Committee for Risk Assessment

RAC

Annex 1
Background document
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

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

22 September 2017

CLH report

Proposal for Harmonised Classification and Labelling

**Based on Regulation (EC) No 1272/2008 (CLP Regulation),
Annex VI, Part 2**

Substance Name:

Dodecyl methacrylate

EC Number: **205-570-6**

CAS Number: **142-90-5**

Index Number: **607-247-00-9**

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Industry in accordance with Article 37(6) of CLP Regulation

Version number: 2.0 **Date: October 2016**

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	Dodecyl methacrylate
EC number:	205-570-6
CAS number:	142-90-5
Annex VI Index number:	607-247-00-9
Degree of purity:	≥ 80 %
Impurities:	
Stabilizer	

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation
Current entry in Annex VI, CLP Regulation	Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 C ≥ 10 % Aquatic Acute 1, H400 Aquatic Chronic 1, H410
Current proposal for consideration by RAC	Deletion of: Skin Irrit. 2, H315 Eye Irrit. 2, H319 STOT SE 3, H335 Aquatic Acute 1, H400 Aquatic Chronic 1, H410
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	none

Table 3: Proposed modification of Annex VI entry No. 607-134-00-4

Index No. 607-134-00-4	**Wording of the international chemical identifier**
Current entry in Annex VI, CLP Regulation	monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex
Proposed modified entry in Annex VI, CLP Regulation	monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex and dodecyl methacrylate

1.3 Proposed harmonised classification and labelling based on CLP Regulation

Table 4: Proposed classification according to the CLP Regulation

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives				
2.2.	Flammable gases				
2.3.	Flammable aerosols				
2.4.	Oxidising gases				
2.5.	Gases under pressure				
2.6.	Flammable liquids				
2.7.	Flammable solids				
2.8.	Self-reactive substances and mixtures				
2.9.	Pyrophoric liquids				
2.10.	Pyrophoric solids				
2.11.	Self-heating substances and mixtures				
2.12.	Substances and mixtures which in contact with water emit flammable gases				
2.13.	Oxidising liquids				
2.14.	Oxidising solids				
2.15.	Organic peroxides				
2.16.	Substance and mixtures corrosive to metals				
3.1.	Acute toxicity - oral				
	Acute toxicity - dermal				
	Acute toxicity - inhalation				
3.2.	Skin corrosion / irritation	none		Skin Irrit. 2 H315	
3.3.	Serious eye damage / eye irritation	none		Eye Irrit. 2 H319	
3.4.	Respiratory sensitisation				
3.4.	Skin sensitisation				
3.5.	Germ cell mutagenicity				
3.6.	Carcinogenicity				
3.7.	Reproductive toxicity				
3.8.	Specific target organ toxicity –single exposure	none		STOT SE 3 H335; C ≥ 10 %	

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
3.9.	Specific target organ toxicity – repeated exposure				
3.10.	Aspiration hazard				
4.1.	Hazardous to the aquatic environment	none		Aquatic Acute 1 H400 Aquatic Chronic 1 H410	
5.1.	Hazardous to the ozone layer				

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: **Signal word:** none
Hazard statements: none
Precautionary statements: none

Proposed notes assigned to an entry: none

1.4 Relation to common group entry with Index No 607-134-00-4 in Annex VI

The common group entry with the Index No. 607-134-00-4 is an umbrella entry for certain esters of methacrylic acid. The international chemical identifier reads as “monoalkyl or monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex” and it classifies all substances encompassed by this definition as Skin Irrit. 2, Eye Irrit 2 and STOT SE 3 H335.

Along with several other esters of methacrylic acid dodecyl methacrylate is exempted from this entry by the fact that it currently has its own entry in Annex VI. With the proposed modification of the current classification of dodecyl methacrylate however the current Annex VI entry would effectively be removed and therefore removing the current exemption at the same time. The deletion of the Annex VI entry for dodecyl methacrylate would therefore only affect the environmental classification of the substance, as the classification for the human health endpoints would be reinstated by the group entry.

It is therefore proposed to simultaneously change the wording of the international chemical identifier of the aforementioned group entry 607-134-00-4 by appending the words “and dodecyl methacrylate” to explicitly exempt the substance from the scope of the group entry.

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

Dodecyl methacrylate was primarily classified and labelled by authorities with Xi, R 36/37/38, S26, 28, 60 and adopted of Annex I of Directive 67/548/EEC, Index No. 607-134-00-4 (monoalkyl or

monoaryl or monoalkyaryl esters of methacrylic acid with the exception of those specified elsewhere in this Annex). This group classification is not based on data of individual member substances.

In 1995, the Methacrylate Producers Association (MPA), Washington, submitted preliminary results from an algal toxicity study in accordance with TSCA 8e to the coordinator of the Office of Pollution Prevention and Toxics at the Environmental Protection Agency (EPA), Washington DC and submitted in January 1996 the concerning study to EPA.

On this base ECB amended the classification of Dodecyl methacrylate with N, R50/53 which was adopted in 2004 in the 29th ATP to the DSD (Annex I of Directive 67/548/EEC, Index No. 607-247-00-9, R36/37/38, N, R50/53, S26, 28, 60, 61) after the introduction of the environmental endpoints into the classification criteria.

Studies on algal toxicity were repeated and showed that the study, which induced the environmental classification, was invalid.

A first EU classification and labelling dossier was submitted to the German competent authority (BAuA) in 2005. In January 2007 deletion of environmental classification was discussed and approved by the Technical Committee on Classification and Labelling of Dangerous Substances (TC C&L) (ECBI/08/07 Rev. 2), but not implemented.

With implementation of the CLP regulation the substance was classified and labelled as Skin Irrit. 2 (H315), Eye Irrit. 2 (H319), STOT SE 3 (H335), Aquatic Acute 1 (H400) and Aquatic Chronic 1, (H410).

Substances used in analogy with dodecyl methacrylate

Pure dodecyl alcohol (dodecanol, lauryl alcohol) is used only on a small scale to produce dodecyl methacrylate. In the large-scale production of long-chain aliphatic methacrylate esters technical mixtures are used of fatty (long-chain aliphatic) alcohols of natural or synthetic origin. As these substances are of main interest on the market, several toxicological studies are available with mixtures of long-chain methacrylates containing dodecyl methacrylate and were used in this CLH dossier.

Table 5: Physico chemical properties of the substances used in studies in this classification dossier:

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	5.59[a]	3.07[a]
Dodecyl methacrylate	142-90-5	$C_{16}H_{30}O_2$	254	6.68[b]	< 0.001[a]
Tridecyl methacrylate	2495-25-2	$C_{17}H_{32}O_2$	268	7.17 [b]	0.01409[c]
Isotridecyl methacrylate	94247-05-9	$C_{17}H_{32}O_2$	268	7.09 [b]	0.01628[c]
Tetradecyl methacrylate	2549-53-3	$C_{18}H_{34}O_2$	282	7.66 [b]	0.004461[c]
Pentadecyl methacrylate	6140-74-5	$C_{19}H_{36}O_2$	297	8.15 [b]	0.001409[c]
Hexadecyl methacrylate	2495-27-4	$C_{20}H_{38}O_2$	311	8.64 [b]	0.0004442[b]
Octadecyl methacrylate	32360-05-7	$C_{22}H_{42}O_2$	339	9.62 [b]	0.0000437[b]

[a] Measured data
[b] Calculated data, [c] Calculated data are higher than predicted from experimental data with dodecyl methacrylate

2.2 Short summary of the scientific justification for the CLH proposal

Data from the REACH registration were taken as a basis for this CLH proposal.

Based on the available/presented data the classification/labelling with Skin Irrit. 2 (H315), Eye Irrit. 2 (H319), STOT SE 3 (H335), Aquatic Acute 1 (H400) and Aquatic Chronic 1 (H410) is deemed to be not justified.

2.3 Current harmonised classification and labelling

2.3.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

Table 6: Current entry in Annex VI, Table 3.1 in the CLP Regulation (Index-No.: 607-247-00-9)

Classification		Labelling			Specific Conc. Limits, M-factors	Notes
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Pictogram, Signal Word Code(s)**	**Hazard statement Code(s)**	**Suppl. Hazard statement Code(s)**		
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 H400 H410	-	STOT SE 3: C ≥ 10 %	

2.4 Current self-classification and labelling

2.4.1 Current self-classification and labelling based on the CLP Regulation criteria

The following industry self-classification(s) and labelling are publically available in the ECHA C&L Inventory (October 2016).

