Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

to the Opinion proposing harmonised classification and labelling at EU level of

oxathiapiprolin (ISO); 1-(4-{4-[5-(2,6-difluorophenyl)-4,5-dihydro-1,2-oxazol-3-yl]-1,3-thiazol-2-yl}piperidin-1-yl)-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone

EC Number: -
CAS Number: 1003318-67-9

CLH-O-0000001412-86-246/F

Adopted

30 November 2018

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON OXATHIAPIPROLIN (ISO); 1-(4-{4-[5-(2,6-DIFLUOROPHENYL)-4,5-DIHYDRO-1,2-OXAZOL-3-YL]-1,3-THIAZOL-2-YL}PIPERIDIN-1-YL)-2-[5-METHYL-3-(TRIFLUOROMETHYL)-1H-PYRAZOL-1-YL]ETHANONE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in the table below as submitted through the web form. Any attachments received are referred to in this table and listed underneath, or have been copied directly into the table.

All comments and attachments including confidential information received during the public consultation have been provided in full to the dossier submitter (Member State Competent Authority), the Committees and to the European Commission. Non-confidential attachments that have not been copied into the table directly are published after the public consultation and are also published together with the opinion (after adoption) on ECHA's website. Dossier submitters who are manufacturers, importers or downstream users, will only receive the comments and non-confidential attachments, and not the confidential information received from other parties.

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Substance name: oxathiapiprolin (ISO); 1-(4-{4-[5-(2,6-difluorophenyl)-4,5-dihydro-1,2-oxazol-3-yl]-1,3-thiazol-2-yl}piperidin-1-yl)-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone
EC number: -
CAS number: 1003318-67-9
Dossier submitter: Ireland

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
02.05.2018	Germany		MemberState	1
Comment received				
The German CA agrees with the proposed classification.				
Dossier Submitter's Response				
Noted. Thank you for your support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2018	Belgium		MemberState	2
Comment received				
HH : BE CA agrees not to classify oxathiapiprolin for acute toxicity, STOT SE, skin corrosion/irritation, eye damage/irritation, skin sensitization and germ cell mutagenicity.				
Dossier Submitter's Response				
Noted. Thank you for your support.				
RAC's response				
Noted.				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON OXATHIAPIPROLIN (ISO); 1-(4-{4-[5-(2,6-DIFLUOROPHENYL)-4,5-DIHYDRO-1,2-OXAZOL-3-YL]-1,3-THIAZOL-2-YL}PIPERIDIN-1-YL)-2-[5-METHYL-3-(TRIFLUOROMETHYL)-1H-PYRAZOL-1-YL]ETHANONE

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2018	Belgium		MemberState	3
Comment received				
One oral 2-year carcinogenicity study in rat and one 18-month oral carcinogenicity study in mouse were presented in the CLH report. In rat, pancreatic islet cell adenomas and carcinomas were reported in females. In mice, a low incidence of histiocytic sarcoma was observed. Both findings were of low incidence and within HCD. BE CA therefore consider that no classification is warranted.				
Dossier Submitter's Response				
Noted. Thank you for your support.				
RAC's response				
Noted.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
09.05.2018	Denmark		MemberState	4
Comment received				
It is of note that there is no evidence of target cell toxicity in the in vivo micronucleus (MN) test in mouse (unaffected PCE/NCE ratio) - and also none in a rat 14-day study (see updated DAR p. 85). Therefore, if there is no other evidence of bone marrow exposure in the tested species (e.g. from ADME data), the in vivo studies do not confirm that oxathiapiprolin is not genotoxic in vivo.				
Dossier Submitter's Response				
There is a rapid, but poor absorption (31 – 49%) within 10h using a low dose of 10 mg/kg bw in rats and absorption declines to 5.4 - 7.7% with a single high dose (200 mg/kg bw) due to saturation of the absorption process. Plasma 14C residue concentrations showed steady-state kinetics in male and female rats after multiple low dose administration. Systemic uptake and distribution of Oxathiapiprolin was evident based on the presence of quantifiable 14C residues in all the collected tissues. However, the percentage and concentration values were very low. Retention of oxathiapiprolin or its metabolites in tissues and blood was thus negligible indicating a very low potential for bioaccumulation. Bone marrow exposure is probable though the amount of exposure is limited. Results from the repeated dose toxicity studies indicate systemic availability with very low toxicity, liver effects and induced enzyme activity are demonstrated. The in-vivo micronucleus (MN) test in mouse was GLP and guideline compliant, it is negative for genotoxicity and there is no evidence to suggest it is un-suitable for assessment of the mutagenic potential of Oxathiapiprolin.				
RAC's response				
RAC takes note of your comment.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
09.05.2018	Denmark		MemberState	5

