2x)	sufficient number of trials	0.02*	-	-
Sweet pepper	Glasshouse	<0.01; 0.02	Insufficient number of trials	No MRL proposed	-	-
Cucumber	Glasshouse	<0.01*(2x), 0.07	Insufficient number of trials	No MRL proposed	-	-

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

ADI	0.005 mg/kg bw/d
TMDI (% ADI) according to WHO European diet	Not yet calculated (as MRL could not be set for all intended uses).
TMDI (% ADI) according to national (to be specified) diets	Not yet calculated (as MRL could not be set for all intended uses).
IEDI (WHO European Diet) (% ADI)	Not yet calculated (as MRL could not be set for all intended uses).
NEDI (specify diet) (% ADI)	Not yet calculated (as MRL could not be set for all intended uses).
Factors included in IEDI and NEDI	Not yet calculated (as MRL could not be set for all intended uses).
ARfD	0.15 mg/kg bw/d
IESTI (% ARfD)	0.4% (WHO-EU, tomato)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	0.6% (UK-toddlers, tomato) 0.1% (UK adults, tomato)
Factors included in IESTI and NESTI	Not yet calculated (as MRL could not be set for all intended uses

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No studies submitted. A potential data requirement was identified.				

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

Proposed MRLs	No MRLs for pepper and cucumber could be proposed at this moment.
Tomato	0.02* mg/kg

Chapter 2.5 Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	8.2% after 90 d, [3-^{14}C] etridiazole (n=1) 4.7-4.8% after 100 d, [3-^{14}C] etridiazole (n=2)
Non-extractable residues after 100 days ‡	6.0% after 90 d [3-^{14}C] etridiazole (n=1) 23-40% after 100 d [3-^{14}C] etridiazole (n=2)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	3-dichloromethyl-5-ethoxy-1,2,4-thiadiazole (dichloro-etridiazole) max 10.2% at 30 d (n=1) max 13.3/12.9% at 4/8 d (n=2) 5-ethoxy-1,2,4-thiadiazole-3-carboxylic acid (etridiazole acid) max 6.7% at 90 d (n=1) max 20-31% at 32-64 d (n=2)

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

Anaerobic degradation ‡

Mineralization after 100 days	2.7% after 91 d, [3-^{14}C] etridiazole (n=1)
Non-extractable residues after 100 days	58% after 91 d, [3-^{14}C] etridiazole (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	3-dichloromethyl-5-ethoxy-1,2,4-thiadiazole (dichloro-etridiazole) max 41% at 2 d (n=1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None The DT_{50} of etridiazole in irradiated soil was 12.6 days (at 151.7 W/m^2, 12 hour dark-light cycles)

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

Laboratory studies ‡

Parent	Aerobic conditions - **persistence endpoints**						
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C / 75% FC	45.5/194	67.9	0.98	FOMC
loam		7.4	20°C / pF 2.5	2.22/7.37	2.22	0.98	SFO
sandy loam		6.0	20°C / pF 2.5	4.80/16.0	4.80	0.96	SFO
Geometric mean/median/mean					8.98/4.80/25.0		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Parent	Aerobic conditions - **modelling endpoints**						
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C / 75% FC	45.5/194	71.2	0.98	FOMC
loam		7.4	20°C / pF 2.5	2.22/7.37	2.22	0.98	SFO
sandy loam		6.0	20°C / pF 2.5	4.80/16.0	4.80	0.96	SFO
Geometric mean/median/mean					9.12/4.80/26.1		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Dichloro-etridiazole	Aerobic conditions - **persistence endpoints**							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C/75% FC	119/395	-	178[2]	0.93	SFO
loam		7.4	20°C/pF 2.5	7.76/47.7	-	7.76[2]	0.96	FOMC
sandy loam		6.0	20°C/pF 2.5	4.66/33.3	-	4.66[2]	0.99	FOMC
Geometric mean/median/mean						18.6/7.76/63.5		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[2] worst-case half-life for *dissipation*

Dichloro-etridiazole	Aerobic conditions – **modelling endpoints**							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C/75% FC			not available		
loam		7.4	20°C/pF 2.5			not available		
sandy loam		6.0	20°C/pF 2.5			not available		
Geometric mean/median/mean						not available		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Etridiazole acid	Aerobic conditions - **persistence endpoints**							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C	St. (r^2)	Method of calculation
Sandy loam		6.0	20°C/45%	36.0/120	-	36.0	0.99	SFO
loam		7.4	20°C/45%	36.5/121	-	36.5	0.99	SFO
sandy loam		5.1	20°C/45%	7.64/25.4	-	7.64	0.99	SFO
Geometric mean/median/mean						21.6/36.0/26.7		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Etridiazole acid	Aerobic conditions - **modelling endpoints**							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		6.0	20°C/45%	36.0/120	-	30.4	0.99	SFO
loam		7.4	20°C/45%	36.5/121	-	29.3	0.99	SFO
sandy loam		5.1	20°C/45%	7.64/25.4	-	7.64	0.99	SFO
Geometric mean/median/mean						19.0/29.3/22.4		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Field studies ‡

Parent	Aerobic conditions **(no data submitted and not required)**								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Geometric mean/median									

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No data. Not required.