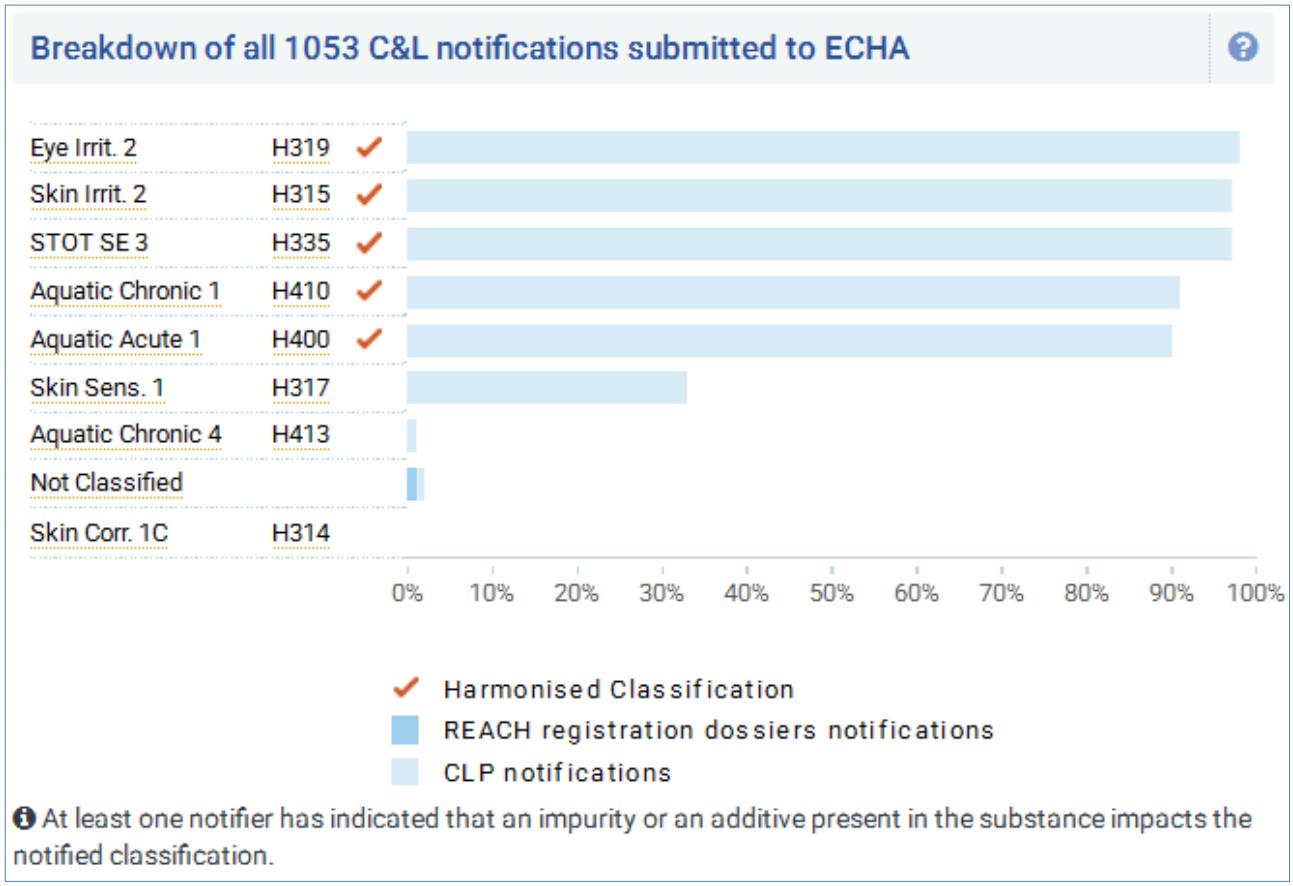


Figure 1: C&L notifications submitted to ECHA (October 2016, www.echa.eu)

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

For Dodecyl methacrylate a harmonised classification had been developed under 67/548/EC. Assessments performed under the OECD chemicals programme and in order to achieve a registration under REACH indicated, that according to new data the existing classification no longer reflects the criteria in Annex 1 of the CLP regulation (Regulation (EC) No 1272/2008). This document represents an update of the harmonised classification according to the currently available and most reliable information following a comprehensive assessment of the key data on behalf of the 2010 registrants under REACH.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

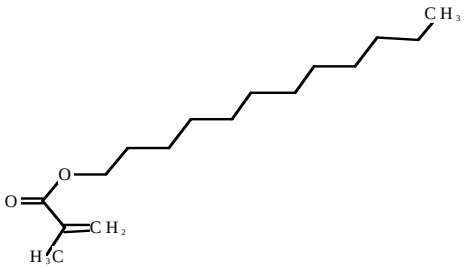
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 7: Substance identity

EC number:	205-570-6
EC name:	Dodecyl methacrylate
CAS number (EC inventory):	142-90-5
CAS number:	142-90-5
CAS name:	2-Propenoic acid, 2-methyl-, dodecyl ester
IUPAC name:	Dodecyl methacrylate
CLP Annex VI Index number:	607-247-00-9
Molecular formula:	$C_{16}H_{30}O_2$
Molecular weight range:	254.42 g/mol

Structural formula:



1.2 Composition of the substance

Table 8: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
Dodecyl methacrylate	Ca. 99.3 %	95-100 %	

For further information on the composition of the substance refer to the IUCLID file.

1.3 Physico-chemical properties

Table 9: Summary of physico - chemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
State of the substance at 20°C and 101,3 kPa	liquid		observation
Melting/freezing point	Melting Point: -7 °C (atmospheric pressure (1013 hPa) assumed)	Brandes and Möller (2003),	Measured, handbook data
Boiling point	307 – 318 °C	Brandes , Möller (2003), Nabert, Schön, Redeker (2005)	Measured, handbook data
Relative density	0.87 g/cm³	Brandes and Möller (2003),	Measured, handbook data
Vapour pressure	0.06 Pa at 20 °C	Rehberg , Fisher (1948),	Measured, dynamic method, extrapolated Clausius Clapeyron equation
Surface tension	waiving		In accordance with column 2 of REACH Annex VII, the surface tension of the substance does not need to be tested because due to its chemical structure, no surface activity is predicted.
Water solubility	< 1 µg/L at 25 °C	Dr. U. Noack Laboratories (2004)	Measured acc.US-EPA OPPTS 830.7860, column elution method
Partition coefficient n-octanol/water	LogPOW 6.68	Syracuse research Corporation (2000)	Calculated, KOWWIN™ v1.67 in EPI web 4.0
Flash point	> 110 °C	Brandes and Möller (2003),	Measured, handbook data
Flammability	waiving	BAM (2013)	Flammability upon ignition (solids, gases): Testing can be waived, substance is a liquid. Flammability in contact with water: The classification procedure needs not to be applied because the substance does not contain metals or metalloids. Pyrophoric properties: The classification procedure needs not to be applied because the substance is known to be stable into contact with air at room temperature for prolonged periods of time (days).
Explosive properties	waiving	BAM (2013)	The classification procedure needs not to be applied because there are no chemical groups associated with explosive properties present in the molecule.

Self-ignition temperature	295 °C @ 1003 hPa	AQura GmbH (2008)	Measured acc. DIN 51794
Oxidising properties	waiving	BAM (2013)	The study does not need to be conducted for flammable liquids.
Granulometry	waiving		The substance is a liquid at 20°C. In accordance with column 2 of REACH Annex VII, the particle size distribution (Granulometry) study does not need to be performed as the substance is marketed or used in a non solid or granular form.
Stability in organic solvents and identity of relevant degradation products	waiving		In accordance with RAECH annex XI, the study was not conducted because it is not critical
Dissociation constant	waiving		In accordance with REACH annex XI, the study was not conducted as the test substance does not dissociate based on structural alerts
Viscosity	6.24 mm²/s @ 20 °C 3.74 mm²/s @ 40 °C	Evonik RohMax Additives GmbH (2008)	measured acc. DIN 51 562, read across of 2-propenoic acid, 2-methyl-, C12-16-alkyl esters

2 MANUFACTURE AND USES

2.1 Manufacture

The ester is produced either by

- direct esterification of methacrylic acid with the corresponding fatty alcohol (such products may contain up to 1 % methacrylic acid as a low molecular weight impurity)
- or trans-esterification/alcoholysis of methyl methacrylate with the corresponding fatty alcohol (such products may contain up to 1 % methyl methacrylate as a low molecular weight impurity).

Pure dodecyl alcohol (dodecanol, lauryl alcohol) is used only on a small scale to produce the ester. In the large-scale production of long-chain aliphatic methacrylate esters technical mixtures are used of fatty (long-chain aliphatic) alcohols of natural or synthetic origin.

The carbon chain length distribution of the resulting mix of long-chain aliphatic methacrylate esters mirrors the chain length distribution of the alcohol(s) used.

A typical raw material for the production of dodecyl methacrylate is a C12-rich alcohol mixture of natural origin with approx. 65-70 % dodecanol, approx 25 % tetradecanol (lauryl and myristyl alcohol) and approx. 5-10 % of higher alkyl alcohols.

