VSP Adviesrapport 14542B01

Fluopyram
Afleiding van de JG-MKN- en MAC-MKN-water

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Opdracht	Dit adviesrapport is de aangepaste versie van de afleiding van de waterkwaliteitsnormen JG-MKN en MAC-MKN (AA-EQS en MAC-EQS) voor fluopyram. De commentaren van het petit comité zijn in deze versie verwerkt

Kwaliteitsprocedures en beoordelingskader

De afleiding van de waterkwaliteitsnormen in dit rapport is opgesteld in overeenstemming met de vigerende VSP kwaliteitsprocedures. De afleiding is beoordeeld door de leden van de Wetenschappelijke Klankbordgroep Normstelling water en lucht.

Contents

1 Introduction

1.1 General

Fluopyram is a fungicide that is approved for use in plant protection products in the European Union (EU). The Ctgb commissioned RIVM to derive an EQSs according to the WFD-methodology. The resulting values can be used by Ctgb in the re-registration process when monitoring data have to be compared with water quality standards according to the agreed procedures.

1.2 Standards considered

Under the WFD, two types of EQSs are derived to cover both long- and short-term effects resulting from exposure:

- an Annual Average EQS (AA-EQS) – a long-term standard, expressed as an annual average concentration (AA-EQS) which should protect the ecosystem against adverse effects resulting from long-term exposure, and
- a Maximum Acceptable Concentration EQS (MAC-EQS) for aquatic ecosystems – the concentration protecting aquatic ecosystems from effects due to short-term exposure or concentration peaks.

Concentrations below the AA-EQS should not result in risks due to direct toxicity, secondary poisoning and/or risks for human health. The latter two aspects are therefore also addressed in the AA-EQS, when triggered by the characteristics of the compound (i.e. human toxicology and/or potential to bioaccumulate). The MAC-EQS is based on direct ecotoxicity only. In the context of authorisation of plant protection products, only freshwater EQSs are used. However, for the purpose of EQS derivation, toxicity data on salt water species data are collected as well. The total available dataset allows for derivation of freshwater and saltwater EQSs and since standards for the saltwater environment may be used for other purposes as well, they are also derived in this report.

For authorisation of plant protection products, transient ecotoxicological effects may be considered acceptable under certain conditions if the potential for recovery is demonstrated. However, the quality standards in the context of the WFD refer to the absence of any impact on community structure of aquatic ecosystems. Hence, long-term undisturbed functioning is the protection objective under the WFD. Therefore, recovery in a test situation, after a limited exposure time, is not included in the derivation of the AA- and MAC-EQS.

1.3 Methodology

1.3.1 Guidance documents

The methodology used for ERL derivation is in accordance with the European guidance document for derivation of environmental quality standards under the WFD [1]. This document is further referred to as the WFD-guidance. For those aspects that may not be fully covered by the

WFD-guidance, additional information can be found in national guidance [2] and relevant reports [3,4].

1.3.2 Data sources

For the derivation of the quality standards for fluopyram, studies used in the Draft Assessment Report (DAR) prepared within the context of Commission Regulation 737/2007 and a number of new aquatic studies provided by the Ctgb are used as basis [5]. A literature search was performed with SCOPUS (www.scopus.com) to find additional literature not included in the DAR.

1.3.3 Data evaluation

The new ecotoxicological data, not used in the DAR, were evaluated with respect to the validity (scientific reliability) of the study. Reliability indices (Ri) of 1 to 4 were assigned according to Klimisch et al. [6], with Ri 1: fully reliable, Ri 2: reliable with restrictions, Ri 3: not reliable and Ri 4: not assignable. A detailed description of the evaluation procedure is given in the WFD-guidance [1].

The data used in the DAR, physico-chemical and ecotoxicological endpoints, are not re-evaluated and included in the report with a reliability of Ri 2. In some cases additional data are obtained from the original study report to provide sufficient information on the studies.

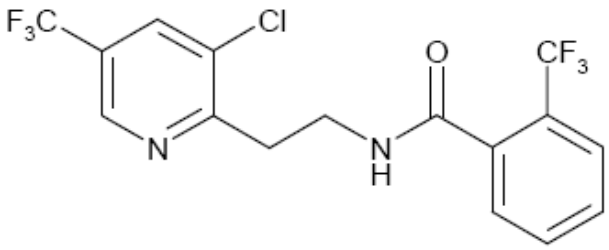
Occasionally, endpoints reported in the DAR exceed the water solubility. According to the WFD guidance, endpoints exceeding the water solubility with more than a factor of 2 should not be used for the EQS derivation. This factor could be increased to 3 when the available data on the water solubility has a variation higher than a factor of 2. The only available endpoint on water solubility of fluopyram is 16 mg/L (no pH dependency; see Table 2), therefore the cut off value is set at 32 mg/L. Endpoints exceeding 32 mg/L were assigned an Ri 3 and therefore rejected.

Endpoints based on nominal test concentrations are accepted as sufficiently reliable for EQS derivation because fluopyram has characteristics that indicate that the substance is not likely to dissipate rapidly from the water phase: it has low vapour pressure, moderate to low hydrophobicity (relatively high water solubility), it does not hydrolyse and does not photolyse rapidly.

2 Information on the substance

2.1 Identity

Table 1. Substance identification

Name	fluopyram
Chemical name	*N*-{2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}-α,α,α-trifluoro-*o*-toluamide
CAS number	658066-35-4
Molecular formula	$C_{16}H_{11}ClF_6N_{2O}$
Molar mass	396.72 g/mol
EC number	not allocated
Structural formula	
SMILES code	C1=CC=C(C(=C1)C(=O)NCCC2=C(C=C(C=N2)C(F)(F)F)Cl)C(F)(F)F
Use class	fungicide
Mode of action	Fluopyram is a new broad-spectrum systemic fungicide of the carboxamide group. It inhibits the succinate dehydrogenase in the cell respiration of the fungus thus blocking electron transport.