Comment received

A classification as Repr 2 may be considered based on the developmental findings of the 2-generation study. In a 2-generation study from 2013, doses of 0, 500, 1500, 6000 and 17000 ppm oxathiapiprolin was tested. In this study, a dose-dependent delay in preputial separation (PPS) was observed in males of both the P1 and the F1 litters without a concomitant reduced bodyweight (bw) and with no signs of maternal toxicity. The delay was statistically significant in the two highest dose groups with a delay in F1 males of 2.0 and 2.4 days at 6000 ppm and 17000 ppm, respectively, compared with controls. These males showed a dose-dependent increase in PPS bw that became statistically significant in the highest dose group (7.6% increase compared with control). In F2 males, PPS also showed a dose dependent delay compared with controls with an increase in time to achieve PPS of 1.6 and 2.4 days at 6000 ppm and 17000 ppm, respectively, of which the latter was statistically significantly increased. The values obtained in the two highest dosed groups were 45.4 days and 46.2 days, respectively, which were outside the HCD from the previous five-year period of the laboratory (range of means 42.7 to 44.6 days). As in the first generation, the bw of F2 males at the time of PPS was dose-dependently increased and was statistically significantly higher in the two highest dose groups compared with controls (+7.2% and +7.3% at 6000 ppm and 17000 ppm, respectively). Thus, there is no indication that the delay in PPS is due to a reduced bw of the males.
Pups of the F1 generation did show a statistically significant reduction in mean bw of 8.2% at the high dose (HD) group compared with controls, however, this mean was not given per sex and may cover a sex-specific reduction. Randomly selected F2 males was kept alive for 60 days and these HD males did not show a statistically significant reduction in bw from day 0 (i.e from day of weaning, see table 37 p. 125 of the study report), however, their mean bw was 5.6% lower than that of the control group.
The delay in PPS was considered treatment-related and adverse in the study report (as was the reduced pup mean bw at 17000 ppm in the second generation).
As adverse effects are observed in the timing of PPS in the absence of other toxic effects, a classification as Repr 2 seems appropriate. It may be considered if this is most appropriately covered by adversity on 'sexual function and fertility' or on 'development'. In the CLP regulation, adverse effects on onset of puberty is specifically mentioned under the heading of 'adversity on sexual function and fertility'
('Annex I: 3.7.1.3. Adverse effects on sexual function and fertility
Any effect of substances that has the potential to interfere with sexual function and fertility. This includes, but is not limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, (…) ') and a classification as Repr 2/H361f may seem the most appropriate.
However, the effect may also be considered as 'altered growth' during development of the offspring. From the study design it cannot be determined if the delay in PPS is 'induced during pregnancy, or as a result of parental exposure' or if it is induced by postnatal exposure via milk or via the diet eaten by the pups.
The possible classification of oxathiapiprolin as Repr 2 was discussed at the Pesticides Peer Review Meeting 137 (12 - 15 January 2016). The RMS did not support classification and at the meeting, the majority of experts considered that the degree of the effect on achieved PPS was not sufficient for classification. It was argued in the report from the meeting that classification was not required, citing part of the CLP: 'Classification is not necessarily the outcome in the case of minor developmental changes' the continuation of the sentence was, however, not included saying: 'when there is only a small reduction in