Laboratory studies ‡

Parent	Anaerobic conditions **(data submitted but not required for intended uses)**						
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C/flooded	0.59/1.97	0.88	0.98	SFO
Geometric mean/median/mean					0.88		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Dichloro-etridiazole	Anaerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C	St. (r^2)	Method of calculation
Sandy loam		6.6	25°C/flooded	11.5/38.2	-	17.2	0.99	SFO
Geometric mean/median						17.2		

[1] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.4	6.6			8.21	349	0.86
Clay	4.2	7.4			8.24	195	0.92
Silt loam	1.6	7.3			5.06	323	0.84
Arithmetic mean/median					7.17/8.21	289/323	0.87/0.86
pH dependence, Yes or No			No				

Dichloro-etridiazole ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.4	6.6			2.77	118	0.81
Clay	4.2	7.4			2.11	50	0.89
Silt loam	1.6	7.3			1.99	128	0.83
Arithmetic mean/median					2.29/2.11	99/118	0.84/0.83
pH dependence (yes or no)			No				

Etridiazole Acid ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.4	6.6			0.459	20	0.95
Clay	4.2	7.4			0.547	13	0.84
Silt loam	1.6	7.3			0.344	22	0.75
Arithmetic mean/median					0.45/0.46	18/20	0.85/0.84
pH dependence (yes or no)				No			

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

Column leaching ‡	No reliable data available. No data requirement.
Aged residues leaching ‡	No study submitted and not required.
Lysimeter/ field leaching studies ‡	No study relevant for the intended use was submitted. No data required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	Exposure of the soil compartment is negligible for the intended uses.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: 92 d at 25 °C (1st order, r^2=0.98) Etridiazole acid: 65 %AR (188 d)
	pH 7: 98 d at 25 °C (1st order, r^2=0.98) Etridiazole acid: 72 %AR (188 d)
	pH 9: 88 d at 25 °C (1st order, r^2=0.99) Etridiazole acid: 69 %AR (188 d)
Photolytic degradation of active substance and metabolites above 10 % ‡	Not required because the molar absorption coefficient of etridiazole was <10 L mol^{-1} cm^{-1}
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not required because the molar absorption coefficient of etridiazole was <10 L mol^{-1} cm^{-1}.
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Parent	**Persistence endpoints** Distribution (max in water 98% after 0 d. Max. sed 0.5% after 2 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Rohrspitz	8.1	7.5	20	1.92-6.38	0.98	1.29-4.29	1.0	-	-	SFO
Espel	8.0	7.7	20	1.78-5.91	0.98	1.33-4.41	0.99	-	-	SFO
Geometric mean				1.85-6.14		1.31-4.35		-		
Median				1.85-6.15		1.31-4.35		-		
Mean				1.85-6.15		1.31-4.35		-		

Parent	**Modelling endpoints**									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} whole sys.	St. (r^2)	DT_{50} water	St. (r^2)	DT_{50} sed	St. (r^2)	Method of calculation
Rohrspitz	8.1	7.5	20	1.92	0.98	1.92	-	1.92	-	SFO
Espel	8.0	7.7	20	1.78	0.98	1.78	-	1.78	-	SFO
Geometric mean				1.85		1.85		1.85		
Median				1.85		1.85		1.85		
Mean				1.85		1.85		1.85		

Etridiazole Acid	**Persistence endpoints** Distribution (max in water 13% after 62-104 d. Max. sed 8.3% after 30 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
River Rhine	8.3	7.5	20	427-1417	0.94	320-1547	0.98	291-968	0.97	SFO/DFOP[1]
Pond Ormalingen	8.4	7.3	20	517-1718	0.89	189-1649	0.97	-	-	SFO/DFOP[1]
Geometric mean				470-1560		246-1597		-		
Median				472-1568		255-1598		-		
Mean				472-1568		255-1598		291-968		

[1] SFO for whole system and sediment. DFOP for water column

Etridiazole Acid	**Modelling endpoints**									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} whole sys.	St. (r^2)	DT_{50} water	St. (r^2)	DT_{50} sed	St. (r^2)	Method of calculation
River Rhine	8.3	7.5	20	427	0.94	427	-	427	-	SFO
Pond Ormalingen	8.4	7.3	20	517	0.89	517	-	517	-	SFO
Geometric mean				470		470		470		
Median				472		472		472		
Mean				472		472		472		

Dichloro-etridiazole	**Persistence endpoints** Distribution (max in water 9.5% after 2 d. Max. sed 1.4% after 2 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
River Rhine	8.1	7.5	20	1.55-5.14	1.00	1.38-4.59	1.00	-	-	SFO
Pond Ormalingen	8.0	7.7	20	2.99-9.33	1.00	2.92-9.71	0.99	-	-	SFO
Geometric mean				2.15-6.93		2.01-6.68				
Median				2.27-7.24		2.15-7.15				
Mean				2.27-7.24		2.15-7.15				

Dichloro-etridiazole	**Modelling endpoints**									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} whole sys.	St. (r^2)	DT_{50} water	St. (r^2)	DT_{50} sed	St. (r^2)	Method of calculation
River Rhine	8.1	7.5	20	1.55[1]	1.00	1.55	-	1.55	-	SFO
Pond Ormalingen	8.0	7.7	20	2.99[1]	1.00	2.99	-	2.99	-	SFO
Geometric mean				2.15		2.15		2.15		
Median				2.27		2.27		2.27		
Mean				2.27		2.27		2.27		

[1] dissipation

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Rohrspitz	8.1	7.5	3.1% after 104 d	max 21% after 14 d	16% after 104 d
Espel	8.0	7.7	2.3% after 104 d	max 26% after 14 d	24% after 104 d

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

Parent	Version control no. of FOCUS calculator: vs 1.1
Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 247.5 Water solubility (mg/L): 117.1 K_{OC} (L/kg): 289 DT_{50} soil (d): 25.0 DT_{50} water/sediment system (d): 1.85 DT_{50} water (d): 1.85 DT_{50} sediment (d): 1.85
Parameters used in FOCUSsw step 3 (if performed)	not performed, not required
Application rate	Crop: ornamentals, peppers-tomatoes and cucumbers Crop interception: no interception (to simulate application through (drip) irrigation) Number of applications: 2 Interval (d): 14 Application rate(s): 7000 g as/ha (ornamentals); 560 g as/ha (peppers-tomatoes); 280 g as/ha (cucumbers) Application window: not relevant (no drainage/runoff) All intended uses are greenhouse applications. No greenhouse scenario is available in Step 1 and 2. Greenhouse applications were simulated by STEP 2 calculations selecting “no runoff/drainage” and correcting the drift factor to 0.1% (default for greenhouse emission).

