Committee for Risk Assessment

RAC

Annex 1
Background document
to the Opinion proposing harmonized classification and labelling at Community level of

bendiocarb (ISO)

EC Number: 245-216-8
CAS Number: 22781-23-3

CLH-O-0000001412-86-51/F

Adopted

12 March 2015

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.

CLH report

Proposal for Harmonised Classification and Labelling

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

Substance Name: Bendiocarb

(2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate)

EC Number: **245-216-8**

CAS Number: **22781-23-3**

Index Number: **006-046-00-8**

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Version number: **1** **Date:** **May 2014**

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	**Bendiocarb**
EC number:	**245-216-8**
CAS number:	**22781-23-3**
Annex VI Index number:	**006-046-00-8**
Degree of purity:	**≥ 97%**
Impurities:	**There are a number of process impurities in the substance. These have been taken into account and are not considered to be of additional concern. Information on impurities is considered to be confidential, further detail is provided in the technical dossier.**

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 Acute Tox. 3 *, H301 Acute Tox. 4 *, H312 Aquatic Acute 1, H400 Aquatic Chronic 1; H410
Current proposal for consideration by RAC	Acute Tox. 2; H300

	Acute Tox. 2; H330 Acute Tox. 3; H311 Aquatic acute 1; H400 (Acute M factor = 10) Aquatic chronic 1; H410 (Chronic M factor =100)
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Acute Tox. 2; H300 Acute Tox. 2; H330 Acute Tox. 3; H311 Aquatic acute 1; H400 (Acute M factor = 10) Aquatic chronic 1; H410 (Chronic M = 100 e)

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 addressed			
2.2.	Flammable gases	Not addressed			
2.3.	Flammable aerosols	Not addressed			
2.4.	Oxidising gases	Not addressed			
2.5.	Gases under pressure	Not addressed			
2.6.	Flammable liquids	Not addressed			
2.7.	Flammable solids	Not addressed			
2.8.	Self-reactive substances and mixtures	Not addressed			
2.9.	Pyrophoric liquids	Not addressed			
2.10.	Pyrophoric solids	Not addressed			
2.11.	Self-heating substances and mixtures	Not addressed			
2.12.	Substances and mixtures which in contact with water emit flammable gases	Not addressed			
2.13.	Oxidising liquids	Not addressed			
2.14.	Oxidising solids	Not addressed			
2.15.	Organic peroxides	Not addressed			
2.16.	Substance and mixtures corrosive to metals	Not addressed			
3.1.	Acute toxicity - oral	**Acute Tox.2; H300**	Not applicable	**Acute Tox 3*; H301**	Not applicable.
	Acute toxicity - dermal	**Acute Tox 3; H311**	Not applicable	**Acute Tox 4*; H312**	Not applicable.
	Acute toxicity - inhalation	**Acute Tox 2: H330**	Not applicable	**Acute Tox 3*; H331**	Not applicable.
3.2.	Skin corrosion / irritation	Not addressed			
3.3.	Serious eye damage / eye irritation	Not addressed			
3.4.	Respiratory sensitisation	Not addressed			

3.4.	Skin sensitisation	Not addressed			
3.5.	Germ cell mutagenicity	Not addressed			
3.6.	Carcinogenicity	Not addressed			
3.7.	Reproductive toxicity	Not addressed			
3.8.	Specific target organ toxicity –single exposure	Not addressed			
3.9.	Specific target organ toxicity – repeated exposure	Not addressed			
3.10.	Aspiration hazard	Not addressed			
4.1.	Hazardous to the aquatic environment	**Aquatic Acute 1; H400** **Aquatic Chronic 1; H410**	**Acute M Factor: 10** **Chronic M Factor: 100**	**Aquatic Acute 1; H400** **Aquatic Chronic 1; H410**	Not applicable
5.1.	Hazardous to the ozone layer	Not addressed			

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

Labelling:

Signal Word: Danger

Pictogram(s): GHS06, GHS09

Signal word: Danger

Hazard statements: H300+330, H311, H410

Precautionary statements: Not listed in Annex VI of CLP

Proposed notes assigned to an entry:

None

BACKGROUND TO THE CLH PROPOSAL

1.4 History of the previous classification and labelling

Bendiocarb is an active substance in the scope of Directive 98/8/EC (Regulation (EU) No 528/2012). The substance is currently listed on Annex VI of CLP where it is classified as Acute Tox. 3 *; H331, Acute Tox. 3 *, H301, Acute Tox. 4 *, H312, Aquatic Acute 1; H400 and Aquatic Chronic 1; H410. This classification has been translated from T; R23/25, Xn; R21, N; R50/53 in accordance with DSD.

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

1.5 Short summary of the scientific justification for the CLH proposal

Bendiocarb is currently listed on Annex VI of CLP where the CLP classification for acute toxicity has been translated as a minimum classification (i.e. Acute Tox. 3 *; H331, Acute Tox. 3 *, H301, Acute Tox. 4 *, H312 Aquatic Acute 1; H400 and Aquatic Chronic 1; H410 from T; R23/25, Xn; R21, N; R50/53 under DSD). Following review under Dir 98/8/EC the classification in accordance with CLP was determined to be Acute Tox. 2; H300 - Acute Tox. 2; H330 - Acute Tox. 3; H311. This dossier therefore seeks to confirm the current classification for acute toxicity under CLP. In addition, it also provides for the inclusion of environmental SCL and M-factors. Aquatic Acute 1; H400 (M factor of 10 applicable) and Aquatic Chronic 1; H410 (M factor of 100 applicable).

1.6 Current harmonised classification and labelling

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

Classification

Acute Tox. 3 *; H331

Acute Tox. 3 *; H301

Acute Tox. 4 *; H312

Aquatic Acute 1; H400

Aquatic Chronic 1; H410

Labelling

Pictogram(s):	GHS06, GHS09
Signal word:	Danger
Hazard statements:	H301, H312, H331, H410

1.7 Current self-classification and labelling

1.7.1 Current self-classification and labelling based on the CLP Regulation criteria

Classificaiton

Acute Tox. 3; H331

Acute Tox. 3, H301

Acute Tox. 4, H312

Aquatic Acute 1, H400

Aquatic Chronic 1; H410

Labelling

Pictogram(s):	GHS06, GHS09
Signal word:	Danger
Hazard statements:	H301, H312, H331, H410

2 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Bendiocarb is an active substance in the scope of Directive 98/8/EC (Regulation (EU) No 528/2012). Bendiocarb is currently listed on Annex VI of CLP where the CLP classification for acute toxicity has been translated as a minimum classification (i.e. Acute Tox. 3 *; H331, Acute Tox. 3 *, H301, Acute Tox. 4 *, H312). Following review under Dir 98/8/EC the classification in accordance with CLP was determined to be Acute Tox. 2; H300, Acute Tox. 2; H330 and Acute Tox. 3; H311. As a consequence, this dossier seeks to confirm the classification for acute toxicity under CLP and provide for the inclusion of M-factors. As the substance is already listed on Annex VI of CLP with a harmonised classification, the other hazard classes will not be addressed in this proposal.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

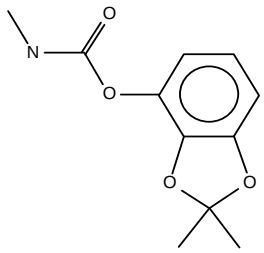
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 5: Substance identity

EC number:	245-216-8
EC name:	Bendiocarb
CAS number (EC inventory):	22781-23-3
CAS number:	22781-23-3
CAS name:	1,3-Benzodioxol-4-ol, 2,2-dimethyl-, 4-(N-methylcarbamate)
IUPAC name:	2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate
CLP Annex VI Index number:	006-046-00-8
Molecular formula:	$C_{11}H_{13}NO_4$
Molecular weight range:	223.23

Structural formula:



1.2 Composition of the substance

Table 6: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
Bendiocarb	97%	≥ 97%	

Table 7: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks

There are a number of process impurities in the substance. These have been taken into account and are not considered to be of additional concern. Further information on the impurities is considered to be confidential but full details are provided in the technical dossier.