foetal/pup body weight or retardation of ossification when seen in association with maternal toxicity.' In the opinion of the DEPA, the delay in PPS is to be considered more severe than a change in bw or in ossification and moreover, the PPS delay was seen in the absence of maternal toxicity. In the second generation, the time for PPS was outside of the HCD and in the HD group, the delay was also higher than 1-2 days, a time of delay which was cited to be 'difficult to interpret with confidence' with reference to the paper by Ashby and Lefevre (2000): The peripubertal male rat assay as an alternative to the Hershberger castrated male rat assay for the detection of anti-androgens, oestrogens and metabolic modulators. J Appl Toxicol. 20(1):35-47.

It should be mentioned that in a range finding 1-generation study, slightly different results were obtained than in the 2-generation study. In the range finding study, oxathiapiprolin was tested at doses of 0, 2000, 10000 and 20000 ppm. A statistically significant delay in achievement of PPS of 3.1 days was observed in the F1 males fed 20000 ppm compared with controls. In this study, however, the delay was considered a result of the lower mean bw of HD male pups observed from PND4 onwards compared with that of the controls. The lower pre-weaning bw in males continued in the post-weaning period until necropsy. An ANCOVA analysis with bw at PND35 as covariate did not find a difference between the substance treated groups and controls when adjusted means for PPS was compared.
Even though the results of this study do not support the findings of the 2-generation study with respect to the delay in PPS, they are not of the same weight. The range finding study was based on fewer animals (10/sex/group) and had a shorter pre-mating exposure (28 days) compared with the 2-generation study as well as a slightly higher maximum dose. Overall, the DEPA therefore finds that a Repr 2 classification for oxathiapiprolin is relevant based on the PPS delay observed in the 2-generation study.

Dossier Submitter's Response
Please see comment 6.
RAC's response
RAC takes note of your comment.

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2018	Belgium		MemberState	6
Comment received				

Fertility :

The toxicity on fertility of oxathiapiprolin has been evaluated with a non-GLP one-generation reproductive toxicity study and a two-generation reproduction toxicity study in rat. Offspring body weights were decreased probably due to exposure during lactation.

In the one-generation study, markedly lower body weight gains were reported in the 20.000 ppm group F1, resulting in mean body weights up to 20% and 16,5% lower respectively in males and females. These effects on body weight are supposed to be the cause of slight development delays and prenuptial separation delay (approx. 3 days). We also notice that the offsprings NOAEL (10.000 ppm) due to the decrease in body weight gain in F1 pups is lower than parental NOAEL (20.000ppm).

In the multigeneration study, mean pup weights at 17.000/10.000 ppm in F1 litters were 8% lower than controls on PND21 (top dose, statistically significant). The F1 males in the

two highest doses were also reported to have a slight increase in the number of days to achieve prenuptial separation. This effect was observed in the two highest doses in the F2 generation. The significant increase in body weight post weaning at top dose also suggests that effects of oxathiapiprolin through milk might be considered for classification.
Taking into consideration the effects on body weight gains in pups, and their consequences on development (delay in growth and prenuptial separation), after exposure of pups to milk, BE CA is of the opinion that a lactation classification might be warranted.

Developmental toxicity :

Low dose up to 1000 mg/kg bw/day in OECD 414 TG studies in rat and rabbit. No observe effects neither in dams nor fetuses. No maternal toxicity is reported up to 1000 mg/kg bw/day (top dose), however, considering the absence of LD50 and adverse effects after repeated exposure, BE CA consider the studies as relevant. No classification is expected based on the available studies.

Dossier Submitter's Response

There is no clear evidence that the effects seen in offspring are due to substance transfer via milk and there is no evidence of the substance presence at toxic levels in milk. The effects of lack of weight gain and delayed preputial separation (PPS) occur during lactation however there is no good evidence that the effect is mediated by exposure to the substance in milk as required by 1272/2008.