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Ornamentals	0 h	2.343	-	2.244	-
	24 h	1.313	1.828	1.685	1.965
	2 d	0.884	1.464	1.168	1.695
	4 d	0.417	1.046	0.552	1.263

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	7 d	0.135	0.706	0.179	0.866
	14 d	0.010	0.377	0.013	0.465
	21 d	0.001	0.253	0.001	0.312
	28 d	0.000	0.190	0.000	0.234
	42 d	0.000	0.126	0.000	0.156

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Peppers/tomatoes	0 h	0.187	-	0.180	-
	24 h	0.105	0.146	0.135	0.157
	2 d	0.071	0.117	0.093	0.136
	4 d	0.033	0.084	0.044	0.101
	7 d	0.011	0.057	0.014	0.069
	14 d	0.001	0.030	0.001	0.037
	21 d	0.000	0.020	0.000	0.025
	28 d	0.000	0.015	0.000	0.019
	42 d	0.000	0.010	0.000	0.012

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Cucumber	0 h	0.094	-	0.090	-
	24 h	0.053	0.073	0.067	0.079
	2 d	0.035	0.059	0.047	0.068
	4 d	0.017	0.042	0.022	0.051
	7 d	0.005	0.028	0.007	0.035
	14 d	0.000	0.015	0.001	0.019
	21 d	0.000	0.010	0.000	0.012
	28 d	0.000	0.008	0.000	0.009
	42 d	0.000	0.005	0.000	0.006

Etridiazole acid	Molecular weight: 174.2
Parameters used in FOCUSsw step 1 and 2	Water solubility (mg/L): 117.1 (set equal to parent, no data) Soil or water metabolite: both Koc (L/kg): 18 DT_{50} soil (d): 26.7 DT_{50} water/sediment system (d): 472 DT_{50} water (d): 472 DT_{50} sediment (d): 472 Crop interception (%): No interception Maximum occurrence observed (% molar basis with respect to the parent) Water/sediment: 13% Soil: 31%
Parameters used in FOCUSsw step 3 (if performed)	Not performed, not required
Application rate	Crop: ornamentals, peppers-tomatoes and cucumbers Crop interception: no interception (to simulate application through (drip) irrigation) Number of applications: 2 Interval (d): 14 Application rate(s): 7000 g as/ha (ornamentals); 560 g as/ha (peppers-tomatoes); 280 g as/ha (cucumbers) Application window: not relevant (no drainage/runoff) All intended uses are greenhouse applications. No greenhouse scenario is available in Step 1 and 2. Greenhouse applications were simulated by STEP 2 calculations selecting “no runoff/drainage” and correcting the drift factor to 0.1% (default for greenhouse emission).
Main routes of entry	surface water (greenhouse emission 0.1%)

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Ornamentals	0 h	0.419	-	0.050	-
	24 h	0.415	0.417	0.050	0.050
	2 d	0.415	0.416	0.050	0.050
	4 d	0.414	0.415	0.049	0.050
	7 d	0.412	0.414	0.049	0.050
	14 d	0.408	0.412	0.049	0.049
	21 d	0.403	0.410	0.048	0.049

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	28 d	0.399	0.408	0.048	0.049
	42 d	0.391	0.403	0.047	0.048

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Peppers/tomatoes	0 h	0.034	-	0.004	-
	24 h	0.033	0.033	0.004	0.004
	2 d	0.033	0.033	0.004	0.004
	4 d	0.033	0.033	0.004	0.004
	7 d	0.033	0.033	0.004	0.004
	14 d	0.033	0.033	0.004	0.004
	21 d	0.032	0.033	0.004	0.004
	28 d	0.032	0.033	0.004	0.004
	42 d	0.031	0.032	0.004	0.004

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Cucumber	0 h	0.017	-	0.002	-
	24 h	0.017	0.017	0.002	0.002
	2 d	0.017	0.017	0.002	0.002
	4 d	0.017	0.017	0.002	0.002
	7 d	0.016	0.017	0.002	0.002
	14 d	0.016	0.016	0.002	0.002
	21 d	0.016	0.016	0.002	0.002
	28 d	0.016	0.016	0.002	0.002
	42 d	0.016	0.016	0.002	0.002

Dichloro-etridiazole	Molecular weight: 213.1
Parameters used in FOCUSsw step 1 and 2	Water solubility (mg/L): 117.1 (set equal to parent, no data) Soil or water metabolite: both Koc (L/kg): 99 DT_{50} soil (d): 63.5 DT_{50} water/sediment system (d): 2.27 DT_{50} water (d): 2.27 DT_{50} sediment (d): 2.27 Crop interception (%): No interception Maximum occurrence observed (% molar basis with respect to the parent) Water/sediment: 9.5% Soil: 13.3%
Parameters used in FOCUSsw step 3 (if performed)	Not performed, not required
Application rate	Crop: ornamentals, peppers-tomatoes and cucumbers Crop interception: no interception (to simulate application through (drip) irrigation) Number of applications: 2 Interval (d): 14 Application rate(s): 7000 g as/ha (ornamentals); 560 g as/ha (peppers-tomatoes); 280 g as/ha (cucumbers) Application window: not relevant (no drainage/runoff) All intended uses are greenhouse applications. No greenhouse scenario is available in Step 1 and 2. Greenhouse applications were simulated by STEP 2 calculations selecting “no runoff/drainage” and correcting the drift factor to 0.1% (default for greenhouse emission).
Main routes of entry	surface water (greenhouse emission 0.1%)

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Ornamentals	0 h	0.193	-	0.083	-
	24 h	0.132	0.162	0.064	0.073
	2 d	0.097	0.138	0.047	0.064
	4 d	0.052	0.106	0.026	0.050
	7 d	0.021	0.075	0.010	0.036
	14 d	0.002	0.042	0.001	0.020
	21 d	0.000	0.028	0.000	0.013

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	28 d	0.000	0.021	0.000	0.010
	42 d	0.000	0.014	0.000	0.007

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Peppers/tomatoes	0 h	0.015	-	0.007	-
	24 h	0.011	0.013	0.005	0.006
	2 d	0.008	0.011	0.004	0.005
	4 d	0.004	0.008	0.002	0.004
	7 d	0.002	0.006	0.001	0.003
	14 d	0.000	0.003	0.000	0.002
	21 d	0.000	0.002	0.000	0.001
	28 d	0.000	0.002	0.000	0.001
	42 d	0.000	0.001	0.000	0.001

