UNITED NATIONS

UNEP

SC

UNEP/POPS/POPRC.8/INF/31

Distr.: General
17 January 2013

English only

Stockholm Convention on Persistent Organic Pollutants

Persistent Organic Pollutants Review Committee
Eighth meeting
Geneva, 15–19 October 2012
Agenda item 5 (f)

Technical work: assessment of alternatives to DDT

Fact sheets on chemical alternatives to DDT

Note by the Secretariat

The annex to the present note contains fact sheets on chemical alternatives to DDT, developed by the Persistent Organic Pollutants Review Committee at its eighth meeting on the basisof the information in document UNEP/POPS/POPRC.8/INF/13. The fact sheets have not been formally edited.

Annex

Fact sheets on chemical alternatives to DDT

Contents

1 Alpha-cypermethrin

2 Bendiocarb

3 Bifenthrin

4 Cyfluthrin

5 Deltamethrin

6 Etofenprox

7 Fenitrothion

8 Lambda-cyhalothrin

9 Malathion

10 Pirimiphos-methyl

11 Propoxur

I. Assessment of POP criteria and other hazard indicators

1. Alpha-cypermethrin

1.1 Sumamry of the assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

a) Persistence

1. Alpha-cypermethrin is stable to hydrolysis at acidic conditions. DT50 values at pH 7 and 9 are 101 days and 7 days, respectivly. Aqueous photolysis contributes to the degradation of alpha-cypermethrin in water. For the aquatic environment a DT50 whole system from water/sediment study indicate no accumulation in water or sediment (DT50 6 to 35 days at pH values of 7.1 to 8.2). Reported DT50 values for soil range from 25 days to 100 days (lab studies) and from 14 to 112 days in field. The modelled P-score is 0.824 indicating high persistency. However this estimate is based on ultimate mineralization. Alpha-cypermethrin does not fulfil the persistence criteria according to Annex D 1 (b) (i).

b) Bioaccumulation

2. Alpha-cypermethrin has a log Kow of 5.5. The experimentally derived BCF in fish considered in the EU risk assessment on biocidal product was 910 L/kg. The modelled B-score for alpha-cypermethrin is 0.581, suggesting bioaccumulation. Based on the empirical evidence (BCF in fish) alpha-cypermethrin does not fulfil the bio-accumulation criteria according to Annex D 1 (c) (i)..

c) Long-range environmental transport

3. Alpha-cypermethrin has a calculated half-life in air of 3.5 hours (< 2 days). Therefore it has a low LRT potential and it is unlikely that the compound fulfils the Annex D 1 (d) (iii) criteria.

d) Ecotoxicity (including pollinator toxicity)

4. Alpha-cypermethrin is highly toxic to aquatic species and is classified according to EU-GHS as aquatic acute and chronic category 1, e.g. very toxic to aquatic life with acute and long lasting effects. It reveals high toxicity toward honey bees and other pollinators. Alpha-cypermethrin therefore fulfils in addition to the reported toxicity to human health (see below) Annex D 1 (e) (ii).

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

5. Alpha-cypermethrin is the name given to the compound consisting of two of the four cis-isomers of Cypermethrin. The acute oral and inhalation toxicity of Alpha-cypermethrin is approximately 2–4 times greater than that of Cypermethrin. However other than this there is no indication that it would have different toxicological effects. Thus, read-across to Alpha-cypermethrin from studies performed with Cypermethrin is not considered acceptable.

6. Alpha cypermethrin is classified by EU-GHS for oral acute toxicity category 3. In addition it may according to the latest EU evaluation qualify also for respiratory acute toxicity category 4. However orally with polar solvents no signs of toxicity were observed up to the limit dose level. The substance is not classified for skin or eye irritation, though according to the latest EU evaluation classification for skin irritation may be possible. No skin sensitization potential was observed with the Magnusson and Kligman test.

7. Alpha-cypermethrin is not classified for carcinogenicity, mutagenicity or reproductive toxicity according to the GHS system in the EU and comprehensive data and evaluations available support this conclusion.

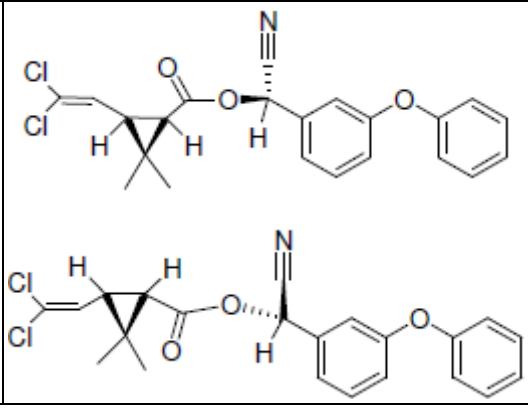
8. Alpha-cypermethrin is not listed in the EU endocrine disrupter database but cypermethrin is listed in the EU endocrine disrupter database within category 2. This means that it is persistent or a HPVC chemical with at least some in vitro evidence of biological activity related to endocrine disruption.

9. The substance did not induce delayed neurotoxicity. Repeated dose toxicity studies showed that the main target organ of Alpha-cypermethrin is the nervous system (CNS and peripheral motor nerves). The critical effect used for limit value derivation was observed in a 1 year dog study were local effects (skin reddening and hair loss) considered as a consequence of systemic toxicity. In the latest evaluation available this lead to an lowest external limit dose (ADI) proposal of 0.015 mg/kg bw day and an internal limit dose (AEL) of 0.01 mg/kg bw day.

1.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Alpha-cypermethrin
IUPAC name:	Racemate comprising (S)-á- cyano-3 phenoxybenzyl-(1R)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate and (R)-á- cyano-3 phenoxybenzyl-(1S)-cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate (= cis-2 isomer pair of cypermethrin)
CAS number:	67375-30-8
Molecular weight:	416.3
Chemical structure:	

b) Chemical group

Pyrethroid

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	5.6 x 10^{-7} Pa (25°C)	EU biocides CAR 2011
Water solubility	4.6 µg/L (pH 7)	EU biocides CAR 2011
Partition coefficient n-octanol/water (log value)	5.5	PPDB 2012
Partition coefficient air/water (log value)	-4.765	EPI Suite 4.0 (KAOWINv1.10)[1]
Partition coefficient air/octanol (log value)	10.27	EPI Suite 4.0 (KAOWINv1.10)
Henry´s Law Constant	0.069 Pa m^3 mol-1	EU biocides CAR 2011

1.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008 – 1nd amendment 2009: for alpha-cypermethrin

Category	Hazard-Phrase
Acute Tox. 3	H301 Toxic if swallowed
STOT SE 3	H335 May cause respiratory irritation
STOT RE 2	H373 May cause damage to organs through prolonged or repeated exposure
Aquatic Acute 1	H400 Very toxic to aquatic life
Aquatic Chronic 1	H410 Very toxic to aquatic life with long lasting effects

[1] http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

b) Proposed reclassification according to GHS

EU biocides CAR 2011: for alpha cypermethrin

Category	Hazard-Phrase
Acute Tox. 3	H301 Toxic if swallowed
Acute tox 4	H332 Harmful if inhaled
Skin irrit. 2	H315 Causes skin irritation
STOT SE 3	H335 May cause respiratory irritation
STOT RE 2	H373 May cause damage to organs through prolonged or repeated exposure
Aquatic Acute 1	H400 Very toxic to aquatic life
Aquatic Chronic 1	H410 Very toxic to aquatic life with long lasting effects

1.4 Environmental fate

a) Abiotic Degradation

-

b) Hydrolysis

10. EU biocides CAR 2011: Hydrolysis of alpha-cypermethrin takes place at alkaline buffer solutions forming 3-phenoxybenzaldehyde (CAS-no. 39515-51-0) as the only major metabolite. Reported values are in line with EFSA review report 2004.

EFSA review report 2004:

I. at pH 4, 50 °C : hydrolytical stability (no degradation after 10 days)

II. at pH 7, 20 °C : DT50 = 101 days

III. at pH 9, 20 °C : DT50 = 7.3 days

c) Phototransformation/photolysis

11. EU biocides CAR 2011: Aqueous photolysis contributes to degradation of alpha-cypermethrin in water. Three resulting metabolites were formed: 3-phenoxybenzaldehyde, 3-phenoxybenzoic acid and cis + trans-2,2-dimethyl-3-(2',2'-dichlorovinyl)cyclopropane carboxylic acid isomers, which are also sensitive to photodegradation. Increasing amounts of carbon dioxide suggesting that alpha-cypermethrin and its photolytic transformation products are rapidly degraded.

d) Biodegradation

12. Retrieved DT_{50} values for soil (lab and field) and water sediment are summarized in Table 3.

Table 3: Half-lives in soil (lab and field), water and sediment

Degradation 50%	days	Reference	Comments
DT_{50} soil lab (days):	25 – 125 (20°C)	EFSA review report 2004	-
DT_{50} water (days):	0.4-2.1 (a.s.) 2.1-3 d (3 phenoxybenzoic acid) 13.9-36.8 d (dimethylcyclopropane carboxylic acid)		-
DT_{50} water sediment/whole system (days):	6.4-35.4		EFSA conclusion: up to 62-55% of applied moved into sediment at day 2; no accumulation in water or sediment; pH values of sediment and water range from 7.1 to 8.2
DT_{50}soil field (days):	14-112 3 year study UK		
DT_{50} soil lab (days):	100	PPDB 2012	persistent
DT_{50} water (days):	1.3	PPDB 2012	moderately fast

DT_{50} water sediment/whole system (days):	21	PPDB 2012	fast
DT_{50}soil field (days):	35	PPDB 2012	moderately persistent

e) Potential for long-range environmental transport

13. EU biocides CAR 2011 state that based on the vapour pressure (3.4×10^{-7} Pa at 25 °C) and the Henry`s Law Constant (0.069 Pa × m³/mol at 25 °C), volatilisation of alpha-cypermethrin is negligible. Calculations of the chemical lifetime in the troposphere resulted in a half-life of 3.47 hours (QSAR estimates). According to this result (t1/2 <2 days), Alpha-cypermethrin is rapidly degraded by photochemical processes and no accumulation of alpha-cypermethrin in the air is to be expected. Therefore it can be concluded that the compound has a low LRT potential.

f) Bioaccumulation

14. EU biocides CAR 2011: According to the experimentally derived BCF in fish, alpha-cypermethrin is not considered to be a bioaccumulable substance with a BCF value of 910 L/kg.

15. WHO 2012: A BCF of 1204 was calculated based on an experiment in rainbow trout with cypermethrin. The same value is listed in PPDB 2012.

g) PB-score[2]

16. Alpha-Cypermethrin has a P-score of 0.824 and a B-score of 0.289 resulting in an overall B-score of 1.11.

1.5 Human health hazard assessment

17. EU biocides CAR 2011: Alpha-cypermethrin is related to Cypermethrin in the following way: Cypermethrin has three chiral centres, one at cyclopropyl C1, a second at cyclopropyl C3, and a third at the benzylic alpha-carbon atom. This pyrethroid therefore consists of a mixture of eight isomers (four diastereoisomeric pairs). The active components of Cypermethrin are 1R cis alpha-S and 1R trans alpha-S. Alpha-cypermethrin is the name given to the compound consisting of two of the four cis-isomers of Cypermethrin: 1R cis alpha-S and 1S cis alpha-R, present each at 12.5 % in Cypermethrin. Consequently, the acute oral and inhalation toxicity of alpha-cypermethrin is approximately 2–4 times greater than that of cypermethrin.

18. Overall, since alpha-cypermethrin is a component of cypermethrin, there is no indication that it would have different toxicological effects. Thus, read-across to alpha-cypermethrin from studies performed with Cypermethrin is not considered acceptable.

a) Acute toxicity

19. EU biocides CAR 2011 for alpha-cypermethrin: The data presented coincide with the EU-GHS classification, i.e. acute toxicity category 3 and 4 for the oral route and respiratory route, respectively. Bioavailablity seems to strongly depend on solvents, with polar solvents no signs of toxicity were observed up to the limit dose level. Alpha-cypermethrin causes skin irritation and may cause respiratory irritation but it does not show skin sensitizing properties in a Magnusson and Kligman test. In humans paresthesia and peripheral sensory phenomena and irritation of respiratory tract was reported.

20. EFSA review report 2004: The acute toxicity data reported are in agreement with the actual EU-GHS classification but not with the EU biocides CAR 2011 proposal for skin irritation and respiratory category 4 classification.

b) Mutagenicity and carcinogenicity

21. EU biocides CAR 2011 for alpha-cypermethrin: All three in vitro genotoxicity assays were negative and also the in vivo micronucleus, mammalian chromosome aberration and UDS tests were unequivocally negative. In consequence, it is concluded that Alpha-cypermethrin has no genotoxic potential. Tumours or other signs of carcinogenicity were not observed upon chronic oral administration of Alpha-cypermethrin to rats and mice.

22. EFSA review report 2004: The report is in agreement with the conclusions presented in the EU

[2] http://www.rivm.nl/bibliotheek/rapporten/601356001.html.

biocides CAR 2011.

23. US EPA RED 2006: Cypermethrin is classified in category C as possible human carcinogen. No quantification is required.

c) Toxicity for reproduction

24. EU biocides CAR 2011 for alpha-cypermethrin: No teratogenic or embryotoxic effects were observed in rats or rabbits. Within a 3-generation study with cypermethrin no adverse effects on reproductive performance or fertility was observed. The data can be read across to alpha-cypermethrin.

25. EFSA review report 2004: The report is in agreement with the conclusions presented in the EU biocides CAR 2011.

d) Neurotoxicity

26. EU biocides CAR 2011 for alpha-cypermethrin: Repeated dose toxicity studies showed that the main target organ of Alpha-cypermethrin is the nervous system (CNS and peripheral motor nerves). After acute and repeated dose studies clinical neurological signs were observed. A 4-week neurotoxicity study aiming at the identification of the toxic mechanism showed that the effects of Alpha-cypermethrin are rather due to a pharmacological effect than the consequence of structural damage, despite sporadic incidences of slight degeneration of the sciatic nerve. Neurobehavioral changes are reversible within 3 days following single dose. In humans paresthesia and peripheral sensory phenomena and irritation of respiratory tract was reported.

27. EFSA review report 2004: The report is in agreement with the conclusions presented in the EU biocides CAR 2011.

28. WHO 2012: A study is cited indicating no delayed neurotoxicity potential in chicken.

e) Immunotoxicity

-

f) Endocrine disruption

29. Alpha-cypermethrin is not listed in the European database for endocrine disrupters. However cypermethrin is listed within category 2, which means that it is persistent or an HPVC with at least some in vitro evidence of biological activity related to endocrine disruption.

g) Mode of action

30. Representing a type II pyrethroid the mode of action is sodium channel blocking resulting in respective neurotoxicity (CS syndrome).

h) Acceptable exposure levels

31. EU biocides CAR 2011 for alpha-cypermethrin: The most sensitive species in chronic toxicity tests was the dog, with a 1-year oral NOAEL of 2.0 mg/kg bw day. The critical effects were local effects (skin reddening and hair loss) considered as a consequence of systemic toxicity. Taking into account the oral absorption factor of 0.45 and an assessment factor of 100 this results in a systemic long term limit value (internal AEL) of 0.009 mg/kg bw day.

32. EFSA review report 2004: Though derived from the 90 day dog study the same systemic long term limit value using the same assessment factor (100) and correction for oral absorption (0.45) is presented (AOEL systemic = 0.01 mg/kg bw day). An external limit value (ADI) is presented on the basis of the 1 year dog study and an assessment factor of 100: 0.015 mg/kg bw day.

1.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

33. EFSA review report 2004 and WHO 2012 reported the toxicity reference values for aquatic organisms listed in Table 4 for risk assessment. The table presents a selection of listed values. Please refer to the original documents for more information.

Table 4: Toxicity reference values for the aquatic compartment

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute 96 hour	Fish	LC_{50}	2.8 µg/l	EFSA, WHO
Chronic, 21 days	Fish	NOEC	< 0.032 µg/l	EFSA, WHO
Acute 48 hour	Aquatic invertebrates	EC_{50}	0.3 µg/l	EFSA,WHO
Chronic, 21 days	Aquatic invertebrates	NOEC	0.03 µg/l	EFSA,WHO
Acute 96 hour	Sediment dwellers	LC_{50}	0.0024 µg/l	EFSA, WHO
Acute 72 hour	Algae	EC50	> 100 µg/l	EFSA, WHO
Mesocosm 126 days	Aquatic community	NOEAEC	0.015 µg/l	EFSA, WHO
Acute 96 hour	Fish	LC_{50}	8.4 µg/l	WHO
Early life stage tox.	Fish	NOEC	0.03 µg/l	WHO
Acute 24 hour	Aquatic invertebrates	EC_{50}	0.14 µg/l	WHO

b) Terrestrial compartment

34. EFSA review report 2004 and WHO 2012 used the toxicity reference values for terrestrial organisms listed in Table 10 for risk assessment. The table presents a selection of listed values. Please refer to the original documents for more information.

Table 5: Toxicity reference values for the terrestrial compartment

Exposure / Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute, oral	Rat	LD_{50}	57 mg/kg	EFSA
Long term 2-generations	Rat	NOAEL	5 mg/kg	EFSA
Acute	Birds	LD_{50}	> 2025 mg/kg	EFSA
Reproduction 20 weeks	Birds	NOEC	130 mg/kg food	EFSA
Acute	Earthworms	LC_{50}	> 100 mg/kg soil	EFSA
reproduction	Earthworms	NOEC	100 g/kg soil	EFSA
Acute	Earthworms	LC_{50}	57,4 (39.2-84) mg/kg soil	WHO
Dietary Toxicity	Birds	LC_{50}	>5000 mg/kg diet	WHO
Chronic reproduction	Birds	NOEC	150 mg/kg diet	WHO

c) Toxicity to pollinators

35. EFSA review report 2004 indicate high toxicity to bees and other pollinators. The acute oral toxicity is 0.059 µg/bee and the acute contact toxicity is 0.033 µg/bee.

1.7 Other information

36. No further critical toxicological information is provided in the WHO 2012 report.

37. Toxicological information presented in the PAN –pesticides database and in the footprint database is largely consistent with the toxicological information summarized above, but they seem to lack the data on mutagenicity and carcinogencity and reproduction toxicity presented above.

1.8 References

EFSA review report 2004: Alpha-Cypermethrin,SANCO/4335/2000 final; 13 February 2004 http://ec.europa.eu/food/plant/protection/evaluation/existactive/list_alpha_cypermethrin.pdf

WHO (2012) WHO specifications and evaluations for public health pesticides- Alpha-Cypermethrin, January 2012.

EU biocides CAR (2011) Evaluation Report Alpha-Cypermethrin, Product-type 18. 2011. available at http://ec.europa.eu/environment/biocides/annexi_and_ia.htm, 2012-03-26

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

PPDB (2012) Pesticide Properties Database: Cypermethrin http://sitem.herts.ac.uk/aeru/footprint/en/index.htm

2. Bendiocarb

2.1 Summary of the assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

a) Persistence

38. Bendiocarb hydrolytically degraded depending on the pH with DT50 values of <1 day to maximum 47 days (at acidic pH). Photolysis was shown to be only a minor route of removal of bendiocarb, however on soil surfaces photolytic degradation was fast. DT50 values in laboratory soil studies range from a few days to weeks. Bendiocarb did degrade reasonably rapidly in the aquatic environment with a DT50 value of 9 days under aerobic conditions in a sediment/water system. Based on the experimental evidence it is concluded that bendiocarb does not meet the persistency criteria of Annex D 1 (b) (i).

b) Bioaccumulation

39. Bendiocarb has a log Kow of 1.7 and an experimental derived BCF in fish of 6. Therefore, the bioaccumulation criterion according to Annex D 1 (c) (i) is not fulfilled.

c) Long-range environmental transport

40. The fate of bendiocarb in air was investigated using the quantitative structure activity relationship estimation method which considers the reaction with the daily air concentrations of hydroxyl (OH) radicals. A maximum estimated half-life of 13.2 h was predicted, however the active substance is not considered volatile. Based on a calculated DT50 value <2 days it can be expected that bendiocarb does not meet the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

41. Beendiocarb is highly toxic to aquatic organisms and is classified according to EU-GHS as aquatic acute and chronic category 1. According to the available data, the most sensitive chronic endpoint for bendiocarb is that derived for a 21 day Daphnia study (NOEC of 0.88 µg /l). The compound is also (highly) toxic to terrestrial organism like birds, bees and earthworms. Based on its high ecotoxicity and toxicity to human health (see below) Annex D 1 (e) (ii) is considered to be fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

42. Bendiocarb is of acute systemic toxicity qualifying for GHS category 3. Available data indicate no skin sensitizing potential.

43. Bendiocarb is not classified for carcinogenicity or mutagenicity by EU-GHS and also the latest US EPA and WHO evaluations support this conclusion. Sufficient data are available.

44. Bendiocarb is also not classified for reproductive toxicity and the latest EU biocides assessment report (AR) supports this conclusion.

45. No immunotoxicity is reported. Bendiocarb is not listed in the EU endocrine disrupter database. No delayed neurotoxicity was observed in a respective study.

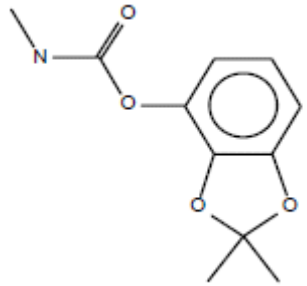
46. Belonging to the group of carbamates the critical effects appear to be cholinesterase inhibition and related neurotoxic effects. The latest proposed long term limit values is 0.0065 mg/kg bw day (EU Biocides AR) which is in a similar magnitude with the WHO proposal.

2.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Bendiocarb
IUPAC name:	2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate
CAS number:	22781-23-3
Molecular weight:	223.23

Chemical structure:	

a) Chemical group

Carbamate

b) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	1.9 10^{-3} Pa at 20°C	EU biocides AR 2011
Water solubility	0.3 g/l	EU biocides AR 2011
Partition coefficient n-octanol/water (log value)	1.7	EU biocides AR 2011
Partition coefficient air/water (log value)	-5.797	EPI Suite v 4.1 (KOAWIN v. 1.10)[3]
Partition coefficient air/octanol (log value)	7.5	EPI Suite v 4.1 (KOAWIN v. 1.10)
Henry´s Law Constant	1.54 x 10^{-3} Pa m^3 mol^{-1}	EU biocides AR 2011

2.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008:

Category	H-phrase	
Acute Tox. 3	H331	Toxic if inhaled.
Acute Tox. 3	H301	Toxic if swallowed.
Acute Tox. 4	H312	Harmful in contact with skin.
Aquatic Acute 1	H100	Very toxic to aquatic life
Aquatic Chronic 1 (M=100)	H410	Very toxic to aquatic life with long lasting effects.

2.4 Environmental fate

a) Abiotic degradation

-

b) Hydrolysis

47. EU biocides AR 2011: Bendiocarb has been shown to hydrolyse with a DT50 of 2 d (at 25°C and pH 7). At pH 7, a major hydrolysis product, NC 7312 (2,2-dimethyl-1,3-benzodioxol-4-ol) was identified, which was recorded to reach 88 % of the applied parent compound under the conditions tested. At pH 5 and pH 9 DT50 values were 1116 hours and 0.7 hours, respectively.

c) Phototransformation/photolysis

48. EU biocides AR 2011: Photolysis was shown to be only a minor route of removal of bendiocarb with a DT50 of 187 days predicted from the available data after adjustment for natural sunlight. HSDB 2012 reported a photolysis half-life in water of 37 days and in soil of <1 day at 25°C.

d) Biodegradation

49. EU biocides AR 2011: Biodegradation of bendiocarb was investigated under aerobic conditions in 3 soils, a sandy loam, a silty clay loam and sand and shown to be reasonably rapid with

[3] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

DT50 values between 2 and 10 days (when adjusted to 12°C). PPDB 2012 reports varying literature values for half-lives in soil from a few days to a few weeks depending on soil type but states a DT50 (typical) of 3.5 days.

50. In water/sediment systems EU biocides AR 2011 identified a DT50 value of 9 days (whole system) and the metabolite NC 7312, which further degraded to CO_2 in aerobic sediment/water systems with DT50 values between 22.6 d (sediment-water system) to 132.8 d (filtered water) calculated for 12°C. Degradation of bendiocarb under anaerobic conditions was shown to follow the same route as under aerobic conditions but at a slightly higher rate (DT50 5 day).

e) Potential for long-range environmental transport

51. EU biocides AR 2011: The fate of bendiocarb in air was investigated using the quantitative structure activity relationship estimation method which considers the reaction with the daily air concentrations of hydroxyl (OH) radicals (AOPWIN, EPI SUITE[4]). A maximum estimated half-life of 13.2 hours was predicted, however the active substance is not considered volatile, as shown by the reported vapour pressure of 1.9 mPa (at 20°C). Due to the lack of persistence no multimedia fate modelling with the OECD tool was performed.

f) Bioaccumulation

52. EU biocides AR 2011 states that bendiocarb has a low potential to bioconcentrate and hence bioaccumulate in fish with a bioconcentration factor (BCF) of 6.0 found for the whole body of the fish. These findings are further supported by the results from calculating a BCF using a QSAR from the 'Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC (new notified substances), Commission Regulation (EC) No 1499/94 (existing substances) and Directive 98/8/EC (biocidal products)' (EC, 2003). This returned a value of 5.6, which agrees very closely with the study results.

g) PB-score

-

2.5 Human health hazard assessment

a) Acute toxicity

53. EU biocides AR 2011: The data presented coincide with the EU-GHS classification, i.e. acute toxicity category 3 for the respiratory and oral route and category 4 for the dermal route. It does not show skin sensitizing properties in a Buehler test.

