Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

nonanoic acid

EC number: 203-931-2
CAS number: 112-05-0

CLH-O-0000002588-64-03/F

Adopted

6 June 2013

6 June 2013

CLH-O-0000002588-64-03/F

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

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

Chemicals name: nonanoic acid

EC number: 203-931-2

CAS number: 112-05-0

The proposal was submitted by **Austria** and received by the RAC on **21 June 2012.**

In this opinion, all classifications are given firstly in the form of CLP hazard classes and/or categories, the majority of which are consistent with the Globally Harmonised System (GHS) and secondly, according to the notation of 67/548/EEC, the Dangerous Substances Directive (DSD).

PROCESS FOR ADOPTION OF THE OPINION

Austria has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation*** on **21 June 2012**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **6 August 2012**.

ADOPTION OF THE OPINION OF THE RAC

Rapporteur, appointed by RAC: **Helmut Greim**

Co-rapporteur, appointed by RAC: **José Luis Tadeo**

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

The RAC opinion on the proposed harmonised classification and labelling was reached on **6 June 2013** and the comments received are compiled in Annex 2.

The RAC Opinion was adopted by **consensus**.

OPINION OF THE RAC

The RAC adopted the opinion that **nonanoic acid** should be classified and labelled as follows:

Classification and labelling in accordance with the CLP Regulation

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard state-ment Code(s)	Suppl. Hazard statement Code(s)	
Current Annex VI entry	607-197-00-8	nonanoic acid	203-931-2	112-05-0	Skin Corr. 1B	H314	GHS05 Dgr	H314		
Dossier submitters proposal	607-197-00-8	nonanoic acid	203-931-2	112-05-0	**Modify:** Skin Irrit. 2 **Add:** Eye Dam. 1 Aquatic Chronic 3	**Modify:** H315 **Add:** H318 H412	GHS05 Dgr	**Modify:** H315 **Add:** H318 H412		
RAC opinion	607-197-00-8	nonanoic acid	203-931-2	112-05-0	**Modify:** Skin Irrit. 2 **Add:** Eye Irrit. 2 Aquatic Chronic 3	**Modify:** H315 **Add:** H319 H412	GHS07 Wng	**Modify:** H315 **Add:** H319 H412		
Resulting Annex VI entry if agreed by COM	607-197-00-8	nonanoic acid	203-931-2	112-05-0	Skin Irrit. 2 Eye Irrit. 2 Aquatic Chronic 3	H315 H319 H412	GHS07 Wng	H315 H319 H412		

Classification and labelling in accordance with DSD

	Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits
Current Annex VI entry	607-197-00-8	nonanoic acid	203-931-2	112-05-0	C; R34	C R: 34 S: (1/2-)26-28-36/37/39-45	
Dossier submitters proposal	607-197-00-8	nonanoic acid	203-931-2	112-05-0	**Modify:** Xi; R38-41	Xi R: 38-41 S: (2-)26-36/37/39-45-46	
RAC opinion	607-197-00-8	nonanoic acid	203-931-2	112-05-0	**Modify:** Xi; R36/38 **Add:** N; R51-53	Xi; N R: 36/38-51/53 S: (2-)46-61	
Resulting Annex VI entry if agreed by COM	607-197-00-8	nonanoic acid	203-931-2	112-05-0	Xi; R36/38 N; R51-53	Xi; N R: 36/38-51/53 S: (2-)46-61	

SCIENTIFIC GROUNDS FOR THE OPINION

RAC general comment

The only hazard classes evaluated were those of skin irritation/corrosion, eye irritation and the environment.

Please note that references cited here can be found in the CLH report and/or the background document to the pinion; references not quoted in the above docuemnts are included at the end of this opinion for the sake of convenience.

