**Committee for Risk Assessment**

**RAC**

# Opinion

proposing harmonised classification and labelling
at EU level of

# octanoic acid

**EC number: 204-677-5**

**CAS number: 124-07-2**

CLH-O-0000002589-62-03/F

**Adopted**

**6 June 2013**

6 June 2013

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# 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: Octanoic acid**

**EC number: 204-677-5**

**CAS number: 124-07-2**

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 octanoic 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) | |
| **Current Annex VI entry** | | | | | | | | | |
| **Dossier submitters proposal** | | octanoic acid | 204-677-5 | 124-07-2 | Skin Corr. 1C<br>Aquatic Chronic 3 | H314<br>H412 | GHS05<br>Dgr | H314<br>H412 | Skin Corr. 1C; H314: C ≥ 70%<br>Skin Irrit 2 ; H315: 1% ≤ C < 70%<br>Eye Irrit 2; H319: 1% ≤ C < 70% |
| **RAC opinion** | | octanoic acid | 204-677-5 | 124-07-2 | Skin Corr. 1C<br>Aquatic Chronic 3 | H314<br>H412 | GHS05<br>Dgr | H314<br>H412 | |
| **Resulting Annex VI entry if agreed by COM** | 607-708-00-4 | octanoic acid | 204-677-5 | 124-07-2 | Skin Corr. 1C<br>Aquatic Chronic 3 | H314<br>H412 | GHS05<br>Dgr | H314<br>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** | | | | | | | |
| **Dossier submitters proposal** | | octanoic acid | 204-677-5 | 124-07-2 | C; R34<br>N; R51-53 | C; N<br>R: 34-51/53<br>S: (2-)20/21-26-36/37/39 | C; R34: C ≥ 70%<br>Xi; R36/38: 1% ≤ C < 70% |
| **RAC opinion** | | octanoic acid | 204-677-5 | 124-07-2 | C; R34N;<br>R51-53 | C; N<br>R: 34-51/53<br>S: (1/2-)26-36/37-39-45-61 | |
| **Resulting Annex VI entry if agreed by COM** | 607-708-00-4 | octanoic acid | 204-677-5 | 124-07-2 | C; R34<br>N; R51-53 | C; N<br>R: 34-51/53<br>S:(1/2-)26-36/37-39-45-61 | |

# 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

No specific guideline studies on irritation or corrosion with octanoic acid are reported in the CLH report. The dossier submitter presents a weight of evidence approach to derive a classification, based onevidence from human experiments, QSAR analysis and from the structurally similar nonanoic and decanoic acid.

Several human volunteer, patch-test studies conducted with Octanoic, Nonanoic and Decanoic acid are described in the CLH report (Jirova et al., 2008, Robinson et al., 1999, Wahlberg, 1983 and Andersen et al., 1995). These all indicated that the substances were at least irritating to skin but most studies terminated exposure when volunteers showed signs of irritation. A transcutaneous electrical resistance test (TERT, York et al., 1996) indicated that decanoic acid was non-corrosive (29.9 kΩ/disc) while Jirova et al. (2008), using the EpiDerm in vitro skin irritation test, concluded that nonanoic and decanoic acid were at least irritant to skin. The ToxTree QSAR tool developed by the European Chemicals Bureau (ECB) indicates that octanoic, nonanoic and decanoic acids are borderline irritating or corrosive to skin.

One non-GLP compliant skin irritation study in rabbits using octanoic acid and indicating severe irritation was reported in the CLH report (Smyth et al., 1962) but this study was not conducted using a standardised design. In addition, several studies using dermal application of nonanoic or decanoic acid in rats, rabbits, guinea pigs and mice are reported as supportive information. These studies apply different concentrations of the test substance and are reported to indicate mild to severe irritation (Talvioja, 2006, Weber 2006, Otterdijk, 2001b, c and d).

The dossier submitter also referenced three studies included in the REACH registration dossier for octanoic acid (see the ECHA web-site). Of the two in vivo rabbit skin irritation studies, one (Nixon, 1981) is inconclusive regarding skin corrosion, whereas the 2nd (Weterings, 1984) indicated borderline corrosivity. The in vitro transcutaneous electrical resistance test (Whittle, 1994) produced resistance below 5.0 kΩ/disc (3.6 kΩ/disc), indicating corrosion. These studies were not reported further in the CLH report but subsequently, the dossier submitter included a summary of them in the Response to comments document (RCOM) document.