2.2 Identified uses

The esters are monomers for the production of polymers. Typical uses of the polymers are in lubricant additives, paint resins, floor care products, sizing agents for paper, reactive adhesives and reactive coatings.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Not evaluated in this dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

In this chapter only toxicokinetics and irritation are discussed

4.1 Toxicokinetics (Absorption, Metabolism, Distribution and Elimination)

4.1.1 Non-human information

Physico chemical properties of the substance will enable qualitative judgements of the TK behaviour (Guidance on information requirements and chemical safety assessment Chapter R.7.c, R.7.12 Guidance on Toxicokinetics):

In general with a calculated log Pow of 6.68 of dodecyl methacrylate absorption into the blood from GI absorption, respiratory absorption or skin is not expected. (log Pow values between -1 and 4 are favourable for absorption). With a water solubility of < 1 µg/l the substance is poorly soluble. The molecular weight is 254 g/mol and the substance is not a skin sensitizer.

Experimental *in vitro* studies of the toxicokinetics of dodecyl methacrylate are only available for dermal absorption. Experimental *in vitro* studies with the structurally related substance ethylhexyl methacrylate are used to assess the metabolism of dodecyl methacrylate.

Absorption

GI absorption

No experimental data are available for GI absorption.

Substances with a molecular weight below 500 g/mol, high water solubility and a log Pow between -1 and 4 are favourable for absorption. With log Pow > 4 passive diffusion through membranes is not expected but the substance may form micelles and be absorbed into the lymphatic system. But with a water solubility of < 1 µg/l very low concentrations of the substance are bioavailable so that the substance is poorly absorbed. No signs of systemic toxicity are indicating that absorption has occurred were seen in an acute oral toxicity test up to 5000 mg/kg bw.

GI absorption is not the favoured route of absorption. Only a low amount of the substance may be absorbed by micellular solubilisation due to the very poor water solubility of the substance.

Respiratory absorption – Inhalation

No experimental data are available for respiratory absorption.

The vapour pressure of dodecyl methacrylate is only 0.06 Pa @ 20 °C and therefore the volatility is far too low for inhalation in a gaseous form (substances with low volatility have a vapour pressure of less than 0.5 kPa).

Inhalation is not the favoured route of absorption.

Dermal absorption

Dodecyl methacrylate is a liquid substance with a molecular weight between MW > 100 < 500 g/mol which would favour dermal uptake, but with a very low water solubility of 1 µg/l dermal uptake from the stratum corneum into the epidermis is likely to be too low. With log Pow > 6 the rate of transfer between the stratum corneum and the epidermis will be slow and will limit absorption across the skin. Uptake into the stratum corneum itself may be slow.

Although dodecyl methacrylate has a skin binding structure (methacrylate) it was not sensitizing in *in vivo* tests in mice and guinea pigs. The substance is not skin irritating or corrosive, so that the substance itself will not enhance penetration through damaged skin. No signs of systemic toxicity indicating absorption were observed in an acute dermal toxicity study up to 3000 mg/kg bw.

The dermal absorption (steady-state flux) of dodecyl methacrylate has been estimated by calculation using the principles defined in the Potts and Guy prediction model (Heylings JR, 2013).

Table 10: 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 254.41 g/mol and a log Pow of 6.68, the predicted flux of Dodecyl methacrylate is 0.003 µg/cm²/h; the relative dermal absorption is minimal.

Metabolism

No data are available of the metabolism of dodecyl methacrylate *in vivo*.

Assumed dodecyl methacrylate will be absorbed the prominent pathway for the metabolism of higher methacrylate esters starts with ester hydrolysis resulting in methacrylic acid and the corresponding alcohol (Jones, 2002), (McCarthy and Witz, 1997). While the acid is further metabolised via the valine pathway of the citric acid cycle (ECETOC, 1996; European Union, 2002) the alcohol may be further metabolised by the two standard metabolic pathways of fatty alcohols (first: oxidation: fatty alcohol -> aldehyde -> acid, and subsequently CoA-mediated fatty acid metabolism - or secondly : glucuronidation of the alcohol and excretion).

Alkyl esters of methacrylic acid up to C_8 (2-ethylhexyl methacrylate) showed rapid metabolism with half lives in rat blood of less than 30 min (Jones, 2002):

Series of *in vitro* and *in vivo* studies with methacrylates were used to develop PBPK that accurately predict the metabolism and fate of these monomers. The studies confirmed that alkyl methacrylate esters are rapidly hydrolysed by ubiquitous carboxylesterases. First pass (local) hydrolysis of the parent esters has been shown to be significant for all routes of exposure. *In vivo* measurements of rat liver indicated this organ as the greatest esterase activity. Similar measurements for skin microsomes indicated approximately a 20-fold lower activity than for liver. However, this activity was substantial and capable of almost complete first-pass metabolism of the alkyl methacrylates. For example, no parent ester penetrated whole rat skin *in vitro* for n-butyl methacrylate, octyl methacrylate or dodecyl

methacrylate tested experimentally with only methacrylic acid identified in the receiving fluid. In addition, model predictions indicate that esters of ethyl methacrylate or larger would be completely hydrolysed before entering the circulation via skin absorption. This pattern is consistent with a lower rate of absorption for these esters such that the rate is within the metabolic capacity of the skin. Parent ester also was hydrolyzed by S9 fractions from nasal epithelium and was predicted to be effectively hydrolysed following inhalation exposure.

These studies showed that any systematically absorbed parent ester will be effectively removed during the first pass through the liver (CL as % LBF, see Table 11). In addition, removal of methacrylic acid from the blood also occurs rapidly (T50 %; see Table 11).

Table 11: Rate constants for the ester hydrolysis by rat-liver microsomes and predicted systemic fate kinetics from methacrylates following i.v. administration

Ester	Vmax	Km	CL (%LBF)	$T_{50\%}$ (min)	C_{max} (MAA) (mg L^{-1})	T_{max} (MAA) (min)
Methacrylic acid (CAS 79-41-4; MAA)	-	-	51.6%	-	-	-
Methyl methacrylate (CAS 80-62-6; MMA)	445.8	164.3	98.8%	4.4	14.7	1.7
Ethyl methacrylate (CAS 97-63-5; EMA)	699.2	106.2	99.5%	4.5	12.0	1.8
Isobutyl methacrylate (CAS 97-86-9; i-BMA)	832.9	127.4	99.5%	11.6	7.4	1.6
n-Butyl methacrylate (CAS 97-88-1; n-BMA)	875.7	77.3	99.7%	7.8	7.9	1.8
Hexyl methacrylate (CAS 142-09-6; HMA)	376.4	34.4	99.7%	18.5	5.9	1.2
2-Ethylhexyl methacrylate (CAS 688-84-6; 2EHMA)	393.0	17.7	99.9%	23.8	5.0	1.2
Dodecyl methacrylate (OMA)	224.8	11.0	99.9%	27.2	5.0	1.2

Vmax (nM/min/mg) and Km (µM) from rat-liver microsome (100 µg/ml) determinations;
CL = clearance as % removed from liver blood flow,
T50 % = Body elimination time (min) for 50 % parent ester,
Cmax = maximum concentration (mg/L) of MAA in blood,
Tmax = time (min) to peak MAA concentration in blood from model predictions.

GSH conjugation, the second potential pathway, has only been observed with small alkyl methacrylates (methyl methacrylate/MMA, ethyl methacrylate/EMA) but was no longer measurable with butyl methacrylate. Moreover, GSH conjugation was only detectable with MMA and EMA at high concentrations which are only achievable under laboratory conditions (Elovaara et al. 1983, Mc Carthy et al 1994).

Table 12: Summary of the peak rates of absorption of MAA and alkyl-methacrylate esters through whole rat and human skin.

		Rat whole skin						Human whole skin
Ester	**Molec. Volume**	**Peak rate of appearance -- Parent Ester --**		**Peak rate of appearance -- MAA --**		**Period of peak abs. rate**	**Absorbed dose**	**Predicted rate of absorption**
		µg cm^{-2}h^{-1}	**±SEM**	**µg cm^{-2}h^{-1}**	**±SEM**	**h**	**% of applied/ over x h**	**µg cm^{-2}h^{-1}**
MAA	78.96*			4584**	± 344	5-8	70%/24	*327.0***
MMA	93.198	360	±20.9	108**	± 4.59	2.5-24	11.3%/24	*33.4***
EMA	107.436			*190***	-			*13.6***
iBMA	135.646			*56***	-			*4.0***
nBMA	135.856			40.9	± 9.4	2-10	0.4%/10	*2.9***
6HMA	164.277			*20***	-			*1.4***
2EHMA	191.66*			*9***	-			*0.6***
OMA	192.696			10.3	± 0.65	8-24	0.24%/24	*0.7***
DMA	249.536			11.8	± 2.11	8-24	0.26%/24	*0.8***

The values in normal type were obtained experimentally, whilst those in italics are predicted values.
** Values are predicted rates of appearance of total chemical including parent ester and metabolite

Distribution

As the bioavailability of dodecyl methacrylate is very low that means neither GI- and respiratory absorption nor dermal absorption are expected and complete metabolism is predicted, only a very low amount of the substance comes into consideration for distribution in blood or plasma and accumulation in organs and tissues.