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Cucumber	0 h	0.008	-	0.003	-
	24 h	0.005	0.006	0.003	0.003
	2 d	0.004	0.006	0.002	0.003
	4 d	0.002	0.004	0.001	0.002
	7 d	0.001	0.003	0.000	0.001
	14 d	0.000	0.002	0.000	0.001
	21 d	0.000	0.001	0.000	0.001
	28 d	0.000	0.001	0.000	0.000
	42 d	0.000	0.001	0.000	0.000

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Not required. Exposure of groundwater is negligible for the intended uses.
Application rate	-

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 18.67 hours (1.556 d) derived by the Atkinson model (AOP v1.91). OH (12 h) concentration assumed = $1.56x10^6$ OH/cm^3
Volatilisation ‡	Not studied – no data requested
	Not studied – no data requested
Metabolites	Dichloro-etridiazole

PEC (air)

Method of calculation	Concentrations of etridiazole and its major metabolite 3-DCM-T in air resulting from volatilisation and concentrations in soil and surface water based on successive deposition of parent and metabolite were calculated based on the models EVA 1.1 and EVA 2.0 (Exposure via Air) • Ornamental crops: 7 kg ai/ha * 13 % * 0.861 = 0.784 kg ai/ha • Vegetable crops: 0.56 kg ai/ha * 13 % * 0.861 = 0.063 kg ai/ha However, indoor application scenarios are not implemented in EVA 1.1. Parameters referring to greenhouses were thus derived from EVA 2.0. The calculation of the emission rate with EVA 1.1 is based on the assumption that the main factor influencing the emission of a compound is its vapour pressure. Default values for greenhouse dimensions from the model EVA 2.0 were used for the calculation of concentrations in air: - floor space of buildings = 300 m^2 - volume of building = 1000 m^3

PEC(a)

Maximum concentration	

Time after application (hours)	Air concentration etridiazole (µg a.s./m^3) after application in ornamentals (app. rate 7 kg a.s./ha)	Air concentration etridiazole (µg a.s./m^3) after application in vegetables (app. rate 0.56 kg a.s./ha)	Air concentration dichloro-etridiazole (µg a.s./m^3) after application in ornamentals (app. rate 0.784 kg a.s./ha)	Air concentration dichloro-etridiazole (µg a.s./m^3) after application in vegetables (app. rate 0.063 kg a.s./ha)
0 - 4	134.48	10.76	15.06	1.21
4 - 12	66.99	5.36	7.50	0.60
12 - 24	33.75	2.70	3.78	0.30
>24	0	0	0	0

Actual and time-weighted average (TWA) PEC_S of etridiazole in soil based on the entry route atmospheric deposition following volatilisation after application of 7 kg ai/ha to ornamental crops

Time after application [d]	PECs [ug/kg]					
	Distance of 1 m		Distance of 3 m		Distance of 5 m	
	Actual	TWA	Actual	TWA	Actual	TWA
0	52.7	-	49.0	-	45.6	-
1	48.8	50.7	45.4	47.2	42.2	43.9
2	45.1	48.8	42.0	45.4	39.1	42.3
4	38.7	45.3	36.0	42.2	33.5	39.3
7	30.7	40.7	28.6	37.9	26.6	35.3
14	17.9	32.2	16.6	30.0	15.5	27.9
21	10.4	26.1	9.7	24.3	9.0	22.6
28	6.1	21.6	5.6	20.1	5.3	18.7
42	2.1	15.6	1.9	14.5	1.8	13.5
100	0.0	6.8	0.0	6.3	0.0	5.9

Actual and time-weighted average (TWA) PECS of etridiazole in soil based on the entry route atmospheric deposition following volatilisation after application of 0.56 kg ai/ha to vegetables (tomatoes, peppers, cucumbers)

Time after application [d]	PECs [ug/kg]					
	Distance of 1 m		Distance of 3 m		Distance of 5 m	
	Actual	TWA	Actual	TWA	Actual	TWA
0	4.21	-	3.92	-	3.65	-
1	3.90	4.05	3.63	3.77	3.38	3.51
2	3.61	3.90	3.36	3.63	3.13	3.38
4	3.09	3.62	2.88	3.37	2.68	3.14
7	2.45	3.26	2.28	3.03	2.13	2.82
14	1.43	2.58	1.33	2.40	1.24	2.23
21	0.83	2.09	0.78	1.94	0.72	1.81
28	0.49	1.72	0.45	1.61	0.42	1.49
42	0.16	1.25	0.15	1.16	0.14	1.08
100	0.00	0.55	0.00	0.51	0.00	0.47

Initial PECS of 3-DCM-T related to atmospheric deposition following volatilisation and formation of 3-DCM-T following deposition of etridiazole and resulting total initial PECS of 3-DCM-T

PECs related to:	PECs [ug/kg]					
	Application to ornamental crops (7kg/ha etridiazole)			Application to ornamental crops (7kg/ha etridiazole)		
Distance of	1 m	3 m	5 m	1 m	3 m	5 m
Etridiazole (deposited)	52.67	49.03	45.64	4.21	3.92	3.65
Transformation factor	0.112					
3-DCM-T (formed in off-crop area)	5.90	5.49	5.11	0.47	0.44	0.41
3-DCM-T (deposited)	5.90	5.49	5.11	0.47	0.44	0.41
Total 3-DCM-T	**11.80**	**10.98**	**10.22**	**0.95**	**0.88**	**0.82**

Actual and time-weighted average (TWA) PECS of 3-DCM-T in soil after application of 7 kg/ha etridiazole to ornamental crops

Time after application [d]	PECs [ug/kg]					
	Distance of 1 m		Distance of 3 m		Distance of 5 m	
	Actual	TWA	Actual	TWA	Actual	TWA
0	11.80	_	10.98	-	10.22	-
1	11.37	11.58	10.58	10.78	9.85	10.04
2	10.95	11.37	10.19	10.58	9.49	9.85
4	10.16	10.96	9.46	10.20	8.81	9.50
7	9.09	10.38	8.46	9.67	7.88	9.00
14	7.00	9.19	6.52	8.56	6.07	7.97
21	5.39	8.18	5.02	7.62	4.67	7.09
28	4.16	7.32	3.87	6.82	3.60	6.35
42	2.47	5.96	2.30	5.55	2.14	5.17
100	0.28	3.09	0.26	2.88	0.25	2.68

