Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

2,3,5,6-tetrafluoro-4-methylbenzyl (1*RS*,3*RS*)-3-[(*Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate; Tefluthrin (ISO)

EC Number: -
CAS Number: 79538-32-2

CLH-O-0000001412-86-61/F

Adopted

05 June 2015

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

05 June 2015

CLH-O-0000001412-86-61/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonized classification and labelling (CLH) of:

Chemical name: **2,3,5,6-tetrafluoro-4-methylbenzyl (1*RS*,3*RS*)-3-[(*Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate; Tefluthrin (ISO)**

EC Number: **-**

CAS Number: **79538-32-2**

The proposal was submitted by **Germany** and received by RAC on 4 August 2014.

In this opinion, all classifications and labelling are given in accordance with the CLP Regulation; the notation of 67/548/EEC, the Dangerous Substances Directive (DSD) is no longer provided.

PROCESS FOR ADOPTION OF THE OPINION

Germany has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **12 August 2014**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **26 September 2014.**

ADOPTION OF THE OPINION OF THE RAC

Rapporteur, appointed by RAC: **Peter Hammer Sørensen**

Co-rapporteur, appointed by RAC: **Riitta Leinonen**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2. The RAC opinion on the proposed harmonized classification and labelling was reached on **05 June 2015.**

The RAC opinion was adopted by **consensus.**

OPINION OF THE RAC

RAC adopted the opinion that Tefluthrin (ISO) should be classified and labelled as follows:

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	**No current Annex VI entry**										
Dossier submitters proposal	TBD	tefluthrin (ISO); 2,3,5,6-tetrafluoro-4-methylbenzyl (1*RS*,3*RS*)-3-[(*Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate	-	79538-32-2	Acute Tox. 1 Acute Tox. 2 Acute Tox. 2 STOT-RE 1 Aquatic Acute 1 Aquatic Chronic 1	H330 H310 H300 H372 (nervous system) H400 H410	GHS06 GHS08 GHS09 Dgr	H330 H310 H300 H372 (nervous system) H410		M = 10000 M = 10000	
RAC opinion	TBD	tefluthrin (ISO); 2,3,5,6-tetrafluoro-4-methylbenzyl (1*RS*,3*RS*)-3-[(*Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate	-	79538-32-2	Acute Tox. 1 Acute Tox. 2 Acute Tox. 2 Aquatic Acute 1 Aquatic Chronic 1	H330 H310 H300 H400 H410	GHS06 GHS09 Dgr	H330 H310 H300 H410		M = 10000 M = 10000	
Resulting Annex VI entry if agreed by COM	TBD	tefluthrin (ISO); 2,3,5,6-tetrafluoro-4-methylbenzyl (1*RS*,3*RS*)-3-[(*Z*)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate	-	79538-32-2	Acute Tox. 1 Acute Tox. 2 Acute Tox. 2 Aquatic Acute 1 Aquatic Chronic 1	H330 H310 H300 H400 H410	GHS06 GHS09 Dgr	H330 H310 H300 H410		M = 10000 M = 10000	

GROUNDS FOR ADOPTION OF THE OPINION

Human health hazard assessment

RAC evaluation of acute toxicity

Summary of the Dossier submitter's proposal

Four acute toxicity studies were presented in the CLH report, which is included as part of the Background document (BD). Studies were conducted by oral, inhalatory and dermal routes.

In an acute oral toxicity study (Southwood, 1985) groups of 5 male and 5 female Alderley park, SPF, albino rats received a single dose of 10.1, 25.5, 47 or 100 mg/kg bw tefluthrin (in accordance with 92/69/EEC B.1 ≅ OECD TG 401). LD_{50} values were calculated to be:

- 21.8 mg/kg bw in males
- 34.6 mg/kg bw in females

No signs of toxicity were seen in any of the animals (male or female), at 10.1 mg/kg bw. Signs of toxicity were present in all animals dosed with 25.5, 47 and 100 mg/kg bw on day 1 and persisted in some surviving animals until day 6. The most common signs of toxicity included tremors, splayed gait, loss of stability, urinary incontinence, salivation and upward curvature of the spine.

In a second acute oral toxicity study (Southwood, 1985) groups of 5 male and 5 female Alderley park, SPF, albino mice received a single dose of 9.8, 48, 97 or 125 mg/kg bw tefluthrin (in accordance with 92/69/EEC B.1 ≅ OECD TG 401). A further group of five male mice received 23.4 mg/kg tefluthrin. LD_{50} values were calculated to be:

- 45.6 mg/kg bw in males
- 56.5 mg/kg bw in females

Signs of toxicity were not seen in any of the animals given 9.8 mg/kg bw, but became apparent in all other animals on the day of dosing and persisted in some survivors until Day 4. The most common signs were shaking, sides pinched in, urinary incontinence and upward curvature of the spine.

The DS proposed that according to the CLP criteria tefluthrin should be classified in acute oral toxicity hazard category 2 (5< ATE ≤50) with the hazard statement H300: Fatal if swallowed.

In an acute inhalation toxicity study (McLean *et al*, 1986) groups of 5 male and 5 female Alpk:AP rats (in accordance with 92/69/EEC B.2 ≅ OECD TG 403), were exposed for 4 hours via the nose only, to tefluthrin aerosol at target concentrations of 5, 20, 50 or 65 mg/m^3. The achieved mean analysed concentrations of 7.7, 14.9, 39.9 and 60.5 mg/m^3 tefluthrin accounted for greater than 80 % of the total particulate. The three highest dose levels had a respirable particle size (more than 90 % of particles had an aerodynamic equivalent diameter (AED) ≤ 2.5 µm and a mass median aerodynamic diameter of approximately 1.3 µm). LC_{50} values were calculated to be:

- 49.1 mg/m^3 (0.0491 mg/L) in males
- 37.1 mg/m^3 (0.0371 mg/L) in females

Animals in the 20, 50 and 65 mg/m^3 tefluthrin groups showed dose related symptoms of neurotoxicity. Neurotoxic symptoms were reversible in animals which survived. The mean body weight of all surviving animals in all groups including control was reduced compared to pre-treatment. This effect was not dose related but was greatest in the 50 mg/m^3 females. The 50 mg/m^3 females did not exceed their starting weight until day 4, but after day 5 the weight gain of all test females was similar to that of controls.

The dose related effect on the kidney in animals which survived to day 15 was small and in the absence of associated histopathological findings was considered not to be toxicologically significant. The increase in lung weight and lung abnormalities (which consisted of red, dark and/or mottled surfaces), seen in one male and three females in the top dose, together with the

persistence of respiratory noise in the 20 and 50 mg/m^3 animals indicate that the respiratory system, including the lung, was a probable target organ for toxicity.

