Committee for Risk Assessment

RAC

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

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CLH-O-0000001412-86-167/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: dodecyl methacrylate

EC Number: 205-570-6

CAS Number: 142-90-5

The proposal was submitted by Germany and received by RAC on 4 October 2016.

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Germany has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at *http://echa.europa.eu/harmonised-classification-and-labelling-consultation/* on 2 November 2016. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by 19 December 2016.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: Christine Bjørge

Co-Rapporteur, appointed by RAC: Steve Dungey

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on 22 September 2017 by consensus.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	607-247-00-9	dodecyl methacrylate	205-570-6	142-90-5	Eye Irrit. 2 STOT SE 3 Skin Irrit. 2 Aquatic Acute 1 Aquatic Chronic 1	H319 H335 H315 H400 H410	GHS07 GHS09 Wng	H319 H335 H315 H410		STOT SE 3; H335: C ≥ 10%	
Dossier submitters proposal	607-247-00-9	dodecyl methacrylate	205-570-6	142-90-5	Remove Eye Irrit. 2 STOT SE 3 Skin Irrit. 2 Aquatic Acute 1 Aquatic Chronic 1	Remove H319 H335 H315 H400 H410	Remove GHS07 GHS09 Wng	Remove H319 H335 H315 H410		Remove STOT SE 3; H335: C ⩾ 10%	
RAC opinion	607-247-00-9	dodecyl methacrylate	205-570-6	142-90-5	Retain STOT SE 3 Remove Eye Irrit. 2 Skin Irrit. 2 Aquatic Acute 1 Aquatic Chronic 1	Retain H335 Remove H319 H315 H400 H410	Retain GHS07 Wng Remove GHS09	Retain H335 Remove H319 H315 H410		Retain STOT SE 3; H335: C ≥ 10%	
Resulting Annex VI entry if agreed by COM	607-247-00-9	dodecyl methacrylate	205-570-6	142-90-5	STOT SE 3	H335	GHS07 Wng	H335		STOT SE 3; H335: C ≥ 10%	

GROUNDS FOR ADOPTION OF THE OPINION

HUMAN HEALTH HAZARD EVALUATION

RAC evaluation of specific target organ toxicity – single exposure (STOT SE)

Summary of the Dossier Submitter's proposal

The Dossier Submitter (DS) informed that no data were available on respiratory tract irritation. The vapour pressure of dodecyl methacrylate is < 0.1 Pa, and inhalation of the gaseous form is therefore not considered as a route of exposure. However, the physico-chemical properties with a very low vapour pressure cannot exclude exposure to the aerosol form. Since no data on dodecyl methacrylate are available for the aerosol form and the existing classification seems to be based on a group approach, a comparison with the criteria was not possible. The lack of irritating properties on the skin and the eye gives supporting evidence that the current classification as STOT SE 3 (respiratory irritation) may not be justified and should be deleted.

Assessment and comparison with the classification criteria

Dodecyl methacrylate has a harmonised classification as STOT SE 3 (respiratory irritation) in CLP Annex VI. No information was made available to RAC regarding the basis for this classification, i.e. if it is based on data on dodecyl methacrylate or on the group entry in Annex VI to CLP for methacrylates with the Index No. 607-134-00-4 and name: "monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex". Therefore, no assessment of the potential for respiratory tract irritation of dodecyl methacrylate or an assessment of read across to other shorter- or longer- chain methacrylates could be made by RAC. Furthermore, exposure to the aerosol form cannot be excluded based on the physico-chemical properties of dodecyl methacrylate.

In a previous German (IND) proposal under the former Technical Committee on Classification and Labelling (TC C&L) to withdraw the classification of dodecyl methacrylate for irritation of respiratory tract (document ECBI/37/06), it was only indicated that "Inhalation is not an expected route of exposure". However, the proposal was never discussed by the TC C&L. Furthermore, the studies that were used to classify the group entry "monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex" as STOT SE 3 (respiratory irritation) has not been available for assessment to RAC.

Conclusion

RAC considers that due to the absence of data, the DS proposal to remove the current classification as STOT SE 3 (respiratory irritation) is not supported.

