Committee for Risk Assessment

RAC

Annex 2

Response to comments document (RCOM)

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

3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate; isophorone di-isocyanate

EC Number: 223-861-6
CAS Number: 4098-71-9

CLH-O-0000007311-84-01/F

Adopted

8 June 2023

ANNEX 2 - COMMENTS AND RESPONSE TO COMMENTS ON CLH PROPOSAL ON 3-ISOCYANATOMETHYL-3,5,5- TRIMETHYLCYCLOHEXYL ISOCYANATE; ISOPHORONE DI-ISOCYANATE

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: 3-isocyanatomethyl-3,5,5- trimethylcyclohexyl isocyanate; isophorone di-isocyanate
EC number: 223-861-6
CAS number: 4098-71-9
Dossier submitter: Germany

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	1
Comment received				
While we as European Aliphatic Isocyanates Producers Association ALIPA appreciate the opportunity to contribute to the classification and labelling procedure for 3-Isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate (IPDI), we would like to emphasize our disagreement with the conclusion drawn by the Dossier submitter BAuA (Federal Institute for Occupational Safety and Health) regarding the endpoints skin corrosion, skin sensitization and the additional labelling as 'corrosive to the respiratory tract ' (Specific target organ toxicity – single exposure). ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf				
Dossier Submitter's Response				
Noted.				
RAC's response				
Thank you for commening.				

OTHER HAZARDS AND ENDPOINTS – Acute Toxicity

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	2
Comment received				
We agree with the proposal of the dossier submitter (DS) to modify the classification from Acute Tox. 3 with H331 to Acute Tox. 1 with H330. ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Thank you for commening.				

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	France		MemberState	3
Comment received				
FR agrees with proposed classification as Acute Tox. 1. We note that the methodology used by the registrant to calculate the LC50 is not adequate in the Bayer (1995) study. Since this study is the most reliable one, could you please consider to re-calculate this LC50 (according to recommendations set in OECD GD39) for setting the ATE?				
Dossier Submitter's Response				
Thank you for your comment. The re-calculated LC50 (LogProbit Model) is higher than the LC50 calculated by the registrant. The LC50 value of 31.0 mg/m^3 was determined in an acute inhalation toxicity study of good quality, Klimisch 2. In general, the classification is based on the lowest ATE value available.				
RAC's response				
Thank you for commening. RAC agrees with DS's reply.				

OTHER HAZARDS AND ENDPOINTS – Skin Hazard

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	4
Comment received				
See attached file ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf				
Dossier Submitter's Response				
The isolated sentence "*Necrosis formation after an exposure time of 4 hours, but not after 3 minutes*." (Hüls AG, 1984a) is not assignable, because no additional information is				

given in the experimental procedure and in the results table. In table 13 of the CLH-report it is stated, that "*Skin Corr. 1A not appropriate*", which is in line with the cited sentence. Adequate, reliable and representative animal data are available and indicate corrosive properties of IPDI. As supported by ALIPA, the DS is of the opinion that Sub-Category 1A is not appropriate and the distinction between 1B/1C is not feasible. The formal conclusion is no sub-categorisation. ALIPA stated that "*Category 1 without subcategorization corresponds to an over classification since other legislations may equal Category 1 with Subcategory 1A*." In light of these consequences, the DS stated in the CLH-report: "*Based on the data available classification in Sub-Category 1B would represent a conservative approach*."
RAC's response
Thank you for commening. RAC agrees with DS's reply.

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	France		MemberState	5
Comment received				
FR agrees with the proposed classification as Skin Corr. 1. Subcategory is not possible in the absence of examination after 3 minutes and 1 hour. It should be noted that only 1/3 available study (with only 1 animal) was performed under semi-occlusive condition B				
Dossier Submitter's Response				
Noted.				
RAC's response				
Thank you for commening.				

OTHER HAZARDS AND ENDPOINTS – Eye Hazard

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	6
Comment received				
We agree with the proposal of the DS. ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Thank you for commenting.				

