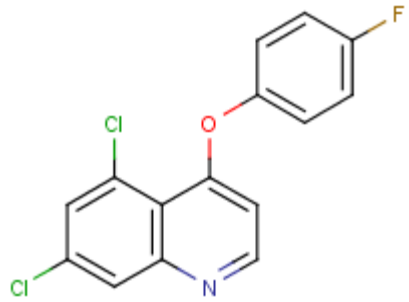
QUINOXYFEN

This EQS dossier was prepared by the Sub-Group on Review of the Priority Substances List (under Working Group E of the Common Implementation Strategy for the Water Framework Directive).

The dossier was reviewed by the Scientific Committee on Health and Environmental Risks (SCHER), which commented that it was not convinced of the need for a different assessment factor for the marine EQS. The use of additional assessment factors (5 for the marine MAC-QS and 10 for the marine AA-EQS) is explained in section 7.1 with reference to the Technical Guidance for Deriving EQS (E.C., 2011), and additional reference has been made in section 3.1.

1 CHEMICAL IDENTITY

Common name	Quinoxyfen
Chemical name (IUPAC)	5,7-dichloro-4-(p-fluorophenoxy)quinoline
Synonym(s)	Quinoline, 5,7-dichloro-4-(4-fluorophenoxy)
Chemical class (when available/relevant)	Fungicide
CAS number	124495-18-7
EU number	613-138-00-7
Molecular formula	$C_{15}H_8Cl_2FNO$
Molecular structure	
Molecular weight ($g.mol^{-1}$)	308.14

2 EXISTING EVALUATIONS AND REGULATORY INFORMATION

Annex III EQS Dir. (2008/105/EC)	Included
Existing Substances Reg. (793/93/EC)	Not applicable
Pesticides (91/414/EEC)	Included in Annex I
Biocides (98/8/EC)	Not applicable
PBT substances	Not investigated by ex- EU PBT Working Group Its properties (Persistency: DT_{50} up to 508 d, Bioaccumulation: BCF = 5040 (7450, when normalized to 5% lipid content), and Toxicity NOEC = 0.00636 mg/L) make this substance eligible.
Substances of Very High Concern (1907/2006/EC)	No
POPs (Stockholm convention)	Not listed. Its properties (Persistency: DT_{50} up to 508 d, Bioaccumulation: BCF = 5040 (7450, when normalized to 5% lipid content), and Toxicity NOEC = 0.00636 mg/L) make this substance eligible. Long range transport would need to be further assessed. Vapour pressure is low ($1.2\ 10^{-5}$ at 20°C) but estimated half-life in air is 1.9 days, close to the trigger value of 2 days. Monitoring studies in Sweden tends to indicate that long range transport remains limited.
Other relevant chemical regulation (veterinary products, medicament, ...)	No
Endocrine disrupter	Not investigated

In relation with long-range transport, monitoring studies in Sweden (Kreuger and Bergström 2006) have been reviewed by EU regulators in 2007 (after publication of E.C. 2003) with the conclusion that there is a low risk for long-range atmospheric transport of quinoxyfen to remote areas: in this study rainwater samples were collected at two locations, from April to September, in 2005 and 2006. Quinoxyfen was not detected (< LOD, *i.e.* < 0.003-0.007 µg/L) in any of the 92 samples. This study was designed to detect long-range transport since Quinoxyfen is not registered in Sweden. The authors put also the results into context by considering the range of different pesticides that have been detected in rainfall at the Vavihill site in the parallel study as part of the Swedish national monitoring programme. Results available for 2005 showed that there were frequent findings of pesticides in samples from May-June and September 2005, some of which are not registered for use in Sweden.

3 PROPOSED QUALITY STANDARDS (QS)

3.1 ENVIRONMENTAL QUALITY STANDARD (EQS)

$QS_{water, eco}$ is the "critical QS" for derivation of an Environmental Quality Standard.

Significant differences between freshwater and marine species cannot be demonstrated from the information available, but data from additional marine taxonomic groups that might have (further) reduced the uncertainties associated with extrapolation to the marine ecosystem, i.e. with the greater species diversity in the marine environment and the possibly greater sensitivity of marine species and taxa not in the experimental dataset. Therefore additional assessment factors have been applied following the TGD-EQS (E.C., 2011).

