CLH report

Proposal for Harmonised Classification and Labelling

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

International Chemical Identification:

Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]

EC Number:	**230-770-5; 248-743-1; 247-555-7; 248-293-6 and others**
CAS Number:	**127087-87-0; 9016-45-9; 7311-27-5; 27942-27-4;**
	26264-02-8; 27177-05-5; 14409-72-4 and others
Index Number:	**none**

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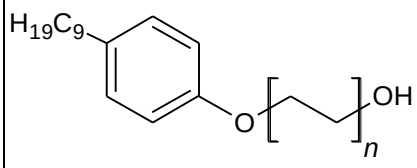
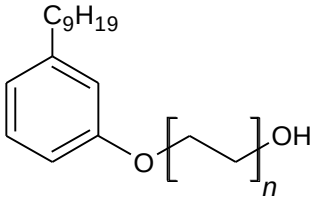
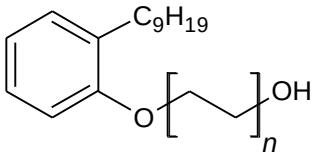
CLH REPORT FOR NONYLPHENOL, BRANCHED AND LINEAR, ETHOXYLATED (WITH 352 G/MOL ≤ AVERAGE MOLECULAR WEIGHT < 704 G/MOL) [INCLUDES ORTHO-, META-, PARA- ISOMERS OR ANY COMBINATION THEREOF]

1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

Name(s) in the IUPAC nomenclature or other international chemical name(s)	Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]
Other names (usual name, trade name, abbreviation)	
ISO common name (if available and appropriate)	
EC number (if available and appropriate)	230-77-5 248-743-1 247-555-7 248-293-6 and others
EC name (if available and appropriate)	
CAS number (if available)	127087-87-0 9016-45-9 7311-27-5 27942-27-4 26264-02-8 27177-05-5 14409-72-4 and others
Other identity code (if available)	
Molecular formula	$(C_2H_4O)_n\ C_{15}H_{24}O$, with n = ≤ 3 to < 11 Where n = represents the number of ethoxylated group(s) to the phenolic group.
Structural formula	Representative structures: *para*- substitution  *meta*- substitution

	 *ortho*- substitution  n = represents the number of ethoxylated groups to the phenolic group n = ≤ 3 to < 11
SMILES notation (if available)	
Molecular weight or molecular weight range	352 g/mol ≤ average molecular weight < 704 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	The major positional isomer is -para (≥90%), while the -ortho isomer is typically less than 10%*.
Description of the manufacturing process and identity of the source (for UVCB substances only)	
Degree of purity (%) (if relevant for the entry in Annex VI)	

*Naylor CG, 2004

1.2 Composition of the substance

Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) will be denoted as NPEn, where n describes the number of ethoxylated groups. This abbreviation is used to refer to a specific NPE substance. Specific NPE oligomers may be reported as NPE-n, where n refers to the mean number of ethoxylate groups in the ethoxylate chain. For example, an oligmer with 9 ethoxylated groups is referred to NPE-9. The term NPE-9 may also refer to a mixture of various oligomers which the mean number of ethoxylated groups per molecule is 9 (i.e., the mixture may also contain NPE-8, NPE-10 etc.). When available this inforamtion will be indicated.

When referring to NPEs as a group, the reference medium-chain NPE will be used.

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Not relevant			

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The impurity contributes to the classification and labelling
Not relevant				

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)	The additive contributes to the classification and labelling
Not relevant					

Table 5: Test substances (non-confidential information)

Identification of test substance	Information in which the test substance is used		
	Environmental Fate	Degradation	Aquatic toxicity
NPE-3 NPE-3.3	X	X	X X
NPE-4		X	X
NPE-5 NPE-5.4			X X
NPE-6		X	X
NPE-8 NPE-8.4 NPE-8.9			X X X
NPE-9 NPE-9.3 NPE-9.5	X	X X X	X X
NPE-10	X	X	X
NPE-10.5	X		

A registration dossier for nonylphenol, branched, ethoxylated (CAS 68412-54-4) is available and was used as a source for information with regard to the substances covered under this CLH report. The substance is registered as a UVCB substance, primarily comprising of one and two ethoxy groups (see Table 6). The relative position of the nonyl group on the aromatic ring was not defined.

Table 6: Information on the constituents of substance, nonylphenol, branched, ethoxylated (NPEO)

Constituent Name*	Concentration range (% w/w minimum and maximum in multi-constituent substances)	Current CLH in Annex VI Table 3.1 (CLP)	Current self-classification and labelling (CLP)
Nonylphenol, branched, n=1	Confidential	None	None
Nonylphenol, branched, n=2	Confidential	None	None
Nonylphenol, branched, n=3	Confidential	None	None
Nonylphenol, branched, n=4	Confidential	None	None
Nonylphenol, branched, n=5	Confidential	None	None
Nonylphenol, branched, n=6	Confidential	None	None

n = represents the number of ethoxy group(s) to the phenolic group

2 PROPOSED HARMONISED CLASSIFICATION AND LABELLING

2.1 Proposed harmonised classification and labelling according to the CLP criteria

Table 7: Proposed harmonised classification and labelling for medium-chain NPEs as defined in this CLP dossier