Table 8: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
None				

1.2.1 Composition of test material

The purity of the tested material was sometimes lower than stated above or was not specified in the test reports. However, during the assessment under 98/8/EC it was determined that the available studies were conducted with active substances representative of the current technical material. The purity of the tested material is provided in the relevant sections.

1.3 Physico-chemical properties

Table 9: Summary of physico - chemical properties (ref. CAR Doc. III-A Section A3)

Property	Value	Reference	Comment (e.g. measured or estimated)
State of the substance at 20°C and 101,3 kPa	Solid, beige crystalline powder	Eyrich 2005	Observation 98.5%
Melting/freezing point	129 °C	Smeykal 2005 a	Dir 92/69 A1 (DSC) Purity 98.5%
Boiling point	Decomposed before boiling at 264°C at atmospheric pressure	Smeykal 2005a	Dir 92/69 A2 (DSC) 98.5%
Relative density	1.29 at 20 °C	Bright 1988a	Dir 92/69 A3 (Pycnometer) 99%
Vapour pressure	1.9 x 10-3 Pa at 20 °C 4.6 x 10-3 Pa at 25 °C	Lowes and Bright 1988	Dir 92/69 A4 (Gas Saturation Method) 99.8%
Surface tension	63.29 mN/m at 20 °C	Muhlberger and Lemke, 2004	Dir 92/69 A5 (Shake flask) Purity 98.9%
Water solubility	pH 7: 0.24 g/l at 13 °C 0.28 g/l at 20 °C 0.38 at 30 °C pH 3-5: 0.26 g/l at 13 °C 0.31 g/l at 20 °C 0.44 g/l at 30 °C pH 9-11 0.03 g/l at 20 °C	Stalker and Ward 1992	Dir 92/69 A6 (Flask Method) 99.3%
Partition coefficient n-octanol/water	Log Pow = 1.7 at 25 °C (pH6.9)	Bright 1988c	Dir 92/69 A8 (Shake flask) 99%
Flash point	Not applicable, substance is a solid		
Flammability	Not highly flammable. Experience in handling and use indicates that the substance is not flammable in contact with air or water.	Smeykal 2005b	Dir 92/69 A10 Purity 98.5%
Explosive properties	Not explosive	Smeykal 2005d	Dir 92/69 A14 Purity 98.5%
Self-ignition temperature	Not autoflammable.	Smeykal 2005c	Dir 92/69 A16 Purity 98.5%
Oxidising properties	Not oxidising	Smeykal 2005e	Dir 92/69 A17

Granulometry	Data not available		
Stability in organic solvents and identity of relevant degradation products	Data not available		
Dissociation constant	Not accessible, bendiocarb hydrolyses rapidly in alkaline solutions.	Bright 1988b	EPA OPPTS (UV spectrophotometic method) 99%
Viscosity	Not applicable, substance is solid.		

2 MANUFACTURE AND USES

2.1 Manufacture

The substance is manufactured outside of the EU and imported into the EU where it is formulated into a biocidal product. The biocidal product is used within the EU.

2.2 Identified uses

Bendiocarb is used to control insects, mites and spiders in pest control (product type 18).

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

3.1.1 Summary and discussion of physico chemical properties.

3.1.2 Comparison with criteria

3.1.3 Conclusions on classification and labelling

As the substance is already listed on Annex VI of CLP, the classification for physico-chemical properties is not considered in this dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

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

The following summary is based upon that in the Competent Authority Report (CAR) made for the review under Directive 98/8/EC.

Following single and repeat oral dosing, bendiocarb is rapidly and almost completely absorbed from the gastrointestinal tract of rats. Dermal absorption, based on *in vitro* studies in which aqueous and dry formulations were applied to human skin, is predicted to be low. Elimination after oral administration occurs mainly in the urine and is complete by 48 hours after dosing. The major urinary and faecal metabolite was the conjugated phenolic derivative, formed by cleavage of the carbamate ester group. Because the distribution of bendiocarb was only investigated at 72 hours after oral administration, when the tissue levels were very low, there was no evidence to indicate the tissues that were reached. However, there was no evidence of selective storage in the tissues examined. There appeared to be no differences in absorption, metabolism, or excretion between sexes or after single or repeat oral doses, or intravenous administration.

Acute toxicity (ref. CAR Doc. III-A Section A6.1)

4.2

Table 10: Summary table of relevant acute toxicity studies

Acute Oral		
Method	**LD_{50}**	**Observations and remarks**
Rat/Sprague-Dawley M; 6/group Gavage 0.75, 1.5, 3.0, 6.0, 12, 24, 48, 67.8, 96, 135.7, 192, 271.5, 384 mg/kg 7 days post exposure observation period Purity Batch 1 ;98.9% Batch 2 ;97.0% Batch 3; 91.0% Batch 4; 97.8% Vehicle 0.5 % aqueous gum tragacanth Not guideline or GLP	71.9 – 155.9 mg/kg Batch 1; 107.2-120.8 mg/kg Batch 2; 110.1 – 155.9 mg/kg Batch 3; 71.9 – 135.5 mg/kg Batch 4; 152.3 mg/kg	Clinical signs included fibrillation, followed by urinary incontinence and salivation in most animals at doses of 12 mg/kg and above. Lacrimation and chromodacryorrhoae were also seen in a few animals. Coarse muscular jerking, cyanosis, exophthalmus and piloerection were seen in severely affected animals at the higher end of the dose range, primarily occurring before death. (CAR: Document A90464 **6.1.1/01**)
Rat/ Sprague-Dawley M+F; 6/sex/group Gavage 17.0, 25.0, 35.3, 50.0 mg/kg 14 days post exposure observation period Purity 98.8% Vehicle corn oil Not guideline or GLP	M: 25 mg/kg F: 27.3 mg/kg	Clinical symptoms included salivation, muscular fibrillations, body tremors, facial soiling, urinary incontinence followed by soiling of the urinogenital region, gasping, exophthlamus, lacrimation, chromodacryorrhea, reduced activity and other associated effects. (CAR: Document A90517 **6.1.1/02**)
Rat/ Wistar M+F; 2-10/ sex/dose Gavage Doses (number in brackets denotes the number of animals per dose) M: 20(4) , 25(6) , 40(4),	M: 45-48 mg/kg F: 34-40 mg/kg	Effects were reported to be “typical of a direct inhibitor of cholinesterase” (no further details are provided), developing within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h.

