Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]

EC Number: 500-315-8; 500-024-6; 500-045-0; 500-209-1; 248-762-5; 243-816-4; 248-291-5; 687-833-9 and others

CAS Number: 127087-87-0; 9016-45-9; 26027-38-3; 68412-54-4; 27986-36-3; 20427-84-3; 27176-93-8; 1119449-38-5 and others

CLH-O-0000007028-75-01/F

Adopted

16 September 2021

16 September 2021

CLH-O-0000007028-75-01/F

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

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

Chemical name:	**Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]**
EC Number:	**500-315-8; 500-024-6; 500-045-0; 500-209-1; 248-762-5; 243-816-4; 248-291-5; 687-833-9 and others**
CAS Number:	**127087-87-0; 9016-45-9; 26027-38-3; 68412-54-4; 27986-36-3; 20427-84-3; 27176-93-8; 1119449-38-5 and others**

The proposal was submitted by **The Netherlands** and received by RAC on **25 June 2020.**

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

PROCESS FOR ADOPTION OF THE OPINION

The Netherlands 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 **3 August 2020**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **2 October 2020**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Laure Geoffroy**

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

The RAC opinion on the proposed harmonised classification and labelling was adopted on **16 September 2021** by **consensus**.

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

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	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)		
Current Annex VI entry	No current Annex VI entry										
Dossier submitters proposal	TBD	Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352 g/mol) [includes ortho-, meta-, para-isomers or any combination thereof]	500-315-8; 500-024-6; 500-045-0; 500-209-1; 248-762-5; 243-816-4; 248-291-5; 687-833-9 and others	127087-87-0; 9016-45-9; 26027-38-3; 68412-54-4; 27986-36-3; 20427-84-3; 27176-93-8; 1119449-38-5 and others	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=1 M=10	
RAC opinion	TBD	Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352 g/mol) [includes ortho-, meta-, para-isomers or any combination thereof]	500-315-8; 500-024-6; 500-045-0; 500-209-1; 248-762-5; 243-816-4; 248-291-5; 687-833-9 and others	127087-87-0; 9016-45-9; 26027-38-3; 68412-54-4; 27986-36-3; 20427-84-3; 27176-93-8; 1119449-38-5 and others	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=1 M=10	
Resulting Annex VI entry if agreed by COM	TBD	Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352 g/mol) [includes ortho-, meta-, para-isomers or any combination thereof]	500-315-8; 500-024-6; 500-045-0; 500-209-1; 248-762-5; 243-816-4; 248-291-5; 687-833-9 and others	127087-87-0; 9016-45-9; 26027-38-3; 68412-54-4; 27986-36-3; 20427-84-3; 27176-93-8; 1119449-38-5 and others	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410		M=1 M=10	

GROUNDS FOR ADOPTION OF THE OPINION

ENVIRONMENTAL HAZARD EVALUATION

RAC general comments

Nonylphenols ethoxylated (**NPEs**) are C9 alkylphenols with an ethoxylate chain of variable length and number of repeating units. NPEs have a broad range of uses as detergents, emulsifiers and wetting or dispersing agents. Uses in the textile industry are also reported in washing, dyeing and bleaching processes.

Nonylphenol, branched and linear, ethoxylated (with average molecular weight < 352g/mol) [includes ortho-, meta-, para- isomers or any combination thereof] is further referred to in this opinion as **short-chain NPEs** with from 1 to <3 ethoxylate units. This opinion is one of three related opinions, the other two concern medium-chain (3 to <11) and long chain (11-30) NPEs. The NPEs were divided into these 3 groups based on their aquatic toxicity since the aquatic toxicity is expected to decrease with the increase of the number of ethoxylate groups in the view of the DS.

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Regarding the available reliable data, the DS proposed to classify short chain NPEs as Aquatic Acute 1, H400 with an M-factor of 1 and Aquatic Chronic 1, H410 with an M-factor of 10.

With a surface tension lower than 60 mN/m (OECD TG 115), short chain NPEs are surface active, affecting the measurements various properties such as water solubility and octanol-water partitioning. For Short chain NPEs, a water solubility of 4.55 mg/L was determined by the critical micelle concentration and a Log Pow value of 5.39 at 20°C was estimated (Bodsch J., 2010c). Short chain NPEs have a moderate potential to absorb to organic matter. A Koc value of 2661 L/kg for NPE-2 is reported in the registration dossier. Due to their low vapour pressure and low Henry's law constant, volatilisation of short chain NPEs is expected to be negligible.