RAC evaluation of skin corrosion/irritation

Summary of the Dossier Submitter's proposal

No study on skin irritation following dermal exposure to dodecyl methacrylate was available. However, the DS assessed, in a weight of evidence approach, four skin irritation studies in rabbits (New Zealand White) with structurally related long-chain alkyl methacrylates. In this respect, the DS included information regarding the physico-chemical properties of the substances used for a read across to dodecyl methacrylate, see table 1 below:

Table 1. Physico-chemical properties of the substances used in studies in the CLH proposal.

Substance name	CAS No	Molecular formula	MW	Log Pow	Water solubility (mg/L)
2-Ethylhexyl methacrylate	688-84-6	$C_{12}H_{22}O_2$	191	5.59a	3.07a
Dodecyl methacrylate	*142-90-5*	*$C_{16}H_{30}O_2$*	*254*	*6.68b*	*< 0.001a*
Tridecyl methacrylate	2495-25-2	$C_{17}H_{32}O_2$	268	7.17b	0.01409c
Isotridecyl methacrylate	94247-05-9	$C_{17}H_{32}O_2$	268	7.09b	0.01628c
Tetradecyl methacrylate	2549-53-3	$C_{18}H_{34}O_2$	282	7.66b	0.004461c
Pentadecyl methacrylate	6140-74-5	$C_{19}H_{36}O_2$	297	8.15b	0.001409c
Hexadecyl methacrylate	2495-27-4	$C_{20}H_{38}O_2$	311	8.64b	0.0004442b
Octadecyl methacrylate	32360-05-7	$C_{22}H_{42}O_2$	339	9.62b	0.0000437b

[a] Measured data

[b] Calculated data

[c] Calculated data are higher than predicted from experimental data with dodecyl methacrylate

The DS included also information regarding dermal absorption of dodecyl methacrylate. Since dodecyl methacrylate has a molecular weight between 100 < MW < 500 g/mol (254 g/mol), this favours dermal uptake. However, with the very low water solubility (< 1 µg/L), dermal uptake from the *stratum corneum* into the epidermis is likely to be low. Furthermore, with a log Pow > 6, the rate of transfer between the *stratum corneum* and the epidermis will be slow and will therefore limit absorption across the skin. Uptake into the *stratum corneum* itself may also be slow.

The DS also indicated that although dodecyl methacrylate has a functional group which can bind to skin (methacrylate), it was not sensitising in *in vivo* tests in mice and guinea pigs. Moreover, it is not skin irritating or corrosive, so the substance itself will not enhance penetration through damaged skin. In addition, no signs of systemic toxicity indicating absorption were observed in an acute dermal toxicity study with doses up to 3000 mg/kg bw. Some data on skin irritation

following dermal exposure to dodecyl methacrylate were submitted to RAC. Some of these references included information regarding the irritating properties of dodecyl methacrylate/lauryl methacrylate (synonym of dodecyl methacrylate). 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 stated that methacrylates including lauryl methacrylate produce slight skin irritation (Gage, Brit. J. Ind. Med. 27, 1. 1970).

The DS also calculated the dermal absorption (steady-state flux) of dodecyl methacrylate by using the principles defined in the Potts and Guy prediction model (Heylings JR, 2013), see table 2 below.

Table 2. Terms used for categorising absorption of chemicals through human skin.

Kp (cm/h)	Absorption rate (µg/cm²/h)	Relative absorption rate category	Predicted absorption from normal exposure
1E-02 – 1E-01	> 500	Very fast	Very high
1E-03 – 1E-02	100-500	Rapid - Fast	High
1E-04 – 1E-03	10-50 50-100	Slow - Moderate Moderate - Rapid	Moderate
1E-05 – 1E-04	0.1-10	Very slow - Slow	Low
1E-06 – 1E-05	0.001-0.1	Extremely - Very slow	Minimal
<1E-06	< 0.001	Extremely slow	Negligible

Based on a molecular weight of dodecyl methacrylate of 254.41 g/mol and a log Pow of 6.68, the DS predicted the flux of dodecyl methacrylate to be 0.003 µg/cm²/h, and concluded that the relative dermal absorption is minimal.