50(10), 80(4), 100(2) mg/kg F: 10 (2), 20 (10), 40 (10) , 80 (8), 160 (2) mg/kg 24 hours post exposure observation period Purity not stated (considered to technical grade material) Vehicle glycerol formal Not guideline or GLP		(CAR: Document A90940 **6.1.1/03**)
Rat/strain not specified M; 4/group Gavage 16, 20, 32, 40, 64, 80, 128 mg/kg Post exposure observation period not specified. Purity not stated (considered to be technical grade) Vehicle glycerol formal Not guideline or GLP	40-64 mg/kg	Effects reported to be "typical of a direct inhibitor of cholinesterase" developed within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. (CAR: Document A90942 **6.1.1/04**)
Mouse/ CFW F; 2-4/ group Gavage Doses (number in brackets denotes the number of animals at each dose) 16 (2), 32 (4), 64 (4) mg/kg 24 hour post exposure observation period Purity not stated (considered to be technical grade) Vehicle glycerol formal Not guideline or GLP	45 mg/kg	Effects were reported to be "typical of a direct inhibitor of cholinesterase" (no further details are provided), developing within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. (CAR: Document A90940 **6.1.1/03**)
Mouse/CD-1 M+F; 6/sex/group Gavage 0, 7.1, 10.0, 14.1, 20.0, 28.3, 40.0, 56.6, 80.0, 113.1 mg/kg	M: 28.3 mg/kg F: 28.2 mg/kg	Clinical signs of toxicity seen at 10 mg/kg and above in both sexes included fibrillation and reduced activity. Straub tail and salivation were seen in a few animals, and urinary incontinence was seen at the top dose level only (10/12 animals at 113.1 mg/kg). In all animals exhibiting clinical signs of toxicity, fibrillation was noted first, starting 1-18 min after dosing, with recovery

14 day post exposure observation period Purity 91.8% Vehicle 0.5 % aqueous gum tragacanth Not guideline or GLP		in survivors occurring between 5 min and 2.5 h post dosing. (CAR: Document A90477 **6.1.1/05**)
Guinea Pig F; 2/group Gavage 25 and 50 mg/kg Purity not specified (considered to be technical grade) Vehicle glycerol formal Not guideline or GLP	35 mg/kg	Effects were reported to be "typical of a direct inhibitor of cholinesterase" (no further details are provided), developing within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. (CAR: Document A90940 **6.1.1/03**)
Rabbit M+F; 2/sex/group Gavage M 20, 40, 80 mg/kg F; 20, 40 mg/kg Purity not specified (considered to be technical grade) Vehicle glycerol formal Not guideline or GLP	M; 40 mg/kg F; 35 mg/kg	Effects were reported to be "typical of a direct inhibitor of cholinesterase" (no further details are provided), developing within a few minutes of dosing. Deaths mainly occurred after 5 min – 2 hours and survivors started to recover after ½ - 2 h. Recovery was visually complete well within 24 h. (CAR: Document A90940 **6.1.1/03**)
Hamster (Syrian) F; 2/group Gavage 25, 100, 200, 400, 1600 mg/kg Purity not specified (considered to be technical grade) Vehicle aqueous cream 7 day post exposure period Not guideline or GLP	141 mg/kg	Effects were reported to be "typical of a quick acting rapidly reversible direct inhibitor of cholinesterase" (no further details provided). (CAR: Document A90384 **6.1.1/06**)
Hen (domestic) F; 5/group	137 mg/kg (without atropine)	Clinical signs included reversible lethargy and loss of muscle function and balance.

Gavage 0, 20, 40, 80, 160, 320 mg/kg Purity not specified (considered to be technical grade) Vehicle corn oil EPA neurotoxicity study Not GLP	757 mg/kg (with atropine)	(CAR: Document A90423 **6.9/01**)
Cat (ex MRC and LAC derived) F; 1 or 2/group Capsule 0.5, 8, 16 and 64 mg/kg Purity 79.4% Not guideline or GLP	11 mg/kg	Clinical signs included muscular fibrillation, ataxia, miosis, urinary and faecal incontinence, prostration, rapid respiration, dyspnoea, convulsions, lachrymation and death (CAR: Document A90967 **6.13.2/01**)
Acute Inhalation		
Method	**LC50**	**Observations and remarks**
Rat/Sprague-Dawley, M+F, 5/sex/group 0, 0.248, 0.377, 0.512, 0.701 mg/l for 4 hours, whole-body exposure 14 day post exposure observation period. 51-65.5% of dust particles <5.5µm Purity 97.9% OECD 403 USEPA 81-3 GLP	M: 0.61 mg/l F: 0.47 mg/l	Clinical signs of toxicity observed at all exposure levels included salivation, wet fur around the eyes and snout, exaggerated respiratory movements; irregular respiratory rate, restless behaviour and tremors were also noted during exposure. Exophthalamus, lethargy, wet fur, discharge from the eyes, brown staining around the snout and jaws and abnormal breathing (increased rate and exaggerated movements) were seen post-exposure up to day 12. (CAR: Document A90617 **6.1.3/01**)
Acute Dermal		
Method	**LD50**	**Observations and remarks**
Rat/Wistar M+F, 4/sex/group 400, 800 mg/kg 7 day post exposure observation period.	M & F 566 mg/kg	Deaths (4/4 males and 4/4/ females) occurred at 800 mg/kg, 26 – 36 h after treatment. No deaths were observed at 400 mg/kg. Toxic effects, observed at both dose levels, were reported to be 'typically cholinergic' and started 45 – 55, and 12 – 16 min after exposure, in males and females respectively. No further details on the nature of the observed toxic effects were given, although their duration was reported as 1 – 2 days.

Purity 96% Vehicle glycerol 7d post-exposure period Not guideline or GLP		(CAR: Document A90347 **6.1.2/01**)
Rat/Wistar F, 2/group Vehicle glycerol formal 400, 800 mg/kg 7 day post exposure observation period. Purity 96% 7d post-exposure period	800 mg/kg	Clinical signs, stated to be 'typical of a direct inhibitor of cholinesterase' (no further details provided), commenced between 2 – 21 h post-application at both doses, with one mortality occurring at 800 mg/kg after 2.5 days. (CAR: Document A90940 **6.1.2/02**)

4.2.1 Non-human information

4.2.1.1 Acute toxicity: oral

LD_{50} values of 25-156 mg/kg and 27-40 mg/kg have been reported in male and female rats respectively.

LD_{50} values of 28-45 mg/kg have been reported in male and female mice.

LD50 values ranging from 11 mg/kg to 141 mg/kg have been reported in other species, namely the guinea pig, hamster, rabbit, hen and cat.

4.2.1.2 Acute toxicity: inhalation

LC_{50} (4-hour) values of 0.61 mg/l and 0.47 mg/l were observed in male and female rats respectively.

4.2.1.3 Acute toxicity: dermal

LD_{50} values of 566 mg/kg and 800 mg/kg were reported in rats.