Taking into account the data from the registration dossier, in particular the results of the TERT study reported in Whittle (1994), the dossier submitter argues that the overall evidence points towards corrosivity and proposes a classification of Skin Corr. 1C – H314 according to CLP (C; R34 according to DSD). They also propose a specific concentration limit of Skin Corr. 1C – H314; C ≥ 70% based on the studies presented in the REACH registration dossier.

### Comments received during public consultation

Two Member States provided comments during the public consultation. One agreed with the proposed classification but the other requested study summaries for the studies included in the REACH registration dossier for octanoic acid but not summarised in the CLH report (Nixon, 1981; Weterings, 1984 and Whittle, 1994). The summaries were provided by the dossier submitter in the RCOM.

Several industry representatives provided identical statements on behalf of the Fatty Acid Consortium (FAC). With regard to the corrosion/irritation classification, the FAC agreed with the proposed classification and SCL. Another industry commenter highlighted that for linear unbranched saturated organic acids, corrosion and irritation are associated with chain length. Shorter chain organic acids (such as acetic acid) are considered corrosive while longer chain acids (e.g. C16-C18 acids) are not considered irritant. Octanoic acid (along with nonanoic and decanoic acids) would fall in the middle of this range. The commenter requests that the reporting of corrosion/irritation studies be more detailed. The Whittle (1994) study only reports resistance values of <5.0 kOhm/disc but does not report skin disc damage or mean disc dye content. The human volunteer 4 h test study showed octanoic acid to be irritant but not corrosive. The dossier submitter maintains that the Whittle (1994) study is valid and notes that exposure was terminated immediately upon signs of irritation being observed in the human test studies.

## 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 a classification and labeling for the individual compounds. The 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 notes 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 may explain the less clear irritating/corrosive effects of the three acids. Due to the close structural similarity and the very similar $pK_a$ values, the RAC supported the general evaluation approach of all three acids proposed by the dossier submitter.

The available information is briefly summarised below.

### *Human patch tests (HPT)*

AHPT 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 did 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 skin irritation. The $ID_{50}$ 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 4 h 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, whereas 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. Following a personal communication with the dossier submitter's 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 alone, the RAC supported the conclusion of the dossier submitter that the three organic acids are at least skin irritants, but do allow conclusions to be drawn on a possible corrosive effect.

***Animal and in vitro studies***

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

The three studies reported in the REACH registration on octanoic acid have not been available to the dossier submitter and to RAC. The dossier submitter summarises them as follows: (see Annex I)

In a dermal irritation test, Nixon et al. (1981) applied 30, 50, 60, 70 and 100% 0.8 ml octanoic acid/2 $cm^2$ to 6 rabbits for 3 h. Whereas erythema and oedema induced by 30-70% were fully reversible after 24 h, at 100% they were not fully reversible in 5/6 animals within 48 h. There was no observation at day14.

In an OECD TG 404 compliant dermal irritation test, Weterings (1984) applied 0.5 ml 100% octanoic acid to 3 rabbits for 4 h. Full thickness necrosis occurred at 48 h in all animals, which was not fully reversible within 14 days, therefore the conclusion was that octanoic acid was skin corrosive.

In the in vitro transcutaneous electrical resistance test using 100% octanoic acid (Whittle 1994) it was reported that the test substance displayed properties which may be corrosive to animal skin in vivo.

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

Van Otterdijk (2001), 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, which was reversible within 15 days.

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 the OECD TG 4OECD 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 the local lymph node assay (LLNA) in mice, 25 µl/ear of 70% decanoic acid 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. RAC agrees with the dossier submitter that these tests support the corrosive effect seen in two rabbit studies.

### Comparison with 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. Where determined, there was reversibility within 15 days in animal studies, except in two tests using 100% octanoic acid, which showed necrosis. Irritation was also seen in the HPT in most of the volunteers exposed up to 48 h at concentrations of 20% and higher. For ethical reasons most human studies were not continued when irritation was observed (apart from Willis et al. (1988) and Wahlberg et al. (1985)).