The result from the single generation range finding study associated the delay in preputial separation (PPS) with lower pup body weights and this effect was replicated in the two generation study where body weight effects were seen but not to the same extent. The association between low body weight and delayed maturation is well established. The degree of effect and the very high concentrations (6000 and 17000ppm) do not support classification. We regard this delay as a minor developmental change likely mediated by low body weights seen at very high concentrations as concluded by the EFSA peer review.

No classification required.

RAC's response

RAC takes note of your comment.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
08.05.2018	Belgium		MemberState	7

Comment received

Observations in rat include increased cholesterol and triglycerides, CYP2B1 induction above 1300 mg/kg bw/day after 2-week oral gavage exposure.

In dog, and increase of 20-30% absolute and relative liver weight was reported at 352 and 1368 mg/kg bw/day after 28-day oral exposure and of 20-40% at 148 and 1242,2 mg/kg bw/day after 1-year exposure. Minimal increases in cholesterol were observed from 460 mg/kg bw/day. Based on these liver weight increases, the 28-day NOAEL was

set at 30 mg/kg bw/day and 13,6 mg/kg bw/day was chosen for the 1-year study. No histopathological adverse changes were reported. Based on the findings in rat and dog, the target-organ seems to be the liver. However, the effects are slight and above the range for classification. Therefore, no classification is warranted.
Dossier Submitter's Response
Noted. Thank you for your support.
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
03.04.2018	United Kingdom		MemberState	8
Comment received				
Oxathiapiprolin (ISO); (CAS 1003318-67-9) The Aquatic acute 1 classification is based on a single study – 48 hour EC50 of 0.67 mg/l (mm) for Daphnia magna (Minerhaut, Kendall, Gallagher and Krueger, 2011e). Given there wasn't a clear dose response curve and that effects were only observed at the highest treatment (0.78 mg/l) which reflects similar levels of solubility in other ecotoxicity tests, we wonder whether the observed effects were physical due to particles in the test media. Are there any microscopic observations or descriptions of the test media to consider this? We note that no effects (including mortality) were observed in the 21-day chronic toxicity to Daphnia magna study resulting in a 21 day NOEC of 0.75 mg/l (mm) which is above the quoted acute EC50. We note that the key chronic endpoint (32 day NOEC of 0.058 mg/l) is based on a US EPA Mysid Chronic Toxicity Test (OPPTS 850.1350) which is a 28-day protocol using juvenile mysids <24 hours old. For consistency with similar endpoints for other data sets, do you know why the study duration was extended and if a 28-day endpoint would be within the same classification range?				
Dossier Submitter's Response				
The original study report by *Minderhout et al.,* (2011) describes how each test solution was mixed by sonication for 30 minutes, and followed by stirring for approximately 2 hours. All test solutions appeared clear and colorless with no visible precipitate. The concentration of DMF in the solvent control and all oxathiapiprolin treatment groups was 0.1 ml/L. There were no further observations recorded for substance solubility. The 21 day NOEC of 0.75 mg/L from the chronic toxicity to *Daphnia magna* study is higher than the 48 hour EC50 of 0.67 mg/L from the acute 48 hour study. The only effect noted at levels lower than the 48 hour EC50 was a statistically significantly lower mean number of offspring produced per surviving female observed at a concentration of 0.24 mg/L compared to control. However, two higher test concentrations (0.45 and 0.75 mg/L) showed no statistical difference in the number of offspring in the chronic study. This is the available data, both studies were performed according to GLP and guidelines, no further information is available to explain these results.				