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry		None									
Dossier submitters proposal	TBD	Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]	230-770-5 248-743-1 247-555-7 248-293-6 and others	127087-87-0 9016-45-9 7311-27-5 27942-27-4 26264-02-8 27177-05-5 14409-72-4 and others	Aquatic Chronic 2	H411	GHS09	H411			
Resulting Annex VI entry if agreed by RAC and COM	TBD	Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof]	230-770-5 248-743-1 247-555-7 248-293-6 and others	127087-87-0 9016-45-9 7311-27-5 27942-27-4 26264-02-8 27177-05-5 14409-72-4 and others	Aquatic Chronic 2	H411	GHS09	H411			

Table 8: Reason for not proposing harmonised classification and status under public consultation

Hazard class	Reason for no classification	Within the scope of public consultation
Explosives	*Hazard class not assessed in this dossier*	No
Flammable gases (including chemically unstable gases)	*Hazard class not assessed in this dossier*	No
Oxidising gases	*Hazard class not assessed in this dossier*	No
Gases under pressure	*Hazard class not assessed in this dossier*	No
Flammable liquids	*Hazard class not assessed in this dossier*	No
Flammable solids	*Hazard class not assessed in this dossier*	No
Self-reactive substances	*Hazard class not assessed in this dossier*	No
Pyrophoric liquids	*Hazard class not assessed in this dossier*	No
Pyrophoric solids	*Hazard class not assessed in this dossier*	No
Self-heating substances	*Hazard class not assessed in this dossier*	No
Substances which in contact with water emit flammable gases	*Hazard class not assessed in this dossier*	No
Oxidising liquids	*Hazard class not assessed in this dossier*	No
Oxidising solids	*Hazard class not assessed in this dossier*	No
Organic peroxides	*Hazard class not assessed in this dossier*	No
Corrosive to metals	*Hazard class not assessed in this dossier*	No
Acute toxicity via oral route	*Hazard class not assessed in this dossier*	No
Acute toxicity via dermal route	*Hazard class not assessed in this dossier*	No
Acute toxicity via inhalation route	*Hazard class not assessed in this dossier*	No
Skin corrosion/irritation	*Hazard class not assessed in this dossier*	No
Serious eye damage/eye irritation	*Hazard class not assessed in this dossier*	No
Respiratory sensitisation	*Hazard class not assessed in this dossier*	No
Skin sensitisation	*Hazard class not assessed in this dossier*	No
Germ cell mutagenicity	*Hazard class not assessed in this dossier*	No
Carcinogenicity	*Hazard class not assessed in this dossier*	No
Reproductive toxicity	*Hazard class not assessed in this dossier*	No
Specific target organ toxicity-single exposure	*Hazard class not assessed in this dossier*	No
Specific target organ toxicity-repeated exposure	*Hazard class not assessed in this dossier*	No
Aspiration hazard	*Hazard class not assessed in this dossier*	No
Hazardous to the aquatic environment	Chronic Category 2	Yes
Hazardous to the ozone layer	*Hazard class not assessed in this dossier*	No

Labelling
Pictogram: GHS09
Hazard statement: H411 (Toxic to aquatic life with long lasting effects)

3 HISTORY OF THE PREVIOUS CLASSIFICATION AND LABELLING

Nonylphenol, branched and linear, ethoxylated (with 352 g/mol ≤ average molecular weight < 704 g/mol) [includes ortho-, meta-, para- isomers or any combination thereof] are not listed in Annex VI of the CLP regulation.

4 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

Requirement for harmonised classification by other legislation or process.

Nonylphenol ethoxylates (NPEs) fall under the Prior Informed Consent Regulation (PIC, EC/649/2012). The PIC regulation manages the import and export of certain hazardous chemicals and places obligations on companies who intend to export these chemicals to non-EU countries. It aims to promote shared responsibility and cooperation in the international trade of hazardous chemicals, and to protect human health and the environment by providing developing countries with information on how to store, transport, use and dispose of hazardous chemicals safety.

As a result of the inclusion of NPEs within the PIC regulation, transportation of NPEs is restricted. This restriction also applies to mixtures containing NPEs above a concentration that leads to classification of the mixture as a result of the presence of NPEs. However, currently a harmonized classification is lacking for these substances. Further, self-classifications vary between the industries. As a result, classification of the mixtures is dependent on the self-classification of the suppliers and is therefore variable. This leads to lack of protection for human health or the environment and lack of clarity to law enforcement.

A harmonised classification for NPEs would result in clarification on the obligations for mixtures as falling under the PIC regulation. Law enforcement of this PIC regulation would be improved.

Most marketed NPE including registered forms are UVCBs containing NPEs varying in number of ethoxylate groups, linearity or branching of the nonyl group or the postion of the ethoxylate group(s) versus the nonyl group on the benzene ring (para-, meta- or ortho- or any combinations thereof). As the exact identity of the tested form is unknown, extrapolation to the other forms within the group for which extrapolation is proposed is difficult. However, in line with the extrapolation applied for the inclusion of these substances in the PIC regulation and applied for the restriction of NPEs in textiles, such extrapolation is considered justified also here.

