

## **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**

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# Part A.

## 1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

### 1.1 Substance

**Table 1: Substance identity**

<b>Substance name:</b>	Azoxystrobin
<b>EC number:</b>	<i>Not allocated</i>
<b>CAS number:</b>	131860-33-8
<b>Annex VI Index number:</b>	607-256-00-8
<b>Degree of purity:</b>	≥ 96.5%
<b>Impurities:</b>	<i>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.</i>

### 1.2 Harmonised classification and labelling proposal

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

	<b>CLP Regulation</b>
<b>Current entry in Annex VI, CLP Regulation</b>	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
<b>Current proposal for consideration by RAC</b>	<b>Removal of * from the acute toxicity classification and inclusion of M-factors</b> 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

<b>Resulting harmonised classification (future entry in Annex VI, CLP Regulation)</b>	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
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### 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 <sup>1)</sup>	Reason for no classification <sup>2)</sup>
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

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

<sup>1)</sup> Including specific concentration limits (SCLs) and M-factors

<sup>2)</sup> 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<sub>50</sub> 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<sub>50</sub> 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 *	H331	H331		GHS06 GHS09 Dgr		
Aquatic Acute 1	H400					
Aquatic Chronic 1	H410	H410				

## 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	H331	H331		GHS06 GHS09 Dgr		68
Aquatic Acute 1	H400					
Aquatic Chronic 1	H410	H410				
Acute Tox. 3	H331	H331		GHS06 GHS09 Dgr		37
Aquatic Acute 1	H400	H400				
Aquatic Chronic 1	H410	H410				

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

### 3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Azoxystrobin is 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

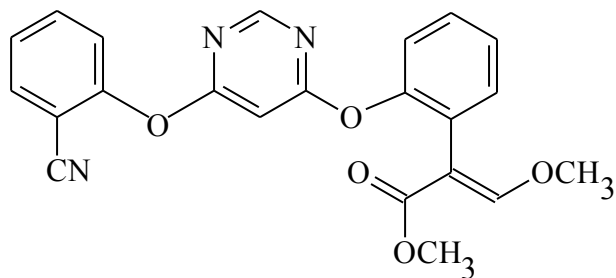
### 1 IDENTITY OF THE SUBSTANCE

#### 1.1 Name and other identifiers of the substance

**Table 4: Substance identity**

<b>EC number:</b>	Not listed
<b>EC name:</b>	Not listed
<b>CAS number (EC inventory):</b>	Not listed
<b>CAS number:</b>	131860-33-8
<b>CAS name:</b>	Benzeneacetic acid, 2-[[6-2(2-cyanophenoxy)-4-pyrimidinyl]oxy]- $\alpha$ -(methoxymethylene)-, methyl ester, ( $\alpha$ E)-
<b>IUPAC name:</b>	Methyl(E)-2-{2[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate
<b>CLP Annex VI Index number:</b>	607-256-00-8
<b>Molecular formula:</b>	403.4
<b>Molecular weight range:</b>	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	H225	H225		GHS02		
Skin Irrit. 2	H315	H315		GHS08		
Asp. Tox. 1	H304	H304		GHS07		
STOT SE 3	H336	H336		Dgr		
STOT RE 2 *	H373 **	H373 **				
Repr. 2	H361d ***	H361d ***				

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 345°C	Husband, R 2000	OECD 103
Relative density	1.34 g/cm <sup>3</sup> at 20° C	Wollerton, C and Husband, R 1995	EEC, A3/ OECD 109 Purity 99%
Vapour pressure	1.1 x 10 <sup>-10</sup> 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 <sub>ow</sub> = 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**

