Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

trifloxystrobin (ISO); methyl (*E*)-methoxyimino-{(*E*)-α-[1-(α,α,α-trifluoro-*m*-tolyl)ethylideneaminooxy]-*o*-tolyl}acetate

EC Number: -
CAS Number: 141517-21-7

CLH-O-0000001412-86-293/F

Adopted

20 September 2019

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON TRIFLOXYSTROBIN (ISO); METHYL (*E*)-METHOXYIMINO-{(*E*)-A-[1-(A,A,A-TRIFLUORO-*M*-TOLYL)ETHYLIDENEAMINOOXY]-*O*-TOLYL}ACETATE

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: trifloxystrobin (ISO); methyl (*E*)-methoxyimino-{(*E*)-α-[1-(α,α,α-trifluoro-*m*-tolyl)ethylideneaminooxy]-*o*-tolyl}acetate
EC number: -
CAS number: 141517-21-7
Dossier submitter: United Kingdom

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	France		MemberState	1
Comment received				
FR: The minimum purity of the active substance according to the RAR of the substance is 980g/kg not 975g/kg (page 1) FR: The CA name of the substance is missing. The CA name is Methyl (αE)-α-(methoxyimino)-2-[[[[(1E)-1-[3 (trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl]benzeneacetate (page 1 FR: p.4: Table 7: For the following hazard classes – explosives, flammable solids, oxidizing solids – it should be better to indicate in the column reason for no classification, "data conclusive but not sufficient for classification" rather than "hazard class not assessed in this dossier" as data are available in RAR of the substance.				
Dossier Submitter's Response				
Thank you for the comments. According to COMMISSION IMPLEMENTING REGULATION (EU) 2018/1060 of 26 July 2018, Annex I: "Purity ≥ 975 g/kg". This is a targeted proposal which only addresses the following hazard classes: reproductive toxicity and hazardous to the aquatic environment. Data on repeated dose toxicity are also included in this dossier to assist the assessment of reproductive toxicity; however, the STOT RE end-point is not assessed. It is our understanding that Table 7 should reflect the end points that are assessed in the CLH proposal. Therefore, we think that "hazard class not assessed in this dossier" is appropriate. "Data conclusive but not sufficient for classification"				

suggests to the reader that we (the dossier submitter) have assessed the available data for these end points and come to a conclusion on the classification. However, this is not the case.
RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Germany		MemberState	2
Comment received				
We agree with the proposal of classification for environmental hazards as Aquatic acute 1 (H400), Aquatic chronic 1 (H410) and chronic M-factor of 10. We would propose to change the acute M-factor to 100.				
Dossier Submitter's Response				
Thank you for the comment – see response to comment 9.				
RAC's response				
Noted. See response to comment no. 9.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Germany	Bayer AG	Company-Manufacturer	3
Comment received				
Bayer asked an independent expert to re-evaluate the sternebral findings based on photographs recently taken from skeletal preparations from the original rabbit developmental toxicity study with trifloxystrobin. This re-evaluation is submitted herewith ("Re-evaluation of sternebral fusions in the Trifloxystrobin Rabbit Development Toxicity Study"). It confirms that the findings under discussion should not trigger classification for reproductive toxicity. ECHA note – An attachment was submitted with the comment above. Refer to public attachment M-651270-01-1_sanitised.zip ECHA note – An attachment was submitted with the comment above. Refer to confidential attachment M-651270-01-1.zip				
Dossier Submitter's Response				
Thank you for the expert opinion and support.				
RAC's response				
Based on a weight-of-evidence assessment, and taking into account the re-evaluation of the sternebral findings as provided by you, RAC is of the opinion that the sternebral findings in rabbits do not present sufficient evidence for classification.				

