Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

pyroxsulam (ISO); *N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide

EC Number: -
CAS Number: 422556-08-9

CLH-O-0000001412-86-102/F

Adopted
10 March 2016

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

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: **pyroxsulam (ISO); *N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide**
EC number: **-**
CAS number: **422556-08-9**
Dossier submitter: **United Kingdom**

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	1
Comment received				
p15: Part B. 1.3 Table 8. Stability in organic solvents: Please note that data are available on solubility in organic solvents in the DAR of Pyroxsulam (in the Volume 3, Annex B2, point B.2.1 of the DAR, 2008 and of the updated DAR, 2012).				
Dossier Submitter's Response				
Thank you for your comments. We note that information on solubility in organic solvents is available in the DAR (as reference above). However, we are not able to update the CLH report at this stage.				
RAC's response				
Brief statement included in the opinion document under Physical Hazards.				

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	2
Comment received				
The German CA supports the proposed classification and labelling: Skin Sens 1 (H317), Aquatic acute 1 (H400), Aquatic chronic 1 (H410) and the acute/chronic M-factor of 100				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	3

Comment received

Point 4.10.1.1, page 38, Two year chronic toxicity/carcinogenicity and chronic neurotoxicity study in the rat

A higher incidence of large granular lymphocyte leukaemia is observed in male rats receiving 100 and 1000 mg/kg bw/d. While these increases are not statistically significant, it should be noted that the incidence in the two high dose groups is outside the historical control range of dietary or oral gavage toxicity studies performed in this laboratory both contemporaneously (studies initiated: 2002-2005) and in the past (studies initiated: 1992-1995).

Point 4.10.1.1, page 39, Eighteen month dietary oncogenicity study in the mouse

An increase in hepatocellular adenoma incidence is observed in males at all doses compared to the controls. There is also an increase in the incidence of carcinomas observed in top dose males.
While the increase in male liver carcinoma incidence at the top dose is not statistically significant, it should be noted that this incidence is higher than the laboratory historical control ranges, Furthermore, no mechanistic study has been provided.

Accordingly, a classification Carcinogenicity Category 2; H351 could be considered.

Dossier Submitter's Response

We note that the incidence of large granular lymphocyte leukaemia in male rats exceeded the historical control at 100 and 1000 mg/kg/day. However, this is somewhat confounded by the fact that the incidence in the concurrent control group also exceeded the historical control. It was noted in male rats only and there was no evidence of effects in relevant organs. Overall this increase is not considered to be treatment related. Please refer to the CLH report for our full rationale.

With regards to the mouse, an increase in hepatocellular adenomas was observed in all dose groups in males only. However, whilst the incidence exceeded the laboratory historical control in the low and high dose groups, it was within the historical control range at the mid dose. The increase in carcinoma was observed in male mice only at the top dose and, whilst this exceeded the laboratory historical control, it was within the control range available for Charles River Labs from studies conducted during the same time period. Please refer to the CLH report for the full rationale.

RAC's response

RAC is in agreement with the DS. The rat LGL leukaemia is not considered treatment related nor is this type of neoplasm in this particular strain of rat considered relevant for human hazard assessment in this case.
The mouse liver tumours present a borderline case at the highest tested dose of 1000 mg/kg bw/day. Extensive discussion is included in the opinion document where it is concluded that there is insufficient evidence to classify for carcinogenicity.

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	4
Comment received				
In agreement with the CLH report there is insufficient evidence to conclude that there is a treatment related carcinogenic effect of pyroxsulam. The proposal of no classification is supported (4.10.6 Conclusions on classification and labelling, page 409).				
Dossier Submitter's Response				
Thank you for your comments				
RAC's response				
Noted. RAC agrees with the DS and DE in the proposal for no classification for carcinogenicity.				

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	5
Comment received				
No comment.				
Dossier Submitter's Response				
Noted.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	6
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) the proposal of no classification is supported (4.9.6 Conclusions on classification and labelling, page 33).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
No classification supported.				

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	7
Comment received				
No comment.				
Dossier Submitter's Response				
Noted.				

RAC's response
Noted.

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	8
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) the proposal of no classification is supported (4.11.6 Conclusions on classification and labelling, page 44).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed. No classification supported.				

RESPIRATORY SENSITISATION

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	9
Comment received				
No comment.				
Dossier Submitter's Response				
Noted.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	10
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) the proposal of no classification is supported (4.6.2 Respiratory sensitization, page 24).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed, no classification.				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	11
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) the proposal of no classification is supported (4.2.5 Conclusions on classification and labelling, page 19).				

Dossier Submitter's Response
Thank you.
RAC's response
Agreed. No classification.

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	12
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) no classification is supported (4.5.5 Conclusions on classification and labelling, page 22).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed, no classification.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	13
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) the proposal of no classification is supported (4.4.2 Eye irritation, page 21).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed. No classification.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	Finland		MemberState	14
Comment received				
The Finnish CA supports the proposed classification and labelling as Skin Sens. 1; H317 for Pyroxsulam.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Agreed.				

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	15
Comment received				
Considering the relative high response (80%) after exposure to a high concentration (5%) observed in the Guinea-Pig maximisation study the classification for subcategory 1A cannot be excluded. According to the Guidance on the Application of the CLP Criteria (Annex I: 3.4.2.2.1.1) a classification as a Category 1 skin sensitiser should be preferred. Therefore a classification as a Category 1 skin sensitiser is supported (4.6.1 Skin				

sensitisation, page 23).
Dossier Submitter's Response
Thank you for your comment.
RAC's response
Agreed.

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	16
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) no classification is supported (4.3.3 Conclusions on classification and labelling, page 20).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	17
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) no classification is supported (4.8.3 Conclusions on classification and labelling of repeated dose toxicity findings relevant for classification as STOT RE, page 30).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Agreed. Classification is not supported based on comparison to the CLP criteria. No toxic effects of significance were observed below the guidance values for STOT-RE2 (and STOT-RE1).				

OTHER HAZARDS AND ENDPOINTS – Aspiration Hazard

Date	Country	Organisation	Type of Organisation	Comment number
31.07.2015	Germany		MemberState	18
Comment received				
In accordance with the EU-Peer Review (EFSA Journal 2013;11(4):3182) no classification is supported (4.6.2 Respiratory sensitisation, page 24).				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Pyroxsulam is a white, crystalline solid and not expected to present an aspiration hazard.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
28.07.2015	France		MemberState	19
Comment received				
We agree with the classification and the M factors proposed for Environmental hazards.				
Dossier Submitter's Response				
Thank you.				
RAC's response				
Noted.				