Rapid Degradability

A summary of the relevant information on rapid degradability is provided by the DS in the table 13 of the CLH report.

NPE with 1 to 2 ethoxy groups are hydrolytically stable at pH 4, 7 and 9 as less than 10% of NPE were transformed after 120h (Anonymous, 2010a).

The DS reported that no photodegradation in water had been observed (Ahel *et al*., 1994a).

Two reliable biodegradation screening studies on short-chain NPEs are reported by the DS. Using OECD TG 301F (manometric respirometry test) and activated sludge as inoculum, after a lag phase of 17.3 ± 0.7 days, NPE-1 was aerobically biodegraded with 25.9 ±8.1% at day 28 and for NPE-2 no biodegradation was observed. In OECD TG 301B with NPE-1.5, 45.3 ± 18.4% CO_2 evolution was observed after 28 days and 58.7% after 35 days. The 10-day window was not met. The DS concluded that NPE with 1, 1.5 and 2 ethoxy groups are not readily biodegradable.

No water simulation tests are available, but the DS reported two reliable sediment simulation tests. The DT_{50}s for primary degradation ranged from 69.3 to 115.5 days (Yuan *et al*., 2004) and 49.5 to 77.0 days at 30 °C (Chang et al., 2004). Three reliable biodegradation tests in soil are available for short chain NPEs and were reported by the DS for information on the behaviour on

these substances although soil assays are not considered relevant for classification purpose where aquatic degradation studies are available.

Bioaccumulation

A summary of the available information on bioaccumulation is presented by the DS in table 15 of the CLH report.

The DS reported that the estimated octanol-water partition coefficient values for NPE-1 range from 5.28 (branched) to 5.58 (linear) and for NPE-2 from 5.01 (branched) to 5.30 (linear). Data reported for the registered UVCB substance nonylphenol, branched, ethoxylated (CAS 68412-54-4) state a value of 5.37 represented the weighted mean value log Pow value of the substance and not individual constituents. Branched structures were not considered in the calculation.

The BCF of nonylphenol branched ethoxylated was estimated to be 648 using the BCFBAF v3.01 program of EPIWEB 4.1 (Arnot Gobas method), based on the weighted average of the BCFs of the various constituents (US EPA, 2014).

The DS noted that experimentally derived BCF values for fish are not available for short-chain NPEs. Measurements of NP, NPE-1, NPE-2 in freshwater fish in the field are available. The data indicated that concentrations of NPE-1 and NPE-2 were below minimum detection levels of 18.2 and 20.6 ng/g, respectively. BAF values from field studies were reported for NPE-1 between 1 and 19 and for NPE-2 between 0.8 and 37. The DS considered that the BAF values cannot be compared directly with bioaccumulation criteria and therefore their use for classification purposes is limited.

BCF values obtained with *Mytilus edulis* were between 100 and 200 for NPE-1 and between 50 and 100 for NPE-2. However, the quality and reliability of the reported BCF values cannot be ascertained due to the lack of information in the study summary.

Based on the estimated BCF value of 648, the DS considered that the short chain NPEs from 1 to 2 have the potential to bioaccumulate.

Aquatic acute toxicity

A summary of the relevant information on aquatic acute toxicity is presented by the DS in table 16 in the CLH report.

For acute aquatic toxicity, studies are presented for the three trophic levels, fish, invertebrates, and algae. An acute fish toxicity study conducted according to OECD TG 203 is available for fathead minnow (*Pimephales promelas*) with NPE-1 and NPE-2. Under the test conditions, the LC_{50} for was determined to be 0.218 mg/L and 0.323 mg/L after 96 h exposure of NPE-1 and NPE-2, respectively.

For invertebrates, two acute studies with *Ceriodaphnia dubia* and with the saltwater mysid *Mysidopsis bahia* were reported by the DS and considered as reliable. For *C. dubnia*, tests were conducted to assess the acute toxicity of NPE-1 and NPE-2 under semi-static conditions in freshwater according to an EPA Guideline. Under these test conditions, the LC_{50} for *C. dubia* was determined to be 0.328 mg/L, and 0.716 mg/L after 48 h exposure to NPE-1 and NPE-2, respectively.

Mysids (*Mysidopsis bahia*) were used to evaluate the acute toxicity of NPE-1.5 under semi-static conditions. Under the test conditions, the 48h LC_{50} values for *Mysidopsis bahia* was determined to be 0.11 mg/L.