	Value	**Comments**
Proposed AA-EQS in [freshwater] [µg.l^{-1}]	0.15	**Critical QS is $QS_{water, eco}$**
Proposed AA-EQS in [marine water] [µg.l^{-1}]	0.015	**See section 7.1**
Proposed MAC-EQS for [freshwater] [µg.l^{-1}]	2.7	**See section 7.1**
Proposed MAC-EQS for [marine water] [µg.l^{-1}]	0.54	

3.2 SPECIFIC QUALITY STANDARD (QS)

Protection objective[*]	**Unit**	**Value**	**Comments**
Pelagic community (freshwater)	[µg.l^{-1}]	0.152	See section 7.1
Pelagic community (marine waters)	[µg.l^{-1}]	0.0152	
Benthic community (freshwater)	[µg.kg^{-1} $_{dw}$]	5.5	e.g. EqP, see section 7.1
Benthic community (marine)	[µg.kg^{-1} $_{dw}$]	0.55	
Predators (secondary poisoning)	[µg.kg^{-1} $_{biota\ ww}$]	13 333	See section 7.2
	[µg.l^{-1}]	0.18 (freshwaters) 0.018 (marine waters)	
Human health via consumption of fishery products	[µg.kg^{-1} $_{biota\ ww}$]	12 174	See section 7.3
	[µg.l^{-1}]	0.16 (freshwaters) 0.016 (marine waters)	
Human health via consumption of water	[µg.l^{-1}]	0.1	

[*] Please note that as recommended in the Technical Guidance for deriving EQS (drat version), "EQSs […] are not reported for 'transitional and marine waters', but either for freshwater or marine waters". If justified by substance properties or data available, QS for the different protection objectives are given independently for transitional waters or coastal and territorial waters.

4 MAJOR USES AND ENVIRONMENTAL EMISSIONS

4.1 USES AND QUANTITIES

Quinoxyfen is included in Annex I to Directive 91/414/EEC and for the uses as a fungicide *for foliar application in wheat and barley at a maximum annual use rate of 300 g a.i. per ha.*

According to the EU Database (http://ec.europa.eu/sanco_pesticides/, March 2010), authorizations at national level are granted in 17 out 27 Member States (AT, BE, CZ, DE, EL, ES, FR, HU, IE, IT, MT, PL, PT, RO, SI, SK, UK)

The website of the French Ministry of Agriculture indicates that 12 different pesticides products are authorised in France, for application on beet, wheat, flax, barley, and grape (http://e-phy.agriculture.gouv.fr/, March 2009).

Dow Agro Science (2010) indicated that over the last years, yearly sold quantities of quinoxyfen are close to 68,000 kg/year. Main quantities are in Italy, Spain, France and Germany. Main use is on vines. Other uses are on wheat, hop, sugarbeet and strawberry.

4.2 ESTIMATED ENVIRONMENTAL EMISSIONS

No information available.

5 ENVIRONMENTAL BEHAVIOUR

5.1 ENVIRONMENTAL DISTRIBUTION

		Master reference
Water solubility (mg.l^{-1})	0.128 at pH=5 0.116 at pH=6.45 0.047 at pH=7 0.036 at pH=9	E.C. 2003
Volatilisation	**Quinoxyfen is not likely to volatilise from water.**	
Vapour pressure (Pa)	1.2 10^{-5} at 20°C 2 10^{-5} at 25 °C	E.C. 2003
Henry's Law constant (Pa.m^3.mol^{-1})	0.0319	E.C. 2003
Adsorption	**The range 18 339 – 28 897 is used for derivation of quality standards. Quinoxyfen adsorbs strongly to solid particles.**	
Organic carbon – water partition coefficient (K_{OC})	K_{OC} = 18 339 – 28 897 log K_{OC} = 4,26 – 4,46	E.C. 2003
Sediment – water partition coefficient($K_{sed-water}$)	459 - 723	E.C. 2003
Bioaccumulation	**Quinoxyfen has a strong bioaccumulation potential. The BCF value of 7 450 is used for derivation of quality standards (BMF1 = 10 ; BMF 2 = 10)**	

Octanol-water partition coefficient (Log Kow)	4.66	E.C. 2003
BCF (measured)	BCF (fish, *Oncorhynchus mykiss*) = 5 040 BCF (fish, *Oncorhynchus mykiss* normalized to 5% lipid) = **7 450**	E.C. 2003