Date	Country	Organisation	Type of Organisation	Comment number
27.02.2019	Sweden		MemberState	4
Comment received				
Reproductive toxicity: We agree that it is difficult to assess whether the reduced bodyweights observed in pups from all generations from LD 7 and onwards is a direct effect following lactational transfer or due to test substance intake via food and/or an effect following malnutrition (reduced bodyweights of the dams). Considering that palatability				

seems to be part of the reduced food intake observed at least in adult animals (dams), we are not convinced that test substance intake via food is the sole explanation for the bodyweight effects in pups observed at LD 14 and 21. Nevertheless, it does not explain the effects observed on day 7. However, in the absence of information regarding the presence of trifloxystrobin in milk we do not think there is sufficient evidence linking effects to lactation and criteria are thus not considered fulfilled.
Dossier Submitter's Response
Thank you for the comments and support.
RAC's response
You are correct that, in absence of data on transfer into milk or on quality of the milk, the available data do not allow directly linking the effect to lactation. However, other explanations for the effect on pup bw development (like it being a direct effect from pups consuming treated diet (or avoiding it, because of palatability reasons), or it being a secondary effect of maternal toxicity) can be discarded in the case of trifloxystrobin. So, the most plausible explanation is that the effect is caused through the milk, given the log P_{ow} and the fact that it partly occurred during a time period where milk is the only nutrition source for pups. With consistency seen over two generations, two studies and two sexes, RAC therefore considers classification for effects on or via lactation (Lact.; H362) justified.

Date	Country	Organisation	Type of Organisation	Comment number
19.02.2019	Netherlands		MemberState	5
Comment received				
Based on the data currently available for Trifloxystrobin, the Netherlands CA agrees with 1) the 'no classification' for effects on sexual function and fertility, 2) the ' no classification' for effects on development and 3) the 'no classification' for effects on/via lactation. Though the presented rat repeated dose toxicity studies did not reveal adverse effects on the reproductive organs, it is noted that some of the repeated dose studies as mentioned in the EFSA peer review (dog and mice) have not been included in current CLH dossier.				
Dossier Submitter's Response				
Thank you for the comment. The full repeated dose data set was not included in the CLH report as repeated dose data was only included as supporting information; the end point itself was not assessed. Adverse effects on sexual function and fertility were only investigated in rats, hence repeated dose data on rats was included. In case it is helpful, please find attached "Confidential document 1 – repeated dose data – trifloxystrobin" which contains the study summaries taken from the RAR for the repeated dose toxicity studies conducted in mice and dogs. Our assessment is that there were no significant adverse effects on the reproductive organs in these studies.				
RAC's response				
1) RAC agrees that the data available do not warrant classification for effects on fertility and sexual function, but notes that the available 2-generation study may not fully inform on this endpoint. 2) RAC supports 'no classification' for developmental toxicity. 3) Please see response to comment no. 4.				

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	France		MemberState	6

Comment received

FR:
- Toxicity for fertility
10.10.3 Comparison with CLP criteria
It is agreed that classification for fertility is not triggered.

- Developmental toxicity
10.10.6 Comparison with CLP criteria
Fused sternebra is categorized as a grey zone anomaly according to DevTox.
Considering the incidences of fused sternebra and asymmetric shaped sternebra exceeding the ranges of historical control data (on a foetus and/or litter basis), Classification repr. Cat2 H361d may be warranted.

- Toxicity on or via lactation
10.10.9 Comparison with CLP criteria
The bridging of the level of trifloxystrobin observed in ruminants to rat and human (omnivorous species) is debatable and no data are available on the quality or quantity of milk produced by the mothers in the rat 2-generation study. Trifloxystrobin has a log POW of 4.5, suggesting that it may have some potential for transfer to milk.
For the above mentioned considerations, it cannot be ruled out that the reduced pup body weights from PND14 in the F1a and F1b pups, and from PND7 in the F2 pups observed from the mid-dose is related to lactation.

Classification lact. H362 is considered warranted.

Dossier Submitter's Response

- Toxicity for fertility
Thank you for the comments and support.