An approach using groups of NPE's instead of covering only individual UVCB substances is used because often NPEs are exported as mixtures from which it is difficult to determine which NPEs were included. Therefore, inclusion of all possible NPEs (including mono-constituent, multi-constituent, UVCB and polymeric substances) would allow the use of the additivity approach for the most relevant endpoint being aquatic toxicity.

This CLH report is one of three proposals that cover various groups of NPEs. These groups were defined based on reliable (Klimisch scores 1 or 2) aquatic toxicity data for NPEs. These data indicate that aquatic toxicity decreases with the increase of the number of ethoxylate groups (see Tables 9 for acute toxicity and Table 10 for chronic toxicity). This difference in toxicity within the whole range of ethoxylate groups was considered to be problematic for classification and labelling. For this reason the studies were grouped in short, medium and long ethoxylate groups according to the degree of toxicity. The borders of the groups are determined in such a way that most of the endpoints fit within the ranges of the group, although some endpoints make the exception.

The most logical ranges were determined as follows:

Short-chain group (NPEn where n = 1 to < 3 ethoxylate group(s)):
Acute and chronic data on NPE with 1 to 2 ethoxy groups are available for fish, invertebrates and algae. The (E)LC_{50} and NOEC values for fish and Daphnia are all < 1 mg/L. This led to the classification of this group of NPEs as Aquatic Acute Cat. 1 and Chronic Cat. 1. The EC50 for algae of >3.0 mg/L and the NOEC of 1.22 mg/L for the same species was the only value that did not fit into the short chain group.

Medium-chain group (NPEn where n = ≤ 3 to < 11 ethoxylate groups):
Acute data on NPE for 3, 4, 5, 6, 9 and 9.5 ethoxy groups are available for acute fish, invertebrates and algae with (E)LC_{50} values ranging between 1 and 14 mg/L.

Chronic data on NPE 4 and 9 were available for fish with the NOEC values between 0.114 and 0.54 mg/L and for Daphnia with the NOEC value of 10 mg/L. In addition, chronic algae toxicity NOEC data were between 1 and 3 mg/L for NPE of 3 and 6 ethoxy groups, respectively. For the medium group of NPEs between 3 and 10 ethoxy group where there is missing data on certain NPE chain length these data are assumed to be comparable withdata of the same group. For chronic toxicity values the division between the short and the medium-chain group is not sharp as the short chain group hold a NOEC of 0.122 mg/L while the medium-chain group holds a lower NOEC of 0.114 mg/L. This overlap is however minimal which makes the division between NPE-2 and NPE-3 acceptable. The medium-chain group was classified as Chronic Cat. 2 and no acute classification for Acute.

Long-chain group (NPEn where n = ≤ 11 to ≤ 30 ethoxylate groups)
Acute data on NPE with 11 to 30 ethoxy groups is available only for NPE-12 (algae) and NPE-30 (fish), with the (E)LC_{50} values > 1 mg/L. Chronic data are only available for NPE-12 (algae) with a NOEC of 20 mg/L. For this long-chain group there is no acute toxicity classification proposed, while for chronic toxicity a conclusion on classification was not possible due to limited data.

Table 9: Overview of valid acute toxicity data and grouping of NPEn

Only relevant and valid studies (Klimisch scores 1 and 2) for nonylphenol ethoxylates have been listed. The reliablity and description of each study can be found in section 11.5.

Substance tested	Method and species	Results (mg/L)* L(E)C_{50}	Proposed NPEn-group
Fish			
NPE-1	OECD TG 203 Fathead minnow (*Pimephales promelas)*	96h-LC_{50} = 0.218	Short-chain
NPE-2	OECD Guideline 203 Fathead minnow (*Pimephales promelas)*	96h LC_{50} = 0.323	Short-chain
NPE-4 NPE-5 NPE-9 NPE-9.5*	Test guideline not mentioned Bluegill sunfish (*Lepomis macrochirus*)	96h LC50 = 1.3 96h LC50 = 2.4 96h LC50 = 7.9 96h LC50 = 7.6	Medium-chain
NPE-9	Test guideline not mentioned Fathead minnow *(Pimephales promelas)*	96h-LC50 = 4.6	Medium-chain

NPE-30	Test guideline not mentioned Bluegill sunfish (*Lepomis macrochirus*)	96h LC50 > 1000	Long-chain
Invertebrates			
NPE-1	*EPA guideline* *Cerodaphnia dubia*	48h-EC_{50} = 0.328	Short-chain
NPE-1.5**	No guideline *Mysidopsis bahia*	48h-EC_{50} = 0.11	Short-chain
NPE-2	*EPA guideline* *Cerodaphnia dubia*	48h-EC_{50} = 0.716	Short-chain
NPE-9	Test guideline not mentioned *Daphnia magna*	48h EC50 = 14	Medium-chain
Algae			
NPE-2	TG201 *Pseudokirchneriella subcapitata*	72h $EC_{50,growth}$ > 3.0	Short-chain
NEP-3 NPE-6 NPE-12	*Scenedesmus subpicatus* performed according to test guideline 201	72h-ErC50= 2.9 72h-ErC50=13 72h-ErC50=89	Medium-chain Medium-chain Long-chain