Acute Inhalation																			
Method	LC50	Observations and remarks																	
<p>Acute Inhalation Toxicity Study OECD 403</p> <p>Rats (CrI:(WI)BR strain) 5/sex/dose</p> <p>4-hours, nose only</p> <p>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.</p> <p>MMAD &lt; 2 µm</p> <p>GLP</p> <p>(Anonymous (1992))</p>	<p>Females = 698 µg/l Males = 962 µg/l</p>	<p>There were no deaths in animals exposed to 257 µg/l azoxystrobin. One male died and one female was killed <i>in extremis</i> during exposure to 511 µg/l azoxystrobin. One male and one female died and two females were killed <i>in extremis</i> during exposure to 767 µg/l azoxystrobin. One male died and two further males were killed <i>in extremis</i> during exposure to 1010 µg/l azoxystrobin</p> <table border="1" style="margin-left: auto; margin-right: auto;"> <thead> <tr> <th rowspan="2">actual conc. (µl)</th> <th colspan="2">Total mortalities</th> </tr> <tr> <th>M</th> <th>F</th> </tr> </thead> <tbody> <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> </tbody> </table> <p>Darkening and mottling of the lungs were observed in rats that died or were killed prior to the scheduled termination of the study.</p>	actual conc. (µl)	Total mortalities		M	F	257	0	0	511	1	1	767	1	3	1010	3	0
actual conc. (µl)	Total mortalities																		
	M	F																	
257	0	0																	
511	1	1																	
767	1	3																	
1010	3	0																	
<p>Acute Inhalation Toxicity Study OECD 403</p> <p>Rats (Alpk: APfSD strain) 5/sex</p> <p>4-hours- nose only, (particle size MMAD &gt;14µm)</p> <p>Azoxystrobin; 96.2% Total particulate concentration: 4.70 mg/litre (method of measurement not stated).</p> <p>GLP</p> <p>(Anonymous, 1997)</p>	<p>&gt; 4.7 mg/l</p>	<p>There were no mortalities.</p> <p>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.</p> <p>All animals had fully recovered by day 7 of the study.</p>																	

#### **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<sub>50</sub> 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<sub>50</sub> 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 ± 3.91 and 14.8 µm ± 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<sub>50</sub> was determined to be 0.698 mg/l in females and 0.962 mg/l in males. An LC<sub>50</sub> 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). 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 ≤ 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<sub>50</sub> reported.

##### **4.2.5 Conclusions on classification and labelling**

**Acute Tox 3; H331 – Toxic if inhaled.**

**ATE = 0.7 mg/l**

#### **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
<b>Hydrolysis</b>			
Equivalent to OECD 111, GLP compliant	25°C: stable at pH 5, 7 and 9 50°C: stable at pH 5 and 7, DT <sub>50</sub> 12.08 d at pH 9; R234886 12%	Stable to hydrolysis under environmental conditions	Steel & Joseph, 1994
No specific guideline, GLP compliant	60°C: DT <sub>50</sub> 2.6d at pH 9 (>1000 d at 20°C)	Stable to hydrolysis under environmental conditions	Tummon & Hurt, 1995
<b>Photolysis</b>			
Equivalent to OECD 316, GLP compliant	DT <sub>50</sub> 8.4 – 13.9d Florida summer sunlight Photodegrades (max after 30 days): R230310 16.3% R401553 8.9% R402173 2.4% CO <sub>2</sub> 5.4%	Azoxystrobin is subject to aqueous photolysis	Kuet & Hadfield, 1994
<b>Biodegradation</b>			
Water/sediment simulation test  German BBA Guideline Part IV, Section 5-1, GLP compliant	Old Basing system: Whole system DT <sub>50</sub> (12°C) 444d Mineralization 2.5% after 152d  Virginia Water system: Whole system DT <sub>50</sub> (12°C) 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

<p>Outdoor pond test</p> <p>SETAC Guideline on Testing Procedures for Pesticides in Freshwater Mesocosms (1991)</p> <p>Summary recommendations of the European Workshop on Freshwater Field Tests (1992)</p>	<p>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.</p> <p>Sediment: Max 0.039 mg/kg after 21 days, 0.023 mg/kg after 119 days</p> <p>DissT<sub>50</sub> water: 13.1d DissT<sub>50</sub> sediment: not calculated</p>	<p>Azoxystrobin partitions to sediment</p> <p>No information on degradation</p>	<p>Jones &amp; Lake, 2000</p>
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Substance identities and structures are provided in Annex 1

### 5.1.1 Stability

#### Hydrolysis

The hydrolysis of <sup>14</sup>C-azoxystrobin was investigated at 25 and 50 °C in sterile aqueous buffer solutions of pH 5, 7 and 9 (Steel & Joseph, 1994). At 25 °C azoxystrobin was shown to be stable to hydrolysis at pH 5, 7 and 9 over 31 days. At 50 °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 °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 °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 <sup>14</sup>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 °N at 25 ± 1 °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 (<sup>14</sup>C-pyrimidinyl label), 11.9 days (<sup>14</sup>C-phenylacrylate label) and 13.9 days (<sup>14</sup>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 (<sup>14</sup>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 °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<sub>2</sub> 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<sub>50</sub> 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<sub>50</sub> 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 13<sup>th</sup> 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<sub>50</sub> was 13.1 days and the DissT<sub>90</sub> was 43.6 days. Degradation DT<sub>50s</sub> 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<sub>50</sub> 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.