In the BCF study cited above, rainbow trout (*Oncorhynchus mykiss* Walbaum) were exposed for 28 days to [^{14}C-2-quinoline-labeled) quinoxyfen under continuous flow-through conditions, at average measured exposure concentrations of 0.51 and 4.9 ng/mL. Following the exposure periods, the fish were transferred to clean flowing water for 14-day elimination periods. Trout were periodically sampled and analyzed for total^{14}C radioactivity in whole fish tissue. There was very little metabolism of quinoxyfen by the rainbow trout. The percentage of total ^{14}C activity detected in radiochromatograms that was attributable to quinoxyfen averaged -97%. Therefore, the uptake and elimination of parent quinoxyfen was not specifically modeled and the BCF value for parent quinoxyfen is expected to be essentially equivalent to the value calculated for total ^{14}C residues. The time required for total ^{14}C residues to achieve 95% of steady-state concentration in whole fish tissue was 11.7 days.
It was commented during the EQS review process that values below 5000 at individual time points have apparently not reached steady state. Both the REACH guidance document (R7c) and the OECD guideline 305 state that the BCF at steady state is to be derived, either directly measured at steady state or as a kinetic BCF.
The OECD guideline states that the BCF should be expressed in relation to lipid content in addition to whole body weight to reduce variability. The REACH guidance (R7c) further states that a value normalized to a default lipid content of 5% should be used for the assessments to perform. The BCF should also be corrected for growth dilution (R7c). A lipid normalized value corrected for growth dilution is presented in the BCF study as well. This value is 149000. Normalized to a default lipid content of 5% the BCF value is 7450.
The report indicates that once the fish were moved to clean flowing water, ^{14}C residues cleared rapidly from the fish, with a model-derived elimination half-life of 2.7 days.
However, this depuration half-life can be explained by the small size of the fish used. The fact that compounds have a shorter half-life in small fish than in large fish is independent of the compound. This phenomenon is documented in the REACH guidance (R7c) by the allometric equations for the uptake rate constant from Sijm et al (1995).
Considering the element above, the value of 7450 is the value to be considered in a PBT assessment. This value is above the criteria for both 'bioaccumulative' (B) and 'very bioaccumulative' (vB).
During the review process, the stakeholder informed that a GLP laboratory study evaluating the bioconcentration in fish (rainbow trout), aquatic invertebrates (daphnids) and algae is currently ongoing and is planned for completion by the end of 2010.

5.2 ABIOTIC AND BIOTIC DEGRADATIONS

		Master reference
Hydrolysis	DT_{50}= 75d at 20°C and pH 4 to 5 The substance is stable in aqueous solution at pH 7 to 9.	E.C. 2003
Photolysis	DT_{50} = 1.7 – 23 h	E.C. 2003
Biodegradation	Quinoxyfen is not readily biodegradable. $DT_{50\ (water)}$= 3 – 7 d (dissipation) $DT_{50\ (sediment)}$= 42 – 211 d (primary degradation) $DT_{90\ (sediment)}$= 117 – 498 d (primary degradation) $DT_{50\ (soil)}$= 224 – 508 d (primary degradation, 20°C, mean 374 d, n=4)	E.C. 2003

6 AQUATIC ENVIRONMENTAL CONCENTRATIONS

6.1 ESTIMATED CONCENTRATIONS

Compartment	Predicted environmental concentration (PEC)	Master reference
Freshwater	No data available	Daginnus, Gottardo et al. 2009(1)
Marine waters (coastal and/or transitional)	No data available	Daginnus, Gottardo et al. 2009(1)
Sediment	No data available	Daginnus, Gottardo et al. 2009(1)
Biota (freshwater)	No data available	Daginnus, Gottardo et al. 2009(1)
Biota (marine)	No data available	Daginnus, Gottardo et al. 2009(1)
Biota (marine predators)	No data available	Daginnus, Gottardo et al. 2009(1)