In theory the lipophilic molecule is likely to distribute into cells and then the intracellular concentration may be higher than extracellular concentration particular in fatty tissues, but this is of secondary importance as the bioavailability of the substance is very low.

Accumulation

In case dodecyl methacrylate should be absorbed accumulation in adipose tissue could be expected as the calculated log Pow is 6.68, but before it should be completely metabolized.

Excretion

As absorption is very low respectively not expected and complete metabolism very fast excretion of dodecyl methacrylate is hardly relevant.

4.1.2 Human information

No human information is available

4.1.3 Summary and discussion on toxicokinetics

According to log Pow > 4 bioaccumulation of dodecyl methacrylate is expected. Otherwise with < 1 µg/l the substance is poorly soluble in water. Therefore the bioavailability of the substance is very low. QSAR modelling for dermal skin absorption predicted minimal absorption with a calculated flux of 0.003 µg/cm²/h (Heylings, 2013). *In vitro* studies with rat liver showed fast ester hydrolysis with alkyl methacrylates up to C8-methacrylates. The same metabolism is predicted for dodecyl methacrylate particularly as the available concentration in the body will be very low.

4.2 Irritation

4.2.1 Skin irritation

Table 13: Summary table of relevant skin irritation studies

Method	Results	Remarks	Reference
rabbit (New Zealand White) Coverage: semiocclusive (shaved) Vehicle: unchanged (no vehicle) OECD Guideline 404 (Acute Dermal Irritation / Corrosion) (adopted 21 May 1981. EEC Directive 84/449/EEC, Part B: methods for the determination of Toxicity, B5. Acute Toxicity. Skin irritation. Official Journal of the European Communities, No L251, pp. 106-108)	not irritating Erythema score: 0.66 of max. 4 (animal #1) (Time point: mean 24+48+72 h) (fully reversible within: 72 h) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria) 0 of max. 4 (animal #2) (Time point: mean 24+48+72 h) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria) 0.33 of max. 4 (animal #3) (Time point: mean 24+48+72 h) (fully reversible within: 72 h) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria) Edema score: 1.33 of max. 4 (animal #1) (Time point: mean 24+48+72 h) (fully reversible within: 8 days) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria) 1.66 of max. 4 (animal #2) (Time point: mean 24+48+72 h) (fully reversible within: 8 days) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria) 1 of max. 4 (animal #3) (Time point: mean 24+48+72 h) (fully reversible within: 8 days) (4-h semiocclusive exposure, reevaluated acc. CLP-criteria)	2 (reliable with restrictions) weight of evidence experimental result **Test material (CAS name): Isotridecyl methacrylate** Form: liquid	Schreiber (1989)
rabbit (albino rabbits) Coverage: occlusive (shaved and shaved/abraded) Vehicle: unchanged (no vehicle) according to Appraisal of the Safety of Chemicals in foods, drugs and	slightly irritating Erythema score: 1.25 of max. 4 (animal: # 1,# 2, #3, #4, #5, #6) (Time point: 24 and 72 h) (not fully reversible within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. DSD (overall mean).) 2 of max. 4 (animal #1) (Time point: mean 24 + 72 h) (not fully reversible	2 (reliable with restrictions) weight of evidence experimental result **Test material (EC name): 2-Propenoic acid, 2-methyl-, C12-16-alkyl esters**	Sterner and Stigilc (1977)

Method	Results	Remarks	Reference
cosmetics, FDA Draize (1959)	within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) 1.5 of max. 4 (animal: #2, #3, #4, #6) (Time point: mean 24 + 72 h) (not fully reversible within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) 1 of max. 4 (animal: #5) (Time point: mean 24 + 72 h) (not fully reversible within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) Edema score: 0.08 of max. 4 (animal: # 1,# 2, #3, #4, #5, #6) (Time point: 24 and 72 h) (not fully reversible within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. DSD (overall mean)) 0 (animal: #1, #2, #3, #4, #6) (Time point: mean 24 + 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) 0.5 of max. 4 (animal #5) (Time point: mean 24 + 72 h) (not fully reversible within: 72 h) (occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria)	Methacrylic acid ester of an alcohol mixture with a mean C-number of 12,6 = **C12.6 methacrylate** (65 % dodecyl methacrylate, 25 % Tetradecyl methacrylate, 10 % higher alkyl methacrylates up to octadecyl methacrylate) Form: liquid	
rabbit (New Zealand White) Coverage: occlusive (shaved and shaved/abraded) Vehicle: unchanged (no vehicle) according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FDA Draize (1959)	slightly irritating Erythema score: 1.67 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: 24 and 72 h) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. DSD criteria) 1.5 of max. 4 (animal: #1, #3, #4, #6) (Time point: mean 24 + 72 hours) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria)	2 (reliable with restrictions) weight of evidence experimental result Test material (IUPAC name): decyl methacrylate Form: liquid	Sterner W, Chibanguza (1978)

Method	Results	Remarks	Reference
	2 of max. 4 (animal: #2, #5) (Time point: mean 24 + 72 hours) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) Edema score: 0.92 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: 24 and 72 h) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. DSD criteria) 1 of max. 4 (animal: #1, #2, #3, #4, #5) (Time point: mean 24 + 72 hours) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria) 2 of max. 4 (animal: #6) (Time point: mean 24 + 72 hours) (not fully reversible within: 72 h) (Occlusive, exposure time 24 h, observation time 72 h, intact skin, reevaluated acc. CLP criteria)		
rabbit (New Zealand White) Coverage: occlusive Vehicle: unchanged (no vehicle) range finding study	not irritating Erythema score: 1 of max. 4 (animal: #1, #2) (Time point: mean 24 + 72 hours) (fully reversible within: 7 days) (Occlusive, exposure time 24 h, observation time 7 days, intact skin, reevaluated acc. CLP criteria) Edema score: 0.5 of max. 4 (animal: #1, #2) (Time point: mean 24 + 72 hours) (fully reversible within: 7 days) (Occlusive, exposure time 24 h, observation time 7 days, intact skin, reevaluated acc. CLP criteria)	2 (reliable with restrictions) weight of evidence experimental result Test material: Dodecyl-, Pentadecyl methacrylate Form: liquid	Parsons RD (1981)

4.2.1.1 Non-human information

No study on skin irritation potential is available of the single substance dodecyl methacrylate. The skin irritation was assessed in a weight of evidence approach with four available studies for structurally related long-chain alkyl methacrylates: One study according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FDA Draize (1959) with Methacrylic acid ester of an

alcohol mixture with a mean C-number of 12,6, CAS: 90551-76-1 (65 % dodecyl methacrylate, 25 % Tetradecyl methacrylate, 10 % higher alkyl methacrylates up to octadecyl methacrylate), one skin irritation screening test with two animals conducted in 1981 with Dodecyl-, Pentadecyl methacrylate (app. equal parts of C12-, C13, C14-and C15-methacrylates), another FDA Draize study with n-Decyl methacrylate and one study acc. OECD 404 with the structurally related substance isotridecyl methacrylate. Only the data for the shaved, intact skin were used for evaluation. In studies carried out with more than 3 animals both approaches, the overall mean score and the average score determined per animal, were used for evaluation.

C12,6 methacrylate: 6 rabbits were dermally exposed to 0.5 mL of C12,6 methacrylate. Two application sites per animal were treated, one site was left intact, the other site was abraded. Test sites were covered with an occlusive dressing for 24 hours. Animals were observed for 72 hours. Irritation was scored by the method of Draize et al, 1959.

The treated abraded skin sites showed identical effects as the intact sites. For reevaluation only the scores of the intact skin were used.

As the test was performed with 6 animals both, the CLP and DSD approaches for evaluation have to be conducted acc. Guidance on the application of the CLP criteria.

With the CLP approach the response of the individual animal values were averaged over the two observation days (24 hours and 72 hours after application) separate for erythema and edema. 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 hours. All mean scores were below 2.3.

With the DSD approach the average score overall animals was used separate for erythema and edema. The overall mean erythema score was 1.25 and the mean overall edema score 0.08. Both values are below 2.3.

Performance of the study does not comply with requirements of the relevant recent EU and OECD guidelines, where semi-occlusive dressing, an exposure period of 4 hours, 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 intensity of the exposure regime and too short recovery period.