Data from skin irritation studies in rabbits

The DS used only the data for the shaved, intact skin for evaluation. Further, in studies carried out with more than 3 animals -both approaches- the overall mean score and the average score were determined per animal and were used for evaluation.

The first study was performed according to FDA Draize study with methacrylic acid ester of an alcohol (65% dodecyl methacrylate, 25% tetradecyl methacrylate, 10% higher alkyl methacrylates up to octadecyl methacrylate) (Sterner and Stigilc, 1977). Six rabbits were dermally exposed to 0.5 mL of the methacrylate mixture. Two application sites per animal were treated, one site was left intact, the other site was abraded. The test sites were covered with an occlusive dressing for 24 h. The animals were observed for 72 h, and the irritation was scored by the method of Draize *et al.*, 1959. The test substance was slightly irritating to the rabbit skin in this study.

The treated abraded skin sites showed identical effects as the intact sites. For re-evaluation, only the scores of the intact skin were used.

The response of the individual animal values were averaged over the two observation days (24 and 72 h after application), separate for erythema and oedema. The mean erythema values were 1 for one animal, 1.5 for four animals and 2 for one animal. Erythema scores were not fully reversible within 72 h. All mean scores were below 2.3.

The performance of the study did not comply with the requirements of the relevant recent EU and OECD guidelines, where semi-occlusive dressing, an exposure period of 4 h, treatment of only intact skin and a recovery period of up to 14 days is stipulated. This study is therefore of limited adequacy for C&L purposes due to the intensity of the exposure regime and the too short recovery period.

The second study was a skin irritation screening test with two animals. It was performed with a mixture of dodecyl-, pentadecyl- methacrylate (approximately equal parts) with exposure for 24 h under occlusive conditions (Parsons RD, 1981). Mean erythema score was 1 in both animals, mean oedema score was 0.5 in both animals. All signs of irritation were fully reversible within 7 days. According to the CLP criteria, the substance was not irritating in this study.

The third study was an FDA Draize study with n-decyl methacrylate (Sterner and Chibanguza, 1978). For clarification, dodecyl methacrylate and n-decyl methacrylate are not synonyms. They have different CAS numbers; dodecyl methacrylate (142-90-5) and n-decyl methacrylate (3179-47-3) and their molecular formulas are different (dodecyl methacrylate $C_{16}H_{30}O_2$ and n-decyl methacrylate $C_{14}H_{26}O_2$). In this study, New Zealand White rabbits were dermally exposed (intact and scarified skin) under occlusive conditions to 0.5 mL undiluted n-decyl methacrylate for 24 h. Animals where observed for 3 days. 2/6 animals reached the maximum irritation score of 2 for erythema and 1/6 animal the maximum irritation score of 2 for oedema. Irritations were not fully reversible within the observation time of 72 h. In addition, the exposure time was longer than 4 h (24 h). In this study, n-decyl methacrylate was slightly irritating to skin. According to the CLP criteria both erythema and oedema effects were < 2.3.

The fourth study was performed according to OECD 404 with the structurally related substance isotridecyl methacrylate (Schreiber, 1989). In this study, 3 New Zealand White rabbits were dermally exposed for 4 h with 0.5 g undiluted test substance under semi-occlusive conditions. Animals were observed after 1 h, 24 h, 48 h, 72 h and after 8 or 9 days. Mean erythema scores (24 +48 +72 h) were 0, 0.33 and 0.66 of max. 4. Mean oedema scores (24 +48 +72 h) were 0, 1.33 and 1.66 of max. 4. All erythema scores were fully reversible within 72 h, all oedema scores within 8 days. Under the CLP criteria, isotridecyl methacrylate was not irritating to skin.

No human data were available.

In summary, the observation period of the two studies with a mixture of methacrylate and with n-decyl methacrylate were too short to observe full recovery of the animals and also the duration of exposure was longer (24 h) than the current guideline value (4 h). However, by analogy to isotridecyl methacrylate and dodecyl-, pentadecyl methacrylate, full recovery after 8/7 days is assumed. Dodecyl methacrylate is thus considered to be slightly irritating to skin but not a skin irritant according to the CLP criteria.