Table B.9.2.5-1 (DAR): Summary of effects following exposure of Daphnia magna to oxathiapiprolin for 21 days

Mean, measured oxathiapiprolin concentration (mg a.s./L)	Mean % adult survival [a,e,g]	First day of reproduction[b]	Mean total live young [c,g]	Mean total immobile young [d,f]	Mean adult length (mm) [e]	Mean adult dry weight (mg) [e]
Water Control (0.0)	85	7 to 8	291	0.29	5.0	1.12
Solvent Control (0.0)	80	7 to 8	280	0.063	5.1	1.07
0.057	100	7 to 8	281	0.10	5.1	0.99
0.12	80	7 to 8	300	0.00	5.0	1.03
0.24	70	7 to 9	245*	0.00	5.0	1.22
0.45	80	7 to 8	286	0.00	5.1	1.07
0.75	90	7 to 8	288	0.11	5.0	1.02

a Percent of adult daphnids alive at the end of the test.
b First day that reproduction was observed in each treatment group.
c Mean number of live young produced per surviving female.
d Mean number of immobile young produced per surviving female.
e There were no statistically significant differences in survival (Fisher's Exact test, $p > 0.05$), in mean total length (Bonferroni t-test, $p > 0.05$) or in mean dry weight (Dunnett's test, $p \leq 0.05$) from the pooled controls.
f The frequencies and the numbers of immobile neonates produced during the test were low; therefore, the statistical analysis of this endpoint was not performed.
g The 21-day EC_{50} value for adult immobility and the 21-day EC_{50} value for reproduction were both greater than 0.75 mg a.s./L, the highest mean, measured test concentration.
* Statistically significant reductions in reproduction (Dunnett's test, $p \leq 0.05$); however, it did not follow a dose responsive pattern.

With reference to the US EPA Mysid Chronic Toxicity Test (OPPTS 850.1350), the actual study length was 32 days (instead of the recommended duration of 28 days). This was described in the original study report as being at least seven days past the median time of first brood release for the negative and solvent controls (Day 22). ASTM E1191-03a describes in detail the culturing of mysids and test procedures. While not explicity explained in the *Claude et al.,* (2012) study, a complete life-cycle test is at least terminated when the last first-generation mysid dies. A test at 27°C should not be ended before 7 days after the median time for first brood release in the controls to allow for delays in brood release by mysids exposed to the test substance.

RAC's response

RAC agrees with the UK comments on the invertebrate studies. However, taking into account the DS responses, RAC considers that lacking more detailed information, the available data allow the proposed classification.

Date	Country	Organisation	Type of Organisation	Comment number
04.05.2018	France		MemberState	9
Comment received				
FR agrees with the classification and M factors (acute and chronic) proposals.				
Dossier Submitter's Response				
Noted and thank you for your support.				
RAC's response				
Noted				

Date	Country	Organisation	Type of Organisation	Comment number
09.05.2018	Finland		MemberState	10

Comment received

FI CA supports the conclusion that oxathiapiprolin is neither rapidly degradable or potentially bioaccumulative. On page 116 of the CLH proposal it is stated that oxathiapiprolin degrades in the environment under natural conditions ultimately forming CO2 and bound residues. However, according to simulation studies in the CLH proposal, there are no indication for ultimate degradation (mineralisation). According to CLP guidance (version 5.0) the substance is considered ultimately degraded with a half-life of < 16 days corresponding to a degradation of > 70 % within 28 days. Is there any information available that degradation of oxathiapiprolin (as recorded by CO2 reflecting mineralisation) did reach > 70 % in simulation studies and thus representing ultimate degradation?

The acute aquatic toxicity based on the lowest of the reliable toxicity values is between 0.1 and 1 mg/L. There are adequate information on long-term toxicity available for all trophic levels. The chronic aquatic toxicity based on the lowest of the reliable toxicity values is between 0.01 and 0.1 mg/L. On page 117 of the CLH proposal it is mentioned that "the chronic NOEC for the mysid shrimp (Americamysis bahia) resulted in a NOEC of 0.058 mg oxathiapiprolin/L, less than 1 mg/L the trigger value for classification as Chronic category 1 under the CLP regulation". The CLP classification criteria for category Chronic 1 is 0.1 mg/L for non-rapidly degradable substances.