HUMAN HEALTH HAZARD ASSESSMENT

RAC evaluation of skin irritation/corrosion

Summary of the Dossier submitter's proposal

The CLH report includes one rabbit dermal irritation study conducted with neat nonanoic acid (Otterdijk, 2001c). Animals were exposed for 4 hours and severe irritation (average erythema score 4 at 24, 48 and 72 hours, no oedema score possible), which was not fully resolved within 15 days, was reported. Application of 22% nonanoic acid in an acute dermal toxicity test (Otterdijk, 2001b) resulted in some clinical signs of irritation with 2/10 showing signs of severe irritation (erythema score of 3 and 4) not fully reversible after 15 days. A Guinea Pig Maximisation Test (GPMT) study revealed erythema scores or 4 and oedema scores of 1 for concentrations at and above 50% (Otterdijk, 2001d). Analysis using the ToxTree QSAR tool made available by the European Chemicals Bureau (ECB) suggested nonanoic acid, as well as its closely related substances octanoic and decanoic acid were borderline "irritating or corrosive to skin". The dossier submitter also mentions a dermal irritation study conducted with the ammonium salt of nonanoic acid in concentrations up to 34%, which showed little irritation properties. References or further analysis of this study were not included.

The dossier submitter includes several human patch test studies conducted with varying concentrations of octanoic, nonanoic and decanoic acid. Irritation was noted in most studies but no corrosion. However, exposure was terminated upon first sign of irritation in most studies (apart from those by Willis et al (1988) and Wahlberg et al (1985)).
References are made to studies included in the REACH registration dossier (see ECHA web site) for nonanoic acid (Unichema/Notox, 1984, Hoechst, 1990 and Celanese/RCC, 2001). The dossier submitter argues that these studies confirm the results seen in the animal studies presented in the dossier but no further details are provided.

The dossier submitter concludes that nonanoic acid presents a borderline case for corrosion or irritation but based on a weight of evidence approach, they conclude that the current classification of Skin Corr. 1B – H314 should be changed to Skin Irrit. 2 – H315 according to CLP. The corresponding classification under DSD would be Xi; R38.

Comments received during public consultation

Comments were received from four Member States. Three agreed with the proposal for skin irritation while one disagreed and argued for classification as Skin Corr. 1C – H314. This is based on visible necrosis, scabs and/or fissures and alopecia, not fully resolved within 14 days, seen after 4h exposure in Otterdijk (2001c) and Unichema/Notox (1984). The lead registrant for nonanoic acid under REACH also submitted a comment arguing for Skin Corr. 1C – H314, based on the same results. The dossier submitter agreed that this is a borderline case, but argued the effects are fully reversible and requested RAC to conclude on this issue. A comment was submitted on behalf of the Fatty Acid Consortium (FAC) detailing two additional studies (Arcelin, 2001 and Weterings, 1984) which they claim support the proposed classification as Skin Irrit. 2 – H315. The study summaries were not available to the dossier submitter for an independent review but further details are available in the Response to comments document (RCOM).

Assessment and comparison with the classification criteria

Since there is insufficient data on the individual organic acids the dossier submitter used the available information on octanoic, nonanoic and decanonic acid, to derive classification and labeling for the individual substances. RAC supported this approach because the pK_a, values of the three acids are similar (octanoic acid 4.89, nonanoic acid 4.96, decanoic acid no pK_a because it is a solid). These values are similar to the pK_a of 4.76 of acetic acid, which is corrosive to the skin (Category 1A, H314). However, RAC noteed that the pK_a and pH values are based on molarity. Since there are large differences in the molecular weights between acetic acid (60) and the three organic acids (octanoic acid 144, nonanoic acid 158, decanoic acid 172) their acidity per weight is lower than that of acetic acid. This explains the less clear irritating/corrosive effects of the three acids. Due to the close structural similarity and the very similar pK_a values, RAC supported the general evaluation approach of all three acids proposed by the dossier submitter.

The available information is briefly summarised below.

Assessment of human patch tests (HPT)

HPT on 72 human volunteers reported by Robinson et al (1999) using octanoic and decanoic acid revealed at least mild irritation in 37 to 56% of the participants up to 1 h and in 84 to 96% after up to 4 h exposure. For ethical reasons exposure was terminated at the first sign of irritation before 4 h of exposure.

In contrast to the dossier submitter, RAC does not see evidence from the York et al (1996) study that decanoic acid produced strong responses in some individuals at 2 h. The report only states that as the concentration was increased, eventually 100% of the volunteers responded and that labelling with R38 was justified.

Irritation by nonanoic acid has also been reported by Wahlberg (1983) (0.1 ml neat nonanoic acid repeatedly for 15 days on the forearm, 1 person).