* The term NPE 9.5 refers to a mixture of various oligomers where the mean number of ethoxylated groups per molecule is 9.5
** The term NPE 1.5 refers to a mixture of various oligomers where the mean number of ethoxylated groups per molecule is 1.5,

Table 10: Overview of valid chronic toxicity data and grouping of NPEn

Substance tested	Method	Results (mg/L)*	Proposed NPEn-group and remarks
Fish			
NPE-1	Not a test guideline method 21 d exposure Rainbow trout (*Oncorhynchus mykiss*)	NOEC VTG[1] = 0.03	Short-chain
NPE-1	Not a test guideline method 100d exposure Medaka (*Oryzias latipes)*	NOECsurvival =0.105 NOEC SSC[2] = 0.035	Short-chain
NPE-1/ NPE-2	Not a test guideline method 90d exposure Medaka (*Oryzias latipes)*	NOEC = 0.05	Short-chain
NPE-2	Not a test guideline method rainbow trout	LOEC ≤ 0.038 VTG induction, GSI and germ cell stages	Short-chain
NPE-1/ NPE-2	Not a test guideline 21 d exposure Rainbow trout (*Oncorhynchus mykiss*)	LOEC GSI[3] < 0.122 gonadal histology LOEC = 0.122 VTG[1]	Short-chain
NPE-4	Method not specified 100d exposure Medaka (*Oryzias latipes*)	0.114, survival 0.38, SSC[2]	Medium-chain
NPE-9	Method not specified 100 d exposure Medaka (*Oryzias latipes*)	0.54, survival 0.54, SSC[2]	Medium-chain
Invertebrate			
NPE-1	TG211	NOEC reproduction = 0.1	Short-chain

	Daphnia magna 21-d exposure		
NPE-1.5	EPA OTS 797.1950 *Mysisdopsis bahia* 28-d exposure	NOEC reproduction = 0.0077	Short-chain
NPE-9	EPA guideline 7d exposure *Daphnia magna*	10 (mortality) >10 (growth)	Medium-chain
Algae			
NPE-2	TG201 *Pseudokirchneriella subcapitata*	72 h NOEC $_{Growth}$ = 1.22	Short-chain
NEP-3 NPE-6 NPE-12	*Scenedesmus subpicatus* performed according to test guideline 201	72h-NOE_bC = 1 72h- NOE_bC = 3 72h- NOE_bC = 20	Short-chain Short-chain Long-chain

1: VTG = vitellogenin
2: SSC = second sex characteristics

Fate and behaviour

NPEs are expected to be hydrolytically stable. They have a moderate potential to absorb to organic matter. Due to their low vapour pressure and low Henry's law constant, evaporation into the atmosphere is expected to be neglible. In general, degradation of NPEs involves progressive shortening of the ethoxylate chain. Hydrolytic or biodegradative ether cleavage leads to the accumulation of NPE-1 and NPE-2.

Individual short-chain NPEs are expected to show common biodegradation properties and pathways. NPE-1 and NPE-2 are expected to degrade the slowest (Van Vlaardingen et al., 2003) and several studies show that in solution NPE-1/NPE-2 ethoxylates compounds degrade overtime to nonylphenol (European Chemical Agency, 2013; Metcalfe et al., 2001). Short-chain NPEs are considered as substances with potential to bioaccumulate.

Medium-chain NPEs are not readily biodegradable using the standard screening test methods (e.g. the application of the 10-day window criterion). However, significant levels of biodegradation (52 – 99%) are observed for all NPEs tested indicating they metabolize to some extent. This rate of degradation seems to rise with increasing number of ethoxylated group. The bioaccumulation potential for this group varies with increasing ethoxy group. Based on $logK_{ow}$ values, the lower end of the group have the potential to bioaccumulate whilst the upper end group a low potential to bioaccumulate.

Long-chain NPEs are considered rapidly degradable and as substances with low potential for bioaccumulation since the estimated LogKow values are above the CLP trigger of ≥ 4.

Conclusion

The grouping of the various lengths of ethoxylated NPEs in short-, mid- and long-chain groups was based on their acute and chronic toxicity. The majority of the endpoints given in Tables 9 and 10 fall within the choosen borders of the groups. Endpoints on the fate and behaviour of NPEs did not further influence this choice. Overall, the choice of grouping based on valid (E)LC_{50} and NOEC values and the corresponding classification are summarised in Table 11. It is shown that the choice of the ranges of each group resulted in distinctive differences in their classification.