- Developmental toxicity
We agree that DevTox identifies these as 'grey zone' findings. However, "skeletal and visceral grey zone anomalies can be upgraded (to malformations) or downgraded (to variations) depending on their severities" (Solecki et al., 2013, M-612514-01-1, see "Non-confidential document 2 - Solecki et al 2013 – trifloxystrobin"). Re-evaluation of the sternebral findings by an independent expert based on photographs taken from skeletal preparations from the original rabbit study (see comment 3) provide additional information on the severity of the sternebral fusions. With the exception of the sterna classified as abnormal by the expert, the other sternebral findings appear to be considered small deviations from the normal situation at the end of the gestation period which are not considered to have long-term post-natal consequences. In line with Solecki et al, these sternebral findings could thus be downgraded to variations and would not support classification for developmental toxicity. Whilst is it not possible to predict the subsequent post-natal development of the abnormal sterna, we note that the independent expert concluded that there was no indication on GD 29 that the integrity of the rib cage and vertebral coumn had been affected by the abnormal sterna.

In addition, there were no other skeletal or visceral adverse changes and no increase in embryo-foetal deaths that could have masked an increase in foetal abnormalities. Sternebral findings occurred only at dose levels with considerable maternal toxicity. Skeletal

abnormalities were not observed in the rat developmental toxicity study up to the limit dose of 1000 mg/kg bw/day.

Overall, we do not think there is sufficient evidence of an adverse effect to warrant classification in Category 2, particulary when the maternal toxicity is taken into account.

- Toxicity on or via lactation
The cause of the reduced body weights in pups during the lactation period is not entirely clear. However, our interpretation of the CLP criteria and associated guidance is that there is insufficient evidence to support classification for effects on or via lactation.

RAC's response

- Toxicity for fertility
RAC agrees that the data available do not warrant classification for effects on fertility and sexual function, but notes that the available 2-generation study may not fully inform on this endpoint.

- Developmental toxicity
Based on a weight-of-evidence assessment, and taking into account the re-evaluation of the sternebral findings as provided by IND in comment no. 3, RAC is of the opinion that the sternebral findings in rabbits do not present sufficient evidence for classification.

- Toxicity on or via lactation
The available data unfortunately do not allow directly linking the effects to lactation. However, other explanations for the effect on pup bw development (like it being a direct effect from pups consuming treated diet (or avoiding it, because of palatability reasons), or it being a secondary effect of maternal toxicity) can be discarded in the case of trifloxystrobin. So, the most plausible explanation is that the effect is caused through the milk, given the log P_{ow} and the fact that it partly occurred during a time period where milk is the only nutrition source for pups. With consistency seen over two generations, two studies and two sexes, RAC therefore considers classification for effects on or via lactation (Lact.; H362) justified.

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Germany		MemberState	7

Comment received

For trifloxystrobin available data was considered conclusive but not sufficient for classification for reproductive toxicity by the DS.

Based on the finding of two grey zone (according to DevTox database) anomalies (enlarged thymus and fused and asymetric sternebrae) observed in two independent studies in rat and rabbit classification as Repr. 2 would be appropriate.

In the rat developmental toxicity study a significant increase of incidences of enlarged thymus was observed at the top dose (p56, CLH report, Annex I). It is proposed to add further information on the magnitude of enlargement of the thymus and the mechanism behind. Reported fetal and litter incidences were slightly outside the HCD, but only the range of the HCD was reported. Please report the HCD in more detail and add single data per study and mean values as well as more information (e.g. laboratory, date, used strain, supplier) as requested by Reg. 283/2013. To our knowledge the mean value of fetal incidence and litter incidence for enlarged thymus in the HCD is 0.7 % and 4.0 %,

respectively. Considering the mean instead of the provided range, the observed fetal incidence of 7.5 % and litter incidence of 31.8 % at the top dose are clearly outside the HCD. The finding enlarged thymus is not considered as variation by the MS.