For the primary producers, only one reliable study is available. The toxicity of Nonylphenol, branched, ethoxylated (containing about 80% NPE-1 and NPE-2, and the remaining being longer chain ethoxylates up to NPE-6) to the unicellular freshwater green algae *Pseudokirchneriella*

subcapitata was determined according to the OECD TG 201. . The 72 h E_rC_{50} and E_yC_{50} values were determined to be > 3.0 mg/L and 2.02 mg/L, respectively.

According to these studies, algae are found to be less sensitive and for the other species the $L(E)C_{50}$ were in the same range (0.1 to 1 mg/L). The lowest $L(E)C_{50}$ is obtained with the mysids (0.11 mg/L) and as this value is lower than the threshold value of 1 mg/L for acute aquatic classification purpose. Then, the DS proposed to classify short chain NPEs (1- < 3 ethoxy groups) as Aquatic Acute Category 1, H400 with a M-factor of 1 based on the $L(E)C_{50}$ between 0.1 and 1 mg/L.

Aquatic chronic toxicity

The valid available data for chronic aquatic toxicity described by the DS are presented in table 20 of the CLH report.

Five long-term studies with fish, the rainbow trout and medaka were presented in the CLH report. In Dussault *et al*. (2005), Rainbow trout (*Oncorhynchus mykiss*) were exposed to nominal concentrations of 0.01% ethanol (carrier control), 1, 3, 10, 30, and 100 µg/L of NPE-1 in a flow-through system. After 21 days, the NOECs for induction of vitellogenin (VTG) by NPE-1 were 0.048 mg/L.

Groups of 2 years old adult male rainbow trout were exposed to a nominal concentration of 30 µg/L of NPE-2 for 3 weeks in a flow through system (Jobling *et al*., 1996). NPE-2 was found to cause significant elevations in the concentrations of vitellogenin measured in the plasma of exposed fish. The pronounced increases in plasma vitellogenin concentrations were accompanied by concomitant significant decreases in the rate of testicular growth as showed by GSI. Histological examination of the testes revealed varying degrees of spermatogenic inhibition in exposed fish relative to the controls.

In Le Gac *et al.* (2001), Rainbow Trout (*O. mykiss*, 13-month-old males) were exposed to a mixture containing 80% NPE-1 and 20% NPE-2 for 3 weeks in a semi-static renewal culture. After a 3-week-exposure, a significant inhibitory effect of the substance on testicular growth and development was observed. When compared to the solvent control group, the mean gonado-somatic index (GSI) values decreased by 18% and 40% at the lowest and highest test concentration, respectively. No significant VTG induction was observed at the low concentration but VTG was increased at the high concentration. The NOEC for vitellogenin induction was 0.122 mg/L and the NOEC for the Gonado somatic index and gonadal histology was less than 0.122 mg/L.

A study (Balch and Metcalfe, 2006) was conducted to evaluate the effects NPE-1 on growth and survival of the Japanese medaka (*Oryzias latipes*). Exposure to the fry began within 1 day of hatch and continued for 100 days under semi-static conditions. Endpoints reported were secondary sex characteristics, total body length and weight, and development of gonadal intersex (i.e., testis-ova). The NOEC value for survival and for the sex ratio were 105 µg/L for NPE-1. The NOEC for the secondary sex characteristics were 35 µg/L for NPE-1.

Metcalfe *et al*. (2001) exposed Japanese medaka at 1d after hatch to a mixture of 54% NPE-1 and 44% NPE-2 in a static-renewal system until 90d post hatching. Based on the observation of alterations to gonadal development, the NOEC for medaka exposed to nonylphenol ethoxylates (NPE-1 and 2) was 0.050 mg/L corresponding to the mean of NPE-1/NPE-2 concentrations of 0.0155/0.0235 mg/L.

For invertebrates, the DS reported two tests one performed with water fleas and one other with saltwater mysids. The *Daphnia magna* reproduction test (semi-static, 21 d) of Nonylphenol, branched, ethoxylated was conducted according to OECD TG 211. Nonylphenol, branched, ethoxylated contains about 80% NPE-1 and NPE-2, and the remaining being loner chain

ethoxylates up to NPE-6. The reproductive output was statistically significantly reduced at the concentration level of 0.320 mg/L and the EC_{10}-value was calculated to be 0.0853 mg/L. The NOEC after 21 days based on the reduction of the reproductive output as the most sensitive effect were determined to be 0.100 mg/L.