Table 11: Grouping and classification of NPEs

Nonylphenol Ethoxylate	Proposed Classification	
	Acute	**Chronic**
Short-chain: 1 to < 3 ethoxy groups	Category 1 (M = 1)	Category 1 (M = 10)
Medium-chain: ≤ 3 to < 11 ethoxy groups	no acute classification	Category 2
Long – chain: ≤ 11 to ≤ 30 ethoxy groups	no acute classification	no chronic classification

5 IDENTIFIED USES

According to the registration dossier for for nonylphenol, branched, ethoxylated (CAS 68412-54-4), the UVCB substance is only used by workers in industrial settings (manufacture and formulation of the substance). For example, industrial manufacture of NPE and industrial formulation of mining products (floating agents) containing NPE. The registered substance primarily comprises of NPE-1 and NPE-2.

Additional sources report that NPEs are used as auxiliary agents in the manufacturing of textiles (Danish Ministry of the Environmet, 2013). Especially, NPEs with 7 to 15 ethoxylate units are used in the manufacture of textiles but also lower NPEs with 4 to 6 ethoxylate units and NPEs with more than 30 ethoxylate units. According to the report, a particular concern is that NPE decomposes to i.a. nonylphenol (NP), which has long been in focus because of its health and environmentally hazardous properties. Residues of nonylphenol (NP) and nonylphenol ethoxylate have been detected in clothes available in the shops and the general consumer may thus be exposed to these substances. As NP and NPE will eventually be washed out of the clothes, the NP and NPEs will to a certain extent also end up in the environment.

6 DATA SOURCES

The data presented in this CLH report is reproduced from several sources.

- Annex XV dossier – Identification of 4-nonylphenol, branched and linear, ethoxylated as SVHC. Germany, 2012.
- ECHA (2013), Support document for identification of 4-nonylphenol, branched and linear, ethoxylated.
- REACH registration dossiers for nonylphenol, ethoxylated (CAS 9016-45-9)
- REACH registration dossiers for nonylphenol, branched, ethoxylated (CAS 68412-54-4)
- Public literature

7 PHYSICOCHEMICAL PROPERTIES

Table 12: Summary of physical chemical properties

Property	**NPE-n**	**Value [mg/L]**	**Comment (e.g. measured or estimated)**
Critical micelle concentration water solubility	NPE 10.5*	37-61	measured (Van Vlaardingen *et al.* 2003)

*mixtures

Nonylphenol ethoxylates belong to a larger family called alkyphenol ethoxylates (APE). APEs are not synthesized on an individual basis but are formed and processed as a mixture containing oligomers with varying number of ethoxy groups. Therefore physicochemical parameters for isomers will –in most cases- be estimated values (Van Vlaardingen et al., 2003). To get an overview of the properties several physical chemical properties were calculated with EPI Suite (v4.11). The following considerations were taken into account for estimating the physical chemical properties: properties for only a sub-set of NPEs were calculated, including the lower and upper grades of ethoxylation, 3 and 10 respectively, the *para*-substitution position of the nonyl group on the phenol molecule was used and representative structures for the nonyl group included a linear and branched form. The KowWin QSAR is not suitable for nonyl ethoxylate since it is a surfactant therefore the results should be used with caution.

Table 13: Summary of estimated physical chemical properties

Physical Chemical Property	***para*-Substitution of the nonyl group on the phenol molecule** (n=number of ethoxylated groups)			
	n=3	n=6	n=7	n=10
	Linear nonyl group			
Molecular weight (g/mole)	352.52	484.68	528.73	660.89
Log Kow (KOWWIN v1.68)[2]	5.03	4.20	3.93	3.11
Water solubility at 25°C mg/L (WaterNT v1.01)[1]	1.83	10.1	17. 4	87.1
Vapour pressure mmHg at 25°C (Modified Grain method) (MPBPWIN v.1.43)	3.93×10^{-10}	4.02×10^{-14}	2.02×10^{-15}	2.11×10^{-19}
Henry's Law Constant (atm m3/mol) (HENRYWIN v3.20, Bond method)	5.73×10^{-12}	1.49×10^{-16}	2.32×10^{-18}	8.71×10^{-24}
	Branched nonyl group			
Molecular weight (g/mole)	352.52	484.68	528.73	660.89
Log Kow v 1.68[2]	4.73	3.91	3.64	2.81
Water solubility at 25°C mg/L (WaterNT v1.01)[1]	14.46	79.5	138	687
Vapour pressure mmHg at 25°C (Modified Grain method) (MPBPWIN v.1.43)	5.14×10^{-09}	4.02×10^{-14}	2.02×10^{-15}	2.11×10^{-19}
Henry's Law Constant (atm m3/mol) (HENRYWIN v3.20, Bond method)	9.74×10^{-12}	1.49×10^{-16}	2.32×10^{-18}	8.71×10^{-24}

1: WaterNT is based on a new set of (larger) fragments which are optimized for water solubility. The set of fragments contains the whole molecule of nonylphenol ethoxylate. The estimation of water solubility is therefore reliable.
2: As nonyl ethoxylate is a surfactant the Kow estimation as well as the experimental determination is difficult as the border between the fractions water and octanol is disturbed by nonyl ethoxylate.