In the rabbit developmental toxicity study increased incidences of skeletal findings (fused and asymetric shaped sternebrae) were observed, which were outside the HCD at the two top dose levels (fetal and/or litter incidence). Only the range of the HCD was presented (p23, CLH report) but also mean values should be reported. Please report the HCD in more detail and add single data per study and mean values as requested by Reg. 283/2013. To our knowledge the mean values of HCD for fetal incidences and litter incidences are: 1 % and 5.1 %, respectively, for fused sternebra 2 and 3, 2.7 % and 12.5 %, respectively, for fused sternebra 3 and 4 and 2.7% and 12.5%, respectively, for fused sternebra 4 and 5. Considering the mean instead of the range, the skeletal findings are clearly outside the HCD. The DS regarded these findings as minor developmental changes in the presence of marked maternal toxicity. In our view, the effect of maternal toxicity is questionable as only slightly reduced body weights (up to 8 %, p 62, CLH report, Annex I) were observed for the dams at the two highest doses during treatment. This was associated with reduced food consumption during the treatment period, probably due to palatability reasons. Body weight gain during the treatment period was significantly reduced. Nevertheless, the MS is of the opinion that the skeletal findings cannot be explained by these changes in maternal body weights. The analysis of individual fetal data (p24, CLH report) confirmed the increase of incidences of partially fused and/or fused sternebrae as well as asymmetrically shaped sternebrae. These skeletal findings are considered as malformations by the MS.

As reported (p16, CLH report), marked decreases in offspring body weight during lactation were observed at the two highest dose levels in the rat multigeneration toxicity study. At 750 ppm, reductions in body weight were statistically significant from PND14 in F1 pups and from PND 7 in the F2. At 1500 ppm, a significant decrease was reported from PND4 on (F2 females). We disagree with the DS, that these effects are non-specific secondary effects of maternal toxicity as body weights of the dams during lactation were reduced to a minor extent only and the body weight gain was increased (p33, 34, CLH report, Annex I).

Furthermore it is unlikely that pup body weight reductions are due to consuming or avoiding treated diet during weaning - as proposed by the DS - as the effects were already observed when the pups were breast-fed only. In addition, eye opening was delayed and therefore also the start of diet consumption. While for lactating goats and cows no transfer of trifloxystrobin or its metabolites to milk was shown, no information regarding rats exists. Although an effect of trifloxystrobin treatment on the quantity or quality of milk cannot be excluded, direct evidence for an adverse effect via lactation is missing and therefore the available data seem not sufficient for classification as Lact. - H362.

Dossier Submitter's Response

Developmental toxicity

Enlarged thymus:

The applicant has provided Historical Control Data for Fetal Visceral Findings, CGA 279202: Rat Oral Teratogenicity, Test Number 943042, supplement date December 20, 1999, Bayer reference number: M-039420-02-1 consists of 22 studies (31 control groups, 725 litters with 4793 live fetuses) performed during (1988–1994) with Tif:RAI f (SPF) rats – please see "Confidential document 2 - historical control data - rat – thymus - trifloxystrobin".

According to the applicant, enlarged thymus was first reported in this laboratory in 1991/1992 studies and was mainly categorized as an anomaly. From mid-1992 onwards this finding occurred regularly in the developmental toxicity studies and was categorized as variation based on the classification criteria of fetal observations provided in the study report:

Malformation:	**Very rare, permanent structural change that may adversely affect fetal survival, development or function.**
Anomaly:	**Rare, slight to moderate, permanent or reversible structural change that is not considered to impair fetal survival, development or function.**
Variation:	**Relatively frequent, transient structural deviation from normal development that is considered not to have any detrimental effect on fetal survival, development or function. Variations occur regularly in control fetuses.**
Incidental:	**Finding of no biological relevance, e.g. due to processing (hemorrhage, mottled lung).**

These criteria are in line with the definitions on malformation and variation as agreed upon during the second Berlin workshop in 1998 (Chahoud et al., 1999, M-610139-01-1, see "Non-confidential document 1 - Chahoud et al 1999 – trifloxystrobin").

