



**Committee for Risk Assessment
RAC**

Annex 2
Response to comments document (RCOM)
to the Opinion proposing harmonised classification and
labelling at EU level of

Fenpyrazamine

**EC number: -
CAS number: 473798-59-3**

CLH-O-0000001412-86-55/F

**Adopted
12 March 2015**

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON FENPYRAZAMINE (ISO)

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during public consultation are made available in this table as submitted by the webform. Please note that some attachments received may have been copied in the table below. The attachments received have been provided in full to the dossier submitter and RAC.

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Substance name: Fenpyrazamine (ISO); S-allyl 5-amino-2-isopropyl-4-(2-methylphenyl)-3-oxo-2,3-dihydropyrazole-1-carbothioate

CAS number: 473798-59-3

EC number: -

Dossier submitter: Austria

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
21/08/2014	Denmark		MemberState	1
Comment received				
DEPA agrees with the proposal for the change of classification from Austria regarding the active substance Fenpyrazamine. No further comments.				
Dossier Submitter's Response				
AT: Noted				
RAC's response				
<p>RAC notes that there are reliable acute and chronic aquatic toxicity data for fish, aquatic invertebrates and algae. The marine diatom <i>Skeletonema costatum</i> is the most sensitive species in both acute and chronic tests.</p> <p>Based on the available information, RAC is of the opinion that Fenpyrazamine should be classified as: Aquatic Acute 1 based on a 96-h E_rC_{50} of 0.034 mg/L for <i>S. costatum</i>. As this value is above 0.01 mg/L but \leq 0.1 mg/L, the acute M-factor is 10.</p> <p>Aquatic Chronic 1 based on a 96-h NOE_rC of 0.011 mg/L for <i>S. costatum</i>. As this value is above 0.01 mg/L but \leq 0.1 mg/L, and the substance is not rapidly degradable, the chronic M-factor is 1.</p> <p>RAC disagrees with the DS's proposed chronic M-factor of 10 based on a yield $NOEC$ of 0.0049 mg/L for <i>N. pelliculosa</i> based on the:</p> <ul style="list-style-type: none"> • <i>EFSA Panel on Plant Protection Products and their Residues guidance (PPR Scientific Opinion)</i> (in footnote to a table) that for algae: • "...Growth rate (r) is the preferred endpoint. Other, usually more sensitive endpoints, such as yield may also be used if growth rate endpoints are not provided..." • <i>EFSA Panel on Plant Protection Products and their Residues guidance</i> too (Section 7.2.6): • "...Growth rate is the preferred endpoint to be used, yield is only included for cases where specific regulatory requirements in some countries may need to be fulfilled..." • OECD guidelines for algae (<i>OECD guideline 201</i>) growth rate data points are preferred. OECD 201 highlights, values based on yield will be lower than those based on growth rate – this is the same for biomass. The PPR Panel recommends to preferably use growth rate endpoints when both growth rate and biomass endpoints are available. • Overall, RAC concluded that the 'yield' endpoint is so similar to 'biomass' that it could be impacted by test design in addition to test item toxicity. Therefore CLP and REACH guidance for growth rate endpoint preference instead of biomass based endpoints should be followed and 				

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“growth rate” used in preference to “yield”.

- The Guidance on the Application of the CLP Criteria v.4.0 (November 2013) is clearer in Annex section I.2.3.1 say the NOEC should preferably be based on growth. It explains why an ErC50 is preferable to an EbC50 and presumably the same reasoning would apply to the NOEC as an endpoint.
- The REACH guidance (*Guidance on information requirements and chemical safety assessment Chapter R.7b: Endpoint specific guidance R. 7.8.4.1 GUIDANCE OF SPECIFIC TEST TYPES FOR FRESHWATER SPECIES*) similarly focuses on use of ErC50 over EbC50 stating the reasons. It’s more specific for aquatic plants where it states “The ECx/NOEC should be related to growth rate”.

RAC considers that the yield end point (based on biomass measurement) suffers from similar statistical drawbacks as the biomass end point. The growth rate end point is therefore preferred when available. This is consistent with the EFSA PPR Guidance, OECD guidelines and CLP guidance.

Date	Country	Organisation	Type of Organisation	Comment number
22/08/2014	Germany		MemberState	2
Comment received				
The German CA supports the proposed environmental classification and labelling as Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410) and M-factor of 10 (acute) and 10 (chronic).				
Dossier Submitter’s Response				
AT: Noted				
RAC’s response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the aquatic environment

Date	Country	Organisation	Type of Organisation	Comment number
01/08/2014	Belgium		MemberState	3
Comment received				
Based on the results of the additional reported studies, we agree with a revision of the environmental classification.				
It is justified to classify fenpyrazamine as Aquatic Acute 1, H400 based on the results of the most sensitive species in the acute aquatic toxicity tests : algae <i>Skeletonema costatum</i> with a 72hErC50=0.0341mg/l (mm). A Macute of 10 should be attributed (0.01mg/l<LC50≤0.1 mg/l).				
We also agree to classify the substance as Aquatic chronic 1, H410. However we prefer to use a Mchronic = 1 (NRD and 0.01mg/l <NOEC ≤0.1 mg/l). Classification is indeed based on the high chronic toxicity of algae, but we consider <i>Skeletonema costatum</i> with a 96hNOEC=0.011mg/l based on growth rate as the most sensitive algae species tested instead of <i>Naviculla pelliculosa</i> with a 96hNOEC =0.0049mg/l based on cell density. The use of growth rate is preferred as endpoint for classification as it is test design independent. The 96hNOEC of <i>Naviculla pelliculosa</i> , based on growth rate = 0.074mg/l, which is less sensitive than the ErC50 for <i>Skeletonema costatum</i> .				
Dossier Submitter’s Response				
AT: Austria is of the opinion that in case of chronic classification based on a NOEC value both endpoints, growth rate and yield should be considered. According to the Regulation 286/2011 amending Regulation 1272/2008 the acute classification should be based on the E _r C ₅₀ which is explicitly mentioned in the regulation. However, for the chronic classification based on the NOEC no information is given on which endpoint should be used.				
RAC’s response				
RAC disagrees with the DS’s proposed chronic M-factor of 10 based on a yield NOEC of 0.0049 mg/L for <i>N. pelliculosa</i> based on the following:				