In four studies with structurally related substances to dodecyl methacrylate, the criteria for classification according to CLP were not met. Mean erythema and oedema scores were < 2.3 in all animals. Since two of the studies were carried out for only 72 h, reversibility was demonstrated with the structurally related substances isotridecyl methacrylate and dodecyl-, pentadecyl methacrylate that were fully reversible within 8/7 days.

According to the DS, dodecyl methacrylate should not be classified as irritating to skin, based on the CLP criteria, and the current classification should be deleted.

Comments received during public consultation

Comments were received from two Member States (MSs). One MS could not conclude on the validity of the proposal to withdraw all the human health classification included in the harmonised classification of dodecyl methacrylate. They pointed out that no justification on the read across

from the tested substances to dodecyl methacrylate was provided in the report, and furthermore that dodecyl methacrylate is metabolised to methacrylic acid (MAA), which is known to be a strong irritant since it is classified as Skin Corr. 1A. The DS responded that the four skin irritation studies used were performed with two single compounds, one compound (isotridecyl methacrylate with C13) with one carbon atom more in the alkyl chain then dodecyl methacrylate (C12) and another compound (decyl methacrylate with C10) with two carbon atoms less in the alkyl chain 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). Further, since the results of the experimental studies did not show a strong irritant effect of the methacryl esters investigated, the metabolism towards methacrylic acid in the skin seems to be insufficient to cause a strong skin irritation.

The second MS asked for a presentation of the details in the OECD chemical programme assessment that was mentioned in section 3 of the CLH report. The DS responded that the data from the OECD report was reflected in the CLH proposal.

Assessment and comparison with the classification criteria

Dodecyl methacrylate has a harmonised classification as Skin Irrit. 2 in the CLP Regulation. It should also be noted that this classification corresponds to the classification of the group entry 607-134-00-4 “monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex”. The DS proposal is to remove the classification of dodecyl methacrylate based on four skin irritation studies with other methacrylates or mixtures of methacrylate containing dodecyl methacrylate, see table 1. The removal of the Skin Irrit. 2 classification of dodecyl methacrylate is therefore based on read across from other methacrylates both with a longer chain length compared to dodecyl methacrylate (C12) (isotridecyl methacrylate (C13), tetradecyl methacrylate (C14) and pentadecyl methacrylate (C15)) and shorter chain length (n-decyl methacrylate (C10)). RAC agrees with the DS that read across to other shorter- or longer- chain methacrylates is relevant due to the similar trend in the physico-chemical properties, structural similarities and common metabolic pathway.

In a previous German (IND) proposal under the former TC C&L group, the classification of dodecyl methacrylate for skin irritation was suggested to be withdrawn (TC C&L, document ECBI/37/06). However, the proposal was never discussed by the TC C&L[1].

The studies that were used to classify the group entry “monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex” as Skin Irrit. 2 were not available for assessment by RAC.

RAC agrees with the DS that the four skin irritation studies performed with mixtures of methacrylates containing dodecyl methacrylate (65% in one study, no detailed information on the composition in the other study) or with n-decyl methacrylate or isotridecyl methacrylate only,

[1] In the rationale for this previous proposal to withdraw the classification for skin irritation, two skin irritation studies were included (Sterner and Stigilc, 1977 and Schreiber, 1989). These studies have also been included by the DS in the current proposal. The DS has additionally included two skin irritation studies in the CLH proposal. The first of these studies showed that n-decyl methacrylate was inducing slight skin irritation (Sterner and Chibanguza, 1978), however, the exposure time was longer than 4 h (24 h). In comparison with the CLP criteria, both erythema and oedema effects were < 2.3. The second of these two studies showed that a mixture of dodecyl-, pentadecyl- methacrylate was not inducing skin irritation (Parsons, 1981).

induced slight skin irritation or no skin irritation, and thus no classification for skin irritation according to the CLP criteria is justified based on the results from these studies.