Overall means were calculated on the basis of the total number of live fetuses and total number of litters.

Enlarged thymus	Fetal incidence (%)				Litter incidence (%)			
	overall		by group		overall		by group	
Category	N	mean	Min.	Max.	N	mean	Min.	Max.
Anomaly	13	0.3	0.0	1.4	13	1.8	0.0	9.5
Variation	32	0.7	0.0	6.0	29	4.0	0.0	29.2

Historical data of enlarged thymus per study

Study number	Dosing start	Category A / V	Fetuses eval.	Litter eval.	Fetus(es) affected	Litter(s) affected	Fetal incidence (%)	Litter incidence (%)
258801	02.02.1988				0	0	-	-
880008	26.07.1988				0	0	-	-
880009	01.11.1988				0	0	-	-
890004	01.02.1989				0	0	-	-
901262	08.01.1991				0	0	-	-
901265	04.02.1991				0	0	-	-
915002	09.04.1991				0	0	-	-
911126	04.06.1991	A	162	23	1	1	0.6	4.3
911035	25.06.1991	A	160	22	1	1	0.6	4.5
901484	30.07.1991	V	146	23	4	4	2.7	17.4
910020	12.11.1991	A	164 143 152 138	24 23 22 21	2 1 2 2	2 1 2 2	1.2 0.7 1.3 1.4	8.3 4.3 9.1 9.5
911345	07.01.1992	A	306	45	3	3	1.0	6.7
911351	07.04.1992	A	129	21	1	1	0.8	4.8
921048	02.06.1992				0	0	-	-

924079	04.08.1992	V	134	23	2	2	1.5	8.7
922821	25.08.1992	V	156	23	2	2	1.3	8.7
922846	18.11.1992	V	167	24	1	1	0.6	4.2
923139	07.04.1993	V	161	24	4	4	2.5	16.7
923166	02.03.1993	V	154	24	3	3	1.9	12.5
931108	14.09.1993	V	168	24	10	7	6.0	29.2
933177	22.02.1994	V	148	22	4	4	2.7	18.2
943001	15.03.1994	V	162	24	2	2	1.2	8.3

A = anomaly, V = variation

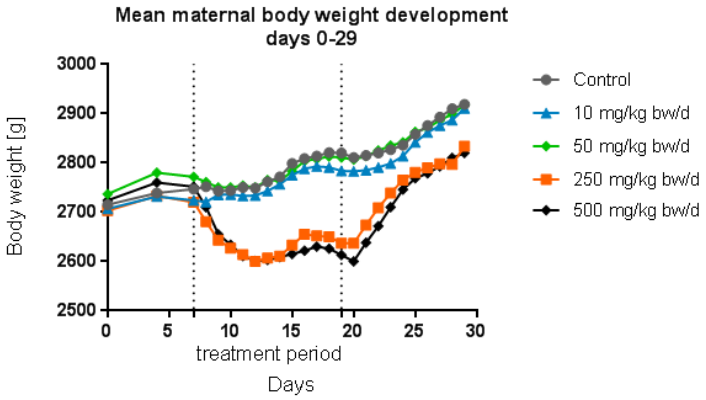
According to the applicant, the term "enlarged thymus" used in the study report is not based on an exact size measurement but is a subjective description by the technician/study director. The categorization of the finding "enlarged thymus" as a variation is based on the criteria of fetal observations provided in the study report (please see above for details). This indicates that the study director considered the finding as reversible and relatively frequent finding in the rat strain. Therefore, the finding is not considered to have any adverse effect on fetal survival or post-natal development. If the finding "enlarged thymus" was a permanent structural change it would have been observed during macro- or microscopic examination in the 2-generation reproductive toxicity study. However, in the 2-generation reproductive toxicity study conducted with trifloxystrobin in the same rat strain and in the same laboratory, the results of the macroscopic and microscopic examination showed no treatment related thymic lesions. Overall, the finding of enlarged thymus in the rat developmental toxicity study is not considered to support classification.