2.2 Physico-chemical properties

Table 2. Physico-chemical properties

Parameter	Unit	Value	Remark	Ref.
Water solubility	[mg/L]	16	pH 7, 20°C	[7]
pK_a	n.a.		does not dissociate	[7]
log K_{ow}	[-]	3.3	20°C, method not reported	[7]
Vapour pressure	[Pa]	$1.2x10^{-6}$	at 20°C	[7]
Henry's law constant	[Pa.m^3/mol]	$2.98x10^{-5}$	calculated	[7]
Melting point	[°C]	117.5		[7]
Boiling point	[°C]	318 – 321		[7]

n.a. = not applicable.

2.3 Classification

A harmonised CLP classification (Annex VI of Regulation (EC) Nr 1272/2008) for fluopyram is available [8], which is presented in Table 3.

Table 3. Fluopyram: harmonised classification

Hazard Class and Category Codes	Hazard Statement Codes	Concentration limits, M-factors
Aquatic Chronic 2	H411	–

2.4 Fate and behaviour

2.4.1 Behaviour in the environment

Selected environmental properties of fluopyram are given in Table 4.

Table 4. Selected environmental properties of fluopyram

Parameter	Name/Unit	Value	Remark	Ref.
log K_{oc}	log [L/kg]	2.46[a]	see footnote	[7]
Hydrolysis half-life	DT_{50} [d]	-	stable at pH 5,7,9	[7]
Photolysis half-life	DT_{50} [d]	21	phenyl ^{14}C-labelled	[7]
Photolysis half-life	DT_{50} [d]	25	pyridyl ^{14}C-labelled	[7]
Photolysis half-life	DT_{50} [d]	21	In natural Rhine water	[7]
Biodegradation in water/sediment systems	$DT_{50\ system}$[d]	1190	24°C; phenyl ^{14}C-labelled	[7]
Biodegradation in water/sediment systems	$DT_{50\ system}$[d]	1000	phenyl ^{14}C-labelled, T not measured	[7]
Biodegradation in water/sediment systems	$DT_{50\ system}$[d]	1470	24°C; pyridyl ^{14}C-labelled	[7]
Biodegradation in water/sediment systems	$DT_{50\ system}$[d]	648	pyridyl ^{14}C-labelled, T not measured	[7]

2.4.2 Bioconcentration and biomagnification

Since log Kow is > 3, the trigger for bioconcentration and biomagnification is exceeded and the risk for bioconcentration and biomagnification should be evaluated. The BCF for fish selected in the DAR is 18 L/kg (whole fish = 18, normalised to 6% lipid content = 16). This values is calculated from the concentration in fish and water. The BCF calculated from kinetic parameters is 65.7-87.9 L/kg. A review of the BCF study shows that fluopyram in fish is expressed as total radioactivity, which is not only active substance but possibly also metabolites. The percentage of fluopyram after 7 days is 54.6% in edibles and 11.0% in viscera. However, after 14 days the percentage of fluopyram in edibles and in viscera is comparable (24.7% versus 21.9% respectively). Data from day 14 are used to calculate the steady-state BCF. The difference between total radioactivity and the parent compound is the reason why there is a difference between the steady state BCF of 18 L/kg and the kinetic BCF of 65.7 – 87.9 L/kg. Human toxicology
The human-toxicological acceptable daily intake (ADI) is 0.012 mg/kg_{bw}/d (DAR). There is no classification that triggers the inclusion of human health in risk limit derivation. Therefore the derivation of the $QS_{water,\ hh\ food}$ is not required.

2.5 Secondary poisoning

Considering the BCF value os less than 20 L/kg_{wwt}, derivation of the $QS_{sp,\ water}$ for secondary poisoning is not necessary from this point of view. Another reason to derive quality standards for

secondary poisoning could be a high intrinsic toxicity to mammals and birds. Although it is not indicated when toxicity is high, the chronic NOAELs mentioned in the DAR for rats and mice are rather low (1.2 and 4.2 mg/kg_{bw}/d, respectively). Therefore, the classification and labelling report (Federal Institute for Occupational Safety and Health, 2013) was checked for more details on the studies. It appears that the population relevant endpoints (mortality, growth) have a higher NOAEL for the rat: 6.0 and 8.6 mg/kg_{bw}/d, for males (survival) and females (body weight), respectively, corresponding to a diet concentrations of 150 mg/kg_{diet}. In the similar study with mice no effects on mortality and only transient effects on body weight were observed in the highest test concentration (750 mg/kg_{diet}) for both males and females. Doses for males and females at a diet concentration of 150 mg/kg_{diet} were 20.9 and 26.8 mg/kg_{bw}/d, respectively. At these diet and dose levels, the route of secondary poisoning is not the critical route for the overall EQS.

3 Derivation of water quality standards

3.1 Ecotoxicological effect data

3.1.1 Aggregated laboratory toxicity data

The available acute and chronic ecotoxicity data for freshwater and marine organisms are summarised in Annex 1. The data selected for EQS derivation are reported in the tables below. As indicated in section 1.3.3, endpoints exceeding the water solubility with more than a factor 2 are not used for the EQS derivation. For Crustacea and Pisces, all studies conducted with the active substance resulted in unbound values or values exceeding 32 mg/L (twice the water solubility of 16 mg/L). These endpoints cannot be used for EQS derivation. However, there are studies available that were conducted with formulations and the endpoints of these studies were considered acceptable. At higher tested concentrations no precipitates were found in these studies. Although for QS-derivation preference is given to studies with the active substance, in this case studies with formulations were also selected. The fact that the results of these studies were selected has no influence on the derived QS , but these values are included to show that these taxa were tested and contribute as such to the use of a lower assessment factor Data for saltwater aquatic organisms were available but all acute endpoints from relevant studies were unbound values. There is one relevant chronic study with saltwater organisms.