54. US EPA factsheet 1999: For oral exposure, bendiocarb is in Acute Toxicity Category I, the highest of four categories for this effect. In addition, bendiocarb is in Acute Toxicity Category II for dermal and inhalation routes of exposure, Acute Toxicity Category III for primary dermal irritation and Acute Toxicity Category IV for primary eye irritation.

b) Mutagenicity and carcinogenicity

55. EU biocides AR 2011: Bendiocarb gave a positive result in an in vitro cytogenicity assay on human lymphocytes with metabolic activation. However, it was negative in several other in vitro (bacterial reverse mutation assays and unscheduled DNA synthesis assay) tests and in three in vivo assays (clastogenicity, chromosome aberrations in bone marrow and dominant lethal mutations in germ cells). Consequently the available data do not support GHS classification for mutagenicity. No treatment-related tumours were identified in lifetime studies in rats or mice exposed to bendiocarb in the diet.

56. US EPA factsheet 1999: There was no evidence of mutagenicity following in vivo or in vitro exposure to bendiocarb. It is classified as a "Group E" chemical, showing no evidence of carcinogenicity in laboratory animals or in humans.

c) Toxicity for reproduction

57. EU biocides AR 2011: A fertility study did not indicate treatment-related effects on fertility and post-implantation losses occurred only in the presence of maternal toxicity in rats and rabbits. A slight delay in ossification in rabbit foetuses, secondary to maternal toxicity, was attributed to bendiocarb but was not sufficient to classify for developmental toxicity. Consequently the available data do not support GHS classification for reproductive toxicity.

[4] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

58. US EPA factsheet 1999: Developmental and reproductive toxicity studies did not show evidence of increased susceptibility of rat or rabbit fetuses following in utero exposure or in offspring following pre- and/or post-natal exposure.

d) Neurotoxicity

59. EU biocides AR 2011: No signs of delayed neurotoxicity were reported in hens following a single oral gavage dose of bendiocarb that resulted in mortalities. However Inhibition of erythrocyte and brain cholinesterase activity is directly attributable to its insecticidal mode of action and considered to be the most sensitive marker of toxicity in rats and dogs. This effect was critical for the derivation of the long term and medium term limit values (AEL).

60. US EPA factsheet 1999: The existing studies with acute and subacute administration of bendiocarb indicate a rapid onset of cholinesterase inhibition and accompanying symptoms.

e) Immunotoxicity

-

f) Endocrine disruption

61. Bendiocarb is not listed in the EU endocrine disrupter database 2012.

g) Mode of action

62. EU biocides AR 2011: Inhibition of erythrocyte and brain cholinesterase activity is directly attributable to its insecticidal mode of action and considered to be the most sensitive marker of toxicity in rats and dogs.

h) Acceptable exposure levels

63. EU biocides AR 2011: A long term limit value of 0.0065 mg/kg bw day was proposed on the basis of a 2 year dog study and application of an assessment factor of 100. Inhibition of cholinesterase activity was considered as the respective critical effect.

64. WHO 2009: An ADI of 0.004 mg/kg bw is reported from an evaluation from 1984.

65. US-EPA factsheet 1999: The chronic population adjusted dose (cPAD) is 0.0004 mg/kg/day. A total assessment factor of 300 was applied, where the additional to standard factor of 3 was used because of data gaps for acute and subchronic neurotoxicity studies in rats.

66. Preference is given to the later proposals of WHO and EU, which are in a similar magnitude.

2.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

Bendiocarb is highly toxic to aquatic organism (cf. Table 3)

Table 3: Toxicity reference values (most sensitive species of each group) Source: EU biocides AR 2011

Test compound/Species	Time-scale	Endpoint	Toxicity
Fish			
Bendiocarb/*Cyprinodon variegatus*	96 h	LC_{50}	0.86 mg l^{-1}
Bendiocarb/*Salmo gairdneri*	78 d	$NOEC_{larval\ growth}$	0.07 mg l^{-1}
NC 7312/*Salmo gairdneri*	96 h	LC_{50}	10 mg l^{-1}
Invertebrates			
Bendiocarb/*Daphnia magna*	48 h	EC_{50}	0.038 mg l^{-1}
Bendiocarb/*Daphnia magna*	21 d	$NOEC_{reproduction}$	0.00088 mg l^{-1}
NC 7312/*Daphnia magna Straus*	48 h	EC_{50}	25.4 mg l^{-1}
Algae			
Bendiocarb/ *Pseudokirchneriella subcapitata*	72 h	E_rC_{50} NOE_rC*	0.408 mg l^{-1} 0.087 mg l^{-1}
NC 7312/*Desmodesmus subspicatus*	72 h	E_rC_{50} NOE_rC	88.3 mg l^{-1} 0.95 mg l^{-1}

b) Terrestrial compartment

67. EU biocides AR (2011) reported an acute toxicity (LC50) to earthworms of 188 mg/kg soil.

US-EPA factsheet 1999 identified a high acute risk to birds after application of a product on turf. Bendiocarb is highly toxic to bees (US-EPA 2009). PPDB 2012 states an oral LD50 for honeybees of 0.1 µg/bee. According to PAN-UK 2012 bendiocarb is thus toxic to some beneficial organisms such as honeybees, but also to earthworms and predators of plant pest. There had been a number of bendiocarb related deaths reported to the Wildlife Incident Investigation Scheme, run by the UK government's Department for the Environment Food and Rural Affairs. Although reporting to this scheme is low. It has been confirmed that from 1999 to 2003, the use of bendiocarb has caused the death of 53 (bee) colonies in the UK. For earthworms bendiocarb is extremely toxic, in one study a standard rate was applied and it reduced the population by 90%.

2.7 Other information

68. WHO 2009: does not contain further critical toxicological information.

69. Toxicological information presented in the PAN –pesticides database and in the footprint database is largely consistent with the toxicological information summarized above, but they point to the fact that some data are available indicating that there may be a concern for reproductive toxicity hazard.

2.8 References

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

EU Biocides AR (2011) Assessment Report Bendiocarb PT18, September 2011, available at http://ec.europa.eu/environment/biocides/annexi_and_ia.htm

HSDB 2012 Hazardous Substance Database, TOXNET, http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB

PAN-UK (2012) Bendiocarb factsheet http://www.pan-uk.org/pestnews/Actives/Bendiocarb.htm, 2012-04-07

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/ 2012-04-18

US-EPA factsheet (1999) R.E.D. facts Bendiocarb, September 1999 http://www.epa.gov/oppsrrd1/REDs/factsheets/0409fact.pdf

WHO (2009) WHO specifications and evaluations for public health pesticides-Bendiocarb, January 2009, http://www.who.int/whopes/quality/Bendiocarb_eval_WHO_jan_2009.pdf, 2012-04-06

3. Bifenthrin

3.1 Summary of the assessment of POP properties – comparison with the criteria of Annex D and other hazard indicators

70. Bifenthrin has been considered by the EU ad hoc working group on PBT[5]. 0Bifenthrin has been discussed in November 2007 at a meeting of the TC NES subgroup on identification of PBT and vPvB substances. The group concluded that bifenthrin fulfils the P, vP (very persistent) and T criteria. Concerning bioaccumulation there was no unanimity, a majority of the Working group described bifenthrin as a borderline case for the B criterion (trigger: BCF exceeds a value of 2 000 L/kg). It was concluded that bifenthrin is not considered as fulfilling the B criterion (EU biocides AR 2010)

a) Persistence

71. The TC NES subgroup based their conclusion vP on DT50 values (12°C) in water/sediment studies that range from 176 to 524 days (for the whole system) and DT50 values (12°C) in soil degradation studies that range from 252 to 695 days (laboratory and field studies). Also without temperature adjustment to 12°C the DT50 values exceed 180 days in soil and water/sediment systems. Therefore it can be concluded that available experimental data show that bifenthrin is persistent and meets the Annex D 1 (b) (i) criterion.

b) Bioaccumulation

72. To evaluate the B criteria, 3 tests on fish bioaccumulation were made available to the TC NES subgroup group. In addition, the applicant provided information on the sediment-bound characteristics of bifenthrin and a new study of fish fed with spiked sediment. In the BCF key study done with *Lepomis macrochirus* according to OECD 305 guideline, the steady-state BCF for uptake of bifenthrin estimated in whole fish was 1,414 L/kg. The Working group took notice of this new information but questioned the usefulness of these additional sediment data. While there was no unanimity, a majority of the Working group described bifenthrin as a borderline case for the B criterion and considered bifenthrin as not fulfilling the B criterion (BCF >2000) according to the EU biocides AR 2010.

73. Bifenthrin has a log Kow of 6.6. Experimental BCF values are reported that exceed 5,000 (i.e. BCF of 6090 in bluegill sunfish). However the modelled B-score of 0.38 suggest a lower bioaccumulation potential. Biomagnification through the aquatic food chain and a high risk from bioaccumulation through the terrestrial food chain could not be excluded based on the available information.

74. It can be concluded that available evidence is equivocal to conclude on the bioaccumulation of bifenthrin according to Annex D 1 (c) (i).

c) Long-range environmental transport

75. The EU biocides AR 2010 on bifenthrin reported no indication of long-range environmental transport . Bifenthrin has a calculated DT50 in air of 13 hours that is below the threshold of 2 days. Therefore it is no likely that bifenthrin meets the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

76. The TC NES subgroup based their conclusion that bifenthrin fulfills the T-criteria on ecotoxicity data on *Daphnia magna*, NOEC (21 days, reproduction) = 9.5 x 10^{-4} µg/L (flow through). This is in line with the proposed EU-GHS classification as aquatic acute and chronic category 1 indicating high toxicity to aquatic organisms.Bifenthrin is highly toxic to bees, but slightly toxic on an acute basis to birds, terrestrial phase amphibians and reptiles. Bifenthrin showed no adverse effects to reproduction at the highest concentration tested for birds.

77. Based on the high aquatic toxicity and toxicity to human health of bifenthrin (see below) Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

78. No EU-GHS harmonised classification is actually available for bifenthrin.

79. However according to the actual EU biocides final AR from 2010 bifenthrin is acutely toxic qualifying for acute oral and respiratory GHS class 3. It is also a skin sensitizer when tested with the Magnusson and Kligmann test; it is negative in the Buehler test that applies a less stringent exposure

[5] http://esis.jrc.ec.europa.eu/index.php?PGM=pbt

regime.

80. Some positive or equivocal in vitro genotoxicity results were observed, but the in vivo genotoxicity results are negative which suggests the conclusion that there is no relevant mutagenic potential. Bifenthrin did not induce tumours in the rat, but in mice equivocal tumour findings were reported which might be considered as limited evidence of carcinogenicity qualifying for GHS category 2. On the same data basis US EPA characterised bifenthrin as "possible human carcinogen". In contrast WHO/JMPR concluded in their latest evaluation from 2012 that bifenthrin is unlikely to pose a carcinogenic hazard to humans.

81. Within reproductive toxicity studies reported in the most actual reviews from EU and US EPA or WHO no specific adverse fertility or developmental effects were observed.

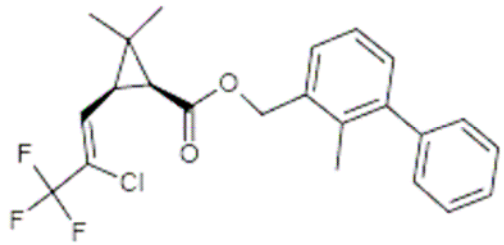
82. Bifenthrin is listed in the EU endocrine disrupter database within category 1 which means it is persistent in the environment or produced at high volumes and shows evidence of endocrine disruption activity in at least one species using intact animals.

83. Bifenthrin did not induce delayed neurotoxicity. Within a developmental neurotoxicity study no specific sensitivity of developing or young rats was observed. The critical effect used for limit value derivation is the clinical neurotoxicity sign tremor. The long term external oral limit values (ADI) in the latest evaluations available are consistently about 0.015 mg/kg bw day. An internal limit value corrected for oral absorption of 0.0075 mg/kg bw day is proposed by the latest European evaluations. In line with the neurotoxic findings at low doses within the EU biocides AR specific target organ toxicity category 1 for the nervous system is proposed.

3.3 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Bifenthrin
IUPAC name:	2-methyl-3-phenylbenzyl (1RS)-cis-3-(2-chloro-3,3,3-trifluroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate
CAS number:	82657-04-3
Molecular weight:	422.88
Chemical structure:	

b) Chemical group

Pyrethroid

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	2.4x 10^{-5} at 25°C (Pa) 1.8x10^{-7} mm Hg	EU biocides AR 2010 US EPA, 2010
Water solubility	<1 µg/L at 20°C, pH 4.05	EU biocides AR 2010
Partition coefficient n-octanol/water (log value)	6.6	EU biocides AR 2010

Property	Value	Remarks and Reference
Partition coefficient air/water (log value)	-4.39	EPI Suite v 4.1 (KOAWIN v. 1.10)[6]
Partition coefficient air/octanol (log value)	10.99	EPI Suite v 4.1 (KOAWIN v. 1.10)
Henry´s Law Constant	101 Pa m³/mol	EU biocides AR 2010

3.3 Classification and labelling

a) Harmonised Classification according to GHS

-

b) Proposal for harmonised classification according to EU-GHS (Regulation (EC) No 1272/2008

84. Proposal from EU Biocides AR 2010:

Category	H-Phrase	
Carc.2	H351	Suspected of causing cancer
Acute Tox. 3	H331	Toxic if inhaled
Acute Tox. 3	H301	Toxic if swallowed
Skin Sens. 1	H317	May cause an allergic skin reaction
STOT Rep. 1	H372 (nervous system)	Causes damage to central nervous system through prolonged or repeated exposure by oral route
Aquatic. Acute 1	H400	Very toxic to aquatic life
Aquatic. Chronic 1	H410	Very toxic to aquatic life with long lasting effects

85. DAR 2010: The proposal is identical to the one presented above from the EU biocides review, with the exception that no STOT RE 1 is proposed.

3.4 Environmental fate

a) Abiotic degradation

-

b) Hydrolysis

86. EU biocides AR 2010: Bifenthrin showed hydrolytic stability.

c) Phototransformation/photolysis

87. EU biocides AR 2010 states no UV/VIS absorption above 290 nm. However photolytic and photo-oxidative degradation of bifenthrin under artificial light yielded a DT50 of 10 days. Estimated half life under natural sunlight conditions was DT50 = 24.4 days (40°N, Madrid conditions) and DT50 = 209 – 300 days (late summer 41°N).

d) Biodegradation

88. EU biocides AR 2010 reported DT50 values in water/sediment systems of 93 to 276 days at 20°C. For the same endpoint EFSA 2011 cited DT50 whole system values of 85 to 324 days (n=4, geometric mean 161 days). In soil laboratory degradation studies the DT50 (geometric mean, n=4, 20°C, degradation kinetics according to best fit) was 192 days. Field DT50 values with a geometric mean of 85 days range from 47 to 267 days. PPDB 2012 and EFSA 2011 reported for lab studies a DT50 range of 54 to 174 days. According to US EPA 2010 bifenthrin is very persistent in both laboratory and filed studies. Half-life in soil ranged from 97 to 250 days. Under anaerobic conditions bifentrhin is considered to be stable (US EPA 2010b) Also EFSA 2011 reported high persistence in field studies. The range of the actual DT50 values from the reliable field dissipation studies were between 15 to 199 days, while the DT90 values were between 221 to 965 days.

e) Potential for long-range environmental transport

89. EU biocides AR 2010 reported a calculated overall OH rate constant of 29.6 x 10^{-12} cm^3 mol^{-1} sec^{-1}. Assuming a 24-h day and an OH concentration of 5.0 x 10^5 cm^{-1} this gives a half-life of 0.54 days or 13 hours. Bifenthrin has a low volatility. It has a moderate volatility from water because its estimated Henry's law constant is 101 Pa m^3 mol^{-1}which is equivalent with an air-water partition

[6] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

coefficient of 0.04 L/L. However, emission from surface water to atmosphere is not expected because of the strong adsorption of bifenthrin to sediment.

f) Bioaccumulation

90. US EPA 2010 indicates that bifenthrin is very lipophilic and bioaccumulative. US EPA 2010b states a BCF of 6090, whole body - bluegill sunfish.

91. DAR 2006: Bioaccumulation was studied in rat for 70 days (15 days depuration phase). Maximum concentrations of radioactivity were detected in fat and skin. Estimated half-lives were around 50 days for fat and skin.

92. Laboratory studies in fish indicate a bioaccumulation potential with BCF ranging from 1,030 (*Cyprinus carpio*, 70 days accumulation phase, plateau reached) to 30,000 (*P. promelas*, 357 days, plateau not reached). Bioconcentration is a function of species, the life stage and the exposure level. All values were defined based on a ratio between fish or tissue and water concentrations; except for *L. macrochirus* for which the k1/k2 expressed BCF was 6,090 for the whole body. However, all available BCF represent the overall radioactivity measured including all bifenthrin and its metabolites. Thus no BCF specifically for bifenthrin is defined from the available data. Metabolism studies in *L. macrochirus* indicated that 67 to 87% of AR (applied radioactivity) corresponds to bifenthrin. Bioaccumulation in the presence of sediment seems to be lower (BCF in *P.promelas* if 45-63), however based on the opinion of the evaluating authority data are insufficient to ensure that the risk of bio-accumulation is low for aquatic species.

93. EU biocides AR 2010: In standard bioaccumulation assays, the bioaccumulation factor (BCF) for fish varies from 666 to 6,090. The higher value corresponds to an old study with the bluegill sunfish *Lepomis macrochirus*, which was redone by the applicant in order to met current standard. A BCF of 1,414 with *Lepomis macrochirus* was obtained. The maximum BCF measurement in carp was BCF = 1,082.

94. In a Full Life Cycle assay, fish exposed continuously during their complete life to bifenthrin exhibits a high BCF, reaching 28,000 after 254 days.

95. Conversely, a higher tier study shows that, in natural environment, the strong adsorption of bifenthrin to sediment can significantly lower the bioaccumulation of the substance in organisms.

96. In November 2007, the Technical Committee for PBT assessment evaluated the bioaccumulation status of this substance and concluded that bifenthrin does not fulfil the B criterion (BCF <2,000).

97. DAR 2010: In the reassessment of bioconcentration in 2010 a BCF of 1,709 was chosen for risk assessment with a clearance time (CT50) of 22 to 28 days in fish. This value is also recommended by EFSA 2011.

98. DAR 2010: A food web bioaccumulation model that has been evaluated against field data for fish measured in agricultural settings after extensive bifenthrin applications was applied using evaluative bioaccumulation and exposure assumptions. Time-dependent bioaccumulation and exposure calculations were determined by linking the output from a five-year FOCUS model scenario as input for the food web predictions. Bifenthrin is found in each level of the food chain but no biomagnification has been observed. There was no biomagnification into the highest trophic level (omnivorous fish) indicating that bifenthrin does not biomagnifiy over 5 years of simulated exposure. However EFSA 2011 identified a data gap concerning biomagnification in the aquatic food chain and a high risk from bioaccumulation through the food chain for aquatic organisms could not be excluded on the basis of the available data.

99. EFSA 2011 stated that a high risk from bioaccumulation through the terrestrial food chain was not excluded and a data gap for further assessment was identified for outdoor uses

g) PB-score

100. Bifenthrin has a P-score of 0.9 and a B-score of 0.38 resulting in an overall B-score of 1,28.

3.5 Human health hazard assessment

a) Acute toxicity

101. EU biocides AR 2010: The acute toxicity data presented are in agreement with GHS the classification proposal listed above: Acute toxicity category 3 for the oral and the inhalation route and skin sensitizing when tested with the Magnusson and Kligman test.

102. The DAR 2010 is in agreement with the information summarized in the EU biocides AR 2010.

In addition a negative Buehler test for skin sensitization is listed.

103. US EPA 2010: Bifenthrin has a moderate order of acute toxicity via the oral route (category II) and a low order of acute toxicity via the dermal route (category III) of exposure. There are no acute inhalation studies on bifenthrin technical; however, acceptable studies on the end-use products are available. Bifenthrin has a lower vapour pressure. Bifenthrin is neither an eye nor skin irritant, nor is it a dermal sensitizer.

b) Mutagenicity and carcinogenicity

104. EU biocides AR 2010: Assays employed to evaluate the genotoxicity of bifenthrin technical were conducted in vitro using bacterial and mammalian cell lines and in vivo using rats and mice. The studies all yielded negative results, except for one mouse lymphoma assay and one unscheduled DNA synthesis (UDS) test. Equivocal results were obtained in another gene mutation assay on CHO cells (non-key study). Three in-vivo genotoxicity tests have been performed, a cytogenetic assay in rats, a micronucleus assay in mice, and an unscheduled DNA synthesis assay in rats. Based on these in-vivo studies, there is no convincing evidence that bifenthrin possesses mutagenic/clastogenic potential. In rats no treatment related tumors were observed but in mice equivocal response in the urinary bladder of the male mice (increased incidence of pericytoma, initially classified as leiomyosarcoma), which might be considered as limited evidence of carcinogenicity effects (GHS category 2).

105. The DAR 2010 is in agreement with the information summarized in the EU biocides AR 2010.

106. US EPA 2010: There was no conclusive evidence of carcinogenic potential of bifenthrin in the rat. A mouse oncogenicity study provided some evidence of carcinogenic potential in this species; therefore, the Agency has characterised bifenthrin as a “possible human carcinogen” and used the reference dose (RfD) approach for risk assessment purposes.

107. WHO 2012: Bifenthrin has been evaluated by the WHO IPCS [2000-2002, Report No.WHO/PCS/01.5] and by the FAO/WHO JMPR in 1992 and 2009. The JMPR concluded that the results of the long-term studies in rats and mice and a series of studies designed to evaluate genotoxicity indicated that bifenthrin is unlikely to pose a carcinogenic hazard to humans.

c) Toxicity for reproduction

108. EU biocides AR 2010: No specific developmental effects were observed in rabbits and rats when administered by the oral route. No effect on reproductive performance or fertility was observed in a two generation study at doses which produced maternal toxicity.

109. The DAR 2010 is in agreement with the information summarized in the EU biocides AR 2010.

d) Neurotoxicity

110. EU biocides AR 2010: Bifenthrin was tested in an acute oral delayed neurotoxicity study and was not considered to be a delayed neurotoxicant when administered to adult hens up to doses of 5000 mg/kg bw. Within a developmental neurotoxicity study no specific sensitivity of developing or young rats was observed. Within repeated dose studies as well as carcinogenicity and reproductive toxicity studies the critical effect was tremor.

111. The DAR 2010 is in agreement with the information summarized in the EU biocides AR 2010.

112. US EPA 2010: The Agency received an acceptable developmental neurotoxicity test (DNT) for bifenthrin in 2006. The study does not show any evidence of increased susceptibility of offspring following exposure to bifenthrin. However, based on the Agency´s review of existing pyrethroid data, EPA has come to the conclusion that the DNT is not a particular sensitive study for comparing the sensitivity of young and adult animals to pyrethroids. The Agency is investigating the need for additional experimentation, specific to the mode of action and pharmacokinetic characteristics of pyrethroids, to evaluate the potential for increased susceptibility of young organisms.

e) Immunotoxicity

-

f) Endocrine disruption

113. EU Endocrine Disruption Database 2012: Listed as category 1 suspected endocrine disrupter, which means that it is persistent in the environment or produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals.

114. US EPA 2010: Bifenthrin is among the group of 58 pesticide active ingredients receiving endocrine disrupter screening program test orders.

g) Mode of action

115. US EPA 2010: Bifenthrin is a Type I pyrethroid (i.e., it lacks a cyano group at the alpha carbon position of the alcohol moiety) neurotoxic pesticide. All pyrethroids act as axonic poisons, affecting both the peripheral and central nervous systems and share similar modes of action. Pyrethroids, including bifenthrin, stimulate repetitive action ain the nervous system by binding to voltage-gated sodium channels, prolonging the sodium ion permeability during the excitatory phase of the action potential.

h) Acceptable exposure levels

116. EU biocides AR 2010: The lowest NOAEL from all repeated dose studies including the 2 year mouse and rat studies stemmed from the 52 week dog study. The critical effects were clinical signs of neurotoxicity. On this basis a long term systemic limit value of 0.0075 mg/kg bw day was proposed considering oral absorption rate of 50% and an assessment factor of 100.

117. DAR 2010: The same study and value has been used as for biocides. In addition to the systemic limit value an external oral limit value (ADI) was derived on the same basis but not accounting for the reduced oral absorption rate, i.e. 2 times the internal value: 0.015 mg/kg bw day.