Skeletal findings (rabbit developmental toxicity study)

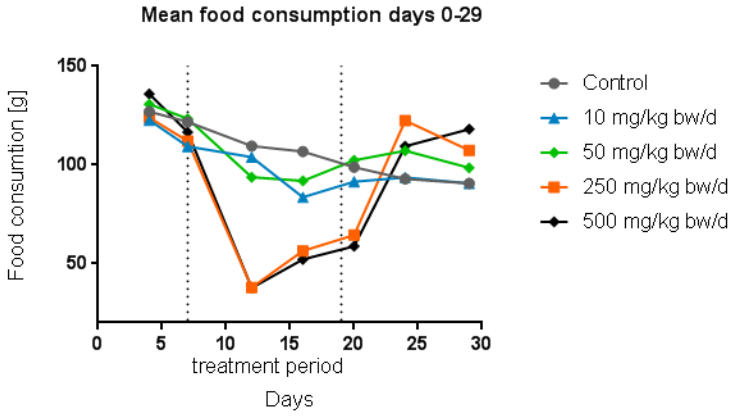
The requested general information on historical control data (strain, laboratory, study list and conduct etc.) is already included in the CLH report Appendix 1, pages 73-76. The applicants have provided single data per study which can be found in "Confidential document 3 - historical control data - rabbit - skeletal findings – trifloxystrobin" (see pages 53-57, 65-69, 77-81).

Maternal toxicity (rabbit developmental toxicity study)

The figure below (rabbit developmental toxicity study) demonstrates that the dams of the two highest dose groups had significant body weight losses compared to control dams during the treatment period resulting in a reduced body weight gain from day 7-20 of -130% and -238% of control at 250 mg/kg bw/d and 500 mg/kg bw/d, respectively. This severe weight loss is indicative of a marked maternal toxicity.



Palatability can affect food consumption when the test substance is applied via the diet. However, in the rabbit developmental toxicity study, the test substance was administered via gavage. Therefore palatability reasons (not mentioned in the context of the developmental toxicity studies in the CLH report, Annex I) cannot explain the effects on food consumption observed in this study. Food consumption of the actual study as illustrated in the following figure is significantly reduced by more than 50% during the treatment period (see CLH report, Annex I, page 63).



Fused sternebra (rabbit developmental toxicity study)
Fused sternebra is categorized as a grey zone anomaly according to DevTox. However, "skeletal and visceral grey zone anomalies can be upgraded (to malformations) or downgraded (to variations) depending on their severities" (Solecki et al, 2013, M-612514-01-1 – see "Non-confidential document 2 – Solecki et al 2013 – trifloxystrobin"). Re-evaluation of the sternebral findings by an independent expert (see comment 3) based on photographs taken from skeletal preparations from the original rabbit study provide additional information on the severity of the sternebral fusions (see response to comment 6).
Sternebral findings occurred only at dose levels with considerable maternal toxicity, and skeletal abnormalities were not observed in the rat developmental toxicity study up to the limit dose of 1000 mg/kg bw/day. Overall, we conclude that the data do not support classification for developmental toxicity.