(1) *data originated from EU modelling-based prioritisation results.*

6.2 MEASURED CONCENTRATIONS

Compartment	Measured environmental concentration (MEC)	Master reference
Freshwater (µg/l)	NL Data: Overall data are comprised between 0.27 ng/L or the LOQ and 100 ng/L. 2006: all data > DL. Average concentration: 5.0 ng/L (56 measurements,14 sampling points) 2007: all data > DL. Average concentration 7.4 ng/L for 2007 (128 measurements on 36 sampling points) 2008: data > DL with a few exceptions Average concentration 8.5 ng/L for 2008 (150 measurements on 37 sampling points). The mean values are only slightly below the mean value based on the LOQ of 10 ng/L in www.priority.substances.wfd.oieau.fr. From the data presented for the Dutch sampling points, no 90th percentile can be calculated. However, because the average concentrations over all yearly sampling points are only a factor of 3.5 to 6 lower than the reported 90th percentile in www.priority.substances.wfd.oieau.fr, it is likely that the 90th percentiles will be in the same range as well.	www.bestrijdingsmiddelenatlas.nl
Freshwater (µg/l)	Analysis on raw water for the years 2006 to 2008 in France (LOQ = 0.05 µg.L^{-1})	

Compartment		Measured environmental concentration (MEC)	Master reference
		2008: 6 / 7316 analysis > LOQ (highest value 2007: 1 / 3647 analysis > LOQ 2006: 2 / 3104 analysis > LOQ The highest values measured were 0.06 µg.L^{-1} in 2008, 0.05 in 2007 and 2006.	
Freshwater (µg/l)		PEC 1: 0.37 PEC 2: 0.075	James, Bonnomet et al. 2009[(1)]
Marine waters (coastal and/or transitional) (µg/l)			
WWTP effluent (µg/l)		No data available	
Sediment (µg/kg dw)	Sed < 2 mm	No data (*0*)	James, Bonnomet et al. 2009[(1)]
	Sed < 20 µm	No data (*0*)	
	Sed < 63µm	No data (*0*)	
	Unspecified	<0.54 (LOD) - 3.66 (outlier at 10) (Italy, two sites, in wineyard)	Capri and Merli 2006
	Sed < 2 mm	<0.11 (LOD) – 1.25 (Germany, 4 sites, cereal growing area)	Fent 2006
Biota	Invertebrates (µg/kg ww)	No data (*0*)	James, Bonnomet et al. 2009[(1)]
		< LOD	Capri and Merli 2007
			Fent 2007
	Fish (µg/kg ww)	No data (*0*)	James, Bonnomet et al. 2009[(1)]
		1.43 to 6.69	Capri and Merli 2007
			Fent 2007
	Marine predators	No data available	

[(1)] *data originated from EU monitoring data collection*

Four monitoring studies were required from the industry as a condition of the continued Annex I inclusion of quinoxyfen as agricultural pesticide. The data have been reviewed by the Commission and declared acceptable. Germany was chosen as being representative of a northern European cereal growing area (cereals was the Annex I supported crop). In addition, Italy was chosen as being representative of a southern European vineyard area (grapes is a major crop). Both countries have historical use of Quinoxyfen. In each case, field scale and area scale monitoring was carried out. The field scale monitoring quantified residues in soil that had potentially resulted from the long-term (up to 10 years prior to 2005) use of Quinoxyfen, and the additional loading produced by the applications made in 2005 and 2006. In addition, aquatic sediment samples were taken from the edge-of-field water body to quantify historical exposure caused by spray drift, run off and erosion. In contrast, the area scale monitoring represented a wider scale since the water bodies chosen were not in direct neighbourhood to treated fields, but were located downwind from treated areas with similar Quinoxyfen application patterns to the farms at field scale.
The studies contained also monitoring information in soils and earthworms which are not summarised below.

Monitoring studies were carried out in Italy over two years (2005 and 2006) to investigate the presence of Quinoxyfen residues in non-target areas close to the point of application and following repeated use in vineyard regions of Italy *(*Capri and Merli 2006, Capri and Merli 2007*)*. Soil, sediment, and biota (fish, invertebrates, in water, earthworm in soil) monitoring was carried out at the same test sites (streams and ditches).
Two areas for potential Quinoxyfen contamination were identified since the historical use of Quinoxyfen in these vineyard regions was high and within an appropriate catchment in each region, vulnerable vineyards and edge-of-field water bodies were selected for monitoring. Quinoxyfen residues were then measured in

soil and aquatic sediments at field scale, and in sediment at catchment scale to quantify potential exposure both from historical use, and following applications according to good agricultural practices in 2005 and 2006. The biota sampling (benthic organisms and fish in the adjacent water bodies) was started in autumn 2005 and was repeated in 2006, firstly before the Quinoxyfen application and then in autumn 2006