118. WHO 2012: An ADI was allocated on the basis of the NOAEL of 0 to 0.01 mg/kg/bw/day using a 100-fold safety factor. This result was supported by the same NOEL in the rat teratology study, although in the latter study gavage, rather than dietary administration, was used.

3.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

119. Bifenthrin is highly toxic to aquatic organisms (cf. Table 3). This finding is in line with US EPA 2010 suggesting high toxicity on an acute and chronic basis to freshwater fish and invertebrates. High toxicity to estuarine/marine fish and invertebrates on an acute basis is also reported.

120. The table presents a selection of listed values. Please refer to the original documents for more information.

Table 3: Toxicity reference values (data from EU biocides AR 2010)

Exposure scenario/Study type	Organism/Species		Endpoint	Toxicity value
Acute, 96 hours (h)	fish	Rainbow trout	LC50	0.1 µg/L
Chronic, 76 days (d) ELS, flow-through	Mammals	Rainbow trout	NOEC	0.012 µg/L
Chronic, 120d, flow through	Birds	Fathead minnow	NOEC	0.040 µg/L
Chronic, 21d, flow through	Invertebrates	*Daphnia magna*	NOEC	0.00095 µg/L
Chronic, 28d, flow through	Invertebrates	*Mysidopsis bahia*	NOEC	0.0012 µg/L
Acute 10d, spiked sediment	Sediment dwellers	*Chironimus riparius*	LC50 EC50 (growth)	<544 µg/Kg ww 170 µg/kg ww
Chronic, 28d, spiked water	Sediment dwellers	*Chironimus riparius*	NOEC	1647 µg/kg ww

b) Terrestrial compartment

121. US EPA 2010 classifies bifenthrin slightly toxic on an acute basis to birds, terrestrial phase amphibians and reptiles. Bifenthrin showed no adverse effects to reproduction at the highest concentration tested for birds (cf. Table 4).

Table 4: Toxicity reference values (source: EU biocides AR 2010)

Exposure scenario/Study type	Organism/Species		Endpoint	Toxicity value
Acute, 32-day dietary	Mammals	Rat	LD50	390 mg/kg
Chronic, teratology study	Mammals	Rabbit	NOAEL	25 mg a.s./kg bw/day
Acute toxicity	Birds	Bobwhite quail	LD50	1800 mg a.s./kg bw

Exposure scenario/Study type	Organism/Species		Endpoint	Toxicity value
Dietary toxicity	Birds	Bobwhite quail	LD50	4450 mg/kg diet
Dietary toxicity	Birds	Mallard duck	LD50	1280 mg/kg diet
Reproductive toxicity	Birds	Bobwhite quail	NOEC	>75 mg/kg diet
Chronic toxicity	Earthworms	*Eisenia sp.*	NOEC	2.13 mg/kg dw

c) Toxicity to pollinators

122. US EPA 2010 concludes that bifenthrin is highly toxic to terrestrial invertebrates, including beneficial insects such as honeybees (cf. Table 5).

Table 5: Toxicity values

Study type	Organism	Toxicity value	Reference
Acute oral toxicity	Bees	0.12 – 0.13 µg a.s./bee	EU biocides AR 2010
Acute contact toxicity	Bees	0.044-0.11 µg a.s. /bee	EU biocides AR 2010

3.7 Other information

123. The summary provided above is in agreement with the toxicological information provided in the footprint database and in the PAN pesticides database with the exception that both of these databases indicate that reproductive toxicity results are unclear or positive, respectively.

3.8 References

DAR (2006) Draft Assessment Report Bifenthrin, June 2006, available at http://dar.efsa.europa.eu/dar-web/provision

DAR (2010) BIFENTHRIN, Additional Report to the DAR, October 2010, available at http://dar.efsa.europa.eu/dar-web/provision

EFSA (2011) Conclusion on the peer review of the pesticide risk assessment of the active substance bifenthrin, EFSA Journal 9(5):2159 http://www.efsa.europa.eu/en/efsajournal/doc/2159.pdf

EU biocides AR (2010) Assessment Report Bifenthrin, Product-type 18, September 2010, available at http://ec.europa.eu/environment/biocides/annexi_and_ia.htm

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/, 2012-04-18

US EPA (2010) Bifenthrin summary document, Registration Review: initial docket, June 2010. http://www.epa.gov/oppsrrd1/registration_review/bifenthrin/index.html

US EPA (2010b) Revised EFED Registration Review Problem Formulation for Bifenthrin December 22, available at: http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0384-0033

Wegmann F. Cavin L, MacLeod M, Scheringer M, Hungerbühler K. (2009) Environmental Modeling & Software 24, 228-237

WHO (2012) WHO specifications and evaluations for public health pesticides- Bifenthrin, January http://www.who.int/whopes/quality/Bifenthrin_WHO_specs_eval_Jan_2012.pdf

4. Cyfluthrin

4.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

124. Cyfluthrin is susceptible to photolytic degradation in aqueous media and soil. Results from biodegradation studies indicates moderate persistence ($DT50_{field}$ are in the range from 26 to 40 days). If metabolites are included a $DT50_{field}$ based on total residues of 26 to 116 days could be observed. In water/sediment systems cyfluthrin showed rapid degradation. The modelled P-score is 0.92 indicating high persistency. The modelled result of 259 days for Pov (overall persistency independent from environmental media) from the OECD tool indicates this as well. However the P-score and Pov are related to ultimate mineralization and not to a DT50 value. Therefore it can be concluded that based on the presented experimental information cyfluthrin does not meet the persistency criterion of Annex D 1 (b) (i).

b) Bioaccumulation

125. The log Kow of 6 indicate a potential of bioaccumulation, however the experimental derived BCF value in fish is 506 (with delayed elimination). The modelled B-score for cyfluthrin is 0.01 suggesting low bioaccumulation. Therefore cyfluthrin does not meet the bioaccumulation criterion of Annex D 1 (c) (i).

c) Long-range environmental transport

126. Cyfluthrin has a calculated DT50 in air of 10 to 26 hours. Depending on the input parameters the results of the OECD multimedia fate model suggest a LRT potential below the reference POPs. But for target-oriented LRTP indicator (TE) the model limits for higher concern are exceeded. However the input value DT50 water is not derived from experimental findings and represents most likely an overestimation. The calculated DT50 in air is <2 days. Therefore it can be concluded that more information for cyfluthrin is needed to conclude on the Annex D 1 (d) criterion.

d) Ecotoxicity

127. Cyfluthrin is highly toxic to aquatic species and is classified according to EU-GHS as aquatic acute and chronic category 1. For terrestrial vertebrates cyfluthrin is highly to moderately toxic to mammals. No toxic effects to birds after acute exposure, but higher toxicity for reproductive effects were observed. Cyfluthrin is considered as non-toxic to earthworms. Based on the high ecotoxicity and toxicity to human health (see below) it is concluded that cyfluthrin meets Annex D 1 (e) (ii).

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

128. Cyfluthrin is classified by EU-GHS for acute toxicity category 2 for oral and 3 for respiratory exposure. The substances are within the EU-GHS system not irritant on skin or eye and are not skin sensitizing when tested with the Magnusson and Kligman method.

129. Sufficient studies are available to estimate the genotoxic, carcinogenic and reproductive toxicity potential. It was concluded that Cyfluthrin is neither genotoxic nor carcinogenic nor a reproductive toxin. It is not listed in the EU endocrine disrupter database.

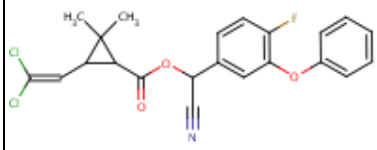
130. Cyfluthrin did not induce delayed neurotoxicity. It was concluded that for pyrethroids no adverse results are to be expected from developmental neurotoxicity studies. For risk assessment the critical effects are general behavioural disturbances and axonal degeneration in the CNS. The long term external oral limit values (ADI) in the latest evaluations available are in the range of 0.003 mg/kg bw day (EFSA) and 0.02 mg/kg bw day (WHO). Internal limit values of 0.002 mg/kg bw day and 0.000243 mg/kg bw day were proposed by EFSA for the oral and respiratory route, respectively.

4.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Cyfluthrin
IUPAC name:	(RS),-α-cyano-4-fluoro-3-phenoxybenzyl-(1RS, 3RS; 1RS, 3SR) - 3-(2,2-dichlorovinyl)-2,2-dimethycyclopropanecarboxylate
CAS number:	68359-37-5 (unstated stereochemistry)

Molecular weight:	434.3
Chemical structure:	

EFSA final review report 2002: Cyfluthrin is a mixture of four diastereoisomers and the ratio of each of the diastereoisomers to their sum shall be:

Diastereoisomer I (1*R*,3*R*,I*R* + 1*S*,3*S*,I*S* = 1:1; cis): 23-27%

Diastereoisomer II (1*R*,3*R*,I*S* + 1*S*,3*S*,I*R* = 1:1; cis): 17-21%

Diastereoisomer III (1*R*,3*S*,I*R* + 1*S*,3*R*,I*S* = 1:1; trans): 32-36%

Diastereoisomer IV (1*R*,3*S*,I*S* + 1*R*,3*S*,I*R* = 1:1; trans): 21-25%

b) Chemical group

Pyrethroid

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	**Value**			**Remarks and Reference**
Vapour pressure	Isomer I: 9.6 · 10^{-7} Pa at 20 °C II: 1.4 · 10^{-8} Pa at 20 °C III: 2.1 · 10^{-8} Pa at 20 °C IV: 8.5 · 10^{-8} Pa at 20 °C			EFSA review report 2002
Water solubility	Isomers I: II: III: IV:	pH 3, 20 °C 2.5 µg/l 2.1 µg/l 3.2 µg/l 4.3 µg/l	pH 7, 20 °C 2.2 µg/l 1.9 µg/l 2.2 µg/l 2.9 µg/l	EFSA review report 2002
Partition coefficient n-octanol/water (log value)	Isomers I and III: 6.0 at 22 oC Isomers II and IV: 5.9 at 22 oC			EFSA review report 2002
Partition coefficient air/water (log value)	-5.96			EPI Suite v 4.1 (KOAWIN v. 1.10)[7]
Partition coefficient air/octanol (log value)	-			-
Henry´s Law Constant	Isomers I: 1.9 · 10^{-1} Pa·m³·mol^{-1} II: 3.2 · 10^{-3} Pa·m³·mol^{-1} III: 4.2 · 10^{-3} Pa·m³·mol^{-1} IV: 1.3 · 10^{-2} Pa·m³·mol^{-1}			EFSA review report 2002

4.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008 – 1nd amendment 2009: for cyfluthrin

Category	H-Phrase	
Acute Tox. 2	H300	Fatal if swallowed
Acute Tox. 3	H331	Toxic if inhaled
Aquatic Acute 1	H400	Very toxic to aquatic life
Aquatic Chronic 1	H410 (M= 1000)	Very toxic to aquatic life with long lasting effects

[7] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

4.4 Environmental fate

a) Abiotic degradation

-

b) Hydrolysis

131. EFSA review report 2002 states fast degradation at 20°C and pH 9 with a DT50 value of <2 days. At all other pH values no or very slow degradation occurs.

132. US EPA RED 2010 reports that the primary routes of dissipation are aqueous and soil photolysis (cf. section below) and hydrolysis in alkaline media.

c) Phototransformation/photolysis

133. EFSA review report 2002 states that cyfluthrin photolytically degrades with a DT50 of 12 days (light source: medium-pressure mercury lamp). Under natural sunlight (August/September, Kansas, 38°49' North) the DT50 is <1 day. Main metabolites were FPBacid (4-fluoro-3-phenoxybenzoic acid), FPBald (3-phenoxy-4-fluoro-benzylaldehyde) and DCVA (3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropanecarboxylic acid (permethric acid)).

d) Biodegradation

134. According to US EPA RED 2010 the terrestrial field dissipation data confirm the pattern observed in the laboratory studies indicating that the chemical follows mixed routes of dissipation in the field. Laboratory studies showed that cyfluthrin is moderately persistent. These finding is in line with recorded DT50 values for cyfluthrin in Table 3.

Table 3: Biotic degradation of cyfluthrin and major metabolites

Study type	Results	Reference	Remarks
DT_{50} soil lab (days):	Cyfluthrin: 4-54 d (n=9, depending on soil type, moisture content and temperature, mean=51 d) (20°C) DCVA: 12-62 d DT50 FPBacid <DCVA	EFSA review report 2002	-
DT_{50} soil $_{field}$ (days):	Cyfluthrin: 26 – 40 (Germany, n=2) Total residues DT50: 26-116 d (USA, n=3)		-
DT_{50} water sediment/water (days):	Cyfluthrin: <1 d FPBacid: app. 10 d		Residues in sediment reached a maximum of 68% of applied after 6 hours, pH sediment 4.5/5 and 6.9/7, pH water 7.6 and 8.2
DT_{50} water sediment/whole system(days):	Cyfluthrin: <1 – 4 d		Apparently rapid degradation of cyfluthrin in sediment - more rapid than other pyrethroids.

e) Potential for long-range environmental transport

135. According to the EFSA review report 2002 the chemical lifetime in troposphere for cyfluthrin is 25.7 h (according to Atkinson, reaction with OH radicals, concentration: $5x10^5$ OH/cm^3)

136. Results of the Phototransformation in air according to EPI Suite TM v4.0 (AOPWIN v 1.92) are based on a 12h day are summarised in Table 4.

Table 4: Phototransformation in air

Guideline / Test method	Molecule / radical	Rate constant for reaction with OH-radicals (k_{OH}) [cm^3 $molecule^{-1}$ sec^{-1}]	Half-life ($t_{1/2}$) [h]	OH-radical concentration (OH-radicals/cm^3)
AOPWIN	OH	12.5011 E-12	10.3	1.5×10^6

137. The OECD "Pov and LRTP Screening Tool"[8] has been developed with the aim of using multimedia models for estimating overall persistence (Pov) and long-range environmental transport potential (LRTP) of organic chemicals at a screening level in the context of PBTs/POPs assessments. The result for cyfluthrin is plotted against the reference chemicals α-HCH, c-octaBDE and PeBD. The criteria lines were not modified and take as proposed in the tool (Pov limit: 195 days, CTD limit: 5096 km, TE limit: 2.25%).

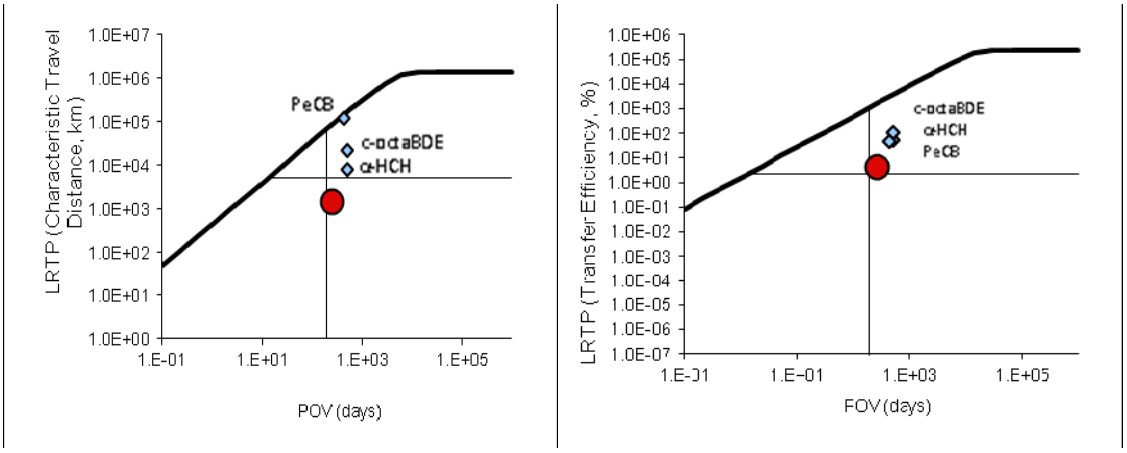
138. The input parameters for Kow and Kaw were taken from Table 2, half-lives for water and soil are listed in Table 5.

Table 5: Half-lives for air, water and soil (input parameters for the OECD Tool)

Half-Lives	Value (h)	Source
Water	4320	PBT profiler[9]
Soil (DT50 lab)	1224	Table 3

139. Input parameter of a DT50 air of 25.7 hours resulted in a calculated CTD (characteristic travel distance) for cyfluthrin of 1438 km and lies below the proposed limits for CTD and the results of α-HCH, c-octaBDE and PeBD. The calculated TE value is 4.1 %. Pov is 259 days. Therefore cyfluthrin can be assessed as a chemical with a potential for LRT lower than the reference POPs (see Figure 1).

Figure 1: Results from the OECD Tool (CTD and TE) for cyfluthrin (red point) and selected reference compounds (α-HCH, c-octaBDE, PeBD).



140. According to Wegmann et al. 2009 compounds that are less problematic from an environmental exposure point of view are in the bottom-left corner (low Pov, low LRT), while substances of environmental concern are found in the upper right region (high Pov, high LRT). In the TE plot cyfluthrin is in the upper right quadrant (though on the boundaries) indicating POP-like persistence and LRT potential.

f) Bioaccumulation

141. EFSA review report 2002 states a BCF in fish of 506 with a depuration half-life (CT50) of 9 days. HSDB 2012 lists an estimated BCF of 170 in aquatic organisms.

g) PB-score

142. Cyfluthrin has a P-score of 0.92 and a B-score of 0.01 resulting in an overall PB-score of 0.93.

4.5 Human health hazard assessment

a) Acute toxicity

143. EFSA review report 2002: The acute systemic LD50 estimates are in the range of GHS class 2 or 3. The substance is non irritant on skin and eye and is not sensitizing when tested with the Magnusson and Kligman method.

144. US EPA RED 2010: The acute oral toxicity of cyfluthrin ranges from Toxicity Category I to III, depending on the administration vehicle. Inhalation toxicity categories also varied by vehicle from Category II to III. Toxicity was low (Category IV) via the dermal route. Cyfluthrin is a slight eye

[8] http://www.oecd.org/document/24/0,3343,en_2649_34379_45373336_1_1_1_1,00.html
[9] http://www.pbtprofiler.net/

(Category III) and dermal (Category IV) irritant, but neither is a dermal sensitizer.

145. WHO 2004: The hazards associated with cyfluthrin have been well characterized. The acute oral LD50 for rats varied from 16 to 1189 mg/kg body weight, depending on the vehicle used, showing that the formulating agent has a strong influence on the acute oral toxicity. Cyfluthrin is toxic by inhalation but acute toxicity by the dermal route is low. Cyfluthrin did not induce skin irritation in rabbits but case reports in humans have shown that local skin irritation can arise from exposure to cyfluthrin formulations. Cyfluthrin caused eye irritation in rabbits. It did not induce dermal sensitization in guinea pigs.

b) Mutagenicity and Carcinogenicty

146. EFSA review report 2002: There is no evidence for genotoxic or carcinogenic potential.

147. US EPA RED 2010: The toxicity profile was sufficient for characterization of potential carcinogenic, mutagenic, developmental, and reproductive effects in the most recent risk assessments. Cyfluthrin is classified as "not likely to be carcinogenic to humans."

148. WHO 2004: Studies on mutagenicity in microbes, with or without metabolic activation, were consistently negative. Cyfluthrin did not induce micronuclei or dominant lethal mutations in mice. Cyfluthrin showed no potential for carcinogenicity.

c) Toxicity for reproduction

149. EFSA review report 2002: Reduced viability index and growth retardation of offspring, coarse tremors of pups during lactation as well as miscarriage and post-implantation resorptions (rabbit), delayed ossification and decreased foetal weights (rat) were observed only at parental toxic doses.

150. US EPA RED 2010: The toxicity profile was sufficient for characterization of potential developmental and reproductive effects in the most recent risk assessments.

151. WHO 2004: In a 3-generation study and in two developmental toxicity studies in rats, no effects on reproductive functions were observed and cyfluthrin showed no evidence of teratogenicity or embryotoxicity.

d) Neurotoxicity

152. EFSA review report 2002: No evidence of delayed neurotoxicity in hens. For risk assessment the critical effects are general behavioural disturbances and axonal degeneration in the CNS.

153. US EPA registration review 2011: Based on the Agency's review of existing pyrethroid data, EPA has come to the conclusion that the development neurotoxicity study (DNT) is not a particularly sensitive study for comparing the sensitivity of young and adult animals to pyrethroids. EPA has recently determined that, as an alternative to the generation and submission of a new DNT study, pyrethroid registrants may instead choose to cite the six previously submitted DNT studies for pyrethroid pesticides. The Agency is also investigating the need for additional experimentation, specific to the mode of action and pharmacokinetic characteristics of pyrethroids, to evaluate the potential for increased susceptibility of young organisms.

e) Immunotoxicity

154. US EPA registration review 2011: The Agency anticipates requiring an immunotoxicity study.

f) Endocrine disruption

155. Cyfluthrin is not listed in the EU endocrine disrupter database.

g) Mode of action

156. US EPA RED 2010: Cyfluthrin is a Type II pyrethroid insecticide.

h) Acceptable exposure levels

157. EFSA review report 2002: A long term ADI of 0.003 mg/kg bw day is reported that was derived from a mouse study and application of an assessment factor of 100. A systemic inhalation AOEL of 0.000243 is reported that was derived from a 13 week inhalation study in rat and application of an assessment factor of 100. This is much lower compared to the systemic AOEL of 0.002 mg/kg bw day also using an assessment factor of 100.

158. US EPA RED 2010: In the most recent risk assessment, neurotoxic endpoints were chosen for all exposure scenarios, with the exception of the inhalation exposure which route-specific studies were used. The point of departure (POD) for the short-term inhalation exposure was chosen from the 28-day rat inhalation study and is based on decreased body weight. The POD for intermediate- and long-

term inhalation exposure is based on decreased body weight and body weight gain observed in the 90-day inhalation study in rats. A dermal study is available, but was not used for endpoint selection because developmental effects were not evaluated in that study.

159. WHO 2004: Toxicological evaluations by the FAO/WHO JMPR and the FAO/WHO JECFA established an ADI for cyfluthrin of 0-0.02 mg/kg body weight, based on the depression of body weight gain in a long-term feeding study on rats.

160. International limit values for worker protection (GESTIS-Database): 8 hours and short term limit values between 0.01 to 0.1 mg/m^3 for Germany and Switzerland

4.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

161. US EPA RED 2010: For aquatic species, numerous aquatic studies have been submitted to the Agency. Cyfluthrin is classified as very highly toxic to aquatic organisms based on data for aquatic vertebrates and invertebrates. An acceptable toxicity study with green algae suggests that cyfluthrin has low toxicity to nonvascular aquatic plants. No vascular aquatic plant data has been submitted to the Agency. Toxicity reference values for aquatic species are listed in Table 5 (source: EFSA review report 2002).

Table 5: Toxicity reference values

Exposure scenario/Study type	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Acute, 96 hours (h)	Fish	Rainbow trout	LC50	0.00047 mg/L	EFSA review report 2002
Acute, 48 h	Fish	Rainbow trout	LC50	**0.00068 mg/L**	
Chronic, 307 days (d)	Fish	Fathead minnow	NOEC	0.040 µg/L	
Chronic, 58 d	Fish	Rainbow trout	NOEC	0.00014 mg/L	
Chronic, 21 d	Invertebrates	*Daphnia magna*	NOEC	0.00002 mg/L	
Acute 96 h	Algae	*Scenedesmus subspicatus*	EC50	>10 mg/L	
Chronic, 28 d	Sediment dwellers	*Chironimus riparius*	EC5	0.00011 mg/L	

b) Terrestrial compartment

162. US EPA RED 2010: For terrestrial species, cyfluthrin is practically nontoxic to birds, moderately toxic to mammals, and highly toxic to terrestrial invertebrates on an acute basis. Chronic effects were seen in rats at levels as low as 150 ppm (cf. Table 6 lists also toxicity for acute time scale for mammals) and at 250 ppm for birds. No terrestrial plant data have been submitted to the Agency. Table 6 presents a selection of listed values from EFSA review report 2002. Please refer to the original documents for more information. EFSA review report 2002 indicates high acute toxicity to mammals.

Table 6: Toxicity reference values (a.s.: active substance, bw: body weight)

Exposure scenario	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Acute	Mammals	Rat	LD50	16-155 mg/kg bw (depending on vehicle)	EFSA review report 2002
Acute toxicity	Birds	Bobwhite quail	LD50	>2000 mg/kg bw	
Acute toxicity	Birds	Canary	LD50	~ 100 mg/kg bw	
Dietary toxicity	Birds	Bobwhite quail	LD50	554 mg/kg bw/day	
Reproductive toxicity	Birds	Mallard duck	NOEL	250 ppm	
Acute toxicity	Earthworms	*Eisenia foetida*	LC50	>1000 mg/kg	

Exposure scenario	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Chronic toxicity	Earthworms	*Eisenia foetida*	NOEC	>100 g a.s./ha	

4.7 Other Information

163. Toxicological information presented in the PAN –pesticides database and in the PPDB footprint database is largely consistent with the toxicological information summarized above.

