Committee for Risk Assessment

RAC

Annex 3

Records

of the targeted consultation following the submission of additional information (mechanistic studies, study summaries and expert statements) pertaining to the assessment of carcinogenicity mode of action of

transfluthrin (ISO); 2,3,5,6-tetrafluorobenzyl (1*R*,3*S*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

EC Number: 405-060-5
CAS Number: 118712-89-3

CLH-O-0000006955-61-01/F

Adopted

18 March 2021

ANNEX 3 – RECORDS OF THE TARGETED CONSULTATION FOLLOWING THE SUBMISSION OF ADDITIONAL INFORMATION ON CLH PROPOSAL ON TRANSFLUTHRIN (ISO); 2,3,5,6-TETRAFLUOROBENZYL (1R,3S)-3-(2,2-DICHLOROVINYL)-2,2-DIMETHYLCYCLOPROPANECARBOXYLATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

The proposal for the harmonised classification and labelling (CLH) of (transfluthrin (ISO); 2,3,5,6-tetrafluorobenzyl (1R,3S)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, EC 405-060-5; CAS 118712-89-3) was submitted by the dossier submitter and was subject to a consultation, from 09.12.2019 to 07.02.2020. The comments received by that date are compiled in Annex 2 to the opinion.

The company Bayer S.A.S. however provided additional information (mechanistic studies, study summaries and expert statements) pertaining to the assessment of carcinogenicity mode of action (MoA) for transfluthrin (ISO). An ad hoc consultation was launched from 09.11.2020 to 30.11.2020 and the comments received are listed below.

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Substance name: transfluthrin (ISO); 2,3,5,6-tetrafluorobenzyl (1R,3S)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
EC number: 405-060-5
CAS number: 118712-89-3
Dossier submitter: The Netherlands

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
30.11.2020	Germany		MemberState	1
Comment received				
Under consideration of the two new studies and the 2 staements of Bayer it arises the impression the data available for tranfluthrin show a borderline case between classification as Carc. 2 and no classification. Further information on historic controls would be helpful.				
RAC's response				
Thank you for your comment. We will review and consider your arguments in our analysis.				

CARCINOGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
30.11.2020	Germany		MemberState	2
Comment received				
Various tumours were observed in carcinogenicity studies in rats and mice, however the incidence was partly very low and of questionable relevance. It is stated in the CLH-report that the incidences in haemangiosarcomas in the spleen and sarcomas of the subcutis were small and the tumours emerged from different tissues. Thus, these findings are likely to be incidental and unrelated to treatment. Furthermore the adenomas of the Harderian gland are considered of questionable relevance for humans. This view is supported. A statistically significant increase of liver adenomas was observed in female mice at the highest tested dose. The new experimental studies complement the investigations on the mechanism of the development of liver adenomas already considered in the CLH report. Altogether the impression develops that transfluthrin is at most only a weak activator of				

the receptors CAR/PXR and/or PPARα and uncertainties remain about the mechanism of tumour formation and the relevance for humans. On the other hand it is noted that the adenomas (benign tumours) were only observed in female mice at the highest tested dose. The B6C3F1 mouse strain is known to develop liver adenomas spontaneously and the incidences were only slightly above an extended in-house HCD. In rats a low incidence of urinary bladder tumours was observed in both sexes in the highest dose, however this increase was not statistically significant. It appears that information on HCD was not provided and should be added. This would improve the database to assess the relevance of the observed tumours.
RAC's response
Thank you for your comment. We will review and consider your arguments in our analysis.