The studies by Willis et al (1988) and Wahlberg et al (1985) continued exposure even after signs of irritation were noted. Willis et al (1988) applied up to 80% nonanoic acid for 48 h to 42 healthy non-atopic male volunteers (not 70 as reported in the CLH report). In 28 volunteers exposed to the 80% solution, up to moderate skin reactions (erythema with oedema and papules) but no corrosion was observed. In a similar study, Wahlberg et al (1985) reported skin irritation with increasing concentration but no corrosion. In this study up to 40% nonanoic acid was applied to 100 hospitalised patients with various skin diseases. At 20% and 40% nonanoic acid, all the 25 exposed patients reacted with irritation. The ED_{50} for irritation was about 6%.

Since the EU classification of chemicals for irritation is based on the available rabbit data, Jirova et al (2008) used the data from 25 compounds to compare the outcome of studies with the EpiDerm model applying 15 and 60 min exposure times and the 4h human patch test (HPT 0.2 g nonanoic and decanonic acid for 4 h, observation time up to 72 h) with data on rabbits. Whereas decanoic acid showed irritation in all three tests, nonanoic acid resulted in irritation from the EpiDerm and HPT test data, and borderline corrosion or irritation from the rabbit study. When compared with the 4h HPT results, the rabbit in vivo test provided 100% sensitivity (5/5), but only 50% specificity (10/20). The EpiDerm protocol with 15 min exposure corresponded better to the response seen in man – sensitivity 80% (4 of 5 irritants classified correctly), while the optimized EpiDerm protocol with 60 min exposure time reached higher concordance with the rabbit test.

The authors concluded that although the rabbit test exhibited 100% sensitivity, but only 50% specificity, the rabbit test identifies irritants reliably, however 50% of non-irritants are wrongly labelled as irritants.

However, the RAC noted that no information on the rabbit tests or on the reason for corrosion/irritation for nonanoic acid is provided. Through personal communication with the dossier submitter the study authors reported that the HPT on nonanoic and decanoic acids showed irritation after 4 h, not at shorter times of exposure

Based on the human patch test studies, RAC supported the conclusion of the dossier submitter that the three organic acids are at least skin irritants, but does not consider that the studies provide evidence for a corrosive effects.

Assessment of animal and in vitro studies

The rabbit study reported by Jirova et al (2008) could not be used because no information on the test procedure or outcome is provided.

Smyth et al (1962), using 5 albino rabbits exposed to 0.1 ml 100% octanoic or decanoic acid for 24 h, report severe irritation. Reversibility was not determined.

Van Otterdijk (2001c), using 3 male rabbits exposed to 75 mg/cm^2 100% nonanoic acid for 4 h and observation up to 72 h, also reported severe irritation and (very) slight oedema, which had resolved within 15 days after exposure. Oedema could not be scored on days 3, 4 and/or 8 due to fissuring, scab formation and/or brown discolouration (sign of necrosis) of the treated skin was observed among all animals between days 1 and 8. Scabs, eschar formation and/or fissuring of the skin were noted on days 3, 4 and/or 8 among the animals. In addition, bald skin and scaliness were observed at the end of the observation period, at day 14 in all 3 animals.

According to CLP, corrosive reactions are typified as ulcers, bleeding, bloody scabs, and by the end of observation at 14 days, by discolouration due to blanching of the skin, complete areas of alopecia, and scars. Of these, only the alopecia at day 14 meets the criteria for corrosion, therefore the dossier submitter considers these effects borderline for classification as corrosive.

Irritation has also been observed in the acute dermal toxicity test in rats (25% decanoic acid for 24 h), which was reversible within 15 days (Talvioja, 2006). The acute dermal toxicity study in rats with 22% nonanoic acid for 24 h showed severe irritation (van Otterdijk, 2001). The erythema was not reversible in 3/10 animals within 15 days.

In an OECD TG 406 skin sensitisation test in Guinea pigs 24 h exposure to nonanoic acid at concentrations above 50% was reported as severely irritating but with an oedema grade of 1 at 24 and 48 h. Reversibility was not investigated (Talvioja, 2006).