4.2.1.4 Acute toxicity: other routes

Not applicable

4.2.2 Human information

Not available

4.2.3 Summary and discussion of acute toxicity

In the acute oral studies LD_{50} values of 25-156 mg/kg and 27-40 mg/kg were observed in male and female rats respectively. Values of 28-45 mg/kg have been reported in male and female mice.

The LD_{50} values observed in the Document A90464 **6.1.1/01**study (from 71.9 -155.9 mg/kg) were higher than those observed in the other rat studies. These higher values were attributed to the use of gum tragacanth as a vehicle as opposed to corn oil or glycerol formal. Comparable values were obtained when glycerol or corn oil were used as the vehicle. The lowest reported LD_{50} is considered relevant for classification.

In the acute inhalation study, 4 hour LC_{50} values of 0.61 mg/l and 0.47 mg/l were reported in male and female rats respectively.

In the acute dermal toxicity studies LD_{50} values of 566 and 800 mg/kg were reported in rats.

4.2.4 Comparison with criteria

Bendiocarb should be classified as Acute Tox 2; H300 (Fatal if swallowed) as the LD_{50} values reported in rats and mice are in the range 5 mg/kg < ATE ≤ 50 mg/kg.

Bendiocarb should be classified as Acute Tox 2; H330 (Fatal if inhaled) as the lowest LC_{50} reported (0.47mg/l in female rats) is in the range 0.05 mg/l < ATE ≤ 0.5 mg/l for dusts and mists.

Bendiocarb should be classified as Acute Tox 3; H311 (Toxic in contact with the skin) as both LD50 values reported (566 mg/kg and 800 mg/kg) were in the range 200 < ATE ≤ 1000 mg/kg.

4.2.5 Conclusions on classification and labelling

CLP: Acute Tox. 2: H300, Acute Tox. 2; H330, Acute Tox. 3; H311

RAC evaluation of acute toxicity

Summary of the Dossier submitter's proposal

Acute toxicity: oral
Classification as Acute Tox 2; H300 was proposed on the basis of LD_{50} values reported in rats and mice in the range 5 mg/kg bw < ATE ≤ 50 mg/kg bw. In the acute oral studies, LD_{50} values of 25-156 mg/kg bw and 27-40 mg/kg bw were observed in male and female rats, respectively. Values of 28-45 mg/kg bw have been reported in male and female mice.

In one rat study, the LD_{50} values (71.9-155.9 mg/kg bw) were higher than in other rat studies. These higher values were attributed to the use of gum tragacanth as a vehicle as opposed to corn oil or glycerol formal. Comparable values were obtained when glycerol or corn oil were used as the vehicle. The lowest reported LD_{50} was considered relevant for classification.

Acute toxicity: inhalation
In the acute inhalation study, 4 hour LC_{50} values of 0.61 mg/L and 0.47 mg/L were reported in male and female rats, respectively. Bendiocarb was proposed to be classified as Acute Tox 2; H330 (Fatal if inhaled) as the lowest LC_{50} reported (0.47mg/L in female rats) was within the range 0.05 mg/L < ATE ≤ 0.5 mg/L for dusts and mists.

Acute toxicity: dermal
In the acute dermal toxicity studies, LD_{50} values of 566 and 800 mg/kg bw were reported in rats. Bendiocarb was proposed to be classified as Acute Tox 3; H311 (Toxic in contact with the

skin) as both LD_{50} values reported (566 mg/kg bw and 800 mg/kg bw) were within the range 200 < ATE ≤ 1000 mg/kg bw.

Comments received during public consultation

Acute toxicity: oral

Three Member State Competent Authorities (MSCAs) supported the proposed classification Acute Tox 2; H300. A manufacturer concluded that a classification as Acute Tox 3; H301 was more appropriate considering that the lowest LD_{50} values in rats were obtained with corn oil that increases the bioavailability of the substance. When results obtained with glycerol formal as a vehicle were averaged, an LD_{50} of 52 mg/kg bw was obtained which would meet the criteria for Acute Tox 3; H301.

Acute toxicity: inhalation

Two MSCA supported the proposed classification as Acute Tox 2; H330. A third MSCA supported classification as Acute Tox 3; H331 on the basis of a lethality of only 2/5 females (the most sensitive sex) at 0.512 mg/L. A manufacturer commented that the study by inhalation was performed using whole-body exposure that resulted in exposure of the animals also via the oral and dermal routes and at a dose exceeding that calculated in the study. On this basis a classification as Acute Tox 3; H331 was considered appropriate.

Acute toxicity: dermal

Three MSCAs supported the proposed classification as Acute Tox 3; H311.

Assessment and comparison with the classification criteria

Acute toxicity: oral

Acute oral toxicity of bendiocarb has been investigated in rats, mice, Guinea pigs, rabbits, hamsters, hens and cats, as summarised in Table 1 below.

Table 1. Summary of acute oral toxicity studies for bendiocarb

Strain/ species	Observation period	Design	Vehicle	Purity	LD_{50}	CAR Reference
RATS						
SD rat (M)	7 days	n=6/group 13 doses tested	0.5% w/w aq. gum tragacanth	4 batches tested with purity 91% to 98.9%	71.9-155.9 mg/kg bw	6.1.1/01
SD rat (M/F)	14 days	n=6/group/sex 4 doses tested	Corn oil	98.8%	**M: 25 mg/kg bw** **F: 27.3 mg/kg bw**	6.1.1/02
Wistar rat (M/F)	24 hr	n=2-10 /group/sex 5-6 doses tested	Glycerol formal	Not stated	**M: 45-48 mg/kg bw** **F: 34-40 mg/kg bw**	6.1.1/03
Rat (M)	Not specified (≥ 24 hr)	n=4/group 6 doses tested	Glycerol formal	Not stated	**M: 40-64 mg/kg bw**	6.1.1/04
MOUSE						
CFW mouse (F)	24 hr	n=2-4/group 3 doses tested	Glycerol formal	Not stated	**F: 45 mg/kg bw**	6.1.1/03
CD-1 mouse (M/F)	14 days	n=6/group/sex 9 doses tested	0.5% w/w aq. gum tragacanth	91.8%	**M: 28.3 mg/kg bw** **F: 28.2 mg/kg bw**	6.1.1/05
GUINEA PIG						
Guinea pig (F)	24 hr	n=2 /group 2 doses tested	Glycerol formal	Not stated	**F: 35 mg/kg bw**	6.1.1/03

RABBIT						
Rabbit (M/F)	24 hr	n=2 /group/sex 2-3 doses tested	Glycerol formal	Not stated	**M: 40 mg/kg bw F: 35 mg/kg* bw**	6.1.1/03
HAMSTER						
Syrian hamster (F)	7 days	n=4 /group 5 doses tested	Water	Not stated	F: 141 mg/kg bw	6.1.1/06
HEN						
Domestic hen (F)	21 days	n=5/group 5 doses	Corn oil	Not stated	F: 137 mg/kg bw	6.9/01
CAT						
Cat (F)	14 days	n=1-2/group 4 doses	Gelatin	79.4%	**F: 11 mg/kg bw**	6.13.2/01

Bold values indicate LD_{50} below the cut-off of 50 mg/kg bw between category 2 and category 3 classifications.