## **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. <sup>14</sup>C-labelled azoxystrobin was applied at 5 concentrations (0.05, 0.1, 0.2, 0.4 and 0.8 µg/cm<sup>3</sup>) to soil slurries (3 g soil: 20 cm<sup>3</sup> 0.01 M CaCl<sub>2</sub>) and shaken for 24 hours at 20 ± 2 °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 ( $K_a$  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 ( $K_f$ ) demonstrated a similar pattern, ranging from 1.5 to 15 ml/g. Freundlich adsorption coefficients normalised to organic carbon ( $K_{foc}$  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  $K_{foc}$  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)	$K_f$ (ml/g)	$K_{foc}$ (ml/g)	1/n	Reference
Method broadly follows OECD 106, GLP compliant	<i>Sandy clay loam</i>	1.7	7.5	12	690	7.9	465	0.84	Rowe & Lane, 1994
	<i>Loamy sand A</i>	1.7	7.8	6.0	357	4	235	0.82	
	<i>Loamy sand B</i>	3.0	7.9	9.0	304	6.2	207	0.85	
	<i>Sand</i>	0.3	5.5	2.1	724	1.5	500	0.84	
	<i>Silty clay loam</i>	1.6	4.9	12	739	9.5	594	0.90	
	<i>Clay loam</i>	2.8	5.5	20	718	15	536	0.90	

$K_a$  = Adsorption coefficient

$K_{aOC}$  = Adsorption coefficient based on organic carbon content

$K_f$  = Freundlich adsorption coefficient

$K_{foc}$  = Freundlich adsorption coefficient based on organic carbon content

1/n = Freundlich regression constant

## 5.2.2 Volatilisation

Azoxystrobin has a low vapour pressure,  $1.1 \times 10^{-10}$  Pa at 20°C, and the Henry’s law constant is calculated as  $7.4 \times 10^{-9}$  Pa m<sup>3</sup> mol<sup>-1</sup> 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 <sub>ow</sub> 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 <sub>fish</sub> 26.61	-

#### 5.3.1 Aquatic bioaccumulation

##### 5.3.1.1 Bioaccumulation estimation

The log K<sub>ow</sub> 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.

$$\text{LogBCF}_{\text{fish}} = 0.85 \times \text{log Kow} - 0.70$$

The logBCF<sub>fish</sub> calculated is 1.425 and so the estimated BCF<sub>fish</sub> 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<sub>ow</sub> 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<sub>ow</sub>; 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<sub>50</sub> 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	<i>Oncorhynchus mykiss</i>	Mortality	Flow-through	96h	LC <sub>50</sub>	<b>0.47 (mm)</b>	Anonymous (1992)
Acute toxicity US EPA E 72-1 GLP	<i>Lepomis macrochirus</i>	Mortality	Flow-through	96h	LC <sub>50</sub>	1.1 (mm)	Anonymous (1993)
Acute toxicity OECD 203 GLP	<i>Cyprinus carpio</i>	Mortality	Flow-through	96h	LC <sub>50</sub>	1.6 (mm)	Anonymous (1993)
Acute toxicity EPA 72-3 GLP	<i>Cyprinodon variegatus</i>	Mortality	Flow-through	96h	LC <sub>50</sub>	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	<i>Pimephales promelas</i>	Mortality and growth early life stage toxicity	Flow-through	28 d	NOEC	<b>0.147 (mm)</b>	Anonymous (1994)
Chronic toxicity OECD 204 GLP	<i>Oncorhynchus mykiss</i>	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<sub>50</sub> 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<sub>50</sub> 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	<i>Daphnia magna</i>	Immobility	Static	48 h	EC <sub>50</sub>	0.23 (mm)	Farrelly and Hamer (1994)
Acute toxicity EU method C.2/OECD 202/EPA- 540/9-85-005 GLP	<i>Daphnia magna</i>	Immobility	Static	48 h	EC <sub>50</sub>	0.28 (mm)	Rapley <i>et al.</i> , (1994)
Acute toxicity Guideline* GLP	<i>Macrocyclops fuscus</i>	Immobility	Static	48 h	EC <sub>50</sub>	0.13 (nom) <sup>A</sup>	Farrelly <i>et al.</i> , (1995)
Acute toxicity EPA 72-3 GLP	<i>Americamysis bahia</i> ( <i>Mysidopsis bahia</i> )	Immobility	Static	96 h	EC <sub>50</sub>	<b>0.055 (nom)<sup>B</sup></b>	Kent <i>et al.</i> , (1993)
Acute toxicity EPA 72-3 GLP	<i>Crassostrea gigas</i>	Immobility	Static	48 h	EC <sub>50</sub>	1.3 (nom) <sup>C</sup>	Kent <i>et al.</i> , (1994)
Guideline* GLP	<i>Chironomus riparius</i> **	Immobility	Static	48 h	EC <sub>50</sub>	0.21 (nom) <sup>D</sup>	Farrelly <i>et al.</i> , (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