Furthermore, RAC agrees that due to the information on dermal absorption provided by the DS, the dermal uptake is considered to be low due to the low water solubility (< 1 µg/L) of dodecyl methacrylate. However, when it comes to the molecular weight that is between 100 and 500 g/mol (254 g/mol), dermal uptake is anticipated. Moreover, dodecyl methacrylate is reported in the literature to be a skin sensitiser (Greim *et al.*, 1995 and Kanazawa *et al.*, 1999), supporting that dermal absorption could occur. However, the DS also estimated the dermal absorption (steady-state flux) of dodecyl methacrylate by calculation (see table 2 of the opinion). From this estimation it was concluded that based on the molecular weight of dodecyl methacrylate of 254.41 g/mol and the log Pow of 6.68, the predicted flux of dodecyl methacrylate is 0.003 µg/cm²/h, and RAC agrees to the conclusion that the relative dermal absorption is considered to be low.

The DS included in the CLH report that although dodecyl methacrylate has a skin binding structure (methacrylate) it is not skin irritating or corrosive.

Conclusion

RAC considers that the read across for skin irritation from longer- and shorter- chain length methacrylates compared to dodecyl methacrylate is justified due to the similar trend in the physico-chemical properties, structural similarities and common metabolic pathway. Further, the dermal absorption was estimated to be low for dodecyl methacrylate.

RAC supports the DS's proposal to remove the classification as Skin Irrit. 2 for dodecyl methacrylate based on the read across to other longer- and shorter- chain length methacrylates compared to dodecyl methacrylate.

RAC evaluation of serious eye damage/irritation

Summary of the Dossier Submitter's proposal

No study on eye irritation was available following eye exposure to dodecyl methacrylate. However, the DS assessed, in a weight-of-evidence approach, four eye irritation studies in rabbits, 3 in New Zealand White and one in Albino rabbits with structurally related long-chain alkyl methacrylates. In this respect, the DS included information regarding the physico-chemical properties of the substances used for a read across to dodecyl methacrylate (see table 1).

Data from eye irritation studies in rabbits:

In the first study that followed a Draize protocol, 0.1 mL of a mixture of 65% dodecyl methacrylate, 25% tetradecyl methacrylate and 10% higher alkyl methacrylate was instilled into the right eye of six New Zealand White rabbits (Sterner and Chibanguza, 1978a). Eyes were not rinsed. The eyes were examined at 24, 48 and 72 h from the beginning of the test. In this study, there were no signs of damage to cornea and iris and no signs of redness and chemosis of the conjunctiva. All irritation scores were 0.

In the second study, 0.1 mL of a mixture of dodecyl- and pentadecyl- methacrylate with approximately equal parts of C12-, C13-, C14- and C15- methacrylates was tested undiluted in 6 Albino rabbits (Mastri, 1975). Eyes were not rinsed. Irritation scores were evaluated after 24, 48 and 72 h of instillation. Mean irritation scores for erythema and iris were 0. Maximum mean irritation score of conjunctiva (redness and chemosis) was 0.67. Irritations were fully reversible

within 7 days. In this study dodecyl-, pentadecyl- methacrylate was not irritating to eyes according to the CLP criteria.

The third study followed a Draize protocol where 0.1 mL of n-decyl methacrylate was instilled undiluted into the conjunctival sac of the left eye of 6 New Zealand White rabbits for 72 h (Sterner and Chibanguza, 1978b). The eyes were not rinsed. Animals were observed for 7 days. Mean irritation scores (24 + 48 + 72 h) for cornea, iris, conjunctiva and chemosis were 0 for all animals. In this study, decyl methacrylate was not irritating to eyes.

In the fourth study, isotridecyl methacrylate was tested in an eye irritation study according to OECD 405 (Schreiber, 1989). 0.1 mL test substance was instilled into the right eye of 3 New Zealand White rabbits. Eyes were not rinsed. The grades of lesions at 24, 48 and 72 h of the cornea, iris and conjunctiva were examined. There were no signs of damage to cornea and iris and no signs of redness and chemosis of the conjunctiva. All irritation scores were 0. In this study, isotridecyl methacrylate was not irritating to eyes.

No human data were available.

In summary, no signs of eye irritation were observed in the four studies with structurally related long-chain alkyl methacrylates (mixture of 65% dodecyl methacrylate and 25% tetradecyl methacrylate and 10% higher alkyl methacrylates, dodecyl-, pentadecyl- methacrylate, n-decyl methacrylate and isotridecyl methacrylate). Maximum irritation score for conjunctiva was 0.67 with dodecyl-, pentadecyl- methacrylate that was fully reversible within 7 days. Irritation scores in the three other studies were 0 for all irritation parameters at all observation time points. In analogy, dodecyl methacrylate is considered not to be an eye irritant.