The DS proposed that according to the CLP criteria tefluthrin should be classified in acute inhalation toxicity hazard category 1 (0 < ATE ≤ 0.05 mg/L, for dusts and mists), hazard statement H330: Fatal if inhaled.

In an acute dermal toxicity study (Southwood, 1985) groups of 5 male and 5 female Alderley park, SPF, albino rats received a single dermal application of 100, 500, 1000 or 2000 mg/kg bw of undiluted tefluthrin (in accordance with 92/69/EEC B.3 ≅ OECD TG 402). In addition, a group of 5 female rats received an application of 50 mg/kg bw. The test substance was kept in contact with the clipped dorso-lumbar region of the rats for 24 hours by means of an occlusive dressing for most of the rats. Due to extreme discomfort observed in some of the rats, the application period was shortened to approximately 2 hours for all the animals in the 2000 mg/kg bw group and one female in the 1000 bw mg/kg group.
LD_{50} values were calculated to be:

- 316 mg/kg bw in males
- 177 mg/kg bw in females

Signs of toxicity became apparent in most animals on day 1 and persisted to day 15 in some rats until the end of the study. The most common signs were stains around nose, chromodacryorrhoea, splayed gait, upward and/or downward curvature of the spine and signs of urinary incontinence. There were clinical signs of neuromuscular incoordination in some animals. These effects were reversible but were evident at the lowest dose (100 mg/kg in males and 50 mg/kg bw in females, respectively).

The DS proposed that according to the CLP criteria tefluthrin should be classified in acute dermal toxicity hazard category 2 (50 < ATE ≤ 200), hazard statement H310: Fatal in contact with with skin.

Comments received during public consultation

Two Member State Competent Authorities (MSCA) supported the proposed classification.

Assessment and comparison with the classification criteria

Following a comparison of the available acute oral and dermal LD_{50} values and inhalation LC_{50} values with the classification criteria, RAC supports the conclusion of the DS that according to CLP Regulation tefluthrin should be classified in Category 1 for acute inhalation toxicity and Category 2 for acute oral and dermal toxicity:

- **Acute Tox. 2 - H300**: Fatal if swallowed (acute oral LD_{50} of 21.8 mg/kg bw in male rats and 34.6 mg/kg bw in female rats and acute oral LD_{50} of 45.6 mg/kg bw in male mouse are within the range 5 < ATE ≤ 50 mg/kg bw)
- **Acute Tox. 1 - H330**: Fatal if inhaled (LC_{50} values of 0.0491 mg/L in male rats and 0.0371 mg/L in female rats are within the range 0 < ATE ≤ 0.05 mg/L for dusts and mists).
- **Acute Tox. 2 - H310**: Fatal in contact with with skin (acute dermal LD_{50} of 177 mg/kg bw in male rats and 177 mg/kg bw in female rats are within the range 50 < ATE ≤ 200 mg/kg bw)

RAC evaluation of specific target organ toxicity – single exposure (STOT SE)

Summary of the Dossier submitter's proposal

The DS reported that there was no evidence of specific target organ toxicity after single oral exposure of tefluthrin. Specific organ toxicity was observed only at dose levels where lethality was already observed in the acute oral studies on rats.

After a single inhalation exposure in rats, a dose-related increase in transient respiratory noise at below the lethal dose level was observed (LC_{50} 0.037 mg/L, 4h). Together with changes in lung weight and histopathology at lethal dose levels, the lung was a probable target organ for toxicity. Further clinical signs (salivation, piloerection, reduced stability) were either observed in control animals or were restricted to days 1 and 2 after exposure.

After single dermal exposure to tefluthrin clinical signs of neuromuscular incoordination (e.g. upward curvature of spine, splayed gait, tip toe gait) were observed in some animals at 100 mg/kg bw (males) and 50 mg/kg bw (females). These dose levels were below the calculated LD_{50} value of 177 mg/kg bw.

Based on the available human information, transient neurotoxic effects for pyrethroid insecticides were mostly described as symptoms of paraesthesia.

Taking all the available information together, the DS concluded that classification with STOT-SE for the active substance tefluthrin was not needed. Therefore, in accordance with the Guidance on the application of the CLP criteria (CLP Guidance), classification for acute toxicity takes precedence and STOT-SE is not assigned.

Comments received during public consultation

One MSCA supported the DS conclusion that tefluthrin should not be classified for STOT-SE.

Assessment and comparison with the classification criteria

Substances that have produced significant toxicity in humans or that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to produce significant toxicity in humans following single exposure should be classified as STOT SE 1 or 2 according to the CLP Regulation. Classification should be supported by evidence associating single exposure to the substance with a consistent and identifiable toxic effect that clearly impacts health. Classification as STOT SE 3 is limited to substances that have narcotic effects or cause respiratory tract irritation (CLP Guidance on the Application of the CLP criteria, version 4.0, section 3.8.2.5).

RAC agrees with the DS that tefluthrin does not fulfil the criteria for STOT SE by oral, dermal or inhalation routes of exposure. Tefluthin does not fulfil the criteria for STOT SE 3 since it didn't cause respiratory tract irritation or narcotic effects.

However, in relation to a STOT SE classification, RAC considered the unusual and severe effects reported in an eye irritation study (Southwood, 1987). In that study, 0.1mL (≈ 33.5 - 50 mg/kg bw) tefluthrin was instilled into the conjunctival sac of one eye of each of six New Zealand White male rabbits (in accordance with 92/69/EEC B.5, equivalent to OECD TG 405). Prior to instillation of tefluthrin, all rabbits were pretreated intraveneously with an analgesic to prevent pain and discomfort. The findings reported are described under "Summary of the Dossier submitter's proposal" in the section "RAC evaluation of eye corrosion/irritation".

RAC considered the effects described via eye contact to be severe, since they could not be prevented by analgesic administration and they led to the premature sacrifice of 4/6 rabbits.

However, RAC is of the opinion that these symptoms occurred due to pain and paraesthesia. The latter effect is a transient effect specific to pyrethroids and has been reported in human subjects exposed to the active substance by skin contact. Under Directive 67/548/EC (DSD), paraesthesia was not regarded as an irritant effect justifying classification as Xi; R38. The S-phrase S24 was, however, required for substances seen to cause this effect. Under CLP, paraesthesia is not specifically addressed by classification and labelling elements and is not considered to fulfil the CLP criteria for STOT SE 1 or 2.

RAC agrees that the end users are sufficiently protected against paraesthesia via eye contact by the precautionary statements that follow from the Acute Tox. classification in Category 1 and 2 – especially Acute Tox. 2 (dermal) with the precautionary statements P262 (Do not get in eyes, on skin, or on clothing) and P280 (Wear protective gloves/protective clothing/eye protection/face protection).