The RAC noted that two studies in rabbits on octanoic acid resulted in skin corrosion. Thus, the RAC supports the dossier submitter's proposal that octanoic acid should be considered as corrosive to the skin and warrants classification as Skin Corr. 1 C - H314 according to CLP (C; R34 according to DSD). RAC however, does not support the proposed specific concentration limits as the available data do not allow for their determination.

## RAC evaluation of eye irritation

### Summary of the Dossier submitter's proposal

No guideline specific eye irritation studies are reported in the CLH report. Two older, non-GLP compliant studies (Smyth et al., 1962 and Briggs et al., 1976) indicate damage to eyes. As the dossier submitter proposes classification for Skin Corr. 1C – H314 (causes skin burns and eye damage) and C; R34 (causes burns), they conclude that classification for eye damage is implicitly covered.

### Comments received during public consultation

Several industry commenters submitted an identical paper from FAC. They agreed with the classification but requested addition of SCLs for eye irritation (Eye Irrit. 2 – H319: 1% < C ≤ 70%), based on results from Leoni and Riedel (2011). The dossier submitter agreed to the setting of SCLs for eye irritation based on the summaries provided by FAC but stressed that they do not have access to the study summary for an independent evaluation. Another industry commenter referenced a Bovine Corneal Opacity and Permeability (BCOP) test for decanoic acid which indicates non-corrosivity of decanoic acid. They therefore concluded that octanoic acid should be classified as Eye Irrit. 2 – H319. The dossier submitter did not have access to the study results and did not comment on the validity of the study. The two studies mentioned by industry during the public consultation were made available to RAC and are assessed below

### 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 C&L of the three organic acids as irritants to the skin and the similar $pK_a$ values of octanoic and nonanoic acid, RAC used the sparse information available on the individual compounds for evaluation of the three organic acids.

Regarding <u>octanoic and decanoic acid,</u> 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 grade 9 corneal effects , 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.

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 supports this proposal although the study was not made available to them. RAC has evaluated the Leoni and Riedel (2011) study. In accordance with the OECD TG 4OECD 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 score of 1, 1.67 and 2. In two animals, lesions of the iris (average score 1 in both animals) and the cornea (average 72 h 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 any of 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 public consultation, 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 437 study and supports the conclusion of the report that based on the criteria of the guideline, a 20% dilution of decanoic acid is 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 substance is considered to be corrosive or a severe irritant.

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

***Comparison with 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 are irreversible effects resulting from treatment with 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.

RAC concluded that classification as Eye Irrit. 2 H313 according to CLP (DSD: Xi; R36 DSD) for octanoic acid would be warranted. However, the Guidance to the CLP Criteria clearly states that when a substance is classified as skin corrosive category 1 then serious damage to the eyes is implicit. Since octanoic acid is classified as skin corrosive, there is no need to proceed with a separate classification for eye effects.

# ENVIRONMENTAL HAZARD ASSESSMENT

## RAC evaluation of environmental hazards

### Summary of the Dossier submitter's proposal

The ecotoxicological tests on fish, crustaceans (read across from decanoic acid) and algae (read across from decanoic acid) presented in the CLH report show that the lowest short term value is the $ErC_{50}$ for algae (= 1.67 mg/L). Since the $L(E)C_{50}$ values are all above 1 mg/L, the dossier submitter concluded that the criterion for classification for acute aquatic hazard Category 1 (CLP) and R50 (DSD) are not fulfilled. The dossier submitter considered octanoic acid to be readily biodegradable and rapidly degradable since in a manometric respirometric test (OECD TG 301F), a mean degradation rate of 84% at the end of the 28-days exposure period was observed.

In the CAR for biocides, the calculated log Pow is 3.03 and the resulting calculated BCF on fish is 75. In the REACH registration dossier, the Pow is 3.05 and the measured BCF for fish is 234 – 249. Based on the values for aquatic acute toxicity stated above (1 mg/L < $ErC_{50}$ for algae = 1.67 mg/L $\leqslant$ 10 mg/L), log Pow ($\geqslant$ 3) and measured BCF (> 100), the dossier submitter proposed to classify as R51/53 according to DSD.

