Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

ethofumesate (ISO); (*RS*)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate

EC Number: 247-525-3
CAS Number: 26225-79-6

CLH-O-0000001412-86-196/F

Adopted

9 March 2018

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON ETHOFUMESATE (ISO); (*RS*)-2-ETHOXY-2,3-DIHYDRO-3,3-DIMETHYLBENZOFURAN-5-YL METHANESULFONATE

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: ethofumesate (ISO); (*RS*)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate
EC number: 247-525-3
CAS number: 26225-79-6
Dossier submitter: Austria

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Germany		MemberState	1
Comment received				
We agree with the proposal of classification for environmental hazards as Aquatic acute 1 (H400), Aquatic chronic 1 (H410) and the acute/chronic M-factor of 1. And we also agree that a classification of ethofumesate for health effects is not necessary.Even though there was some evidence of clastogenic acitivity of ethofumesate in vitro, the general conclusion may be drawn that there is no relevant genotoxic potential based on the negative outcome of the majority of in vivo tests.				
Dossier Submitter's Response				
Noted				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
11.05.2017	Spain		MemberState	2
Comment received				
The outcome of the Meeting of the Commission Working Group on the Classification and Labelling of Dangerous Substances Pesticides, ECB Ispra, 19-21 May 1999 (ECBI/43/99 Rev. 2), that no classification and labelling for ethofumesate is necessary for human health, could be supported, as proposed by the dossier submitter. In the European peer review (2015) no proposal for classification of ethofumesate for human health was made by EFSA or by Member States. During the re-evaluation of the active substance as active ingredient in PPPs, no new toxicological studies were provided				

by the notifier which would change the conclusion. Besides, considering the new criteria for classification and labelling and the new classification categories according to Regulation (EC) 1272/2008, ethofumesate does not require classification. New (CLP) classification categories: No non-lethal effects in acute oral toxicity studies were observed which would warrant the classification as STOT SE (specific target organ toxicity - single exposure) for ethofumesate. No effects on rats in 28 days oral toxicity studies were observed below the value of 300 mg/kg bw/d which is considered as guidance value for potential classification of substances as STOT-RE 2 (specific target organ toxicity – repeated exposure). Similarly, no effects on rats and mice were observed in 90 days oral toxicity studies below the value of 100 mg/kg bw/d which is considered as guidance value for potential classification of substances as STOT-RE 2 after 90 days exposure period. According to Regulation (EC) No 1272/2008 no guidance values are set for effects observed in dog studies, however, ethofumesate did not cause any effects in dogs which would trigger classification as STOT-RE at tested doses. No effects on rodents were observed below the values of 25 mg/kg bw/d (chronic studies) and 12.5 mg/kg bw/d (carcinogenicity studies) which are considered as guidance values for potential classification of substances as STOT-RE 2 (specific target organ toxicity – repeated exposure). According to Regulation (EC) No 1272/2008 no guidance values are set for effects observed in dog studies, however, ethofumesate did not cause any effects in dogs which would trigger classification as STOT-RE at tested doses. No treatment related non-neoplastic or neoplastic findings were observed in any of the studies. Therefore, ethofumesate is considered not to be potentially carcinogenic substance. No effects on rodents were observed which are considered relevant for potential classification of substance as reproductive toxicant. Therefore, ethofumesate is considered not to be potentially reprotoxic substance with regard to effects observed in multigeneration studies. Therefore, we agree with the dossier submitter that no classification and labelling for ethofumesate is necessary for human health.
Dossier Submitter's Response
Noted
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	France		MemberState	3
Comment received				
FR agrees with the classification for environmental hazards and with the acute and chronic M factor values proposed in the CLH report.				
Dossier Submitter's Response				
Noted				
RAC's response				
Noted.				

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Date	Country	Organisation	Type of Organisation	Comment number
19.05.2017	Germany		MemberState	4
Comment received				
We agree with the proposal of classification for environmental hazards as Aquatic acute 1 (H400), Aquatic chronic 1 (H410) and the acute/chronic M-factor of 1.				
Dossier Submitter's Response				
Noted				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
28.04.2017	United Kingdom		MemberState	5
Comment received				
The Myriophyllum spicatum study (Banman, 2013) is key to the current classification proposal of Aquatic Acute 1 (M=1), Aquatic Chronic 1 (M=1). The remaining data support the existing classification of Aquatic Chronic 2. In general, aquatic primary producer test species have historically been unicellular algae or moncotyldonous species such as Lemna which produce rapid vegetative growth over the relevant test guideline period (e.g. 72 hours or 7 days) which is considered to cover acute and chronic endpoints. The Myriophyllum spicatum test species is a rooted dicotyledonous macrophyte. Based on the currently available information, we are unclear if the M. spicatum 14-day study endpoints are relevant for both acute and chronic classification. We are unclear if a significant portion of the organism growth and reproduction lifecyle has occurred during the study to consider chronic effects. Equally, we are unclear if 14 days represents a short-term acute time period for the organism. In addition, we note a sediment phase was included in the study which make interpretation of endpoints difficult. From the water-sediment simulation studies, we note that a significant proportion of ethofumesate may partition to sediment during the 14 day study period. Are there analytical data for water and sediment concentrations during the study to support the endpoints based on measured water phase concentrations?				
Dossier Submitter's Response				
The RMS agrees on the mentioned uncertainties specified by UK. The use of the Myriophyllum endpoint for C&L might be a point for further discussion. However, on the experience of the RMS the Myriophyllum endpoint is commonly used for C&L purposes. Additionlly, other countries agreed on the endpoint and the C&L of ethofumesate. No information on analytical data for sediment concentratons are given in the study report. The measured concentrations of ethofumesate were between 74 and 83% of the nominal concentrations (mean measured). Hence, no conclusion regarding the concentration of ethofumesate in the sediment during the 14 day study can be drawn.				

RAC's response
Myriophyllum spicatum, a rooted macrophyte species, may be considered the target aquatic plant species for ethofumesate. Indeed, from the studies reported by the DS, the *Lemna* sp. and algae are less sensitive to ethofumesate. Although the study with *Myriophyllum spicatum* was conducted according to the OECD test guideline 221 (*Lemna* growth inhibition test) which foresees an exposure period of 7 days, in this case the time exposure was 14 days as reccomended by OECD test guideline 239 (water-sediment *Myriophyllum spicatum* toxicity test), which is a valid time period to calculate both acute and chronic endpoints*.*Moreover the study fulfils the validity test criteria reported in the OECD test guideline 239. Regarding sediment, the OECD test guideline 239 recommends to determine the concentration at the beginning and the end of the test, at least at the highest test concentrations, unless the water concentration is > 80% of nominal. In this study the conditions are not completely verified, but the measured concentrations (74% - 83% of the nominal) are not too far from this limit. Moreover at the highest test concentrations the measurements are > 80% of the nominal.