Committee for Risk Assessment

RAC

Annex 1
Background document
to the Opinion proposing harmonised classification and labelling at EU level of

azoxystrobin (ISO); methyl (*E*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate

EC Number: -
CAS Number: 131860-33-8

CLH-O-0000001412-86-206/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

8 June 2018

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

Substance Name: Azoxystrobin

EC Number: **Not allocated**

CAS Number: **131860-33-8**

Index Number: **607-256-00-8**

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Chemicals Regulation Directorate

Health and Safety Executive

United Kingdom

Version number: **2** **Date:** **July 2017**

ANNEX 1 - BACKGROUND DOCUMENT TO RAC OPINION ON AZOXYSTROBIN (ISO); METHYL (*E*)-2-{2-[6-(2-CYANOPHENOXY)PYRIMIDIN-4-YLOXY]PHENYL}-3-METHOXYACRYLATE

CONTENTS

Part A.

Part B.

Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	**Azoxystrobin**
EC number:	***Not allocated***
CAS number:	***131860-33-8***
Annex VI Index number:	***607-256-00-8***
Degree of purity:	***≥ 96.5%***
Impurities:	***There are a number of process impurities. These have been taken into account and are not considered to impact on the proposed classification and labelling. Further information is provided in section 1.2 of Part B.***

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation
Current entry in Annex VI, CLP Regulation	Acute Tox 3*; H331- Toxic if inhaled Aquatic Acute 1; H400 – Very toxic to aquatic life Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects
Current proposal for consideration by RAC	**Removal of * from the acute toxicity classification and inclusion of M-factors** Acute Tox 3; H331- Toxic if inhaled Aquatic Acute 1; H400 – Very toxic to aquatic life Acute M factor = 10 Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects Chronic M factor = 10

Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Acute Tox 3; H331- Toxic if inhaled Aquatic Acute 1; H400 – Very toxic to aquatic life Acute M factor = 10 Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects Chronic M factor = 10

1.3 Proposed harmonised classification and labelling

Table 3: Proposed classification

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives	-	-	-	Not considered in this proposal
2.2.	Flammable gases	-	-	-	Not considered in this proposal
2.3.	Flammable aerosols	-	-	-	Not considered in this proposal
2.4.	Oxidising gases	-	-	-	Not considered in this proposal
2.5.	Gases under pressure	-	-	-	Not considered in this proposal
2.6.	Flammable liquids	-	-	-	Not considered in this proposal
2.7.	Flammable solids	-	-	-	Not considered in this proposal
2.8.	Self-reactive substances and mixtures	-	-	-	Not considered in this proposal
2.9.	Pyrophoric liquids	-	-	-	Not considered in this proposal
2.10.	Pyrophoric solids	-	-	-	Not considered in this proposal
2.11.	Self-heating substances and mixtures	-	-	-	Not considered in this proposal
2.12.	Substances and mixtures which in contact with water emit flammable gases	-	-	-	Not considered in this proposal
2.13.	Oxidising liquids	-	-	-	Not considered in this proposal
2.14.	Oxidising solids	-	-	-	Not considered in this proposal
2.15.	Organic peroxides	-	-	-	Not considered in this proposal
2.16.	Substance and mixtures corrosive to metals	-	-	-	Not considered in this proposal
3.1.	Acute toxicity - oral	-	-	-	Not considered in this proposal
	Acute toxicity - dermal	-	-	-	Not considered in this proposal

	Acute toxicity - inhalation	**Acute Tox. 3; H331 – Toxic if inhaled** **(Removal of *)**	**Not applicable**	**Acute Tox 3*; H331 – Toxic if inhaled**	-
3.2.	Skin corrosion / irritation	-	-	-	Not considered in this proposal
3.3.	Serious eye damage / eye irritation	-	-	-	Not considered in this proposal
3.4.	Respiratory sensitisation	-	-	-	Not considered in this proposal
3.4.	Skin sensitisation	-	-	-	Not considered in this proposal
3.5.	Germ cell mutagenicity	-	-	-	Not considered in this proposal
3.6.	Carcinogenicity	-	-	-	Not considered in this proposal
3.7.	Reproductive toxicity	-	-	-	Not considered in this proposal
3.8.	Specific target organ toxicity – single exposure	-	-	-	Not considered in this proposal
3.9.	Specific target organ toxicity – repeated exposure	-	-	-	Not considered in this proposal
3.10.	Aspiration hazard	-	-	-	Not considered in this proposal
4.1.	**Hazardous to the aquatic environment**	**Aquatic Acute 1; H400 – Very toxic to aquatic life** **Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects**	**Acute M = 10** **Chronic M = 10** **(Addition of M-factors)**	**Aquatic Acute 1; H400 – Very toxic to aquatic life** **Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects**	-
5.1.	Hazardous to the ozone layer	-	-	-	Not considered in this proposal

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling:

Pictogram(s):	GHS06, GHS09
Signal word:	Danger
Hazard statements:	H331 – Toxic if inhaled
	H410 – Very toxic to aquatic life with long lasting effects
Precautionary statements:	Not included in Annex VI

Proposed notes assigned to an entry: N/A

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

Azoxystrobin is a pesticide and biocide active substance which has an existing entry in Annex VI of CLP. The substance was originally classified under the Dangerous Substances Directive (Dir 67/548/EEC or DSD) in the late 1990's as T; R23, N; R50/53. This classification was translated to Acute Tox. 3*; H331 – Toxic if inhaled, Aquatic Acute 1; H400 – Very toxic to aquatic life and Aquatic Chronic 1; H410 – Very toxic to aquatic life with long lasting effects in Annex VI of CLP.

This proposal seeks to update the existing entry by confirming the classification for acute toxicity via the inhalation route (i.e. to remove the *) and including M-factors. The other hazard classes and differentiations are not addressed in this proposal.

At the time of submission, the substance is not registered under REACH.

2.2 Short summary of the scientific justification for the CLH proposal

In an acute inhalation study in rats, the LC_{50} of azoxystrobin was found to be 0.698 mg/l in females and 0.962 mg/l in males. Therefore, the criteria for classification as **Acute Tox 3; H331 – Toxic if inhaled** are met; confirming the existing classification and allowing for the removal of the *.

Azoxystrobin is considered not rapidly degradable for the purpose of classification and has a low bioaccumulation potential.

The lowest acute endpoint is the EC_{50} of 0.055 mg/L from the study with Mysid shrimp. As this is < 1 mg/L, classification as **Aquatic Acute Category 1; H400 – Very toxic to aquatic life** is proposed with an **acute M-factor of 10** (>0.01 to ≤ 0.1 mg/L).

The lowest chronic endpoint is the NOEC of 0.00954 mg/L from the study with Mysid shrimp. As this is < 0.1 mg/L and the active is not considered to be rapidly degradable, classification as **Aquatic Chronic Category 1; H410 – Very toxic to aquatic life with long lasting effects** is proposed with a **chronic M-factor of 10** (>0.001 to ≤ 0.01 mg/L).

The classification proposed in this CLH report is consistent with that considered in the EFSA conclusion on the risk assessment of the pesticide active substance (EFSA Journal 2010; 8(4):1542) and included in the draft CAR (dCAR), 2016.

2.3 Current harmonised classification and labelling

2.3.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

Classification		Labelling			Specific Concentration limits, M-Factors	Notes
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**	**Supplementary Hazard Statement Code(s)**	**Pictograms, Signal Word Code(s)**		
Acute Tox. 3 * Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H410		GHS06 GHS09 Dgr		

2.4 Current self-classification and labelling

2.4.1 Current self-classification and labelling

At the time of submission the following entries were included in the C&L Inventory

Classification		Labelling			Specific Concentration limits, M-Factors	Number of Notifiers
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**	**Supplementary Hazard Statement Code(s)**	**Pictograms, Signal Word Code(s)**		
Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H410		GHS06 GHS09 Dgr		68
Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H400 H410		GHS06 GHS09 Dgr		37

Classification		Labelling			Specific Concentration limits, M-Factors	Number of Notifiers
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**	**Supplementary Hazard Statement Code(s)**	**Pictograms, Signal Word Code(s)**		
Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H410	EUH401	GHS06 GHS09 Dgr		21
Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H410		GHS06 GHS09 Dgr		19
Acute Tox. 3 Aquatic Acute 1 Aquatic Chronic 1	H331 H400 H410	H331 H410		GHS06 GHS09 Dgr		1

RAC general comment

The active substance azoxystrobin is a pesticide (broad-spectrum 'Qo' inhibitor fungicide – see below) and biocide (product-type 7, 9 and 10 - film preservatives; fibre, leather, rubber and polymerised materials preservatives; and construction material preservatives, respectively), which has an existing entry in Annex VI of the Regulation (EC) No 1272/2008 (CLP Regulation) as Acute tox. 3*; H331, Aquatic Acute 1; H400, Aquatic Chronic 1; H410, with no M-factors.

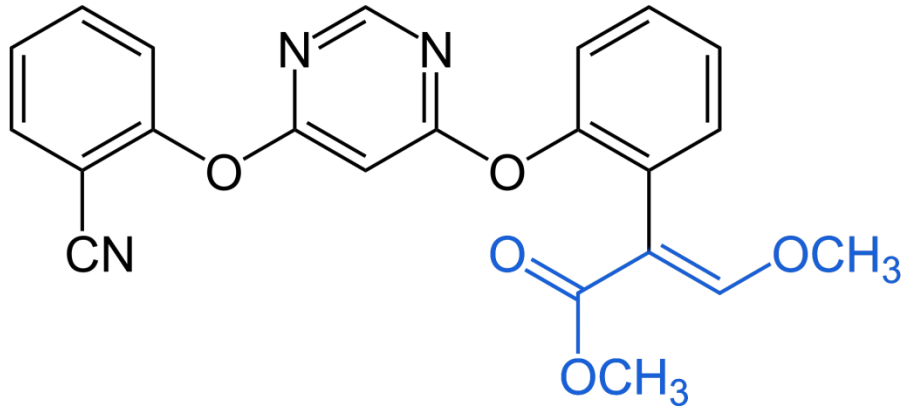


Figure 1: Azoxystrobin: Basic structure, the toxophore is the β-methoxyacrylate portion (shown in blue)

The Qo fungicides inhibit plant pathogens by blocking their ability to produce energy. They do this by blocking the transfer of electrons at the Quinone "outside" site of the bc1 complex (complex III in the electron transport chain).