8 EVALUATION OF PHYSICAL HAZARDS

Not evaluated in this dossier

9 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Not evaluated in this dossier

10 EVALUATION OF HEALTH HAZARDS

Not evaluated in this dossier

11 EVALUATION OF ENVIRONMENTAL HAZARDS

11.1 Rapid degradability of organic substances

Table 14: Summary of relevant information on rapid degradability

Test substance	Test Method	Results	10-day Window?	Remarks	KS*	Reference
NPE-3	OECD 301 B GLP	52% at 29 days	No	60% level of CO2 Not readily biodegradable	1	Diefenbach (1995a)[2]
NPE-6	OECD 301 A GLP	63% at 28 days	No	70% level of DOC Not readily biodegradable	1	Anonymous (1994a)[3]
NPE-9	OECD 301 B GLP Adapted inoculum Non-GLP	74.8 ± 1.92% at day 28 79.5 ± 2.31% at day 35	No	70% level of DOC Not readily biodegradable	2	Anonymous (1999)[1] Staples *et al.* (2001) [1]
NPE-9	ISO 14593 headspace CO_2 biodegradation test Non-GLP	69.5 % at day 35, unacclimated microbial seeds, 70.2 % at day 35, acclimated microbial seeds	No	60% level of CO2 Not readily biodegradable	2	Staples *et al.* (2001)[1]
NPE-9.3	OECD 301 A GLP	70% at 28 days	No	70% level of DOC Not readily biodegradable	1	Anonymous (1994b)[3]
NPE-9.5	OECD 301 E Non-GLP	99% biodegradation within 8 days at 5 mg/L 98% biodegradation within 13 days at 25 mg/L 95% biodegradation within 14 days at 50 mg/L	Yes	Readily biodegradable	2	Jurado *et al.* (2009)[2]
NPE-10	OECD 301 B GLP	36% at 28 days	No	60% level of CO_2 Not readily biodegradable	1	Diefenbach (1995b)[2]

*Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.

[1]As summarised in the ECHA support document for identification of 4-nonylphenol, branched and linear, ethoxylated as substances of very high concern.

[2]Summarized from the literature.

[3]Summarized from confidential company study.

11.1.1 Ready biodegradability

11.1.1.1 Screening Studies

Four screening studies with Ri1 are available with the test substance isononylphenol ethoxylate (CAS Nr 37205-87-1) with varing degrees of ethoxylate groups (3, 6, 9.3 and 10). These are grouped below (Diefenbach and Schröberl studies).

Diefenbach (1995a)

A Modified Sturm Test was performed under GLP according to the modified Sturm-test EG 92/69/EWG C.4-C). This is the current OECD 301B CO_2 Evolution test. Test was performed with NPE-3 (isononylphenol ethoxylate (CAS nr. 37205-87-1)) . Test was performed in 5000 mL flasks. The test substance was tested at 21.1 mg /L and 20 mL inoculum. Inoculum was retrieved from the sewage plant effluent Marl-Ost in Germany. No preconditioning was performed. The control was performed with inoculum only. A reference control was performed with 25.0 mg/L natriumbenzoate and inoculum. All tests were performed in duplicate. The test was performed at 21.7-22.4°C for 29 days. CO_2 evolution was monitored using TAC-analysis after 0, 2, 6, 9, 14, 19, 23, 28 and 29 days.

Results

CO_2 evolution was 18.2 mg/L in the control meeting the validity criteria. The CO_2 evolution in the test treatment after 29 days was 41.95 and 41.10 mg/L and 57.05 mg/L in the reference control, respectively. This CO_2 evolution is equivalent to 89% of theoretical evolution in the reference control, 52% in the test substance. Pass level for ready biodegradability of 60% of CO_2 production within the 10-d window was met for the reference control but not for the test treatment (ca 30% in days13-23). The study is reliable (Ri= 1). This test is considered as a valid study, with reliability 1.

Anonymous (1994a)

A DOC-DIE away test was performed under GLP according to EG- 92/69 EWG, part II, C.4-A). This is the current OECD 301A DOC Die-away. Test was performed NPE-6 (isononylphenol ethoxylate (CAS nr. 37205-87-1)).Test was performed in 2000 mL Erlenmeyer flasks. The test substance was tested at 10.2 mg DOC/L and inoculum. Inoculum was retrieved from the sewage plant effluent Marl-Ost in Germany. The control was performed with inoculum only. A reference control was performed with natriumbenzoate (10.8 mg DOC/L) and inoculum. All tests were performed in duplicate. The test was performed in the dark at 21.9-22.2°C for 28 days. Biodegradation was monitored by measuring the dissolved organic carbon (DOC) reduction after 0 and 3 h, and after 7, 14, 21, 27 and 28 days.

Results

Removal of the test substance was 63% after 28 days. Pass level for ready biodegradability of 70% removal of DOC within the 10-d window was not met as maximum removal was 65% within 10 days (day 4-14). The 10-d window was met for the reference control with a removal of 98%. The study is reliable (Ri= 1).