As regards sediment, quinoxyfen was always below the LOD of 0.54 µg/kg in 4 out of 15 sites. For other sites, the detection of quinoxyfen is related to the application time in vineyards, most of the detection being related to post-application or pre-harvest periods. Mean values ranges from 0.54 to 3.66 (one outlier at ca. 10), individual replicates up to 8.53 (except outlier at 26.08 mg/kg dw). In some location, not analysis was carried out due to the lack of sediment.

A total of 117 fish samples (25 different species) sampled at the sites were analysed and only in seven cases Quinoxyfen residues were above the limit of detection. Detectable concentrations were measured only in samples collected during the autumn 2005 campaign and ranged from 1.43 to 6.69 µg/kg. Quinoxyfen was below the detection limit in all invertebrate samples.

Monitoring studies were carried out in Germany over two years (2005 and 2006, 4 sampling occasions, i.e. prior to application in spring, approximately 1 week after application, after crop harvest and in autumn) to investigate the presence of Quinoxyfen residues in non-target areas close to the point of application and following repeated use on wheat regions of Germany (Fent 2006, Fent 2007). The same protocol as above was applied. Pond distance from treated area ranged from 20 to 390 m. The limit of detection (LOD) was 0.11 µg/kg and the limit of quantification (LOQ) was 0.33 µg/kg.
At field scale, the use of Quinoxyfen resulted in sediment concentrations ranged from < LOD=11 µg/kg dw to 1.25 µg/kg dw. Quinoxyfen was detected before seasonal application in 2 of 4 sampling locations (0.34 – 0.49 µg/kg in 2005-2006 for one site, 0.34 µg/kg in 2006 for the second site). At area scale, sediment concentrations were lower than those seen at field scale, with values only around or below the LOQ.

Biota sampling was carried out before (April 2006) and after treatment (autumn 2005 and 2006).

Quinoxyfen concentrations in samples of *macroinvertebrate* collected within the “field” scale monitoring before treatment range from 0.42 to 0.62 µg/kg fresh weight and after the treatment season from 0.37 to 1.56 µg/kg fresh weight. 14 out 20 samples were below the LOD or LOQ. The residues observed in the 26 macroinvetebrates samples collected at the “area” scale were lower than those sampled at the “field” scale. The majority of biota samples (18 of 26) contained no Quinoxyfen above the LOD (0.10 µg/kg) and in 8 of 26 samples the concentration was lower than the LOQ (0.33 µg/kg).

Considering the *fish* sampled both at the “field” and “area” scales, a total of 40 samples (15 different species) were processed for Quinoxyfen analyses. With one exception (*Salmo fontinalis* captured in the Krummel in autumn 2005 and autumn 2006; measured residues: 2.50 µg/kg and 4.65 µg/kg, respectively) all other species captured contained no Quinoxyfen in concentrations above the LOQ (0.59 µg/kg), independent of sampling site or sampling occasion.

This study indicates that in these local conditions, there is no tendency for accumulation of Quinoxyfen. However, it is also observed that quinoxyfen is still found in the environment on some occasions before the next application period.

As a general consideration, it is underlined that field studies cannot be directly used to assess PBT properties, for which criteria have been defined for laboratory results. These are open systems in which the disappearance of a substance results both from degradation and dissipation or transfer to another compartment/location.

7 EFFECTS AND QUALITY STANDARDS

7.1 ACUTE AND CHRONIC AQUATIC ECOTOXICITY

All data presented extracted from EU-DAR (E.C. 2003) thereafter are considered as peer-reviewed. The reliability of studies where endpoints are expressed as nominal concentrations is questionable, since as stated in the DAR « measured concentrations in some studies were considerably below nominal », which is likely in view of the hydrophobicity of the substance.