The DS proposal in the CLH report for human health hazards seeks to update the existing entry by confirming the classification for acute toxicity via the inhalation route (i.e. to remove the minimum classification or *) and to add the ATE value as well as to re-evaluating the environmental hazard classes. Other hazard classes were **not** addressed.

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Azoxystrobin in an active substance with both biocidal and pesticidal use. As azoxystrobin already has an existing harmonised entry this proposal seeks to confirm the existing classification for acute toxicity via the inhalation route (i.e. to remove the *) and to include M-factors only. The other hazard classes and differentiations are not addressed in this proposal.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

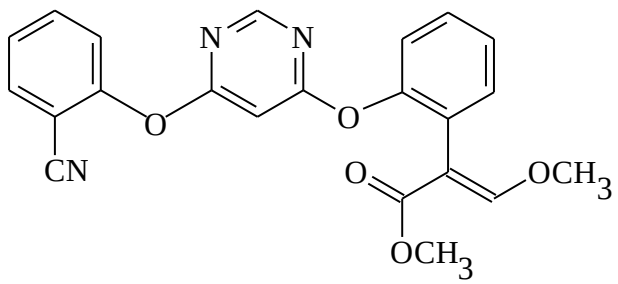
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 4: Substance identity

EC number:	Not listed
EC name:	Not listed
CAS number (EC inventory):	Not listed
CAS number:	131860-33-8
CAS name:	Benzeneacetic acid, 2-[[6-2(2-cyanophenoxy)-4-pyrimidinyl]oxy]-α-(methoxymethylene)-, methyl ester, (αE)-
IUPAC name:	Methyl(E)-2-{2[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate
CLP Annex VI Index number:	607-256-00-8
Molecular formula:	403.4
Molecular weight range:	C22H17N3O5

Structural formula:



1.2 Composition of the substance

Table 5: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
Azoxystrobin	> 96.5%	96.5 – 100%	

Current Annex VI entry:

Table 6: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks
Z-isomer	-	< 2.5%	At this concentration it is not considered to impact on the classification.
Toluene	-	< 0.5%	At this concentration it is not considered to impact on the classification.

Identified relevant impurities are listed above. There are a number of other process impurities in the substance. These have been taken into consideration and are not considered to impact on the classification proposed in this dossier. Further information on the impurities is considered to be confidential but full details are provided in the IUCLID.

Current Annex VI entry: Toluene

Classification		Labelling			Specific Concentration limits, M-Factors	Notes
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Supplementary Hazard Statement Code(s)	Pictograms, Signal Word Code(s)		
Flam. Liq. 2 Skin Irrit. 2 Asp. Tox. 1 STOT SE 3 STOT RE 2 * Repr. 2	H225 H315 H304 H336 H373 ** H361d ***	H225 H315 H304 H336 H373 ** H361d ***		GHS02 GHS08 GHS07 Dgr		

Due to the concentration at which this impurity is present, it is not considered to impact on the classification.

Table 7: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
None				

Current Annex VI entry: N/A

1.2.1 Composition of test material

The material used in the relevant studies is considered to be equivalent to that outlined above.

1.3 Physico-chemical properties

All studies were conducted according to GLP.

Table 8: Summary of physico-chemical properties

Property	**Value**	**Reference**	**Comment (e.g. measured or estimated)**
State of the substance at 20°C and 101,3 kPa	White crystalline powder	Wollerton, C and Husband, R 1993	Visual observation Purity 99%
Melting/freezing point	116° C	Wollerton, C and Husband, R 1993	OECD 102 Purity 99%
Boiling point	Not determined, azoxystrobin decomposes at 345ºC	Husband, R 2000	OECD 103
Relative density	1.34 g/cm^3 at 20° C	Wollerton, C and Husband, R 1995	EEC, A3/ OECD 109 Purity 99%
Vapour pressure	1.1 x 10^{-10} Pa at 20°C	Wollerton, C and Husband, R 1993	OECD 104 Purity 99%
Surface tension	71.8 mN/m at 20°C (90% saturated solution)	Wollerton, C and Husband, R 1995	EEC A.5/OECD 115 Purity 96.2 % (technical)
Water solubility	0.0067g/l at pH 5.2 and 20°C 0.0067g/l at pH 7 and 20°C 0.0059g/l at pH 9.2 and 20°C	Wollerton, C and Husband, R 1993	EEC A6 Purity 99%
Partition coefficient n-octanol/water	Log P_{ow} = 2.5 at pH 7 and 20°C	Wollerton, C and Husband, R 1993	OECD 107
Flash point	Not applicable		
Flammability	Not-flammable Based on experience in handling and use, the substance is not pyrophoric and is not highly flammable in contact with water	Wollerton, C and Husband, R 1995	EEC A10 Purity 96.2% (technical)

Explosive properties	Examination of the chemical structure does not reveal bond groupings known to confer explosibility	Wollerton, C and Husband, R 1993	-
Self-ignition temperature	The substance did not self-ignite under the conditions of the test	Wollerton, C and Husband, R 1995	EEC, A16 Purity 96.2% (technical)
Oxidising properties	From a consideration of the structure, azoxystrobin is not considered to have oxidizing properties		
Granulometry	No data		
Stability in organic solvents and identity of relevant degradation products	No data		
Dissociation constant	Azoxystrobin has no acid or basic properties in aqueous solutions. It is therefore impossible to specify dissociation constants of the active ingredient in water	Wollerton, C and Husband, R 1993	Based on UV spectral data
Viscosity	Not applicable - solid		

2 MANUFACTURE AND USES

2.1 Manufacture

Azoxystrobin is manufactured within the EU.

2.2 Identified uses

Azoxystrobin is a fungicide with intended pesticide and biocide use. As a pesticide, representative uses include application to broccoli, cauliflower, Brussels sprouts, kale, barley and wheat. As a biocide, it is intended to preserve a range of materials in Product Types (PTs) 7 (Film preservatives), 9 (Fibre, leather, rubber and polymerised materials preservatives) and 10 (Construction material preservatives). Products containing azoxystrobin will be used by professional users during the manufacture of such materials.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

3.1 Physico-Chemical Properties

Not considered in this proposal

4 HUMAN HEALTH HAZARD ASSESSMENT

The hazard assessment is based on the information provided in the dCAR (2016) and the RAR – Volume 3; B6 (2009)

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

4.1.1 Non-human information

4.1.2 Human information

4.1.3 Summary and discussion on toxicokinetics

Azoxystrobin is absorbed following oral, dermal and inhalation exposure in a dose dependent manner. The absorbed compound is completely metabolised yielding at least 15 metabolites (with some quantitative differences between the sexes) and is eliminated rapidly, mainly via the bile. Major metabolic pathways are hydrolysis of the methoxyacid with subsequent conjugation with glucuronic acid or glutathione conjugation of the cyanophenyl ring.

4.2 Acute toxicity

Only acute toxicity via the inhalation route is considered in this proposal. Two studies in the rat are available and are both summarised in the table below.

Table 9: Summary table of relevant acute toxicity studies

<table>
<tr><th colspan="3">Acute Inhalation</th></tr>
<tr><th>Method</th><th>LC50</th><th>Observations and remarks</th></tr>
<tr><td>Acute Inhalation Toxicity Study
OECD 403

Rats (Crl:(WI)BR strain)
5/sex/dose

4-hours, nose only

Azoxystrobin; 95.2%
Total particulate concentration: 257, 511, 767 and 1010 µg/l, which were chemically analysed as 242, 481, 717 and 968 µg azoxystrobin/l, respectively.

MMAD < 2 µm

GLP

(Anonymous (1992))</td><td>Females = 698 µg/l

Males = 962 µg/l</td><td>There were no deaths in animals exposed to 257 µg/l azoxystrobin. One male died and one female was killed in extremis during exposure to 511 µg/l azoxystrobin. One male and one female died and two females were killed in extremis during exposure to 767 µg/l azoxystrobin. One male died and two further males were killed in extremis during exposure to 1010 µg/l azoxystrobin

<table><tr><th rowspan="2">actual conc. (µ/l)</th><th colspan="2">Total mortalities</th></tr><tr><th>M</th><th>F</th></tr><tr><td>257</td><td>0</td><td>0</td></tr><tr><td>511</td><td>1</td><td>1</td></tr><tr><td>767</td><td>1</td><td>3</td></tr><tr><td>1010</td><td>3</td><td>0</td></tr></table>
Darkening and mottling of the lungs were observed in rats that died or were killed prior to the scheduled termination of the study.</td></tr>
<tr><td>Acute Inhalation Toxicity Study OECD 403

Rats (Alpk: APfSD strain)
5/sex

4-hours- nose only, (particle size MMAD >14µm)

Azoxystrobin; 96.2%
Total particulate concentration: 4.70 mg/litre (method of measurement not stated.

GLP

(Anonymous, 1997)</td><td>> 4.7 mg/l</td><td>There were no mortalities.

All animals had increased breathing depth during exposure. Following exposure, abnormal respiratory noise was heard in two males and one female. 3 males and 1 female displayed subdued behaviour.

All animals had fully recovered by day 7 of the study.</td></tr>
</table>

4.2.1 Non-human information

4.2.1.1 Acute toxicity: oral

Not considered in this proposal.

4.2.1.2 Acute toxicity: inhalation

In the initial acute inhalation study, the LC_{50} was determined to be 698 µg/l (0.698 mg/l) in females and 962 µg/l (0.962 mg/l) in males. Darkening and mottling of the lungs were observed in the rats that died during exposure.