In a local lymph node assay (LLNA) in mice, 25 µL/ear of 70% decanoic acid applied 3 times in 3 consecutive days was mildly irritant, which did not reverse within 6 days (Weber et al, 2006).

Since the dossier submitter considered the findings borderline to corrosion they used the Toxtree QSAR evaluation of the three organic acids (which revealed irritating or corrosive to skin) and the in vitro rat skin corrosivity test on the basis of transcutaneous electrical resistance (TER), which indicated skin corrosion. However, RAC concluded that the outcomes of these in vitro tests are overruled by the weight of evidence form the various in vivo tests, including the human data, which did not show corrosion.

Comparison with the classification criteria

When tested in rabbits, guinea pigs and mice the three organic acids induced mild to severe skin irritation in a high percentage of the animals except one test on octanoic acid, which showed no full reversibility of full thickness necrosis at day 14.

When determined, there was reversibility within 15 days in animal studies in all other studies. Unfortunately, the reports do not provide information on the severity of the effects. Irritation was also seen in the HPT in most of the volunteers exposed up to 48 h at concentrations of 20% and higher.

RAC noted that the evidence for skin corrosion of nonanoic acid is borderline. Since the available information on decanoic acid does not indicate skin corrosion and considering their similar pKa values, RAC does not consider that there is sufficient evidence to classify nonanoic acid as corrosive.

Based on a weight of evidence approach and in agreement with the dossier submitter, RAC concludes that nonanoic acid should be considered as irritating to the skin and warrants classification as Skin Irrit. 2 - H315 according to CLP (Xi; R38 according to DSD).

RAC evaluation of eye irritation

Summary of the Dossier submitter's proposal

No studies estimating the eye irritation properties of nonanoic acid are made available in the CLH report. The dossier submitter argues that a severe skin irritation classification would exclude further eye irritation testing (OECD TG 405) and result in classification as severely eye damaging. Nevertheless, one non GLP-compliant study (Smyth et al., 1962) conducted with octanoic and decanoic acid in rabbits, is mentioned in the CLH report. This study indicated corneal necrosis (score of 9 out of 10 is reported) from exposure to octanoic and decanoic acids which would raise concerns for eye damaging properties of nonanoic acid. The dossier submitter proposes to classify nonanoic acid as Eye Dam. 1 – H318 under CLP and R41 under DSD.

Comments received during public consultation

Two Member States and one industry commenter supported the classification proposal for Eye Dam. 1 – H318. One Member State argued that the substance should be classified as corrosive, which covers eye damage and this would therefore be superfluous. One Member State argued that classification for eye damage is not warranted due to lack of data and proposes classification as Eye Irrit. 2 – H319. The FAC argues in their comment that the database is not sufficient to conclude on classification for eye effects.

Assessment and comparison with the classification criteria

There are no guideline specific eye irritation studies on octanoic-, nonanoic-, or decanoic acid reported in the CLH dossiers. Due to the very similar structutres, the similar pK_a values of octanoic and nonanoic acid and the proposed classification and labelling of the three organic acids as irritants to the skin , the RAC used the sparse information available on the individual compounds to evaluate the three organic acids.

Regarding octanoic and decanoic acid, two older, non-GLP compliant studies in rabbits (Smyth et al, 1962 and Briggs et al, 1976) were available to the dossier submitter. The Smyth et al (1962) study in 5 rabbits per group resulted in corneal effects (severity grade 9), indicating risk for severe damage to the eye for both octanoic and decanoic acid. No information on the concentration or on the reversibility was provided. The Briggs et al (1976) study revealed corneal opacity, with no reversibility over up to 72 h. No information on the number of rabbits or on the concentrations of the test compounds is provided and no scoring has been applied.