Dodecyl-, Pentadecyl methacrylate: In an acute skin irritation range finding study (1981) 2 New Zealand White rabbits were exposed to Dodecyl-, Pentadecyl methacrylate which contains app. equal parts of C12-, C13-, C14 and C15-methacrylates for 24 h under occlusive conditions. Mean erythema score was 1 in both animals, mean edema score was 0.5 in both animals. All signs of irritation were fully reversible within 7 days. According CLP criteria the substance is not irritating in this study.

n-Decyl methacrylate: In a primary dermal irritation study conducted in 1978 New Zealand White rabbits were dermally exposed (intact and scarified skin) under occlusive conditions to 0.5 mL undiluted n-Decyl methacrylate for 24 hours. Animals then were observed for 3 days. Irritation scores for intact skin were reevaluated according to CLP criteria. 2/6 animals reached the maximum irritation score of 2 for erythema and 1/6 animal the maximum irritation score of 2 for edema. Irritations were not fully reversible within the observation time of 72 hours. Otherwise the exposure time was longer than 4 hours.

In this study n-Decyl methacrylate was slightly irritating to skin. According to CLP criteria effects both erythema and oedema effects are < 2.3. With the DSD approach the mean erythema score was 1.67, the mean edema score was 0.92.

Isotridecyl methacrylate was tested in a primary dermal irritation study acc. OECD 404. 3 New Zealand White rabbits were dermally exposed for 4 hours with 0.5 g undiluted test substance under semiocclusiv conditions. Animals were observed after 1h, 24h, 48h 72h and after 8 or 9 days. The test was reevaluated acc. CLP criteria. Mean erythema scores (24 +48 +72 h) were 0, 0.33 and 0.66 of max. 4. Mean edema 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 edema scores within 8 days. Under CLP criteria Isotridecyl methacrylate is not irritating to skin.

4.2.1.2 Human information

Human information is not available

4.2.1.3 Summary and discussion of skin irritation

By design, the observation period of the two studies with C12,6 methacrylate and n-Decyl methacrylate were too short to observe full recovery of the animals and also the duration of exposure was longer than the current guideline value. But in analogy to isotridecyl methacrylate and Dodecyl-, Pentadecyl methacrylate full recovery after 8/7 days is assumed. In analogy dodecyl methacrylate is considered to be slightly irritating to skin but not a skin irritant according to the CLP criteria.

4.2.1.4 Comparison with criteria

In four studies with structurally related substances to dodecyl methacrylate the criteria for classification acc. CLP criteria were not reached. Mean erythema and oedema scores were < 2.3 in all animals. As two studies were carried out for only 72 h, reversibility was demonstrated with the structurally related substances isotridecyl methacrylate and Dodecyl-, Pentadecyl methacrylate which were fully reversible within 8/7 days.

4.2.1.5 Conclusions on classification and labelling

According to CLP criteria dodecyl methacrylate has not to be classified as irritating to skin. Current classification should be deleted.

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].

[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).

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, 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.

4.2.2 Eye irritation

Table 14: Summary table of relevant eye irritation studies

Method	Results	Remarks	Reference
rabbit (New Zealand White) Vehicle: unchanged (no vehicle) OECD Guideline 405 (Acute Eye Irritation / Corrosion)	not irritating (not classified) Cornea score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) Iris score: 0 of max. 2 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) Conjunctivae score: 0 of max. 3 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) Chemosis score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h)	2 (reliable with restrictions) weight of evidence experimental result **Test material (CAS name): Isotridecyl methacrylate** Form: liquid	Schreiber (1989)
rabbit (New Zealand White) Vehicle: unchanged (no vehicle) according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FAD Draize (1959)	not irritating Cornea score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 +72 hr) Iris score: 0 of max. 2 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 +72 hr) Conjunctivae score: 0 of max. 3 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48+ 72 hr) Chemosis score: 0 of max. 3 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48+ 72 hr)	2 (reliable with restrictions) weight of evidence experimental result Test material (EC name): 2-Propenoic acid, 2-methyl-, C12-16-alkyl esters Methacrylic acid ester of an alcohol mixture with a mean C-number of 12,6 = C12.6 methacrylate (65 % dodecyl methacrylate, 25 % Tetradecyl methacrylate, 10 % higher alkyl methacrylates up to octadecyl methacrylate) Form: liquid	Sterner and Chibanguza (1978a)

Method	Results	Remarks	Reference
rabbit (New Zealand White) Vehicle: unchanged (no vehicle) according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FDA Draize (1959)	not irritating Cornea score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed) Iris score: 0 of max. 2 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed) Conjunctivae score: 0 of max. 3 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed) Chemosis score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed)	2 (reliable with restrictions) weight of evidence experimental result Test material (IUPAC name): decyl methacrylate Form: liquid	Sterner W, Chibanguza G (1978b)
rabbit (Albino Rabbits) Vehicle: unchanged (no vehicle) no data	not irritating Cornea score: 0 of max. 4 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed) Iris score: 0 of max. 2 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed) Conjunctivae score: 0.67 of max. 4 (animal #2) (Time point: mean 24 + 48 + 72 h) (fully reversible (48 h)) (not rinsed) 0 of max. 0 (animal: #1, #2, #3, #4, #5, #6) (Time point: mean 24 + 48 + 72 h) (not rinsed)	2 (reliable with restrictions) weight of evidence experimental result Test material: Dodecyl-, Pentadecyl methacrylate Form: liquid	Mastri CW (1975)

4.2.2.1 Non-human information

No study on eye irritation potential is available of the single substance dodecyl methacrylate. The eye irritation was assessed in a weight of evidence approach with four available studies for structurally related long-chain alkyl methacrylates: One study according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FDA Draize (1959) with methacrylic acid ester of an alcohol mixture with a mean C-number of 12,6, CAS: 90551-76-1 (65 % dodecyl methacrylate, 25 % Tetradecyl methacrylate, 10 % higher alkyl methacrylates up to octadecyl methacrylate), one study with Dodecyl-, Pentadecyl methacrylate (app. equal parts of C12-, C13, C14-and C15-methacrylates) (1975), one study with n-decyl methacrylate (1978) and one study according to OECD 405 with the structurally related substance isotridecyl methacrylate.

C12,6 methacrylate: In a study following an FDA guideline (Draize protocol) C12,6-methacrylate (0.1 ml) was instilled into the right eye of six New Zealand White rabbits. The lids were then gently held together for one second. The test eyes were not washed out following the instillation. The left eye remained untreated for control. The eyes were examined at 24, 48 and 72 hours from beginning of test. Eye irritation was scored for signs of corneal damage (density, area), iris reaction and lesions of the conjunctivae (erythema, chemosis and discharge). 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.

Dodecyl-, Pentadecyl methacrylate: In a primary eye irritation study (1975) with 6 Albino rabbits animals were exposed with 0.1 ml undiluted Dodecyl-, Pentadecyl methacrylate which contains approximately equal parts of C12-, C13-, C14 and C15-methacrylates. Eyes were not washed. Irritation scores were evaluated after 24, 48 and 72 hours. 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 is not irritating to eyes according to the CLP criteria.

n-Decyl methacrylate: In a primary eye irritation study (according to Appraisal of the Safety of Chemicals in foods, drugs and cosmetics, FDA Draize (1959)) 0.1 ml undiluted n-Decyl methacrylate was instilled into the conjunctival sac of the left eye of 6 New Zealand White rabbits, (2.4 -2.6 kg body weight) for 72 hours (not rinsed). Animals were observed for 7 days. Irritation was scored according to Draize scoring system and reevalutated according CLP criteria. Mean irritation scores (24 + 48 + 72 hours) for cornea, iris, conjunctiva and chemosis were 0 for all animals. In this study Decyl methacrylate is not irritating to eyes.

Isotridecyl methacrylate was tested in an eye irritation study according to OECD 405. 0.1 ml test substance was instilled into the right eye of 3 New Zealand White rabbits. The lids were then gently held together for one second. The test eyes were not washed out following the instillation. The left eye remained untreated for control. The examination of the cornea was secured with the aid of fluorescin after recording the observation at 24 hours. The grades of lesions at 24, 48 and 72 hours 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.

4.2.2.2 Human Information

No data are available on human information

4.2.2.3 Summary and discussion of eye irritation

No signs of eye irritation were observed in four studies with structurally related long-chain alkyl methacrylates (C12.6 methacrylate, Dodecyl,-Pentadecyl methacrylate, n-Decyl methacrylate and

isotridecyl methacrylate). Maximum irritation score for conjunctiva was 0.67 with Dodecyl,-Pentadecyl methacrylate which was fully reversible within 7 days. Irritation scores in three further studies were 0 for all irritation parameters at every observation time point. In analogy dodecyl methacrylate is considered not to be an eye irritant.