A study was conducted to determine the long-term toxicity of the substance NPE-1.5 (except NPE-1.5 also contains 3.8% of NP), to aquatic invertebrates according to EPA OTS 797.1950 (Mysid Chronic Toxicity Test), in compliance with GLP. *Mysidopsis bahia* was exposed to the test substance at concentrations of 0, 2.3, 4.7, 9.4, 19 and 37 µg/L (equivalent to measured concentrations 0, 2.2, 4.0, 7.7, 16 and 32 µg/L) for 28 days under flow-through conditions. Under the study conditions, the 28 d NOEC (for reproduction in *Mysidopsis bahia*) was determined to be 0.0077 mg/L.

The toxicity of Nonylphenol, branched, ethoxylated (containing about 80% NPE-1 and NPE-2, and the remaining being longer chain ethoxylates up to NPE-6) to the unicellular freshwater green algae *Pseudokirchneriella subcapitata* was determined according to OECD TG 201. . The 72 h E_rC_{10} and NOEC (yield) values were determined to be 1.22 mg/L and 0.75 mg/L respectively.

Chronic aquatic toxicity information is available for all three trophic levels and the lowest long-term toxicity values for fish, aquatic invertebrates and algae are 0.105, 0.0077, and 1.22 mg/L, respectively. The DS considered, based on the *Mysidopsis bahia* 28-day NOEC value of 0.0077 mg/L, short chain NPEs fulfil the criteria for classification as Aquatic Chronic 1, H410 with an M-factor of 10 based on the NOEC between 0.001 and 0.01 mg/L.

Comments received during consultation

During the consultation, one MSCA and one other national authority commented on the classification proposal of the DS. Both support the classification proposal for short chain NPEs as Aquatic Acute 1, M=1 and Aquatic Chronic 1, H410, M=10 but the validity of the lowest acute endpoint for *Mysidopsis bahia* used to derive the Aquatic Acute classification was discussed. The national authority proposed to revise the Klimisch Score of 2 to 4 or 3 due to a mortality exceeding the validity criteria of 10% in the control, GLP compliance is not reported in the study, raw data were not documented and test concentrations were not mentioned. They also asked for clarifications on validity criteria in algal study and whether the endpoints were based on mean measured concentrations for Anonymous (2007), Hall *et al*. (1989), and Anonymous (2010b).

Regarding the control mortality of the study with *Mysidopsis bahia*, despite the validity criterion for ≤10% control mortality not being met, the DS considered the study acceptable because this occurred on only a few occasions. Nevertheless, the DS agreed that the test was not GLP compliant, that raw data were not documented and that actual test concentrations were not mentioned. In this case, assigning a Klimisch score of 4 because of the limited information could be warranted and the DS invited RAC to consider this option.

Assessment and comparison with the classification criteria

Aquatic Chronic classification

Degradation

The dataset presented indicates that short-chain NPEs are not affected by abiotic degradation. Indeed, in a valid OECD TG 111, less than 10% of NPE are transformed after 120 hours at pH4, 7 and 9 at 50°C, demonstrating that hydrolysis is not a relevant pathway for NPE degradation. Insignificant photochemical degradation was found for NPE-1 in phototransformation experiments conducted both in presence of sunlight and artificial light.

In valid 301F and 301B tests, NPE-1 was aerobically biodegraded with 25.9 ±8.1% at day 28, for NPE-2 no biodegradation was observed, and 45.3 ± 18.4% CO_2 evolution was observed for NPE-1.5 after 28 days and 58.7% after 35 days, indicating that neither NPE-1 and NPE-2, nor NPE-1.5 fulfilled the pass level biodegradation within 28 days to be considered as readily biodegradable.

Additional supportive studies presented by the DS reported low primary degradation in sediment.

According to the criteria on rapid degradability defined in the section 4.1.2.9 in the CLP regulation and based on the valid and available data presented by the DS, and especially on the findings from the screening biodegradation tests, RAC agreed to consider short-chain NPEs as **not rapidly degradable** for classification purpose.

Bioaccumulation

No experimental study was available to derive BCF values for fish. As noted in the SEv Dossier (ECHA, 2018), BAF values suggested a relatively low bioaccumulation potential in the aquatic environment and no significant biomagnification in the food chain. However, due to uncertainties, uncertain relationship between the biota and water concentrations, very low sample numbers, data gap on whole fish concentrations (muscle will not necessarily contain the highest concentrations), lack of lipid normalisation, RAC concurred with the DS that field situation study and BAF values are not appropriate for a classification purpose because these values cannot be directly compared with the BCF threshold.