The DS concluded that according to the CLP criteria, dodecyl methacrylate should not be classified as irritating to eyes. Thus, the current classification should be deleted.

Comments received during public consultation

Comments were received from two MSs. One MS could not conclude on the validity of the proposal to withdraw all the human health classifications of dodecyl methacrylate. They pointed out that no justification on the read across from the tested substances to dodecyl methacrylate was provided in the report, and furthermore that dodecyl methacrylate is metabolised to MAA, which is known to be a strong irritant since it is classified as Skin Corr. 1A. The DS responded that the four skin irritation studies used were performed with two single compounds, one compound (isotridecyl methacrylate with C13) with one carbon atom more in the alkyl chain than dodecyl methacrylate (C12) and another compound (decyl methacrylate with C10) with two carbon atoms less in the alkyl chain than 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). Further, since the results of the experimental studies did not show a strong irritant effect of the methacryl esters investigated, the metabolism towards methacrylic acid in the eye seems to be insufficient to cause a strong eye irritation.

The second MS asked for a presentation of the details in the OECD chemical programme assessment that was mentioned in section 3 of the CLH report. The DS responded that the data from the OECD report was reflected in the CLH proposal.

Assessment and comparison with the classification criteria

Dodecyl methacrylate has a harmonised classification as Eye Irrit. 2 in the CLP Regulation. It should also be noted that this classification corresponds to the classification of the group entry 607-134-00-4 “monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the

exception of those specified elsewhere in this Annex". The DS proposal is to remove the classification of dodecyl methacrylate based on four eye irritation studies with other methacrylates or mixtures of methacrylate containing dodecyl methacrylate (see table 1). The removal of the Eye Irrit. 2 classification of dodecyl methacrylate is therefore based on read across from other methacrylates, both with a longer chain length compared to dodecyl methacrylate (C12) (isotridecyl methacrylate (C13), tetradecyl methacrylate (C14) and pentadecyl methacrylate (C15)) and with a shorter chain length (decyl methacrylate (C10)). RAC agrees with the DS that a read across to other shorter- or longer- chain methacrylates is relevant due to the similar trend in the physico-chemical properties, structural similarities and common metabolic pathway.

In a previous German (IND) proposal under the former TC C&L group the classification of dodecyl methacrylate for eye irritation was suggested to be withdrawn (TC C&L, document ECBI/37/06). However, the proposal was never discussed by the TC C&L[2].

The studies that were used to classify the group entry "monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex" as Eye Irrit. 2 have not been available for assessment to RAC. RAC agrees with the DS that the four eye irritation studies performed with mixtures of methacrylate containing dodecyl methacrylate (65% in one study, no detailed information on the composition in the other study) or with decyl methacrylate or isotridecyl methacrylate, did not induce eye irritation. In one study the maximum irritation score for conjunctiva was 0.67 with dodecyl-, pentadecyl- methacrylate that was fully reversible within 7 days. No classification for eye irritation according to the CLP criteria is therefore justified based on the results from these studies.

Conclusion

RAC considers that the read across for eye irritation from longer- and shorter- chain length methacrylates compared to dodecyl methacrylate is justified due to the similar trend in the physico-chemical properties, structural similarities and common metabolic pathway.

RAC supports the DS proposal to remove the classification as Eye Irrit. 2 for dodecyl methacrylate based on the read across to other longer- and shorter- chain length methacrylates compared to dodecyl methacrylate.

