Committee for Risk Assessment

RAC

Annex 2
Response to comments document (RCOM) to the Opinion proposing harmonised classification and labelling at EU level of

dodecyl methacrylate

EC Number: 205-570-6
CAS Number: 142-90-5

CLH-O-0000001412-86-167/F

Adopted
22 September 2017

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: dodecyl methacrylate
EC number: 205-570-6
CAS number: 142-90-5
Dossier submitter: Germany

GENERAL COMMENTS

Date	Country	Organisation	Type of Organisation	Comment number
19.12.2016	France		MemberState	1

Comment received

Based on the data provided in the CLH report, we cannot conclude on the validity of the proposal meaning to withdraw all the human health classifications included in the actual harmonized classification. Indeed, no justification on the read-across from the tested substances to DCMC is provided in the report. Furthermore, DCMC is metabolized into MAA which is known to be a strong irritant since it is classified Skin Corr. 1A. Could you please provide further justification on the read-across approach?

Even if it is not an open point for public consultation, we think that sensitisation (dermal and respiratory) should be discussed within a category approach considering that many methacrylates are sensitizers. In addition, please note that Kanazawa (1999) conclude that a C12 derivative showed the strongest sensitizing potential among 11 methacrylates tested.

Dossier Submitter's Response

We appreciate the questions and comments of the French CA.
In the first part, three questions concerning the three end points in human health classifications (skin irritation, eye irritation and respiratory irritation) were asked.
The four skin irritation and four eye irritation studies used in this dossier were performed with two single compounds, one compound (isotridecyl methacrylate) with one carbon atom more in the alkylchain then dodecyl methacrylate and another compound (decyl methacrylate) with two carbon atoms less in the alkylchain then dodecyl methacrylate. Additionally, two studies were performed with mixtures containing dodecyl methacrylate (65% in one study, no detailed information on the composition in the other study). The read across from a C13 containing alkyl chain towards a C12 containing alkyl chain together with the read across from a C10 containing alkyl chain towards the C12 containing alkyl chain appears to be justified. The results of all four studies did not differ essentially and they are supporting the conclusion that dodecyl methacrylate is not a skin

irritant fulfilling the CLP criteria. Since the results of the experimental studies did not show a strong irritant effect of the methacryl esters investigated, the putative metabolism towards methacrylic acid in the skin seems to be insufficient to cause a strong skin irritation.
The results of the four studies on eye irritation clearly demonstrate that dodecyl methacrylate is not irriating to the eye. A putative metabolism towards methyl acrylate is not relevant for this application.
Data were provided for the vapour pressure of dodecyl methacrylate (0.06 Pa at 20 °C) and therefore it was concluded that inhalation is not a route of exposure.

Since we focus on the scope of the dossier we do not comment on the Guinea pig maximisation test of Kanazawa et al., 1999.

RAC's response

RAC consider that the read across for skin and eye irritation from longer- and shorter chain length metacrylates compared to dodecyl methacrylate is justified due to the similarities in the physico- chemical properties. Further, RAC agrees with the DS that since the results of the experimental studies did not show a strong irritant effect of the methacryl esters tested, the potential metabolism to methacrylic acid in the skin seems to be insufficient to cause a strong skin irritation. Further, the dermal absorption was estimated to be low for dodecyl methacrylate.
However, some further studies on the skin irritation properties of dodecyl methacrylate/lauryl methacrylate (synonyme to dodecyl methacrylate) was provided to RAC by the DS. One reference stated that lauryl methacrylate is not a primary skin irritant, however, the test compound would be considered a moderate irritant, and contact with the skin should be avoided" (OSHA Toxicity Screening Tests for Rohm and Haas Company, Lauryl methacrylate, 1973). Another reference included that methacrylates including lauryl methacrylate produce slight skin irritation" (Gage, Brit. J. Ind. Med. 27,1. 1970). The RAC conclusion regading the classification for skin, eye and respiratory irritation were as following:

The RAC conclusion regarding skin irritation:
Option 1: In the absence of a well conducted OECD TC 404 with dodecyl methacrylate and with data indicating that dodecyl methacrylate is considered to induce slight or moderate skin irritation, the removal of the classification for skin irritation is not supported by RAC.
Option 2: RAC support the DS proposal to remove the classification as Skin Irrit. 2 for dodecyl methacrylate.

The RAC conclusion regarding eye irritation:
RAC consider that the read across for eye irritation from longer- and shorter chain length metacrylates compared to dodecyl methacrylate is justified due to the similarities in the physico chemical properties.
Option 1: In the absence of data on dodecyl methacrylate for the assessment of eye irritation, the removal of the classification for eye irritation is not supported by RAC.
Option 2: RAC support the DS proposal to remove the classification as Eye Irrit. 2 for dodecyl methacrylate. The two additionally studies included by the DS does not contradict the agreement of no classification of dodecyl methacrylate for eye irritation in the former TC C&L group.