In conclusion, RAC is of the opinion that tefluthrin **does not fulfil the criteria for STOT SE** and agrees with the DS proposal not to classify tefluthrin for this hazard class.

RAC evaluation of skin corrosion/irritation

Summary of the Dossier submitter's proposal

In a skin irritation study (Southwood, 1985) six male New Zealand White albino rabbits received a single four-hour application of approximately 0.5 mL tefluthrin to the shorn flank (in accordance with 92/69/EEC B.4 ≅ OECD 404).

Tefluthrin caused slight irritation to rabbit skin. The DS concluded that the recorded Draize values did not meet the CLP criteria for classification as irritating to skin.

Comments received during public consultation

No comments received during public consultation.

Assessment and comparison with the classification criteria

In the skin irritation study (Southwood, 1985), 2/6 rabbits could not be scored due to moderate to severe erythema and severe oedema adjacent to the application site. The mean Draize score observed was maximally 0.33 over 20 – 72 hours for both erythema and oedema in the remaining 4 rabbits. This means that the criteria for classification as irritating to skin are not met (*ie*. in at least 2/3 tested animals a mean score of ≥ 2.3 - ≤ 4.0 for erythema/eschar or for oedema).

RAC supports the conclusion of the DS that according to CLP Regulation **tefluthrin does not meet the criteria for classification for skin irritation**.

RAC evaluation of eye corrosion/irritation

Summary of the Dossier submitter's proposal

In an eye irritation study (Southwood, 1987) tefluthrin (0.1mL) was instilled into the conjunctival sac of one eye of each of six New Zealand White male rabbits (in accordance with 92/69/EEC B.5 ≅ OECD TG 405). Prior to instillation of tefluthrin, all rabbits were pretreated intraveneously with an analgesic to prevent pain and discomfort. The following findings were reported:

- Immediately following dosing, three rabbits had slight, two had moderate and one had practically no initial pain (despite pre-dosing with analgesic). As a consequence, four rabbits received a second dose and one animal received two further doses of the analgesic.

- All rabbits showed effects of paraesthesia (excessive blinking, shaking of the head and pawing of the eye).
- Four of the six rabbits were distressed and were humanely killed on the day of dosing. One approximately one hour after instillation.
- Conjunctival effects (slight or moderate redness, slight or mild chemosis and slight or severe discharge) in all five rabbits 2 hours following dosing.
- Of the two surviving animals, all signs of irritation had disappeared by three or nine days after instillation.

The DS concluded that tefluthrin does not meet the criteria to be classified for eye irritation/corrosion according to the CLP Regulation.

Comments received during public consultation

One MSCA commented on the quality of the eye irritation study and questioned the validity of the test presented in the dossier. According to them, the evaluation criteria on the eye damage/irritation are based on the severity of the eye damage, and the reversibility within the observation period of 21 days in the Southwood study did not seem to be relevant for the assessment of eye irritation. Besides, no information was provided relating to the assessment of the animals up to 4 and 17 days.

Assessment and comparison with the classification criteria

The mean scores for a substance to be classified as eye irritant according CLP criteria (Irritating to eyes (category 2, H319)) are:
at least in 2/3 tested animals a positive response of
- corneal opacity: ≥ 1 and/or
- iritis: ≥ 1 and/or
- conjunctival redness: ≥ 2 and/or
- conjunctival oedema (chemosis): ≥ 2

following grading at 24, 48 and 72 hours after installation of the test material, and which fully reverses within an observation period of 21 days.

As can be seen from Table 26 in the CLH report, the two surviving rabbits (no 9 and 11) had a mean score < 2 for both conjunctival redness and chemosis. Accordingly, the remaining rabbits (no 10, 12, 13 and 14) should have had a mean score > 2 for conjunctival redness or conjunctival chemosis after day 1, 2 and 3 (if they had not been killed on the day of dosing) if classification in category 2; H319 would have been warranted. This is actually possible from the data in Table 26 of the CLH report, but it seems unlikely since the scores of the two surviving rabbits drop from day 1 to day 3. Since the assessment is based on only two rabbits (1/3 of the tested animals) the available data are not adequate to determine the eye irritation potential of tefluthrin.

Based on the limited data available, Tefluthrin **does not meet the criteria for classification as severe eye damage/eye irritation.**

RAC evaluation of skin sensitisation

Summary of the Dossier submitter's proposal

In a GPMT skin sensitisation study (Barber, 1984) a group of 20 test and 10 control young adult female Alpk Dunkin Hartley guinea pigs were used (in accordance with 96/54/EC B.6 ≅ OECD TG 406). The intradermal induction was conducted using 5 % tefluthrin solutions. Following challenge, the following findings were reported:

- 5.2 % of the test animals responded (erythema) and 11.1 % of the control animals responded when challenged with a 50 % (w/v) tefluthrin solution.

- No erythema was seen in any of the test animals following challenge with a 10 % (w/v) solution

It was not reported whether or not signs of irritation were seen during the induction phase and therefore it is not possible to determine whether this was the maximum non-irritating intradermal concentration.

The DS concluded that when previously-induced guinea-pigs were challenged with either 50 % or 10 % solutions of tefluthrin in corn oil, no sensitisation responses were elicited. According to the CLP criteria, tefluthrin should therefore not be classified as a skin sensitiser.

Comments received during public consultation

No comments were received during public consultation.

Assessment and comparison with the classification criteria

In the Skin Sensitisation study where previously-induced guinea-pigs were challenged with either 50 % or 10 % solutions of tefluthrin in corn oil, erythema was seen in only 1/19 guinea-pigs in the 50 % group (and 1/10 in the control).

RAC agrees with the DS conclusion that tefluthrin should **not** be classified as a skin sensitiser, since positive skin reactions were observed in less than 30% of exposed animals.

RAC evaluation of specific target organ toxicity– repeated exposure (STOT RE)

Summary of the Dossier submitter's proposal

Four repeated dose toxicity studies were presented. The studies were conducted via oral and dermal routes.

In a 13-week dietary study (Stonard *et al*., 1984) groups of 20 male and 20 female Alpk:AP rats were fed diets containing 0, 50, 150 or 350 ppm tefluthrin (in accordance with 87/302/EEC B.26 ≅ OECD TG 408). The following findings were reported:

- Significant reduction in body weight gain and food consumption of both sexes at 350 ppm (31.8 mg/kg bw/d).
- Small reductions in haemoglobin, haematocrit and red blood cell count in both sexes at 350 ppm.
- Small increases in plasma urea at weeks 4 and 13 in both sexes at 350 ppm.
- Small increases in plasma cholesterol at weeks 4 and 13 in males at 150 and 350 ppm.
- Dose-related increase in liver weights in males.