During the public consultation for octanoic acid industry provided information from a study by Leoni and Riedel (2011). In 2 out of 3 rabbits tested, lesions of the iris with a score equal to 1 have been induced using 70% octanoic acid. The effects were fully reversible within 6 – 11 days. The test would result in classification as Eye Irrit. 2, H319 at 70%. The dossier submitter supported this proposal although the study was not made available to them. RAC evaluated the Leoni and Riedel (2011) study. In accordance with the OECD TG 403 test guideline, 0.1 ml of 70% octanoic acid was applied for 24 h to 3 rabbits. The animals were observed over 72 h and at 6, 9, and 11 days after dosing. Conjunctival redness, chemosis and discharge were observed in all animals, with average scores of 1, 1.67 and 2. In two animals, lesions of the iris (average score 1 for both animals) and the cornea (average scores 1.33 and 0.67, respectively) were observed. At the end of the prolonged observation period of 9 days no corneal, iris or other lesions were seen in the three animals. According to the CLP criteria, this corresponds to a classification as Eye Irrit. 2 – H319 (Xi; R36 according to DSD). This more recent study does not confirm the results of the older non-guideline studies.

During the same public consultation for octanoic acid, industry also referred to a Bovine Corneal Opacity and Permeability (BCOP) test for decanoic acid, which indicates non-corrosivity. RAC has evaluated this OECD TG TG 437 compliant study which concluded that based on the criteria of the guideline, a 20% dilution of decanoic acid was not corrosive or a severe irritant to the eye. The in vitro opacity score was 16.83 as compared to a score of ≥ 55.1 at which a compound is considered to be corrosive or a severe irritant.

For nonanoic acid no eye damage or eye irritation data are available.

Comparison with classification criteria

The available information is inconsistent and does not allow a clear differentiation between irreversible and reversible effects on the eyes. The poorly described Smyth et al(1962) study indicates that there were irreversible effects resulting from exposure to octanoic and decanoic acid, which is not supported by the study of Briggs et al (1976) and the more recent study by Leoni and Riedel (2011) on octanoic acid, from which classification as Eye Irrit. 2 H313 at 70% could be derived. The study by Briggs et al (1976) does not provide sufficient information to evaluate the irritating potencies of octanoic and decanoic acids.

Based on the data on octanoic and decanoic acid, RAC concluded that classification as Eye Irrit. 2 H313 according to CLP (Xi; R36 according to DSD) for nonanoic acid was warranted.

ENVIRONMENTAL HAZARD ASSESSMENT

RAC evaluation of environmental hazards

Summary of the Dossier submitter's proposal

The ecotoxicological tests on fish, crustaceans and algae presented in the CLH report show that the lowest short term value is the LC_{50} for fish (> 7.2 mg/L). Since the L(E)C50 values are all above 1 mg/L, the dossier submitter concludes that the criterion for classification for acute aquatic hazard Category 1 (CLP) and R50 (DSD) are not fulfilled.

Long-term toxicity data are described in the CLH report for all three trophic levels. The lowest chronic value is the NOErC 0.568 mg/l for algae (*Desmodesmus Subspicatus*) .

The dossier submitter considered nonanoic acid as readily biodegradable and rapidly degradable, since in a manometric respirometry test (OECD TG 301F), degradation rates of 76-77% at the end of the 28-days exposure period were observed.

In the Competent Authority Report (CAR) for biocides, the calculated log Pow was given as 3.52 and the resulting calculated Bio Concentration Factor BCF on fish was 195.88. In the REACH registration dossier, the measured Pow was 3.42 and the calculated BCF for fish was 3.2.
The lowest value for aquatic acute toxicity in fish (> 7.2 mg/L) and the log Pow ($\geqslant$ 3) would lead to a classification as R51/53 according to DSD. However, the dossier submitter discards this value and proposes not to classify with R51/53 following a weight of evidence assessment based on the following arguments:

a) 7.2 mg/L was the highest concentration tested in the study and no effects were observed at that concentration;
b) The long term NOEC for fish = 19.2 mg/L;
c) The LC_{50} for fish to octanoic acid = 68 mg/L.

In relation to the long term aquatic hazard, the dossier submitter proposed to use the NOEC value for algae which, together with the rapid degradability data, would result in classification as aquatic chronic Category 3 - H412, according to CLP and
'No classification' according to DSD.

Comments received during public consultation

During the public consultation, comments on hazards to the aquatic environment were received from five Member States Competent Authorities (MSCAs) and two industry organisations.
Three MSCAs supported the classification proposal, without providing further argumentation.