Table 5. Acute ecotoxicity data of fluopyram for freshwater aquatic organisms

Endpoints	L(E)C_{50} [mg/L]	Remark	Ref.
Algae			
Navicula pelliculosa	9.6	endpoint growth rate	[5]
Raphidocelis subcapitata	6.5	geomean value from two studies, endpoint growth rate	
Crustacea			
Daphnia magna	55.5	study with formulation, endpoint based on nominal concentrations, recalculated to active substance, recovery 98 - 109%	[9]
Pisces			
Oncorhynchus mykiss	71.6	study with formulation, endpoint based on nominal concentrations, recalculated to active substance, no precipitates observed, recovery 86 – 109%	[10]
Cyprinus carpio	> 84	study with formulation	[11]
Lepomis macrochirus	> 5.17		[5]
Pimephales promelas	> 4.95		[5]
Cyanophyta			
Anabaena flos-aquae	> 9.69	based on mean measured concentrations	[5]
Macrophyta			
Lemna gibba	3.32	geomean value from two studies (3.8 and 2.9), preferred endpoint growth rate, lowest value based on front numbers	[5]
Amphibia			
Xenopus laevis	> 5.0		[12]

Table 6. Acute ecotoxicity data of fluopyram for saltwater aquatic organisms

Endpoints	$L(E)C_{50}$ [mg/L]	Remark	Ref.
Crustacea			
Americamysis bahia	> 0.51		[5]
Pisces			
Cyprinodon variegatus	> 0.98		[5]
Mollusca			
Crassostrea virginica	> 0.43	Endpoint growth	[5]

Table 7. Chronic ecotoxicity data of fluopyram for freshwater aquatic organisms

Endpoints	$NOEC/EC_{10}$ [mg/L]	Remark	Ref.
Algae			
Navicula pelliculosa	2.47	NOEC for growth rate, based on mean measured concentrations	[5]
Raphidocelis subcapitata	1.30	geomean of two values for growth rate, based on mean measured concentrations	[5]
Crustacea			
Daphnia magna	1.214	most sensitive endpoint: reproduction, based on TWA concentrations	[5]
Pisces			
Pimephales promelas	0.135	length of fry/behavioural effects, TWA concentration	[5]
Macrophyta			
Lemna gibba	1.84	geomean value from two studies (2.06 and 1.65), preferred endpoint growth rate based on frond number or frond area	[5]
Cyanophyta			
Anabaena flos-aquae	9.69	NOEC for growth rate and biomass, based on mean measured concentrations	[5]
Insecta			
Chironomus tentans	0.14	endpoint survival and emergence, spiked sediment, result based on TWA concentration in overlying water	[5]
Chironomus riparius	0.525	endpoint emergence. TWA concentrations, spiked water, based on measured	[5]

Table 8. Chronic ecotoxicity data of fluopyram for saltwater aquatic organisms

Endpoints	$NOEC/EC_{10}$ [mg/L]	Remark	Ref.
Crustacea			
Leptocheirus plumulosus	1.6	endpoint mortality, based on mean measured concentrations in overlying water, spiked sediment study	[5]
Algae			
Skeletonema costatum	> 1.13	based on mean measured concentrations	[5]

3.2 Derivation of the MAC-EQS

Valid acute toxicity data for freshwater organisms are available for eleven species from six taxa covering algae, crustaceans and fish. Therefore a complete base set is available. Apart from data on freshwater organisms data on salt water organisms are also available for three species

from three taxa. The MAC-$QS_{fw, eco}$ is derived from the lowest acute toxicity value available, the EC50 of 3.32 mg/L for the macrophyte *Lemna gibba*. An assessment factor of 100 is applied because the substance is a fungicide and data on this potentially sensitive taxon are not included in the dataset. The MAC-$QS_{fw, eco}$ is 3.32 / 100 = 0.032 mg/L = 32 µg/L.

The MAC-$QS_{sw, eco}$ is derived on the basis of the combined freshwater and saltwater dataset. An additional assessment factor of 10 is applied by default. According to the WFD-guidance, this factor can be lowered if the saltwater dataset contains data from studies with marine test organisms other than algae, crustaceans and fish, and/or having a life form or feeding strategy differing from that of algae, crustaceans or fish. There are acute values for *Americamysis bahia*, *Cyprinodon variegatus* and *Crassostrea virginica*, the latter can be considered as an additional marine species. However, the assessment factor is not lowered despite of the availability of toxicity data for an additional marine species since the toxicity values for marine data are all unbound values and the lowest acute toxicity value for freshwater organisms is higher (factor of ± 8) than the value for *Crassostrea virginica*, This results in a MAC-$QS_{sw, eco}$ of 32 µg/L.

3.3 Derivation of the AA-EQS

3.3.1 Ecotoxicity – $QS_{fw, eco}$ and $QS_{sw, eco}$

NOECs are available for nine freshwater and two saltwater species, representing seven taxa, covering the base set. The number of taxa is too low to perform statistical extrapolation and only the assessment factor approach is applied. In this situation, the $QS_{fw, eco}$ is derived by applying an assessment factor of 10 to the lowest NOEC. However, because data on fungi are absent, a higher assessment factor (50) is applied to the lowest NOEC of 0.135 mg/L for the freshwater fish *Pimephales promelas*, resulting in a $QS_{fw, eco}$ of 0.135 / 50 = 0.0027 mg/L = 2.7 µg/L.

The $QS_{sw, eco}$ is derived on the basis of the combined freshwater and saltwater datasets. There is one valid endpoint from a study with a saltwater species, but this is not a typical marine species according to the WFD-guidance. Therefore an additional assessment factor of 10 is applied to derive the $QS_{sw, eco}$. This results in a $QS_{sw, eco}$ of 0.27 µg/L.

4 Conclusion

The MAC-EQS_{fw} for fluopyram is 32 µg/L, the MAC-EQS_{sw} is 32 µg/L.
The AA-EQS_{fw} for fluopyram is 2.7 µg/L, the AA-EQS_{sw} is 0.27 µg/L.