Anonymous (1994b)

A DOC-DIE away test was performed under GLP according to EG- 92/69 EWG, part II, C.4-A). This is the current OECD 301A DOC Die-away. Test was performed with NPE-9.3 (isononylphenol ethoxylate (CAS nr. 37205-87-1)).Test was performed in 2000 mL Erlenmeyer flasks. The test substance was tested at 9.35 mg DOC/L and inoculum. Inoculum was retrieved from the sewage plant effluent Marl-Ost in Germany. It was aerated before test initiation. Concentration of the inoculum was 24.7 mg/L. The control was performed with inoculum only. A reference control was performed with natriumbenzoate (10.47 mg DOC/L) and inoculum. All tests were performed in duplicate. The test was performed in the dark at 22.0-22.2°C for 28

days. Biodegradation was monitored by measuring the dissolved organic carbon (DOC) reduction after 0 and 3 h, and after 7, 14, 21, 27 and 28 days.

Results

Removal of the test substance was 70% after 28 days. Pass level for ready biodegradability of 70% removal of DOC within the 10-d window was not met as maximum removal was just below 60% within 10 days (day 1-11). The 10-d window was met for the reference control with a removal of 99%. The study is reliable (Ri= 1).

Diefenbach (1995b)

A Modified Sturm Test was performed under GLP according to the modified Sturm-test EG 92/69/EWG C.4-C). This is the current OECD 301B CO2 Evolution test. Test was performed with NPE-10 (isononylphenol ethoxylate (CAS nr. 37205-87-1)). Test was performed in 5000 mL flasks. The test substance was tested at 31.61 mg /L and 14 mL inoculum. Inoculum was retrieved from the sewage plant effluent Marl-Ost in Germany. The inoculum was aerated in the dark during one day. The control was performed with inoculum only. A reference control was performed with 34.3 mg/L natriumbenzoate and inoculum. All tests were performed in duplicate. The test was performed at 20.5-22.3°C for 28 days. CO2 evolution was monitored using TAC-analysis after 0, 3, 7, 10, 14, 17, 21, 25 and 28 days.

Results

CO_2 evolution was 18.2 mg/L in the control meeting the validity criteria. The CO_2 evolution in the test treatment after 28 days was 10.06 mg/L and 20.85 mg/L in the reference control, respectively. This CO_2 evolution is equivalent to 90% of theoretical evolution in the reference control, 36% in the test substance. Pass level for ready biodegradability of 60% of CO_2 production within the 10-d window was met for the reference control but not for the test treatment (ca 20% in days 2-12). The study is reliable (Ri= 1).

Remaining screening studies with Ri2

Anonymous (1999); Staples et al. (2001)

A study was conducted to evaluate the ready biodegradability of NPE-1.5 and NPE-9 by using sludge from a wastewater treatment plant as the microbial seed. In this dossier emphasis will be given to the results of NPE-9. The procedure followed OECD guideline 301B and GLP. The test substance with the standard nutrient medium inoculated with inoculum (30 mg suspended solids/L), was kept in bottles (in darkness) at 22 ± 2 °C for 35 d. A blank control, reference material (Sodium benzoate) and a toxic control were run in parallel for validation purposes. Test substance concentration and dissolved oxygen concentrations for each test medium were determined on days 15 and 35. CO2 evolution was observed after days 1, 2, 4, 6, 9, 13, 18, 22, 28 and 35.

Results

74.8 ± 1.92% CO_2 evolution was observed after 28 days and 79.5 ± 2.31% after 35 days. The 10-day window was failed. 17.5% Suspended organic carbon was determined on day 35. This suggests that NPE-9 incorporated into biomass or adsorbed to suspended material. The reference material attained 60% mineralization in 6 d and 95.4% after 35 d and passed the OECD '10-day window' criterion. Staples *et al.* calculated first order half-lives (primary degradation) of and 13.6 days. NPE-9 showed significant biodegradation but failed to meet the 10-day window pass level for ready biodegradability criterium. The study is reliable (Ri = 2).

Staples et al. (2001)

Ultimate degradation for NPE-9 was measured using the ISO14593 headspace CO_2 biodegradation test. Test vessels were 125-ml serum vials (total volume 160 ml). The same test medium as for the 301B test was used. Test vessels to which the prepared inoculum (acclimated or unacclimated) and medium had been added were fortified by sufficient test material to yield 10 mg C/L and a final volume of 103 ml. Blank controls were prepared without test substances. Vials were sealed and incubated in the dark at 22°C. Duplicate vials were taken on days 1, 3, 7, 14, and 21, and five vials were taken on day 28 for analysis of CO_2. The CO_2 was analyzed by injecting 1 ml H_3PO_4 to the sealed vials, shaken on a rotary shaker for 1 h, and injecting 1 ml headspace gas into a Dohrmann carbon analyzer. Concentrations of CO_2 were determined by comparison to a standard curve.

Results

Temperature measurements were within 22 ±°C, and pH remained within 7.4 to 7.6 during the tests as specified by the test methods. Sodium benzoate positive controls reached 60% mineralization in 6 days and 94.5% by day 35, indicating that the test systems and microbial populations were functioning properly. NPE-9 reached CO_2 evolution of 69.5% (unacclimated microbial system) and 70.2% (acclimated microbial system) by day 35. The study is reliable (Ri = 2).