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- EFSA Panel on Plant Protection Products and their Residues guidance ([PPR Scientific Opinion](#)) (in footnote to a table) states that for algae:
- "...Growth rate (r) is the preferred endpoint. Other, usually more sensitive endpoints, such as yield may also be used if growth rate endpoints are not provided..."
- EFSA Panel on Plant Protection Products and their Residues guidance (Section 7.2.6):
- "...Growth rate is the preferred endpoint to be used, yield is only included for cases where specific regulatory requirements in some countries may need to be fulfilled..."
- The OECD test guideline for algae (*OECD TG 201*) states that growth rate data points are preferred. It highlights that values based on yield will be lower than those based on growth rate – this is the same for biomass. We note that the PPR Panel recommends to preferably use growth rate endpoints when both growth rate and biomass endpoints are available.
- *The Guidance on the Application of the CLP Criteria v.4.0* (November 2013) is clearer in *Annex section I.2.3.1*, which states that the NOEC should preferably be based on growth. It explains why an ErC50 is preferable to an EbC50 and presumably the same reasoning would apply to the NOEC as an endpoint.
- The REACH guidance (*Guidance on information requirements and chemical safety assessment Chapter R.7b: Endpoint specific guidance R. 7.8.4.1 GUIDANCE OF SPECIFIC TEST TYPES FOR FRESHWATER SPECIES*) similarly focuses on use of ErC50 over EbC50 stating the reasons. It is more specific for aquatic plants where it states "The ECx/NOEC should be related to growth rate".

Overall, RAC concludes that the 'yield' end point (based on biomass measurement) is likely to suffer from similar statistical drawbacks as the biomass end point. The growth rate end point is therefore preferred for both acute and chronic algal toxicity when available. This is consistent with the EFSA PPR Guidance, OECD guidelines, REACH and CLP guidance (although the latter document could be clarified to reflect this issue).

Date	Country	Organisation	Type of Organisation	Comment number
22/08/2014	Germany		MemberState	4
Comment received				
<p>Page 48 table 27: summary of relevant information on aquatic toxicity: Please add the relevant data for 1) freshwater blue-green alga <i>Anabaena flos-aquae</i> (Softcheck, K.A. 2010 Report No.: QNW-0058, Study No. 12709.6306) and for 2) sediment organism <i>Chironomus riparius</i> (Putt, A.E. 2009; Report No.: QNW-0034, Study No. 13048.6535)</p> <p>Page 80, point 5.4.4 other aquatic organisms (including sediment): There exist additional valid data for chironomides toxicity for Fenpyrazamine: Static study following OECD Guideline 219 with <i>Chironomus riparius</i> NOEC (28d) of 0.32 mg a.s./L nominal related to emergence rate (Putt, A.E. 2009; Report No.: QNW-0034, Study No. 13048.6535)</p> <p>Because marine aquatic invertebrates (<i>Americamysis bahia</i>) are the most sensitive species for Fenpyrazamine with NOEC(28d) of 0.024 mg a.s./L mean measured, the additional data have no influence on proposed classification and labelling of Fenpyrazamine.</p>				
Dossier Submitter's Response				
<p>AT: The study with the freshwater algae <i>Anabaena flos-aquae</i> was not included in the table because the study is not considered valid and should be used as additional information only.</p> <p>The study for sediment organism <i>Chironomus riparius</i> (Putt, A.E. 2009; Report No.: QNW-0034, Study No. 13048.6535) was included in the CLH report for the first submission of fenpyrazamine and was accidentally deleted in the CLH report for the new submission. We agree with Germany that the study summary should be included in the CLH report.</p>				

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RAC's response

As the additional information does not affect the classification, it has not been mentioned in the opinion.

Date	Country	Organisation	Type of Organisation	Comment number
22/08/2014	France		MemberState	5

Comment received

We agree with the classification proposal and with the acute M factor. The chronic M factor seems to be based on the NOECy from the study on *Navicula pelliculosa* (0.008 mg/L). To our opinion, as for EC50, the NOEC based on growth rate, when available for algae or aquatic plants, should be considered for classification purpose. Then, could you, please, confirm that the NOECy from the study on *Navicula pelliculosa* could be used for the chronic M factor proposal as a NOECr is also available in this study?

Dossier Submitter's Response

AT: The NOEC for growth rate and yield is 0.074 mg a.s./L and 0.0049 mg a.s./L, respectively. Austria is of the opinion that in case of chronic classification based on a NOEC value both endpoints, growth rate and yield should be considered. According to the Regulation 286/2011 amending Regulation 1272/2008 the acute classification should be based on the E_rC_{50} which is explicitly mentioned in the regulation. However, for the chronic classification based on the NOEC no information is given on which endpoint should be used.

RAC's response

See response to comment no. 1 and 3.