5 References

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6 List of abbreviations

AA-EQS	Annual Average – Environmental Quality Standard (In Dutch: JG-MKN, jaargemiddelde milieukwaliteitsnorm)
BCF	Bioconcentration Factor
BMF	Biomagnification Factor
EC_x	Concentration at which x% effect is observed
$EQS_{sp, water}$	Environmental Quality Standard based on the exposure of birds and mammals feeding on aquatic organisms
ERL	Environmental Risk Limit
LC_{50}	Concentration at which 50% mortality is observed
MAC-EQS	Maximum Acceptable Concentration – Environmntal Quality Standard for ecosystems (In Dutch: MAC-MKN)
Marine species	Species that are representative for marine and brackish water environments and that are tested in water with salinity > 0.5 ‰.
NOEC	No Observed Effect Concentration
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
NOEAEC	No Observed Ecosystem Adverse Effect Level
$QS_{water, hh food}$	Quality Standard for surface water based on the human consumption opf fishery products
SSD	Species Sensitivity Distribution
TGD	Technical Guidance Document
TWA	Time Weighted Average
WFD	Water Framework Directive (2000/60/EC)

Annex 1 Aquatic toxicity data

The abbreviations used in the toxicity data tables in this Annex are explained in the Dutch guidance on EQS derivation [2], part 3, section 2.1.1.

Table A2.1. Acute toxicity to freshwater organisms

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Hardness CaCO3 [mg/L]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference	Study id.
Algae																	
Navicula pelliculosa		Y	S	fluopyram	94.7	am	7.3 - 8.4	23.7 - 24.0		96 h	EC50	growth rate	9.6	2	10	[5]	p.77
Navicula pelliculosa		Y	S	fluopyram	94.7	am	7.3 - 8.4	23.7 - 24.0		96 h	EC50	biomass	6.1	2	10	[5]	p.77
*Raphidocelis subcapitata**		Y	S	fluopyram	94.7	am	7.4 - 10.0	23.6 - 24.2		72 h	EC50	biomass	4.3	2	14	[5]	p.71
*Raphidocelis subcapitata**		Y	S	fluopyram	94.7	am	7.4 - 10.0	23.6 - 24.2		72 h	EC50	growth rate	6.0	2	15	[5]	p.71
*Raphidocelis subcapitata**		Y	S	fluopyram SC 500 G	41.5 (504 g/L)	am	8.0 - 9.3	22.0 - 22.7		72 h	EC50	growth rate	6.9	2	10	[5]	p.88
Raphidocelis subcapitata		Y	S	fluopyram FS 600	48.7	am	7.3 - 9.1	22.6 - 22.9		72 h	EC50	growth rate	8.2	1	16	[13]	
Raphidocelis subcapitata		Y	S	fluopyram SC 500D G	42.4	am	8.2 - 8.4	21.7 - 22.5		72 h	EC50	growth rate	6.2	1	17	[14]	
Raphidocelis subcapitata		Y	S	fluopyram SC 500B G	42.0	am	7.8 - 8.2	21.3 - 22.0		72 h	EC50	growth rate	6.2	1	18	[15]	
Skeletonema. costatum		Y	S	fluopyram	94.7	am	7.7 – 8.5	20.1 – 21.6		72 h	EC50	biomass	> 1.13	2	10	[5]	p.114
Skeletonema costatum		Y	S	fluopyram	94.7	am	7.7 – 8.5	20.1 – 21.6		72 h	EC50	growth rate	> 1.13	2	10	[5]	p.114
Cyanophyta																	
Anabaena flos-aquae		Y	S	fluopyram	94.7	am	7.4 - 10.0	23.6 - 24.2		96 h	EC50	biomass and growth rate	> 9.69	2	10	[5]	p.76
Crustacea																	
Daphnia magna	< 24 h	Y	S	fluopyram	94.7	am	8.0 - 8.1	21.2 - 21.7	231	48 h	EC50	immobility	> 17	2	9	[5]	p.66
Daphnia magna	< 24 h	Y	S	fluopyram SC 500A G	41.5 (504 g/L)	am	8.1 - 8.2	20.7 - 21.0	249	48 h	EC50	immobility	> 38.2	2	10	[5]	p.69
Daphnia magna	< 24 h	Y	S	fluopyram FS 600	48.7	dw	8.3 - 8.5	20.6 - 20.8		48 h	EC50	immobility	> 23.28	1	11	[16]	
Daphnia magna	< 24 h	Y	S	fluopyram SC 500D G	42.4	am	7.8	19.8 - 20.1		48 h	EC50	immobility	55.5	1	12	[9]	
Daphnia magna	< 24 h	Y	S	fluopyram SC 500B G	42.0	am	7.9 - 8.0	20.1 - 20.4		48 h	EC50	immobility	59.2	2	13	[17]	
Pisces																	
Cyprinus carpio	1.9 ± 0.8 g, 5.3 ± 0.7 cm	Y	S	fluopyram	94.7	rw	6.8 - 7.2	23.6 ± 2	40 - 60	96 h	LC50	mortality	> 26.5	3	1	[5]	p.59
Cyprinus carpio	1.9 ± 0.7 g, 4.8 ± 1.0 cm	Y	S	fluopyram SC 500 B	42,0	dw	6.7 - 7.2	21.5 - 22.9	40 - 60	96 h	LC50	mortality	> 84	1	2	[11]	
Lepomis macrochirus	1.4 ± 0.1 g, 4.8 ± 0.3 cm	Y	S	fluopyram	94.7	rw	6.0 - 8.0	21.0 - 23.0	40 - 60	96 h	LC50	mortality	> 5.17	2	3	[5]	p.54
Oncorhynchus. mykiss	2.1 ± 0.6 g, 5.9 ± 0.6 cm	Y	S	fluopyram	94.7	rw	6.0 - 8.0	12.0 - 12.6	40 - 60	96 h	LC50	mortality	> 1.78	2	4	[5]	p.52
Oncorhynchus. mykiss	1.7 ± 0.6 g, 5.3 ± 0.5 cm	Y	S	fluopyram SC 500 G	41.5 (504 g/L)	rw	6.8 - 7.3	12.0 - 12.5	40 - 60	96 h	LC50	mortality	> 46.4	4	5	[5]	p.63
Oncorhynchus. mykiss	1.33 ± 0.09 g, 55.0 ± 1.2 mm	Y	S	fluopyram FS 600	48.7	dw	7.6 - 7.9	13.1 - 13.7	40 - 60	96 h	LC50	mortality	71.6	1	6	[13]	
Oncorhynchus. mykiss	1.7 ± 0.7 g, 5.5 ± 0.6 cm	Y	S	fluoram SC 500D G	42.4	rw	7.1 - 7.8	11.6 - 12.1	40 - 60	96 h	LC50	mortality	> 100	1	7	[18]	
Pimephales promelas	0.62 ± 0.11 g, 41.5 ± 2.6 cm	Y	S	fluopyram	94.7	dw	7.6 – 8.1	22.1 – 22.8	50 - 54	96 h	LC50	mortality	> 4.95	2	8	[5]	p.57
Amphibia																	
Xenopus laevis	15.2 ± 1.11 mm	Y	S	fluopyram	94.7	dw	8.3 - 8.4	21.3 - 21.7		48 h	LC50	mortality	**> 5.0**	1		[12]	
Macrophyta																	
Lemna gibba		Y	S	fluopyram SC 500A G	94.7	am	7.2 – 8.8	23.6 – 24.7		7 d	EC50	growth rate (frond #)	3.8	2	10	[5]	p.102
Lemna gibba		Y	S	fluopyram SC 500A G	94.7	am	7.2 – 8.8	23.6 – 24.7		7 d	EC50	growth rate (frond area)	3.6	2	10	[5]	p.102