4.8 References

EFSA review report (2002) Cyfluthrin, 6843/VI/97-final; 2 Dec. 2002, http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1-29_en.pdf 2012-04-04

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

HSDB (2012) Hazardous Substances Data Bank http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB 2012-04-16

US EPA RED (2010) Summary document registration review; EPA-HQ-OPP-2010-0684, available at http://www.epa.gov/pesticides/chemicalsearch 2012-04-04

US EPA registration review (2011): Cyfluthrin final work plan registration review, EPA-HQ-OPP-2010-0684 available at http://www.epa.gov/pesticides/chemicalsearch 2012-04-04

Wegmann F. Cavin L, MacLeod M, Scheringer M, Hungerbühler K. (2009) Environmental Modeling & Software 24, 228-237

WHO (2004) Specifications and evaluations for public health pesticides- Cyfluthrin, November 2004 http://www.who.int/whopes/quality/en/Cyfluthrin_spec_eval_WHO_Nov_2004.pdf 201204-016

5. Deltamethrin

5.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

164. Deltamethrin is stable to hydrolysis at pH 5 to 7. It is degraded fast at pH 9 (2.5 days) and pH 8 (DT50 31 days) Photolysis is not considered an important removal process. In soil deltamethrin is degraded at a relatively fast to moderate rate and the substance is not expected to accumulate in soil. In water sediment studies, deltamethrin will rapidly partition to the sediment, to suspended organic matter and to biota. In water/sediment systems, the degradation DT50 was estimated to 45 and 141 days in two different systems at 20°C (whole system) and the dissipation DT50 in sediment to 55 and 133 days at 20°C. However the pH in the aqueous phase was high enough for hydrolysis. The modelled P-score for deltamethrin is 0.745, indicating persistency. Also findings suggesting high persistency of deltamethrin were reported: Deltamethrin has the potential to persist in aquatic environments, where it may partition to sediment (DT50 26-120 days in aerobic aquatic metabolism study, DT50 32-36 days in anaerobic soil metabolism). Deltamethrin appears to be moderately to highly persistent in terrestrial environments (terrestrial field dissipation 14 to 231 days). Therefore it can be concluded that experimental degradation data in soil may exceed the threshold of 180 days as specified in Annex D 1 (b) (i). Experimental data on persistence in water at pH≤7 were not assessed. Also modelled information suggests high persistency.

b) Bioaccumulation

165. Concerning the log Kow values of 4.6 and 6.2 are reported that indicate a potential of bioaccumulation. The experimental derived BCF value in fish is 1400. Bioaccumulation of deltamethrin in sediment dwellers was also observed (BAF of up to 305).The modelled B-score for deltamethrin is 0.129 not indicating a high bioaccumulation potential. Therefore it is likely that deltamethrin does not meet the bioaccumulation criterion of Annex D 1 (c) (i).

c) Long-range environmental transport

166. Deltamethrin has a calculated half-life in air of 16 hours (<2 days) indicating moderately fast degradation in air. Therefore it is unlikely that deltamethrin fulfils the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

167. Deltamethrin is highly toxic to fish and arthropods (including daphnids and chironomids, bees and other terrestrial insects). It is classified according to EU-GHS as very toxic to aquatic life with acute and long lasting effects. Based on its high aquatic toxicity and toxicity to humans Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

168. Deltamethrin was classified within the EU GHS system for acute toxicity category 3 for the oral and respiratory route. It was not irritating and not sensitizing when tested with the M&K and Buehler method.

169. Deltamethrin was not genotoxic within the standard in vitro test battery and the rat and mouse studies did not indicate evidence for carcinogenicity according to the European evaluations. IARC concluded that deltamethrin is not classifiable as to its carcinogenicity to humans (group 3). The available data indicated that developmental or reproductive effects were only observed at parentally toxic doses and no respective classification is proposed.

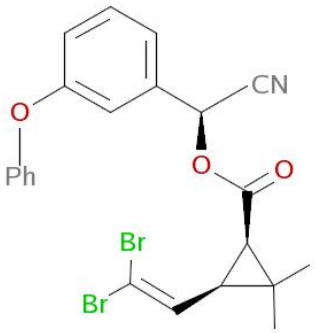
170. Deltamethrin is listed within category 1, which means that it is persistent in the environment or produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals. US EPA indicated that a new immunotoxicity study is required.

171. Representing a type II pyrethroid the critical effect is neurotoxicity. No delayed neurotoxicity study was required. Within acute and subchronic neurotoxicity studies clinical signs of neurotoxicity were observed, with the subchronic studies also in terms of alternations in the FOB. In higher doses also mortalities and reduced body weight gain were observed. Within a developmental neurotoxicity study adverse effects were only observed at parentally toxic doses. The clinical neurotoxicity effects in the 90 day and the 1-year dog studies were the basis for the derivation of a systemic long term limit value of 0.0075 mg/kg BW day. An assessment factor of 100 and an oral absorption rate of 75% was taken into consideration.

5.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Deltamethirn
IUPAC name:	(S)-α-cyano-3-phenoxybenzyl (1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
CAS number:	52918-63-5
Molecular weight:	505.2
Chemical structure:	

b) Chemical group

Pyrethroid

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure at 25°C (mPa)	0.0000124	PPDB 2012
Water solubility at 20°C (mg/l)	0.0002	PPDB 2012
Partition coefficient n-octanol/water (log value, pH 7, 20°C)	4.6	PPDB 2012
Partition coefficient n-octanol/water (log value)	6.2	HSDB 2012
Partition coefficient air/water (log value)	-3,69	EPI Suite v 4.0[10]
Partition coefficient air/octanol (log value)	8.2	EPI Suite v 4.0
Henry´s Law Constant at 25°C ($Pa.m^3.mol^{-1}$)	3.10×10^{-02}	PPDB 2012

5.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008 – 1nd amendment 2009

Category	Hazard-Phrase
Acute Tox. 3 *	H331 Toxic if inhaled.
Acute Tox. 3 *	H301 Toxic if swallowed.
Aquatic Acute 1	H400 Very toxic to aquatic life.
Aquatic Chronic 1	H410 Very toxic to aquatic life with long lasting effects.

5.4 Environmental fate

[10] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

a) Abiotic degradation

-

b) Hydrolysis

172. EU biocides AR 2011: The hydrolysis of deltamethrin was shown to be insignificant at pH 5 and 7. At pH 9, however, hydrolysis was significant with a half-life of 2.5 days (25°C). At pH 8, the DT50 was 31 days (23°C).

173. PPDB 2012: Aqueous hydrolysis DT50 (days) at 20°C and pH 7: stable (pH sensitive: Stable pH 5 to pH 7, DT50 31 days at pH 8, 2.5 days at pH 9, 25°C)

c) Phototransformation/photolysis

174. EU biocides AR 2011: Direct photochemical reactions do not occur at a rate that makes this a significant route of degradation of deltamethrin under natural conditions in water. In soil, direct and indirect photochemical reactions may contribute to the degradation of deltamethrin, but other routes of transformation account for the major loss of parent compound.

175. PPDB 2012: Aqueous photolysis DT50 (days) at pH 7: 48 days: stable

d) Biodegradation

176. EU biocides AR 2011: Deltamethrin was not readily biodegradable in laboratory tests. In aquatic environments, deltamethrin will very rapidly partition to the sediment, to suspended organic matter and to biota. In water/sediment systems, the degradation DT50 was estimated to 45 and 141 days in two different systems at 20°C and the dissipation DT50 in sediment to 55 and 133 days at 20°C. The pH values of the aqueous phase of these systems were 8.0 to 9.1 and hydrolysis may have contributed to the degradation observed. So it cannot be excluded that the rate of degradation would be slower in more acidic/neutral systems. PH of the sediments was lower (7.1/7.5). The difference in degradation rate between the two systems probably reflects difference in amount of fine-textured material and amount of organic matter. $DT50_{soil}$ from DAR 2002 are displayed in Table 3. EU biocides AR 2011 concluded that hydrolysis was probably an insignificant route of degradation in the soils. The DT50 values of the major metabolite of deltamethrin, Br2CA (decamethrinic acid), has been calculated to 0.7-11.6 days in three soils with a geometric mean of 2.0 days (normalised to 25°C and field capacity).

177. US EPA summary 2010: Deltamethrin has the potential to persist in aquatic environments, where it may partition to sediment (DT50 26-120 days in aerobic aquatic metabolism study, anaerobic soil metabolism 32-36 days). Deltamethrin appears to be moderately to highly persistent in terrestrial environments (terrestrial field dissipation 14 to 231 days). The metabolite Br2CA (observed in multiple studies) appears to persist much more than former compounds. It was observed in laboratory studies and in the field.

Table 3: DT50 values of deltamethrin in soil, water and sediment

Degradation 50%	days	Reference	Comment
DT_{50} soil lab	20-35 (3 studies, median 28), all 25°C	DAR 2002	main metabolite soil Br2CA (2,2-dimethylcyclopropanecarboxylic acid)
DT_{50}soil field	21	PPDB 2012	Non Persistent
DT_{50} water sediment/water	17	PPDB 2012	Slow
DT_{50} water sediment/whole system	65	PPDB 2012	Moderately fast
DT_{50}soil field	2-3 weeks US (Minnesota), both cropped and bare soil 1-4 weeks, 4 bare soils in Germany	DAR 2002	-
DT_{50} sediment	55 and 133	EU biocides AR	2 experimental systems with

	(20°C)	2011	different carbon content
DT_{50} water sediment/whole system	45 and 141 (20°C)	EU biocides AR 2011	60% of the applied radioactivity was found in the sediments immediately after application

e) Potential for long-range environmental transport

178. EU biocides AR 2011: Due to its low vapour pressure, deltamethrin is not expected to volatilise to air from plants and soil at significant levels, which was confirmed in a wind tunnel study. However, the calculated Henry's law constant is 1.252×10^{-3} $Pa.m^3.mol^{-1}$, indicating that deltamethrin has a tendency to volatilise from water. If present in air, the data on indirect photooxidation indicate degradation when reacting with hydroxyl radicals with a DT50 of 16 hours (reference to Atkinson, AOPWIN-model). Based on the moderate degradation rate in air no multimedia fate modelling was performed.

f) Bioaccumulation

179. DAR, 2002: Deltamethrin showed a high potential for bioaccumulation with a laboratory BCF (*Lepomis macrochirus*) of 1400 (whole fish). Bioconcentration in fish at this level was confirmed in a microcosm study. Bioconcentration (of total ^{14}C) in chironomids from spiked sediments has also been shown. Micro/mesocosm studies also showed a significant and rapid uptake in plants. Thus, at continuous or repeated exposure to deltamethrin, there is a clear risk for bioaccumulation in biota. BCF/BAF values are 1400 (fish) as total ^{14}C. Major part of ^{14}C consisted of deltamethrin; 213-305 (chironomidae, sediment-exposed, 24 h value, based on total ^{14}C), 145-303 (chironomidae, overlaying water, 24 hour value, based on total ^{14}C)

g) PB-score

180. Deltamethrin has a P-score of 0.745 and a B-score of 0.129 resulting in an overall B-score of 0.875.

5.5 Human health hazard assessment

a) Acute toxicity

181. EU biocides AR 2011: The data presented are in agreement with the actual EU GHS classification: category 3 for oral and respiratory exposure, no skin or eye irritation, not sensitizing when tested with the M&K method and the Buehler method.

182. EFSA review report 2002: The conclusions presented are in agreement with the EU biocides final CAR 2011.

183. WHO 2012: Deltamethrin is not a skin/eye irritant, nor a skin sensitizer.

b) Mutagenicity and carcinogenicity

184. EU biocides CAR 2011: Within the available in vitro test battery deltamethrin was not genotoxic. The available rat and mice carcinogenicity studies did not indicate evidence for carcinogenicity.

185. EFSA review report 2002: The conclusions presented are in agreement with the EU biocides final CAR 2011.

186. IARC 1999: Deltamethrin induced micronuclei and chromosomal aberrations in bone marrow and abnormal sperm morphology in mice treated in vivo. The only other indication of genotoxic potential was induction of chromosomal aberrations in plants. Deltamethrin was tested for carcinogenicity in one experiment in mice and in one experiment in rats by oral administration. In mice, no increase in tumour incidence was seen. In rats, a statistically significant increase in the incidence of unspecified thyroid adenomas was observed in low-dose males and high-dose females. Conclusively there was inadequate evidence for the carcinogenicity of deltamethrin in experimental animals. No data were available from studies in humans. Therefore Deltamethrin was considered as not classifiable as to its carcinogenicity to humans (Group 3).

187. WHO 2012: There is no evidence of genotoxic, carcinogenic or mutagenic effects.

c) Toxicity for reproduction

188. EU biocides CAR 2011: No developmental toxicity was observed at maternal toxic doses in rats and rabbits. In mice an increased incidence of supernumerary ribs at maternal toxic doses was observed. Within a reproductive toxicity study in rat increased pup mortality, reduced lactation index

and reduced pup weight were only observed at parental toxic dose levels.

189. EFSA review report 2002: The conclusions presented are in agreement with the EU biocides final CAR 2011.

190. WHO 2012: There is no evidence of teratogenic or reproductive toxicity effects.

d) Neurotoxicity

191. EU biocides CAR 2011: No delayed neurotoxicity study or data were required or available. Within an acute and subchronic neurotoxicity study in rats neurotoxic effects in terms of clinical signs and functional alternations in functional observation batteries were observed that were in higher doses accompanied with mortalities and reduced body weight gain. Within a developmental neurotoxicity study in rats vocalizations in male pups and delayed onset of balanopreputial separation at maternal toxic dose were observed. Medical data from manufacturing, formulating and packaging plants indicate that transitory skin sensations were the most prevalent finding (paraesthesia, transient local burning, tingling, pickling sensations, itching, numbness of the facial skin – erythema in some cases). Cases of intoxications (mostly occupational due to inappropriate handling of products) have been reported. Two cases of occupational acute deltamethrin poisoning died of convulsions and another died of pulmonary oedema. No late sequeala of pyrethroid poisoning have been described in the scientific literature.

192. EFSA review report 2002: The conclusions presented are in agreement with the EU biocides final CAR 2011.

e) Immunotoxicity

193. US EPA summary 2010: the toxicology database for deltamethrin is essentially complete, with the exception of the immunotoxicity data. The Agency expects to require an immunotoxicity study (Guideline # 870.7800).

f) Endocrine disruption

194. EU Endocrine Disruption Database 2012: Listed within category 1, which means that it is persistent in the environment or produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals.

195. EU biocides CAR 2011: As part of the evaluation of the application for the inclusion of Deltamethrin in Annex I of the Biocidal Products Directive (98/8/EC) toxicology and ecotoxicology data have been assessed. It is concluded that there was no evidence of endocrine disruption effects from these studies. However, it should be noted that due to limitations in the test guidelines available at the time, the potential for endocrine effects may not have been fully investigated.

g) Mode of action

196. ATSDR 2003: The primary site of action for pyrethrins and pyrethroids is the sodium channel of nerve cells, Type II pyrethroids include a cyano group; their effects in rodents are usually characterized by pawing and burrowing behavior, followed by profuse salivation, increased startle response, abnormal hindlimb movements, and coarse whole body tremor that progresses to sinuous writhing (choreoathetosis). Clonic seizures may be observed prior to death. Body temperature is not increased, but may decrease. The term CS-syndrome (from choreoathetosis and salivation) has been applied to Type II responses.

h) Acceptable exposure levels

197. EU biocides CAR 2011: A systemic long term internal limit dose value (AEL) of 0.0075 mg/kg bw day was derived from the clinical neurotoxicity effects in the 1-year dog study, considering an oral absorption rate of 75% and a standard assessment factor of 100.

198. EFSA review report 2002: The same systemic long term limit dose value (AOEL systemic) of 0.075 mg/kg bw day was developed on the basis of the neurotoxic effects in the 1 year dog study and the 90 day dog study and the standard assessment factor of 100. An external long term limit dose value (ADI) of 0.01 mg/kg bw day was developed on the basis of the same studies and assessment factor.

199. WHO 2010: the FAO/WHO JMPR has allocated an ADI of 0.01 mg/kg bw.

5.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

200. Toxicity data for aquatic species are for example available from EFSA review report 2002 and

EU biocides CAR 2011 and PPBD 2012. The compound is classified as very highly toxic to aquatic organisms based on data for aquatic vertebrates and invertebrates. Toxicity reference values for aquatic species are listed in Table 4.

Table 4: Toxicity reference values for the aquatic compartment

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute 96 hour	Fish	LC_{50}	0.00026 mg/l (0.26 µg/l)	PPBD
Chronic, 21 days	Fish	NOEC	< 0.032 mg/l (32 µg/l)	PPBD
Acute 48 hour	Aquatic invertebrates	EC_{50}	0.00056 mg/l (0.56 µg/l)	PPBD
Chronic, 21 days	Aquatic invertebrates	NOEC	0.0041 mg/l (4.1 µg/l)	PPBD
Acute 96 hour	Aquatic crustaceans	LC_{50}	0.0000017 mg/l (0.0017 µg/l)	PPBD
Acute 96 hour	Sediment dwellers	LC_{50}	0.01 mg/l (10 µg/l)	PPBD
Acute 72 hour	Algae	EC50	9.1 mg/l (9100 µg/l)	PPBD
Mesocosm	Aquatic community	NOEAEC	0.0032 mg/l (3.2 µg/l)	PPBD
Chronic 28 day	Sediment dwelling organisms	NOEC	0.0000035 mg/l 0.0035 µg/l based	EU CAR
Chronic 28 day	Sediment dwelling organisms	NOEC	31 µg/kg ww sediment	EU CAR
Chronic Chronic	Mesocosm Mesocosm	NOEC $NOEC_{mortality}$	0.0048 µg/l 0.009 µg/l	EU CAR EU CAR

b) Terrestrial compartment

201. Toxicity reference values for the terrestrial compartment derived from PPDB 2012 and the EU biocides CAR 2011 are summarized in Table 5. Deltamethrin shows low toxicity to birds at short as well as long-term exposure.

Table 5: Toxicity reference values for the terrestrial compartment

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute, oral	Rat	LD_{50}	87 mg/kg	PPBD
Acute, dietary	Rat		2.5 mg/kg	PPBD
Acute	Birds	LD_{50}	> 2250 mg/kg	PPBD
Acute, dietary	Birds	LD_{50}	> 5620 ppm mg/kg	PPBD
Acute/14 day	Earthworms	LC_{50}	> 1290 mg/kg	EU-CAR
Chronic Reproduction	Birds	NOEL	55-70 mg/kg	EU-CAR
Chronic/28 days	Soil dwellers (spring tails)	NOEC	0.78 mg/kg	EU-CAR
Chronic/28 days	microorganisms	NOEC	> 0.5 mg/kg soil	EU-CAR

c) Toxicity to pollinators

202. DAR 2002: Deltamethrin showed very high contact and oral toxicity to honey bee, *Apis mellifera*, in laboratory studies. Acute oral toxicity: LD50 79 ng/bee; LD50 (48 h): 280 ng /bee; Acute contact toxicity: LD50 (48 h) 1.5 ng/bee: LD50 (48 h) 10 ng/bee

203. Deltamethrin showed very high contact toxicity (almost 100% mortality at an application rate of 13.5 g/ha) to some terrestrial arthropods (*Coccinella septempunctata, Chrysoperla carnea* and *Trichogramma cacoeciae*) in laboratory studies. According to both EPPO and Annex VI to Directive 91/414/EEC there is a high predicted risk if more than 30% of the individuals are affected. Also in the field studies there were effects observed, although those results were somewhat difficult to quantify due to different practical circumstances.

5.7 Other information

204. Toxicological information presented in the PAN –pesticides database and in the footprint database is largely consistent with the toxicological information summarized above with the exception that the reproductive toxicity and developmental study results summarized from EFSA above seem not respected or insufficient for a conclusion in these two databases.

5.8 References

ATSDR (2003) TOXICOLOGICAL PROFILE FOR PYRETHRINS AND PYRETHROIDS, September 2003, http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=787&tid=153

DAR (2002) Draft Assessment Report. Deltamethrin. 2002, http://dar.efsa.europa.eu/dar-web/provision, 2012-03-26

EU biocides CAR (2011) Competent Authority Report, Deltamethrin. Product-type 18 (Insecticides), 2011.

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

EFSA review report (2002) Deltamethrin 6504/VI/99-final October 2002, available at http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/ 2012-04-18

IARC (1999) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 53, Occupational Exposures in Insecticide Application, and Some Pesticides , available at http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php

US EPA summary (2010) Deltamethrin Summary Document, Registration Review; Initial Docket March 2010, EPA-HQ-OPP2009-0637-0002, available at http://www.epa.gov/pesticides/chemicalsearch

WHO Report (2010) available at http://www.who.int/whopes/quality/newspecif/en/

6. Etofenprox

6.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

205. Etofenprox is hydrolytically stable but degrades according to the results from aquous and soil photolysis studies. An evaluated comprehensive dataset demonstrates that etofenprox is rapidly and completely degraded in soil without giving rise to significant or persistent degradation products. DT50 values in water-sediment systems of etofenprox and its metabolite are in the same range than results from soil studies for water and whole system. DT50 in sediment is longer with a maximum of 56 days (for the metabolite). Though etofenprox has a P-score of 0.7 (based on mineralization) it can be concluded that etofenprox does not meet the Annex D criterion 1 (b) (i).

b) Bioaccumulation

206. Etofenprox has a log Kow >5 indication a potential for bioaccumulation. The BCF in fish is 3,921. However this value is based on a single study. The modelled B-score of 0.5 is in agreement with the experimental high BCF value. Based on the (limited) available data it can be concluded that etofenprox does not meet the criterion 1 (c) (ii) of Annex D.

c) Long-range environmental transport

207. Etofenprox has a calculated half-life in air of 2 hours (<2 days). Therefore it is unlikely that etofenprox fulfils the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

208. Etofenprox shows high toxicity to aquatic organisms that qualify for EU-GHS classification acute and chronic category 1. Etofenprox is of low toxicity to birds. Etofenprox shows no effects on earthworms up to 47 mg/kg dry artificial soil. Etofenprox is toxic to bees. Based on its high aquatic toxicity Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

209. Etofenprox was of low acute toxicity, did not induce skin or eye irritation or skin sensitization with the M&K test. No GHS classification is necessary for acute toxicity. It did not show genotoxic potential within a series of in vitro and in vivo tests. In a rat 2 year study thyroid tumors were observed but the available mode of action data support the assumption o f a threshold and low relevance form humans. By weight of evidence the renal tumors in the mouse were not considered significant and overall the European evaluations conclude that there is no concern for carcinogenicity. US EPA concludes that etofenprox is not likely to be carcinogenic to humans at doses that do not alter thyroid homeostasis. Based on a weight of evidence analysis etofenprox is not considered a specific reproductive toxicant however haemorrhage effects observed in weanlings and kinetic data supporting high milk excretion rates might indicate a hazard for breast fed children and a respective need for GHS labelling. Though representing structurally a pyrethroid-like pesticide etofenprox did not appear neurotoxic, neither in acute nor repeated dose studies. Within the developmental neurotoxicity study some minor functional neurological effects appeared at dose levels causing also adverse parental effects. Etofenprox is listed in the EU database for endocrine disrupters within category 3b, which means that insufficient data are available for an evaluation of respective effects.

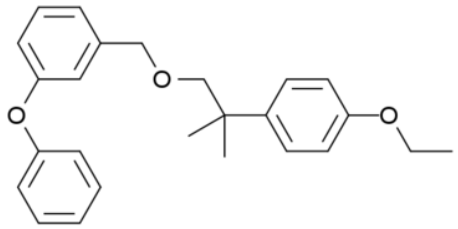
210. A systemic and external long term limit value of 0.03 mg/kg bw day was proposed consistently throughout several evaluations based on either the long term rat or the mouse study and assessment factor of 100. The critical target organs were liver, kidney and thyroid.

6.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Etofenprox
IUPAC name:	2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether
CAS number:	80844-07-1
Molecular weight:	376.49

Chemical structure:	

b) Chemical group

Pyrethroid-ether

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Reference
Vapour pressure at 25°C (mPa)	$8.13x10^{-04}$	PPDB 2012
Water solubility at 20°C (mg/l)	0.0225	PPDB 2012
Partition coefficient n-octanol/water (log value, pH 7, 20°C)	6.9	PPDB 2012
Partition coefficient air/water (log value)	-6.03	EPI Suite v 4.1 (KOAWIN v. 1.10)[11]
Partition coefficient air/octanol (log value)	12.93	EPI Suite v 4.1 (KOAWIN v. 1.10)
Henry´s Law Constant at 25°C ($Pa.m^3.mol^{-1}$)	0.0136	PPDB 2012

6.3 Classification and labelling

a) Harmonised Classification according to GHS

-

b) Proposed classification

211. EU biocides CAR 2011 (according to Regulation (EC) No 1272/200):

Category	Hazard-Phrase
STOT RE2	H373 – May cause damage to organs (liver, kidney)
	H362 –May cause harm to breast fed children
Aquatic acute 1 (M=100)	H400 - Very toxic to aquatic life
Aquatic chronic 1 (M=1000)	H410 – Very toxic to a aquatic life with long lasting effects

212. This classification proposal is actually in discussion within the ECHA/RAC process and especially the human toxicology classification proposals are challenged.

c) Self classification

213. ECHA CLP inventory

Category	Hazard-Phrase
Aquatic acute 1	H400 - Very toxic to aquatic life
Aquatic chronic 1 or 2	H410 – Very toxic to a aquatic life with long lasting effects or H411

6.8 Environmental fate

a) Abiotic degradation

[11] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

-

b) Hydrolysis

214. AR 2007 states that etofenprox is hydrolytically stable under relevant environmental conditions.

c) Phototransformation/photolysis

215. AR 2007 reported for photo-chemically degradation a DT50 of 4.7 days for buffer solution and 7.8 days for pond water. Etofenprox degrades in aqueous solution predominantly to α-CO (2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate). This finding is in line with DAR 2005. Etofenprox also degrades in a soil photolysis study.

d) Biodegradation

216. DAR 2005: The comprehensive database demonstrates that etofenprox is rapidly and completely degraded in soil without giving rise to significant or persistent degradation products. AR 2007 confirms that etofenprox is of short persistence in the environment (cf. Table 3) and potential effects of exposure of fish and aquatic invertebrates are the main areas of concern.