ACUTE EFFECTS			**Reliability** †	**Master reference**
Algae & aquatic plants ($mg.l^{-1}$)	**Freshwater**	***Pseudokirchneriella subcapitata* / 120h** **ErC_{50} = 0.027 (measured concentration)**	2	Milazzo et al.1993, cited in E.C. 2003
	Marine	*Skeletonema costatum* / 120h EC_{50} = 0.130	4	US-EPA 2005
Invertebrates ($mg.l^{-1}$)	**Freshwater**	*Daphnia magna* / 48 h EC_{50} = 0.08 (mean measured)	1	E.C. 2003
	Marine	*Crassostrea virginia* / 96h EC_{50} = 0.072	4	US-EPA 2005
		Americamysis bahia EC_{50} = 0.079	4	E.C. 2003
	Sediment	No data available		
Fish ($mg.l^{-1}$)	**Freshwater**	*Oncorhynchus mykiss* / 96h LC_{50} = 0.27	3 (nominal concentration)	E.C. 2003
	Marine	*Cyprinodon variegatus* / 96h EC_{50} > 0.168	4	US-EPA 2005
	Sediment	No data available		
Other taxonomic groups		No data available		

† Reliability codes according to Klimisch, H. J., M. Andreae, et al. (1997). "A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data." Regulatory Toxicology and Pharmacology **25**: 1-5.

CHRONIC EFFECTS			**Reliability** ‡	**Master reference**
Algae & aquatic plants ($mg.l^{-1}$)	**Freshwater**	*Pseudokirchneriella subcapitata* / 120h NOEC = 0.00463 (measured concentrations)	2§	Milazzo et al.1993, cited in E.C. 2003 US-EPA 2005
	Marine	*Skeletonema costatum* / 120h NOEC = 0.0546	4	US-EPA 2005
Invertebrates ($mg.l^{-1}$)	**Freshwater**	*Daphnia magna* / 21d NOEC = 0.0278 (mean measured)	1	E.C. 2003
	Marine	***Americamysis bahia* / 28d** **NOEC = 0.00152**	**1**	**DAS Study No. 040427, 2006**
	Sediment	*Chironomus riparius* / 27d* NOEC = 0.548 $mg/kg_{sed\ dry\ weight}$	1	E.C. 2003
Fish ($mg.l^{-1}$)	**Freshwater**	*Pimephales promelas* / 28d NOEC = 0.013	4	US-EPA 2005
		Oncorhynchus mykiss / 21d NOEC 0.014 (mean measured)	1	E.C. 2003
	Marine	*Cyprinodon variegatus* / 39d NOEC = 0.00409	1	DAS Study No. 040426 2005
	Sediment	No data available		
Other taxonomic groups		No data available		

* E.C. 2003 does not specify if the result was normalized to an organic carbon content of 5%. Information is not available.

The lowest value was observed on a 28-day flow-through life-cycle toxicity test with the saltwater mysid, *Americamysis bahia*, were effect of quinoxyfen on survival, growth, and reproduction of mysids exposed were recorded. A NOEC = 0.00152 mg/L was determined based on the growth of the organisms.

‡ Reliability codes according to Klimisch, H. J., M. Andreae, et al. (1997). "A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data." Regulatory Toxicology and Pharmacology **25**: 1-5.

§ The three study categories used by the Agency to classify studies are core, supplemental, and invalid. Supplemental studies are scientifically sound; however, they were performed under conditions that deviated substantially from recommended protocols. Results do not meet guideline requirements; however, the information may be useful in a risk assessment. For more details, please see http://www.ipmcenters.org/Ecotox/DatabaseGuidance.pdf.

Significant differences between freshwater and marine species cannot be demonstrated from the information available and results can therefore be considered together as described in the TGD-EQS (E.C., 2011).

As regards acute data, information is available on 3 trophic levels with the lowest result observed on *Pseudokirchneriella subcapitata* / 120h EC_{50} = 0.027 mg/l (measured concentrations).

For MAC derivation a default factor of 100 applies. According the Technical Guidance for Deriving Environmental Quality Standards, Table 3.4 (E.C., 2011), the AF of 100 may be reduced to 10 when "*Acute toxicity data for different species do not have a higher standard deviation than a factor of 3 in both directions (i.e. "If the standard deviation of the log transformed L(E)C_{50} values is <0.5…") OR known mode of toxic action and representative species for most sensitive taxonomic group included in data set".* The standard deviation of its log transformed L(E)C_{50} values for a range of freshwater and marine fish, invertebrates and algae is 0.31 indicating that the AF can be lowered.