In another study conducted on azoxystrobin, the LC_{50} was determined to be >4.7 mg/l. However, it is noted that measurements of the atmosphere generated gave mean aerodynamic particle size of 14.6 µm $\pm$ 3.91 and 14.8 µm $\pm$ 3.34, which falls outside the range recommended in the guidelines.

4.2.1.3 Acute toxicity: dermal

Not considered in this proposal.

4.2.1.4 Acute toxicity: other routes

4.2.2 Human information

4.2.3 Summary and discussion of acute toxicity

4.2.4 Comparison with criteria

In a 4-hour acute inhalation study, the LC_{50} was determined to be 0.698 mg/l in females and 0.962 mg/l in males. An LC_{50} of >4.7 mg/l was determined in a second study, but is it is noted that the particle size of the test material was relatively high (i.e., the MMAD of the test material was >14 µm). Therefore, it is considered that the values from the earlier study should be considered for the classification. For dusts and mists, classification in category 3 is appropriate where 0.5 mg/l < ATE $\leq$ 1.0 mg/l. Therefore, considering the results in the first study, the criteria for classification in category 3 are met and the * should be removed from the existing Annex VI entry.

It is also proposed to include an ATE value of 0.7 mg/l, based on the lowest LC_{50} reported.

4.2.5 Conclusions on classification and labelling

Acute Tox 3; H331 – Toxic if inhaled.
ATE = 0.7 mg/l

RAC evaluation of acute toxicity

Summary of the Dossier Submitter's proposal

Only acute toxicity via the inhalation route was considered in this proposal. The substance was originally classified for human health under the Dangerous Substances Directive (Dir 67/548/EEC or DSD) in the late 1990's as T; R23. This classification was transposed to Acute Tox. 3*; H331 – Toxic if inhaled in Annex VI of the CLP Regulation. The DS proposal seeks to update the existing entry by confirming the classification for acute toxicity via the inhalation route (i.e. to remove the *, i.e. the minimum classification) and to add the ATE value (0.7 mg/L (dust or mist)).

Two studies in rats were presented and summarised (Anon., 1997 and Anon., 1992). Only one was considered sufficient for classification purposes (Anon., 1992) due to the unacceptably high MMAD (Mass Median Aerodynamic Diameter) values (> 14 µm), observed in the more recent 1997 study (guideline requires an MMAD of 1-4 µm).

In the Anon. (1992) acute inhalation study in rats (Crl:(WI)BR strain; 5/sex/dose), the LC_{50} of azoxystrobin was found to be 0.698 mg/L in females and 0.962 mg/L in males, confirming the existing classification in category 3 and allowing for the removal of the minimal classification (i.e. *) and the addition of an ATE value of 0.7 mg/L (dust or mist).

Comments received during public consultation

Three MSCAs commented in the PC in support of the proposed classification for acute inhalation toxicity. Two supported the proposed ATE of 0.7 mg/L. The third, while supporting the classification, did not agree with proposed ATE stating that a more conservative approach, a value of 0.5 mg/L, should be adopted. The DS responded that this should be considered by the RAC.

Assessment and comparison with the classification criteria

In a 4-hour acute inhalation study, the LC_{50} was determined to be 0.698 mg/L in females and 0.962 mg/L in males. An LC_{50} of > 4.7 mg/L was determined in a second study, but it is noted that the particle size of the test material was relatively high (i.e., the MMAD of the test material was > 14 µm). According to Annex I: 3.1.2.3.2 of CLP, dusts and mists with particle sizes in the range 1 – 4 µm mean mass aerodynamic diameter (MMAD) inhaled by rats are applicable to human exposure. Therefore, it is considered that only the values from the earlier study (1992) should be considered for classification.

It is noted by RAC that the applicant conducted the subsequent (1997) acute inhalation study with a particle size that more accurately represents the particle size of azoxystrobin technical grade active ingredient as manufactured.

In the 1992 study, there were no deaths in animals exposed to 257 µg/L azoxystrobin technical. One male died and one female was killed *in extremis* during exposure to 511 µg/L. One male and one female died and two females were killed *in extremis* during exposure to 767 µg/L azoxystrobin. One male died and two further males were killed *in*

extremis during exposure to 1010 µg/L (see table below) but all the females survived.

Darkening and mottling of the lungs were observed in rats that died or were killed prior to the scheduled termination of the study. The LC_{50} for males was calculated at 0.962 mg/L and at 0.698 (0.70) mg/L for females.

For dusts and mists, classification in category 3 is appropriate where 0.5 mg/L < ATE ≤ 1.0 mg/L. Therefore, considering the results in the one acceptable study provided (Anon. 1992), **the criteria for classification in category 3 are met and the * should be removed from the existing Annex VI entry**.

The proposed ATE of 0.7 mg/L is supported by the RAC; it is the lowest LC_{50} estimated from the data and considered sufficiently protective.

4.3 Specific target organ toxicity – single exposure (STOT SE)

Not considered in this proposal.

4.4 Irritation

Not considered in this proposal.

4.4.1 Eye irritation

Not considered in this proposal.

4.4.2 Respiratory tract irritation

Not considered in this proposal.

4.5 Corrosivity

Not considered in this proposal.

4.6 Sensitisation

Not considered in this proposal.

4.6.1 Respiratory sensitisation

Not considered in this proposal.

4.7 Repeated dose toxicity

Not considered in this proposal.

4.8 Germ cell mutagenicity (Mutagenicity)

Not considered in this proposal.

4.9 Carcinogenicity

Not considered in this proposal.

4.10 Toxicity for reproduction

Not considered in this proposal.

4.11 Other effects

Not considered in this proposal.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Azoxystrobin was originally classified under the Dangerous Substances Directive (Dir 67/548/EEC) in the late 1990's as N, R50/53. This classification was later translated to CLP classification of Acute Category 1 (H400) and Chronic Category 1 (H410). This proposal seeks to confirm the existing entry and to define the M-factors.

Pesticide assessment of Azoxystrobin

Azoxystrobin was initially assessed by DE under Directive 91/414/EEC in the 1990's for use as a pesticide. In this assessment, toxicity studies were tabulated and not summarised in depth. Toxicity endpoints were however deemed reliable and acceptable for risk assessment purposes as stated in the list of endpoints table (LOEP table, SANCO 7581/VI/97-rev5 22 April 1998). The EU Annex I renewal of azoxystrobin as a pesticide was carried out by the UK, under Regulation 1107/2009 and finalised in 2010 (please refer to EFSA Journal 2010; 8 (4):1542). Studies previously considered for the initial DE assessment were not revisited during the renewal assessment as they were still considered relevant and reliable. A number of additional toxicity studies were submitted and considered. As a result of this, a new List of Endpoints (LOEP) table was produced (please refer to EFSA Journal 2010; 8 (4):1542) which states the most critical endpoints for the whole data package.

New toxicity studies submitted for the renewal assessment have been summarised under the headings below (5.4.1-5.4.4). As stated above, no study summaries are available for any of the initial toxicity studies considered by DE and tabulated in the monograph. Please refer to Section 6 of this report for these tabulated studies. However, the following studies are summarised in IUCLID as part of the biocide assessment:

Acute fish toxicity: Anonymous., 1992, Anonymous, 1993, Anonymous, 1993.

Chronic fish toxicity: Anonymous, 1994, Anonymous, 1994.

Acute invertebrate toxicity: Rapley, Farrelly and Hamer, 1994, Farrelly and Hamer, 1994, Farrelly *et al.,* 1995, Kent *et al.,* 1993.

Chronic invertebrate toxicity: Rapley *et al.,* 1994, Boeri *et al.,* 1997.

Sediment dwellers: Farrelly *et al.,* 1995, Gentle and Rapley, 1997.

Algae toxicity: Smyth *et al.,* 1993a, Smyth *et al.,* 1994a, Smyth *et al.,* 1994b.

Aquatic plant toxicity: Smyth *et al.,* 1994.

Microbial activity: Morris *et al.,* 1994.

Biocide assessment of Azoxystrobin

When azoxystrobin was considered as a biocide in 2016, one study over and above those submitted for the pesticide consideration was submitted (this study on *Chironomus riparius* has been discussed further below under section 5.4.2.2). Therefore, the majority of the studies submitted for the assessment were previously submitted and considered during the EU Annex I renewal of azoxystrobin as a pesticide under Regulation 1107/2009. At the time of writing (December 2016), the biocide assessment has been submitted but is undergoing peer review.

5.1 Degradation

Table 10: Summary of relevant information on degradation

Method	Results	Remarks	Reference
Hydrolysis			
Equivalent to OECD 111, GLP compliant	25ºC: stable at pH 5, 7 and 9 50ºC: stable at pH 5 and 7, DT_{50} 12.08 d at pH 9; R234886 12%	Stable to hydrolysis under environmental conditions	Steel & Joseph, 1994
No specific guideline, GLP compliant	60ºC: DT_{50} 2.6d at pH 9 (>1000 d at 20°C)	Stable to hydrolysis under environmental conditions	Tummon & Hurt, 1995
Photolysis			
Equivalent to OECD 316, GLP compliant	DT_{50} 8.4 – 13.9d Florida summer sunlight Photodegrades (max after 30 days): R230310 16.3% R401553 8.9% R402173 2.4% CO_2 5.4%	Azoxystrobin is subject to aqueous photolysis	Kuet & Hadfield, 1994
Biodegradation			
Water/sediment simulation test German BBA Guideline Part IV, Section 5-1, GLP compliant	Old Basing system: Whole system DT_{50} (12ºC) 444d Mineralization 2.5% after 152d Virginia Water system: Whole system DT_{50} (12ºC) 341d Mineralization 5.1% after 152d Water: max 91.2% after 0d (Virginia) Sediment: max 90.5% after 0d (Old Basing) Metabolites: R234886 max 10.8% in water, 15.6 % in sediment after 152 d	Azoxystrobin degrades slowly in water/sediment systems. No significant mineralization.	Water/sediment study: Warinton, 1994 Kinetics: Harvey, 2008

Outdoor pond test SETAC Guideline on Testing Procedures for Pesticides in Freshwater Mesocosms (1991) Summary recommendations of the European Workshop on Freshwater Field Tests (1992)	Water: Nominal time 0 concentration 8.95 µg/l. Max observed 10.3µg/l (115%) after 3 hours. 2.4µg/l (27%) after 28 days. Sediment: Max 0.039 mg/kg after 21 days, 0.023 mg/kg after 119 days $DissT_{50}$ water: 13.1d $DissT_{50}$ sediment: not calculated	Azoxystrobin partitions to sediment No information on degradation	Jones & Lake, 2000

Substance identities and structures are provided in Annex 1

5.1.1 Stability

Hydrolysis

The hydrolysis of ^{14}C-azoxystrobin was investigated at 25 and 50 ^{o}C in sterile aqueous buffer solutions of pH 5, 7 and 9 (Steel & Joseph, 1994). At 25 ^{o}C azoxystrobin was shown to be stable to hydrolysis at pH 5, 7 and 9 over 31 days. At 50 ^{o}C hydrolysis of azoxystrobin was shown to be pH dependent; at pH 5 and 7 azoxystrobin was stable to hydrolysis over 12 days whilst at pH 9, significant hydrolysis was observed with 48.5% of the parent compound remaining after 12 days. The half-life was calculated to be 290 hours (12.08 days) at pH 9. R234886 was identified as the main hydrolysis product observed at a maximum of 12%.