Table 3: Biotic degradation of etofenprox and major metabolite

Study type	Results	Reference	Remarks
DT_{50} soil lab (days):	7-25 (20°C, aerobic): geometric mean: 12 (n=4)	AR 2007	-
DT_{50} water (days) from water/sediment study:	Etofenprox: 2.1-10.5 (n=2)		Etofenprox partitioned fast into the sediment (after 0d 63-70%)
DT_{50} sediment (days) from water/sediment study:	Etofenprox: 18-32 4´-OH: 26-56 (n=2)		4´-OH: 2-(4-ethoxyphenyl)-2-methylpropyl 3-(4-hydroxy) phenoxybenzyl ether
DT_{50} water sediment/whole system (days):	Etofenprox: 6.5-20 (n=2) 4´-OH: 22-30		-

e) Potential for long-range environmental transport

217. AR 2007: The photo-chemical degradation of etofenprox in air has been estimated to be very fast. The calculated DT50 is 2.07 hours. In addition etofenprox has a moderate persistence in the environment; therefore no multimedia fate modelling was performed.

f) Bioaccumulation

218. Etofenprox has a log Kow of 6.9 indicating a bioaccumulation potential. The experimental derived BCF is 3,951 in whole fish according to AR 2007. In edibles a value of 1,554 and in non-edibles a BCF of 7,213 was recorded. Also DAR 2005 indicates that etofenprox has a potential for bioaccumulation according to the results of the same bluegill sunfish study, but states reversible accumulation with depuration factors of 9 to16 days.

219. No other studies and/or information on terrestrial bioaccumulation are available.

g) PB-score

220. Etofenprox has a P-score of 0.7 and a B-score of 0.5 resulting in an overall B-score of 1.5.

6.5 Human health hazard assessment

a) Acute toxicity

221. EU biocides CAR 2011: The LD50 values for all routes are above the limits requiring classification, the substance is not irritant and not skin sensitising with the M&K test.

b) Mutagenicity and carcinogenicity

222. EU biocides CAR 2011: The substance did not show genotoxic potential in any *in vitro* and *in vivo* assays employed (Ames-Test, in vitro cytogenicity test with human lymphocytes, in vitro gene mutation test V79 cells, in vitro UDS, in vivo micronucleus test). In the 2 year rat study thyroid follicular cell adenoma were observed but the available MOA data support the assumption of a threshold and low relevance for humans. Some renal tumor findings appeared in the carcinogenic

mouse study but the weight of evidence analysis including statistical considerations it was concluded that there was no evidence for carcinogenic potential in the mouse.

223. US EPA summary document 2007: The Committee classified etofenprox as "Not likely to be carcinogenic to humans at doses that do not alter thyroid homeostasis."

c) Toxicity for reproduction

224. EU biocides CAR 2011: Several developmental and reproductive toxicity studies were summarized. Adverse effects on the offspring in the absence of parental toxicity were observed but on the basis of a total weight of evidence analysis it was concluded that there is no concern for specific reproductive toxicity requiring classification. However since haemorrhage effects were observed in weanlings and the kinetic data support high milk excretion rates a label for H362 – may cause harm to breast fed babies is proposed. The C&L proposal is actually challenged in the ECHA / RAC process.

d) Neurotoxicity

225. EU biocides CAR 2011: No data are available for delayed neurotoxicity since the substance has no structural similarities known or implicated in producing this type of effect. No neurotoxic effects were observed in the rat studies for acute neurotoxicity or in the 13-week neurotoxicity rat study at the highest doses tested, that were 2000 and 604 mg/kg bw, respectively. Within the developmental neurotoxicity study some minor functional neurological effects appeared in the developing rat with NOAELs that were the same as the overall parental NOAELs which indicated that the developing animal was not more susceptible that the parental animals.

226. Etofenprox is structurally a pyrethroid-like substance but the typical neurotoxic type I (C syndrome) or II (CS syndrome) effects were not observed.

e) Immunotoxicity

227. -

f) Endocrine disruption

228. Etofenprox is listed in the EU database for endocrine disrupters 2012 within category 3b, which means that insufficient data are available for an evaluation of respective effects.

g) Mode of action

229. US EPA summary document 2007: Etofenprox is a synthetic pyrethroid-like substance. It differs in structure from pyrethroids in that it lacks a carbonyl group. Etofenprox contains an ether moiety whereas pyrethroids contain ester moieties. Its mode of action against insects is very similar to that of pyrethroids, and its main action site is the neuronal axon; however, its toxicity in test animals is different from that of a pyrethroid.

h) Acceptable exposure levels

230. EU biocides CAR 2011: The systemic long term limit dose (AEL) of 0.037 mg/kg bw day was proposed on the basis of a 2 year rat feeding study and application of an assessment factor of 100 to the NOAEL. The liver was the respective critical target organ.

231. EFSA review report 2009: An external long term limit dose (ADI) of 0.03 mg/kg bw day is proposed.

232. US EPA summary document 2007: An external long term limit dose (RfD) of 0.037 is proposed on the basis of the same study as the EU biocides draft CAR 2011 and the application of an assessment factor of 100. The LOAEL of this critical study is at 25.5 mg/kg/day and is based on increased thyroid weights. Related to increased liver weights and histopathological changes in liver and thyroid that occurred at the higher dose.

233. WHO 2007: An external long term limit dose (ADI) of 0-0.03 mg/kg bw/day was allocated by the JMPR, based on a long term study in mice and a 100 fold safety factor.

6.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

234. AR 2007: Etofenprox is highly toxic to fish, daphnids and chironomids in standard laboratory aquatic tests and less toxic to algae. The metabolite α-CO is less acutely toxic to fish, daphnids or algae than the active ingredient itself (cf. Table 4). The metabolite α-CO is less acutely toxic to fish, daphnids or algae than the active ingredient itself. The metabolite 4'-OH shows lower toxicity to chironomids than etofenprox. DAR 2005 and US EPA summary document 2007 confirm high toxicity

to aquatic organisms.

Table 4: Toxicity reference values for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity (mg/l)
Fish – Test substance: etofenprox			
Oncorhynchus mykiss	96 h, flow-through	Mortality, LC_{50}	0.0027
Brachydanio rerio	40 d, flow-through	Mortality and development, NOEC	0.025
Fish – Test substance: metabolite α-CO			
Oncorhynchus mykiss	96 h, flow-through	Mortality, LC_{50}	> 0.048
Invertebrates – Test substance: etofenprox			
Daphnia magna	48 h, static renewal	Mortality, EC_{50}	0.0012
Daphnia magna	21 d, semi-static	Reproduction, NOEC	0.000054
Invertebrates – Test substance: metabolite α-CO			
Daphnia magna	48 h, static	Mortality, EC_{50}	> 0.044
Algae – Test substance: etofenprox			
Pseudokirchneriella subcapitata	72 h, static	Biomass, E_bC_{50}	>0.05625
Pseudokirchneriella subcapitata	72 h, static	Biomass, NOEC	0.05625
Algae – Test substance: metabolite α-CO			
Pseudokirchneriella subcapitata	96 h, static	Biomass, E_bC_{50}	>0.053
Sediment dwelling organisms – Test substance: etofenprox			
Chironomus riparius	10 d, static water-sediment system	Mortality, EC_{50}	>0.0209
Chironomus riparius	25 d, static water-sediment system	Emergence, Development , NOEC	0.0038
Sediment dwelling organisms – Test substance: metabolite 4'-OH			
Chironomus riparius	48 h, static	Mortality, LC_{50}	0.0502
Microorganisms – Test substance: etofenprox			
Activated sludge	3 h, static	Respiration rate, NOEC	≥100 mg/l or ≥water solubility

b) Terrestrial compartment

235. US EPA summary document 2007: Etofenprox is practically acute non-toxic to mallard ducks. Two avian subacute dietary toxicity tests also show that etofenprox is practically non-toxic to avian test species (cf. toxicity reference values in Table 5).

Table 5: Toxicity reference values (bw: body weight)

Exposure scenario	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Acute toxicity	birds	mallard duck	LD_{50}	> 2000 mg/kg bw	AR 2007
Dietary toxicity	birds	Mallard duck, bobwhite quail	LC_{50}	LC_{50} > 5000 mg as/kg diet	

Exposure scenario	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Reproductive toxicity	birds	bobwhite quail	NOEL	1000 mg/kg diet	
Acute toxicity	earth-worms	*Eisenia foetida*	LC_{50}	>47.2 mg/kg dry soil (measured)	

c) Toxicity to pollinators

236. DAR 2005 states that the 24-hour acute oral and contact LD_{50}values of etofenprox technical were 0.27 and 0.13 µg a.i./bee, respectively.

6.7 Other information

237. The toxicological information provided in the DAR 2005 is in agreement with the EU biocides CAR 2011. However no classification proposal is presented.

238. The toxicological information provided in the US EPA summary document 2007 is in agreement with the EU biocides draft CAR 2011. However no classification proposal is presented with regard to STOT RE or risk for breast fed babies.

239. The summary provided above is in agreement with the toxicological information provided in the PPDB database and in the PAN pesticides database with the exception that both of these databases indicate that reproductive toxicity results are unclear or positive, respectively and the latter database presents the US EPA conclusion that at high doses etofenprox is likely to be carcinogenic.

6.8 References

AR (2007) Assessment Report, Etofenprox, Product-type 8 (Wood preservatives), September 2007, available at http://ec.europa.eu/environment/biocides/annexi_and_ia.htm, 2012-03-26

DAR (2005) Draft Assessment Report Etofenprox, June 2005 http://dar.efsa.europa.eu/dar-web/provision, 2012-03-26

EFSA review report 2009, Review report for the active substance etofenprox, 22 October 2009 http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection, 2012-03-26

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

EU biocides draft CAR 2011 Etofenprox Product-type PT 18 (Insecticide),

http://ec.europa.eu/environment/biocides/evaluation_reports.htm, 2012-04-16

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/ 2012-04-18

US EPA summary report (2007) Summary Document Registration Review: Initial Docket, Case Number 7407, EPA-HQ-OPP-2007-0804, August 2007 http://www.epa.gov/pesticides/chemicalsearch

WHO (2007) WHO SPECIFICATIONS AND EVALUATIONS FOR PUBLIC HEALTH PESTICIDES ETOFENPROX, http://www.who.int/whopes/quality/en/Etofenprox_eval_WHO_july_2007.pdf, 2012-04-16

7. Fenitrothion

7.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

240. Hydrolysis is of minor importance for fenitrothion elimination in the environment (pH dependant DT50 values of 100-200 days). Photochemical half-lives in water of 3 to 4 days indicate there may be some potential for photolysis to contribute towards degradation of free fenitrothion in the aquatic environment. In soil the active substance is rapid degraded with DT50 values of 2 days. However also longer DT50 values (up to 48 days) are reported. In water/sediment systems fenitrothion and its residues are expected to degrade with short DT values of <10 days. Therefore it can be concluded that fenitrothion does not meet Annex D criterion 1 (b) (i).

b) Bioaccumulation

241. Fenitrothion has a log Kow value <5. Experimental BCFs in the range of 20 to 450 for a number of different aquatic species were reported. Depuration in fish is considered to be fast. Based on these findings fenitrothion does not meet the criterion 1 (c) (ii) of Annex D.

c) Long-range environmental transport

242. The half-life in air was calculated as <6 hours indicating that fenitrothion is not expected to persist in air or pose a risk of long-range environmental transport in air. Therefore it is unlikely that fenitrothion fulfils the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

243. Fenitrothion shows high toxicity to aquatic organisms that qualify for EU-GHS classification acute and chronic category 1 suggesting long lasting very toxic effects to aquatic life. Fenitrothion is considered highly toxic to honeybees and earthworms. Fenitrothion is very toxic to birds. Chronic effects in avian reproductive testing were observed. Based on its high aquatic toxicity and toxicity to terrestrial species (e.g. birds) as well as toxicity to human health (see below) Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

244. Fenitrothion is of low acute systemic toxicity qualifying for GHS category 4. In the EU GHS system it is actually not classified for skin sensitization though data are available that support respective classification.

245. Fenitrothion is not classified for carcinogenicity or mutagenicity by EU-GHS and also the latest US EPA and IPCS evaluation support this conclusion. Sufficient data are available.

246. Fenitrothion is also not classified for reproductive toxicity. No immunotoxicity is reported.

247. However Fenitrothion is listed in the EU endocrine disrupter database within category 1 which means it shows evidence of endocrine disruption activity in at least one species using intact animals.

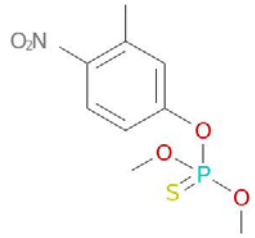
248. No delayed neurotoxicity was observed in a respective study. However representing an organophosphorous compound the critical effect is cholinesterase inhibition. Proposed long term limit values range between 0.0013 mg/kg bw day (US EPA) and 0.005 mg/kg bw day (DAR).

7.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Fenitrothion
IUPAC name:	O,O-dimethyl O-4-nitro-m-tolyl phosphorothioate
CAS number:	122-14-5
Molecular weight:	277.24

Chemical structure:	

b) Chemical group

Organophosphate

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	5.40E^{-05} mmHg	20°C, EXP
Water solubility	14 mg/L at 30°C	US EPA 2009
Partition coefficient n-octanol/water (log value)	2.69 3.43	US EPA 2009
Partition coefficient air/water (log value)	-4.42	EPI Suite v 4.1 (KOAWIN v. 1.10)
Partition coefficient air/octanol (log value)	7.72	EPI Suite v 4.1 (KOAWIN v. 1.10)
Henry´s Law Constant	9.30E^{-07} atm-m^3/mole	25°C, EST

7.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008: **Category**	**Hazard-Phrase**
Acute Tox. 4	H302- Harmful if swallowed
Aquatic Acute 1	H400- Very toxic to aquatic life
Aquatic Chronic 1	H410- Very toxic to aquatic life with long lasting effects

7.4 Environmental fate

249. According to DAR 2005 the following major metabolites (>10% of applied) were identified:

250. In soil: NMC (3-methyl-4-nitrophenol, in surface water: A-NMC (*O*-acetyl-3-methyl-4-nitrophenol), AM-FNT (*O*-(4-amino-3-methylphenyl) *O*,*O*-dimethyl phosphorothioate) and DM-AM-FNT (*O*-(4-amino-3-methylphenyl) *O*-hydrogen *O*-methyl phosphorothioate) and in sediment: NMC.

251. US EPA 2009: Fenitrothion has the potential for formation of the toxic degradation products through an oxidative desulfonation reaction. Two oxon degradation products were identified in several of the environmental fate studies, fenitrooxon and desmethyl fenitrooxon. Based upon applied radioactivity the two oxons - fenitrooxon (<4.3% applied) and desmethyl fenitrooxon (<4.3% applied) are minor degradation products.

a) Abiotic degradation

-

b) Hydrolysis

252. DAR 2005: Fenitrothion was only slowly hydrolysed in buffer solutions at pH 5, 7 and 9 at 25°C. Mean DT50 values were extrapolated well beyond the end of the study as 195.5, 183 and 100.5 days, respectively. Therefore, at environmentally relevant pH and temperature, it is unlikely that hydrolysis will contribute significantly to the degradation of fenitrothion in water.

c) Phototransformation/photolysis

253. DAR 2005 states a half-life in water of 3.3-3.6 days for photolysis. The one major degradate CA-FNT, which was not found in the dark control, declined to not detectable levels by the study end. These results indicate there may be some potential for photolysis to contribute towards degradation of free fenitrothion in the aquatic environment, perhaps more in Southern than Northern Europe.

d) Biodegradation

254. DAR 2005: Aerobic degradation of fenitrothion in soil under laboratory conditions is considered to be rapid, with DT50 values of around 2 days in 5 soils at 20-25°C. Only one major soil metabolite was formed under these conditions, NMC, which also degraded rapidly with DT50 values of up to 3.3 days. Under anaerobic laboratory conditions, fenitrothion also degraded rapidly, with a first order DT50 of 0.8 days at 25°C (in sandy loam).

255. US EPA 2009 reported <1% (of applied) fenitrooxon and desmethyl fenitrooxon in the soil metabolism study. However somewhat longer aerobic metabolism half-lives from other reports are cited (DT50 24 to 48 days from three or more studies).

256. In water/sediment systems DAR 2005 states that fenitrothion declined rapidly in the total system and in both the water and sediment phases with first order DT50 values of <2 days. In the water phase and total system, single phase and 2-phase exponential models respectively, were used with an accumulation phase, to estimate degradation rates for the major metabolites. The resulting DT50 values were <10 days.

e) Potential for long-range environmental transport

257. DAR 2005: The half-life in air was calculated as <6 hours indicating that fenitrothion is not expected to persist in air or pose a risk of long-range environmental transport in air. Based on this finding no multimedia fate modeling was performed.

f) Bioaccumulation

258. US EPA 2009 reports log Kow values of 2.69 and 3.43 indicating a low potential for bioaccumulation. DAR 2005: The BCF was 30 at 0.05 mg/L in a fish bioconcentration study. The depuration of fenitrothion was rapid (90% elimination in whole fish in less than 7 days). IPCS 1992 states BCFs for fenitrothion with continuing exposure to range from 20 to 450 for a number of different aquatic species.

g) PB-score

-

7.5 Human health hazard assessment

a) Acute toxicity

259. DAR 2005: Acute systemic toxicity and skin/eye irritation results are in agreement with the actual EU-CLP entry with the exception that the dermal LD50 would qualify the substance in addition for acute dermal category 4 (H312) and the results from the Magnusson and Kligman maximisation test for skin sensitization may be considered sufficient for respective classification.

260. US EPA Registration review 2009: Fenitrothion is acutely toxic (Toxicity Category II) via the oral, dermal, and inhalation routes of exposure, causes minor eye and dermal irritation, and is not a dermal sensitizer.

261. IPCS 1992: Fenitrothion is an insecticide of moderate toxicity with oral LD50 values in rats and mice ranging from 330 to 1416 mg/kg body weight. Acute dermal toxicity in rodents ranged from 890 mg/kg body weight to more than 2500 mg/kg body weight. Fenitrothion is only minimally irritating to the eyes and is nonirritating to the skin. The chemical showed dermal sensitizing potential in one of two studies on guinea-pigs.

b) Mutagenicity and carcinogenicity

262. DAR 2005: On the basis of bacterial and mammalian in vitro tests and in vivo and somatic germ cells fenitrothion is not considered as genotoxic. On the basis of studies in rats and mice it is also not considered as carcinogenic.

263. US EPA Registration review 2009: Fenitrothion is not classified as a carcinogen. No evidence of carcinogenicity was seen in the mouse and rat carcinogenicity studies. There is no concern for mutagenicity.

264. IPCS 1992: No carcinogenic effects were found in any of the long-term studies reported. Fenitrothion was not mutagenic in *in vitro* and *in vivo* studies.

c) Toxicity for reproduction

265. DAR 2005: Effects on pup body weight, viability and lactation in rats and incidence of abortions was observed only at maternally toxic doses and not considered as specific effect.

266. IPCS 1992: Fenitrothion has not been found to be teratogenic at doses of up to 30 mg/kg body weight in rabbits and up to 25 mg/kg body weight in rats. Dose levels exceeding 8 mg/kg body weight were maternally toxic.

267. Developing young rats exhibited behavioral deficits post-natally following *in utero* exposure. A NOEL for this effect was established at 5 mg/kg body weight per day.

268. Multigeneration reproduction studies on rats did not indicate any morphological effects. A NOAEL of 120 mg/kg diet, based on reproductive parameters, was demonstrated in these studies.

d) Neurotoxicity

269. DAR 2005: There was no evidence of delayed neurotoxicity in hens after acute or subacute exposure. In acute neurotoxicity study in rats tremors, reduced body temperature and motor activity were observed at ≥ 50 mg/kg bw in both sexes but there were no findings in males at 12.5 mg/kg bw and no neuropathological changes in both sexes. In a sub-chronic neurotoxicity study in rats with neuropathological assessments a NOAEL of 20 ppm (1.32 mg/kg bw/day)was identified based on impaired body weight gain and reduction in erythrocyte and brain cholinesterase at 60 ppm (3.99 mg/kg bw/day). Inhibition of cholinesterase activity was the critical effect for long and medium term limit dose derivation.

270. IPCS 1992: Delayed neurotoxicity has not been reported as a result of exposure to fenitrothion. Fenitrothion has been tested in short-term studies on rats, dogs, guinea-pigs, and rabbits and in long-term carcinogenicity studies on rats and mice. In short-term studies on rats and dogs ,the no-observed-adverse-effect levels (NOAELs), based on brain-ChE activity, were, respectively, 10 mg/kg diet and 50 mg/kg diet.

271. Long-term studies on rats and mice indicated a NOAEL (based on brain ChE activity) of 10 mg/kg diet.

e) Immunotoxicity

272. -

f) Endocrine disruption

273. EU Endocrine Disruption Database (2012): Fenitrothion was listed as category 1 suspected endocrine disrupter, i.e. produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals.

g) Mode of action

274. US EPA Registration review 2009: As with other OPs, the principal toxic effects induced by fenitrothion are related to its cholinesterase-inhibiting activity.

275. IPCS 1992: Fenitrothion is an organophosphate and causes cholinesterase activity depression in plasma, red blood cells, and brain and liver tissues. It is metabolized to fenitrooxon, which is more acutely toxic. Its toxicity may be potentiated by some other organophosphate compounds.

h) Acceptable exposure levels

276. DAR 2005: The following long and medium term limit dose values were derived on the basis of acetyl cholinesterase inhibition as critical effect and application of an assessment factor of 100: ADI = 0.005 mg/kg bw day; ARfD = 0.013 mg/kg bw day

277. US EPA Reregistration Review 2009: Population adjusted dose (PAD) acute, dietary = 0.13 mg/kg bw day; PAD chronic, dietary = 0.0013 mg/kg bw day. For both PADs an assessment factor of 100 was used. The critical effects were tremors and impaired motor coordination for the acute exposure value and Plasma ChE inhibition and histophathology changes of the lymph nodes for the chronic exposure value.

278. International limit values for worker protection (GESTIS-Database, 2012): The limit values for 8 hours are 1 mg/m3 in Austria and 0.02 mg/m3 in Poland, a short term limit value of 0.1 mg/m3 is reported for Poland.

7.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

279. IPCS 1992: Fenitrothion is highly toxic for aquatic invertebrates in both freshwater (cf. Table 3) and seawater with LC50 values of a few µg/litre for most species tested. Field observations and studies on experimental ponds have shown effects on populations of invertebrates. However, most of

the changes observed were temporary, even at concentrations considerably higher than those likely to occur after recommended usage. Fish are less sensitive to fenitrothion than invertebrates. The most sensitive life stage is the early larva. Field studies after application of fenitrothion to forests showed no effects on wild populations of fish or on the survival of caged test fish with measured water concentrations of fenitrothion of up to 0.019 mg/litre. Repeated application of fenitrothion to forests had no effect on fish populations.

280. US EPA 2009 identified the most conservative toxicological endpoint for aquatic species is 1.5 ppb from an acute toxicity study with brown shrimp, a marine/estuarine species.

281. Concerning toxicity of identified metabolites (cf. Table 3) DAR 2005 reports a 48 h EC50 for fenitrothion of 8.6 µg a.s./l and the 48 h EC50 for AM-FNT (the precursor to DM-AM-FNT) was 5.88 mg/l. AM-FNT was therefore three orders of magnitude less toxic than fenitrothion.