<u>Effects on or via lactation</u>
Thank you for the comments and support. The cause of the reduced body weights in pups during the lactation period is not entirely clear. However, our interpretation of the CLP criteria and associated guidance is that there is insufficient evidence to support classification

for effects on or via lactation.
RAC's response
- Developmental toxicity Considering that *enlarged thymus* is a relatively frequent finding in the rat strain studied, that the increase in incidence was relatively small and occurred only at the limit dose of 1 000 mg/kg bw/d which was maternally toxic (32 % lower net weight change over GD6-21 as compared to controls), that no thymic lesions were observed in the 2-generation study and that thymus was not a target organ in other repeated dose toxicity studies, RAC is of the opinion that it does not provide sufficient evidence for classification. Based on a weight-of-evidence assessment, and taking into account the re-evaluation of the sternebral findings as provided by IND in comment no. 3, RAC is of the opinion that the *sternebral findings* in rabbits do not present sufficient evidence for classification. - Toxicity on or via lactation See response to comment no. 4.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	France		MemberState	8
Comment received				
FR agrees with the proposal of classification for environmental hazards and the proposals of acute and chronic M factors.				
Dossier Submitter's Response				
Thank you for the comments and support.				
RAC's response				
Noted, but based on comment no. 9 the acute M-factor becomes 100.				

Date	Country	Organisation	Type of Organisation	Comment number
01.03.2019	Germany		MemberState	9
Comment received				
Page 58, point 11.4.2 Acute (short term) toxicity to aquatic invertebrates: There are additional acute data available for trifloxystrobin with the marine invertebrate species Mysidopsis bahia (Boeri, R.L. 1996). These data (report KCA 8.2.4.2/01) were provided at DAR Volume3, B.9 (2017). The study fulfils validity criteria and is considered acceptable and suitable for classification purposes. The lowest LC50 (96 hours) is 0.00862 mg/l (mean measured). In general, both freshwater and marine species toxicity data are considered suitable for use in classification provided the test methods used are equivalent (regulation EC No. 286/2011). Page 62, point 11.6. Comparison with the CLP-criteria for acute aquatic hazard: The lowest acute LC50 (96 hours) is 0.00862 mg/l (mean measured) for Mysidopsis bahia. This result would confirm an acute M-factor of 100, instead of 10 based on acute endpoints in the range of 0.01 to 0.1 mg/L.				

Dossier Submitter's Response
Thank you for your comments. The study with the marine invertebrate species Mysidopsis bahia (Boeri, R.L. 1996), was evaluated during the Annex I renewal process for Trifloxystrobin. The Rapporteur Member State concluded: "Therefore, as a reliable toxicity endpoint could not be derived for this study, the RMS considers that it is not suitable for use in the risk assessment" (see page 113 of dRAR Vol 3 B.9 (AS) dated July 2017). As a consequence, this study is not part of the List of Endpoints as published by EFSA in September 2017 in the course of the peer review of the pesticide risk assessment of the active substance Trifloxystrobin. According to this evaluation, the study endpoint is not reliable consequently it should not be used for classification purposes (and the acute M-factor should be 10). However, upon further consideration, the (Boeri 1996) study was conducted to GLP, following US FIFRA guideline 72-3 and the study validity criteria were met. The study reported a 96-hour LC50 of 0.00862 mg/l (based on mean measured concentrations). For the purpose of hazard classification, the endpoint can be considered reliable. We note that RAC has previously considered 96-hour LC50 endpoints for Mysids relevant for hazard classification. Considering the endpoint is in the range 0.001 to 0.01 mg/l, we agree that an acute M-factor of 100 is appropriate.
RAC's response
RAC agrees with the DS proposal on inclusion of the Boeri 1996 study, resulting in an acute M-factor of 100.

PUBLIC ATTACHMENTS

1. M-651270-01-1_sanitised.zip [Please refer to comment No. 3]
2. Non-confidential document 1 - Chahoud et al 1999 – trifloxystrobin
3. Non-confidential document 2 - Solecki et al 2013 - trifloxystrobin

CONFIDENTIAL ATTACHMENTS

1. M-651270-01-1.zip [Please refer to comment No. 3]
2. Confidential document 1 - repeated dose data – trifloxystrobin
3. Confidential document 2 - historical control data - rat - thymus – trifloxystrobin
4. Confidential document 3 - historical control data - rabbit - skeletal findings - trifloxystrobin