One MSCA supported the proposal, but claimed that the data presented in the CLH report did not allow conclusions to be drawn on the toxicity to fish and algae, since the test procedures used were not appropriate and a constant concentration of the test substance was not guaranteed. However, other valid data for fish and algae presented in the REACH registration dossiers for nonanoic acid support the proposed classification.

The remaining MSCA suggested that a wider set of ecotoxicity data relating to the homologous series (heptanoic, octanoic and decanoic acid) available from the REACH registration dossiers, should be considered, in order to address potentially conflicting aquatic chronic data.

In response to the latter two comments, the dossier submitter included in the RCOM a summary of all available chronic ecotoxicity data for fish and crustaceans from the CARs and REACH registration dossiers for octanoic, nonanoic and decanoic acids. Based on all these data, the dossier submitter concludeed that the proposed classification was indeed appropriate.

One industry organisation considered that the evidence provided by the available data was not sufficient to justify classification as Aquatic Chronic 3, since the NOEC value of 0.568 is not supported by any other aquatic chronic value and the study was of poor quality. The dossier submitter responded to this comment by stating that being an algicide and herbicide, it is not surprising that it would have a low algae NOEC value andoreover, that the NOEC algae value for nonanoic acid was consistent with the values for decanoic and octanoic acids.

The second industry stakeholder organisation (Fatty Acids Consortium, FAC) proposed that nonanoic acid should not be classified as Aquatic Chronic 3, since the NOEC value of 0.568 mg/L was considered unreliable. They claimed that only the "nominal" NOEC value of 20 mg/l of the technical product, corresponding to 4.4 mg/L of the active ingredient, should be considered reliable. The Consortium supported this proposal by considering that, based on the data available in the REACH registration dossiers, an increase in aquatic toxicity can be expected as the chain length increases. Decanoic acid would therefore represent the worst case scenario.
The dossier submitter responded to this comment by confirming their view of the reliability of the chronic algae study and therefore supporting the proposed classification. More details, including the argumentation by FAC and the dossier submitter, are included in the RCOM.

Assessment and comparison with the classification criteria

Degradation

Nonanoic acid was readily biodegradable in an OECD TG 301F manometric respirometry test showing a degradation of 76 - 77% at 28 days and within the 10 d window 64 - 67%. Hydrolysis and photolytic degradation in water are excluded for nonanoic acid because organic acids cannot be hydrolysed in the absence of further functional groups and it do not display chromophore properties at wavelengths above 290 nm.

Additional information from the CAR of biocides showed the aerobic degradation of different mixtures of fatty acids in soil in two non GLP studies. Nonanoic acid rapidly dissipates from soil, with a DT_{50} value of approximately 2.1 days at 12ºC (1.1 days at 20ºC).

Based on the available data, RAC agreed with the dossier submitter that nonanoic acid should be considered **readily biodegradable** according to DSD and **rapidly degradable** according to CLP.

Bioaccumulation

No experimental log kow could be determined for decanoic acid, because the octanol /water coefficient cannot be accurately estimateded.

Two different values of log Kow have been summarized in the CLH report: in the CAR for biocides the calculated log Kow is 3.52, and in the REACH registration dossier, the measured value is 3.42. This log Kow corresponds to an undissociated acid but at relevant environmental pHs, nonanoic acid is found in a dissociated form (pka = 4.9 nonanoic acid; pka = 4.8 ammonium salt of nonanoic acid) and therefore, the log kow is expected to be lower.

Nevertheless, nonanoic acid is a surface active substance (surface tension 34.6mN/m), and according to the Technical Guidance Document on Risk Assessment (EC 2003, part II, p. 24), for substances of this type it may not be advisable to use an estimated or measured Kow values as a predictor for Koc (soil, sediment, suspended organic matter and sludge) and BCF (fish, worm),

because the predictive value of log Kow for such estimations may be too low. Instead, for surfactants it may be appropriate to obtain measured Kp and BCF.

For nonanoic acid, there is no BCF available; however, in the REACH registration dossier for octanoic acid, there is an experimental BCF performed with sodium laurate (dodecanoic acid), which can be used as a read-across for nonanoic acid. The measured BCF value for lauric acid is 255 L/kg, but it is based on total radio-labelled residues and therefore, this is an overestimate. Nevertheless, according to the guideline on the application of the CLP criteria (p. 506), if an experimental BCF based on the parent compound is not available, for classification purposes, the BCF based on radio-labelled residues can be used.