4.2.2.4 Comparison with criteria

The application of Dodecyl methacrylate to rabbit eyes does not induce effects which are relevant for a classification as eye irritant in accordance with the CLP criteria. In four studies with structurally related long chain alkyl methacrylates in only one study the highest induced irritation score for conjunctiva was 0.67 which was fully reversible within 48 h. All other scores were 0 at 24, 48 and 72 h.

4.2.2.5 Conclusion on classification and labelling

According to CLP criteria dodecyl methacrylate has not to be classified as irritating to eyes. Current classification should be deleted.

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.

4.2.3 Respiratory tract irritation

No data are available on respiratory tract irritation. As vapour pressure of dodecyl methacrylate is < 0.1 Pa, inhalation of the gaseous form is not a route of exposure. The physico chemico properties with a very low vapour pressure cannot exclude an 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 criteria is not possible... The lack of irritating

[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.

properties on the skin and the eye gives supporting evidence that the current classification as STOT SE 3 may not be justified and should be deleted.

4.3 Corrosivity

See irritation

4.4 Specific target organ toxicity – single exposure (STOT SE)

See 4.2.3 Respiratory tract irritation.

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.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.2 Degradation

Table 15: Summary of relevant information on degradation

Method	Results	Remarks	Reference
Test type: ready biodegradability activated sludge (mixture of 2 storage lakes, 3 municipal sewage plants and 1 industrial sewage plant) equivalent or similar to OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	readily biodegradable % Degradation of test substance: 88.5 after 2 d (O_2 consumption) 7.5 after 2 d (O_2 consumption) 21 after 3 d (O_2 consumption) 60 after 10 d (O_2 consumption) 72 after 15 d (O_2 consumption)	1 (reliable without restriction) **Test material:** Dodecyl methacrylate	Fraunhofer (1988)
Test type: ready biodegradability activated sludge (mixture of 2 storage lakes, 3 municipal sewage plants and 1 industrial sewage plant) equivalent or similar to OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	readily biodegradable % Degradation of test substance: 76.6 after 28 d (O_2 consumption) 12.8 after 5 d (O_2 consumption) 59.2 after 10 d (O_2 consumption) 62.2 after 11 d (O_2 consumption)	2 (reliable with restriction) Read across: **Test material:** Methacrylic acid ester 13.6 (68 % esters of C-13- alcohols, 32 % esters of C-15-alcohols, containing a total of 35 % esters of branched alcohols)	Fraunhofer (1988b)

5.2.1 Stability

No data are available on hydrolytic stability of dodecyl methacrylate.

5.2.2 Biodegradation

5.2.2.1 Screening tests

Two studies are available on biodegradation of dodecyl methacrylate and a mixture of the structurally related substances C13- and C15- alkyl methacrylates (linear and branched).

The ready biodegradation of dodecyl methacrylate was investigated in a study conducted according to EEC Directive 84/449/EEC, Degradation – biodegradation, Modified MITI Test, published in official Journal of the European Communities No. L251/199) over a period of 28 days using sludge samples from different places like rivers, lakes, municipal and industrial sewage plants as inoculums (30 mg/L) and 100 mg/L test substance. The biodegradation rate was determined by measurement of O_2 consumption. Inoculum blank and procedural/functional control with reference substance aniline was performed.

After 28 days the degradation of dodecyl methacrylate reached 88.5 % (Fraunhofer 1988). 60 % degradation was found after 10 days. The reference substance reached the pass level of 60 % at day 7 (93.8 % after 28 d). This study is regarded as reliable without restriction and satisfies the guideline requirements for ready biodegradation. Dodecyl methacrylate proved to be readily biodegradable.

In a second study (Fraunhofer 1988b) the ready biodegradation of methacrylic acid ester 13.6 (68 % esters of C-13- alcohols, containing a total of 32 % esters of C-15-alcohols, 35 % esters of branched alcohols) was investigated in a study conducted according to EEC Directive 84/449/EEC, Degradation – biodegradation, Modified MITI Test, published in official Journal of the European Communities No. L251/199) over a period of 28 days using sludge samples from different places like rivers, lakes, municipal and industrial sewage plants as inoculums (30 mg/L) and 100 mg/L test substance. The biodegradation rate was determined by measurement of O_2 consumption. Inoculum blank and procedural/functional control was performed with the reference substance aniline.

After 28 days the degradation of methacrylic acid ester 13.6 reached 76.6 %.The reference substance reached 84.0 % after 28 d. This study is regarded as reliable with restriction and satisfies the guideline requirements for ready biodegradation. Methacrylic acid ester 13.6 proved to be readily biodegradable.

5.2.3 Summary and discussion of degradation

Dodecyl methacrylate (Fraunhofer 1988) and a mixture of C13 and C15 alkyl methacrylates (Fraunhofer 1988) were demonstrated to be readily biodegradable in biodegradation tests according to OECD guideline 301 C (modified MITI tests). 88.5 % and 76.6 % biodegradation were achieved within 28 days, respectively. The 10 day window criteria were fulfilled in both tests.

5.3 Bioaccumulation

5.3.1 Aquatic Bioaccumulation

The studies on aquatic bioaccumulation are summarised in the following table:

Table 16: Summary of relevant information on aquatic bioaccumulation

Method	Results	Remarks	Reference
Danio rerio aqueous (freshwater) flow-through Total uptake duration: 56 h Details of method: Calculation of the uptake and depuration rate constants and the BCF: The uptake rate constant (k1), the depuration rate constant (k2), the kinetic steady state bioconcentration factor (BCFk) were calculated by linear and nonlinear regression functions using data for concentrations of 2-Ethylhexylmethacrylate in whole fish measured in the extracts. Calculations of means and ranges were done with Excel spreadsheets (Microsoft Inc.) while linear and non-linear regressions were	BCF: 37 (whole fish) Elimination: yes; DT50: 1.5 h yes; DT95: 6 h	Read across 2 (reliable with restrictions) key study experimental result **Test material (EC name): 2-ethylhexyl methacrylate**	Schäfers (2006)

Method	Results	Remarks	Reference
conducted with the program SigmaStat 2.03 (SPSS Inc. 1997). Calculation of the steady state BCF: The test substance is known to be taken up quickly due to the high partition coefficient and to be rapidly metabolized, leading to a very fast elimination. A non-GLP pre-study showed that the steady state can be expected to be achieved within the first 8-12 h. Two further sampling dates after 32 h and 56 h were included to provide certainty about the BCF. The BCFSS was calculated by dividing the mean of the values for the 2-Ethylhexyl methacrylate concentration in fish which represent the worst case steady state by the mean measured relevant concentrations in the water. Calculation of the depuration rate constants: The depuration rate constant (k2) was calculated using the measured concentrations in fish during the depuration phase by applying a model regarding fish as one compartment. The model assumes that the concentration of the test substance in the fish (Cf) is decreasing exponentially: Cf(t) = Cf(ti) * e(-k2*t) Cf(t): concentration in fish at sampling time in days (µg/Kg) Cf(ti): steady state concentration in fish corresponding to the concentration at start of the depuration phase (= 100%) k2: depuration rate constant k2 was calculated by linear regression applied to the ln-transformed concentrations in fish. Calculation of the uptake rate constant: The uptake rate constant k1 was calculated by a non-linear regression of the ratios Cf/Cw against time during the uptake phase and using the depuration rate constant fitted before. The fitted model assumes an attenuation of uptake by simultaneous depuration, increasing with increasing Cf up to an steady state between uptake and depuration. For the one compartment kinetics eq. 3 was fitted: Cf/Cw = k1/k2 * (1-e(-k2*t)) k1: uptake rate constant Cf: concentration in fish (µg/kg) Cw: concentration in water (µg/L) k1 was calculated by non-linear regression using the k2 values obtained in the depuration phase . Calculation of kinetic BCFk: The kinetic BCF for the one compartment model is given by BCFk = k1/k2 OECD Guideline 305 (Bioconcentration: Flow-through Fish Test)			

5.3.2 Summary and discussion of aquatic bioaccumulation

No *in vivo* study is available with dodecyl methacrylate but a fish bioaccumulation study (OECD guideline 305) with the structurally related substance ethylhexyl methacrylate. The measured BCF was 37.

Bioavailability of ethylhexyl methacrylate is expected to be higher than dodecyl methacrylate due to the lower log Pow, lower molecular weight and higher water solubility of ethylhexyl methacrylate (EHMA, CAS No: 688-84-6, $C_{12}H_{22}O_2$: log Pow. 5.59; MW 198.31 g/mol; water solubility: 3.07 mg/l; Dodecyl methacrylate , $C_{16}H_{30}O_2$: log Pow 6.68, MW 254.42 g/mol, water solubility: < 1 µg/l). Ethylhexyl methacrylate and dodecyl methacrylate are both alkyl methacrylates and the same way of rapid metabolism is expected. Metabolism of ethylhexyl methacrylate is indeed faster than dodecyl methacrylate, but the concentration of dodecyl methacrylate in organisms is much lower than ethylhexyl methacrylate due to the lower bioavailability. Nevertheless, an exact BCF of dodecyl methacrylate cannot be estimated.