In the CLP guidance, high quality data on the BCF for some invertebrates (blue mussel, oyster, scallop are quoted) may be used instead of fish BCF, as a worst-case surrogate. In the CLH report, BCF values obtained with *Mytilus edulis* were between 100 and 200 for NPE-1 and between 50 and 100 for NPE-2. However, the DS and RAC considered that the quality and reliability of the reported BCF values cannot be ascertained due to the lack of information in the study summary.

The estimated BCF value of 648 for nonylphenol branched ethoxylated using the BCFBAF v3.01 program of EPIWEB 4.1 (Arnot Gobas method), based on the weighted average of the BCFs of the various constituents (US EPA, 2014) meet the CLP trigger value for indication of bioaccumulation (BCF ≥ 500). Nevertheless, according to CLP guidance and information requirements R7c, for surface active substances, the classification of the bioconcentration potential based on hydrophobicity measures such as log K_{ow} should be used with caution and due to the uncertainty, measured BCF values are preferred. Furthermore, for complex substances, estimating an average or weighted BCF value is not recommended. In this case, bioaccumulation should be assessed on the representative constituents, meaning for short chain NPE, NPE-1 and NPE-2 at least, separately.

In the absence of valid experimentally determined BCF value, RAC considered that the estimated octanol-water partition coefficient values for NPE-1 range from 5.28 (branched) - 5.58 (linear) and for NPE-2 from 5.01 (branched) - 5.30 (linear) are the values to take into account for classification purpose. Based on these estimated values, RAC concludes that the short chain NPEs have a potential to bioaccumulate.

Aquatic Toxicity

***Table 1**: Summary of the available acute and chronic toxicity data compared with the CLP criteria. mm = mean measured, n = nominal concentrations, m = initial measured concentration. Key endpoints used in acute and chronic hazard classification are highlighted in bold.*

Method	Substance tested	Results	Remarks	Reference
Acute toxicity				
Fish				
OECD TG 203 Fathead minnow (*Pimephales promelas)*	**NPE-1** NPE-2	**96h-LC_{50} = 0.218 mg/L (mm)** 96h LC_{50} = 0.323 mg/L (mm)	**Flow-through; freshwater RI = 2**	**Anonymous (2007)**
Invertebrates				
US EPA 600/4-90/027F 48h exposure *Ceriodaphnia dubia*	NPE-1 NPE-2	48 h LC_{50} = 0.328 mg/L (mm) 48 h LC_{50} = 0.716 mg/L (mm)	Semi-static RI = 2	Anonymous (2007)
No guideline 48h exposure *Mysidopsis bahia*	NPE-1	48 h LC_{50} = 0.11 mg/L (m?)	Semi-static; Natural salt water; RI = 4	Hall *et al*. (1989)
Algae				
OECD TG201 72h exposure *Pseudokirchneriella subcapitata*	NPEO	$EC_{50,\ growth}$ > 3.0 mg/L $EC_{50,\ yield}$ = 2.02 mg/L (n)	Static; RI = 2	Anonymous (2010b)
Chronic toxicity				
Fish				
Not a test guideline method 21d exposure Rainbow trout (*Oncorhynchus mykiss*)	NPE-1	NOEC VTG = 0.048 mg/L (mm)	Flow-through; Plasma vitellogenin endpoint RI = 2	Dussault *et al*. (2005)
Not a test guideline method 100d exposure Medaka (*Oryzias latipes)*	NPE-1	NOEC survival =0.105 mg/L NOEC sex ratio =0.105 mg/L NOEC SSC = 0.035 mg/L (mm)	Static; Endpoint: mixed secondary sexual characteristics RI = 2	Balch and Metcalfe (2006)
Not a test guideline method 90d exposure Medaka (*Oryzias latipes)*	NPE-1/ NPE-2	NOEC survival = 0.1mg/L NOEC sex ratio = 0.1mg/L NOEC (gonadal histology) = 0.0155/0.0235 mg/L (mm)	Static; Endpoint: Testis-ova RI = 2	Metcalfe *et al*. (2001)
Not a test guideline method rainbow trout males only 21 d exposure	NPE-2	LOEC VTG induction, GSI and gonadal histology ≤ 0.038 mg/L (mm)	Flow-though Endpoint: Plasma vitellogenin and decrease in testicular growth RI = 2	Jobling *et al*. (1996)