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic environmental hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Dodecyl methacrylate is currently listed in Annex VI to the CLP Regulation (EC) 1272/2008 and classified as Aquatic Acute 1 – H400 and Aquatic Chronic 1 – H410 based on a 96-h E_rC_{50} > 0.19 mg/L and a 96-h NOE_rC of 0.0062 mg/L for *Pseudokirchneriella subcapitata* (Hoberg, 1995). New algal data (Noack, 2005b) were submitted and deletion of the environmental classification was approved by the Technical Committee on Classification and Labelling of Dangerous Substances (TC C&L) in January 2007 (ECBI/08/07 Rev. 2). This decision was not implemented. The DS

[2] In the rationale for this previous proposal to withdraw classification for eye irritation, two eye irritation studies were included (Sterner and Chibanguza, 1977 and Schreiber, 1989). In addition to these studies, the DS has included two eye irritation studies in the current CLH proposal. Both studies showed no eye irritation following exposure to dodecyl- and pentadecyl- methacrylate with approximately equal parts of C12-, C13-, C14- and C15- methacrylates and n-decyl methacrylate, respectively.

consequently proposed to remove the current classification based on the same arguments that were accepted by the TC C&L.

Degradation

No information is available on the abiotic stability of dodecyl methacrylate.

A Modified MITI (I) test (OECD TG 301C) indicated 88.5 % degradation (based on oxygen consumption) over 28 days. The 10-d window criterion was fulfilled, so dodecyl methacrylate is readily biodegradable. The test concentration was 100 mg/L, significantly exceeding the reported solubility in pure water of < 0.001 mg/L at 25 °C. The CLH proposal includes a supporting OECD TG 301C study on a structural analogue (C13- and C15- alkyl methacrylates (linear and branched)), which was also readily biodegradable.

Bioaccumulation

The predicted octanol-water partition coefficient (log K_{ow}) is 6.68 (using KOWWIN™ v1.67 in EPI web 4.0). No *in vivo* study was available with dodecyl methacrylate. The CLH proposal included an aqueous fish bioaccumulation (OECD TG 305) study for the structurally related substance ethylhexyl methacrylate indicating rapid depuration (half-life of 1.5 h), but read-across was not applied due to expected differences in bioavailability. The DS concluded that dodecyl methacrylate has the potential to bioaccumulate in organisms based on the estimated log K_{ow} > 4.

Aquatic toxicity

Aquatic toxicity data are available for all three trophic levels, and a summary of the relevant information is provided in the following table (the key endpoints used in hazard classification are highlighted in bold). All studies were performed under flow-through conditions with results expressed in terms of mean measured concentrations, unless stated otherwise.

Table: Summary of relevant information on aquatic toxicity

Method	Test organism	Endpoint	Toxicity values in mg a.s./L	Reference
Short-term toxicity to fish				
OECD TG 203 [a]	*Oncorhynchus mykiss* (Rainbow Trout)	96-h LC_{50}	> 62	Springborn Laboratories, 1995 [b]
DIN 38412 part 15 (static)	*Leuciscus idus* (Golden Orfe)	48-h LC_{50}	1 080 (nominal)	Institut Fresenius, Chemische und biologische Laboratorien GmbH, 1988 [b]
Long-term toxicity to fish				
No data				
Short-term toxicity to aquatic invertebrates				
OECD TG 202 [a]	*Daphnia magna*	48-h EC_{50}	> 2	Putt, 1995 [b]
Long-term toxicity to aquatic invertebrates				
OECD TG 211 (semi-static)	*Daphnia magna*	21-d NOEC (reproduction and immobilisation)	**≥** 0.00573	Noack, 2005a
Toxicity to algae and aquatic macrophytes				
OECD TG 201 [a] (static)	*Pseudokirchneriella subcapitata*	96-h E_rC_{50} 96-h NOE_rC	> 0.19 0.0068 (initial measured)	Hoberg, 1995 [b]
OECD TG 201 (static)	*Desmodesmus subspicatus*	72-h E_rC_{50} 72-h NOE_rC	> 0.01 0.01 (nominal)	Noack, 2005b
N.a. – data not available				

Method	Test organism	Endpoint	Toxicity values in mg a.s./L	Reference
Short-term toxicity to fish				
Note: [a] – Test substance was a mixture of 69.13 % dodecyl methacrylate and 27.4 % tetradecyl methacrylate. [b] – Study is considered unreliable by the DS.				