* 35 mg/kg bw according to CLH report. Two doses were tested and 0/2 animals died at 20 mg/kg bw and 2/2 died at 40 mg/kg bw supporting an LD_{50} of 30 mg/kg bw.

F=females, M=males; n=number

All studies were considered by the dossier submitter (DS) of sufficient reliability. RAC notes that some studies (on Guinea pig, rabbit, cat) were performed using a limited number of doses and with a small number of animals and their respective reliability is considered lower. It is also noted that the observation period in many studies was less than 14 days as recommended in the test guideline (minimum 24 hr). However, in all studies and all species, deaths were observed within two hours after administration of the test substance and a short observation period is not considered to affect the estimation of the LD_{50}.

In all species tested, clinical signs typical to direct cholinesterase inhibition were observed and generally included muscular fibrillation, urinary incontinence and salivation. Available results showed a similar magnitude of sensitivity in rats, mice, Guinea pigs, rabbits and cats while hamsters and hens appeared slightly less sensitive to acute toxicity of bendiocarb.
According to the Guidance on the Application of the CLP Criteria (Version 4; CLP guidance), the lowest value available in the most sensitive appropriate species should be used for classification. Considering the relative reliability of the available data, results in rats and mice are considered the most relevant for the classification purpose.

Available studies were performed using different vehicles that may have impacted the bioavailability of the test compound. In particular in SD rats, toxicity was more pronounced using corn oil than 0.5% w/v aqueous gum tragacanth. There is however no reason to exclude studies performed with corn oil that resulted in the lowest LD_{50} of 25 mg/kg bw in rats. This LD_{50} is within the range of 5 mg/kg bw < LD_{50} ≤ 50 mg/kg bw and justifies classification as Acute Tox 2; H300.

The classification is further supported by similar LD_{50} values obtained in rats with glycerol formal as a vehicle, in mice with glycerol formal or gum tragacanth as a vehicle as well as in Guinea pigs, rabbits and cats although these latter studies are given less weight.

On this basis, RAC supports classification Acute Tox 2; H300 for acute oral toxicity of bendiocarb.

Acute toxicity: inhalation

One OECD TG 403 study investigated acute inhalation toxicity of bendiocarb in rats as summarised in Table 2 below.

Table 2. Summary of acute inhalation toxicity studies for bendiocarb

Strain/ species	Observation period	Design	Exposure	Purity	LD_{50} / lethality	CAR Reference
RATS						
SD rat (M/F)	14 days	n=5/group/sex 4 doses tested	4hr to dust in air 51-65.5% of particles < 5.5 µm in diameter	97.9%	M: 0.61 mg/L F: 0.47 mg/L M&F: 0.55 mg/L Conc. (mg/l) M F 0.248 0 0 0.377 0 1/5 0.512 2/5 2/5 0.701 3/5 5/5	6.1.3/01

Females appeared slightly more sensitive than males in this study and the LC_{50} of 0.47 mg/L observed in females is within the range 0.05 mg/L < LC_{50} ≤ 0.5 mg/L for dusts and mists and justifies a classification as Acute Tox 2; H330.

It is noted that most of the deaths (1/1 death at 0.377 mg/L, 3/4 at 0.512 mg/L and 5/8 at 0.701 mg/L) occurred already during the 4-hour exposure time. Because of this short latency, although a contribution of exposure through grooming cannot be fully excluded, the deaths are considered to be caused by respiratory exposure. Besides, at the macroscopic examination, congestion of the lungs was the principal finding in those animals that died before the end of the observation period, which provides some indication that mortality was linked to inhalation exposure.

It is also noted that a 50% rate of mortality was not attained in females at the dose of 0.512 mg/L. However, the LC_{50} is a calculated value that also takes into account the steepness of the dose-response curve over all doses tested. An LC_{50} value of 0.47 mg/L was given for female rats in this study.

The determination of the LC_{50} can be accomplished relatively simply by the use of different statistical packages. Small variations in the numerical results for the LC_{50} can be expected depending on how the statistical analysis of the dose-response data is performed. A re-calculation of the study data for female rats using PROAST software was performed by RAP to determine an LC_{50} value according to the dose-response model that better fits the data (Table 3).

Table 3. Re-calculation of LC_{50} values using PROAST software

Model	Likelihood (loglik)	Accept	LC_{50}	Lower CI	Upper CI
null	-15,67	--	NA	NA	NA
full	**-5,87**	--	NA	NA	NA
two-stage	-10,52	no	0.556	NA	NA
log-logist	-6,67	yes	0.497	0.421	0.591
Weibull	**-6,26**	yes	**0.511**	0.438	0.592
log-prob	-6,6	yes	0.492	0.419	0.586
gamma	-6,51	yes	0.496	0.424	0.588
logistic	-6,48	yes	0.508	0.435	0.596
LVM: E2-	-6,38	yes	0.504	0.433	0.591
LVM: H3-	-6,57	yes	0.497	0.42	0.59

Parameters: no covariate; BMR: 0 ED50; constraint: yes; P-value: 0.05; CI=confidence interval

Using the Weibull model that fitted the data with the highest likelihood, an LC_{50} of 0.511 mg/L was determined with a 95% confidence interval of 0.438-0.592 mg/L. RAC concludes that the reported LC_{50} of 0.47 mg/L for female rats is not robust enough to establish that the female LC_{50}

value is below the classification limit of 0.5 mg/L between category 2 and 3.

Overall, RAC concludes that a classification as Acute Tox 3; H331 is appropriate for bendiocarb on the basis of the recalculated female LC_{50} of 0.51 mg/L. This is supported by the combined LC_{50} of 0.55 mg/L for male and female rats.

Acute toxicity: dermal

Acute dermal toxicity of bendiocarb had been investigated in rats as summarised in Table 4 below.

Table 4. Summary of acute dermal toxicity studies for bendiocarb

Strain/ species	Obs. period	Design	Vehicle	Purity	LD_{50}	CAR Reference
RATS						
Wistar rat (M/F)	7 days	n=4/group/sex 2 doses tested	Glycerol	Not stated	M & F: 566 mg/kg bw	6.1.2/01
Wistar rat (F)	7 days	n=2 1 dose tested	Glycerol formal	Not stated	F: 800 mg/kg bw	6.1.2/02

None of the studies completely fulfilled the guideline requirements. Due to a very limited number of animals tested at a single dose in the second study, its reliability to establish the LD_{50} is limited. The first study appears to be of higher reliability. The LD_{50} calculated in both studies are within the range of $200 < LD_{50} \leq 1000$ mg/kg bw and justify a classification as Acute Tox 3; H311 for acute dermal toxicity of bendiocarb.

Supplemental information - In depth analyses by RAC
None.

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

Not considered in this dossier.

4.4 Irritation

4.4.1 Skin irritation

Not considered in this dossier.

4.4.2 Eye irritation

Not considered in this dossier.

4.4.3 Respiratory tract irritation

Not considered in this dossier

4.5 Corrosivity

Not considered in this dossier.

4.6 Sensitisation

Not considered in this dossier.

4.7 Repeated dose toxicity

Not considered in this dossier.