Table 3: Toxicity reference values for aquatic species, most sensitive species of each group (Table from DAR 2005) (a.s....active substance)

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests				
Oncorhynchus mykiss	Technical fenitrothion	Acute	LC50 (96h)	1.3 mg a.s./L
Daphnia magna	Technical fenitrothion	Acute	EC50 (48h)	0.0086 mg a.s./L
Selenastrum capricornutum	Technical fenitrothion	Acute	EbC50 (72h)	1.3 mg a.s./L
Oncorhyncus mykiss	Technical fenitrothion	Chronic	NOEC (96 days)	0.088 mg a.s./L
Daphnia magna	Technical fenitrothion	Chronic	NOEC (21 days)	0.087 µg a.s./L
Daphnia magna	AM-FNT	Acute	EC50 (48h)	5.8 mg metabolite/l
Daphnia magna	NMC	Acute	EC50 (48h)	18 mg metabolite/L
Microcosm or mesocosm tests				
Microcosm study conducted with Daphnia magna – NOEC = 0.17 µg a.s./l.				

b) Terrestrial compartment

282. NRA (1999): Reports from acute, dietary and reproductive testing in quail and mallards are available. Laboratory and field information for a large number of species has been obtained from the scientific literature. Fenitrothion is slightly to very highly toxic to birds by acute oral and dietary routes. Chronic effects in avian reproductive testing were observed. Available field data from Scotland, Canada and Senegal indicate that a proportion of the bird population will receive a significant exposure to fenitrothion in sprayed areas, and that some birds will die and others suffer sub-lethal effects. US EPA 2009 indicated in bobwhite quail an acute oral LD50 of 23 mg/kg bw, for subactue dietary an LC50 of 157 ppm and a chronic NOAEC/LOAEC of 13/17 ppm based on reduced egg production (most sensitive species).

283. Fenitrothion is considered highly toxic to honeybees and earthworms.

c) Toxicity to pollinators

284. DAR 2005 states that the acute oral and contact LD50 values of fenitrothion were 0.20 and 0.16 µg a.i./bee, respectively.

7.7 Other Information

285. Toxicological information present in the PAN –pesticides database and in the footprint database are consistent with the CMR, endocrine and neurotoxicity information summarized above.

7.8 References

DAR (2005) Draft Assessment Report Fenithrothion, January 2005 http://dar.efsa.europa.eu/dar-web/provision, 2012-03-26

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

GESTIS-Database (2012) http://gestis-

en.itrust.de/nxt/gateway.dll/gestis_en/000000.xml?f=templates$fn=default.htm$3.0, 2012-04-16

NRA (1999) The NRA review of fenitrothion, Interim Report, June 1999, http://www.apvma.gov.au/products/review/docs/fenitrothion_summary.pdf, 2012-04-16

IPCS (1992) INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY, ENVIRONMENTAL HEALTH RITERIA 133, FENITROTHION, WHO Geneva, 1992 http://www.inchem.org/documents/ehc/ehc/ehc133.htm 2012-04-20

US EPA (2009) Registration Review – Problem formulation for the Ecological Risk Assessment of Fenitrothion February 2009 http://www.epa.gov/pesticides/chemicalsearch 2012-04-16

US EPA Reregistration Review (2009) US EPA Fenitrothion Summary Registration review: initial docket March 2009, Docket Number: EPA-HQ-OPP-2009-0172 http://www.epa.gov/pesticides/chemicalsearch, 2012-04-16

8.Lambda-cyhalothrin

8.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

286. Based on a combination of data for cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin these active substances are moderately persistent in the environment and degrade slowly through a combination of biotic and abiotic mechanisms. (Reported findings for cyhalothrin suggest no photolysis). Lambda-cyhalothrin is stable to aqueous hydrolysis below pH 7; however also fast hydrolytic degradation at low pH values was reported. Photolysis may contribute to the removal of lambda-cyhalothrin in water. Under both aerobic and anaerobic soil metabolism conditions, cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin biodegrade at moderate rates, with comparable half-lives of several weeks. In aquatic metabolism conditions, lambda-cyhalothrin and gamma-cyhalothrin may biodegrade at moderate rates under aerobic condition, with half-lives in the order of about 21-53 days (aerobic, both chemicals), but more slowly under anaerobic condition, with a half-life of 142 days (lambda-cyhalothrin only). The modelled P-score is 0.92 indicating high persistency. However the P-score is related to ultimate mineralization and not to a DT50 value. Therefore it can be concluded that based on the presented experimental information cyhalothrin, lambda- cyhalothrin and gamma-cyhalothrin do not meet the persistence criterion of Annex D 1 (b) (i). However there are indications that under anaerobic conditions in aquatic environment half-lives are prolonged and persistency under low temperatures cannot be excluded.

b) Bioaccumulation

287. The log Kow of >5 and the experimental derived BCF values of 1660 -2240 indicate high potential of bioaccumulation. Also higher reported values for cyhalothrin, bioaccumulation ~4600x, based on a study performed in fish are available. The modelled B-scores are 0.581 suggesting bioaccumulation potential as well. Based on the reported BCF values in fish cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin do not meet the Annex D 1 (c) (i) criterion. However log Kow>5 for all three compounds are reported and the highest BCF of 4600 is close to the Annex D threshold of 5000.

c) Long-range environmental transport

288. The estimated reported DT50 values in air for lamda cyhalothrin are 4 and 12 hours. These values can be considered for screening for cyhalothrin and gamma cyhalothrin as well. Therefore it is unlikely that these active substances will meet the Annex 1 (c) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

289. Lambda-cyhalothrin and gamma-cyhalothrin are highly toxic to aquatic species and lambda-cyhalothrin is classified according to EU-GHS as aquatic acute and chronic category 1. For terrestrial vertebrates lambda-cyhalothrin is highly toxic to mammals. No toxic effects to birds after acute exposure, but higher toxicity for reproductive effects were observed. Lambda-cyhalothrin is considered as non-toxic to earthworms. Based on the high toxicity to aquatic organisms and toxicity to human health (see below) it is concluded that lambda-cyhalothrin, cyhalothrin and gamma-cyhalothrin meet the Annex D criterion 1 (e) (ii).

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

290. Read across between cyhalothrin and lambda-cyhalothrin is considered justified based on the similarity of effects observed in subchronic lambda-cyhalothrin and cyhalothrin studies as well as comparative toxicokinetic and metabolism studies. In terms of acute oral toxicity gamma-cyhalothrin is estimated as 2 times more toxic compared to lambda cyhalothrin and the latter 3 times more toxic compared to cyhalothrin. However long term limit values were derived from lambda-cyhalothrin so that there is no critical impact on risk assessment for long term exposure and for short term exposure the point of departure for gamma-cyhalothrin should be reduced by a factor of 2. Based on the US EPA summary the other available data support that toxicities of lambda-cyhalothrin and gamma-cyhalothrin are comparable which allows combining the respective databases.

291. Lambda-cyhalothrin is classified for acute toxicity category 4 for the dermal route, category 3 for the oral route and category 2 for the respiratory route. It is not irritating and not sensitizing within a guinea pig maximisation test (M&K method). For cyhalothrin and gamma-cyhalothrin no harmonised EU GHS classification is available.

292. Cyhalothrin did not induce genotoxic effects in vitro or in vivo and there was no evidence of carcinogenicity in rats. Some equivocal carcinogenic effects were observed in a mouse study. However the European evaluations did not consider these sufficient for classification. US EPA concluded from the studies with cyhalothrin that cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin as "not likely to be carcinogenic to humans"

293. With cyhalothrin no teratogenic or reproductive toxicity effects were observed within developmental rat and rabbit studies or a 3 generation rat study. Nevertheless lambda-cyhalothrin is listed within the EU endocrine disrupter database within category 1, which means that it is persistent in the environment or produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals.

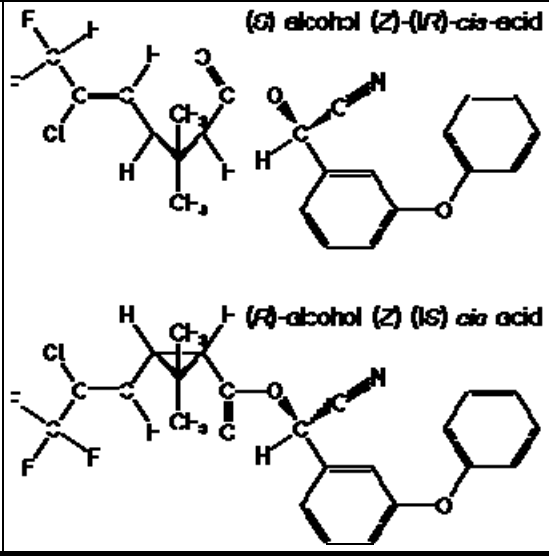
294. Representing a type II pyrethroid the critical effect is neurotoxicity. No delayed neurotoxicity study was required. Within a developmental neurotoxicity study with lambda-cyhalothrin adverse effects were only observed at parentally toxic doses. The clinical neurotoxicity effects accompanied with gastrointestinal effects and reduced food intake in the 90 day and the 1-year dog studies with lambda-cyhalothrin were the basis for the derivation of a systemic long term limit value of 0.0025 mg/kg bw day. An assessment factor of 100 and an oral absorption rate of 50% was taken into consideration. The value was considered reliable also for cyhalothrin and gamma-cyhalothrin.

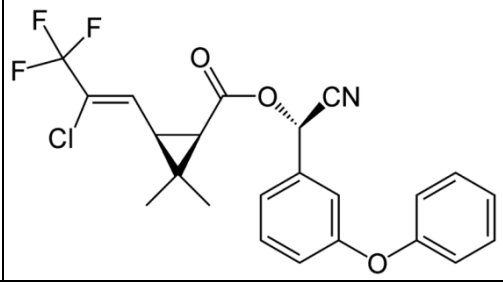
8.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

295. Lambda-cyhalothrin is the pure cis 1R-alphaS and cis 1S-alphaR enantiomeric pair whereas cyhalothrin is a 50/50 mixture of lambda-cyhalothrin and the cis 1R-alphaR and cis 1S-alphaS enantiomeric pair.

Table 1: Substance identity

Common name:	Cyhalothrin
IUPAC name:	(RS)-α-cyano-3-phenoxybenzyl (1RS,3RS)-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate
CAS number:	68085-85-8
Molecular weight:	449.85
Chemical structure:	
Common name:	Lambda-cyhalothrin
IUPAC name:	(*R*)-a-cyano-3-phenoxybenzyl (1*S*)-cis-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate and (*S*)-a-cyano-3-phenoxybenzyl (1*R*)-cis-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate
CAS number:	91465-08-6
Molecular weight and chemical structure:	See above
Common name:	Gamma-cyhalothrin

IUPAC name:	(*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate
CAS number:	76703-62-3
Molecular weight:	449.85 g.mol^{-1}
Chemical structure:	

b) Chemical group

-

c) Physico-chemical properties

Table 3: Overview of selected physico-chemical properties

Property	Cyhalothrin	Lamda-cyhalothrin	Gamma-cyhalothrin	Reference
Vapour pressure at 25°C (mPa)	1.00 x 10^{-09}	0.0002	3.45 x 10^{-04}	PPDB 2012
Water solubility at 20°C (mg/l)	0.004	0.005	0.000002	PPDB 2012
Partition coefficient n-octanol/water (log value, pH 7, 20°C)	6.8	6.9	4.96 (range 4.96-5.65)	PPDB 2012
Partition coefficient air/water (log value)	-4.22	-4.22	-4.21	EPI Suite v 4.0[12]
Partition coefficient air/octanol (log value)	11.02	11.12	9.97	EPI Suite v 4.0
Henry´s Law Constant at 25°C (Pa.m³.mol^{-1})	1.80 x 10^{-02}	2.00 x 10^{-02}	3.19 x 10^{-02} (Dimensionless)	PPDB 2012

8.3 Classification and labelling

a) Harmonised Classification according to GHS

296. No harmonised classification according to EU-GHS for cyhalothrin and gamma-cyhalothrin available.

297. Regulation (EC) No 1272/2008 – 1nd amendment 2009: Lambda cyhalothrin:

Category	Hazard-Phrase
Acute Tox. 2	H330 Fatal if inhaled.
Acute Tox. 3	H301 Toxic if swallowed.
Acute Tox. 4	H312 Harmful in contact with skin.
Aquatic Acute 1	H400 Very toxic to aquatic life.
Aquatic Chronic 1	H410 Very toxic to aquatic life with long lasting effects.

8.4 Environmental fate

a) Abiotic Degradation

-

[12] http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

b) Hydrolysis

298. Cyhalothrin: PPDB 2012: Hydrolysed slowly at pH 7 to pH 9, faster at pH 9

299. Lamda-cyhalothrin: PPDB 2012: Very Persistent: pH 5.2 and pH 6.9, DT_{50} ~7 days at pH 9. These findings are in line with the EFSA review report 2001. However WHO, 2006 reported half-live values according to the OECD 111 test method for lambda-cyhalothrin: pH4: 4.27 days at 20°C, pH 7: 5.03 days at 20°C, and pH 9: 3.36 days at 20°C suggesting fast hydrolytic degradation.

300. Gamma-cyhalothrin: PPDB 2012: Aqueous hydrolysis DT_{50}: 136 days at 20°C and pH 7 (persistent), stable at pH 5, 1.1 days at pH 9

c) Phototransformation/photolysis

301. Cyhalothrin: PPDB 2012: stable to phototransformation/photolysis

302. Lamda-cyhalothrin: EFSA review report 2001: Indicated DT_{50} in water 13 days (latitudes 40 and 50°N). Average quantum yield at 270-290 nm 0.092. Calculated DT_{50} values in European waters range from 5 days (summer) to 75 days (winter). However photolysis is considered to be negligible under field conditions.

d) Biodegradation

303. US EPA 2010 concluded that based on a combination of data for lambda-cyhalothrin and gamma-cyhalothrin, they are moderately persistent in the environment and degrade slowly through a combination of biotic and abiotic mechanisms. On soil, lambda-cyhalothrin is fairly stable (with very little degradation on the order of only ~13% in 35 days). Under both aerobic and anaerobic soil metabolism conditions, cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin biodegrade at moderate rates, with comparable half-lives of several weeks. Various aerobic soil studies are available with all three test substances. Lambda-cyhalothrin and gamma-cyhalothrin may biodegrade more slowly under anaerobic conditions with a half-life of 142 days (lambda-cyhalothrin only).

304. PPDB (2012) states that for cyhalothrin lab soil studies indicate a DT50 range of 32 to 82 days (geometric mean: 57 days, 20°C).

305. Degradation values for lambda-cyhalothrin are displayed in Table 3.

Table 3: Degradation estimates of lambda-cyhalothrin in soil, water and sediment

Degradation 50%	days	Reference	Comment
DT_{50} soil lab (20°)	56 (29 -100)	EFSA review report 2001	
DT_{50}soil field	23 (6-40)		Soils from Germany and US (n=10)
DT_{50} water sediment/water	< 1		Rapid dissipation from water: after 1 day 10-13% of applied
DT_{50} water sediment/whole system	7- 15 days		was present the water phase pH dependent

306. Degradation values for gamma-cyhalothrin are similar to lambda-cyhalothrin and range according to PPDB (2012) from a DT50 lab (20°C) of 42 days (geometric mean) to a DT50 typical of 50 days. The DT50 from the water phase only is given with 15 days, however no pH values is stated in PPDB (2012).

e) Potential for long-range environmental transport

307. According to EU biocides AR 2011 the estimated T1/2 in air of lambda-cyhalothrin is 0.51 days (12.2 hours) based on rate constant for gas-phase reaction with hydroxyl radicals 31.46 cm^3/molecule x sec and assuming a global (day and night) annual average OH-radical concentration of 0.5 x 10^6 molecules/cm^3. EFSA review report 2001 lists a DT50 value for photo-oxidative degradation of 4.1 hours.

308. This value can be considered for screening for cyhalothrin and gamma-cyhalothrin as well. The estimation program AOPWIN[13] do not considered specific isomeric forms.

f) Bioaccumulation

[13] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

309. Cyhalothrin: PPDB 2012: BCF: 1950 in whole fish assuming high bioaccumulation potential (this value is also recorded for the other two compounds). However a higher value was identified by US EPA 2010.

310. Lambda-cyhalothrin: EFSA review report 2001 BCF: 1660-2240 (whole fish). US EPA 2010 also lists BCF values from open literature in *Chironomus riparius* that range from 1300 to 3400.

311. US EPA 2010: Lambda-cyhalothrin and gamma-cyhalothrin are highly bioaccumulative (~4600x), based on a study performed with cyhalothrin in fish, and they depurate at moderately slow rates (~9 days). There is the potential for bioaccumulation and biomagnification.

g) PB-score

312. Lambda-cyhalothrin has a P-score of 0.919 and a B-score of 0.581 resulting in an overall B-score of 1.500. The same values were reported for cyhalothrin.

8.5 Human health hazard assessment

313. EU biocides CAR 2011: The human health effect assessment of lambda-cyhalothrin is based on data obtained for lambda-cyhalothrin or cyhalothrin. Lambda-cyhalothrin is the pure cis 1R-alphaS and cis 1S-alphaR enantiomeric pair whereas cyhalothrin is a 50/50 mixture of lambda-cyhalothrin and the R157836 (the cis 1R-alphaR and cis 1S-alphaS) enantiomeric pair. Read across between the two substances is considered justified based on the similarity between effects observed in the two 90 day studies performed in rats with identical dose levels of either lambda-cyhalothrin or cyhalothrin. Read across is further supported by a bridging study demonstrating that the absorption, tissue distribution, metabolism and excretion of lambda-cyhalothrin and cyhalothrin is quantitatively and qualitatively similar in rat. However lambda-cyhalothrin appears to be approximately three times more potent than cyhalothrin in both rats and mice when comparing the acute oral toxicity of lambda-cyhalothrin reported in this dossier to the acute oral toxicity of cyhalothrin reported in literature. Since all reference values used were derived from NOAELs obtained in studies performed with lambda-cyhalothrin, the difference in potency has no impact on the risk assessment of the representative formulations containing lambda-cyhalothrin.

314. US EPA summary document 2010: The relative toxicities of lambda-cyhalothrin and gamma-cyhalothrin are comparable, making it possible for the **Agency to combine** the toxicity databases for purpose of risk assessment. The database for gamma-cyhalothrin was supplemented by available data for lambda-cyhalothrin and vice versa because the toxicity profiles of lambda-cyhalothrin and gamma-cyhalothrin are expected to be similar to each other.

a) Acute toxicity

315. EU biocides CAR 2011: The acute toxicity data are in agreement with the actual EU GHS classification: category 4 for the dermal route, category 3 for the oral route and category 2 for the respiratory route. The substance was not sufficiently irritant to skin or eye to require respective classification. The substance was not sensitizing within a guinea pig maximisation test (M&K method).

316. EFSA review report 2001: The conclusions presented were in agreement with EU biocides CAR 2011.

317. US EPA summary document 2010: The acute toxicity profiles for the cyhalothrins were similar. Oral, dermal and inhalation routes of exposure resulted in toxicity category II. Only gamma-cyhalothrin was slightly more toxic (category I) for inhalation. Cyhalothrin and lambda-cyhalothrin were moderately irritating to the eye (category III). They were mildly irritating to the skin (category IV). Gamma-cyhalothrin appeared to be more irritating (category I and II, for eye and skin irritation, respectively). None of the cyhalthrins were dermal sensitizers.

318. WHO 2011: WHO/IPCS has evaluated lambda-cyhalothrin and classified it as ‘Moderately Hazardous’ (Class II), on the basis of acute oral toxicity data. The hazards and risks were summarised as follows: Harmful, irritating to eyes, skin and upper respiratory system.

b) Mutagenicity and carcinogenicity

319. EU biocides CAR 2011: Genotoxicity and carcinogenicity studies and were carried out with cyhalothrin. No genotoxic effects were observed in the standard in vitro test package, reinforced with an additional UDS test and in vivo mouse micronucleus test. There is also no evidence of carcinogenicity in rats. An increased incidence of mammary adenocarcinomas was observed in female mice (above incidence in concurrent and historical controls). However the results of the studies performed do not give sufficient evidence for classification of lambda cyhalothrin as a carcinogenic

substance.

320. EFSA review report lambda-cyhalothrin 2001: The conclusions presented were in agreement with EU biocides CAR 2011.

321. US EPA summary document 2010: The agency classified cyhalothrin, lambda-cyhalothrin and gamma-cyhalothrin as “not likely to be carcinogenic to humans” based on the lack of evidence of carcinogenicity in mice and rats. Carcinogenicity studies are not available for lambda- or gamma-cyhalothrin. However the general cyhalothrin carcinogenicity studies in rats and mice were considered to be sufficient for classification as “not likely to be carcinogenic to humans”. There is no evidence of mutagenicity for cyhalothrin, lambda-cyhalothrin or gamma-cyhalothrin.

c) Toxicity for reproduction

322. EU biocides CAR 2011: Reduced bodyweights with associated effects on mean litter weight were observed in a three generation rat study with cyhalothrin. It was concluded that there were no adverse effects on adult fertility or reproduction. The teratogenicity studies performed with cyhalothrin on rats and rabbits did not reveal any foetal effects.

323. EFSA review report 2001: The conclusions presented were in agreement with EU biocides CAR 2011.

d) Neurotoxicity

324. EU biocides CAR 2011: Clinical signs of neurotoxicity from lambda-cyhalothrin were reported in dogs and rats. Within the developmental neurotoxicity study no respective specific effects were observed with lambda-cyhalothrin. Cases of subjective facial sensation (also known as 'SFS' or paraesthesia) were reported to have occurred at all stages of *lambda*-cyhalothrin handling, from small-scale laboratory work to commercial synthesis and formulation operations. Subjective facial sensation is a collection of skin-associated symptoms, including itching, tingling, burning, cold or numbness due to skin contact with *lambda*-cyhalothrin. The face was most commonly affected. These symptoms can cause discomfort and may in some individuals last for up to 24 hours after exposure. Recovery was apparently complete and there was no evidence of lasting damage.

325. EFSA review report 2001: The conclusions presented were in agreement with EU biocides CAR 2011.

326. US EPA summary document 2010: The number of reported incidents involving lambda-cyhalothrin is relatively large. The majority of health effects involved dermal, neurological, gastrointestinal and respiratory symptoms. These symptoms were of low to moderate severity, however, two of the incidents resulted in death. Most of the cases occurred at home in a residual setting, although there were cases that occurred in occupational settings as well. This exposure occurred while the patients were applying or using the product either indoors or outdoors. Many incidents appeared to occur because the product was used improperly. A moderate number of low severity incidents involving gamma-cyhalothrin have been reported. In addition, the number of high severity incidents is low. Most of the cases occurred at home in a residential setting. Patients reported inhaling the product, or accidentally getting the product on their faces, hands, arms and/or legs. These exposures occurred while the patients were applying or using the products either indoors or outdoors.

327. WHO 2011: Ingestion could lead to neurological symptoms such as tremors and convulsions.

e) Immunotoxicity

328. US EPA summary document 2010: The agency anticipates requiring an immunotoxicity study (GLN 870.7800) in order to conduct a complete human health risk assessment for lambda-cyhalothrin and gamma-cyhalothrin.

f) Endocrine disruption

329. EU Endocrine Disruption Database (2012): Listed within category 1, which means that it is persistent in the environment or produced at high volumes with evidence of endocrine disruption activity in at least one species using intact animals.

330. EU biocides CAR 2011: As part of the evaluation of the application for the inclusion of lambda-cyhalothrin in Annex I of the Biocidal Products Directive (98/8/EC) toxicology and ecotoxicology data are assessed. It is concluded that there was no clear evidence of endocrine disruption effects from these studies. However, it should be noted that due to limitations in the test guidelines available at the time, the potential for endocrine effects may not have been fully investigated.

g) Mode of action

331. ATSDR 2003: The primary site of action for pyrethrins and pyrethroids is the sodium channel of nerve cells, Type II pyrethroids include a cyano group; their effects in rodents are usually characterized by pawing and burrowing behaviour, followed by profuse salivation, increased startle response, abnormal hindlimb movements, and coarse whole body tremor that progresses to sinuous writhing (choreoathetosis). Clonic seizures may be observed prior to death. Body temperature is not increased, but may decrease. The term CS-syndrome (from choreoathetosis and salivation) has been applied to Type II responses.

332. US EPA summary document 2010: As with the other pyrethroids, lambda- and gamma-cyhalothrin cause neurotoxicity in insects and mammals by the modulation of nerve axon sodium channels. Pyrethroids interfere with the ability of the nervous system to relay nerve transmissions, potentially resulting in tremors, conclusions, salivation and other clinical effects. Based on similar mammalian toxicity profiles for cyhalothrin technical, lambda-cyhalothrin and gamma-cyhalothrin, the toxicity databases were combined for purposes of risk assessment. Endpoints for risk assessment were based on neurological effects observed in lambda-cyhalothrin studies. However, the points of departure were reduced by a factor of 2 for acute dietary, dermal and inhalation scenarios because of the increased toxicity observed and/or presumed in rat gamma-cyhalothrin studies. There was no evidence of increased quantitative and qualitative susceptibility in rats or rabbits. The endpoints chosen for risk assessment were considered protective, and the degree of concern and residual uncertainties were low.

h) Acceptable exposure levels

333. EU biocides CAR 2011: A systemic long term limit value (AEL) of 0.0025 mg/kg bw/day was derived based on the NOAEL obtained in the one-year dog study, an oral absorption of 50% and an assessment factor of 100. The respective critical effects were neurological effects (unsteadiness, lack of muscular co-ordination), gastro-intestinal effects and reduced food intake. In the long term rat studies also neurological effects were observed as critical, but they were accompanied with hepatic changes including increased liver weight and reduced body weight.