The acute fish and acute *Daphnia* studies were considered unreliable as they were conducted significantly in excess of the solubility limit in pure water (< 0.001 mg/L at 25 °C; undissolved substance was observed in some of the test solutions), and one fish and the *Daphnia* study also used a test substance that contained 27.4 % tetradecyl methacrylate. However, since no effects were apparent (other than at very high nominal test concentrations), repeat tests were not considered necessary.

The 21-d *Daphnia* study was a limit test at a nominal test concentration of 0.01 mg/L (i.e. at least an order of magnitude above the solubility limit in pure water) and no effects were observed.

The Hoberg (1995) study was originally considered valid when it was used as the basis for the current harmonised classification. However, the test substance composition is significantly different from the substance addressed by the proposal (95 – 100 % dodecyl methacrylate) and test concentrations were at least an order of magnitude above the solubility limit of dodecyl methacrylate in pure water. Coupled with the results of a repeat limit test at 0.01 mg/L (nominal) with a different algal species (Noack, 2005b) in which no effects were observed, the DS considered the Hoberg (1995) study to be unreliable.

Comments received during public consultation

Two Member State Competent Authorities (MSCA) agreed with the proposed declassification, one of them suggesting that studies that used a mixture of 69.13% dodecyl methacrylate and 27.4% tetradecyl methacrylate are not appropriate for classification of dodecyl methacrylate and should not be taken into account in the overall weight of evidence.

One MSCA asked for all relevant data from an OECD HPV assessment to be included (the DS replied that they had done so), and asked for some clarifications for the description of the Hoberg (1995) algal study to confirm its reliability for 72-h endpoints (pointing out that the Noack (2005b) study might not be directly comparable as it used a different species). The information provided by the DS in response appears to show a dose-response relationship with 72-h E_rC_{50} and NOE_rC values equivalent to those selected by the DS at 96 h. RAC notes that 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) 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 %). It is not known whether the dodecyl methacrylate study suffered from similar drawbacks. In addition, no information is provided on test concentration maintenance. Nevertheless, RAC considers that the different test substance identity and use of nominal concentrations well above the water solubility limit of dodecyl methacrylate are sufficient reasons to set the Hoberg (1995) study aside for hazard classification purposes, given that a valid study on another algal species is available.

One MSCA disagreed with the proposal because they claimed that a predicted “toxicity value” (presumably chronic NOEC or equivalent) was below 0.010 mg/L using the PBT Profiler without any additional supporting information (e.g. on species, endpoint or applicability domain). In addition, it is not possible to independently evaluate the reliability of the reported water solubility value, or whether solubility in aquatic test media is significantly different from pure water, which creates some uncertainty for the interpretation of the data.

Assessment and comparison with the classification criteria

Degradation

Dodecyl methacrylate is readily biodegradable, and is therefore rapidly degradable according to the CLP Regulation.

Bioaccumulation

The substance is potentially bioaccumulative based on a predicted log K_{ow} value above the CLP Regulation threshold of 4.

Aquatic toxicity

Short-term aquatic toxicity data are available for three trophic levels, but only one (algal) study is considered fully reliable. The algal 96/72-h E_rC_{50} is above the water solubility limit of the substance, which is consistent with the available data for fish and *Daphnia*. The substance therefore does not require classification for Aquatic Acute hazard.

Reliable long-term aquatic toxicity data are available for invertebrates and algae, with relevant NOEC values above the water solubility limit of the substance indicating no need for Aquatic Chronic classification. Since there are no long-term toxicity data for fish and the substance is potentially bioaccumulative, the surrogate approach has to be considered. However, it is poorly water soluble and does not appear to be acutely toxic to fish at levels up to the water solubility limit, resulting in no classification. As it is rapidly degradable, it also does not require classification as Aquatic Chronic 4.

In summary, RAC supports the DS's proposal to remove classification as Aquatic Acute 1 and Aquatic Chronic 1.

Additional references

Greim *et al.*, 1995. Assessment of structurally related chemicals: Toxicity and ecotoxicity of acrylic acid and acrylic acid alkyl esters (acrylates), methacrylic acid and methacrylic acid alkyl esters (methacrylates). Chemosphere, 31; 2637-2659.

Kanazawa *et al.*, 1999. Structure-activity relationship in allergic contact dermatitis induced by methacrylates. Contact Dermatitis. 40; 19-23.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).