NOAEL and LOAEL were considered to be 150 and 350 ppm (13.6 and 31.8 mg/kg bw/d), respectively, based on the reduction in body weight gain.

In a 13-week oral neurotoxicity study (Pinto, 2002) groups of 12 male and 12 female Alpk:APfSD rats were fed diets containing 0, 50, 150 or 350 ppm tefluthrin (in accordance with 96/54/EEC B.38 ≅ OECD TG 424 ≅ OPPTS 870.6200). The following findings were reported:

- Treatment-related findings included increased activity, irregular breathing, increased breathing rate, reduced splay reflex and paw flicking in the 350 ppm males.
- Treatment-related findings included increased activity, ataxia (from week 5), increased breathing rate, reduced splay reflex, upward curvature of the spine, piloerection, increased response to sound, abnormal gait and paw flicking in the 350 ppm females. There was an increase in the incidence and severity as the study progressed for the ataxia, increased activity, upward curvature of the spine and reduced splay reflex.

- Landing foot splay was significantly increased in weeks 5, 9 and 14 in the 350 ppm females.
- At 150 ppm two females had increased breathing rate in week 5, another female in week 14, and one female had upward curvature of the spine from week 9. One female fed 50 ppm had increased breathing rate at week 2 only.
- Change in brain pathology in a single 350 ppm female.
- Significant reduction in body weight and food consumption in the first 5 weeks in the 350 ppm females.
- Significant reduction in food consumption in the first week in the 350 ppm females and a slight reduction in food consumption at all doses for males.

Other observations:
All animals survived to scheduled termination. No effects on motor activity or on brain weights were observed in either sex.

The NOAEL and LOAEL were considered to be 150 and 350 ppm (11.6 and 26.6 mg/kg bw/d for females), respectively.

In a 13-week oral study (Kalinowski *et al*., 1985) groups of 4 male and 4 female Alderley Park beagle dogs were dosed daily with 0, 0.1, 0.5 or 1.5 mg/kg bw/d tefluthrin (in accordance with 87/302/EEC B.27 ≅ OECD TG 409). The following findings were reported:

- Whole body tremors in one female dog in the 1.5 mg tefluthrin/kg bw/d group on day 4, approximately 3 hours after dosing - full recovery occurred within one hour.
- Plasma triglyceride levels of males given 1.5 mg/kg bw/d were slightly raised at weeks 4, 8 and 13.
- Slight increase in the thyroid gland weights in the 1.5 mg/kg bw/d females.

The NOAEL and LOAEL were considered to be 0.5 and 1.5 mg/kg bw/d, respectively, based on the neurotoxicity observed in 1 female at 1.5 mg/kg bw/d on day 4.

In a 1-year oral study (Stonard, 1986) groups of 6 male and 6 female Alderley Park beagle dogs were dosed with gelatine capsules containing 0, 0.1, 0.5 or 2.0 mg/kg bw/d tefluthrin (in accordance with 67/348/EEC B.30 ≅ OECD TG 452). The following findings were reported:

- Ataxia and tremors in 9/12 dogs given 2 mg/kg bw/d; in the majority of instances these effects were noted within the first few weeks of treatment (weeks 1 – 4), but ataxia and tremors were also seen in the middle and the end of the testing period.
- Bilateral optic neuritis, choroiditis and scleritis with focal unilateral retinal degeneration in one female at 2 mg/kg bw/d.
- Mean body weight gain of males at 2 mg/kg bw/d was low.
- Slight, but not statistically significant, increase in liver and kidney weights, in males at 2 mg/kg bw/d.

Other observations:
One 2 mg/kg bw/d male died during week 36, but no clinical abnormalities had been observed in this dog within four weeks preceding death. The dog had shown signs of neurological effects earlier in the study and lesions on its claws and chin suggesting that neurotoxic events may have preceded the death.

The NOAEL and LOAEL were considered to be 0.5 and 2.0 mg/kg bw/d, respectively, based on a single death, signs of neurotoxicity (tremor and ataxia) and the possible treatment-related single incidence of eye lesions at 2 mg/kg bw/d.

In a 21 day dermal study (Leah, 1989) groups of ten male and ten female Alpk:AP$_f$SD rats received 6-hour dermal applications of the test substance at 0, 0.1, 1.0 or 50 mg/kg bw/d in PEG 300 (in accordance with 92/69/EEC B.9 ≅ OECD TG 410). The following findings were reported:

- Dose-related incidence of upward or downward curvature of the spine.

- In both males and females tip-toe gait and splayed gait from 1.0 mg/kg bw/d and bizarre behaviour at 50 mg/kg bw/d - these were considered to be indicative of paraesthesia rather than systemic toxicity.
- Eight males and eight females dosed with 50 mg/kg bw/d had scabs on the treated skin, and the treated skin of one male in this group was thickened.
- Signs of severe skin irritation at 50 mg/kg bw/d.

The systemic NOAEL was considered to be 50 mg/kg bw/d (highest dose) in the absence of true systemic toxicity, whereas for local effects the LOAEL was set at 0.1 mg/kg bw/d covering irritation/paraesthesia and secondary effects (curvature of the spine).

Based on the overt signs of neurotoxicity in dogs (tremor, ataxia) at 1.5 and 2.0 mg/kg bw/d (90-days; first few weeks of 1-year study), the DS proposed that according to the CLP criteria tefluthrin should be classified with **STOT-RE 1** (the doses being below the guidance value of ≤ 10 mg/kg bw/d), hazard statement **H372**: Causes damage to organs (nervous system) through prolonged or repeated exposure.

Comments received during public consultation

Two MSCAs supported the DS proposal for classification of tefluthrin with STOT-RE 1; H372. One MSCA and industry did not agree with the proposed DS classification and were in favour of no STOT-RE classification. One MSCA argued that dermal exposure was also a relevant route of exposure for the STOT-RE 1 classification along with oral exposure. One MSCA noted that during the EFSA Peer Review this issue was discussed [PRAPeR Expert Meeting 76 (31 May -04 June 2010)]. EFSA decided not to regard these effects for systemic toxicity and established a NOAEL in this study of 50 mg/kg bw/d and a LOAEL for local effects (based on signs indicative of paraesthesia and skin irritation) of 0.1 mg/kg bw/d (EFSA Journal 2010; 8(12):1709).