However, the calculated log Pow of dodecyl methacrylate is 6.68. According to Guidance on the application of the CLP criteria (Annex III 4.3) read across should only be considered if no experimental BCF or log Pow data or no predicted log Pow data are available. The log Pow is above the CLP cut-off (log Pow ≥ 4) and thus dodecyl methacrylate has potential to bioaccumulate in organisms.

5.4 Aquatic toxicity

Table 17: Summary of relevant information on aquatic toxicity

Method	Results	Remarks	Reference
Fish			
Oncorhynchus mykiss freshwater flow-through OECD Guideline 203 (Fish, Acute Toxicity Test)	LC_{50} (96 h): > 62 mg/L act. ingr. (highest test concentration) (meas. (arithm. mean)) based on: mortality (Test solutions were cloudy and grey. The amount of undissolved material increased with increasing test concentration.)	3 (not reliable) weight of evidence experimental result **Test material (EC name): dodecyl methacrylate** Form: liquid	Springborn laboratories Inc. (1995)
Leuciscus idus freshwater static DIN 38412 part 15	LC_{50} (48 h): 1080 mg/L test mat. (test concentration 6 orders of magnitude above the solubility of the test substance) (nominal) based on: mortality	3 (not reliable) weight of evidence experimental result **Test material (EC name): dodecyl methacrylate** Form: liquid	Institut Fresenius, Chemische und biologische Laboratorien GmbH, 6204 (1988)

Method	Results	Remarks	Reference
Daphnia			
Daphnia magna freshwater flow-through OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	EC_{50} (48 h): > 2 mg/L test mat. (meas. (arithm. mean)) based on: mobility	3 (not reliable) weight of evidence experimental result **Test material (EC name): dodecyl methacrylate**	Putt (1995)
Daphnia magna freshwater semi-static OECD Guideline 211 (Daphnia magna Reproduction Test) (adopted September 1998)	NOEC (21 d): >= 5.73 µg/L test mat. (meas. (arithm. mean)) based on: reproduction (and immobilisation) (test concentration above the water solubility)	1 (reliable without restriction) key study experimental result **Test material (EC name): dodecyl methacrylate** Form: liquid	NOACK (2005)
Algae			
Desmodesmus subspicatus (algae) freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test) (1984)	EC_{50} (72 h): > 10 µg/L test mat. (nominal) based on: biomass and growth rate (95 % confidence interval: not applicable) NOEC (72 h): 10 µg/L test mat. (nominal) based on: biomass and growth rate (95 % confidence interval: not applicable) LOEC (72 h): > 10 µg/L test mat. (nominal) based on: biomass and growth rate (95 % confidence interval: not applicable)	1 (reliable without restriction) key study experimental result **Test material (EC name): dodecyl methacrylate** Form: liquid	NOACK (2005b)
Selenastrum capricornutum (new name: Pseudokirchnerella subcapitata) (algae) freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test)	EC_{50} (96 h): > 0.19 mg/L act. ingr. (meas. (initial)) based on: growth rate NOEC (96 h): 0.0062 mg/L act. ingr. (meas. (initial)) based on: growth rate	3 (not reliable) weight of evidence experimental result **Test material (EC name): dodecyl methacrylate** Form: liquid	Hoberg (1995)

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

Two studies are available on short term toxicity to fish. The first study according to DIN 38412 part 15 (Fresenius, 1988) with *leuciscus idus* (golden orfe) was conducted with dodecyl methacrylate (97.2 %) at nominal test concentrations of 950, 1000, 1050 and 1100 mg/l. The test solution was prepared using an ultrasonic stirrer.

At 950 mg/l 0/10 fish were dead, 1/10 at 100 mg/l, 2/10 at 1050 mg/l and 10/10 at 1100 mg/l. LC_{50} was calculated to 1080 mg/l, LCo was 950 mg/l.

As the test concentration was 6 orders of magnitude above the solubility of the test substance, the test is regarded as invalid.

A second test was conducted with a mixture of 69.13 % dodecyl methacrylate and 27.4 % tetradecyl methacrylate acc. OECD guideline 203 with rainbow trout (Springborn 1995) under flow through conditions at nominal concentrations of 13, 21, 35, 58 and 97 mg dodecyl methacrylate/l = active ingredient (a. i.). These concentrations are corresponding with mean measured concentrations of 8.8, 12, 13, 24 and 62 mg a. i. /l (measured by HPLC). Acetone was used as solubilizer in a concentration of 0.167 ml/l. No mortality was observed up to the highest measured concentration of 62 mg/l a. i. LC_{50} was considered to be > 62 mg/l.

Throughout the study, test solutions were observed to be cloudy and grey and contained a surface film of undissolved test material. As the test was performed with solvent and in a range of concentrations four to five orders of magnitude above the water solubility of the substance (< 1 µg/l) and the substance was introduced into the test medium by rapid stirring, a true solution has not been achieved under the test conditions. Therefore the test is regarded as invalid.

OVERALL COMMENT OF TOXICITY TO FISH: Despite the fact that the available tests are problematic from a technical point of view, it appears that saturated solutions of dodecyl methacrylate are non-toxic to fish, so that there was no necessity to repeat the tests.

5.4.1.2 Long-term toxicity to fish

No data are available on long term toxicity to fish

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

One study is available on the acute toxicity to daphnia. The test was conducted with a mixture of 69.13 % dodecyl methacrylate and 27.4 % tetradecyl methacrylate according to OECD guideline 202 (Putt, 1995) under flow through conditions with *daphnia magna* at nominal concentrations 0.39, 0.65, 1.1, 1.8 and 3.0 mg/l dodecyl methacrylate = active ingredient (a. i.) corresponding with measured concentration of 0.17, 0.30, 0.59, 0.80 and 2.0 mg a. i./l (measured by HPLC). The test material was introduced into the test medium by rapid stirring. Following 48 h of exposure, 35 % immobilization was observed among daphnids exposed to 2.0 mg a. i./l. During the same period 20, 15, 10 and 25 % immobilization was observed among daphnids exposed to the 0.17, 0.30, 0.58 and 0.80 mg a. i./l treatment levels. 5 % immobilization was observed among daphnids exposed to the control solutions. All mobile daphnids exposed to the highest treatment level (2.0 mg a. i./l) exhibited lethargic

behaviour. Sublethal effects were also observed among several organisms exposed to the 0.80 mg a. i./l treatment level. No sublethal effects were observed among daphnids exposed to the remaining concentrations tested.

Based on these results EC_{50} (48 h) was empirically estimated to be > 2.0 mg a. i./l, the highest achievable concentration. The slope of the concentration effect curve at 48 h did not establish a relationship between exposure and effect sufficient to empirically determine a NOEC for dodecyl methacrylate in this test.

In the absence of a clear concentration effect relationship and taking into account that emulsions with concentrations three to four orders of magnitude above the water solubility instead of solutions were tested the test is regarded as invalid.

A 21 d daphnia reproduction test indicates that dodecyl methacrylate is non-toxic to daphnia at a concentration one order of magnitude above the limit of water solubility. Saturated solutions of dodecyl methacrylate are non-toxic to daphnia under acute and chronic conditions.

5.4.2.2 Long-term toxicity to aquatic invertebrates

One study is available on the long term toxicity to aquatic invertebrates (NOACK, 2005). The test was conducted with dodecyl methacrylate, purity 98.34 %. The 21-day-chronic toxicity of dodecyl methacrylate to *Daphnia magna* STRAUSS was studied under semi static conditions according to OECD guideline 211. Daphnids were exposed to dodecyl methacrylate at a limit concentration of 10 µg/L (nominal). This concentration is higher than the solubility in water (< 1 µg/L) but has, nevertheless, been chosen with regard to the feasibility of attaining appropriate and analysable test concentrations at 10 µg/L.

10 test organisms, individually held were used for the limit concentration and control. At test start they were 2 to 24 h old. The test method was semi-static. Test solutions were renewed daily.

Concentrations of dodecyl methacrylate in the stock solution, limit concentration and control of fresh (0 h) and old (24 h) media were determined via HPLC. Samples were taken and analysed on days 0, 7, 16, 20 (fresh media) and on days 1, 8, 17, 21 (old media). The test item concentrations decreased within 24 h. All effect values were given based on the time weighted mean measured concentration for the limit concentration of 5.73 µg/L.