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	France		MemberState	7
Comment received				
Based on the mean scores (24, 48, 72h) in the 2 available studies, a classification as Eye Dam is not fulfilled. However, some data point to severe eye damage: - the substance is corrosive to skin - some effects (chemosis and cornea damage) are not completely reversible throughout the 8 day observation (no observation on day 21 as recommended in the CLP guidance) in the first study - loss of hair around treated eye, incrustation at the eye lid and thickening in the second study It has also to be noted that, according to CLP guidance: "[..] if a substance or mixture is classified as Skin corrosion Category 1 then serious damage to eyes is implicit as reflected in the hazard statement for skin corrosion (H314: Causes severe skin burns and eye damage)." […] "Testing for eye irritation should not be carried out on substances known or predicted to be corrosive to skin and classified as such. Such substances are automatically considered to be severely damaging to the eye and are classified but not labelled for serious eye damage in addition to skin corrosion."				
Dossier Submitter's Response				
Thank you for the reference to the guidance, which clarifies the interrelation between H314 and H318.				
RAC's response				
Thank you for commenting.				

OTHER HAZARDS AND ENDPOINTS – Skin Sensitisation Hazard

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	8
Comment received				
See attached file ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf				
Dossier Submitter's Response				
LLNA-test: ALIPA cited an NIH Publication (No. 11-7709): "*LLNA cannot be considered a stand-alone assay to determine skin sensitization potency categories. …*" However, this statement refers to skin sensitisers with an EC3 > 2%. For skin sensitisers with EC3 of ≤ 2%, the ICCVAM-recommendation is different: "*ICCVAM concludes that the LLNA, using the GHS classification criteria, can be used to categorize substances as strong sensitizers (GHS Subcategory 1A) when the estimated concentration that produces a positive LLNA result (i.e., EC3) is ≤2%.*" IPDI has an EC3 < 2%. **Guinea Pig Maximization Test (GPMT)** Comment noted. **Buehler test**				

Comment noted. **Overall conclusion** Sufficient evidence from reliable animal studies is provided to warrant classification in Sub-Category 1A according to the CLP classification criteria. **SCL:** Comment noted.
RAC's response
Thank you for commenting. RAC agrees with DS's reply.

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	France		MemberState	9
Comment received				
FR agrees with the proposed classification as Skin Sens. 1A based on 2 experimental studies reporting high frequency of reactions. High frequency of skin sensitisation is also supported by human data (Geier and Schubert, 2021). Based on the LLNA, the substance is considered as an extreme sensitiser. Strong potency is obtained from the Buehler assay, but extreme potency cannot be neither excluded (the induction dose of 5% already induces 80% of reactions; no lower doses tested). Thus, FR also agrees with the proposed SCL.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Thank you for commenting.				

OTHER HAZARDS AND ENDPOINTS – Specific Target Organ Toxicity Single Exposure

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	France		MemberState	10
Comment received				
FR agrees with the approach to delete the current classification as STOT SE 3 considering the proposed classification as Corrosive, with the adding of EUH071.				
Dossier Submitter's Response				
Thank you for your comment.				
RAC's response				
Thank you for commenting				

Date	Country	Organisation	Type of Organisation	Comment number
06.10.2022	Belgium	ALIPA Aisbl	Industry or trade association	11
Comment received				
See attached file				

ECHA note – An attachment was submitted with the comment above. Refer to public attachment ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate_October 2022.pdf
Dossier Submitter's Response
Thank you for your comment. With respect to EUH071, please see CLP guidance 3.1.4.2
RAC's response
Thank you for commenting. RAC agrees with DS reply.

PUBLIC ATTACHMENTS
1. ALIPA_Harmonised CLH Consultation_3-isocyanatomethyl-3,5,5- trimethylcyclohexyl isocyanate_October 2022.pdf [Please refer to comment No. 1, 2, 4, 6, 8]