4.8 Germ cell mutagenicity (Mutagenicity)

Not considered in this dossier.

4.9 Carcinogenicity

Not considered in this dossier.

4.10 Toxicity for reproduction

Not considered in this dossier.

4.11 Other effects

Not considered in this dossier.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Bendiocarb was discussed at the European Commission Working Group on the Classification and Labelling of Dangerous Substances in May 1997. On this basis it has a harmonised environmental classification (Index # 006-046-00-8) under Dangerous Substances Directive 67/548/EEC of N; R50/53. This is translated under the Classification, Labelling and Packaging Regulation EC 1272/2008 to Aquatic Acute 1, Aquatic Chronic 1. However, Special Concentration Limits (SCLs) and M-Factors were not harmonised – these are now proposed in this document.

Bendiocarb is an insecticide used to control crawling and flying insects. Available environmental fate and hazard studies have been reviewed under Directive 98/8/EC Biocidal Products Directive. The studies are summarised in the Competent Authority Report (CAR) dated October 2011. The key environmental fate and ecotoxicity information for determining classification, SCLs and M-Factors is presented below.

Bendiocarb hydrolyses with a half-life of 46.5 days at pH 5, 48.1 hours at pH 7 and 43.8 minutes at pH 9 (all at 25 ^{o}C). Where available, ecotoxicity data for the principal hydrolysis product NC 7312 (2-dimethyl-1,3-benzodioxol-4-ol) are also presented.

5.1 Degradation

The European Commission Working Group on the Classification and Labelling of Dangerous Substances (May 1997) agreed the substance meets the ‘not rapidly degradable’ criteria for classification and labelling. The main purpose of this report is to assign M-factors, however the available degradation data from the 2011 biocide CAR for bendiocarb have been consulted in case

they affect the existing or proposed classification. Other than from the CAR, no new information on degradation is available. A summary of the biotic and abiotic degradation is included here:

Abiotic degradation (ref. CAR Doc. III-A Section A7.1.1.1)

Two hydrolysis studies have been submitted on radiolabelled [^{14}C]-bendiocarb according to US EPA guidelines and largely according to OECD 111 (Campbell, 1988[Doc. A90220 **7.1.1.1.1/01**]). Bendiocarb has been shown to hydrolyse at a moderate rate under environmental temperatures and pH with a DT_{50} of 5.7 d (at pH 7 and predicted at 12°C). Hydrolysis increased with increasing pH and at pH 7 a major metabolite, NC 7312 (2,2-dimethyl-1,3-benzodioxol-4-ol), was identified. This was recorded to reach 87.9% of the applied parent compound under the conditions tested (20°C).

Photolysis studies were carried out on [^{14}C]-bendiocarb according to US EPA guidelines (Brehm, 1988a[Doc. A90107 **7.1.1.1.2/01**]). Photolysis was shown to be only a minor route of removal of bendiocarb with a DT_{50} of 187 d predicted from the available data after adjustment for natural sunlight.

Ready biodegradation

No ready or inherent biodegradability studies are available. However, higher tier sewage treatment simulation and sediment-water studies have been submitted (ref. CAR Doc. III-A. Section 7.1.2.1.1. and 7.1.2.2.2). These studies describe route and rate of both abiotic and biological degradation in natural water systems, thereby giving an indication of biodegradability of bendiocarb. The study on aerobic degradation in sewage treatment processes (Doebbler, 1978[Doc. A90198 **7.1.2.1.1/01**]) was carried out to determine the effects of bendiocarb on an activated sludge process using 48 hour shake flask assays. This study used [^{14}C]-bendiocarb added to mixed liquors taken from the test vessels; an unacclimatised vessel (not treated with bendiocarb prior to the study [i.e. the control]) and an acclimated vessel (continuously exposed for 30 d to bendiocarb prior to the study). Only limited uptake into the biomass (maximum 15% with acclimated sludge at 1 mg/L) and only minimal metabolism to CO_2 took place (2% in 48 h at 1 mg/L for acclimated sludge).

Analysis of the effluent indicated that the [^{14}C]-radiolabel was present as a metabolite, rather than the parent compound bendiocarb. It was suggested that this metabolite was most likely to be NC 7312 - as supported by the hydrolysis study suggesting, at the pH values present in the STP, that NC 7312 would be the main metabolite. Based upon the results of this study, it can be concluded that bendiocarb is neither readily nor inherently biodegradable and that the active substance and/or its metabolite (NC 7312) was largely present undegraded in the effluent (bendiocarb partitions 99% to water and 1% to sediment).

Aerobic and anaerobic aquatic degradation

Degradation of [^{14}C]-bendiocarb was studied in two simulated aerobic sediment-water systems (Purser, 1997a[Doc. A92628 **7.1.2.2.2/01** and Arnold, 1984[Doc. A90212 **7.1.2.2.2/02**]). The 1984 study was not carried out to a recognised guideline and pre-dates GLP, but does support the findings of the later study. The 1997 study was carried out to US EPA guidelines. Under aerobic conditions in a sediment/water system, bendiocarb was shown to degrade (DT_{50} 17.1 d at 12°C, k = 0.041 d^{-1}) to a single major metabolite, NC 7312 which further degraded to CO_2. NC 7312 was shown to reach a maximum mean level of 28-32% applied radioactivity (AR) in water phase after 7 d and 17-18% AR in the sediment after 2-3 d. The rate of degradation of the metabolite was shown to be enhanced in the presence of sediment, with DT_{50}s between 22.6 d (sediment-water system) to 132.8 d (filtered water) calculated for 12°C.

The available data suggest that NC 7312 binds to sediment before undergoing further degradation to CO_2. There is evidence of greater degradation in the presence of sediment and NC 7312 does have

a log K_{ow} of 3.15 indicating that adsorption to sediment is likely. According to these data and the CLP criteria, NC 7312 would also be considered not rapidly degradable.

Degradation of bendiocarb under anaerobic conditions (Purser, 1997b[Doc. A92629 **7.1.2.1.2/01**]) was shown to follow the same route as under aerobic conditions but at a slightly higher rate (DT_{50} 8.9 d adjusted to 12ºC). Degradation of the major metabolite, NC 7312, was not investigated further in the anaerobic system.

Overall, and according to CLP criteria, these data confirm the view that bendiocarb (and its main metabolite NC 7312) is not rapidly biodegradable for the purposes of environmental hazard classification

5.2 Environmental distribution

Not considered in this dossier.

5.3 Aquatic Bioaccumulation

Although not necessarily needed from a classification perspective where a substance is confirmed to be non-rapidly degradable, the available data from the bendiocarb CAR indicate that the substance has a low potential to bioconcentrate and hence bioaccumulate in fish. In the bioaccumulation study on radiolabelled [^{14}C]-bendiocarb in bluegill sunfish performed according to US EPA 72-6 guideline (Doc. A90219 **7.4.2/01**), a BCF of 6.0 was found for the whole fish. These findings are further supported by the results of calculation of BCF using a QSAR method which returned a value of 5.56, which agrees very closely with the study results.

5.4 Aquatic toxicity

Available aquatic ecotoxicity information is summarised in Table 11a and Table 11b. Key studies for determining SCLs and M-factors are discussed further below.