In relation to the long term aquatic hazard according to the changes to the CLP Regulation based on the 2nd ATP, only long term data on algae (*Desmodesmus Subspicatus*) are available, providing a geometric mean NOEC of 0.47 mg/L (72 h growth inhibition test, read across from decanoic acid, presented in the CAR for biocides). For fish and crustaceans, only acute toxicity values in the range 10-100 mg/l are available, which in combination with rapid degradability, measured BCF in fish < 500 and logPow < 4 does not lead to any classification. The dossier submitter proposed therefore to use the NOEC value for algae that, together with the rapid degradability, would determine a classification for aquatic chronic Category 3.

In conclusion, the dossier submitter proposes to classify octanoic acid as hazardous to the aquatic environment, aquatic chronic Category 3 - H412, according to the Regulation (EC) 1272/2008 (CLP), and R51/53 according to Directive 67/548/EEC (DSD).
However, following a remark raised in the public consultation, the dossier submitter has changed the proposed classification for long term aquatic hazard according to CLP to aquatic chronic Category 2. The dossier submitter justified the change on the basis of the algae TWA NOEC from the REACH registration dossier, (study conducted on *Pseudokirchnerella Subcapitata)*, which is equal to 0.07 mg/l. The dossier submitter has also changed the proposed classification according to DSD to "no classification", on the basis of the measured TWA $ErC_{50}$ from the REACH registration dossier of octanoic acid (study conducted on *Pseudokirchnerella Subcapitata)*, which is equal to 31 mg/l.

## Comments received during public consultation

During the public consultation, comments on hazards to the aquatic environment were received from four Member States Competent Authorities (MSCAs) and four companies.
Three MSCAs supported the classification proposal.

Another MSCA suggested that a wider set of ecotoxicity data be considered relative to the analogues (heptanoic, nonanoic and decanoic acid), available from the REACH registration dossiers, in order to understand and validate the read-across to octanoic acid.
In particular, this MSCA proposed that the TWA NOEC value relating to the study conducted on the algae *pseudokirchnerella subcapitata* be used from the REACH registration dossier instead of the read-across from decanoic acid.

In response to this comment, the dossier submitter included in the RCOM a summary of all available acute and chronic ecotoxicity data from CARS and REACH registration dossiers from heptanoic, octanoic, nonanoic and decanoic acids. On the basis of this extended dataset, the dossier submitter changed the proposed classification to Aquatic Chronic 2, according to CLP, and no classification, according to DSD.

The four companies referred to a report of the Fatty Acids Consortium (FAC) to propose no classification, on the basis of the general characteristics of fatty acids, naturally occurring and ubiquitously present in the aquatic environment, where they are readily biodegraded by microorganisms. They underpinned their justification with the argument that the logPow was inappropriate as a predictor of bioaccumulative properties and the fact that the calculated BCF (75) is < 100.

Moreover, they claimed that there were methodological deficiencies in the studies used to conclude on classification in the CLH report. They questioned the use of a 72h-NOEC instead of a 48h-NOEC in the algae test for decanoic acid under Biocide Directive, as well as the use of measured concentrations. (In their view, fatty acids act as nutrients for algae. Since the applied amount is not lost from the system but become part of the cells, nominal concentrations should be used). Therefore, they propose that the NOEC of 17.5 mg/l, which was obtained in a new algae study on octanoic acid, be considered. This value would warrant a "no classification" according to the CLP regulation.

Also, long term studies on aquatic invertebrates for decanoic acid are being conducted and test data were expected by October 2012.

The dossier submitter responded to this comment by supporting the classification as Aquatic Chronic 2 and describing the cause of the observed effects in the long term test on algae, and the lack of classification according to DSD.

For the full set of comments and responses, see the response to comments document (RCOM) in Annex 2.

## Assessment and comparison with the classification criteria

### *Degradation.*

Octanoic acid is readily biodegradable under Ready Biodegradability test conditions (OECD TG 301F); degradation was 81-88% at 28 days and within the 10 d window 66-73%. Hydrolysis and photolytic degradation in water are excluded for octanoic acid because organic acids cannot be hydrolysed in the absence of further functional groups and it does not display chromophore properties at wavelengths above 290 nm.

Octanoic acid degrades rapidly in the atmosphere by reaction with OH radicals ($T_{1/2}$: 46.1 h), therefore accumulation in air is not expected.

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

### *Bioaccumulation*

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

No experimental log kow can be determined for octanoic acid, because the octanol/water coefficient cannot be calculated by the relation of water saturation concentration and octanol saturation concentration.