Based on classification criteria FI CA supports the proposed environmental classification Aquatic Acute 1, H400 with M-factor of 1 and Aquatic Chronic 1, H410 with M-factor of 1 for oxathiapiprolin.

Dossier Submitter's Response

As a first step in biodegradation screening, the GLP and OECD 301B CO_2 evolution test by *Piriyadarsini*, (2013) was negative, oxathiapiprolin did not pass the test criteria for a readily biodegradable substance (OECD 301B: 60% $ThCO_2$ within a 10 day window of the 28 day test). The reference substance performed as expected while the toxicity control indicated inhibition of respiration by oxathiapiprolin. Result: not readily biodegradable.

Table 8.2.2.1-1 (DAR, 2016): Percent biodegradation of oxathiapiprolin.

Treatment (10 mg/L)	**Percent biodegradation levels**									
Day	**2**	**4**	**6**	**8**	**10**	**14**	**18**	**22**	**26**	**28/29**
Oxathiapiprolin	0	0	0	0.6	0.6	0.6	0.6	0.6	0.6	1.7
Sodium Benzoate	14.5	29	37	41	46	62	75	84	89	93.1
Oxathiapiprolin/ sodium benzoate	0.8	4.3	6.3	8.7	9.3	10	11	13	15	16

There was no second tier screening via an inherent biodegradation test (OECD 302 A-C).

The biotransformation of oxathiapiprolin was also studied in two aquatic sediment test systems under aerobic conditions (*Cleland, 2012,* GLP, OECD 308) which indicated biotransformation to a variety of transformation products but with little evidence for rapid degradability, the whole system DT_{50} resulting in a geomean of 70.3 days.

The biotransformation of oxathiapiprolin under aerobic conditions was studied in one surface water obtained from natural sources (*Wardrope, 2012*; GLP, OECD 309). The reference item was readily mineralized as (>90% (mean) in the surface water in all reference item flasks), confirming the validity of the system. Oxathiapiprolin did not mineralize significantly during the 60-day study (estimates ranged from 32-57%).

Overview:
(1) Effects on fish: in three acute fish toxicity studies using rainbow trout, bluegill sunfish and sheepshead minnow exposed to oxathiapiprolin for 96 hours under static conditions, the toxicity (LC50) exceeded the solubility limit of oxathiapiprolin in water (0.184 mg/L, 20°C, pH 7). Freshwater and marine fish species showed a similar sensitivity to oxathiapiprolin where the acute measured LC50 values were >0.65 to 0.72 mg/L (these values represented the highest mean measured concentrations tested, and were above the solubility limit for the active substance). The most sensitive chronic NOEC for freshwater fish (rainbow trout) was 0.46 mg/L and for marine fish (sheepshead minnow) is 0.34 mg/L.

(2) Effects on aquatic invertebrates: the most sensitive acute freshwater and marine species EC50 values were mean measured concentrations of 0.67 mg/L (*Daphnia magna*) and >0.33 mg/L (*Crassostrea virginica*), indicating that oxathiapiprolin is highly toxic to *daphnia* up to its limit of water solubility. The most sensitive chronic values were the 32 day NOEC = 0.058 mg/L for mysid shrimp (*Americamysis bahia*) and a 28 day NOEC = 0.11 mg/L in aqueous phase and 2.8 mg/kg sediment for sediment dwelling organisms (*Chironomus riparius*).

(3) Effects on algae and aquatic plants: the most sensitive ErC50 values for freshwater algae (*Pseudokirchneriella subcapitata*) and aquatic plants (*Lemna gibba*) were >0.142 and >0.79 mg/L, respectively; the highest concentrations tested.