Actual and time-weighted average (TWA) PEC_S of 3-DCM-T in soil after application of 0.56 kg/ha etridiazole to vegetables (tomatoes, peppers, cucumbers)

Time after application [d]	PECs [ug/kg]		
	Distance of 1 m	Distance of 3 m	Distance of 5 m

	Actual	TWA	Actual	TWA	Actual	TWA
0	0.95	-	0.88	-	0.82	-
1	0.91	0.93	0.85	0.86	0.79	0.80
2	0.88	0.91	0.82	0.85	0.76	0.79
4	0.81	0.88	0.76	0.82	0.71	0.76
7	0.73	0.83	0.68	0.77	0.63	0.72
14	0.56	0.74	0.52	0.69	0.49	0.64
21	0.43	0.66	0.40	0.61	0.37	0.57
28	0.33	0.59	0.31	0.55	0.29	0.51
42	0.20	0.48	0.18	0.44	0.17	0.41
100	0.02	0.25	0.02	0.23	0.02	0.21

Actual and time-weighted average PECSw of etridiazole in surface water based on the entry route atmospheric deposition following volatilisation after application of 7 kg ai/ha to ornamental crops

Time after application [d]	**PECsw [ug/L] Distance of**					
	1 m	3 m	5m	10 m	15m |	20m
Actual						
0	13.17	12.26	11.41	9.54	7.98	6.67
1	9.05	8.43	7.84	6.56	5.48	4.59
2	6.22	5.79	5.39	4.51	3.77	**3.15**
4	2.94	2.74	2.55	2.13	1.78	1.49
7	0.96	0.89	0.83	0.69	0.58	0.48
14	0.07	0.06	0.06	0.05	0.04	0.04
21	0.01	0.00	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00	0.00	0.00
100	0.00	0.00	0.00	0.00	0.00	0.00
Time-weighted average						
1	10.98	10.22	9.52	7.96	**6.65**	5.56
2	9.27	8.63	8.03	6.71	5.61	**4.69**
4	6.82	6.35	5.91	4.94	4.13	3.46
7	4.66	4.33	4.03	3.37	2.82	2.36
14	2.50	2.32	2.16	1.81	1.51	1.26
21	1.67	1.56	1.45	1.21	1.01	0.85
28	1.26	1.17	1.09	0.91	0.76	0.64
42	0.84	0.78	0.73	0.61	0.51	0.42
100	0.35	0.33	0.30	0.25	0.21	0.18

Actual and time-weighted average PECSw of etridiazole in surface water based on the entry route atmospheric deposition following volatilisation after application of 7 kg ai/ha to vegetables (tomatoes, peppers, cucumbers)

Time after application [d]	PECsw [ug/L] Distance of					
	1 m	3 m	5m	10 m	15m |	20m
Actual						
0	1.05	0.98	0.91	0.76	0.64	0.53
1	0.72	0.67	0.63	0.52	0.44	0.37
2	0.50	0.46	0.43	0.36	0.30	0.25
4	0.24	0.22	0.20	0.17	0.14	0.12
7	0.08	0.07	0.07	0.06	0.05	0.04
14	0.01	0.01	0.00	0.00	0.00	0.00
21	0.00	0.00	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00	0.00	0.00
100	0.00	0.00	0.00	0.00	0.00	0.00
Time-weighted average						
1	0.88	0.82	0.76	0.64	0.53	0.44
2	0.74	0.69	0.64	0.54	0.45	0.38
4	0.55	0.51	0.47	0.40	0.33	0.28
7	0.37	0.35	0.32	0.27	0.23	0.19
14	0.20	0.19	0.17	0.14	0.12	0.10
21	0.13	0.12	0.12	0.10	0.08	0.07
28	0.10	0.09	0.09	0.07	0.06	0.05
42	0.07	0.06	0.06	0.05	0.04	0.03
100	0.03	0.03	0.02	0.02	0.02	0.01

Initial PECsw of 3-DCM-T related to atmospheric deposition following volatilisation and formation of 3-DCM-T following deposition of etridiazole and resulting total initial PECS of 3-DCM-T

Time after application [d]	PECsw [ug/L] Distance of					
	1 m	3 m	5m	10 m	15m |	20m
Application to ornamental crops (7 kg/ha Etridiazole)						
Etridiazole (deposited)	13.167	12.257	11.410	9.540	7.976	6.669
Transformation factor	0.094					
3-DCM-T (formed in off-crop area)	1.238	1.152	1.073	0.897	0.750	0.627
3-DCM-T (deposited)	1.475	1.373	1.278	1.068	0.893	0.747
Total 3-DCM-T	2.712	2.525	2.350	1.965	1.643	1.374
Application to vegetable crops (0.56 kg/ha Etridiazole)						

Etridiazole (deposited)	1.053	0.981	0.913	0.763	0.638	0.534
Transformation factor	0.094					
3-DCM-T (formed in off-crop area)	0.099	0.092	0.086	0.072	0.060	0.050
3-DCM-T (deposited)	0.119	0.110	0.103	0.086	0.072	0.060
Total 3-DCM-T	0.218	0.202	0.188	0.158	0.132	0.110

Actual and time-weighted average PECSw of 3-DCM-T in surface water after application of 0.7 kg/ha etridiazole to ornamental crops