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Hardness CaCO3 [mg/L]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference	Study id.
Lemna gibba		Y	S	fluopyram SC 500A G	94.7	am	7.2 – 8.8	23.6 – 24.7		7 d	EC50	yield (frond #)	2.9	2	10	[5]	p.98
Lemna gibba		Y	S	fluopyram SC 500A G	94.7	am	7.2 – 8.8	23.6 – 24.7		7 d	EC50	yield (frond area)	3.0	2	10	[5]	p.98
Lemna gibba		Y	S	fluopyram	94.7	am	7.2 – 8.9	23.7 – 24.3		7 d	EC50	growth rate (frond #)	2.9	2	10	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am	7.2 – 8.9	23.7 – 24.3		7 d	EC50	growth rate (frond area)	> 1.65	2	10	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am	7.2 – 8.9	23.7 – 24.3		7 d	EC50	yield (frond area)	2.9	2	10	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am	7.2 – 8.9	23.7 – 24.3		7 d	EC50	yield (frond #)	2.6	2	10	[5]	p.92

Notes

* *Raphidocelis subcapitata* is formerly known as *Pseudokirchneriella subcapitata*

1 TWA concentration, study not acceptable, test concentration far above stated water solubility of 16 mg a.s./L at pH 7 (test required for registration in Japan)
2 limit test, value recalculated to active substance, based on nominal concentrations, recovery 85 - 93% of nominal during the test
3 TWA concentration
4 limit test, TWA concentrations
5 TWA concentrations, top three treatments exceeded solubility, supplemental information
6 results based on nominal concentrations, recalculated to active substance, no precipitates observed, recovery 86 - 109%
7 limit test, based on nominal concentrations, recovery 107 - 109%
8 based on mean measured concentrations, effect concentration above practical limit of water solubility under test conditions
9 above the practical limit of water solubility, based on mean measured concentrations
10 based on mean measured concentration
11 based on nominal test concentrations, recovery 84 - 95%, test water dw blended with spring water
12 based on nominal test concentrations, recovery 98 - 109%
13 based on nominal test concentrations, recovery 85.5 at highest concentration, recovery 85,5 - 154.0 %
14 biomass area under the growth, based on mean measured concentration
15 growth rate, based on mean measured concentration
16 based on nominal concentrations, recovery 87 - 98%, recalculated to active substance
17 based on nominal concentrations, recovery 99 - 104%, recalculated to active substance
18 based on nominal concentrations, recovery 92-105%, recalculated to active substance
27 results based on nominal concentrations, recovery 83 - 87%

Table A2.2. Acute toxicity of fluopyram to saltwater organisms

Species	Species properties	A	Test type	Test compound	Purity	Test water	Salinity [‰]	pH	T	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference	Study id.
Crustacea																	
Americamysis bahia	< 24 h	Y	F	fluopyram	94.7	nw	20	8,0	24.1 – 25.5	96 h	LC50	mortality	> 0.51	2	1	[5]	p.105
Pisces																	
Cyprinodon variegatus	0.35 ± 0.17 g 21.8 ± 3.2 cm	Y	S	fluopyram	94.7	reverse osmosis with seawater		7.9 – 8.1	21.3 – 22.2	96 h	LC50	mortality	> 0.98	2	2	[5]	p.103
Mollusca																	
Crassostrea virginica	valve height 33.6 mm		F	fluopyram	94.7	nw	20	7.9 – 8.2	20 – 21.5	48 h	EC50	growth	> 0.43	2	1	[5]	p.107