Table 11a: Summary of relevant aquatic toxicity information for bendiocarb

Substance and purity	Species	Test Guideline	Endpoint	Toxicity value	Conditions	Reference
Bendiocarb 98 %	*Cyprinodon variegaus* (Sheepshead Minnow)	US EPA 72-3	96-h LC_{50}	0.86 mg a.s./l	Flow-through Mean measured pH 7.8 to 8.0	Doc. A90622 **7.4.1.1/01**
Bendiocarb 100 %	*Salmo gairdneri* (Rainbow trout)	In house (broadly OECD 210)	78-d NOEC	0.07 mg/l	Flow-through Mean measured pH 6.8 to 7.5	Doc. A90214 **7.4.3.2/01**
Bendiocarb 97.62 %	*Daphnia magna*	OECD 202	48-h EC_{50}	0.038 mg a.s./l	Flow-through Mean measured pH 7.56 to 7.84	Gries, 2005a Doc. M-259123-01-1

						7.4.1.2/01
Bendiocarb 95.15 %	*Daphnia magna*	US EPA 72-4	21-d NOEC	0.000882 mg a.s./l	Flow-through Mean measured pH 7.6 to 8.2	Smith *et al*, 1990 Doc. A90226 **7.4.3.4/01**
Bendiocarb 97.62 %	*Pseudokirchneriella subcapitata (Selenastrum capricornutum*)	OECD 201	72-h E_rC_{50} 72-h NOE_rC	0.408 mg a.s./l 0.087 mg a.s./l	Static Mean measured pH 7.76 to 9.96	Gries, 2005b Doc. M-259108-01-1 **7.4.1.3/01**

Table 11b: Summary of relevant aquatic toxicity information for degradant NC 7312

Substance and purity	**Species**	**Test Guideline**	**Endpoint**	**Toxicity value**	**Conditions**	**Reference**
NC 7312 >99 %	*Salmo gairdneri* (Rainbow trout)	US EPA 660	96-h LC_{50}	10 mg/l	Semi-static Nominal	Doc. A90492 **7.4.1.1/02**
NC 7312 >99 %	*Daphnia magna*	OECD 202	48-h EC_{50}	25.4 mg/l	Static Nominal	Williams &Thompson, 1982 Doc. A90493 **7.4.1.2/02**
NC 7312 99.2 %	*Desmodesmus subspicatus*	OECD 201	72-h E_rC_{50} 72-h NOE_rC	88.3 mg a.s./l 0.95 mg a.s./l	Static Nominal	Grade & Wydra, 2007 Doc. M-287279-01-1 **7.4.1.3/02**

Based on aquatic toxicity testing, the most sensitive trophic level for bendiocarb is invertebrates. The two key studies for deriving acute and chronic M-factors are presented below.

Gries, 2005a Doc. M-259123-01-1 **7.4.1.2/01**

The acute toxicity to *Daphnia magna* was assessed following OECD guideline 202 and using flow-through conditions. The GLP study used bendiocarb with a purity of 97.62%. Exposure concentrations were prepared with the aid of dimethylformamide (DMF) [0.2047 g bendiocarb in 100 ml] and were: 0.0125, 0.025, 0.05, 0.1 and 0.2 mg a.s./l. A solvent control was included. Actual mean measured concentrations using HPLC-UV were: 0.015, 0.029, 0.05, 0.11 and 0.16 mg a.s./l. Observations were undertaken at 0, 24 and 48 hours noting immobilisation and sublethal effects.

Based on mean measured concentrations, the 48-h EC_{50} was 0.038 mg a.s./l and the 48-h NOEC was 0.015 mg a.s./l [1].

Smith *et al*, 1990 Doc. A90226 **7.4.3.4/01**

The chronic toxicity to *Daphnia magna* was assessed following US EPA guideline 72-4 and GLP. The study used ^{14}C-radiolabelled bendiocarb with purity of 95.15 %. A flow-through diluter system was employed with approximately 5.75 chamber volumes per day (4,600 ml) provided to each chamber with approximately 1.9 cycles per hour. The study ran for 21 days and is considered broadly in line with OECD guideline 211 and OECD 211 guideline validity criteria were met. A working stock solution was prepared every 3-4 days. The exposure test concentrations were prepared with the aid of acetone (a solvent control was included) and were: 0.625, 1.25, 2.5, 5.0 and 10.0 µg a.s./l.

Total ^{14}C radioactivity was determined by Liquid Scintillation Counting (LSC). Measured concentrations were 100.5 to 118.1 % of nominal – this is considered to reflect both bendiocarb and the hydrolysis degradant NC 7312. If it is assumed that all radioactivity represented bendiocarb, the mean measured exposure concentrations were 0.74, 1.47, 2.71, 5.2, and 10.05 µg a.s./l.

Bendiocarb was qualitatively analysed by Thin Layer Chromatography (TLC) in the highest exposure concentration on days 0, 1, 2, 6, 9, 13, 16, and 21, and accounted for between 63.7 and 98.4 % of the radioactivity. The hydrolysis degradant NC 7312 was considered to account for between 1.7 and 36.3 % of the radioactivity.

Bendiocarb was quantitatively determined by High Performance Liquid Chromatography (HPLC) in two samples (day 6 and 16) of the highest exposure concentration. The percentage bendiocarb was 99 and 62.1 % radioactivity with NC 7312 as 0.2 and 27.1 % radioactivity, respectively.

The pH of exposure solutions was determined on days 0, 7, 14, and 21. The study pH range was 7.6 to 8.2. The pH range for the exposure concentration 1.47 µg a.s./ (mean measured initial) was 7.8 to 8.2.

In summary, analysis by both TLC and HPLC showed bendiocarb to be the principle component. However, as the substance hydrolyses (half-life of 48.1 hours at pH 7 and 43.8 minutes at pH 9 at 25 ^{o}C), the exact concentrations of bendiocarb over the test period are unclear. The available data are insufficient to determine a weighted mean exposure concentration. In the absence of accurate bendiocarb concentrations the rapporteur for the Directive 98/8/EC assessment agreed with the applicant to adjust the study NOEC of 1.47 µg/l by 60 % to account for the lowest value of 62.1 % bendiocarb recorded. Hence the originally reported NOEC and LOEC values of 1.47 and 2.71 µg l^{-1} were reduced to 0.882 and 1.626 µg l^{-1} respectively..

Whilst the available data are not ideal, this adjusted NOEC value of 0.882 µg/l (0.000882 mg/l) is considered a reasonable worst case approach given the uncertainties in the actual exposure concentrations, and is used for this classification and labelling proposal, to be consistent with the data used for the Directive 98/8/EC assessment.

From table 12, the main degradant NC 7312 is more toxic to fish than to invertebrates but it is less toxic to fish than its parent bendiocarb. Crucially it is much less toxic to invertebrates (≈1000 x) than bendiocarb. Considering the measured concentrations of bendiocarb, it was conservatively assumed in the CAR that all toxic effects were due to bendiocarb.

[1] Values quoted to 3 decimal places based on study EC_{50} 0.0377 mg a.s./l and NOEC 0.0148 mg a.s./l.