The test shows some deficiencies such as the depuration phase was not determined, the fish were only sampled at the end of the exposure and that the study was not GLP compliant; however, this test can indicate the bioaccumulation potential of similar substances and therefore it can be used as supportive information.

In conclusion, since the log Kow may be an unreliable predictor of bioconcentration potential for this substance, it is not appropriate to compare it with the classification criteria. No measured BCF data are available for nonanoic acid itself. Dodecanoic acid is more hydrophobic than nonanoic acid, so a direct read across from its measured fish BCF is likely to be a worst case approach. The implication in the absence of any further evidence is that the BCF of nonanoic acid is below 500 L/kg, but it cannot be ruled out that the BCF is above 100 L/kg.

Aquatic toxicity

A summary of ecotoxicological data of different structurally similar organic acids has been summarised in the additional key elements section, table 1.

Regarding nonanoic acid, all tests (except testing of the effects on microbial aquatic activity) were conducted with the ammonium salt of nonanoic acid in the form of the "intermediate formulation" NEU 1170 H.

In these studies, the formulation NEU 1170 H, containing approximately 20% nonanoic acid (nominal), was tested. As in this formulation nonanoic acid is, apart from water, the main component and bioavailability of the active substance in the formulation is higher than for the technical active substance, these tests are considered to be appropriate for the evaluation of the active substance. The end-points of the tests were corrected according to the exact concentration of nonanoic acid.

The formulation NEU 1170 H has been used under the Biocides Directive to study the toxicity of nonanoic acid (Competent Authority Report, CAR, 2007: Doc. II/III-A).
Furthermore, based on the concentration and DSD classification of the other components of the formulation, they are unlikely to contribute to its toxicity and if the toxicity obtained for nonanoic acid with this formulation is compared with other similar acids, it is consistent with a logical trend which shows an increase in toxicity with increasing hydrophobicity. Therefore, the use of the formulation NEU 1170H for the purpose of classification and labelling is considered appropriate.

As can be seen in table 1, when the toxicity to fish and *daphnia* is evaluated, the expected relationship between the toxicity and hydrophobicity of the acids can be seen and since water/fat solubility is related to chain-length of the acids, their toxicities follow the order: dodecanoic acid > decanoic acid > nonanoic acid > octanoic acid. However regarding the toxicity to algae, which is clearly the most sensitive taxonomic group, there are some data which are potentially too inconsistent to enable a classification to be established.

Three different algae tests were included in the report, one performed with nonanoic acid with a NOEC of 0.57 mg/L (CAR of biocides), one more performed with decanoic acid and a NOEC of 0.21 mg/l (CAR of biocides) and finally another one with octanoic acid as the test substance and a NOEC of 0.07 mg/L (REACH registration dossier). Information on dodecanoic acid has been also included in order to attempt to follow the trend of the toxicity, and the NOEC value used for algae is 0.079 mg/L (CAR of biocides). All these values were based on mean measured concentrations.

The tests for nonanoic, decanoic and dodecanoic acids were performed with the same algae species (*Desmodesmus Subspicatus*) and for octanoic acid the selected algae species was *Pseudokirchnerella subcapitata*, these two species are recommended by the OECD TG 201. As can be seem in the results, *Pseudokirchnerella subcapitata* appears to be the most sensitive species and therefore octanoic acid the most toxic compound. This result from the REACH registration dossier is not consistent with the results obtained in daphnia and fish or with the trend observed in the algae tests carried out on the substances in the group. If this test is not considered, toxicity appears to increase with hydrophobicity as would be expected.

Furthermore, there are some deficiencies in the test from the REACH registration dossier, such as the inconsistency in dose-responsiveness at the lowest concentrations, the rapid loss of the test concentration and the fact that the highest effect is observed at 24 hours. Therefore, taking into account that the reliability of this test cannot fully be confirmed and that this test is not consistent with the results of the other taxonomic groups, it should not be used for classification purposes.

For nonanoic acid there is an algae test available with *Desmodesmus subspicatus*, the same species used for decanoic acid test, which is suitable to be used for classification purposes.