Industry did not support the classification in category 1 for STOT-RE and argued that the main toxicological effects of tefluthrin in all species are clinical signs of neurotoxicity. This is not unexpected, given the insecticidal mode of action of pyrethroids in interfering with voltage gated sodium channels. The effect is generally seen within a few hours of dosing, and recovers rapidly. It does not get worse with repeated daily dosing. This effect is transient and reversible, and a manifestation of acute toxicity, for which classifications of Acute Tox.2; H300, Acute Tox.2; H310 and Acute Tox.1; H330 (Fatal via oral, dermal and inhalation routes), are being proposed.

Assessment and comparison with the classification criteria

In general the purpose of STOT RE is to identify the primary target organ(s) of toxicity for inclusion in the hazard statement. The primary target organ of tefluthrin is the nervous system. And since classification as STOT RE includes all significant health effects that can impair function, both reversible and irreversible, immediate and/or delayed (CLP Annex I, 3.9.1.1), it is relevant to evaluate if tefluthrin should be classified for STOT RE.

The key issue is whether the neurotoxicological findings are more appropriately covered by an acute toxicity classification than by STOT RE. None of the above mentioned seven oral studies clearly shows that the neurotoxicological effects are due to repeated dosing. On the contrary, four oral studies (Pinto, 2002 (90-day rat study), Stonard, 1986 (105-week rat study), Stonard, 1986 (52-weeks dog study) and Wickramaratne, 1987 (3-generation rat study)) indicate that the neurotoxicological effects observed are due to acute toxicity symptoms that are repetedly observed.

Based on these four oral studies, RAC does not support the conclusion of the DS that according to the criteria in the CLP Regulation, tefluthrin should be classified with STOT RE 1. Furthermore, the 21-day dermal study (Leah, 1989) in Alpk:AP rats does not clearly show that the observed effects (curvature of the spine, tip-toe gait and splayed gait) are due to repeated dose toxicity. Curvature of the spine are seen from day one in the study and that splayed gait appears to be a delayed

acute effect in both the 21-day dermal study and the acute dermal toxicity study (McLean *et al*, 1986).

RAC concludes that tefluthrin **does not meet the criteria for classification with STOT RE**.

RAC evaluation of germ cell mutagenicity

Summary of the Dossier submitter's proposal

The mutagenic and DNA damaging potential of tefluthrin was studied in several *in vitro* test systems using bacteria and mammalian and human cells and in *in vivo* test systems using rats and mice. Tefluthrin was negative in two *in vitro* bacterial reverse mutation assays and in an *in vitro* gene mutation test in mouse lymphoma cells. No clastogenic effects were seen in an *in vitro* human lymphocyte cytogenectics test, an *in vivo* rat cytogenetics test or in an *in vivo* mouse micronucleus test. No evidence of DNA damage or repair was noted in an *in vitro* UDS assay.

It was concluded by the DS that no classification of tefluthrin for mutagenicity was required according to the CLP Regulation.

Comments received during public consultation

No comments were received during public consultation.

Assessment and comparison with the classification criteria

Mutagenic properties of tefluthrin were negative in several *in vitro* assays (see above), in one *in vivo* micronucleus assay in mice and in one *in vivo* cytogenetics test in rats.

RAC supports the conclusion of the DS that classification of tefluthrin for germ cell mutagenicity is **not** warranted.

RAC evaluation of carcinogenicity

Summary of the Dossier submitter's proposal

The DS presented two long-term oral toxicity studies in the carcinogenicity part of the CLH report.

In a 2-year toxicity/oncogenicity study (Wickramaratne, 1986) groups of 50 male and 50 female Alpk:AP mice were fed diets containing 0, 25, 100 or 400 ppm tefluthrin (in accordance with OECD TG 451). The following findings were reported:

- Body weight gain was reduced in males and females fed 100 ppm and 400 ppm (4 – 6 % below control values).
- Reduced food consumption in the 400 ppm males and females during the first 2 weeks of the study.
- Incidence of liver adenoma showed a positive trend in females. However, the incidence of liver carcinoma was not increased.
- A slightly positive trend of lung adenocarcinoma in males. However, there was no effect on the incidence of adenoma.
- Incidence of adenoma of the harderian gland was positive. The control group consisted of two subgroups. In one of the subgroups the incidence was 4/49 which is similar to the incidences in the 25 and 100 ppm dose groups.

- There was an increased incidence of adenoma of the pituitary gland in males and of adenoma of *pars intermedia* in females. However, the incidence of carcinoma in males was not increased.

The NOAEL was considered to be 25 ppm tefluthrin (3.2 mg/kg bw/d in males and 3.9 mg/kg bw/d in females).

In a 2-year carcinogenicity study (Stonard *et al.*, 1986) groups of 76 male and 76 female Alpk:AP rats were fed diets containing 0 or 400 ppm tefluthrin and groups of 64 male and 64 female Alpk:AP rats were fed diets containing 25 or 100 ppm tefluthrin for up to 104 weeks (in accordance with OECD TG 453). The differences in group sizes were due to extra animals being added at the top dose due to animal losses early in the study. The following findings were reported:

- Four male and five female rats fed 400 ppm tefluthrin died during the first three weeks of the study but this mortality rate did not continue throughout the study.
- Increased response to sound, increased activity, abnormal gait and tremors was mainly seen within the first three weeks of the study in the 100 ppm and 400 ppm groups. Observations of abnormal gait were seen mainly during the first few weeks of the study, occasionally throughout the mid phase of the study and increasing in incidence after week 80.
- Body weight gain was reduced in males and females fed 400 ppm and in males fed 100 ppm.
- Food consumption was reduced in the 400 ppm groups;in females during the first 13 weeks of the study and in males during the first year. Reduced food consumption was also seen in the 100 ppm males for the first year but was statistically significant only for the first 13 weeks.
- Food utilisation values were reduced in both sexes at 400 ppm tefluthrin, and in males also at 100 ppm tefluthrin during the first year of the study.
- Haemoglobin and haematocrit were slightly decreased at weeks 40 and 53 at 400 ppm in males only.
- Plasma albumin, cholesterol and total protein concentrations were reduced, and plasma alanine and aspartate transaminase activities were elevated in 400 ppm females. This could indicate a mild toxic effect on the liver or a poorer clinical condition. A similar, but less consistent trend was seen in 400 ppm males.
- There was a minimal increase in brain weight in females fed 400 ppm tefluthrin at 52 weeks and at study termination, an effect that wasnot associated with any histopathological change.
- Liver weight was marginally increased at 52 weeks in both males and females fed 400 ppm tefluthrin . No statistically significant difference was observed at study termination.

Other observations included no evidence of a treatment-related effect on urine biochemistry, despite isolated statistically significant differences from the control in some parameters in treated groups. There were no macroscopic or microscopic changes which could be attributed to the treatment with tefluthrin. In particular, tumour incidence, latency and malignancy were not adversely affected by the administration of tefluthrin.