The hydrolysis of azoxystrobin was investigated in sterile aqueous buffer solution at pH 9 and 60 ^{o}C over 7 days (Tummon & Hurt, 1995). Significant hydrolysis was observed with 16% of the parent compound remaining after 7 days. The half-life was calculated to be 2.6 days. Together with the data from Steel & Joseph, 1994, an Arrhenius plot was constructed and the half-life of azoxystrobin at 20 ^{o}C and pH 9 was estimated to be 2313 days. Therefore, hydrolysis is not expected to represent a significant pathway for degradation of azoxystrobin under realistic environmental conditions.

Aqueous Photolysis

One acceptable study is available for the photo transformation of azoxystrobin in water (Kuet & Hadfield, 1994). Sterile aqueous solutions of ^{14}C-azoxystrobin, separately radio labelled in either the cyanophenyl, pyrimidinyl or phenylacrylate ring, were prepared in pH 7 buffer. Treated samples were continuously irradiated using light from a xenon arc lamp for defined periods up to the equivalent of approximately 30 days Florida summer sunlight (50 ^{o}N at 25 ± 1 ^{o}C). Dark control samples were stored under the same conditions and analysed at the final sampling time. In a separate trapping experiment, volatiles were captured in sodium hydroxide ethanolamine solutions. After 30 days 97 to 101 % of applied radioactivity was found in the dark control samples and no degradation was observed. Azoxystrobin degraded extensively in irradiated samples under the experimental conditions. At least 15 photo degradates were observed of which 6 were identified. The main component was the z-isomer of azoxystrobin (R230310) observed at a maximum of 16.3 % and was the only photo degradate observed at >10 %. Unidentified degradates accounted for up to 30 % applied radioactivity and consisted of at least 7 discrete bands. Azoxystrobin was the major component in all the samples analysed, accounting for between 11.1 % and 25.7 % of applied radioactivity at the final sampling interval. Volatiles were determined in the separate experiment to be 6.2 % of which 5.4 % was characterized as carbon dioxide. Under the experimental conditions azoxystrobin exhibits biphasic kinetics with the half-life of azoxystrobin in Florida summer sunlight

calculated to be 8.4 days (^{14}C-pyrimidinyl label), 11.9 days (^{14}C-phenylacrylate label) and 13.9 days (^{14}C-cyanophenyl label).

5.1.2 Biodegradation

5.1.2.1 Biodegradation estimation

Not available.

5.1.2.2 Screening tests

Not available.

5.1.2.3 Simulation tests

Water/sediment

The degradation of azoxystrobin (^{14}C-labelled in either the cyanophenyl, pyrimidinyl or phenylacrylate ring) was studied in two different natural water-sediment systems (Old Basing and Virginia Water) under non-sterile laboratory conditions over 152 days in the dark at 20 ^{o}C (Warinton, 1994). The test was GLP compliant and carried out in accordance with German BBA Guideline Part IV, Section 5-1 which is considered equivalent to OECD 308. Sites for water and sediment collection were chosen on the basis of the physical characteristics of the sediment (sand and clay contents) and were not pre-exposed to the test compound. Azoxystrobin was applied at concentrations equivalent to a single application of 252 to 273 g/ha distributed in water to 30 cm (84 to 91 µg/l). After 152 days approximately 57 % AR and 51 % AR azoxystrobin remained in the Old Basing and Virginia Water whole systems respectively. Metabolite R234886 was observed at a maximum of 17.7 % AR (whole system). No other metabolites were observed at levels greater than 2 % AR. Azoxystrobin was observed at a maximum of 90.5 % AR in sediment on day 0 in the Old Basing system. Mineralisation to CO_2 reached 2 % AR to 6 % AR of applied activity after 152 days. Non-extractable residues increased throughout the study, although maximum levels at the end of the incubation accounted for only 5 to 7 % AR of the applied radioactivity. The results of Warinton, 1994, were re-interpreted according to FOCUS Kinetics Guidance (2006) (Harvey, 2008). Degradation of azoxystrobin from the whole system was modelled using SFO kinetics: DT_{50} values at 20 ^{o}C are 234 and 180 days for the Old Basing and Virginia Water systems respectively. At the average EU outdoor temperature of 12 ^{o}C DT_{50} values are 444 days and 341 days for the Old Basing and Virginia Water systems respectively.

Outdoor mesocosm

An outdoor experimental pond study (Jones & Lake, 2000) was conducted according to the following guidelines:

- SETAC (1991). Guidance Document on Testing Procedures for Pesticides in Freshwater Static Mesocosms. From the workshop "A Meeting of Experts on Guidelines for Static Field Mesocosm Tests" held at Monks Wood Experimental Station, Huntingdon, UK, 3-4 July 1991).
- Crossland, N O; Heimbach F; Hill I R; Boudou A, Leewangh P; Matthiessen P and Persoone G (1992). Summary and Recommendations of the European Workshop on Freshwater Field Tests (EWOFFT), Potsdam, Germany, June 25-26, 1992.

The study was carried out in accordance with the principles of GLP.

The dissipation of azoxystrobin was investigated in the 5 m x 5 m pond containing a 10 cm deep sediment layer with an overlying 30 cm deep water column, simulating the European shallow water model. Macrophyte coverage was approximately 25% to 30% of the benthic surface at the time of azoxystrobin application. Azoxystrobin was applied as a broadcast spray at a rate of 25 g ai/ha on 13th July 1998 (nominal time 0 concentration 8.95 µg/l assuming instantaneous and complete mixing through water compartment). Water samples were taken for analysis after 3, 6, 12 and 24 hours, then 2, 4, 7, 14, 21 and 28 days after application. Sediment samples were taken after 1, 4, 7, 14, 21, 28, 66, 91 and 119 days. The concentration of azoxystrobin in the pond water, 3 hours after the application was 10.3 µg/L (115% of nominal time 0 concentration). Twenty four hours after application the concentration of azoxystrobin was 9.4 µg/L (105% of nominal time 0 concentration). Azoxystrobin residues in water declined to 2.4 µg/L after 28 days (27% of nominal time 0 concentration). Residues in the top segment sections (0-5 cm) increased from 0.026 mg/kg 1 day after application to a maximum of 0.039 mg/kg 21 days after application. From this point onwards, sediment residues declined slowly and were 0.023 mg/kg 119 days after application. Negligible amounts of azoxystrobin were detected in the lower 5-10 cm of the sediment cores. The rate of dissipation in water was calculated using single first order kinetics with non-linear regression, the calculated water phase $DissT_{50}$ was 13.1 days and the $DissT_{90}$ was 43.6 days. Degradation DT_{50}s for the water, sediment and whole system were not calculated.

5.1.3 Summary and discussion of degradation

Azoxystrobin is considered hydrolytically stable under environmental conditions but undergoes aqueous photolysis to produce a number of photodegradation products. Photolysis is of uncertain relevance as a route of degradation in typical European aquatic environments and, given the available data, there is insufficient information in this case to evaluate photodegradation in terms of mineralisation or transformation to non-classifiable substances. Therefore, aquatic photolysis is not considered further in relation to meeting the criteria for rapid degradation.

A ready biodegradability study is not available. In a laboratory aerobic water-sediment study azoxystrobin was observed to degrade slowly. Whole system degradation DT_{50} values were estimated to be 341 and 444 days at 12 ^{o}C. Minimal mineralisation was observed. In an outdoor mesocosm study azoxystrobin was observed to partition into the sediment phase where it slowly dissipated.

Based on the available data, azoxystrobin is not degraded (abiotically and/or biotically) in the aquatic environment to a level of >70 % within a 28 day window or transformed to non-classifiable products. Consequently, azoxystrobin is considered not rapidly degradable for the purpose of classification and labelling.

5.2 Environmental distribution

5.2.1 Adsorption/Desorption

One study is available assessing the adsorption of azoxystrobin in 6 different soils (Rowe & Lane, 1994). The study was carried out to GLP and broadly follows OECD guideline 106. ^{14}C-labelled azoxystrobin was applied at 5 concentrations (0.05, 0.1, 0.2, 0.4 and 0.8 µg/cm^3) to soil slurries (3 g soil: 20 cm^3 0.01 M $CaCl_2$) and shaken for 24 hours at 20 ± 2 ^{o}C. Soils were sterilised before use to

minimise degradation; subsequent thin layer chromatographic analysis of the equilibrium aqueous solutions and soil extracts showed there was less than 10 % degradation in the slurries. Average adsorption partition coefficients (Ka values) in the six soils ranged from 2.1 ml/g in the sandy soil to 20 ml/g in the clay loam. Freundlich adsorption coefficients (Kf) demonstrated a similar pattern, ranging from 1.5 to 15 ml/g. Freundlich adsorption coefficients normalised to organic carbon (Kfoc values) ranged from 207 to 594 ml/g. 1/n values ranged from 0.82 to 0.90. Using the McCall Classification scale to assess a chemicals potential mobility in soil, azoxystrobin can be classified as having between a 'medium' and 'low' potential mobility in soil. These soil Kfoc values indicate that azoxystrobin is likely to dissipate into sediments in typical aquatic systems as supported by the simulation test data summarised in section 5.1.2.3.