The average number of juveniles per parent in the control group was 85 after 21 days. The reproductive output at the limit concentration was not statistically significant reduced compared to the control. The coefficient of variation around the mean number of living offspring produced per parent in the control group was 5.02 % and shows very small variances between the control replicates.

No winter eggs, males, ephippia, stillborn juveniles and aborted eggs occurred in control or test groups.

The mean day of release of first brood was 9 in the control group and the limit concentration. There was no difference between the two groups. At the limit concentration and the control group 4 broods were released during the test period.

The intrinsic rates of natural increase (IR) of the surviving parent animals accounting for generation time and offspring numbers were used for calculation of population growth. The mean IR of the surviving daphnids of the limit concentration was compared to the control by One Way Analysis of Variances ($p < 0.05$). There was no statistically significant difference. The intrinsic rate was comparable for the control and limit concentration.

The no observed effect concentration (NOEC) after 21 days based on reproduction capacity is the tested limit concentration of 5.73 µg/L. No statistically significant test item related effects were observed at the limit concentration when compared to the control group. No immobilisation of parent animals occurred in the control or test group.

Water quality parameters as pH-value, dissolved oxygen, water hardness and temperature were determined to be within the acceptable limits.

In order to prove the validity of the test system and test conditions at the testing facility, an acute immobilization test according to DIN 38412 L11 was carried out with potassium dichromate as reference item once per month. The EC_{50} of the reference item at 1.84 mg/L after 24 h was within the validity range of 1.0 to 2.5 mg/L according to DIN 38412 L30.

The 21 day LC_{50}/EC_{50} based on reproduction/immobilisation was greater than 5.73 µg/L (mean measured concentration). The 21-day NOEC based on reproduction/immobilisation was ≥ 5.73 µg/L (mean measured concentration). Production of offspring in the treated groups indicated that Dodecyl methacrylate did not have an effect on the reproduction at concentrations lower or equal than 5.73 µg/L.

This study is classified as acceptable and satisfies the guideline requirements for a chronic toxicity study with freshwater invertebrates.

5.4.3 Algae and aquatic plants

Two studies are available on algae toxicity.

The first was conducted with a mixture of 69.13 % dodecyl methacrylate and 27.4 % tetradecyl methacrylate according to OECD guideline 201 with *Selenastrum capricornutum* (new name: *Pseudokirchneriella subcapitata*) under static conditions at nominal concentrations of 0.0063, 0.013, 0.025, 0.050 and 0.10 mg a. i. /l (a. i. = dodecyl methacrylate, corresponding with 0.0091, 0.019, 0.036, 0.072 and 0.145 mg/l test substance (Hoberg, 1995). Acetone was used as solubilizer in a concentration of 0.1 ml/l. Measured concentrations by HPLC were higher than nominal concentrations: 0.068, 0.016, 0.0274, 0.062 and 0.19 mg a. i./l.

EC_{50} value for growth rate (ECr_{50}(96 h) > 0.19 mg/l) was above the highest nominal concentration tested. NOEC was 0.0062 mg/l (measured concentration).

In the absence of a clear concentration-effect relationship and taking into account that emulsions and not solutions of the material were tested, the NOEC which had been reported in the test report is irrelevant. The study is regarded as invalid.

A second study was conducted with dodecyl methacrylate (purity 98.34 %) for 72 h acc. OECD guideline 201 as limit test under static conditions with *Desmodesmus subspicatus* at test concentrations of 10 µg/l with an initial cell density of nominally 10E+1 cell/ml (NOACK, 2005b). Three replicates were tested for the limit concentration and six for the control.

The recovery rate of the limit concentration was 105 % at the test start and 94 % at test end. All effect values are based on nominal test concentrations.

The test concentration of 10 µg/l was higher than the solubility in water (< 1 µg/l) but was, nevertheless, been chosen with regard to the feasibility of attaining an analysable test concentration of 10 µg/l.

EC_{50} and NOEC based on growth inhibition and biomass production were > 10 µg/l and ≥ 10 µg/l, respectively. The study is acceptable and satisfies the guideline requirements for Algae, Growth Inhibition study. The study is regarded as valid without restrictions.

Validity of ecotoxicity studies with solvent in which the test concentrations exceed the limit of solubility by several orders of magnitude

Several ecotoxicity tests with dodecyl methacrylate have been performed at concentrations orders of magnitude above the limit of solubility. In those cases, rapid stirring or solvent or both have been used to disperse the test material. In those studies, no attempt has been made to determine whether the test material was dissolved and only in one study it was acknowledged that the test material was present in the form of an emulsion. Based on the measured water solubility of dodecyl methacrylate (< 1 µg/l) it can be assumed, that in those cases the test material was present almost entirely as small, undissolved droplets forming an emulsion. That has the consequence that the 'concentration' no longer determines the dose in the test organism but the stochastic, individual contact of the test organism with droplets of the test material and the kinetics of the subsequent absorption of the droplet by the test organism. Test results obtained this way are artefacts and not representative. They cannot be used establishing a concentration-effect relationship. Therefore, test results have only been used when the test was performed without solvent and the nominal test concentration was not higher than approximately ten-fold above the solubility of dodecyl methacrylate in water.

5.5 Comparison with criteria for environmental hazards (sections 5.1 – 5.4)

Table 18: Comparison with criteria for environmental hazards

	Criteria for environmental hazards	Dodecyl methacrylate	Conclusion
Rapid Degradation	Readily biodegradable in a 28-day test for ready biodegradability	88 % after 28 days (O2 consumption) 10 day window passed	**Rapidly degradable**
Bioaccumulation	Log Kow ≥ 4 BCF ≥ 500	Estimated Log Kow = 6.68	**Bioaccumulative**
Aquatic Toxicity	Acute toxicity data: $LC_{50}/EC_{50}/ErC_{50}$ ≤ 1 mg/L Chronic toxicity data: NOEC ≤ 1mg/L	Algae: ErC_{50} 72h > 10 µg/l (test concentration higher than the water solubility of 1 µg/l) NOEC 72 h: ≥ 10 µg/l (test concentration higher than the water solubility of 1 µg/l) Invertebrates: NOEC 21d ≥ 5.73 µg/l (test concentration higher than the water solubility of 1 µg/l) Fish: No valid study	**Not acute and chronic toxic up to the water solubilty**

Criteria for the classification with Aquatic Acute 1 and Aquatic Chronic 1-3:

The values for acute and chronic toxicity are above the water solubility. Therefore, the criteria for the classification of the substance with Aquatic Acute 1 and Aquatic Chronic 1-3 are not fulfilled.

Criteria for the classification with "Aquatic Chronic 4"

- Poorly soluble substance for which no acute toxicity is recorded at levels up to the water solubility

  AND

- which are not rapidly degradable

  AND

- have an experimentally determined BCF ≥ 500 (or, if absent, a Log Pow ≥ 4)

The substance is rapidly degradable. Therefore, this criterion for the classification with Aquatic Chronic 4 is not fulfilled.

5.6 Conclusions on classification and labelling for environmental hazards (sections 5.1 – 5.4)

As dodecyl methacrylate is rapidly degradable and the values for acute and chronic aquatic toxicity are above the water solubility of the substance classification and labelling according to the CLP criteria for environmental hazards is not required. The current classification with Aquatic Acute 1 (H400) and Aquatic Chronic 1 (H410) is not justified and should be deleted.

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 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
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.

Supplemental information - In depth analyses by RAC

ECOSAR v1.11 is the tool applied by the PBT profiler (cited by the French CA in their public comments) to generate predictions on aquatic toxicity. Predicted toxicity values to fish calculated by ECHA using this model (based on an estimated log K_{OW} of 6.68) are as follows:

ECOSAR SAR Class	96-h LC_{50} (mg/L)	NOEC (ChV/2^{-2}) (mg/L)
Methacrylates	0.022	0.0011
Neutral organics	0.013	0.0014

The substance is outside the parametric domain of the acute models. It is within the parametric domain of the chronic models, but the values are not considered reliable for the "methacrylates" class because they are an extrapolation by means of an unreliable acute-to-chronic ratio. The values are also all higher than the experimental water solubility reported in the CLH report (<0.001 mg/L).

Acute fish toxicity values were also calculated for the analogue dodecyl acrylate (CAS no. 2156-97-0):

ECOSAR SAR Class	96-h LC_{50} (mg/L)
Acrylates	0.309
Neutral organics	0.039

The same domain considerations apply as for the target substance. In addition, two experimental values for acute fish toxicity for the analogue provided in the ECOSAR database and OECD QSAR Toolbox 4.0 (ECOTOX database) indicated either no effects or a 96-h LC_{50} of 4.33 mg/L for Fathead Minnow. Although RAC has not evaluated their reliability, this suggests that the ECOSAR models may over-estimate fish toxicity for this type of substance.

Overall, these predictions do not provide reliable information on the toxicity of dodecyl methacrylate to fish.

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