According to the DS, there was no evidence of a carcinogenic effect of tefluthrin. No data from epidemiological studies were submitted by applicant. The studies in rats and mice revealed no evidence of carcinogenicity. Therefore, The Ds considered that tefluthrin does not meet the criteria in the CLP Regulation for classification for carcinogenicity.

Comments received during public consultation

One MSCA requested further arguments on the non-carcinogenic potential of tefluthrin. In particular, the MSCA quoted from the CLH report that: "There was a positive trend of neoplastic findings in liver, lung, harderian gland and pituitary gland. However, these findings are not considered to be an evidence of carcinogenic activity of tefluthrin since the observed incidences were mainly within historical control data." The MSCA further noted that at the top dose, the

incidence of liver adenoma in female mice and the incidence of lung adenocarcinoma in male mice were outside the historical control data (HCD) range.

Assessment and comparison with the classification criteria

There is no evidence of tefluthrin having caused cancer in humans.

In the 2-year study in rats no data on neoplastic findings were presented in the CLH report but it was concluded that "*tumour incidence, latency and malignancy were not adversely affected by the administration of tefluthrin*".

In the 2-year study in mice the neoplastic findings are summarized in the Table below.

Table (Table 50 in the CLH report): Incidences of neoplastic findings (%) with positive trend

Organ and findings	Sex	0 ppm	25 ppm	100 ppm	400 ppm	Trend test	HCD
Liver							
Adenoma	F	2/100 (2)	0/49 (0)	3/50 (6)	5/50 (10)	** p=0.004	0-3.4 %
Adenocarcinoma		2/100 (2)	3/50 (6)	1/50 (2)	1/50 (2)		0-8.3 %
Lung							
Adenoma	M	8/100 (8)	3/50 (6)	2/49 (4.1)	4/50 (8)	n.s.	No data
Adenocarcinoma		2/100 (2) (0/50 & 2/50)	0/50 (0)	1/49 (2)	3/50 (6)	* p=0.03	0-3.3 %
Harderian gland							
Adenoma	M	5/95 (5.3) (4/49 & 1/46)	4/48 (8.3)	4/48 (8.3)	´7/49 (14.3)	* p=0.04	0-16 %
Pituitary gland							
Adenoma	M	2/88 (2.3)	0/34 (0)	2/34 (5.9)	4/41 (9.8)	** p=0.01	0-13 %
Carcinoma	M	0/88 (0)	0/34 (0)	1/34 (2.9)	0/41 (0)	n.s.	

logrank test for positive test with dose (Peto *et al*., 1980); n.s.: not significant

As can be seen from the Table above the incidences of liver adenoma were increased and outside the historical range in both 100 ppm and 400 ppm females. Since liver adenocarcinomas were not increased, tefluthrin does not seem to have a potential to progress to malignant tumours. The incidence of liver adenocarcinoma was at the same level as in controls and within the range of historical control data.

The increased incidence of lung adenocarcinoma in male mice was not significant. The incidences in the control groups were 0/50 and 2/50 (*ie*. 2/100). In comparison with 3/50 in 400 ppm males this is not significant. The incidence of lung adenocarcinoma was outside the historical control range in the 400 ppm males, but so was one of the control groups (2/50). The lack of significant increases in tumours and no dose-response relationship will usually lead to no classification if this was the only tumour type seen according to CLP Guidance (Version 4.0, section 3.6.2.3.2 a).

The incidence of Harderian gland adenoma was within the range of historical control data. In addition, according to the CLP Guidance (*V*ersion 4.0, section 3.6.2.3.2 a) tumours in the Harderian gland are of no relevance to humans (although it cannot automatically be ruled out that the substance could cause similar tumours in humans), and therefore Harderian gland adenoma on its own is unlikely to lead to classification.

The incidence of Pituitary gland adenoma was within the range of historical control data. Since pituitary gland carcinomas were not increased there does not seems to be a potential to progress to malignant tumours. According to the CLP Guidance (Version 4.0, section 3.6.2.3.2 c) benign

brain tumours may be of concern and could support a classification in category 2. In this case however, the fact that Pituitary gland adenoma are within the range of historical control data supports no classification according to CLP Guidance.

RAC agrees with the DS that the studies in rats and mice revealed no evidence of carcinogenicity. Therefore, tefluthrin **does not meet the CLP criteria for classification for carcinogenicity**.

RAC evaluation of reproductive toxicity

Summary of the Dossier submitter's proposal

In the reproductive toxicity study (3-generation), the neurological effects in the offspring were attributed to a direct systemic exposure after oral ingestion. No adverse effects were observed in the fertility parameters. The parental and offspring NOAELs were 4.7 mg/kg bw/d (50 ppm), whereas the reproductive NOAEL was 23.4 mg/kg bw/d (250 ppm).

In a rat developmental study, maternal toxicity consisted of increased mortality, clinical signs of maternal toxicity (abnormal gait, uncoordinated limb movements, involuntary spasms, hypersensitivity to noise, piloerection and subdued behaviour) and decreased maternal body weight gain and food consumption at the high dose of 7.5 mg/kg bw/d. Some maternal toxicity was also noted at 5 mg/kg bw/d. Decreases in maternal body weight gain and food consumption during the dosing period were noted in females at 3 and 5 mg/kg bw/d. Maternal food consumption was also decreased at 5 mg/kg bw/d in the post-dosing period. At 5 mg/kg bw/d a slight reduction in ossification of the foetuses and increased incidence of 25 pre-sacral vertebrae were observed. No evidence of a teratogenic effect was noted.

In a rabbit developmental study, maternal toxicity consisted of body tremors in all treatment groups (the incidence and severity of this finding was most marked at the high-dose level of 12 mg/kg bw/d), decreased body weight gain during dosing at 12 mg/kg bw/d and decreased food consumption at 6 and 12 mg/kg bw/d. No evidence of a teratogenic effect was noted. However, the incidence of skeletal variations (27 pre-sacral vertebrae) was increased in all dose groups. The NOAEL of teratogenicity was 12 mg/kg bw/d. The NOAELs for maternal toxicity and foetotoxicity were < 3 mg/kg bw/d.

It was concluded by the DS that based on the results of the multi-generation study and the developmental toxicity studies **classification for reproductive toxicity is not proposed**.

Comments received during public consultation

No comments were received during the public consultation for this endpoint.

Assessment and comparison with the classification criteria

Adverse effects on sexual function and fertility:
There were no epidemiological data to evaluate effects on sexual function and fertility.No specific information regarding effects on or via lactation was provided. No effects were observed in the 3-generation study; therefore no classification for adverse effects on sexual function and fertility is warranted.

