Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

α-methyl-1,3-benzodioxole-5-propionaldehyde [1]

(*S*)-α-methyl-1,3-benzodioxole-5-propionaldehyde; (2*S*)-3-(1,3-benzodioxol-5-yl)-2-methylpropanal [2]

(*R*)-α-methyl-1,3-benzodioxole-5-propionaldehyde; (*2R*)-3-(1,3-benzodioxol-5-yl)-2-methylpropanal [3]

EC Number: 214-881-6 [1];- [2]; - [3]
CAS Number: 1205-17-0 [1]; 737776-68-0 [2]; 737776-59-9 [3]

CLH-O-0000007094-76-01/F

Adopted

18 March 2022

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON A-METHYL-1,3-BENZODIOXOLE-5-PROPIONALDEHYDE

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.

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Substance name:
α-methyl-1,3-benzodioxole-5-propionaldehyde [1]
(*S*)-α-methyl-1,3-benzodioxole-5-propionaldehyde; (2*S*)-3-(1,3-benzodioxol-5-yl)-2-methylpropanal [2]
(*R*)-α-methyl-1,3-benzodioxole-5-propionaldehyde; (*2R*)-3-(1,3-benzodioxol-5-yl)-2-methylpropanal [3]

EC number: 214-881-6 [1]; - [2]; - [3]
CAS number: 1205-17-0 [1]; 737776-68-0 [2]; 737776-59-9 [3]
Dossier submitter: Denmark

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
08.10.2021	France		MemberState	1
Comment received				
Animal data: based on the EC3 value of 16.4%, we agree that helional fulfils criteria for classification as Skin Sens. 1B. Human data: only one publication is available. You state in page 10 that it is possible that the frequency of occurrence of skin sensitisation can be > 0.8% since patch tests included concentrations < 7.5% helional (considered as optimal concentration). Do you have specific data with patch tests performed with 10.1% and 15.2%? Based on both elements, FR agrees with the proposed classification as Skin Sens. 1B. Other data: According to page 5, we understand that helional was subjected to in vitro testings leading to classification as Skin Sens. 1 or 1B depending on the defined approach considered. This supports the proposed classification. Thus, it would have been interesting to add more information in the CLH report on these in vitro tests and their results, if possible.				

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON A-METHYL-1,3-BENZODIOXOLE-5-PROPIONALDEHYDE

Dossier Submitter's Response
Thank you for your comments and support on the proposed classification of helional as Skin Sens. 1B. Human data: The study by Bennike et al., 2019, identifying the optimal patch test concentration for helional, included approximately 100 patients per test concentration. 1 positive reaction were seen at 15.2 %. The data are also summarised in Annex I. Based on the results optained in the study, the DS is of the opinion that it cannot be excluded that a higher frequency of sensitisation would be seen in a clinical patch test study, using the identified optimal patch test concentration of helional. Other data: The DS has not looked further into the in vitro data behind the classification derived from the guideline on Defined Approaches for Skin Sensitisation (DASS). Since the data used on reference chemicals in the supporting document and its annexes have been thoroughly evaluated in the process of developing the DASS, the DS is of the opinion that the classification derived from the DASS can be used as supporting evidence.
RAC's response
Thank you for your comment. RAC agrees with the DS response.

Date	Country	Organisation	Type of Organisation	Comment number
13.09.2021	Germany		MemberState	2
Comment received				
The DE CA supports the CLH proposal of the DK CA to classify helional as skin sensitiser. Reliable LLNA data show that helional acts as moderate skin sensitiser (EC3=16.4 %) and allow for sub-categorisation as Skin Sens. 1B. Furthermore, in a clinical study to determine the optimal patch test concentration in humans, patch-testing to helional resulted in 0.8 % positive reactions in consecutive dermatitis patients, showing that helional acts as skin sensitiser in humans. The DS states that the frequency of 0.8 % may underestimate the incidence of sensitisation in unselected dermatitis patients, and concludes that "human data can therefore not exclude helional to have strong sensitising properties in humans". The DE CA inquires if relative exposure data, data on the induction threshold of helional in humans, or data on the severity of responses in patients were available / considered (in a weight of evidence approach for sub-categorisation) to draw this conclusion. Altogether, the DE CA supports the proposal of the DK CA for a harmonised classification of helional as skin sensitiser, as shown by positive reactions in animals and humans. Data do allow for sub-categorising into Skin Sens. 1B, based on animal data. This is supported by in chemico / in vitro studies (Defined Approaches for Skin Sensitisation, ITSv1 and ITSv2). The DE CA agrees with the DK CA that a GCL of 1 % (w/v) should be used.				
Dossier Submitter's Response				
Thank you for your comments and support on the proposed classification of helional as Skin Sens. 1B and use of the GCL of 1 %. The DS has not been able to indentify data on the induction threshold of helional in humans. The only human data identified was the study by Bennike et al., 2019,				

identifying the optimal patch test concentration of helional. All four positive reactions were scored as ++ positive reactions (+/++/+++). Data on the human exposure to helional were lacking, therefore relative exposure data were not considered in the CLH dossier. In the 2012 SCCS opinion helional is mentioned as a "top 100 substance" referring to volumes used. The registred tonnage is 100-1000 t/yr with widespread uses by both consumers and professional workers in applications that may entail dermal exposure. However, no data on observed concentrations in consumer products have been available to the DS enabling an exposure consideration according to guidance on application of CLP criteria.
RAC's response
Thank you for your comment. RAC agrees with the DS response.