Notes
1 based on TWA concentrations
2 based on mean measured concentrations

Table A2.3. Chronic toxicity of fluopyram to freshwater organisms

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	Hardness CaCO3 [mg/L]	pH	T [°C]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Reference	Study id.
Algae																	
Navicula pelliculosa		Y	S	fluopyram	94.7	am		7.3 - 8.4	23.7 - 24.0	96 h	NOEC	growth rate	2.47	2	9	[5]	p.81
Navicula pelliculosa		Y	S	fluopyram	94.7	am		7.3 - 8.4	23.7 - 24.0	96 h	NOEC	biomass	2.47	2	9	[5]	p.81
*Raphidocelis subcapitata**		Y	S	fluopyram	94.7	am		7.4 - 10.0	23.6 - 24.2	72 h	NOEC	biomass	1.46	2	10	[5]	p.71
*Raphidocelis subcapitata**		Y	S	fluopyram	94.7	am		7.4 - 10.0	23.6 - 24.2	72 h	NOEC	growth rate	1.46	2	11	[5]	p.71
Raphidocelis subcapitata		Y	S	Fluopyram SC 500 G	41.5 (504 g/L)	am		8.0 - 9.3	22.0 - 22.7	72 h	NOEC	growth rate	1.17	2	9	[5]	p.88
Raphidocelis subcapitata		Y	S	fluopyram FS 600	48.7	am		7.3 - 9.1	22.6 - 22.9	72 h	EC10	growth rate	4.22	1	12	[13]	
Raphidocelis subcapitata		Y	S	fluopyram FS 600	48.7	am		7.3 - 9.1	22.6 - 22.9	72 h	NOEC	growth rate	1.56	1	12	[13]	
Raphidocelis subcapitata		Y	S	fluoram SC 500D G	42.4	am		8.2 - 8.4	21.7 - 22.5	72 h	EC10	growth rate	2.55	1	13	[14]	
Raphidocelis subcapitata		Y	S	fluoram SC 500D G	42.4	am		8.2 - 8.4	21.7 - 22.5	72 h	NOEC	growth rate	1.98	1	13	[14]	
Raphidocelis subcapitata		Y	S	fluopyram SC 500B G	42.0	am		7.8 - 8.2	21.3 - 22.0	72 h	NOEC	growth rate	1.29	1	14	[15]	
Skeletonema costatum		Y	S	fluopyram	94.7	am		7.7 – 8.5	20.1 – 21.6	72 h	NOEC	growth rate	1.13	2	15	[5]	p.114
Cyanophyta																	
Anabaena flos-aquae		Y	S	fluopyram	94.7	am		7.4 - 10.0	23.6 - 24.2	96 h	NOEC	biomass and growth rate	9.69	2	9	[5]	p.76
Crustacea																	
Daphnia magna	< 24 h	A	F	AE C656948	94.7	am	53	8.0 – 8.1	20.6 – 21.0	21 d	NOEC	reproduction	1.214	2	2	[5]	p.122
Pisces																	
Pimephales promelas	< 24 h old	Y	F	fluopyram	94.7	rw	46.28	6.5 - 7.4	24.7 - 26.8	33 d	NOEC	Length of fry	0.135	2	1	[5]	p.119
Macrophyta																	
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.8	23.6 – 24.7	7 d	NOEC	growth rate (frond #)	2.06	2	4	[5]	p.98
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.8	23.6 – 24.7	7 d	NOEC	growth rate (frond area)	2.06	2	5	[5]	p.98
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.8	23.6 – 24.7	7 d	NOEC	yield (frond #)	1.04	2	3	[5]	p.98
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.8	23.6 – 24.7	7 d	NOEC	yield (frond area)	1.04	2	6	[5]	p.98
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.9	23.7 – 24.3	7 d	NOEC	growth rate (frond #)	1.65	2	4	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.9	23.7 – 24.3	7 d	NOEC	growth rate (frond area)	1.65	2	5	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.9	23.7 – 24.3	7 d	NOEC	yield (frond area)	0.278	2	3	[5]	p.92
Lemna gibba		Y	S	fluopyram	94.7	am		7.2 – 8.9	23.7 – 24.3	7 d	NOEC	yield (front #)	0.278	2	6	[5]	p.92
Insecta																	
Chironomus riparius	first instar	N	S	fluopyram	97.5	am with artificial sediment	267.0 – 302.6	7.7 – 8.5	20.1 - 20.5	28 d	NOEC	emergence	0.525	2	7	[5]	p.139
Chironomus riparius	first instar	N	S	fluopyram	97.5	am with artificial sediment	267.0 – 302.6	7.7 – 8.5	20.1 - 20.5	28 d	NOEC	development rate	1.63	2	7	[5]	p.139
Chironomus tentans	first instar	Y	R	fluopyram	94.7	nw with artificial sediment	36 - 44	6.3 - 7.0	21 - 25	54 d	NOEC	emergence and survival	0.14	2	8	[5]	p.144
Chironomus tentans	first instar	Y	R	fluopyram	94.7	nw with artificial sediment	36 - 44	6.3 - 7.0	21 - 25	54 d	NOEC	dry weight	0.29	2	8	[5]	p.144

Notes

* *Raphidocelis subcapitata* is formerly known as *Pseudokirchneriella subcapitata*

1 ELS study, based on TWA concentrations

2 based on TWA concentrations

3 frond number based on yield (final biomass), mean measured concentrations

4 frond number based growth rate, mean measured concentrations

5 frond area based growth rate, mean measured concentrations

6 frond area based on yield (final biomass), mean measured concentrations

7 spiked water, sediment not analysed, based on TWA concentrations in overlying water

8 spiked sediment, endpoint based on TWA concentrations overlying water, non-guideline study 9 based on mean measured concentrations

10 biomass area under the growth, based on mean measured concentration
11 growth rate, based on mean measured concentration
12 based on nominal concentrations, recovery 87 - 98%, recalculated to active substance
13 based on nominal concentrations, recovery 99 - 104%, recalculated to active substance
14 based on nominal concentrations, recovery 92-105%, recalculated to active substance
15 based on mean measured concentrations, effect concentration above practical limit of water solubility under test conditions
16 ELS study, based on TWA concentrations
17 based on TWA concentrations

Table A2.4. Chronic toxicity of fluopyram to saltwater organisms

Species	Species properties	A	Test type	Test compound	Purity [%]	Test water	pH	T [°C]	Salinity [‰]	Exp. time	Criterion	Test endpoint	Value [mg/L]	Ri	Notes	Ref.	Study Id.
Crustaceae																	
Leptocheirus plumulosus	0.71 – 1.0 mm	Y	R	fluopyram		nw	7.9 -8.0	25 ± 1	32 - 33	10 d	NOEC	mortality	1.6	2	1	[5]	p.110