<sup>A</sup> Concentrations were maintained within 85-93% of the nominal concentrations.

<sup>B</sup> Concentrations were maintained within 107-116% of the nominal concentrations.

<sup>C</sup> Concentrations were maintained within 97-106% of the nominal concentrations.

<sup>D</sup> 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	<i>Daphnia magna</i>	Reproduction and growth	Semi-static	21 d	NOEC	0.044 (mm)	Rapley <i>et al.</i> , (1994)
Chronic toxicity US EPA 72-4 GLP	<i>Americamysis bahia</i> ( <i>Mysidopsis bahia</i> )	Reproduction and growth	Flow-through	28 d	NOEC	<b>0.00954 (mm)</b>	Boeri <i>et al.</i> , (1997)
BBA (1995) GLP	<i>Chironomus riparius</i> *	Emergence and time	Static	25 d	NOEC	0.8 mg/L water (nom)	Gentle and Rapley (1997)
SETAC-Europe (1993) and ASTM (1993) GLP	<i>Chironomus riparius</i> #	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 phase 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<sub>50</sub> based on frond number and EC<sub>50</sub> 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	<i>Pseudokirchneriella subcapitata</i> ( <i>Selenastrum capricornutum</i> )	Growth rate	Static	72 h	E <sub>r</sub> C <sub>50</sub> NOE <sub>r</sub> C	1.47 (mm) 0.038 (mm)	Smyth <i>et al.</i> , (1993)
EPA FIFRA 123-2 GLP	<i>Anabaena flos-aquae</i>	Growth rate	Static	72 h	E <sub>r</sub> C <sub>50</sub> NOE <sub>r</sub> C	13.9 (mm) 8.5 (mm)	Smyth <i>et al.</i> , (1994)
EPA FIFRA 123-2 GLP	<i>Navicula pelliculosa</i>	Growth rate	Static	72 h	E <sub>r</sub> C <sub>50</sub> NOE <sub>r</sub> C	<b>0.146 (nom)<sup>A</sup></b> <b>0.02 (nom)<sup>A</sup></b>	Smyth <i>et al.</i> , (1994)
EPA FIFRA 123-2 GLP	<i>Skeletonema costatum</i>	Growth rate	Static	72 h	E <sub>r</sub> C <sub>50</sub>	0.3 (nom) <sup>B</sup>	Smyth <i>et al.</i> , (1994)
EPA 123-2 GLP	<i>Lemna gibba</i>	Frond number increase	Semi-static	14 d	EC <sub>50</sub> NOEC	<b>3.2 (nom)<sup>C</sup></b> <b>0.8 (nom)<sup>C</sup></b>	Smyth <i>et al.</i> , (1994)

<sup>A</sup> 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<sub>r</sub>C<sub>50</sub> is proposed for use in the hazard assessment. A NOE<sub>r</sub>C 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<sub>r</sub>C, the nominal 120 hour NOE<sub>r</sub>C of 0.02 mg/L (20 µg/L) will be used.

