Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

7-oxabicyclo[4.1.0]hept-3-ylmethyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate

EC Number: 219-207-4
CAS Number: 2386-87-0

CLH-O-0000007129-71-01/F

Adopted

2 June 2022

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 7-OXABICYCLO[4.1.0]HEPT-3-YLMETHYL 7-OXABICYCLO[4.1.0]HEPTANE-3-CARBOXYLATE

COMMENTS AND RESPONSE TO COMMENTS ON CLH: PROPOSAL AND JUSTIFICATION

Comments provided during 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 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 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. Journal articles are not confidential; however they are not published on the website due to Intellectual Property Rights.

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

Substance name: 7-oxabicyclo[4.1.0]hept-3-ylmethyl 7-oxabicyclo[4.1.0]heptane-3-carboxylate
EC number: 219-207-4
CAS number: 2386-87-0
Dossier submitter: Ireland

MUTAGENICITY

Date	Country	Organisation	Type of Organisation	Comment number
22.10.2021	France		MemberState	1
Comment received				
FR agrees with the proposal to classify the substance as a category 2 germ cell mutagen based on the positive data available showing a mutagenic action at the first site of contact.				
Dossier Submitter's Response				
The IE CA would like to thank the FR CA for their support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
15.10.2021	Germany		MemberState	2
Comment received				
The DE CA supports the proposal to classify the substance EC no. 219-207-4 as Muta 2 (H341). Muta. 2 classification is considered to be warranted due to positive evidence for induction of gene mutations in somatic cells (forestomach) in an adequate mammalian in vivo mutagenicity test (oral TGR according to OECD TG 488, GLP; Anonymous, 2016). Albeit the increased mutation frequency in the forestomach lies just slightly out of the acceptable range, it is supported by the DE CA that this effect is considered biologically relevant. The DE CA agrees with the DS that based on the available data in the dossier regarding				

germ cells the classification criteria for category 1B are not fulfilled.
Dossier Submitter's Response
The IE CA would like to thank the DE CA for their support.
RAC's response
Noted.

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
22.10.2021	France		MemberState	3
Comment received				
Only a GPMT is available to assess the skin sensitising potential of the substance. No data on human are available. Regarding the results of this study (≥30% of the animals demonstrated redness score ≥1 at 24 and 48h), the substance is a skin sensitiser. Finally, 63 and 42% of the animals responded after the intradermal induction dose of 5%, indicating a moderate potency of sensitisation, and therefore a subcategorization as 1B. However, as no lower doses were tested, a higher potency, and therefore a classification in category 1A cannot be excluded. FR agrees with the conclusion of classifying the substance in category 1.				
Dossier Submitter's Response				
The IE CA would like to thank the FR CA for their support.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
15.10.2021	Germany		MemberState	4
Comment received				
The DE CA supports the CLH proposal of the IE CA to classify the substance EC no. 219-207-4 as skin sensitiser. In a guinea pig maximisation test (similar to OECD TG 406, GLP) conducted with EC no. 219-207-4, administration of 5 % test substance for intradermal induction and 100 % for challenge resulted in 63 % animals with positive reactions (24 h reading; Anonymous, 1991a). Data are within the range for classification of EC no. 219-207-4 as moderate skin sensitiser (≥ 30 % response at > 1 % intradermal induction dose in a GPMT). However, lower concentrations (i.e. ≤ 1 %) of the test substance for intradermal induction were not tested and thus category 1A cannot be excluded. Therefore, the DE CA agrees with the DS that classification of EC no. 219-207-4 as skin sensitiser category 1 (H317), without sub-categorisation is warranted.				
Dossier Submitter's Response				
The IE CA would like to thank the DE CA for their support.				
RAC's response				
Noted.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Repeated Exposure

Date	Country	Organisation	Type of Organisation	Comment number
22.10.2021	France		MemberState	5
Comment received				
FR agrees with the proposal of category 2 based on the degeneration of olfactory epithelium observed at doses from 50 mg/kg bw/day. Regarding the relevance of liver effects, it could be added that the hepatocellular vacuolation observed is of minimal severity at the two lowest doses, confirming that this effect should not be taken into account for classification as STOT RE.				
Dossier Submitter's Response				
The IE CA would like to thank the FR CA for their support. We agree that as the hepatocellular vacuolation observed at ≤ 50 mg/kg bw/day was of minimal severity, it should not be taken into account for classification as STOT RE.				
RAC's response				
Noted.				

Date	Country	Organisation	Type of Organisation	Comment number
15.10.2021	Germany		MemberState	6
Comment received				
Based on the observed degeneration of the olfactory epithelium (loss of sustentacular cells, vacuolation and desquamation of neuroepithelial cells) of the nasal tissue at ≥ 50 mg/kg bw/d in male and female rats in an adequate oral repeated dose 90-day toxicity study according to OECD TG 408, GLP, the DE CA supports the proposal to classify the substance EC no. 219-207-4 as STOT RE 2 (H373, nasal cavity).				
Dossier Submitter's Response				
The IE CA would like to thank the DE CA for their support.				
RAC's response				
Noted.				