334. EFSA review report 2001: The same systemic long term limit value (AOEL systemic) was derived on the same data and assessment factors. In addition an external long term limit value (ADI) of 0.05 mg/kg bw day was derived on the same data without consideration of the oral absorption rate

335. WHO 2011: The JMPR allocated an ADI of 0-0.02 mg/kg bodyweight for cyhalothrin, based on short term and chronic testing on rats, mice, rabbits, guinea pigs and dogs. The data were considered by the JMPR and WHO to be applicable to lambda-cyhalothrin.

8.6 Environmental hazard assessment

336. According to US EPA (2010) *lambda*-cyhalothrin and *gamma*-cyhalothrin has the following

337. Environmental Hazards statement: This pesticide is extremely toxic to fish and aquatic organisms and toxic to wildlife

a) Aquatic compartment (including sediment)

338. Toxicity data for aquatic species are for example available from EFSA review report 2001 and EU biocides AR 2011. Lambda-cyhalothrin is classified as very highly toxic to aquatic organisms based on data for aquatic vertebrates and invertebrates as well as for sediment dwelling organisms. Toxicity reference values for aquatic species are listed in Table 4. Toxicity values reported for cyhalothrin and gamma-cyhalothrin are within the same range (deviation factor max. of 10) suggesting high toxicity in chronic exposure conditions to invertebrates.

339. US EPA summary document 2010: Gamma-cyhalothrin is very highly toxic to fish and aquatic invertebrates. Chronic toxicity data for sensitive freshwater fish species as well as invertebrates are lacking, also no data on aquatic plants are available. There are concerns of increased toxic effects of gamma- and lambda-cyhalothrin together with piperonyl butoxide on nontarget species.

Table 4: Toxicity reference values for the aquatic compartment

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute 96 hour	Fish	LC_{50}	0.21 µg/l	EFSA review report 2001
Chronic, 21 days	Fish	NOEC	0.25 µg/l	
Acute 48 hour	Aquatic invertebrates	EC_{50}	0.36 µg/l	
Acute 96 hour	Neonate aquatic invertebrates	EC_{50}	0.016 µg/l	
Acute 96 hour	Neonate aquatic invertebrates	NOEC	0.006 µg/l	
Chronic, 21 days	Sediment dwelling organisms	NOEC	0.16µg/l	
Acute 96 hour	Algae	EC50	>0.3 mg/l	
Acute 96 hour	Aquatic crustaceae	LC_{50}	0. 00 3µg/l	PPDB 2012
Chronic, 21 days	Aquatic invertebrates	NOEC reproduction	0.00198 µg/l	EU biocides AR 2011
Chronic, 21 days	Sediment dwelling organisms	NOEC	0.0175µg/l	
Field study, 14 days	Various species	NOAEC	0.0175	

b) Terrestrial compartment

340. EFSA review report 2001 and EU biocides AR 2011: Lambda-cyhalothrin is toxic to vertebrates and highly toxic to bees and other arthropods. Chronic toxicity field studies with earthworms revealed a low NOEC of 29 µg/kg soil (ww). The chronic dietary intake NOEC for birds in a reproduction study was estimated to be 3 mg/kg bw/day. Acute LD50 for cyhalothrin and gamma cyhalothrin suggested no acute toxicity to birds (PPDB 2012). The low chronic NOEC for earthworms of gamma-cyhalothrin is in line with the finding in Table 5 for lambda-cyhalothrin.

Table 5: Toxicity reference values for the terrestrial compartment for lambda-cyhalothrin

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute, oral	Mice	LD_{50}	20 mg/kg	EFSA review report 2001
Short term dietary	Rat	NOEL	0.7 mg/kg/d	
Acute	Birds	LD_{50}	>3950 mg/kg	
Dietary	Birds	LC_{50}	>5300 mg/kg	
Reproduction	Birds	NOEC	>30mg/kg /food	
Acute 14 day	Earthworms	LC_{50}	>1000 mg/kg	
Short term Dietary	Birds	LC_{50}	> 3978 mg/kg	EU biocides AR 2011
Reproduction	Birds	NOEC	> 30mg/kg /food =3mg/kg/bw/d	
Acute 14 day	Earthworms	LC_{50}	>247mg/kg	

Exposure scenario/ Study type	Organism /Species	Endpoint	Toxicity value	Reference
Chronic 3 years	Earthworms, field study	NOEC	0.029 mg/kg /ww soil	
28 days reproduction	Soil dwelling arthropod	NOEC	1.29 mg/kg /ww soil	
28 days	Plants	EC_{50}	0.11mg/kg ww soil	
28 days	Microorganisms	EC_{50}	1.1 mg/kg ww soil	

c) Toxicity to pollinators

341. Cyhalothrin and gamma-cyhalothrin: PPDB 2012: Acute 48 hour LD50 contact = 0.005 µg/bee

342. Lambda-cyhalothrin: EFSA review report 2001: Acute oral toxicity: LD50 (48 h) = 0.91 µg/bee

343. Acute contact toxicity: LD50 (48 h) = 0.038 µg/bee

344. EU biocides AR 2011: The most sensitive of the other tested arthropod species was the predatory mite *T. pyri*, with a 48 hour LR50 = 0.0037 g a.s./ha in a study with direct exposure of dried residues on glass plates.

8.7 Other Information

345. Toxicological information presented in the PAN –pesticides database and in the footprint database is largely consistent with the toxicological information summarized above with the exception that the reproductive toxicity and developmental study results summarized above seem not respected or insufficient for a conclusion in the PAN database and the negative conclusion on carcinogenicity and the EU endocrine disruption database listing was not acknowledged in the footprint database. It seems that read across between the cyhalothrin and the lambda- and gamma- enantiomers was not similarly taken into consideration for these databases.

346. In the review report of the EC work programme for review of existing active substances provided for the placing of plant protection products on the market, it is mentioned that for the protection of aquatic organisms, risk mitigation measures should be applied. For the protection of bees Member States should prescribe appropriate risk mitigation measures (e.g. buffer zones) if products containing lambda-cyhalothrin are applied at high doses. Depending on crop and application rate, Member States should prescribe appropriate risk mitigation measures to avoid unacceptable effects on non-target arthropods when authorisations are granted for plant protection products containing this active substance.

8.8 References

EU biocides AR (2011) Assessment Report for lambda-cyhalothrin. Product-type 18. (Insecticide) May 2011, available at http://ec.europa.eu/environment/biocides/annexi_and_ia.htm

EU biocides CAR (2011) Competent Authority Report lambda-cyhalothrin, Product-type 18, May 2011.

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

EFSA review report (2001) Review report for the active substance lambda-cyhalothri,. 7572/VI/97-final January 2001, available at http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection

US EPA summary document (2010) Lambda-Cyhalothrin Summary Document Registration Review: Initial Docket December 2010. http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2010-0480

US EPA (2010) EFED Registration Review Problem formulation for Lambda-Cyhalotrin and Gamma-Cyhalothrin November 2010. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0480-0005

WHO (2011) Specifications and evaluations for public health pesticides. Lambda- Cyhalothrin. available at http://www.who.int/whopes/quality/newspecif/en/

PPDB (2012) Pesticide Properties Database, http://sitem.herts.ac.uk/aeru/footprint/en/index.htm, 2012-04-18

9. Malathion

9.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

347. Malathion is susceptible to pH dependant hydrolytic degradation (DT50 values range from 107 days at pH 5 to 0.49 days at pH 9). The parent compound and its metabolites are degraded in laboratory soil test with DT50 values form <1 day to 11 days. Also results from water/sediment studies suggest rapid break-down for malathion (DT50 <1 day). The modelled P-score of malathion is also low. Based on the presented information it can be concluded that malathion does not meet the persistence criterion of Annex D 1 (b) (i).

b) Bioaccumulation

348. Malathion does not fulfil the Annex D 1 (c) (i) criterion on bioaccumulation based on a log Kow of 2.75 and an experimentally derived BCF of 103. In addition the modelled B-score is 0.00.

c) Long-range environmental transport

349. Malathion has a calculated a half-life in air of 0.8 hours. According to the rapid degradation of malathion in air (<2 days) and a lack of experimental evidence of persistency the LRT potential of malathion is considered to be low. Therefore it can be concluded that malathion does not fulfill the Annex D 1 (d) (iii) criterion.

d) Ecotoxicity (including pollinator toxicity)

350. Malathion is highly toxic to aquatic organisms and is classified according to GHS as aquatic acute and chronic category 1. For terrestrial vertebrates on a chronic basis, malathion is moderately toxic to avian species and less toxic to mammals. However DAR- 2009 considers a reproduction NOEC of 13.5 mg a.s./kg bw/day for Bobwhite quail relevant for risk assessment that is below the dietary value of 2400 ppm from the dietary study used by US-EPA Red 2009.Malathion is acutely slightly toxic to earthworms, but its toxicity to bees is high.

351. Based on its high ecotoxicity and toxicity to human health (see below) Annex D 1 (e) (ii) is fulfilled

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

352. Malathion is of low acute systemic toxicity qualifying for acute oral GHS class 4.

353. Malathion is not classified for carcinogenicity, mutagenicity or reproductive toxicity according to the GHS system in the EU.

354. The in vitro genotoxicity results are inconclusive, but the in vivo genotoxicity results are negative which suggests the conclusion that there is no relevant mutagenic potential. Some carcinogenicity findings lead to IARC class 3 (evidence inadequate in humans and inadequate or limited in animals) and US-EPA conclusion for “suggestive evidence for carcinogenicity”. Genotoxicity of the impurity Isomalathion cannot be excluded.

355. Within reproductive toxicity studies decreased pup weights in rats and increased resorptions in the rabbit were reported but the results were considered not sufficient for a classification proposal.

356. Malathion is listed in the EU endocrine disrupter database within category 2. This means that it is persistent or a HPVC chemical with at least some in vitro evidence of biological activity related to endocrine disruption.

357. Some literature studies are indicated that show that malathion can affect immune function, but this was not considered as important for risk quantification by US EPA.

358. Malathion is classified for skin sensitization.

359. The substance did not induce delayed neurotoxicity. The critical effect used for limit value derivation is cholinesterase inhibition. In the latest evaluation available this lead to an lowest ADI proposal of 0.03 mg/kg bw day.

9.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

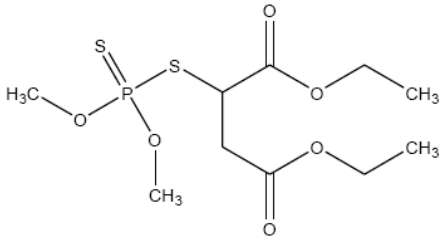
Common name:	malathion (ISO)
IUPAC name:	1,2-bis(ethoxycarbonyl)ethyl O,O-dimethyl phosphorodithioate
CAS number:	121-75-5
Molecular weight:	330.6
Chemical structure	

Table 2: Toxicological relevant impurities

Impurities	Typical concentration	Remarks
Isomalathion	must not exceed 2 g/kg (EFSA review report 2010-01-22) ≤ 0.03 % isomalathion (Annex VI to EU CLP regulation)	DAR2009: acetyl cholinesterase inhibitor which enhances the toxicity of malathion. Positive results in genotoxicity studies may be due to isomalathion, this has been reported also in literature.
malaoxon	must not exceed 1 g/kg (EFSA review report 2010-01-22)	DAR 2009: acetyl cholinesterase inhibitor which enhances the toxicity of malathion.

b) Chemical group

Organophosphate

c) Physico-chemical properties

Table 3: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	4.5 x10^{-4} Pa	PPDB 2012
Water solubility	148 mg/L (25°C)	DAR 2009
Partition coefficient n-octanol/water (log value)	2.75	PPDB 2012
Partition coefficient n-air/water (log value)	-6.7	EPI SUITE[14]
Partition coefficient n-octanol/air (log value)	9.45	EPI SUITE
Henry´s Law Constant at 25°C	1.00 X 10^{-03} Pa m^3 mol^{-1}	PPDB 2012

9.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008 – 1nd amendment 2009

Category	Hazard-Phrase
Acute Tox. 4	H302
Skin Sens. 1	H317
Aquatic Acute 1	H400
Aquatic Chronic 1	H410, M=1000

[14] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

9.4 Environmental fate

a) Abiotic degradation

-

b) Hydrolysis

360. PPDB 2012: Aqueous hydrolysis DT50 at 20°C and pH 7 is 6.2 days. The degradation is pH sensitive and the DT50s range from 107 days at pH 5 to 0.49 days at pH 9, all at 25°C.

c) Phototransformation/photolysis

361. EnviChem 2012: Aquatic photolysis half-lives from 833 days to 41.3 days at pH 6 for summer sunlight 30 °N (source: Howard 1991). PPDB 2012 lists a DT50 value of 98 days at pH7.

d) Biodegradation

362. EFSA 2006: The available data demonstrate that in soil malathion degrades to the major (>10% applied radioactivity (AR)) metabolites malathion monocarboxylic acid (MMCA) malathion dicarboxylic acid (MDCA). In soil malathion and MMCA exhibited very low persistence and MDCA exhibited low persistence. (cf. Table 4) In sediment water systems malathion exhibited very low persistence breaking down to the major metabolites MMCA (which exhibited low persistence) and MDCA (which exhibited medium persistence). All the compounds remained primarily in the water phase of the test sediment water system. US EPA 2006 state that Malathion is generally nonpersistent; but open literature studies suggest that its persistence is longer on soil that is of dry, sandy, low nitrogen, low carbon, and acidic quality.

Table 4: Biotic degradation of malathion and major metabolites

Study type	Results	Reference	Remarks
DT_{50} soil lab (days):	Malathion: <1 d (20°C) MMCA: <1 d MDCA: 3 d (geometric mean, n=4)	EFSA DAR-LOEP 2009	-
DT_{50} soil lab (days):	Malathion: <1 to ~11d	US-EPA RED 2009	-
DT_{50} water (days) from water/sediment study:	Malathion: <1 d MMCA: 3-4d MDCA:15-17d	EFSA DAR-LOEP 2009	Malathion remained in the water phase
DT_{50} water sediment/whole system (days):	Malathion: <1 d MMCA: 3-4d MDCA:13-21d	EFSA DAR-LOEP 2009	-

e) Potential for long range transport

363. Results of the Phototransformation in air according to EPI Suite TM v4.0 (AOPWIN v 1.92) are based on a 12h day are summarised in table 5.

Table 5: Phototransformation in air

Guideline / Test method	Molecule / radical	Rate constant for reaction with OH-radicals (k_{OH}) [cm^3 $molecule^{-1}$ sec^{-1}]	Half-life ($t_{1/2}$) [d]	OH-radical concentration
AOPWIN	OH	77.4198 E-12	0.14	1.5 x 10^6 OH-radicals/cm^3

364. According to these results malathion is rapidly degraded by photochemical processes. Du to the lack of persistency no multimedia fate modelling with the OECD tool was performed.

f) Bioaccumulation

365. According to PPDB 2012 a BCF of 103 was estimated. EnviChem 2012 listed a range for BCF of 1.3 - 21.0 in *Cyprinus carpio* (source: AQUIRE 1994)

g) PB-score

366. Malathion has a P-score of 0.11 and a B-score of 0.00 resulting in an overall B-score of 0.11.

9.5 Human health hazard assessment

a) Acute toxicity

367. DAR 2009: Acute systemic toxicity and skin/eye irritation results are in agreement with the actual EU-CLP entry. In the Magnusson and Kligman test for skin sensitization a response was observed that was considered sufficient for classification.

368. US EPA RED 2009: Malathion exhibits low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Category III or IV, LD50 oral > 5000 mg/kg bw, LD50 dermal > 2000mg/kg bw, LC50 respiratory > 5.2 mg/L). It exhibits only slight eye and dermal irritation and is not a dermal sensitizer.

b) Mutagenicity and carcinogenicity

369. DAR 2009: In vitro results appear inconclusive with negative AMES and UDS tests but a positive mouse lymphoma gene mutation test and a positive in vitro chromosome aberration tests. However an in vivo chromosome aberration study in rat bone marrow and an in vivo UDS test were negative which suggests that there is no genotoxic potential and no classification is proposed.

370. Increased nasal tumors were observed in the rat as well as liver tumors at high dose levels. The nasal tumors were probably secondary to a local irritation. The content of the impurity isomalathion is considered to be critical also with regard to genotoxicity of the compound. The results were not considered sufficient for a classification proposal.

371. US EPA RED 2009: Malathion has been classified as having "suggestive evidence of carcinogenicity" in accordance with the EPA Proposed Guidelines for Carcinogen Risk Assessment (July 1999; i.e. less than likely to be carcinogenic or carcinogenic to humans). The classification is based on the following evidence: 1) the occurrence of liver tumors in mice and rats only at excessive doses; 2) the presence of a few rare tumors in rats, which cannot be distinguished as either treatment related or due to random occurrence; 3) the evidence for mutagenicity is not supportive of a mutagenic concern in carcinogenicity; and 4) malaoxon, a structurally related chemical, is not carcinogenic in rats. The chronic dietary risk assessment is considered protective of any potential carcinogenic effects.

372. IARC Monograph 1987: The substance is listed as group 3 carcinogen, which means not classifiable as to its carcinogenicity to humans. All substances not qualifying for group 4 (non-carcinogen) or groups 1 and 2 (at least possibly carcinogenic to humans) are listed in this group 3.

c) Toxicity for reproduction

373. DAR 2009: Malathion induced a decrease in rat pup weights at non maternally toxic dose levels and increased incidence of resorptions in the rabbit that were considered not related to maternal toxic effects. However the results appeared not sufficient for a classification proposal.

d) Neurotoxicity

374. DAR 2009: No indications of delayed neurotoxicity were observed. Brain acetyl cholinesterase inhibition was observed as well as clinical signs and results in behavioral assessment in a rat developmental study. Though accompanied with kidney and liver effects the acetyl cholinesterase inhibition was observed as the most dominant effect and consequently the basis for limit dose derivation (ADI, AOEL).

375. US EPA RED 2009: ChE inhibition provides the critical effect for determining the point of departure for the oral, dermal and inhalation (aggregate only) routes of exposure. The comparative ChE in the young demonstrate that juvenile animals are more sensitive than adults.

e) Immunotoxicity

376. US EPA RED 2009: "Published literature studies have shown that malathion can affect immune function, depending on route, magnitude, and frequency of administration. … Although the immunotoxicity study is identified as a data gap, it is not considered important to the quantification of risk from malathion. Rather it will be used to further characterize the hazard from malathion in terms of its effects on the immune system, and it is not expected to have an effect on the hazard values used in the risk assessment. Therefore, no additional safety factor is necessary to account for the lack of a guideline immunotoxicity study."

f) Endocrine disruption

377. EU Endocrine Disruption Database 2012: The substance is listed within category 2, which means that it is persistent or an HPVC with at least some in vitro evidence of biological activity related to endocrine disruption.

378. US EPA RED 2009: In the available toxicity studies on malathion, there was no estrogen or androgen mediated toxicity. Thyroid effects were observed in the combined chronic/carcinogenicity study in rats, which included an increase in parathyroid hyperplasia in male and female rats, and a significant trend in thyroid follicular cell adenomas and/or carcinomas and thyroid c-cell carcinomas (all in males). However, the FIFRA SAP did not consider the thyroid effects of concern or necessarily related to malathion exposure.

g) Mode of action

379. DAR 2009, US EPA RED 2009: Malathion belongs to a group of pesticides called organophosphates (OPs), which share a common mechanism of toxicity by affecting the nervous system via cholinesterase inhibition.

h) Acceptable exposure levels

380. DAR 2009: A long term limit value (ADI) and a medium term limit value (AOEL) of 0.03 mg/kg bw of were proposed on the basis of a rat 2year study and a rat 90 day study, respectively. An assessment factor of 1000 was used for both values due to the uncertainties for the toxicological impact of the impurity isomalathion in the relevant studies. The acetyl cholinesterase inhibition was considered as the critical effect.

381. US EPA RED 2009: Lowest AEL: incidental oral children: 0.07 mg/kg bw day, several other AELs available for adults, and dermal and respiratory exposure. The acetyl cholinesterase inhibition was considered as the critical effect.

382. International limit values for worker protection (GESTIS-Database): 1-15 mg/m^3 for 8 hours

9.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

383. US EPA RED 2009 used the toxicity reference values for aquatic organisms listed in Table 6 for risk assessment. The findings by US EPA are in line with DAR 2009 indicating that malathion is extremely toxic to fish (lowest LC50 0.022 µg/l) and daphnia (EC50 0.72 µg/l) in the laboratory (21 studies for aquatic toxicity were submitted). The NOEC of the mesocom study was 5.0 µg a.s./l and the EAC (Ecologically Acceptable Concentration) was set as 30 µg a.s./l (long term effects were not observed).

Table 6: Toxicity reference values (source: USEPA RED 2009)

Exposure Scenario	Species	Exposure Duration	Toxicity Reference Value	Toxicity Category/Effect
Freshwater Fish				
Acute	Bluegill sunfish	69 hr	LC_{50} = 30 ppb	Very highly toxic
Chronic	Rainbow trout	97 day	NOEC 21 ppb	LOEC = 44 ppb
Freshwater Invertebrates				
Acute	Water flea, *Daphnia magna*	48 hr	EC_{50} = 1.0 ppb	Highly toxic
Chronic	Water flea, *Daphnia magna*	21 day	NOEC = 0.06 ppb	LOEC = 0.01 ppb

b) Terrestrial compartment

384. US-EPA RED 2009 and DAR 2009 used the toxicity reference values for terrestrial organisms listed in Table 7 for risk assessment. The table presents a selection of listed values. Please refer to the original documents for more information.

Table 7: Toxicity reference values

Exposure scenario/Study type	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
Acute, 32-day dietary	Mammals	Rat	LD50	390 mg/kg	US EPA RED 2009
Chronic, teratology study	Mammals	Rabbit	NOAEL	25 mg a.s/kg bw/day	DAR 2009
Acute toxicity	Birds	Bobwhite	LD50	359 mg as/kg	DAR 2009

Exposure scenario/Study type	Organism/Species		Time Scale Endpoint	Toxicity value	Reference
		quail			
Dietary toxicity	Birds	Bobwhite quail	LD50	554 mg/kg bw/day	DAR 2009
Reproductive toxicity	Birds	Bobwhite quail	NOEC	13.5 mg/kg bw/day	DAR 2009
Acute, 8-day dietary	Birds	Ring-necked pheasant	LC50.	2369 ppm	US-EPA RED 2009
Chronic, 21-week dietary	Birds	Bobwhite quail	LOEL	2400 ppm	US EPA RED 2006
Acute toxicity	Earthworms		LC50	116 mg/kg	DAR 2009

c) Toxicity to pollinators

385. EFSA 2006 states that the toxicity to bees is high and risk mitigations measures are also needed to protect other non-target arthropods off field. Table 8 displays toxicity values.

Table 8: Toxicity values

Study type	Organism	Time Scale Endpoint	Toxicity value	Reference
Acute oral toxicity	Bees	Acute oral	0.40 µg a.s./bee (formulation tested)	DAR 2009
Acute contact toxicity	Bees	Acute contact	0.16 µg a.s. /bee (formulation tested)	DAR 2009

9.7 Other information

386. US-EPA RED 2009: Human RA for outdoor Mosquito control measures available, acceptable risks indicated.

387. The toxicological summary provided above is in agreement with the toxicological information provided in the footprint database and in the PAN pesticides database.

388. WHO specifications and evaluations for public health pesticides- Malathion 2003: does not contain further critical toxicological information

9.8 References

DAR (2009) Additional Report to the DAR Malathion. February 2009 http://dar.efsa.europa.eu/dar-web/provision

EnviCHem (2012) Data bank of Environmental Properties of Chemicals – EnviChem http://www.ymparisto.fi/default.asp?contentid=141944&lan=en 2012-04-06.

EFSA (2006) Scientific Report, Conclusion on the peer review of malathion, Efsajournal, 63, 1-86, January 2006 http://www.efsa.europa.eu/de/efsajournal/pub/63r.htm

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

IARC Monograph (1987) Monograph 30, Sup 7 http://monographs.iarc.fr/ENG/Monographs/PDFs/index.php

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/ 2012-04-18

US EPA RED (2009): Reregistration Eligibility Decision for Malathion, Case No. 0248. http://www.epa.gov/oppsrrd1/REDs/malathion_red.pdf

10. Pirimiphos-methyl

10.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

389. Pirimiphos-methyl is susceptible to photolysis and pH-dependant hydrolytic degradation (DT50 from 7 to 79 days). The parent compound is degraded in laboratory soil tests with DT50 values of 3 to 21 days. Dissipation half-lives in field studies range from 18 to 67 days. Pirimiphos-methyl is suspected to volatilize from soil surfaces. No experimental DT50 values for water were available, however adsorption and volatilization will contribute in addition to hydrolyses to removal from the water phase. The modelled P-score of 0.52 is slightly above the trigger of 0.5, however based on the overall evidence it is concluded that pirimiphos-methyl does not meet the persistence criterion of Annex D 1 (b) (i).

b) Bioaccumulation

390. Pirimiphos-methyl has a log Kow in the range of 3.9-4.2. Its estimated BCFs are below 1000. The modelled B-score is 0.17. Thus the parent compound does not fulfill the Annex D 1 (c) (i) criterion on bioaccumulation.

c) Long-range environmental transport

391. The calculated a half-life in air was 0.8 hours. According to the rapid break-down of pirimiphos-methyl in air (<2 days) the potential for LRT is considered to be low. Therefore pirimiphos-methyl does not meet the Annex D 1 (d) (iii).

d) Ecotoxicity

392. Pirimiphos-methyl is highly toxic to birds, aquatic species and invertebrates. It is classified according to EU-GHS as aquatic acute and chronic category 1. Based on its high ecotoxicity and toxicity to human health (see below) Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

393. Pirimiphos-methyl is of low acute systemic toxicity that qualifies for GHS category 4. It is not sensitizer and is not classified for carcinogenicity, mutagenicity or reproductive toxicity or specific target organ toxicity according to the GHS system in the EU.