On the basis of the results provided, the most sensitive acute and chronic endpoints were the 48 h EC50 = 0.67 mg/L for *Daphnia magna* and 32 day NOEC = 0.058 mg/L for mysid shrimp, in the fresh water and marine environments respectively.

There is a typo on page 117, the MS is quite correct, the chronic category 1 hazard criteria for a non rapidly degradable substance is ≤ 0.1 mg/L. The sentence should read: "The chronic NOEC (28 day) for the mysid shrimp (*Americamysis bahia*) was 0.058 mg oxathiapiprolin/L, less than the 0.1 mg/L trigger value for classification as Chronic category 1 under the CLP regulation".

RAC's response
RAC noted the DS clarification to the MS observations

Date	Country	Organisation	Type of Organisation	Comment number
02.05.2018	Germany		MemberState	11
Comment received				
Page 63, table 28 (summary of relevant information on degradation): According to the DAR Vol 3 CA B8 (page 218, B.8.1.1.2.4 Summary of Lab and Field soil degradation kinetics) the normalized DT50 values for Oxathiapiprolin in field studies range from 31.5–104 days in the soil degradation studies conducted in Europe and from 52.8–138.5 days				

in the soil dissipation studies conducted in the USA and Canada. Please clarify the differences.

Page 72ff (5.2.1 Adsorption/Desorption), tables with different adsorption parameters: Please clarify whether "Average" means geometric mean, arithmetic mean or median.

Page 76ff, table 30 (summary of relevant information on aquatic toxicity):
For the studies with marine (Skeletonema costatum) and freshwater diatom (Navicula pelliculosa), with green (Pseudokirchneriella subcapitata) and blue-green algae (Anabaena flos-aquae) and with duckweed (Lemna gibba) the NOEC values should be added as relevant endpoints for chronic classification.

Additionally the mean measured concentrations should be given instead of the nominal concentrations for the 7-day toxicity test with duckweed (Porch et al 2011).

Page 97ff, point 5.4.3 algae and aquatic plants:
The study with marine diatom (Skeletonema costatum) from Arnie et al 2013a does not fulfill the validity criteria (coefficient of variation of section by section specific growth rates of control < 35 %) for 72 and 96 hours and should only be given as additional information.
The study with freshwater diatom (Navicula pelliculosa) from Arnie et al 2013b does not fulfill the validity criteria (coefficient of variation of section by section specific growth rates of control < 35 %) for 96 hours, therefore only valid results of 72 hours should be used for classification.

Page 117, point comparison with criteria for environmental hazards:
At the last paragraph the NOEC value of 0.058 mg/L (Americamysis bahia) is compared with the trigger value of 1 mg/L instead of 0.1 mg/L for classification as Aquatic Chronic 1.

Dossier Submitter's Response

(1) Page 66, last two rows of table 28 (summary of relevant information on degradation): Unable to clarify the figures reported in the CLH report vs those reported in the DAR. The values reported for Normalised DT50 should be those reported in the DAR in section B.8.1.1.2.4 under Oxathiapiprolin, field studies:

EU studies: normalized DT50 values in field studies range from 31.5–104 days.
North America: normalized DT50 values in field studies range from 52.8–138.5 days.

(2) Page 72ff (5.2.1 Adsorption/Desorption), tables with different adsorption parameters: "Average" means arithmetic mean.

(3) Page 76ff, table 30 (summary of relevant information on aquatic toxicity). Noted.

(4) Additionally the mean measured concentrations should be given instead of the nominal concentrations for the 7-day toxicity test with duckweed (Porch et al 2011). Noted.

(5) Page 97ff, point 5.4.3 algae and aquatic plants. Noted.

(6) Page 117, point comparison with criteria for environmental hazards:

At the last paragraph the NOEC value of 0.058 mg/L (Americamysis bahia) is compared with the trigger value of 1 mg/L instead of 0.1 mg/L for classification as Aquatic Chronic 1. Typo, noted and agreed, see comment 10.
RAC's response
RAC noted the DS clarification to the MS observations