Adverse effects on development:
There were no appropriate epidemiological studies available on developmental effects in humans. The developmental toxicity studies revealed only minimal effects on foetal ossification in rats and an increased incidence of a skeletal variation in rats (25^{th} pre-sacral vertebra) and rabbits (27^{th} pre-sacral vertebra) at maternal toxic dose levels. No evidence of teratogenicity was observed in either species. Hence, no classification for adverse effects on development is warranted.

RAC supports the conclusion of the DS that based on the results of reproductive toxicity studies in rats and rabbits, the substance **does not meet the criteria for classification for reproductive toxicity**.

Environmental hazard assessment

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

The DS proposed to classify the substance as Aquatic Acute 1 (H400) with an M-factor of 10 000 and Aquatic Chronic 1 (H410) with an M-factor of 10 000. The classification was based on the substance being not rapidly degradable, potential for bioaccumulation and very high toxicity in aquatic organisms. The lowest acute toxicity value was a 96 hour EC_{50} of 0.000053 mg/l for an invertebrate *Mysidopsis bahia* and the lowest chronic toxicity value was a 345 day NOEC of 0.00000397 mg/l for fish *Pimephales promelas*.

Degradation

Terflutrin hydrolysed slowly in water under environmental conditions. In a study using both [U-^{14}C]-phenyl-tefluthrin and [1-^{14}C]-cyclopropyl tefluthrin in sterile aqueous buffer solutions at pH 25 °C the substance was stable to hydrolysis at pH 5 and pH 7 throughout the 30 day test duration. At pH 9 hydrolysis products Compound 1a and Compound II were found at average levels of 34.6 % (([1-^{14}C]-cyclopropyl label) and 21.4 % ([U-^{14}C]-phenyl label) respectively after 30 days. Recovery of radioactivity was not always high assumably due to predominantly tefluthrin residues bound to glass.

In a photodegradation study following GLP terfluthin degraded with a DT_{50} > 31 days. The photolysis of both [U-^{14}C]-phenyl-tefluthrin and [1-^{14}C]-cyclopropyl tefluthrin was studied at 25° ± 1°C in aqueous solutions at pH7. Recoveries of radioactivity ranged from 92.0 to 105.5 %. There were no major photodegradation products other than trans-tefluthrin which is formed in amounts of between 21.2 and 37.2 % after 31 days irraditation. There were a significant amount, between 40.7 and 57.7 of applied radioactivity after 31 days, of volatile loss during the experiment.

There was no ready biodegradability test available.

Two water-sediment tests were available. The first water/sediment test was carried out according to a SETAC Guideline and GLP. Both [U-^{14}C]-phenyl-tefluthrin and [1-^{14}C]-cyclopropyl tefluthrin were applied to two water-sediment systems, Kromme Rijn and TNO Zuidpolder. The systems were incubated at 20 °C. Samples of both water and sediment were taken for analysis at 0, 7, 14, 28, 42, 56, 70 and 84 days after application. Recovery of radioactivity varied between 73 to 92 % of applied radioactivity (AR). This deviation from the test guideline is not considered to compromise the validity of the test. Tefluthrin rapidly dissipated from the aqueous phase by adsorption to sediment. Levels of degradation products in the water phase increased with time so that between 18 and 41 % of AR was present after 12 weeks. Compound 1a and Compound II were identified as degradation products in both systems. Compound IV was found to be the major degradation product in the water phase in both systems. Compound Ia was found at increasing levels up to 12 weeks after treatment predominantly in the water phase. Compound II was found at lower levels and was generally found at higher levels in the sediment rather than water. Other degradates for example Compounds III and V were present in small amounts. Mineralisation in both systems was little with the maximum of 6 % of $^{14}CO_2$ detected 12 weeks after application. The DT_{50}s calculated with ModelManager v1.1 are the following:

Table 1. Teflutrin DT_{50} values in two water-sediment systems

Water-Sediment System	Compartment	Simple Exponential Model
Kromme Rijn	Sediment	203
	Water-Sediment	146
TNO Zuidpolder	Sediment	204
	Water-Sediment	60

In the second water-sediment test performed according to the Canadian Trade Memorandum T-1-255 Guideline and GLP both [U-^{14}C]-phenyl-tefluthrin and [1-^{14}C]-cyclopropyl tefluthrin were applied to a water-sediment system. The systems were incubated at temperatures 20°C ± 2°C and 5°C ± 2°C. Both aerobic and anaerobic conditions were used. Organic matter content in the the sediment 20.3% exceeds the amount of 12.9% stated in the guideline which is, however, considered not to compromise the validity of the study. At 20 °C no major degradation products (>10 %) were found. Loss of teflutrin from the water phase to sediment and by volatile loss was rapid with the average of only 11% being found at 0 day after treatment (DAT) in the aerobic studies. Volatility was significant with level up to 20% (180 DAT) under aerobic conditions. The most abundant degradatation product, i.e. Compound V, reached a peak total of 8.5% in water and 6.6% in the sediment 30 DAT in aerobic conditions. Other degradation products in aerobic systems were Compound IV and unidentified metabolites M2 and M3. Mineralisation was significant under aerobic conditions reaching 48.6% 120 DAT for cyclopropyl label and 32.3 % for phenyl label. At the lower temperature of 5°C under aerobic conditions, dissipation of tefluthrin from the water to the sediment was less rapid and volatile losses were much reduced. Mineralisation was also much reduced: 21.5% for cyclopropyl label and only 4.1% for phenyl label. Levels of Compound IV reached 22.6% by 360 DAT whereas Compound V reached maximum levels of 7.9% in sediment and 2.7% in water 360 DAT.

Table 2. Teflutrin DT_{50} and DT_{90} values in a water-sediment system at 20 °C

	[1-^{14}C]-cyclopropyl label		[U-^{14}C]-phenyl label	
	DT50	**DT90**	**DT50**	**DT90**
Water-sediment	58 days	190 days	51 days	185 days
Sediment only	57 days	189 days	59 days	195 days

The DS concluded that tefluthrin is not rapidly degradable based on the information above.

Bioaccumulation

In the bioaccumulation study where bluegill sunfish (*Lepomis macrochirus*) were exposed to ^{14}C-methylene labelled tefluthrin (OECD TG 305E and GLP), a steady state BCF of 1400 L/kg ww (whole fish based on tefluthrin parent compound) was measured. Lipid normalization was not applied and no information on the lipid content of the test fish was included in the CLH Report. The measured log P_{ow} was 6.4 (20 °C). Thus tefluthrin can be considered as potentially bioaccumulative.