394. The data reported indicate no concern for mutagenicity and no or equivocal carcinogenicity findings in animals. Similarly the data reported do not indicate specific reproductive or developmental toxicity.

395. The standard repeated dose studies did not indicate specific immunotoxicity and the substance is not listed in the EU endocrine disrupter database

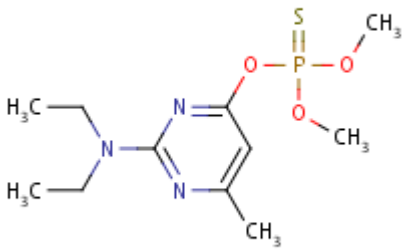
396. The substance did not induce delayed neurotoxicity. The critical effect used for limit value derivation is cholinesterase inhibition in brain and erythrocytes. In the latest evaluation available this lead to an ADI proposal of 0.004 mg/kg bw day.

10.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Pirimiphos-methyl
IUPAC name:	O-(2-diethylamino-6-methylpyrimidin-4-yl) O,O-dimethyl phosphorothioate
CAS number:	29232-93-7
Molecular weight:	305.34

Chemical structure:	

b) Chemical group

Organophosphate

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure	0.002 Pa	with 20°C, EXP
Water solubility	8.6 mg/L	with 20°C, EXP
Partition coefficient n-octanol/water (log value)	3.9 4.2	PPDB, 2012 EPISUITE, EXP
Partition coefficient air/water (log value)	-4.54	EPI Suite v 4.0
Partition coefficient air/octanol (log value)	8.44	EPI Suite v 4.0
Henry´s Law Constant	7.01 x 10^{-7} atm-m^3/mole	with 25°C, EST

10.3 Classification and labelling

a) Harmonised Classification in Annex VI of the CLP

Regulation (EC) No 1272/2008:

Category	Hazard-Phrase	
Acute Tox. 4	H302	Harmful if swallowed
Aquatic Acute 1	H400	Very toxic to aquatic life
Aquatic Chronic 1	H410	Very toxic to aquatic life with long lasting effects

10.4 Environmental fate

a) Abiotic degradation

-

b) Hydrolysis

397. US EPA RED 2006: Pirimiphos-methyl hydrolyzes rapidly at acidic pHs and is relatively stable at neutral and alkaline pH; calculated half-lives are 7.3 days at pH 5, 79.0 days at pH 7, and 54-62 days in pH 9. A degradate, O-2-diethylamino-6-methylpyrimidin-4-yl o-methyl-phosphorothioate, was recovered at significant amounts in the pH 7 and pH 9 solutions that did still contain the organophosphate moiety and therefore, may still have significant toxicological activity.

c) Phototransformation/photolysis

398. DAR 2005: The active substance is photolabile with a DT50 <30 minutes at pH 5 and 7 in a photolysis study.

d) Biodegradation

399. PPDB 2012 states a DT50 (geometric mean) of 12 day (range 3-21 days) for laboratory

degradation studies at 20°C and a DT50 field of 39 days (range 18-67 days). HSDB 2012 reported a dissipation half-life of pirimiphos-methyl of 5.2-5.9 days on soil, but more that 40% of the loss of pirimiphos-methyl within 24-hrs may be attributed to volatilization coupled with photodegradation from the surface soil. This finding is in agreement with DAR 2005 where pirimiphos-methyl was significantly volatilised from soil and leaf surfaces in a laboratory study.

400. No DT50 for water was identified, however based on its physico-chemical properties and observed hydrolyzes it is not expected that the parent compound will persist in aquatic environments. According to DAR 2005 no water/sediment study was submitted. If released into water, pirimiphos-methyl is expected according to HSDB 2012 to adsorb to suspended solids and sediment based upon the estimated Koc. 89.2% of pirimiphos-methyl was lost in a water/sediment mixture in 1 day; however, the primary loss mechanisms were by adsorption and volatilization rather than biodegradation (HSDB, 2012).

e) Potential for long-range environmental transport

401. DAR 2005: Calculations of the chemical lifetime in the troposphere with hydroxyl radicals (AOPWIN Program version 1.8) resulting in a half life of <0.067 days using a 12 hour day (1.5×10^6 HO/cm^3) or 0.8 hours. According to these results pirimiphos-methyl is rapidly degraded by photochemical processes. Du to the lack of persistency no multimedia fate modelling with the OECD tool was performed.

f) Bioaccumulation

402. PPDB 2012 estimates the BCF of 741 L/kg ww, the BCF modelled with EPISUITE (based on a log Kow of 4.2) yields a value of 274 L/kg ww. No experimental derived value was available in the indicated information sources.

g) PB-score

403. Pirimiphos-methyl has a P-score of 0.52 and a B-score of 0.17 resulting in an overall B-score of 0.67.

10.5 Human health hazard assessment relevant for the PBT assessment

a) Acute toxicity

404. DAR 2005: Acute systemic toxicity and skin/eye irritation results are in agreement with the actual EU-CLP entry. In the Magnusson and Kligman test for skin sensitization a weak response was observed that was not considered sufficient for a classification proposal.

405. US EPA RED 2006: Acute systemic toxicity results are not in agreement with the actual EU-CLP entry. However there is agreement that the substance is not a dermal sensitizer.

	EPA Toxicity category	Results
Acute dermal	III	LD50 ≥3.5 g/Kg for females and between 2.2-3.5 g/kg for males
Acute oral	III	LD50 2.4 g/kg
Acute inhalation	IV	LC50 ≥4.7mg/L
Eye irritation	II	Irritant
Dermal irritation	III	Moderate irritant
Dermal sensitizer	N/A	Non-sensitizer

b) Mutagenicity and carcinogenicity

406. DAR 2005: Positive bacterial mutation results in the literature were not reproduced in a well performed unpublished study. Equivocal increases in SCE (sister chromatide exchange, questionable biological significance) were observed but the weight of in vitro evidence is negative. Also the in vivo genotoxicity is negative. Carcinogenicity studies were negative in mice and in rat an equivocal brain and pancreas tumour incidence was observed in a poorly reported rat study. The latter could qualify the substance for GHS class 2 classifications, however a respective evaluation and decision is still pending.

407. No IARC monograph is available.

c) Toxicity for reproduction

408. DAR 2005: The substance was not toxic to reproduction and not teratogenic. Shifted pelvic position was observed at a maternally toxic dosage (cholinesterase inhibition) in rabbits (borderline

effect, considered to be a variation rather than a malformation).

d) Neurotoxicity

409. DAR 2005: The substance did not induce delayed neurotoxicity. Brain and erythrocyte cholinesterase inhibition was observed in animals and in humans. It represents the critical effect leading to the proposals for the ADI of 0.004 mg/kg bw day (AF = 100), for the AOEL of 0.02 mg/kg bw day and for the ARfD of 0.15 mg/kg bw day.

410. US EPA RED 2006: Marked plasma, RBC and brain cholinesterase inhibition was observed at the lowest dose levels in the short term dermal and inhalation studies (15 mg/kg bw day) and in the intermediate dermal and inhalation studies (0.2 mg/kg bw day).

e) Immunotoxicity

411. DAR 2005: Toxicological findings from repeated dose studies on lymphocyte and leukocyte counts were isolated, inconsistent and seen in the presence of other toxicity. Therefore these findings were not considered indicative of specific immunotoxicity.

f) Endocrine disruption

412. The substance is not listed in the EU Endocrine Disrupter Database 2012.

g) Mode of action

413. US EPA RED 2006: The substance is an organophosphate insecticide which causes cholinesterase inhibition by all routes of exposure.

h) Acceptable exposure levels

414. EFSA review report 2011: ADI 0.004 mg/kg bw; ARfD 0.15 mg/kg bw; AOEL 0.02 mg/kg bw

415. Assessment factors of 100 were used accounting for the standard uncertainties. The critical effect was the acetyl cholinesterase inhibition.

416. US EPA RED 2006: Population adjusted dose (PAD) acute, dietary = 0.005 mg/kg bw day; PAD chronic, dietary = 0.000067 mg/kg bw day. For both PADs an assessment factor of 3000 was used, accounting in addition to the standard uncertainties also for LOAEL-NOAEL extrapolation and the lack of complete toxicity database. The critical effect was the acetyl cholinesterase inhibition.

417. International limit values (GESTIS): No international limit value listed in GESTIS

10.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

418. According to US EPA RED 2006 pirimiphos-methyl is highly toxic to aquatic species and invertebrates. Table 3 lists toxicity reference values according to DAR 2005 and PPDB 2012.

Table 3: Toxicity reference values

Group	Time-scale	Endpoint	Toxicity (mg/l)	Reference
Oncorhynchus mykiss	96 hours	LC50	0.404 mg a.s./L	DAR 2005
Oncorhynchus mykiss	96 hours	LC50	0.20 mg a.s./L	
Cyprinus carpio	96 hours	LC50	1.4 mg a.s./L	
Daphnia magna	48 hours	EC50	0.00021 mg a.s./L	
Selenastrum capricornutum	96 hours	EC_b50	1.0 mg a.s./L	
Oncorhynchus mykiss	21 days	NOEC	0.023 mg a.s/L	PPDB 2012
Daphnia magna	21 days	NOEC	0.08 µg s.s/L	PPDB 2012
Chironimus riparius	96 hours	LC50	0.039 mg a.s/L	PPDB 2012

b) Terrestrial compartment

419. US EPA RED 2006 Pirimiphos-methyl is highly toxic to birds. A LC50 in Bowhite quail of 207 ppm was reported (CCID, 2012). Pirimiphos-methyl is much less acutely toxic to mammals than it is to birds. The LD50 value for mammals is 2,400 mg/kg.

10.7 Other Information

420. WHO specifications and evaluations for public health pesticides-Pirimiphos-methyl 2004: does not contain further critical toxicological information

421. Toxicological information present in the PAN –pesticides database and in the PPDB database are largely consistent with the toxicological information summarized above.

422. There are no significant agricultural approved outdoor uses in the US and European Union.

10.8 References

CCID (2012) New Zealand EPA HSNO Chemical Classification and Information Database, April 2012. http://www.epa.govt.nz/search-databases/Pages/HSNO-CCID.aspx, 2012-04-16

DAR (2005) Pirimiphos-methyl Draft Assessment Report, February 2005. http://dar.efsa.europa.eu/dar-web/provision

EFSA review report (2011) Review report for the active substance pirimiphos-methyl, January 2011, http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1_pirimiphos-methyl_en.pdf

EU Endocrine Disruption Database (2012) http://ec.europa.eu/environment/endocrine/strategy/short_en.htm, 2012-04-16

Gestis (2012) Gestis-databse on hazardous substances, http://ww.dguv.de/ifa/en/gestis/stoffdb/index.jsp, 2012-04-16

HSDB (2012) Hazardous Substances Data Bank,Toxnet, http://toxnet.nlm.nih.gov/cgi-bin/sis/search 2012-04-02

PPDB (2012) Pesticide Properties DataBase, University of Hertfordshire, http://sitem.herts.ac.uk/aeru/footprint/en/ 2012-04-18

US EPA RED (2006) Reregistration Eligibility Decision for Pirimiphos-methyl, http://www.epa.gov/oppsrrd1/REDs/pirimiphos_methyl_red.pdf

WHO (1983) DATA SHEETS ON PESTICIDES No. 49, PIRIMIPHOS-METHYL, IPCS Inchem, http://www.inchem.org/documents/pds/pds/pest49_e.htm 2012-04-02

11. Propoxur

11.1 Summary of the assessment of POP properties– comparison with the criteria of Annex D and other hazard indicators

a) Persistence

423. Propoxur is persistent to hydrolysis at acid and neutral pH values. The compound is degraded under laboratory soil test conditions with DT50 values of 30-79 days, assuming moderate persistence. Concerning the degradation of propoxur in water or sediment a DT50 value of 2 days (for whole system in a water/sediment study) has been reported (but no information on pH available to proof biodegradation below pH <7). Based on the presented information it can be concluded that propoxur does not meet the persistence criterion of Annex D 1 (b) (i), however there exists no proof of biodegradation in aquatic environments below a pH value of 7.

b) Bioaccumulation

424. Propoxur does not fulfil the Annex D 1 (c) (i) criteria on bioaccumulation based on an estimated BCF of 75 and a log Kow of 0.14.

c) Long-range environmental transport

425. Propoxur has a calculated half-life in air of 4 hours (<2 days). Therefore it is unlikely that propoxur fulfils the Annex D 1 (d) (iii) criteria.

d) Ecotoxicity (including pollinator toxicity)

426. Propoxur is highly toxic to aquatic organisms and is classified according to GHS as aquatic acute and chronic category 1. Also the acute toxicity of propoxur for birds and mammals is high. It reveals moderate toxicity to honey bees and is assumed to be harmful for other arthropods. Based on its high ecotoxicity and toxicity to human health (see below) Annex D 1 (e) (ii) is fulfilled.

e) Toxicity to human health (including mutagenicity, carcinogenicity and adverse effects on the reproductive, endocrine, immune or nervous systems)

427. Propoxure is classified within the EU GHS system for acute oral toxicity category 3 and this is supported by the available data. It is not irritating and not skin sensitizing, but it might qualify also for acute respiratory category 4.

428. Propoxure showed little if any genotoxic activity within in vitro and in vivo tests. However it was classified by US EPA as group B, probable human carcinogen. No concern for reproductive toxicity was reported on the basis of developmental rat and rabbit studies as well as two generation rat studies.

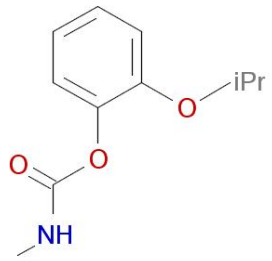
429. Representing a carbamate dominant neurotoxic effects were observed in the acute and repeated dose studies. No histological effects on the nervous tissue were reported but the critical effect for limit dose derivation is acetyl cholinesterase inhibition. US EPA derived a long term limit value (RfD) of 0.005 mg/kg bw day on the basis of a human LOAEL for red blood cell cholinesterase inhibition and an assessment factor of 10 for intraspecies variability and 3 for LOAEL to NOAEL extrapolation. WHO proposed a long term limit value (ADI) of 0.02 mg/kg bw day on the basis of the same study but without the additional factor of 3 since the lowest dose was considered as a NOAEL since depression of erythrocyte cholinesterase did not exceed 20% and the recovery was very rapid.

11.2 Identity of the substance and physical and chemical properties

a) Name and other identifiers of the substance

Table 1: Substance identity

Common name:	Propoxur
IUPAC name:	2-isopropoxyphenyl methylcarbamate
CAS number:	114-26-1
Molecular weight:	209.24

Chemical structure:	

b) Chemical group

Carbamate

c) Physico-chemical properties

Table 2: Overview of selected physico-chemical properties

Property	Value	Remarks and Reference
Vapour pressure at 25°C (mPa)	1.3	PPDB 2012
Water solubility at 20°C (mg/l)	1800	PPDB 2012
Partition coefficient n-octanol/water (log value, pH 7, 20°C)	0.14	PPDB 2012
Partition coefficient air/water (log value)	-7.23	EPI Suite v 4.0[15]
Partition coefficient air/octanol (log value)	8.75	EPI Suite v 4.0
Henry´s Law Constant at 25°C ($Pa.m^3.mol^{-1}$)	1.50×10^{-04}	PPDB 2012

11.3 Classification and labelling

a) Harmonised Classification according to GHS

Regulation (EC) No 1272/2008:

Category	Hazard-Phrase
Acute Tox. 3	H301 Toxic if swallowed
Aquatic Acute 1	H400 Very toxic to aquatic life.
Aquatic Chronic 1	H410 Very toxic to aquatic life with long lasting effects.

11.4 Environmental fate

a) Abiotic Degradation

-

b) Hydrolysis

430. PPBD 2012: Persistent: Aqueous hydrolysis DT50 (days) at 20°C and pH 7: 180

431. WHO 2005: Half-life at 22ºC >1 year at pH 4, 93.2 days at pH 7, 30.1 hours at pH 9

432. US EPA RED 1997: Propoxur is apparently hydrolytically stable at acid to neutral pHs (3 to 7) but degrades rapidly at alkaline pH values.

c) Phototransformation/photolysis

433. PPDB 2012: Fast: Aqueous photolysis DT50 (days) at pH 7: 0.01 day

d) Biodegradation

434. PPBD 2012 lists the degradation estimates according to Table 3. The metabolite 2-(1-methylethoxy)phenol in soil was identified.

435. US EPA RED 1997: Based on supplemental data, propoxur is likely to be moderately persistent

[15] http://www.epa.gov/oppt/exposure/pubs/episuite.htm

(the metabolic half-life is on the order of several months). mobile, and may potentially leach to groundwater.

Table 3: Half-lives of propoxur in soil, water and sediment

Degradation 50%	days	Reference	Comment
DT_{50} soil lab:	79 30 (20°C)	PPDB PPDB	Moderately persistent Moderately persistent
DT_{50}soil field:	28	PPDB	Non Persistent
DT_{50} water sediment/whole system:	2	PPDB	Fast

e) Potential for long-range environmental transport

436. According to AOPWIN v1.92 the photo-chemical degradation of propoxur in air has been estimated to be fast. The calculated DT50 is 4.05 hours (assuming a 12 hours day and a OH concentration of 1.5 x 10^6 OH/cm^3).

f) Bioaccumulation

437. PPBD 2012: The calculated bioconcentration factor of 75 is considered to be low.

g) PB-score

438. Not available.

11.5 Human health hazard assessment

a) Acute toxicity

439. US EPA factsheet 1997: In studies using laboratory animals, propoxur generally has been shown to be of moderate acute toxicity. It has been placed in Toxicity Category II (the second highest of four categories) for effects via the oral route of exposure, and Toxicity Category III for the dermal and inhalation routes. The data presented support EU GHS classification for oral category 3 only and no skin irritation was well as not skin sensitization.

440. WHO 2005: The data presented support the actual classification with the exception of a respiratory LC50 of 0.65 mg/L that may support an additional GHS classification in respiratory category 4.

b) Mutagenicity and carcinogenicity

441. US EPA factsheet 1997: Propoxur showed little if any genotoxic activity when tested with bacterial mutation tests and in vitro mammalian mutation and chromosomal aberration tests as well as in vivo hamster bone marrow chromosomal aberration tests and in mouse micronucleus test. However on the basis of dietary carcinogenicity studies in mouse and rat it has been classified as a Group B, probable human carcinogen. The agency has calculated a unit risk, Q_1* of 3.7 x 10^{-3} based on male rat bladder tumors. Also the results were reported from a chronic inhalation study in rats and a chronic feeding study in dogs.

c) Toxicity for reproduction

442. US EPA RED 1997: The available developmental rat and rabbit studies and the two rat reproductive toxicity studies (2-generations) do not suggest any increased sensitivity of infants and children to propoxur from pre- and post-natal exposures.

d) Neurotoxicity

443. US EPA summary 2009: Propoxur inhibits acetylcholinesterase (AChE). Toxicological characteristics of propoxur involve maximal ChE inhibition (typically within 15 minutes to an hour) followed by rapid reactivation of the enzyme and then recovery (minutes to hours). As such, the critical duration of exposure for propoxur is acute ChE inhibition of brain and red blood cell AChE measured at the peak time of effect. At the time of the 1996 risk assessment, the Agency did not have a comparative cholinesterase assay that evaluated the sensitivity of young animals compared to adult animals to address the FQPA factor in risk assessment. Therefore, the Agency retained a 10X FQPA factor for propoxur. The neurotoxic effects were critical for the limit value derivation.

444. At least in the low and medium dose ranges no adverse histological effects were identified in the acute and repeated dose studies that included neurotoxicity studies with FOBs.

e) Immunotoxicity

445. US EPA summary 2009: The toxicity database for propoxur is nearly complete. However, EPA plans to require an immunotoxicity study (870.7800) and a comparative cholinesterase assay.

f) Endocrine disruption

446. -

g) Mode of action

447. Representing a carbamate the critical effect of propoxur is acetyl cholinesterase inhibition.

h) Acceptable exposure levels

448. US EPA factsheet 1997: The Agency has calculated a reference dose (RfD), the amount of pesticide believed not to cause adverse effects if consumed daily over a 70- year lifetime, of 0.005 mg/kg/day, based on a human study with a LOEL of 0.15 mg/kg, the lowest dose tested. This dose was associated with transient red blood cell cholinesterase inhibition. An uncertainty factor of 10 was applied to account for intra-species variability and an additional factor of 3 was applied to compensate for the lack of a NOEL. The FAO/WHO joint committee on pesticide residue (JMPR) in 1989 proposed an acceptable daily intake (ADI) of 0.02 mg/kg/day on the basis of an acute no-effect level in humans. In the JMPR evaluation of the human study, the NOEL was considered to be 0.2 mg/kg/day since the depression of erythrocyte cholinesterase did not exceed 20% and the recovery was very rapid.

449. International limit values for worker protection (GESTIS-Database): Long-term limit values between 0.5 and 2 mg/m^3 inhalable aerosol are presented by a total of 16 institutions and countries.

11.6 Environmental hazard assessment

a) Aquatic compartment (including sediment)

450. Toxicity data for the aquatic compartment are summarized in Table 4. According to US EPA RED 1997 propoxur is moderately toxic to freshwater fish (some LC s are in the range of >1-10 ppm); 50 and very highly toxic to freshwater invertebrates (daphnid EC is <1 ppm).

Table 4: Toxicity reference values for the aquatic compartment (source PPDB 2012)

Exposure scenario/Study type	Organism/Species	Endpoint	Toxicity value
Acute 96 hour	Fish	LC_{50}	6.2 mg/l
Acute 48 hour	Aquatic invertebrates	EC_{50}	0.15 mg/l
Acute 96 hour	Sediment dwelling organisms	LC_{50}	38.1mg/l

b) Terrestrial compartment

451. Toxicity data for the terrestrial compartment are summarized in Table 5.

452. US EPA RED 1997: Based on the results of studies propoxur is categorized as very highly toxic to birds on an acute basis (some LD s are <10 mg/kg); highly toxic to birds on a subacute dietary basis (an LC is in the range of 51-500 ppm).

Table 5: Toxicity reference values for the terrestrial compartment

Exposure scenario/Study type	Organism /Species	Endpoint	Toxicity value	Reference
Acute	Rat	LD_{50}	~50 mg/kg	PPBD
Short-term, dietary	Rat	NOEL	200 ppm diet	PPBD
Acute	Birds	LD_{50}	25.9 mg/kg	PPBD
Acute	Birds	LD_{50}	3.55 -60.4 mg/kg	US EPA RED

c) Toxicity to pollinators

453. PPBD 2012: Honeybees: Acute 48 hour LD50: 1.35 µg/bee: Moderate

11.7 Other information

454. The data and information presented in WHO 2005 is largely in agreement with the data and information provided above.

455. Propoxur has been excluded from Annex 1 (EC Directive 1107/2009 (repealing 91/414) and is not included in Annex I of the Biocidal Products Directive 98/8/EC (Commission Decision of April 14th 2009 concerning the non-inclusion of certain substances in Annex I, IA or IB to Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market with regard to product type 18).

11.8 References

PPDB (2012) Pesticide Properties Database: Propoxur
http://sitem.herts.ac.uk/aeru/footprint/en/index.htm

GESTIS (2012) Database on hazardous substances,
http://www.dguv.de/ifa/en/gestis/stoffdb/index.jsp, 2012-04-18

US EPA summary (2009) US EPA Propoxur Summary Document for Registration Review Document ID: EPA-HQ-OPP-2009-0806-0002, available at
http://www.epa.gov/oppsrrd1/registration_review/propoxur/index.html

US EPA factsheet (1997) Factsheet Propoxure RED. EPA738-R-97-009. available at
http://www.epa.gov/oppsrrd1/registration_review/propoxur/index.html

US EPA Red (1997) Reregistration Eligibility Decision (RED) PROPOXUR, August 2007, available at http://www.epa.gov/oppsrrd1/registration_review/propoxur/index.html

WHO (2005) WHO Specifications and evaluations for public health pesticides, Propoxur. 2-isopropoxyphenyl methylcarbamate.