Table 11: Summary of relevant information on adsorption/desorption

Summary table – Adsorption/desorption - Azoxystrobin									
Method, GLP status,	**Soil**	**%OC**	**Soil pH**	**K_a (ml/g)**	**K_{aOC} (ml/g)**	**Kf (ml/g)**	**Kfoc (ml/g)**	**1/n**	**Reference**
Method broadly follows OECD 106, GLP compliant	*Sandy clay loam*	1.7	7.5	12	690	7.9	465	0.84	Rowe & Lane, 1994
	Loamy sand A	1.7	7.8	6.0	357	4	235	0.82	
	Loamy sand B	3.0	7.9	9.0	304	6.2	207	0.85	
	Sand	0.3	5.5	2.1	724	1.5	500	0.84	
	Silty clay loam	1.6	4.9	12	739	9.5	594	0.90	
	Clay loam	2.8	5.5	20	718	15	536	0.90	

K_a = Adsorption coefficient
K_{aOC} = Adsorption coefficient based on organic carbon content
Kf = Freundlich adsorption coefficient
Kfoc = Freundlich adsorption coefficient based on organic carbon content
1/n = Freundlich regression constant

5.2.2 Volatilisation

Azoxystrobin has a low vapour pressure, 1.1 x 10^{-10} Pa at 20ºC, and the Henry's law constant is calculated as 7.4 x 10^{-9} Pa m^3 mol^{-1} indicating that azoxystrobin is unlikely to partition from the water phase to air (Wollerton & Husband, 1993).

5.2.3 Distribution modelling

No available information.

5.3 Aquatic Bioaccumulation

Table 12: Summary of relevant information on aquatic bioaccumulation

Method	Results	Reference
Partition coefficient n-octanol/water for Azoxystrobin. OECD 107	Log K_{OW} 2.5 at 20°C	Wollerton, C & Husband, R (1993)
Calculation method according to ECHA guidance on environment risk assessment (Part B) 2015, section 3.8.2	Estimated BCF_{fish} 26.61	-

5.3.1 Aquatic bioaccumulation

5.3.1.1 Bioaccumulation estimation

The log K_{ow} for Azoxystrobin is 2.5 (at 20 °C) (see section 1.3. Therefore, there is no indication of a bioaccumulation potential for this active substance. For completeness, a BCF value for fish was also calculated using the equation provided in the ECHA guidance on environment risk assessment for biocides (Part B) 2015, section 3.8.2.

LogBCFfish = 0.85 x log Kow - 0.70

The logBCFfish calculated is 1.425 and so the estimated BCFfish is 26.61.

5.3.1.2 Measured bioaccumulation data

None submitted or required.

5.3.2 Summary and discussion of aquatic bioaccumulation

The experimentally derived Log K_{ow} for azoxystrobin is 2.5, this is less than the trigger value of 4 given in the CLP Regulation. No experimental BCF study is available but an estimated fish BCF of 26.61 has been calculated using biocides methodology based on the Log K_{ow}; this is also below the CLP trigger value of 500. Overall therefore, a low bioaccumulation potential is predicted for azoxystrobin.

5.4 Aquatic toxicity

Azoxystrobin aquatic organism endpoints

Only endpoints with technical azoxystrobin (rather than formulations) are included under the headings below as only substance endpoints are usually considered for classification. All studies referred to have been considered reliable during the EU renewal of the active substance as a pesticide and currently under review as a biocide.

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

As stated at the outset of section 5, only tabulated detail is available for the majority of the azoxystrobin toxicity endpoints. However, during the pesticide renewal a new acute fish study was submitted which is summarised briefly below.

Anonymous (1992) ICI: 5504: Acute toxicity to sheepshead minnow (*Cyprinodon variegatus*).

The acute toxicity of azoxystrobin (96.2% purity) to sheepshead minnow (*Cyprinodon variegatus*) was assessed in a reliable study performed according to EPA guideline 72-3 and in compliance with GLP. Exposure to the test item was for 96 hours in a flow-through system at concentrations of 180, 320, 560, 100, 1800 and 3200 µg/L. From the results, a 96 hr LC_{50} value of 660 µg/l (0.66 mg/L) was calculated based on mean measured concentrations. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

The most critical acute endpoints for each fish species are stated below:

Table 13: Summary of relevant information on aquatic toxicity – short-term toxicity to fish

Guideline	Species	Endpoint Data	Exposure		Results		Reference
			Design	Duration	Endpoint	Toxicity (mg/L)	
Acute toxicity OECD 203 GLP	*Oncorhynchus mykiss*	Mortality	Flow-through	96h	LC_{50}	**0.47 (mm)**	Anonymous (1992)
Acute toxicity US EPA E 72-1 GLP	*Lepomis macrochirus*	Mortality	Flow-through	96h	LC_{50}	1.1 (mm)	Anonymous (1993)
Acute toxicity OECD 203 GLP	*Cyprinus carpio*	Mortality	Flow-through	96h	LC_{50}	1.6 (mm)	Anonymous (1993)
Acute toxicity EPA 72-3 GLP	*Cyprinodon variegatus*	Mortality	Flow-through	96h	LC_{50}	0.66 (mm)	Anonymous (1992)

mm=endpoint based on mean measured concentrations
nom= endpoint based on nominal concentrations

5.4.1.2 Long-term toxicity to fish

As stated above, only tabulated detail is available for the majority of the azoxystrobin toxicity endpoints. No newer long term fish toxicity studies were submitted for the pesticide renewal of azoxystrobin or its current review as a biocide.

The long term endpoints for each fish species are stated below:

Table 14: Summary of relevant information on aquatic toxicity – long-term toxicity to fish

Guideline	Species	Endpoint Data	Exposure		Results		Reference
			Design	Duration	Endpoint	Toxicity (mg/L)	
Chronic toxicity US EPA 72-4 GLP	*Pimephales promelas*	Mortality and growth early life stage toxicity	Flow-through	28 d	NOEC	**0.147 (mm)**	Anonymous (1994)
Chronic toxicity OECD 204 GLP	*Oncorhynchus mykiss*	Mortality and sub-lethal effects	Flow-through	28 d	NOEC	0.16 (nom)*	Anonymous (1994)

mm=endpoint based on mean measured concentrations
nom= endpoint based on nominal concentrations
*concentrations maintained within 94-115% of the nominal.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

As stated above, only tabulated detail is available for the majority of the azoxystrobin toxicity endpoints. However, during the pesticide renewal new studies were submitted which are summarised briefly below.

Kent SA, Sankey SJ and Grinell AJ (1993). ICI5504: Acute toxicity to the mysid shrimp (*Mysidopsis bahia*) Report No. BL4785/B. Brixham Environmental Laboratory, Brixham, UK. (Syngenta File No. ICI5504/0925)

The acute toxicity of azoxystrobin (96.2% purity) to mysid shrimp (*Mysidopsis bahia* - now *Americamysis bahia*) was assessed in a reliable study performed according to EPA 72-3 and in compliance with GLP. Exposure to the test item was for 96 hours in a static system at concentrations of 5.6, 10, 18, 32, 56, 100 and 180 µg/L. From the results, a 96 hr EC_{50} value of 55 µg/l (0.055 mg/L) was calculated based on nominal concentrations. Concentrations in the test were maintained within 107-116% of the nominal concentrations. This endpoint was based on mortality. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

Kent SA, Sankey SJ, Caunter JE and Grinell AJ (1994). ICI5504: Acute toxicity to the larvae of the Pacific oyster (*Crassostrea gigas*) Report No. BL4842/B. Brixham Environmental Laboratory, Brixham, UK. (Syngenta File No. ICI5504/0927)

The acute toxicity of azoxystrobin (96.2% purity) to the Pacific oyster (*Crassostrea gigas*) was assessed in a reliable study performed according to EPA 72-3 and in compliance with GLP. This study assessed the acute toxicity to the development of larvae/embryos of the Pacific oyster.

Exposure to the test item was for 48 hours in a static system at concentrations of 0.56, 1.0, 3.2, 5.6 and 10 mg/L. From the results, a 48 hr EC_{50} value of 1.3 mg/L was calculated based on nominal concentrations. Concentrations in the test were maintained within 97-106% of the nominal concentrations. This endpoint was based on an effect on development. The number of normal/abnormal larvae were counted. Larvae were defined as normal if the bivalve shell was fully formed. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

The most critical acute endpoints for each invertebrate species are stated below:

Table 15: Summary of relevant information on aquatic toxicity – short-term toxicity to aquatic invertebrates

Guideline	Species	Endpoint Data	Exposure		Results		Reference
			Design	Duration	Endpoint	Toxicity (mg/L)	
Acute toxicity EU method C.2/OECD 202/EPA-540/9-85-005 GLP	*Daphnia magna*	Immobility	Static	48 h	EC_{50}	0.23 (mm)	Farrelly and Hamer (1994)
Acute toxicity EU method C.2/OECD 202/EPA-540/9-85-005 GLP	*Daphnia magna*	Immobility	Static	48 h	EC_{50}	0.28 (mm)	Rapley *et al.*, (1994)
Acute toxicity Guideline* GLP	*Macrocyclops fuscus*	Immobility	Static	48 h	EC_{50}	0.13 (nom)[A]	Farrelly *et al.*, (1995)
Acute toxicity EPA 72-3 GLP	*Americamysis bahia (Mysidopsis bahia)*	Immobility	Static	96 h	EC_{50}	**0.055 (nom)[B]**	Kent *et al.*, (1993)
Acute toxicity EPA 72-3 GLP	*Crassostrea gigas*	Immobility	Static	48 h	EC_{50}	1.3 (nom)[C]	Kent *et al.*, (1994)
Guideline* GLP	*Chironomus riparius***	Immobility	Static	48 h	EC_{50}	0.21 (nom)[D]	*Farrelly* et al., *(1995)*

*This study was not carried out to any specific guideline.