Not a test guideline 21d exposure Rainbow trout (*Oncorhynchus mykiss*) Males only	NPE-1/ NPE-2	NOEC GSI gonadal histology < 0.122 mg/L NOEC VTG = 0.122 mg/L (n)	semi-static, endpoint: reduced testicular growth and development RI = 2	Le Gac *et al*. (2001)
Invertebrates				
OECD TG 211 *Daphnia magna* 21d exposure	NPE-1	NOEC reproduction = 0.1 mg/L (n)	Semi-static; RI = 1	Anonymous (2010c)
EPA OTS 797.1950 ***Mysidopsis bahia*** **28d exposure**	**NPE-1.5**	**NOEC reproduction = 0.0077 mg/L (m, n)**	**Flow-though** **RI = 1**	**Anonymous (1999b)**
Algae				
OECD TG 201 *Pseudokirchneriella subcapitata* 72h exposure	NPE-2	E_rC_{10} = 1.22 mg/L NOEC growth = 1.5 mg/L NOEC yield = 2.02 mg/L (n)	Static; RI = 2	Anonymous (2010b)

VTG = vitellogenin, SSC = second sex characteristics

Aquatic acute classification

A full acute data set (fish, aquatic invertebrates, algae) is available for short-chain NPEs. For the DS, the most sensitive species is *Mysidopsis bahia.* This species is known to be very sensitive to different organic compounds. Nevertheless, the reliability of the key study (Hall *et al*., 1989) was questioned during the public consultation. As confirmed by the DS, the concentration NPE+1.5 was measured by gas chromatography but in the published article the period of this measurement was not reported. The most important point is the deviation from the 10% mortality as a validity criterion. In any control, it is assumed that control mortality reached 20%. The impact of this mortality excess is not possible to assess due to the lack of data reported in the article, the unavailability of the raw data and the vague description as followed: *"With the exception of one test, only experiments with <20 percent control mortality were used in comparing the toxicity of different surfactants. Control mortality above the recommended 10% was deemed acceptable because this occurred on only a few occasions and lower levels of mortality occurred for mysids exposed to low levels of surfactant. A toxicant dose-response was otherwise observed in these tests. Reference toxicant data generated during the study demonstrated that sensitivity of mysids in tests with 11 to 19% control mortality was the same as that for mysids used in experiments with ~10% control mortality."* In table 2 of the available report, a control mortality as high as 25% is quoted and used due to the lack of mortality in NPE+50 exposures that is a long chain NPEs, out of this CLH proposal scope. Due to this uncertainty where the mortality excess could lead to an endpoint underestimation, RAC is of the opinion that this study is not reliable for use under CLP.

As the available L(E)C_{50}s for fish and aquatic invertebrates are 0.218 mg/L (NPE-1) and 0.328 mg/L (NPE-1), respectively, and as these values are lower than the classification threshold value of 1 mg/L, RAC agrees that short chain NPEs (1 to < 3 ethoxylate groups) fulfil the criteria for classification **as Aquatic Acute Category 1, H400**. According to CLP table 4.1.3, a **M-factor=1** is warranted for L(E)C_{50}s ranged from 0.1 to 1 mg/L.

Aquatic chronic toxicity

Chronic toxicity data are available for fish, aquatic invertebrates, and algae.

RAC noted that for fish studies, few of them presented results for endpoints normally used for classification purpose as growth and survival. Most results of these studies are related to endocrine disrupting effects. Survival and growth endpoints may not be the most sensitive. For example, from the Medaka studies, a NOEC for reproduction in the range 0.035-0.1 mg/L was suggested by the observed effects on secondary sex characteristics for NPE-1 as proposed in the SEv dossier. RAC considers the most sensitive species to be *M. bahia* with a 28-day NOEC value of 0.0077 mg/L. RAC agrees that as not rapidly degradable substances, Short chain NPEs (1 to < 3 ethoxylate groups) fulfil the criteria for classification as **Aquatic Chronic 1, H410. An M-factor of 10** is warranted based on the NOEC between 0.001 and 0.01 mg/L.

Conclusion

RAC agrees with the DS that **short chain NPEs (1 to < 3 ethoxylate groups) warrant classification as:**

Aquatic Acute 1 (H400), M=1

Aquatic Chronic 1 (H410), M=10

ANNEXES:

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

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