A calculated log Kow value of 3.03 has been summarized in the CLH report. This log Kow corresponds to an undissociated acid; however at relevant environmental pHs, octanoic acid is found in a dissociated form (pka = 4.89) and, therefore, the log kow is expected to be lower.

Nevertheless, octanoic acid is a surface active substance (surface tension 53.2mN/m), and according to the Technical Guidance Document on Risk Assessment (EC 2003, part II, p. 24), for such substances it may not be advisable to use an estimated or measured Kow value as a predictor for 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 BCF values.

For octanoic acid, there is no BCF available; however, in the REACH registration dossier[i], there is an experimental BCF performed with sodium laurate, which can be used with caution as a read-across analogue for octanoic acid. The measured BCF value for lauric acid is 255 L/kg, but it is based on total radio-labelled residues and therefore, it is overestimated. 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 furthermore 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 octanoic acid itself. The $C_{12}$ analogue lauric acid is more hydrophobic than octanoic acid, so a direct read across of its measured fish BCF is likely to be a worst case scenario approach. The implication in the absence of any further evidence is that the BCF of octanoic 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 (see BD).

As can be seen in this table, if the toxicity in fish and daphnia is evaluated without considering the read-across, as one would expect, there appears to be a direct relationship between the toxicity and hydrophobicity of the acids and since hydrophobicity is related to chain-length of the acids, their toxicities follow the order: lauric 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 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 (Competent Authority Report, 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 lauric 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 lauric acid 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 guideline.
As can be seen 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 other substances in the group. If this test is not considered, toxicity appears to increase with hydrophobicity.
Furthermore, there are some deficiencies in the test from REACH registration, 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.

During Public Consultation, industry noted a new algae test performed with octanoic acid; this test was submitted during the preparation of the second draft opinion, however, according to the information included in the test report, it is not totally clear if, at the end of the test, the concentration has been measured with algae (as required by the guideline) or without them. On the other hand, if the test has been performed according to the guideline, it is difficult to understand why it is possible to maintain the concentration, for the duration of the test, for octanoic acid, and not for nonanoic, decanoic and lauric acids. So in analogy with the test that was registered under REACH, the reliability of this test can also not be confirmed, and therefore it should not be used for classification purposes (for more details, see the supplemental information section).

A read-across from nonanoic and decanoic acids is appropriate, if considering the worst case scenario, because the toxicity increases with increasing hydrophobicity.
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 might be regarded as 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 guideline 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 72h the growth inhibition is lower than at 48h when the concentration was higher. Therefore, at least for this test, the criterion for using nominal concentrations is not met.

Moreover, under the Biocides Directive, the acute and chronic algae toxicity was based on mean measured concentrations. Taking into account the deficiencies of the test submitted under REACH registration and the new test submitted by the industry and the justified use of measured concentrations in the algae tests conducted on nonanoic and decanoic acids, the classification is as follows.

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

Regarding chronic toxicity, the most sensitive species is the algae (*Desmodesmus subspicatus)* with a NOErC of 0.21mg/L (read across from decanoic acid) or 0.52 mg/L (read-across from nonanoic acid).

Taking into account these values and its rapid degradation, octanoic acid classifies as **Chronic category 3 (H412)** according to **CLP**. Although there are no chronic tests in fish, the surrogate approach is not relevant since octanoic acid is readily biodegradable and has a fish BCF < 500 L/kg and therefore leads to no classification, and does not impact on the proposal. For chronic tests in *Daphnia*, please see the supplemental information section point 2 (read-across from decanoic acid) and table 1 from the additional information section (read-across from nonanoic acid). The read-across from decanoic acid is a worst case; nonanoic acid is more similar and therefore using read-across from nonanoic acid would be a more realistic approach, but both values trigger no classification.

Under **DSD**, the $EC_{50}$ value for algae, *Desmodesmus subspicatus*, (read-across from decanoic acid) is 1.67 mg/L and although the substance is readily biodegradable, the BCF > 100 L/kg cannot be ruled out, therefore classification as R51/R53 is justified. It is not possible to carry out the read-across from nonanoic acid, because there is no reliable measured $EC_{50}$ value for this species (*Desmodesmus subspicatus*).

## 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 Comments received on the CLH report, response to comments provided by the dossier submitter and rapporteurs' comments (excl. confidential information).