**This is a species with a sediment life phase however this study was not carried out with sediment.

mm=endpoint based on mean measured concentrations

nom= endpoint based on nominal concentrations

[A] Concentrations were maintained within 85-93% of the nominal concentrations.

[B] Concentrations were maintained within 107-116% of the nominal concentrations.

[C] Concentrations were maintained within 97-106% of the nominal concentrations.

[D] Concentrations were maintained within 83-102% of the nominal concentrations.

5.4.2.2 Long-term toxicity to aquatic invertebrates

As stated above, only tabulated detail is available for the majority of the azoxystrobin toxicity endpoints. However, during the pesticide renewal a new long term invertebrate study was submitted which is summarised briefly below.

Boeri, RL, Magazu, JP. and Ward, T.J (1997). Chronic toxicity of Azoxystrobin to the Mysid, *Mysidopsis bahia*. Report No. 1350-ZE.T.R. Wilbury Laboratories, Marblehead, Massachusetts. (Syngenta File No. ICI5504/0952)

The chronic toxicity of azoxystrobin (96.2% purity) to mysid shrimp (*Mysidopsis bahia* - now *Americamysis bahia*) was assessed in a reliable study performed according to EPA 72-4 and in compliance with GLP. Exposure to the test item was for 28 days in a flow-through system at concentrations of 5.2, 10, 20, 40, 80 µg/L. From the results, a 28 day NOEC value of 9.54 µg/L (0.00954 mg/L) was calculated based on mean measured concentrations. This endpoint was based on effects on reproduction and mortality. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

The most critical long term endpoints for each invertebrate species are stated below:

Table 16: Summary of relevant information on aquatic toxicity – long-term toxicity to aquatic invertebrates

Guideline	Species	Endpoint Data	Exposure		Results		Reference
			Design	Duration	Endpoint	Toxicity (mg/L)	
Chronic toxicity EPA-540/9-86-141 GLP	*Daphnia magna*	Reproduction and growth	Semi-static	21 d	NOEC	0.044 (mm)	Rapley *et al.*, (1994)
Chronic toxicity US EPA 72-4 GLP	*Americamysis bahia (Mysidopsis bahia)*	Reproduction and growth	Flow-through	28 d	NOEC	**0.00954 (mm)**	Boeri *et al.*, (1997)
BBA (1995) GLP	*Chironomus riparius**	Emergence and time	Static	25 d	NOEC	0.8 mg/L water (nom)	Gentle and Rapley (1997)
SETAC-Europe (1993) and ASTM (1993) GLP	*Chironomus riparius#*	Emergence and time	Static	33 d	NOEC	23 mg/kg sediment d.w (mm)	Gentle (1997)#

*This is a species with a sediment life phase and this study included a sediment phase, the results was based on initial nominal water phase concentrations (within 94-118% on day 0); concentrations of the active in the water phrase were 4-39% of the nominal concentrations at the end of the test. This study was designed more for risk assessment then classification and labelling.

This study was not considered as part of the EU Annex I review for Azoxystrobin as a pesticide under Regulation 1107/2009, Dir. 91/414/EC. As a result, the applicant's summary of this study has been considered (please refer to the study summary on IUCLID). However, as the endpoint is only based on a sediment (rather than water) concentration, it can be discounted for classification purposes.

mm=endpoint based on mean measured concentrations

nom= endpoint based on nominal concentrations

5.4.3 Algae and aquatic plants

As stated above, only tabulated detail is available for the majority of the azoxystrobin toxicity endpoints. However, during the pesticide renewal new studies were submitted which are summarised briefly below.

Smyth DV, Sankey SA, Kent SJ & Johnson PA (1994). ICIA5504: Toxicity to marine algae *Skeletonema costatum*. Report No. BL5053/B. Brixham Environmental Laboratory, Brixham, UK. (Syngenta File No. ICI5504/0966)

The toxicity of azoxystrobin (96.2% purity) to *Skeletonema costatum* was assessed in a reliable study performed according to EPA 123-2 and in compliance with GLP. Exposure to the test item was for 120 hours in a static system at concentrations of 3.2, 10, 32, 100, 320, 1000, 3200 µg/L. From the results, a 72 hour E_rC_{50} of 300 µg a.s/L (0.3 mg/L) was calculated based on growth rate and nominal concentrations. Concentrations were 109-141% of the nominal concentrations, concentrations greater than 120% were only observed in test concentrations 3.2 and 10 µg/l. No 72 hour NOE_rC is available from the study report. The E_rC_{50} endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

Smyth DV, Sankey SA, Kent SJ & Stanley RD 1994. ICIA5504: Toxicity to the freshwater diatom *Navicula pelliculosa*. Report No. BL5087/B. Brixham Environmental Laboratory, Brixham, UK.(Syngenta File No. ICI5504/0965)

The toxicity of azoxystrobin (96.2% purity) to *Navicula pelliculosa* was assessed in a reliable study performed according to EPA 123-2 and in compliance with GLP. Exposure to the test item was for 120 hours in a static system at concentrations of 1, 5, 10, 20, 40, 80, 160, 320 µg/L. The study report only states 120 hour endpoints however during the Annex I pesticide renewal of Azoxystrobin, the notifier re-calculated endpoints for other time points. Therefore the 72 hour nominal E_rC_{50} of 146 µg a.s/L (0.146 mg/L) is proposed for use in the hazard assessment. Concentrations were 109-130% of the nominal concentrations, concentrations greater than 120% were only observed in test concentrations 1 and 5 µg/l. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide. A NOE_rC for growth rate for 72 hours was not stated when the Annex I notifier re-calculated endpoints. Therefore in the absence of a 72 hour NOE_rC, the nominal 120 hour NOE_rC of 20 µg/L (0.02 mg/L) will be used.

Smyth DV, Sankey SA, Kent SJ & Shearing JM, 1994. ICIA5504: Toxicity to blue green algae *Anabaena flos-aquae*. Report No. BL5054/B. Brixham Environmental Laboratory, Brixham, UK.(Syngenta File No. ICI5504/0967)

The toxicity of azoxystrobin (96.2% purity) to *Anabaena flos-aquae* was assessed in a reliable study performed according to EPA 123-2 and in compliance with GLP. Exposure to the test item was for 120 hours in a static system at concentrations of 1.3, 2.4, 4.3, 7.8, 14 and 25 mg a.s/L. From the results, a 72 hour E_rC_{50} of 13.9 mg a.s/L was calculated based on mean measured concentrations. The 72 hr mean measured NOE_rC based on growth rate was 8.5 mg a.s/L. The E_rC_{50} endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide.

Smyth, DV, Kent, SJ, Sankey, SA and Stanley, RD (1994a). ICI5504: Toxicity to the duckweed *Lemna gibba*. Report number BL5000/B. Brixham Environmental Laboratory, Brixham, UK.Syngenta file no ICI5504/0963.

The toxicity of azoxystrobin (96.2% purity) to *Lemna gibba* was assessed in a reliable study performed according to EPA 123-2 and in compliance with GLP. Exposure to the test item was for 14 days in a static, renewal system at concentrations of 0.1, 0.2, 0.4, 0.8, 1.6, 3.2 and 6.4 mg a.s/L. From the results, a 14 day EC_{50} based on frond number and EC_{50} for dry weight of 3.2 and >6.4 mg a.s/L, respectively were calculated based on nominal concentrations. Concentrations were within 98-110% of the nominal concentrations. The nominal 14 day NOEC was 0.8 mg/L. This endpoint was deemed to be reliable and acceptable during the EU Annex I renewal of azoxystrobin as a pesticide. Results at 7 days were not stated in the study report.

The most critical endpoints for each algal and plant species are stated below:

Table 17: Summary of relevant information on aquatic toxicity – algae and aquatic plants

Guideline	Species	Endpoint Data	Exposure		Results		Reference
			Design	Duration	Endpoint	Toxicity (mg/L)	
OECD 201 GLP	*Pseudokirchneriella subcapitata (Selenastrum capricornutum)*	Growth rate	Static	72 h	E_rC_{50} NOE_rC	1.47 (mm) 0.038 (mm)	Smyth *et al.*, (1993)
EPA FIFRA 123-2 GLP	*Anabaena flos-aquae*	Growth rate	Static	72 h	E_rC_{50} NOE_rC	13.9 (mm) 8.5 (mm)	Smyth *et al.*, (1994)
EPA FIFRA 123-2 GLP	*Navicula pelliculosa*	Growth rate	Static	72 h	E_rC_{50} NOE_rC	**0.146 (nom)**[A] **0.02 (nom)**[A]	Smyth *et al.*, (1994)
EPA FIFRA 123-2 GLP	*Skeletonema costatum*	Growth rate	Static	72 h	E_rC_{50}	0.3 (nom)[B]	Smyth *et al.*, (1994)
EPA 123-2 GLP	*Lemna gibba*	Frond number increase	Semi-static	14 d	EC_{50} NOEC	**3.2 (nom)**[C] **0.8 (nom)**[C]	Smyth *et al.*, (1994)

[A] Concentrations were 109-130% of the nominal concentrations, concentrations greater than 120% were only observed in test concentrations 1 and 5 µg/l. The study report only states 120 hour endpoints however during the Annex I pesticide renewal of Azoxystrobin, the notifier re-calculated endpoints for other time points. Therefore the 72 hour E_rC_{50} is proposed for use in the hazard assessment. A NOE_rC for growth rate for 72 hours was never stated when the Annex I notifier re-calculated endpoints. Therefore in the absence of a 72 hour NOE_rC, the nominal 120 hour NOE_rC of 0.02 mg/L (20 ug/L) will be used.

[B] Concentrations were 109-141% of the nominal concentrations, concentrations greater than 120% were only observed in test concentrations 3.2 and 10 µg/l.