Aquatic toxicity

There were acute toxicity data available from two fish studies, two *Daphnia magna* studies, one *Mysidopsis bahia* study, one algae study and one *Chironomus* study. Chronic toxicity data was available from two fish studies, one *Daphnia magna* study, one algae study and one sediment *Chironomus* study.

Table 3. The lowest aquatic toxicity values for tefluthrin

Substance and purity	Species	Test Guideline	Endpoint	Toxicity value (mg/L)	Conditions
Tefluthrin 90.4 % w/w	Oncorhynchus mykiss	US EPA FIFRA Subdivision E, 72-1; OECD 203; GLP	96h LC50	0.00006	flow through, mm (33.8-49.7% of nominal)
Teflutrin 90.4 % w/w	Lepomis macrochirus	US EPA FIFRA Subdivision E, 72-1; OECD 203; GLP	96h LC50	0.00013	static, mm (35.4-50.7% of nominal)
Tefluthrin 94.4-95.0 %	Pimephales promelas	US EPA FIFRA Subdivision E, 72-4;	28d NOEC (length and	0.0000096	flow through, mm

w/w		OECD 210; GLP	weight, larval survival)		(46-72% of nominal)
^{14}C-tefluthrin 99%	**Pimephales promelas**	**US EPA FIFRA Subdivision E, 72-5, GLP**	**345 d NOEC (survival of F1 generation larvae 56 days post hatch)**	**0.00000397**	**full lifecycle test, flow through, mm (66-71% of nominal)**
Tefluthrin 99.1%	Daphnia magna	EPA-540/9-85-005, OECD Daphnia 14 day study, GLP	48h EC50 (immobility)	0.000064	static, mm (53-77% of the nominal)
^{14}C labelled terfluthrin 98.3%	Daphnia magna	US EPA -660/3-75-009, OECD 202, GLP	48h EC50 (immobility)	0.00007	static, mm (at the start ~80% and at the end ~20% of the nominal)
^{14}C-tefluthrin 98.5%	**Mysidopsis bahia**	**ASTM E729-80, GLP**	**96h EC50 (mortality)**	**0.000053**	**marine, flow through, mm (50-75% of nominal)**
^{14}-C-phenyl labelled tefluthrin, ≥95%	Daphnia magna	US EPA 540/9-86-141; OECD 202/Part II (1984), GLP	21d NOEC (offspring production, parental body length)	0.00000792	flow through, mm (35-47% of nominal)
Tefluthrin 93.0%	Pseudokirchneriella subcapitata	OECD 201, GLP	96h ErC50 96h NOEC	>1.05 0.51	static, mm (at the start 89-122% and at the end 2-28% of nominal)
Tefluthrin 91.9%	Chironomus riparius	OECD 202, GLP	48h EC50 (immobility)	0.0025	static, spiked water, mm (at the start 76-121% and at the end 8-22%)

mm = mean measured

The lowest acute toxicity value is for *Mysidopsis bahia* from a study carried out according to an ASTM Guideline and GLP. The nominal concentrations were 0.000010, 0.000018, 0.000032, 0.000056 and 0.0001 mg/L. Mean measured concentrations were 50 to 75 % of the nominal namely 0.000007, 0.000009, 0.000024, 0.000038 and 0.000073 mg/L. The 96-hour EC50 value for tefluthrin on the mysid shrimp *Mysidopsis bahia* was 0.000053 mg/L based on mean measured concentration. Two acute *Daphnia* study EC_{50}s were also in the range of 0.00001 mg/L < EC_{50} ≤ 0.0001 mg/L.

The lowest chronic toxicity value comes from a full lifecycle study with fathead minnow (*Pimephales promelas*) performed according to US EPA Guideline and GLP. The nominal concentration were 0.0000015, 0.000003, 0.000006, 0.000012 and 0.000024 mg/L. Actual test concentrations were measured regularly throughout the study. Mean measured concentration over the test period were 0.00000101, 0.00000200, 0.00000397, 0.00000802 and 0.0000171 mg/L that is from 66 to 71 % of the nominal. The overall NOEC value was 0.00000397 mg/L based on mean measured concentrations.The critical parameter was survival of F_1 generation larvae to 56 days post-hatch. Newly fertilised fathead minnow eggs exposed to maintained concentrations of tefluthrin in a freshwater flow-through test system through-out a complete life-cycle, resulted in a NOEC value of 0.00000397 mg tefluthin/L, based on mean measured concentrations. There

was, however, no significant effect on survival to 56 days post-hatch of F_0 generation larvae at 0.00000802 mg/L. The NOEC values from a 28 day *Pimephales promelas* study and a 21 day *Daphnia* study were in the same range namely 0.000001 < NOEC ≤ 0.00001 mg/L.

The 96 hour ErC_{50} value for algae was > 1.05 mg/L and the NOEC value 0.51mg/l based on mean measured concentrations. The concentrations tested (0.18, 0.32, 0.56, 1.8 mg/L as nominal) were all in excess of the solubility of the substance and undissolved substance might have caused physical effects. The mean measured concentrations at the start of the study ranged from 89-122 % of nominal; after 96 hours the measured concentrations ranged from 2 to 28 % of nominal. There was no clear concentration-related response in the growth reductions.

Comments received during public consultation

Three MSCAa agreed with the proposed classification. One MSCA asked for a short summary on the environmental distribution of the substance which was not included in the response to comments table.

Assessment and comparison with the classification criteria

The substance is not rapidly degradable and was stable to hydrolysis at pH 5 and pH 7 for 30 days. At pH 9 hydrolysis products Compound Ia and Compound II were found at average levels of 34.6 and 21.4 % respectively. There is no biodegradability test available. The DT_{50} values from the two available aerobic water/sediment tests in water-sediment system were in the range of 51 to 146 days.

Comparison with the classification criteria (BCF ≥ 500 and log K_{ow} ≥ 4) shows that the substance is potentially bioaccumulative based on a fish BCF of 1400, corroborated by a log K_{ow} of 6.4.

The lowest acute toxicity value is an EC50 of 0.000053 mg/l for the invertebrate *Mysidopsis bahia* which falling in the range of 0.00001 mg/L < $L(E)C_{50}$ ≤ 0.0001 mg/L results in an **Aquatic Acute 1 classification with an M-factor of 10 000**.

There is adequate chronic toxicity data available for all three trophic levels. The lowest chronic toxicity value is a NOEC of 0.00000397 mg/l for the fish *Pimephales promelas* which is in the range of 0.000001 mg/L < NOEC ≤ 0.00001 mg/L. As tefluthrin is not rapidly degradable the resulting classification is **Aquatic Chronic 1 with an M-factor of 10 000**.

ANNEXES:

Annex 1 Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in RAC boxes.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and by RAC (excl. confidential information).