Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate

EC Number: 276-957-5
CAS Number: 72869-86-4

CLH-O-0000007057-74-01/F

Adopted

26 November 2021

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 7,7,9(OR 7,9,9)-TRIMETHYL-4,13-DIOXO-3,14-DIOXA-5,12-DIAZAHEXADECANE-1,16-DIYL BISMETHACRYLATE

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: 7,7,9(or 7,9,9)-trimethyl-4,13-dioxo-3,14-dioxa-5,12-diazahexadecane-1,16-diyl bismethacrylate
EC number: 276-957-5
CAS number: 72869-86-4
Dossier submitter: Finland

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
19.01.2021	France		MemberState	1
Comment received				
Animal data: Based on results of the LLNA, criteria for Skin Sens. 1B are fulfilled. Human data: More than 100 positive case reports are available. All cross-sectional studies report frequency of skin sensitisation higher than 1%. The frequency of positive reactions in selected patients varies between studies and appears higher in more recent studies (>2% in 3/11 studies). Thus, according to CLP guidance, the level of frequency of occurrence of skin sensitisation can be considered as high. Assessment of exposure data is lacking from the CLH report (refer to table 3.3 of CLP guidance). If no adequate exposure data is available and based on the high frequency of occurrence of skin sensitisation in human, a subcategorisation as Skin Sens. 1A cannot be excluded. In this context, subcategorisation may be not possible. Thus, it should be discussed at the RAC level if classification as Skin Sens. 1 instead of 1B as proposed is more appropriate.				
Dossier Submitter's Response				
Thank you for your comment. The assessment of human exposure is not included in the CLH report as there is no adequate data available. Proposed sub-categorization as 1B is based on reliable LLNA. In this case, our view is that insufficient human exposure data would not overtake animal data. However, we agree it is the RAC to consider the most appropriate classification.				

RAC's response
Thank you for your comment. RAC agrees with DS. The sub-categorisation is not possible based on human data available for UDMA. However according to section 3.4.2.2.4.2. of Annex I to Regulation (EC) 1272/2008: "*Evidence from animal studies is usually much more reliable than evidence from human exposure. However, in cases where evidence is available from both sources, and there is conflict between the results, the quality and reliability of the evidence from both sources must be assessed in order to resolve the question of classification on a case-by-case basis. Normally, human data are not generated in controlled experiments with volunteers for the purpose of hazard classification but rather as part of risk assessment to confirm lack of effects seen in animal tests. Consequently, positive human data on skin sensitisation are usually derived from case-control or other, less defined studies. Evaluation of human data must therefore be carried out with caution as the frequency of cases reflect, in addition to the inherent properties of the substances, factors such as the exposure situation, bioavailability, individual predisposition and preventive measures taken".* In case of UDMA both human data and animal date were provided, but in line with above statement the reliable animal data are analysed for sub-categorisation purposes only when human data is not suitable for the purposes of sub-categorisation due to missing data on exposure. Based on the available animal data, i.e. the key LLNA, RAC agrees with DS that sub-categorization is warranted. As Sub-category 1A can be excluded, Sub-category 1B can be applied instead of Category 1. Human data support the classification of UDMA as a skin sensitiser.

Date	Country	Organisation	Type of Organisation	Comment number
22.01.2021	Sweden		MemberState	2
Comment received				
The SE CA supports the proposed harmonised classification of UDMA as Skin Sens. 1B, H317 based on animal data (LLNA with an EC3-value of 36,9%). Human evidence further supports classification of UDMA as a skin sensitiser.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
Thank you for your comment.				

Date	Country	Organisation	Type of Organisation	Comment number
04.01.2021	Germany		MemberState	3
Comment received				
We support the dossier submitter's proposal to classify UDMA as skin sensitiser and to assign sub-category 1B. While human data is indicative of the substance's potential to elicit skin sensitisation, animal data unequivocally demonstrates that sub-category 1B is appropriate. With regard to the dossier submitter's conclusion that "the frequency of positive reactions to UDMA in diagnostic patch tests can be considered high" (see CLH report p. 19) we would like to point out that only 6 out of 14 evaluable studies meet the criterion for "high frequency". Thus, eight studies only meet the criterion for "low/moderate frequency". Moreover, while in absolute numbers the number of published cases exceeds the threshold for high frequency (i.e. ≥ 100 cases), the exceedance appears rather low for a				

wide dispersive substance that has been patch tested since the 1980s (169 published cases according to the CLH report). However, we consider this is only a side note. Since human data is not suitable for the purposes of sub-categorisation due to missing data on exposure, the question whether there is evidence for high or low/moderate frequency plays a minor part for the CLH proposal.
Dossier Submitter's Response
Thank you for your comment.
RAC's response
Thank you for your comment.