Notes
1 endpoint growth, based on mean measured concentrations in sediment, spiked sediment study
2 endpoint growth, based on mean measured concentrations in overlying water, spiked sediment study

Annex 2 Commentaren Petit Comité INS

Commentaar petit comité		**Rapportnr :** Fluopyram	
Door: Theo Brock		**datum: 28-09-2018**	
P.	**paragraaf**	**Opmerking lid petit comité**	**Reactie Auteur**
5	1.3.3	Should not the CRED criteria ne used now to be up-to-date?	The validity criteria are presented in the spirit of the CRED criteria
5	1.3.3	What about toxicity data based on the formulated product (most probably a higher solubility)	The results of studies with the formulation show that the solubility is higher than that of the active substance
5	1.3.3	This assumes that the application of fluopyram is conducted correctly. From my experience this assumption often may be wrong. As a minimum requirement for reliability the concentration should be measured in the dosing solutions.	Although this might be the case it cannot be checked and the assumption made was that the applications were conducted correctly
8	3.1.1	This is a saltwater species (Skeletonema costatum)	Data removed from table 5 and reported under the marine species
9	3.1.1	This is a saltwater species (Skeletonema costatum)	Data removed from table 5 and reported under the marine species
10	3.2	Note that the Kingdom of fungi is very diverse and may contain both sensitive and insensitive species. Is it really justified to always apply an AF of 100 if a toxicity value for one of the fungi taxa is lacking without prior knowledge on the types of fungal taxa that may be sensitive? (It cannot be excluded that the species sensitivity distribution within the Kingdom of fungi is as variable as that for non-fungi.)	It is reported that the AF is applied because fungi are a **potentially** sensitive taxon. This AF is applied according to the guideline.

Commentaar petit comité		**Rapportnr :** Fluopyram	
Door: W. Peijnenburg		**datum: 28-09-2018**	
P.	**paragraaf**	**Opmerking lid petit comité**	**Reactie Auteur**

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
4	1.2	Ik doe ook meteen de details erbij: ik vind 'human health aspects' een rare omschrijving en stel voor om 'aspects'weg te laten. Verder zou onderaan paragraf 1.2 'function' vervangen moeten worden door 'functioning'.	Beiden tekstueel aangepast
7	Table 4	Ik heb het niet nagerekend maar ik neem aan dat de waarde van log van Koc van 2.46 gelijk is aan 278.9. Wat mij betreft mag de voetnoot dan ook weg.	Dat klopt. Voetnoot verwijderd.
7	Table 4	Bij hydrolyse halflife staat '-'. Is het misschien mogelijk om op basis van de duur en de analytische onzekerheid van het hydrolyse-experiment een >-waarde te schatten?	Er is geen studie aangeleverd, alleen eindpunten. Een schatting is dus niet mogelijk.
7	2.4.2	Hier staat de kryptisch zin 'and is not only that of the active substance.' Deze formulering is onduidelijk en dient aangepast.	Is aangepast
8	Table 5	Voor de tabellen 5-8 geldt dat het woord 'data' in de kop ontbreekt. Het gaat niet om ecotoxicity maar om ecotoxicity data.	Is aangepast
9	3.2	Hier staat dat data voor 3 marine organismen beschikbaar zijn. Op zich klopt dat wel, maar in alle gevallen gaat het om een >-waarde. Hierdoor zijn alle marine data dus feitelijk niet bruikbaar. M.i. zou dit aspect hier toegevoegd moeten worden.	Is toegevoegd
10	3.2	Ik vind inderdaad dat de extra factor vanwege het ontbreken van fungicide-data nodig is.	Ok.
10	3.3.1	Ik mis de onderbouwing van de factor 50.	Er staat aangegeven dat dit is omdat er geen toxicity data voor fungi aanwezig zijn. Dit is wat er in de guidance aangegeven staat.
10	3.3.1	Ook hier ben ik van mening dat een extra factor nodig is vanwege het ontbreken van fungicide-data.	Dat is dus inderdaad gedaan. De factor is nu 50 ipv 10 vanwege het ontbreken van fungicide data.

Commentaar petit comité	**Rapportnr :** Fluopyram
Door: D. ten Hulscher	**datum: 28-09-2018**

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
4	1.1	Het middel is expliciet gemaakt als fungicide. Is dat voldoende reden om ook effectgegevens voor fungi te willen betrekken. Het lijkt me ook raar dat die er niet zijn als het middel met dat doel is geproduceerd. Heeft de fabrikant die gegevens niet?	Er zijn gegevens aangeleverd voor schimmels maar dat zijn schimmels op planten. Voor de afleiding van de waternormen zijn deze niet relevant. Verder is er dmv aanpassing van de assessment factor rekening gehouden met ontbreken van gegevens van fungi.
4	1.3.1	Er is inmiddels een nieuwe guidance vastgesteld. graag hier vermelden, en of volgens de oude of de nieuwe guidance is gewerkt. Voor het onderdeel bioconcentratie/biomagnificatie is de methode sterk aangepast.	Er is gewerkt volgens de nieuwe guidance. De referentie is aangepast
6	2.2	(Mbt opmerking bij Henry's law constant ivm ontbreken temperatuur.) Deze is makkelijk te checken door zelf H uit te rekenen uit dampdruk en oplosbaarheid die beiden bij 20 graden zijn gegeven.	Dit blijkt bij narekenen een berekende waarde te zijn en dat is nu gerapporteerd
8	3.1.1	Is gemeten hoeveel van het werkzame bestanddeel in deze formuleringen zit, graag meer details om deze aanname/conclusie te kunnen beoordelen.	De hoeveelheid w.s. kan je in de tabellen in Annex I terugvinden. Per studie staat aangegeven waarom het resultaat ervan wel/niet is meegenomen als eindpunt.
8	3.1.1	Die zie je denk ik pas bij concentraties ver boven de oplosbaarheid.Graag meer info om de betrouwbaarheid van deze studies (terecht meegenomen?) te kunnen beoordelen	In Annex I staat er meer info over de betrouwbaarheid en deze info is meegenomen.
9	3.2	Dit is in tegenspraak met wat je hierboven zegt: Data for saltwater aquatic organisms were available but all acute endpoints from relevant studies were > values. . There is one relevant chronic study with saltwater organisms.	Er is nu een stukje toegevoegd over de zoutwater data. Als het goed is is dat afdoende.
10	3.2	Hierboven zeg je dat deze allemaal > getallen hebben opgeleverd. Ik denk niet dat de assessment factor omlaag kan.	Assessmentfactor is aangepast en nu dus niet meer verlaagd.