Time after application [d]	**PECsw [ug/L] Distance of**					
	1 m	3 m	5m	10 m	15m	20m
Actual						
0	2.712	2.525	2.350	1.965	1.643	1.374
1	1.999	1.861	1.732	1.448	1.211	1.012
2	1.473	1.371	1.276	1.067	0.892	0.746
4	0.800	0.744	0.693	0.579	0.484	0.405
7	0.320	0.298	0.277	0.232	0.194	0.162
14	0.038	0.035	0.033	0.027	0.023	0.019
21	0.004	0.004	0.004	0.003	0.003	0.002
28	0.001	0.000	0.000	0.000	0.000	0.000
42	0.000	0.000	0.000	0.000	0.000	0.000
100	0.000	0.000	0.000	0.000	0.000	0.000
Time-weighted average						
1	2.337	2.176	2.026	1.694	1.416	1.184
2	2.030	1.890	1.759	1.471	1.230	1.028
4	1.566	1.458	1.357	1.135	0.949	0.793
7	1.119	1.042	0.970	0.811	0.678	0.567
14	0.626	0.582	0.542	0.453	0.379	0.317
21	0.422	0.393	0.366	0.306	0.256	0.214
28	0.317	0.295	0.275	0.230	0.192	0.161
42	0.211	0.197	0.183	0.153	0.128	0.107
100	0.089	0.083	0.077	0.064	0.054	0.045

Actual and time-weighted average PECsw of 3-DCM-T in surface water after application of 0.56 kg/ha etridiazole to vegetables (tomatoes, peppers, cucumbers)

Time after application [d]	**PECsw [ug/L] Distance of**					
	1 m	3 m	5m	10 m	15m	20m
Actual						

Time after application [d]	PECsw [ug/L] Distance of					
	1 m	3 m	5m	10 m	15m	20m
0	0.218	0.202	0.188	0.158	0.132	0.110
1	0.160	0.149	0.139	0.116	0.097	0.081
2	0.118	0.110	0.102	0.086	0.072	0.060
4	0.064	0.060	0.056	0.046	0.039	0.032
7	0.026	0.024	0.022	0.019	0.016	0.013
14	0.003	0.003	0.003	0.002	0.002	0.002
21	0.000	0.000	0.000	0.000	0.000	0.000
28	0.000	0.000	0.000	0.000	0.000	0.000
42	0.000	0.000	0.000	0.000	0.000	0.000
100	0.000	0.000	0.000	0.000	0.000	0.000
Time-weighted average						
1	0.187	0.174	0.162	0.136	0.114	0.095
2	0.163	0.152	0.141	0.118	0.099	0.082
4	0.126	0.117	0.109	0.091	0.076	0.064
7	0.090	0.084	0.078	0.065	0.054	0.045
14	0.050	0.047	0.043	0.036	0.030	0.025
21	0.034	0.032	0.029	0.025	0.021	0.017
28	0.025	0.024	0.022	0.018	0.015	0.013
42	0.017	0.016	0.015	0.012	0.010	0.009
100	0.007	0.007	0.006	0.005	0.004	0.004

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: active substance, etridiazole acid Surface water: active substance, etridiazole acid Sediment: active substance, etridiazole acid Ground water: - (no exposure of groundwater) Air: active substance, dichloro-etridiazole

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data provided - none requested
Surface water (indicate location and type of study)	No data provided - none requested
Ground water (indicate location and type of study)	No data provided - none requested
Air (indicate location and type of study)	No data provided - none requested

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable

Chapter 2.6 Ecotoxicology

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds				
Bobwhite quail	a.s.	Acute	LD50 560 (1)	
Mallard duck	a.s.	Short-term	LC50 286 (2)	
Bobwhite quail	a.s.	Long-term	NOEC 3.7	NOEC 42
Mammals				
Rat	a.s.	Acute	LD50 945	-
Rat	a.s.	Long-term	NOEC 5.3	NOEC 80
Additional higher tier studies ‡				
No data available – not required				

(1,2) Endpoint considered as less reliable, since no data to confirm purity of the test substance(1) or validation of analytical method(2) is available, but endpoints taken as sufficiently reliable for risk assessment in view of the expected low exposure of birds as result of the intended uses (glasshouse).

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

Ornamentals, 2 x 7 kg a.s./ha (worst-case exposure)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Route: water	Acute	0.63	452095	10
Route: fish	Long-term	0.01	430	5
Tier 1 (Mammals)				
Route: water	Acute	4E-04	3E+06	10
Route: fish	Long-term	0.01	977	5

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[(1)] (mg/L)
Laboratory tests				
Fish				
Oncorhynchus mykiss	a.s.	96 hr (flow-through)	Mortality, EC_{50}	2.4 (mm)
	a.s.	90 d (flow-through)	ELS NOEC	0.12 (mm)
	Etridiazole acid	96 hr (static)	Mortality, EC_{50}	>100 (nom)
	Dichloro-etridiazole	96 hr (flow-through)	Mortality, EC_{50}	0.77 (mm)
Cyprinodon variegatus	a.s.	96 hr (flow-through)	Mortality, EC_{50}	4.0 (mm)
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (flow-through)	Mortality, EC_{50}	3.1 (mm)
	a.s.	21 d (flow-through)	Reproduction, NOEC	0.37 (mm)
	Etridiazole acid	48 h (static)	Mortality, EC_{50}	350 (mm)
	Dichloro-etridiazole	48 h (flow-through)	Mortality, EC_{50}	1.1 (mm)
Mysidopsis bahia	a.s.	96 h (flow-through)	Mortality, EC_{50}	2.5 (mm)
Crassostrea virginica	a.s.	96 h (flow-through)	Mortality, EC_{50}	3.0 (mm)
Sediment dwelling organisms				
No data submitted – no data required				
Algae				
Selenastrum capricornutum	a.s.	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.30 (nom) >1.0 (nom)
	Etridiazole acid	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	27 (mm) 29 (mm)
	Dichloro-etridiazole	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.62 (mm) >0.98 (mm)
Anabaena flos-aquae	a.s.	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.42 (nom) >1.0 (nom)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[(1)] (mg/L)
Higher plant				
Lemna gibba	a.s.	14 d (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}:	7.3 $_{(initial)}$ 14 $_{(initial)}$
Microcosm or mesocosm tests				
No data submitted – no data required				

[(1)] nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).