5.4.1 Fish

Not considered in the dossier.

5.4.2 Aquatic invertebrates

Not considered in this dossier.

5.4.3 Algae and aquatic plants

Not considered in this dossier.

5.4.4 Other aquatic organisms (including sediment)

Not considered in this dossier.

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

Bendiocarb was discussed at the European Commission Working Group on the Classification and Labelling of Dangerous Substances in May 1997. On this basis it has a harmonised environmental classification (Index # 006-046-00-8) under DSD of N; R50/53. This is translated under CLP to Aquatic Acute 1, Aquatic Chronic 1. However, SCLs and M-Factors were not harmonised, these are therefore proposed in this document.

The current harmonised classification considers that bendiocarb is not rapidly degradable or readily biodegradable. This is confirmed by the information available in the 2011 biocide CAR for bendiocarb.

Acute toxicity data for fish, invertebrates and algae are available for bendiocarb and its hydrolysis degradant NC 7312. These indicate that NC 7312 is significantly less toxic than bendiocarb (ref.: table 12, section 5.4). This degradant is also non-rapidly biodegradable and the overall classification proposal for bendiocarb is considered to adequately include and cover NC 7312.

The long-term aquatic data suggest that the long-term toxicity NOEC is below 0.001 mg/l. The bendiocarb 21-d NOEC for *Daphnia magna* is 0.000882 mg a.s./l.

Regulation EC 1272/2008

Based on acute ecotoxicity to *Daphnia magna* data in the range $0.01 < L(E)C_{50} \leq 0.1$ mg/l an acute M-factor of 10 is applicable.

Based on chronic ecotoxicity to *Daphnia magna* data in the range of $0.0001 < NOEC \leq 0.001$ mg/l a chronic M-factor of 100 is applicable for a not rapidly degradable substance.

Directive 67/548/EEC
As bendiocarb is not rapidly degradable and exhibits acute aquatic toxicity below 1 mg/l, Special Concentrations Limits are applicable and presented below in section 5.6.

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

Regulation EC 1272/2008

Aquatic Acute 1; H400 ‘Very toxic to aquatic life’

Aquatic Chronic 1; H410 ‘Very toxic to aquatic life with long lasting effects’,

An acute M-factor of 10 is applicable based on 0.01 <L(E)C_{50} ≤0.1 mg/l. A chronic M-factor of 100 is applicable based on 0.0001 <NOEC≤ 0.001 mg/l for a not rapidly degradable substance.Where Cn is the concentration of bendiocarb in the preparation.

Summary of the Dossier submitter's proposal

Bendiocarb is an insecticide used to control crawling and flying insects. The DS proposed to classify the substance as Aquatic Acute 1 (H400) with an M-factor of 10 and Aquatic Chronic 1 (H410) with an M-factor of 100. The classification was based on the substance being not rapidly degradable, non-bioaccumulative and very toxic to aquatic organisms. The lowest acute toxicity value was a 48-hour EC_{50} of 0.038 mg/L for *Daphnia magna* and the lowest chronic toxicity value was a 21-day NOEC of 0.000882 mg/L, also for *Daphnia magna.*

Degradation
Bendiocarb hydrolysed at 25°C with a half-life of 46.5 days at pH 5, 48.1 hours at pH 7 and 43.8 minutes at pH 9 using radiolabelled [^{14}C]-bendiocarb in a test performed according to US EPA Subdivision N guidelines (161-1,1982) and largely according to OECD TG 111. At pH 7 and at 12°C the half-life was predicted to be 5.7 days. The major metabolite at pH 7, NC 7312 (2,2-dimethyl-1,3-benzodioxol-4-ol), was identified. This reached 87.9% of the applied parent compound.

Photolysis studies were carried out on [^{14}C]-bendiocarb according to US EPA guidelines. Photolysis was shown to be only a minor route of removal of bendiocarb with a DT_{50} of 187 days predicted from the available data.

No ready biodegradability studies are available. The study on aerobic degradation in sewage treatment process was carried out to determine the effects of bendiocarb on an activated sludge process using 48-hour shake flask assays. Only limited uptake into the biomass and only minimal metabolisms to CO_2 took place. Analysis of the effluent indicated that [^{14}C]-radiolabel was present as a metabolite. It was suggested that this metabolite was most likely NC 7312 as supported by the hydrolysis study. Based upon the results in this study, it can be concluded that bendiocarb is neither readily or inherently biodegradable.

Degradation of [^{14}C]-bendiocarb was studied in two simulated aerobic sediment-water systems. The later study was carried out according to US EPA guidelines. Under aerobic conditions in a sediment/water system, bendiocarb was shown to degrade to a single major metabolite NC 7312 with a half-life of 17.1 days at 12°C. NC 7312 further degraded to CO_2. NC 7312 reached a maximum mean level of 28-32% applied radioactivity (AR) in water phase after 7 days and 17-18% AR in the sediment after 2-3 days. The rate of degradation of the metabolite was enhanced in the presence of sediment, with DT_{50} values between 22.6 days in sediment-water system and 132.8 days in filtered water at 12°C. The available data suggests that NC7312 binds to sediment before undergoing further degradation to CO_2. There is evidence of greater degradation in the presence of sediment and NC 7312 does have a log Kow of 3.15 indicating that adsorption to sediment is likely. According to these data NC 7312 would also be considered not rapidly degradable. The former study was not carried out according to a recognised test guideline, but supported the findings of the later study.

Bioaccumulation
In the bioaccumulation study on radiolabelled [^{14}C]-bendiocarb in bluegill sunfish (*L. macrochirus*) performed according to US EPA 72-6 guideline, a BCF of 6.0 was found for the whole fish. The $logP_{ow}$ was 1.7 (25°C, pH 6.9) in the shake flask test according to EEC-Method A8 (1992). Thus bendiocarb has a low potential to bioconcentrate and hence bioaccumulate in fish.

Aquatic toxicity
Table 5. Summary of relevant aquatic toxicity data for bendiocarb

Substance and purity	Species	Test Guideline	Endpoint	Toxicity value	Conditions
Bendiocarb 98%	*Cyprinodon variegatus*	US EPA 72-3	96h LC50	0.86 mg a.s./L	Flow-through, mean measured, pH 7.8 to 8.0
Bendiocarb 100%	*Salmo gairdneri*	In house (broadly OECD 210)	78d NOEC	0.07 mg/l	Flow-through, mean measured, pH 6.8 to 7.5
Bendiocarb 97.62%	***Daphnia magna***	**OECD 202**	**48h EC50**	**0.038 mg a.s./L**	**Flow-through, mean measured, pH 7.56 to 7.84**

6 OTHER INFORMATION

Not applicable.

7 REFERENCES

All references should be viewed as references to the Competent Authority Report – October 2011 – Document IIA – Effects Assessment for the Active Substance – Bendiocarb and Document IIIA, prepared by the UK for the review of the active substance under Directive 98/8/EC. The non-confidential Document IIIA is annexed (Annex I) to this CLH report.

Please refer to Annex I of the report for futher details on the studies.

8. ANNEXES

Annex I - Competent Authority Report – October 2011 – Document IIIA – non-confidential