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
10	3.3.1	Het middel is op de markt gebracht als fungicide, mij lijkt dat deze data nodig zijn voor een gedegen beoordeling. Ik neem aan dat een fabrikant de werkzaamheid van een middel test en dat er dus gegevens moeten zijn. Zo niet dan is idd een extra factor nodig.	Een extra assessment factor vanwege het ontbreken van data voor fungi is al toegepast

Commentaar petit comité	**Rapportnr :** Fluopyram
Door: Mascha Rubach	**datum: 08-10-2018**

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
8	3.1.1	The sentence 'For Crustacea and Pisces, *all* studies conducted with the active substance resulted in > values or values exceeding 32 mg/L (twice the water solubility of 16 mg/L).' Suggest to add the word 'all' as done in italics above, otherwise sentence may seem unfinished.	added
8	3.1.1	Please elaborate, for further justification, whether any coformulants in the formulations used in the formulation studies could have inceased the toxicity of fluorpyram.	Since the lowest toxicity value is from a study with the active substance and since there is no indication that the results of studies performed with a formulation result in higher toxicity value, there is no reason to believe that coformulants in the formulations contributed to a higher toxicity of the formulation.
8	3.1.1	'This has no influence on the derived QS, but these values are included to show that these taxa were tested.' It is not clear what had no influence? Is the QS the same whether you include endpoints on crustaceans and fish or not? Or do you mean that the > than values are shown, but not included in the derivation? Or do you mean that by using the assessment factor approach for derivation, specific values were not of influence? Please clarify and amend and also make it clear in the Tables.	Adjusted to: The fact that the results of these studies were selected has no influence on the derived QS , but these values are included to show that these taxa were tested and contribute as such to the use of a lower assessment factor
8/9	Table 5-8	Please add footnotes (or bold typeface) to the table to clarify which endpoints were (not) used in the EQS derviations.	All data selected for EQS derivation are reported in the table

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
8	Table 5 / Reference list	Reference [9] appearantly relates to an azoxystobin EC directive. This does not make sense. Please correct.	corrected
8	Table 5 / Reference list	The Lemna endpoint derivation is not transparent as the reported endpoints of EC50s of 3.8 and 2.9 are from a formulation study and the lowest endpoint in the LoEP is 2.32 mg a.s./L, which cannot be found back in tge Annex table A2.1. Please correct or clarify.	The author of the study used the nominal concentrations of fluopyram to conduct statistical analyses, while the reviewer used mean-measured concentrations from days 0 and 7. The endpoint reported by the reviewer (2.9 mg/L) is used in this report.
9	3.2	`Apart from data *on* freshwater organisms, data *on* salt water organisms is also available for three species from three *different animal groups*.` Editorial suggestions in italics above. The use of the word taxa is confusing in this context.	Editorial suggestion applied. I prefer the use of the word taxa since this is used in the guidance document
9	3.2	Please correct the lowest endpoint and MAC-EQS derivation, if necessary following above comment. The additional safety factor of 10 (100 in total, leading to a MC-EQS of 32 µg/L) is considered necessary from our perspective, indeed due to the absence of tox data on funghi, while the mode of action as an SDHI is well known and can indeed be considered broad spectrum. Efficacy against targets such as *Botrytis cinerea* is expected at 0.03-0.29 µg/mL (https://onlinelibrary.wiley.com/doi/abs/10.1002/ps.3241). With this safety factor (and the additional 10 for saltwater species) non-target fungi in the same range of sensitity should be covered. Note that fluopzram is not registered as an active substance for biocidal uses under the BPR.	Not necessary Ok

P.	paragraaf	Opmerking lid petit comité	Reactie Auteur
10	3.2	I see an issue with reducing the safety factor for the marine species from default 10 to 5. Yes, there are three marine species included in the testing, but they all resulted in higher than values, of which the lowest is 0.43 mg as/L, which is a factor 7.5 lower than 3.2 µg/L (result of applying the default of 10). Of course we do not know the sensitivity of this species, but exactly therefore the safety factor should not be lowered only because 3 higher than values are available. Furthermore, in an earlier section of the report it is mentioned that unbound values are not taken into account, which is confusing if here they are taken into account.	The extra assessment factor is removed and the text is adjusted
10	3.3	I agree with the additional safety factor of 50 for the derivation of the AA-EQS due to the absence of funghi tox data.	OK
10	3.3.1	`NOECs are available for nine freshwater and one saltwater species, representing seven taxa, covering the base set.` The word taxa is confusing as all species names are known. We assume it should be subgroups or be more specific in other ways.	As reported earlier: the guidance uses the word taxa so this is preferred.
12	5	References 9 and 10 refer to azoxystrobine.	Deleted.
12	5	The reference list seems incomplete. I did not check all references, but for instance Riebschlaeger 2013 (daphnia acute with the PPP) is missing. – or is it the T.R. reference 17? Also one Matlock & Moore 2016 with rainbow trout study is missing. Maybe there are more ?	Checked the reference list and added the missing references.
ff	Annex ?	Normally the study sumamries of new data are included? Please include in an Annex.	Summaries of new data are not included in an Annex. The results are only reported in the tables in Annex 1 of this report