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

FOCUS Step 2

Ornamentals, 2 x 7 kg a.s./ha (worst-case exposure)

Test substance	Organism	Toxicity end point (µg/L)	Time scale	PEC_i (µg/L)	TER	Annex VI Trigger
a.s.	Fish	2400	Acute	2.343	1024	100
a.s.	Fish	120	Chronic	2.343	51	10
a.s.	Aquatic invertebrates	2500	Acute	2.343	1067	100
a.s.	Aquatic invertebrates	370	Chronic	2.343	158	10
a.s.	Algae	300	Chronic	2.343	128	10
a.s.	Higher plants	7300	Chronic	2.343	3116	10
Etridiazole acid	Fish	>100000	Acute	0.419	>2E+05	100
Etridiazole acid	Aquatic invertebrates	350000	Acute	0.419	8E+05	100
Etridiazole acid	Algae	27000	Chronic	0.419	6E+04	10
Dichloro-etridiazole	Fish	770	Acute	0.193	3990	100
Dichloro-etridiazole	Aquatic invertebrates	1100	Acute	0.193	5699	100
Dichloro-etridiazole	Algae	620	Chronic	0.193	3212	10

Bioconcentration			
	Active substance	Etridiazole acid	Dichloro-etridiazole
logP_{OW}	3.4	0.7	2.7 (estimated)
Bioconcentration factor (BCF)[1]	165 (etridiazole)	No data available – no data required	No data available – no data required
Annex VI Trigger for the bioconcentration factor	100		
Clearance time (days) (CT_{50})	<1		
(CT_{90})	>14		
Level and nature of residues (%) in organisms after the 14 day depuration phase	14%; nature not investigated		

[1] only required if log $P_{O/W}$ >3.

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

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
No data submitted – data required		
Field or semi-field tests		
No data submitted – no data required		

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g a.s./ha)
Typhlodromus pyri	a.s.	Mortality	5003
Aphidius rhopalosiphi	a.s.	Mortality	1494

Ornamentals, 2 x 7.0 kg a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
Aaterra ME	*Typhlodromus pyri*	5003	2.4	Not applicable	2
Aaterra ME	*Aphidius rhopalosiphi*	1494	8.0	Not applicable	2

Tomatoes/peppers, 2 x 0.56 kg a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
Aaterra ME	*Typhlodromus pyri*	5003	0.2	Not applicable	2
Aaterra ME	*Aphidius rhopalosiphi*	1494	0.6	Not applicable	2

Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)	End point	% effect [1]	Trigger value
Typhlodromus pyri	Proto-nymphs	a.s., leaf discs, 14 days	Initial: 72 360 720 3600 7200 14400	Mortality / reduction of reproduction	 4 / 4 0 / -25 0 / -16 0 / 12 59 / - 96 / -	50 %
Aphidius rhopalosiphi	<48 hour old wasps	a.s., plants, 48 hours	Initial: 360 2520 5040 7200 14400	Mortality / reduction of reproduction	 0 / not tested 16 / 29 12 / 30 20 / 41 96 / -	50 %
Chrysoperla carnea	2-3 day old larvae	a.s., leaves, 30 days	Initial: 5112 8208 11304 14400	Mortality / reduction of reproduction	 0 / not tested 0 / not tested 3 / -19 0 / 16	50 %

[1] The – sign means increase of reproduction

Ornamentals, 2 x 7.0 kg a.s./ha

Test substance	Species	Type effect (LR_{50} or ER_{50})	Effect (g/ha)	HQ in-field	Trigger
Aaterra ME	*Typhlodromus pyri*	LR_{50}	6292	1.9	1
Aaterra ME	*Typhlodromus pyri*	ER_{50}	>3600	3.3	1
Aaterra ME	*Aphidius rhopalosiphi*	LR_{50}	8280	1.4	1
Aaterra ME	*Aphidius rhopalosiphi*	ER_{50}	>7200	1.7	1

Field or semi-field tests
No data submitted – no data required HQ's are based on unrealistic worst case assumptions, since product is applied through dripping: refined risk assessment under section B.9.5.3.1.1 in the DAR, based on residue data from section B.7.1, exposure can be lowered by factor 5, which brings HQ's below trigger value.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
Eisenia fetida	a.s.	Acute 14 days	No data submitted – no data required
	Preparation	Acute	LC_{50} 198 mg a.s./kg soil
	Etridiazole acid	Acute	LC_{50} >1000 mg/kg soil
Other soil macro-organisms			
No data submitted – no data required			
Soil micro-organisms			
Nitrogen mineralisation	a.s.		No data submitted – no data required
	Preparation	Chronic	Loamy sand soil: NOEC 3.36 mg a.s./kg soil Sandy loam soil: NOEC 3.49 mg a.s./kg soil
Carbon mineralisation	a.s.		No data submitted – no data required
	Preparation	Chronic	Loamy sand soil: NOEC 33.6 mg a.s./kg soil Sandy loam soil: NOEC 34.9 mg a.s./kg soil
Field studies[2]			

Test organism	Test substance	Time scale	End point
No data submitted – no data required			

Toxicity/exposure ratios for soil organisms

Since the proposed uses are non-soil bound and in glasshouses, it is unlikely that soil non-target organisms will be exposed to etridiazole or its metabolites. Therefore no TER's are calculated.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

Etridiazole was not phytotoxic to spring wheat seeds (dose not reported).
Etridiazole was not phytotoxic to herbaceous and woody ornamental plants when applied once to the growth medium (dose not clear). Repeated application decreased the number of stem cankers.
Etridiazole was not toxic to soybean plants at doses of 1000, 2000 and 3000 mg a.s./kg seed.
Etridiazole was slightly toxic to tomatoes at doses of 30 and 60 mg Aaterra/kg.
Etridiazole did not affect corn growth at a dose of 2.5 mg a.s./kg soil.
Etridiazole increased corn yield by 78% and 25% in the first and second year after application at 0.6 kg Terrazole/ha.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/ha)	TER	Trigger
No data submitted – no data required						

Additional studies (e.g. semi-field or field studies)

No data submitted – no data required

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	30-min EC_{50} 105 mg a.s./L 3-hour EC_{50} 32 mg a.s./L
Pseudomonas sp	No data submitted – no data required

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Etridiazole
water	Etridiazole
sediment	No relevant compounds

groundwater	No relevant compounds

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	N, R50, R53

	RMS/peer review proposal
Preparation	N, R50, R53

LEVEL 3

Etridiazole

PROPOSAL FOR THE DECISION

3 Proposed decision with respect to the application for inclusion of the active substance in Annex I

3.1 Background to the proposed decision

Etridiazole is the ISO common name for ethyl-3-trichloromethyl-1,2,4-thiazol-5-yl ether (IUPAC) or 5-ethoxy-3-trichloromethyl-1,2,4-thiadiazole (CA).