[C] Concentrations were 98-110% of the nominal concentrations

mm=endpoint based on mean measured concentrations
nom= endpoint based on nominal concentrations

5.4.4 Other aquatic organisms (including sediment)

Sediment studies have been considered under section 5.4.2.

5.5 Comparison with criteria for environmental hazards (sections 5.1 – 5.4)

Azoxystrobin is considered not rapidly degradable for classification purposes and has a low bioaccumulation potential.

Acute and chronic classification has been considered under the headings below. The lowest acute and chronic endpoints are an EC_{50} of 0.055 mg/L and a NOEC of 0.00954 mg/L, respectively. These endpoints are both for the aquatic invertebrate *Americamysis bahia* (mysid shrimp). It is acknowledged that only 14 day endpoints from the *Lemna gibba* study are available. Although 7 day endpoints might be preferred, this is not available. Furthermore, some of the NOECs from the algae studies are also not available. Despite this, these endpoints would not change the severity of the classification (acute and chronic category 1) which is primarily based on the aquatic invertebrate endpoints.

Acute category

The critical acute endpoints are an LC_{50} of 0.47 mg/L (fish), an EC_{50} of 0.055 mg/l (crustacean), an E_rC_{50} of 0.146 mg/L (algae) and an EC_{50} of 3.2 mg/L (aquatic plants). Summaries of the acute crustacean, algae and aquatic plant endpoints are provided under sections 5.4.2.1 and 5.4.3, respectively. It is noted that a summary of the critical acute fish endpoint is not available in the pesticide RAR or biocide CAR for azoxystrobin, however the endpoint was previously considered to be reliable in EU review. Overall, the lowest acute endpoint is the nominal 96-hour EC_{50} of 0.055 mg/L from the study with Mysid shrimp. As this is < 1 mg/L a hazard classification of Acute Category 1 is proposed with an Acute M-factor of 10 (>0.01 to ≤ 0.1 mg/L).

Chronic category

The critical chronic endpoints are a NOEC of 0.147 mg/L (fish), a NOEC of 0.00954 mg/L (crustacean), a NOE_rC of 0.02 mg/L (algae) and a NOEC of 0.8 mg/L (aquatic plants). Summaries of the chronic crustacean, algae and aquatic plant endpoints are provided under section 5.4.2.2 and 5.4.3, respectively. It is noted that a summary of the critical chronic fish endpoint is not available, but as noted before, this was previously considered reliable in EU peer review. Overall, the lowest chronic endpoint is the 28-day mean measured NOEC of 0.00954 mg/L from the study with Mysid shrimp. As this is < 0.1 mg/L and the active is not considered to be rapidly degradable, a hazard classification of Chronic Category 1 is proposed with a Chronic M-factor of 10 (>0.001 to ≤ 0.01 mg/L).

5.6 Conclusions on classification and labelling for environmental hazards (sections 5.1 – 5.4)

Aquatic Acute 1; H400: Very toxic to aquatic life

Acute M-factor = 10

Aquatic Chronic 1; H410: Very toxic to aquatic life with long lasting effects

Chronic M-factor = 10

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

With this proposal, the DS sought to confirm the existing entry for aquatic hazards, namely Aquatic Acute 1 and Aquatic Chronic 1, as well as to introduce M-factors.

Azoxystrobin was considered by the DS as not rapidly degradable for classification purposes with a low bioaccumulation potential. The lowest acute and chronic endpoints were an EC_{50} value of 0.055 mg/L and a NOEC value of 0.00954 mg/L, respectively. These endpoints are both for the aquatic invertebrate *Americamysis bahia* (mysid shrimp). Based on these endpoints the DS proposed an environmental classification as Aquatic Acute 1 (H400) with an M-factor of 10 and Aquatic Chronic 1 (H410) with an M-factor of 10.

Degradation

The results of a hydrolysis study (OECD TG 111) showed that azoxystrobin was stable at pH 4, 7 and 9 at 25°C and at pH 5 and 7 at 50°C. Azoxystrobin was hydrolysed relatively fast at pH 9 at 50°C with a DT_{50} 12.08 days. A second GLP compliant study showed fast hydrolisation of azoxystrobin at pH 9 with a DT50 of 2.6 days (60 °C). Hydrolysis is not expected to represent a significant pathway for degradation of azoxystrobin under realistic environmental conditions.

Azoxystrobin was shown to photodegrade in a photolysis study (OECD TG 316). It degraded extensively in irradiated samples under 30 days Florida summer sunlight. For azoxystrobin the DT_{50} was calculated to be 8.4 days and during the study more than 15 photo degradants were observed 6 of which being identified.

No ready biodegradability screening tests were conducted on azoxystrobin. The degradation of azoxystrobin was studied in two different natural water-sediment systems (GLP, German BBA Guideline Part IV, Section 5-1). Mineralisation to CO_2 reached 2% to 6% of the applied radioactivity after 152 days. Degradation of azoxystrobin from the whole system was modelled using SFO kinetics: DT_{50} values at 20°C are 234 and 180 days for the Old Basing and Virginia Water systems respectively. At the average EU outdoor temperature of 12°C, DT_{50} values are 444 days and 341 days for the Old Basing and Virginia Water systems respectively. An outdoor mesocosm study was also conducted (GLP, SETAC (1991), Crossland *et al.*, 1992). The calculated water phase $DissT_{50}$ was 13.1 days and the $DissT_{90}$ was 43.6 days. Therefore, the DS concluded that azoxystrobin is considered not rapidly degradable for the purpose of classification and labelling.

Bioaccumulation

No experimental BCF study is available but an estimated fish BCF of 26.61 has been calculated using biocides methodology based on the Log K_{OW}. The experimentally derived Log K_{OW} for azoxystrobin is 2.5, this is less than the trigger value of 4 given in the CLP Regulation. The DS concluded that azoxystrobin has low bioaccumulation potential.

Aquatic Toxicity

The ecotoxicological test results from available acute and chronic studies for all trophic levels of azoxystrobin are summarised in the following table and sections. Only endpoints with technical azoxystrobin were included by the DS.

Table: *Summary of the relevant toxicity information on fish, aquatic invertebrates and algae/aquatic plants (the most sensitive data per species are highlighted in* ***bold****).*

Test organism	Guideline	Exposure	Toxicity (mg/L)
Toxicity to fish			
Oncorhynchus mykiss	OECD TG 203, GLP	96h	**LC_{50} - 0.47 (mm)**
Lepomis macrochirus	US EPA E 72-1, GLP	96h	LC_{50} - 1.1 (mm)
Cyprinus carpio	OECD TG 203, GLP	96h	LC_{50} - 1.6 (mm)
Cyprinodon variegatus	EPA 72-3, GLP	96h	LC_{50} - 0.66 (mm)
Pimephales promelas	US EPA 72-4, GLP	28d	**NOEC - 0.147 (mm)**
Oncorhynchus mykiss	OECD TG 204, GLP	28d	NOEC - 0.16 (nom)
Toxicity to aquatic invertebrates			
Daphnia magna	EU method C.2/ OECD TG 202/ EPA-540/9-85-005, GLP	48h	EC_{50} - 0.23 (mm)
Daphnia magna	EU method C.2/ OECD TG 202/ EPA-540/9-85-005, GLP	48h	EC_{50} - 0.28 (mm)
Macrocyclops fuscus	No specific guideline, GLP	48h	EC_{50} - 0.13 (nom)
Americamysis bahia (Mysidopsis bahia)	EPA 72-3, GLP	96h	**EC_{50} - 0.055 (nom)**
Crassostrea gigas	EPA 72-3, GLP	48h	EC_{50} - 1.3 (nom)
Chironomus riparius	No specific guideline, not a sediment study, GLP	48h	EC_{50} - 0.21 (nom)
Daphnia magna	EPA-540/9-86-141, GLP	21d	NOEC - 0.044 (mm)
Americamysis bahia (Mysidopsis bahia)	US EPA 72-4, GLP	28d	**NOEC - 0.00954 (mm)**
Chironomus riparius[*]	BBA (1995), GLP	25d	NOEC - 0.8 water (nom)
Chironomus riparius[#]	SETAC-Europe (1993) and ASTM (1993), GLP	33d	NOEC - 23 mg/kg sediment d.w. (mm)
Toxicity to algae and aquatic plants			
Pseudokirchneriella subcapitata (Selenastrum capricornutum)	OECD TG 201, GLP	72h	E_rC_{50} - 1.47 (mm) NOE_rC - 0.038 (mm)

Anabaena flos-aquae	EPA FIFRA 123-2, GLP	72h	E_rC_{50} - 13.9 (mm) NOE_rC - 8.5 (mm)
Navicula pelliculosa	EPA FIFRA 123-2, GLP	72h	**E_rC_{50} - 0.146 (nom)** **NOE_rC - 0.02 (nom)**
Skeletonema costatum	EPA FIFRA 123-2, GLP	72h	E_rC_{50} - 0.3 (nom)
Lemna gibba	EPA 123-2, GLP	14d	**EC_{50} - 3.2 (nom)** **NOEC - 0.8 (nom)**

mm = endpoint based on mean measured concentrations

nom = endpoint based on nominal concentrations

Acute toxicity

For fish, four studies were available. *O. mykiss* was the most sensitive fish species tested in the acute studies, with a 96h LC_{50} of 0.47 mg/L based on mean measured concentrations.

Six studies were available for aquatic invertebrates. *Mysidopsis bahia* was the most sensitive species tested in the acute studies, with a 96h EC_{50} of 0.055 mg/L based on mean measured concentrations.

Four acute toxicity studies were available for algae and aquatic plants. *Navicula pelliculosa* was the most sensitive species with E_rC_{50} 0.146 mg/L based on nominal concentrations.

Chronic toxicity

For fish, two flow-through studies were available. *P. promelas* was the most sensitive fish species tested in the chronic studies, with a 28d NOEC 0.147 mg/L based on mean measured concentrations.

Long-term toxicity to aquatic invertebrates was assessed based on four available studies. *Mysidopsis bahia* was the most sensitive species tested in the acute studies, with a 28d NOEC of 0.00954 mg/L based on nominal concentrations.