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

<sup>C</sup> 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<sub>50</sub> 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<sub>50</sub> of 0.47 mg/L (fish), an EC<sub>50</sub> of 0.055 mg/l (crustacean), an E<sub>r</sub>C<sub>50</sub> of 0.146 mg/L (algae) and an EC<sub>50</sub> 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<sub>50</sub> 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<sub>r</sub>C 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**

**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
<b>Fish</b>					
<i>Oncorhynchus mykiss</i>	0.068	0.47	96 h	flow-thr. measured	(1)
<i>Cyprinus carpio</i>	0.31	1.6	96 h	flow-thr. measured	(2)
<i>Lepomis macrochirus</i>	0.50	1.1	96 h	flow-thr. measured	(3)
<b>Invertebrates</b>					
<i>Daphnia magna</i>	0.126	0.28	48 h	static measured	(4)
<i>Daphnia magna</i>	-	0.23	48 h	static measured	(5)*
<i>Daphnia magna</i>	-	0.19	48 h	static measured	(5)**
<i>Daphnia magna</i>	-	0.82	48 h	static nominal	(5)***
<i>Daphnia magna</i>	0.125	0.27	48 h	static nominal	(6)
<i>Daphnia pulex</i>	0.062	0.20	48 h	static nominal	(7)
<i>Macrocyclus fuscus</i>	0.062	0.13	48 h	static nominal	(8)
<i>Brachionus calycifl.</i>	-	>4.00	48 h	static nominal	(9)
<i>Chaoborus cristall.</i>	-	1.60	48 h	static nominal	(10)
<i>Gammarus pulex</i>	0.125	0.35	48 h	static nominal	(11)
<i>Asellus aquaticus</i>	-	>4.00	48 h	static nominal	(12)
<i>Cloeon dipterum</i>	0.125	3.20	48 h	static nominal	(13)
<i>Chironomus riparius</i>	0.125	0.21	48 h	static nominal	(14)
<i>Ischnura elegans</i>	-	>4.00	48 h	static nominal	(15)
<i>Notonecta glauca</i>	-	>4.00	48 h	static nominal	(16)
<i>Lymnea stagnalis</i>	-	>4.00	48 h	static nominal	(17)
<b>Algae</b>					
<i>Selenastrum capric.</i>	0.038	0.36	96 h	static measured	(18)
<b>Bacteria</b>					
<i>Pseudomonas putida</i>	>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
<b>Fish</b>						
<i>Oncorhynchus mykiss</i>	0.160	-	mortality	28 d	flow-thr. nominal	(1)
<i>Pimephales promelas</i>	0.147	0.193	growth	33 d	flow-thr	measured (2)
<b>Invertebrates</b>						
<i>Daphnia magna</i>	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 <sub>50</sub> (Rainbow trout) = 0.47 mg as/l, 96 h study
Bioaccumulation fish	Not required (logP <sub>OW</sub> < 3)
Acute toxicity invertebrate	EC <sub>50</sub> ( <i>Macrocyclops fuscus</i> ) = 0.13 mg as/l, 48 h study
Acute toxicity algae	EC <sub>50</sub> ( <i>Selenastrum capric.</i> ) = 0.36 mg as/l, 96 h study
Chronic toxicity sediment dwelling organism	NOEC 0.8 mg as/l

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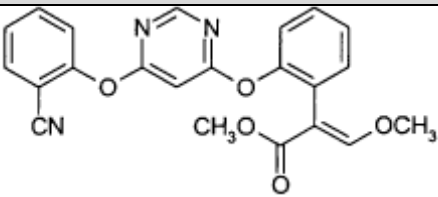
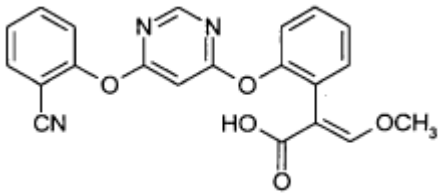
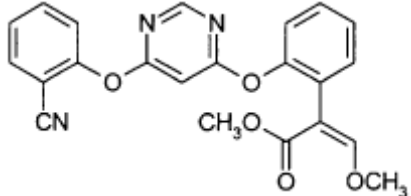
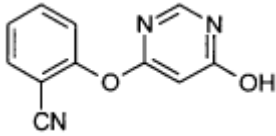
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Smyth DV, Sankey SA, Kent SJ & Johnson PA	1994	ICIA5504: Toxicity to marine algae <i>Skeletonema costatum</i> . Report No. BL5053/B. Brixham Environmental Laboratory, Brixham, UK. (Syngenta File No. ICI5504/0966)
Smyth, D., Kent, S., Sankey, S. and Stanley, R.	1994	ICIA5504: Toxicity to duckweed <i>Lemna gibba</i> Brixham Environmental Laboratory Report No. BL5000/B GLP / Unpublished



## 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-yloxy]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-yloxy]benzoic acid	