On the other hand, Quinoxyfen is a fungicide of known mode of action, but the potentially most sensitive species group is not included in the dataset. Additional information was provided during the review process with the aim of demonstrating the specificity of the action of the substance on powdery mildew fungi (Erysiphales). Level 1, 2, and 3 early screening efficacy tests (Dixon 1995) showed no insecticide and herbicide activity and fungicide activity was shown against *Erysiphe graminis tritici* but against *Alternaria sp., Cercospora sp., Cladosporium sp., Fusarium sp., Helminthosporium sp..,Puccinia sp., Pseudocercosporella sp.,* and *Pyricularia sp.* no useful activity was recorded.

The main mode of action at the cellular level is the inhibition of primary appressorial formation. Quinoxyfen, has virtually no effect on spore germination, primary germ tube development, secondary appressoria or haustoria (Longhurst 1995). This review reports the experiment from Barkham (1994) where Quinoxyfen was screened against over 50 different fungi from 19 different orders. The results demonstrated that no significant inhibition by Quinoxyfen was shown by any fungus species. The highest level of inhibition (20%) was seen with *Epicoccum nigrum*, a member of the Dothideales (most closely related to Erysiphales based on the structure of the ascus). This lack of activity was explained as because the activity of Quinoxyfen is specific to some members of the obligate Erysiphales, or that the activity is limited to the inhibition of appressorium formation observed in vivo and that the growth of fungus *per se* is not inhibited. An additional study was carried out on *Colletotrichum coccodes* and *C. capsici* which readily produced appressoria *in vitro*. Results showed that mycelial growth of neither species was affected by Quinoxyfen. Similar results were obtained for appressoria which formed after 21 days. Production of fruiting bodies, which occurred with *C. capsici*, was also unaffected (Barkham 1994c).

Considering the overall information available on the specificity of the mode of action of the substance, and the low interspecies variability, it is proposed to retain the lowest endpoint, with an assessment factor of 10.

For saltwater, an additional factor of 10 would normally be applied in order to account for the wider diversity of species found in the marine environment. When one short-term EC_{50} from an additional specific saltwater taxonomic group the overall AF can be lowered to 50. Since the data-set includes an EC_{50} for the marine mollusc *Crassostrea virginia*, this AF should apply.

As regards the determination of the AA-$QS_{freshwater, eco}$ and AA-$QS_{marine\ water, eco}$ the lowest value was obtained with the marine shrimp *Americamysis bahia* (NOEC (28d) = 0.00152 mg/l. Data are available for the 3 trophic level with again, an uncertainty on one of the 2 algae tests. As above, it may be underlined that Quinoxyfen is a fungicide, and the potentially most sensitive species group is not included in the chronic dataset. Such tests are however not conventional and as for other species, interspecies variability is limited. An assessment factor of 10 is then proposed for freshwater.

For marine waters, an assessment factor of 100 is proposed since data are only available on 3 taxa (algae, invertebrate, fish).

Tentative QS_{water}	**Relevant study for derivation of QS**	**Assessment factor**	**Tentative QS**
$MAC_{freshwater, eco}$	*Pseudokirchneriella subcapitata* / 120h EC_{50} = 0.027 $mg.l^{-1}$	10	2.7 $\mu g.l^{-1}$
$MAC_{marine\ water, eco}$		50	0.54 $\mu g.l^{-1}$

AA-QS$_{freshwater, eco}$	*Americamysis bahia* / 28d NOEC = 0.00152 mg.l^{-1}	10	0.152 µg.l^{-1}
AA-QS$_{marine\ water, eco}$		100	0.0152 µg.l^{-1}
AA-QS$_{freshwater, sed.}$	*Chironomus riparius* / 27d NOEC = 0.548 mg.kg^{-1}$_{sed\ dry\ weight}$ -	100	5.5 µg.kg^{-1}$_{dw}$ 1.2 µg.kg-1$_{ww}$
AA-QS$_{marine\ water, sed.}$		1 000	0.55 µg.kg^{-1}$_{dw}$ 0.12 µg.kg^{-1}$_{ww}$