As the test substance was not detectable at the end of the algae tests performed with nonanoic and decanoic acids, the 48 h time interval becomes relevant. However, in the 72- hour algal growth inhibition test with decanoic acid, the following validity criterion given in OECD TG 201 is not fulfilled: "The test period may be shortened to at least 48 hours to maintain unlimited, exponential growth during the test as long as the minimum multiplication factor of 16 is reached". In the case of the algae test with decanoic acid the multiplication factor is only approximately 10. Therefore, the total test duration of 72 h has to be used for effect assessment and to estimate chronic effects (by using a concentration equal to half of the limit of quantification when the test substance is not detectable). For nonanoic acid it is not possible to check this due to the minimal data provided.

There is a rapid loss of the test concentrations in the tests with nonanoic, decanoic and dodecanoic acids; this rapid loss also appears in fish and daphnia studies (semi-static tests), as well as in the algal tests without algae for nonanoic and dodecanoic acids. Furthermore, it is necessary to take into account that decanoic acid together with octanoic and nonanoic acids, are surface active substances and the critical micelle concentration is not mentioned in the dossier; so the presence of micelles and adsorption to hard surfaces could partly explain the technical difficulties associated with measuring the actual concentrations of these acids.

According to the OECD TG 201, the use of nominal concentrations could be appropriate when a decrease in concentration of the test substance in the course of the test is not accompanied by a decrease in growth inhibition. In the algae test performed with decanoic acid it is observed that at 72 h the growth inhibition is lower than at 48 h when the concentration was higher. Therefore, at least for this test, the criterion of using nominal concentrations is not met. For nonanoic acid it is not possible to check this due to the minimal data provided.

Moreover, under the Biocides Directive, the acute and chronic algae toxicity was based on mean measured concentrations" (CAR, 2007: Doc. II/III-A). Taking into account the deficiencies of the test submitted under REACH registration for octanoic acid and the justified use of measured concentrations in the algae tests conducted with nonanoic and decanoic acids, the classification is as follows.

Under CLP, the aquatic acute toxicity category is based on EC50 values, and for nonanoic acid these values are >1 mg/l, therefore nonanoic acid does not warrant classification for aquatic acute toxicity. This value is consistent with the acute toxicity of other structurally similar compounds (octanoic and decanoic acid) with EC_{50} values also higher than 1 mg/L.

Regarding chronic toxicity, two tests were reviewed, one in *Daphnia* with a NOEC of 9.93 mg/L, and one in algae (*Desmodesmus subspicatus)* which is the most sensitive species with a NOErC of 0.568 mg/L. Taking into account this value and its rapid degradation, nonanoic acid warrants classification as **Chronic category 3 (H412)** according to **CLP**. Although there are not chronic

tests in fish, because the available OECD TG 204 prolonged toxicity study cannot be considered an aquatic chronic test, the surrogate approach is not relevant, since nonanoic acid is both readily biodegradable and has a fish BCF <500 L/kg Since this leads to no classification, it does not affect the proposal.

Considering the DSD classification, there is no measured ErC_{50} value from the test performed with *Desmodesmus subspicatus,* which is the most sensitive chronic species. However, for decanoic acid, which is a very similar substance with only one more carbon than nonanoic acid, the ErC50 value for this species was 2 mg/L; if read-across is then carried out to the nearest higher homologue, then the ErC50 for nonanoic acid would be 1.84 mg/L (Read across from decanoic acid: Conc. Nonanoic acid [g/L] = conc. Decanoic acid [g/L]*MM Nonanoic acid [g/mol] / MM Decanoic acid [g/mol], where: MM Nonanoic acid = Molar Mass Nonanoic acid = 158.24 g/mol and MM Decanoic = Molar Mass Decanoic Acid = 172.27 g/mol) which would lead to a classification with R51 and in combination with a BCF >100 L/kg (the BCF > 100 L/kg cannot be ruled out) classification as N; R51/53 is therefore justified.

ANNEXES:

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

Annex 2 Response to comments document (RCOM): comments received on the CLH report, response to comments provided by the dossier submitter and rapporteurs' comments (excl. confidential information).