The RAC conclusion regarding STOT SE 3:
RAC consider that due to the absence of data, the DS proposal to remove the STOT RE 3 classification is not supported.

Date	Country	Organisation	Type of Organisation	Comment number
02.12.2016	United Kingdom		MemberState	2
Comment received				
It would be useful to present details of the OECD chemicals programme assessment that is mentioned in section 3 of the CLH report.				
Dossier Submitter's Response				
All data (also the basis of the OECD HPV assessment) were reflected in the respective chapters of the CLH report.				
RAC's response				
We note that the Dossier Submitter states that they have included all relevant information from the OECD report. We have not been able to check this as the OECD document does not appear to be publically available.				

OTHER HAZARDS AND ENDPOINTS – Hazardous to the Aquatic Environment

Date	Country	Organisation	Type of Organisation	Comment number
19.12.2016	France		MemberState	3
Comment received				
Based on the data provided, we cannot agree on the proposal for removing the classification as aquatic acute and chronic 1. Using PBT profiler, there is an alert on the Toxic criterion, with a value below 10µg/L. Moreover, in the different study presented, there is always the concern about solubility of the substance in water and the detection limit of the tools used to follow the evolution of the substance concentration. Thus, as a tensioactive substance, there is also uncertainty about the BCF who may change a lot between measured and predicted value. When considering the high tonnage, the bioaccumulative property and the possibly T criterion fulfil (in PBT profiler and in the two key studies, beside the limit of solubility), we do not support the modification of the actual classification.				
Dossier Submitter's Response				
Thank your for your comment. We agree, that the substance has potential to bioaccumulate. Reflecting the valid ecotoxicity data the substance showes no effect up to its limit of water solubility. The ecotoxicity test showing toxicity of the substance at lower concentrations is not valid as there was no clear concentration-effect relationship and emulsions instead of solution of the test material observed. Therefore neither the T-criterion is fulfilled nor the classification justified.				
RAC's response				
The reliability of the QSAR predictions from the PBT profiler is not indicated in the comments, so RAC has performed its own predictions using ECOSAR with the help of the ECHA secretariat. We conclude that the QSAR prediction is not reliable. The claim that the substance is surface active cannot be checked as a study has been waived due to the low water solubility value. However, this is not relevant to the bioaccumulation assessment because the DS accepts that the substance meets the CLP criterion. Supply volume is not relevant to the hazard classification, which is based on the evidence presented.				

RAC agrees with the DS that the fully reliable studies in the data set do not suggest any relevant aquatic toxicity up to the solubility limit in pure water. This is also consistent with the previous agreement at the TC C&L.

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2016	Sweden		MemberState	4
Comment received				
The Swedish CA supports the proposal to remove the current classification of dodecyl methacrylate in Aquatic Acute 1 (H400) and Aquatic Chronic 1 (H410). Our support is based on evidence of rapid degradation of dodecyl methacrylate, and values for acute and chronic aquatic toxicity that are above the water solubility of the substance. Therefore, according to the CLP criteria, classification and labelling of dodecyl methacrylate for environmental hazards is not justified.				
Dossier Submitter's Response				
Thank you for your support.				
RAC's response				
RAC notes the support.				

Date	Country	Organisation	Type of Organisation	Comment number
15.12.2016	Belgium		MemberState	5
Comment received				
1. A degree of purity of ≥ 80% is given in section 1.1 while in section 1.2 of Part A the reported concentration range is 95-100% (typical conc. ca. 99.3%). 2. Bioaccumulation : an estimated log Kow is reported for dodecyl methacrylate : 6.68 which indicates a potential to bioaccumulate. Read across was performed with ethylhexyl methacrylate. This substance has a lower log Kow =5.59 , MW=191, a much higher water solubility (3.7 mg/l) and a measured BCF= 37 Furthermore this substance metabolises faster than dodecyl methacrylate. In the CLH report it is also mentioned that the concentration of dodecyl methacrylate is much lower than ethylhexyl methacrylate due to the bioavailability. However this is questionable because the estimated BCF of dodecyl methacrylate = 424 L/kg wet-wt (using episuite V4.1) which is higher than the experimental determined BCF of 37 of the read across substance . 3. Aquatic toxicity : Adequate and reliable aquatic toxicity data are not available for all three levels. The environmental studies performed with a mixture of 69.13% dodecyl methacrylate and 27.4% tetradecyl methacrylate are not appropriate for classification and labelling of dodecyl methacrylate and should not be taken into account in the weight of evidence. Only 1 reliable acute toxicity study is available: Algae, Desmodesmus subspicatus : 72hErC50>10 µg/L (nom). No toxicity is observed up to the water solubility (<1µg/L) and at present the substance does not fulfil the classification criteria for aquatic acute toxicity Acute 1. Reliable chronic studies are available for invertebrates and algae. No chronic study was performed on fish. This means that also the surrogate approach should be taken into account. However no reliable LC50 could be determined for fish. Thus based on the NOEC of the most sensitive species (Daphnia magna 21d NOEC >= 5.73 µg/L(meas. arithm. mean)) and the fact that the substance is readily biodegradable (88% degradation within 28d) no toxicity was seen up to the water solubility. The substance thus not fulfil the criteria for chronic toxicity.				