According to the CLH guidance, a 7 days growth endpoint for *L. gibba* is preferred to a 14 days endpoint, but no 7d toxicity data are available in the CLH report. The 14d NOEC was 0.8 mg/L, based on nominal concentrations.

Comments received during public consultation

Comments were received during the public consultation from 4 MSCAs and 1 Company-Downstream user. All 4 MSCAs were in support of the proposed classification and labelling regarding aquatic hazards (acute and chronic). The Company-Downstream user had an editorial comment on the aqueous photolysis of azoxystrobin as it presented in the CLH report.

Assessment and comparison with the classification criteria

Degradation

Azoxystrobin is considered hydrolytically stable under environmental conditions but undergoes aqueous photolysis to produce a number of photodegradation products. In a

laboratory aerobic water-sediment study azoxystrobin was observed to degrade slowly. Whole system degradation DT50 values were estimated to be 341 and 444 days at 12°C. Minimal mineralisation was observed. In an outdoor mesocosm study azoxystrobin was observed to partition into the sediment phase where it slowly dissipated. Based on the available data, azoxystrobin is not degraded (abiotically and/or biotically) in the aquatic environment to a level of > 70% within a 28 day window or transformed to non-classifiable products. Consequently, azoxystrobin is considered not rapidly degradable for the purpose of classification and labelling.

Bioaccumulation

No experimental BCF study is available, azoxystrobin has a Log K_{OW} = 2.5 at 20°C which is below the criterion of $K_{OW} \geq 4$.

Aquatic Toxicity

Acute toxicity

The critical acute results are an LC_{50} of 0.47 mg/L (fish), an EC_{50} of 0.055 mg/L (crustacean), an E_rC_{50} of 0.146 mg/L (algae), and an EC_{50} of 3.2 mg/L (aquatic plants). Therefore, for acute (short-term) aquatic hazard, azoxystrobin fulfils the criterion of ≤ 1 mg/L. The lowest acute endpoint is the nominal 96h EC_{50} of 0.055 mg/L from the study with *Mysid* shrimp. These values is in the range of $0.01 < L(E)C_{50} \leq 0.1$ mg/L which justifies an acute M-factor of 10.

Chronic toxicity

The critical chronic results are a NOEC of 0.147 mg/L (fish), a NOEC of 0.00954 mg/L (crustacean), a NOE_rC of 0.02 mg/L (algae) and a NOEC of 0.8 mg/L (aquatic plants). The lowest chronic endpoint is the 28 day mean measured NOEC of 0.00954 mg/L from the study with *Mysid* shrimp. This value is below 0.01 mg/L which is the classification threshold for Aquatic Chronic 1 for not rapidly degradable substances, and justifies a chronic M-factor of 10 ($0.001 < NOEC \leq 0.01$ mg/L).

There are no acute data available for *P. promelas* and thus any extrapolation for chronic toxicity for other fish species based on the acute:chronic ratio was not possible. However, if this assessment had been performed is unlikely to alter the classification as proposed below.

Conclusion on classification

Azoxystrobin is considered not rapidly biodegradable and has low potential of bioaccumulation. In agreement with the DS, RAC is of the opinion that azoxystrobin should be classified as:

Aquatic Acute 1 – H400 'Very toxic to aquatic life' with an **M factor = 10**, and **Aquatic Chronic 1 - H410** 'Very toxic to aquatic life with long lasting effects' with **M factor= 10**.

6 OTHER INFORMATION

Acute toxicity of azoxystrobin to aquatic organisms

(Tabulated studies from the original DE monograph)

Species	NOEC mg/l	EC/LC50 mg/l	Exposure durat./design	Remarks	Reference
Fish					
Oncorhynchus mykiss	0.068	0.47	96 h flow-thr.	measured	(1)
Cyprinus carpio	0.31	1.6	96 h flow-thr.	measured	(2)
Lepomis macrochirus	0.50	1.1	96 h flow-thr.	measured	(3)
Invertebrates					
Daphnia magna	0.126	0.28	48 h static	measured	(4)
Daphnia magna	-	0.23	48 h static	measured	(5)*
Daphnia magna	-	0.19	48 h static	measured	(5)**
Daphnia magna	-	0.82	48 h static	nominal	(5)***
Daphnia magna	0.125	0.27	48 h static	nominal	(6)
Daphnia pulex	0.062	0.20	48 h static	nominal	(7)
Macrocyclpos fuscus	0.062	0.13	48 h static	nominal	(8)
Brachionus calycifl.	-	>4.00	48 h static	nominal	(9)
Chaoborus cristall.	-	1.60	48 h static	nominal	(10)
Gammarus pulex	0.125	0.35	48 h static	nominal	(11)
Asellus aquaticus	-	>4.00	48 h static	nominal	(12)
Cloeon dipterum	0.125	3.20	48 h static	nominal	(13)
Chironomus riparius	0.125	0.21	48 h static	nominal	(14)
Ischnura elegans	-	>4.00	48 h static	nominal	(15)
Notonecta glauca	-	>4.00	48 h static	nominal	(16)
Lymnea stagnalis	-	>4.00	48 h static	nominal	(17)
Algae					
Selenastrum capric.	0.038	0.36	96 h static	measured	(18)
Bacteria					
Pseudomonas putida	>3.2	>3.2	6 h static	nominal	(19)

Ref.: (1) Anonymous., 1993, WAT95-50541; (2) Anonymous., 1993, WAT95-50542; (3) Anonymous., 1993, WAT95-50583; (4) Rapley et al., 1994, WAT95-50539; (5) Farrelly and Hamer, 1994, WAT95-50597; (6) Rapley et al., 1995, WAT95-50585; (7) Rapley et al., 1995, WAT95-50596, (8) Farelly et al., 1995, WAT95-50586; (9) Farelly et al., 1995, WAT95-50594; (10) Farelly et al., 1995, WAT95-50590; (11) Farelly et al., 1995, WAT95-50587; (12) Farelly et al., 1995, WAT95-50588; (13) Farelly et al., 1995, WAT95-50592; (14) Farelly et al., 1995, WAT95-50589; (15) Farelly et al., 1995, WAT95-50591; (16) Rapley et al., 1995, 50593; (17) Farelly et al., 1995, WAT95-50595; (18) Smyth et al., 1993, WAT95-50538; (19) Morris et al., 1994, WAT95-50537

* : Tested in water alone

** : Tested in soil/water, water phase

***: Tested in soil/water, whole system

Chronic toxicity of azoxystrobin to aquatic organisms

Species	NOEC mg/l	LOEC mg/l	Endpoint	Exposure durat./design	Remarks	Reference
Fish						
Oncorhynchus mykiss	0.160	-	mortality	28 d flow-thr.	nominal	(1)
Pimephales promelas	0.147	0.193	growth	33 d flow-thr	measured	(2)
Invertebrates						
Daphnia magna	0.044	0.084	reproduction	21 d semist.	measured	(3)

Ref.: (1) Anonymous., 1994, WAT95-50558; (2) Rhodes et al.; 1994, WAT95-50584; (3) Rapley et al., 1994, WAT95-50540

Agreed list of endpoints (taken from SANCO 7581/VI/97-rev5 22 April 1998)

Aquatic Organisms

Acute toxicity fish	LC_{50} (Rainbow trout) = 0.47 mg as/l, 96 h study
Bioaccumulation fish	Not required ($logP_{OW}$ < 3)
Acute toxicity invertebrate	EC_{50} (*Macrocyclops fuscus*) = 0.13 mg as/l, 48 h study
Acute toxicity algae	EC_{50} (*Selenastrum capric.*) = 0.36 mg as/l, 96 h study
Chronic toxicity sediment dwelling organism	NOEC 0.8 mg as/l

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Smyth, D., Kent, S., Sankey, S. and Shearing, J.	1994	ICIA5504: Toxicity to the blue-green alga Anabaena flos-aquae Brixham Environmental Laboratory Report No. BL5054/B GLP / Unpublished
Smyth, D., Sankey, S., Kent, S. and Stanley, R.	1994	ICIA5504: Toxicity to the freshwater diatom Navicula pelliculosa Brixham Environmental Laboratory Report No. BL5087/B GLP / Unpublished
Smyth DV, Sankey SA, Kent SJ & Johnson PA	1994	ICIA5504: Toxicity to marine algae *Skeletonema costatum*. Report No. BL5053/B. Brixham Environmental Laboratory, Brixham, UK. (Syngenta File No. ICI5504/0966)
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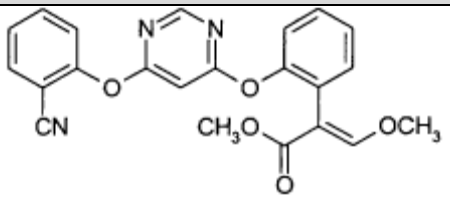
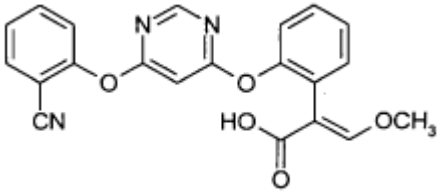
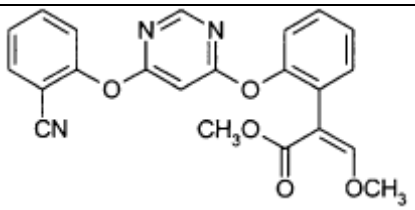
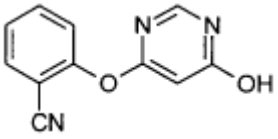
8 ANNEXES

ANNEX 1 – Substance code, chemical name and structure

Substance Identities		
Code	**IUPAC Name**	**Structure**
Azoxystrobin	Methyl (E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate	
R234886	(E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-xyloxy]phenyl}-3-methoxyacrylic acid	
R230310	Methyl(Z)- 2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate	
R401553	6-(2-cyanophenoxy)pyrimidin-4-ol	
R402173	2-[6-(2-cyanophenoxy)pyrimidin-4-xyloxy]benzoic acid