7.2 SECONDARY POISONING

Secondary poisoning of top predators		Master reference
Mammalian oral toxicity	Rat / Oral / 2 years / Liver hypertrophy and glomerulonephrosis; reduced body weight NOAEL = 20 $mg.kg^{-1}_{bw}.d^{-1}$ **NOEC = 400 $mg.kg^{-1}_{feed\ ww}$ (CF= 20)** Reliability: valid, as stated by E.C. 2003	E.C. 2003
	Rat / Oral / Reproduction study / Slight reduction in bodyweight gain in pups during lactation NOAEL = 100 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC = 2000 $mg.kg^{-1}_{feed\ ww}$ (CF= 20) Reliability: valid, as stated by E.C. 2003	E.C. 2003
	Rabbit / Oral / Developmental effects NOAEL = 80 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC = 2264 $mg.kg^{-1}_{feed\ ww}$ (CF= 33.3) Reliability: valid, as stated by E.C. 2003	E.C. 2003
Avian oral toxicity	Mallard duck / Oral / 27 w / Reproduction effects LOEC = 229 $mg.kg^{-1}_{feed\ ww}$ Reliability: supplemental, as stated US-EPA 2005	US-EPA 2005
	Bobwhite quail / Oral / Reproduction effects NOEC = 1000 $mg.kg^{-1}_{feed\ ww}$ Reliability: valid, as stated by E.C. 2003, US-EPA 2005	E.C. 2003

The reproduction Mallard duck study quoted by the US-EPA database reports to the lowest endpoint. According to the US-EPA website[**], this study is a 188-d reproductive study with dietary administration for birds. The following results are reported Eggs Laid: % Live Embryos: 933, % Egg Hatch: 933, 14 Day Survive: 229. The US-EPA stated that the study was supplemental, with no further justification. In contrast, the study on bobwhite quail was considered as a core data by the US EPA and selected by E.C. 2003 as relevant for the risk assessment to birds. Considering the uncertainty linked to the mallard duck study, which is not available for review, rated as supplemental by US-EPA and, not selected by the EU and US-EPA regulators, it is proposed to base the QS derivation on the next lowest endpoint which is the NOEC of 400 ppm derived from the 2-years rat study.

Conversion to water are made using a BCF of 7 450, BMF1 = 10 and BMF2 = 10.

Tentative QS_{biota}	Relevant study for derivation of QS	Assessment factor	Tentative QS
Biota	NOEC =400 $mg.kg^{-1}_{feed\ ww}$	30[(1)]	13 333 $\mu g.kg^{-1}_{biota\ ww}$ corresponding to 0.18 $\mu g.l^{-1}$ (freshwater) 0.018 $\mu g.l^{-1}$ (saltwater)

(1) proposal made for the purpose of this dossier, according to REACH guidance on information requirements and chemical safety assessment (ECHA 2008)

** http://www.ipmcenters.org/

7.3 HUMAN HEALTH

Human health via consumption of fishery products		**Master reference**
Mammalian oral toxicity	Rat / Oral / 2 years / Liver hypertrophy and glomerulonephrosis; reduced body weight NOAEL = 20 $mg.kg^{-1}_{bw}.d^{-1}$ Reliability: valid, as stated by E.C. 2003	E.C. 2003
CMR	Quinoxyfen is not classified for any carcinogenic, mutagenic or reprotoxic properties.	E.C. 2008

Tentative $QS_{biota, hh}$	**Relevant study for derivation of $QS_{biota, hh}$**	**Assessment Factor**	**Tentative $QS_{biota, hh}$**
Human health	NOAEL = 20 $mg.kg^{-1}_{bw}.d^{-1}$	100[(1)]	12 174 $\mu g.kg^{-1}_{biota}$ corresponding to 0.163 $\mu g.l^{-1}$ (freshwater) 0.163 $\mu g.l^{-1}$ (saltwater, using BMF1 only) 0.016 $\mu g.l^{-1}$ (saltwater, using BMF 1&2)

(1) Proposal made by WHO for the purpose of Quinoxyfen toxicological evaluation (WHO 2008). ADI 0.2 $mg.kg_{bw}^{-1}.d^{-1}$ established by EU, see http://ec.europa.eu/sanco_pesticides/public/index.cfm

Human health via consumption of drinking water		**Master reference**
Existing drinking water standard(s)	0.1 $\mu g.l^{-1}$ (preferred regulatory standard)	Directive 98/83/EC

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