Etridiazole is a contact fungicide with protective and curative action. Its protective action is restricted to the plant root zones in the soil or growth substrate. Etridiazole is a strong growth inhibitor of *Phytophthora* and *Pythium spp*.

Etridiazole is formulated as an Micro-Emulsion (AATERRA ME), intended for agricultural use in glasshouse substrate grown fruiting vegetables (tomatoes, peppers, cucumbers) and non-soil bound glasshouse ornamentals.

The provided analytical methods for the determination of the a.s. in technical material and in the plant protection product are acceptable and will not prevent the inclusion of etridiazole in Annex I.

The provided analytical method for monitoring etridiazole residues in tomatoes, sweet peppers and cucumber fruit is acceptable.

Additional methodology for the metabolites 3-hydroxymethyl etridiazole and 5-hydroxyethoxy etridiazole acid included in the provisional residue definition for plant products should be submitted.

The provided analytical method for monitoring etridiazole, dichloro-etridiazole and etridiazole acid residues in soil is acceptable.

The provided analytical method for monitoring etridiazole, dichloro-etridiazole and etridiazole acid residues in surface water was acceptable. The LOQ for surface water was 0.1 µg/L and is below the level of the lowest appropriate toxicity value for aquatic organisms. The method is applicable for drinking and groundwater.

The provided analytical method for monitoring etridiazole residues in air was accepted. The method is considered suitable for post-registration monitoring, since the LOQ (0.9 µg/m^3) is below the limit of 9 µg/m^3 calculated as: limit = AOEL*0.1*60/20 (AOEL = 0.03 mg/kg bw/day).

Additional methodology for the metabolites included in the residue definition for air should be submitted unless non-inclusion of the metabolites in the residue definition is accepted.

An ADI for dietary exposure of 0.005 mg/kg bw/day was established. A systemic AOEL for semi-chronic exposure, based on oral toxicity data, of 0.03 mg/kg bw/d can be set. An ArfD of 0.15 mg/kg bw/day is proposed.

Based on the AOEL and exposure assessments, for AATERRA ME safe uses have been identified for mixing and loading and application (as far as this is relevant). A safe use for bystanders has been identified since no bystanders should be allowed in greenhouses during the application of AATERRA ME. Safe uses for workers have been identified.

The provided residue data and dietary exposure estimates –for the use in tomato- will not prevent the inclusion of etridiazole in Annex I.

At this stage safe use can be established for the environment (fate and behaviour) and for ecotoxicology. Regarding the risk for bumblebees risk mitigation measures can be applied at Member State level.

3.2 Proposed decision concerning inclusion in Annex I

[redacted]

3.3 Rational for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate

[redacted]

The information in sections 3.2 and 3.3 has been removed upon the request by the EU Commission as it relates to risk management recommendations or proposals.

LEVEL 4

Etridiazole

DEMAND FOR FURTHER INFORMATION

4 Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in Annex I

4.1 Identity of the active substance

1. According to a letter of 11 July 2006 the batch results are from a pilot plant. Therefore a new batch analysis is required after going to full production. This is also required because of the remark that chloroform will not be present because of a better stripping of the product.
2. It should be explained by the notifier how the specifications are set (e.g. which statistical method was used) and why they are considered acceptable (also taking the results of the 5-batch analysis into consideration) :
   - The lowest purity in the batch analysis is 98.7% etridiazole. Notifier is asked to raise the minimal specification for the active substance to e.g. 980 g/kg as this appears to be technical possible.
   - The results from the batch analysis do not support the specification for the impurities. It appears that technical it is possible to lower the specification. Notifier is asked to use the FAO guidelines for setting specification, based on the batch results.
   - Volatiles are no longer part of the specification. Water however is still part of the specification, although it was not determined in the batch analysis. Because the specification for water is 1 g/kg it is not needed in the specification and notifier is advised to remove it.
   - Notifier should submit a new specification.

4.2 Physical and chemical properties of the active substance

No further information required.

Physical and chemical properties of the plant protection product: AATERRA ME

No further information required.

4.3 Data on application and further information

No further information required.

4.4 Classification, packaging and labelling

Sufficient data available. No further information required.

4.5 Methods of analysis

Analytical methods for plant products

Additional analytical methods for the metabolites 3-hydroxymethyl etridiazole and 5-hydroxyethoxy etridiazole acid are required as they are included in the provisional residue definition for plant products (provisional data gap).

Analytical method for soil, water and air

Additional analytical methods for the metabolites dichloro-etridiazole and etridiazole acid included in the provisional residue definition for air should be submitted (provisional data gap).

4.6 Toxicology and metabolism

Active substance

Sufficient data available. No further information required.

Plant protection product

Sufficient data available. No further information required.

4.7 Residue data

The data base for the setting of the MRL in sweet peppers and cucumbers should be completed so that a total of 8 residue trials are available for each crop (i.e. 5 more trials for cucumber and 6 more trials for peppers).

4.8 Environmental fate and behaviour

No further information required.

4.9 Ecotoxicology

Active substance

An acute oral toxicity study with bumblebees, in order to enable a risk assessment for the use in tomatoes.

(Reference for a bumblebee test could be for example: Steen JJM, Gretenkord C & Schaefer H (1996): Method to determine the acute oral LD50 and acute contact LD50 of pesticides for bumble bees (*Bombus terrestris* L.). Proc. 6th Int. Symp. on the hazard of pesticides for bumble bees (ICPBR), September 17-19, Braunschweig, Germany, appendix 28.)