Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

Penthiopyrad (ISO); (*RS*)-*N*-[2-(1,3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl)pyrazole-4-carboxamide

EC Number: N.A.
CAS Number: 183675-82-3

CLH-O-0000001412-86-78/F

Adopted

4 December 2015

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON PENTHIOPYRAD (ISO),(RS)-N-[2-(1,3-DIMETHYLBUTYL)-3-THIENYL]-1-METHYL-3-(TRIFLUOROMETHYL)PYRAZOLE-4-CARBOXAMIDE

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 attachments including confidential documents received during the public consultation have been provided in full to the dossier submitter, to RAC members and to the Commission (after adoption of the RAC opinion). 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.

ECHA accepts no responsibility or liability for the content of this table.

Substance name: **Penthiopyrad (ISO); (*RS*)-*N*-[2-(1,3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl)pyrazole-4-carboxamide**

CAS number: **183675-82-3**

EC number: **-**

Dossier submitter: **United Kingdom**

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	1
Comment received				
Regarding SID and PC properties DE-MSCA proposes minor corrections: •In the reference substance data set for Penthiopyrad in the IUCLID file the name "1-methyl-N-[2-(4-methylpentan-2-yl)-3-thienyl]-3-(trifluoro methyl)-1H-pyrazole-4-carboxamide" is given as IUPAC name. The same name is given in table 4 in the CLH report concerning the substance identity. This information is differing from the IUPAC name given in the DAR (also attached in IUCLID section 13 under "Assessment Report Volume 3 Annex B Section B1: Identity"). In the DAR "(RS)-N-[2-(1,3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl)pyrazole-4-carboxamide" is given as IUPAC name. The information given in the reference substance data set and in the Draft CLH report should be amended accordingly. •In IUCLID section 1.2 some impurities are listed (flagged as confidential). For two of the stated impurities CAS names are given although there are no existing corresponding CAS entries. Therefore, both CAS names should be deleted. •In IUCLID section 4.7 one of the given endpoint study records includes an expert statement. In this endpoint study record under "Results and discussions" the partition coefficient is given as: log Pow = 3.9 at 20°C and pH 7. According to the corresponding information and explanations in the endpoint study record and referring to the result given in the CLH report the correct pH value is 5 and should be amended accordingly. •In IUCLID section 4.8 on water solubility one of the endpoint study records (titled "Solubility in organic solvents_Tognucci 1999") does not only cover the water solubility but also the solubility in organic solvents. The corresponding information on the solubility in organic solvents should be given in section 4.9 as well.				

•In Part B, section 1.2, table 5 of the CLH report the value "≥ 98 %" is given in column 1. In this column the name of the constituent of the substance should be stated instead. According to the information given in the IUCLID file the value "≥ 98 % w/w" corresponds to the concentration range of the constituent. Furthermore, the typical concentration should be given as well. •In Part B, section 1.3, table 8 of the CLH report it is stated that "OECD 105/EEC A.6 (method)" was used to determine the water solubility. No concrete method is stated, the corresponding information should be added. •In section 4.21 of the IUCLID file in the endpoint study record based on the study by Tognucci (1999) it is stated that the "Titrations were conducted at room temperature." This information should be added in Part B, section 1.3, table 8 of the CLH report.
Dossier Submitter's Response
Thank you for the comments. • We agree that the IUPAC name should be in line with that used in the DAR, but are unable to update the CLH report at this stage. • The CAS names have been removed from the IUCLID. • The log Pow should be 3.9 as currently reported. • As it is not necessary to complete the full IUCLID data set for the active substance the data on the solubility in organic solvents has not been copied to section 4.9. It forms part of the study reported in section 4.8. • We note the oversight but can not amend the table in the CLH report. • The method used was the flask method. We can not update the CLH report. • Again, thank you for the comment, but we can not update the CLH report at this stage.
RAC's response
Noted.

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	2
Comment received				
Long-term study in mice: Not agreed. In the long-term study in mice, increased incidence of hepatocellular adenoma and carcinoma was observed in males at 200 and 600 mg/kg bw/d Penthiopyrad compared to the concurrent control. Although, the number of adenoma was within HCD and the number of carcinoma (at 600 mg/kg bw/d) only slightly outside HCD, historical control data is not sufficient to contravene these findings, in general. Furthermore, if historical control data				

should be used as an argument against the assumption of a carcinogenic effect or classification, it must be taken into consideration that the carcinoma incidence in mice, although low, increased with dose.
In summary, the presented study in mice raises sufficient evidence for carcinogenic properties of Penthiopyrad, to classify it with Carc. 2 (H351). This would be in line with the recommendation of EFSA's Pesticides Peer Review Experts' Meeting 95 and the conclusion of EFSA's peer review.

Long-term study in rats:
Agreed.
Based on the available data the observed thyroid tumors in rats are considered of no relevance for humans.

Dossier Submitter's Response

Thank you for your comments we note your opinion. Full rationale for the proposed classification is provided in the CLH report and we have no further comments.

RAC's response

In the mice long-term study there was a late development of hepatocellular adenomas and adenomas and carcinomas together (but no carcinomas alone) in males in the two highest dose groups. The incidence of hepatocellular adenomas were 13/52 (25 %) in the group receving 200 mg/kg bw/d and 15/52 (29 %, statistically significant) in the group receiving 600 mg/kg bw/d, vs. 7/52 (13 %) in the control group. Still these findings were within the historical control range for hepatocellular adenomas (17.31-34.62 %). Please not that the incidence of hepatocellular carcinomas was 2/52 in the contemporary control group and is considered the reason for the high dose goups not reaching statistically significance. However, the incidence in the contemporary control group was within the range of the historical controls.

RAC therefore concluded that since the hepatocellular adenomas in male mice was within the HCD, only benign tumours reached statistically significance, and only in one sex, and no multisite responses were observed in either mice or rats, no classification for carcinogenicity is justified.

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	3

Comment received

Agreed.
Based on the presented data there is no need to classify Penthiopyrad for mutagenicity.

Dossier Submitter's Response

Thank you for your comments.

RAC's response

Noted.

TOXICITY TO REPRODUCTION

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	4
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for reproductive toxicity.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
RAC agrees that no classification is warranted for effects on sexual function and fertility and developmental toxicity. .				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	5
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for acute toxicity.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	6
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for skin corrosion/irritation.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	7
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for serious eye damage/eye irritation.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	8
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for skin sensitization.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	9
Comment received				
Agreed. Based on the presented data there is no need to classify Penthiopyrad for STOT SE.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
08.07.2015	Germany		MemberState	10
Comment received				
DE-MSCA supports the proposed environmental classification and labelling as Aquatic acute 1 (H400) and Aquatic chronic 1 (H410) and the M-factor acute and chronic of 1 too.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
16.07.2015	France		MemberState	11
Comment received				
We agree with the classification and the M factors proposed for Environmental hazards.				
Dossier Submitter's Response				
Thank you for your comments.				
RAC's response				
Noted.				