Dossier Submitter's Response
1. The purity of ≥ 80 % in Part A section 1.1 represents the required minimum concentration of a mono-constituent substance. The definition comprises all mono-constituent substances with a Dodecyl methacrylate concentration ≥ 80 %. The typical concentration of 99.3 % and concentration range of 95-100 % reported in Part B section 1.2 represents the "real" substance composition that was taken from registration dossiers and used for classification. 2. Since an exact BCF could not be estimated for dodecyl methacrylate, the calculated log Kow was used for the assessment of the bioaccumulation potential. Based on this value the substance has potential to bioaccumulate in organisms. 3. Thank you for your comment. We completely agree with you.
RAC's response
RAC notes the support.

Date	Country	Organisation	Type of Organisation	Comment number
02.12.2016	United Kingdom		MemberState	6

Comment received
Algal growth inhibition: For the Hoberg (1995) study, there are a few typos in the measured concentration range which should read 0.0068, 0.016, 0.24, 0.062 and 0.19 mg/l based on initial (0 hour) measurements as presented in the study report. We note that 72-hour observations are available for the Hoberg (1995) study and feel these should be used in preference to 96-hour endpoints (for consistency with other substances). This is in line with the results from the Noack (2005) algal growth inhibition study. We note that the Hoberg study report states that test solutions were clear and colourless and there was no sign of undissolved material. The assumption that test solutions involved emulsions is therefore not clearly supported and no information is provided about why this would invalidate the study. In addition, the lack of dose-response does not invalidate a study. In fact, it is not clear to us that a dose-response effect was not observed. It would be useful to present data to show the level of inhibition (ideally including 72 hours) for each treatment with the standard deviation to consider the dose response along with a graphical plot. We note the difference in test item composition between studies. We wonder if this could have affected the study results. We note that the algal studies used different test species and consider it difficult to directly compare results from the two studies. For example, one species could be more sensitive. Overall, we consider the current CLH report does not present sufficient information to consider the Hoberg, 1995 study invalid.
Dossier Submitter's Response
Thank you for your comment. The measured concentrations were 0.0068, 0.016, 0.024, 0.062 and 0.19 mg a.i./L.

	Inhibition compared to pooled control [%]			
Concentrations	at 24 h	at 48 h	at 72 h	at 96 h
0.0068 mg/L	61.6	-2.7	0.8	0.5
0.016 mg/L	85.1	8.6	2.8	6.4
0.024 mg/L	182.8	5.6	2.6	12
0.062 mg/L	172.7	14.9	12.2	12
0.19 mg/L	124.3	30.1	31.7	29

Agreeing with you and as stated in comment number 5, the test substance composition (mixture of 69.13 % dodecyl methacrylate and 27.4 % tetradecyl methacrylate) in the Hoberg 1995 study is not appropriate for the classification and labelling of dodecyl methacrylate. The available valid study with Algae shows no effect up to 10 µg/L.

RAC's response

RAC notes that there appears to be a dose-response relationship in this study at 72 h. Although statistical analysis is not provided by the DS, the 72-h ErC_{50} and NOEC would appear to be equivalent to the values selected by the DS at 96 h. RAC notes that visual indication that a solution was clear does not necessarily mean that the substance was fully dissolved.

An algal study performed on the same species in the same laboratory and in the same year for the related substance isobutyl methacrylate (CAS no. 97-86-9) has previously been considered by RAC. Although that study reported effects, it failed a validity criterion that did not exist at the time the test was performed (the mean coefficient of variation for section-by-section growth rates in the control cultures exceeded 35 %). The data owner should check the dodecyl methacrylate study to see if it suffered from similar drawbacks. In addition, test concentration maintenance should be described, and results adjusted accordingly (if appropriate).

Nevertheless, RAC considers that the different test substance identity and use of nominal concentrations above the water solubility limit of dodecyl methacrylate are sufficient reasons to set the Hoberg (1995) study aside, given that a valid study on another algal species is available.