Jurado et al. (2009)

A study was conducted to evaluate the ready biodegradability of NPE-9.5 by using water from a wastewater treatment plant as the microbial seed. The procedure followed OECD guideline 301E. The study was not said to be performed under GLP. The test substance was tested in a mineral medium inoculated with inoculum (0.5 mL of water from a secondary treatment of a sewage-treatment plant), was kept in a 2-L Erlenmeyer flask (in darkness) at 25°C for 35 d. A reference material with an easily biodegradable surfactant (LAS) in order to determine the activity of the microbial population present in the test medium was included. A blank control and a toxic control were not included.

The test was performed at 5, 25 and 50 mg/L NPE-9.5. Biodegradation was monitored by measuring the residual NPE-9.5 over time. Several measurements were made within a period of 340 h (about 14 days). Number of measurements and the timing differed between the three test concentrations.

Results

At the test concentration of 5 mg/L the biodegradation exceeded 99% in less than 8 days. For an initial concentration of the assay of 25 mg/ L, the biodegradation reached was 98% in less than 13 days. When the initial concentration of the assay doubled at 50 mg/L, the biodegradation declined to 95% and the assay lasted 14 days, giving a residual surfactant concentration of 2.4 mg/L. NPE-9.5 showed significant biodegradation and met the criteria for ready biodegradation (10-day window). A blank control was not included. The degree of biodegradation should be corrected for the amount of abiotic degradation in the blank inoculum control as a percentage of the concentration initially present. A toxic control was not included either. Thus, the calculated biodegradation is an overestimation. The study is reliable with restrictions. Ri =2.

11.1.1.2 Conclusions on ready biodegradability

Standard OECD ready biodegradability tests are available for various medium-chain NPEs.

NPE-3 and NPE-10 reached degradation levels of 52% in 28/29 days. The pass levels of the test (60% of CO_2) were not achieved by the end of the test.

Biodegradation levels for NPE-6, NPE-9 and NPE-9.3 ranged from 63% to 75%. The pass levels of the tests (70% of DOC or 60% CO_2) were met however, the 10-day window condition set out by the test guideline was not met for any of these substances. All available studies were performed with inoculum from sewage plant effluent. Some of these inocula could be adapted to NPEs to some extent. This could explain in part why NPEs in this range biodegrade to approximately 70%, although the 10-day window was not reached. The exception is the study of Jurado *et al.* (2009) in which NPE-9.5 was found to be readily biodegradable. This study reported biodegradation at 99% within 8 days at 5 mg/L, 98% within 13 days at 25 g/L and 95% within 14 days at 50 mg/L. Based on the information provided in the study summary, it is unclear why NPE-9.5 degraded rapidly in comparison with other studies. The reason for the variances in the extent of degradation between the studies may be due (but not limited) to differences in the composition of the test materials but also differences in the test methods and experimental design (method employed for measuring degradation, the degree of acclimation and/or the source of the microbial inoculum).

11.1.2 BOD_5/COD

No information available.

11.1.3 Hydrolysis

No information is available on medium-chain ethoxylates.

According to the SVHC support document for 4-nonylphenol (ECHA, 2013) it is expected that nonylphenol ethoxylates will not be subject to abiotic degradation via hydrolysis. The nonyl group and the phenolic ring structure are chemically stable against hydrolysis. Also the ethoxylate chain is not suspected to be degraded via hydrolysis, but via biotic degradation. It is supposed that hydrolysis is not a relevant degradation process for medium-chain NPEs under environmental conditions.

11.1.4 Other convincing scientific evidence

11.1.4.1 Field investigations and monitoring data (if relevant for C&L)

No information available.

11.1.4.2 Inherent and enhanced ready biodegradability tests

No information available.

11.1.4.3 Water, water-sediment and soil degradation data (including simulation studies)

Table 15: Summary of simulation tests in surface waters

Test substance	Test Method	Results	Remarks	KS*	Reference
NPE-8	Static die-away test Non-GLP Unpolluted lake	~ 100% degradation after 19 days at 22°C under dark conditions and 33 days under light conditions	NPE mixture with an average length of 8 ethoxylated units. NPE-15, NPE-16 and NPE-17 were present in the mixture.	2	Mann and Boddy (2000)[2]
NPE-10	Laboratory-scale bioreactor	> 99% after 100 hours	Primary degradation occurred Metabolites generated: NPECs	2	Jonkers *et al.* (2001)[1]

	Non-GLP river water				
NPE-10 (n=1-18, average 10)	Estuarine water die-away Aerobic	$DisT_{50}$ = 23-69 days (winter 13ºC) $DisT_{50}$ = 10-35 days (18°C) $DisT_{50}$ = 2.5-35 days (summer 22.5ºC)	Main intermediate NPE-2	2	Kveštak and Ahel (1995)[1]

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]As summarised the ECHA support document for identification of 4-nonylphenol, branched and linear as support of very high concern
[2] Summarized from the literature.

Simulation studies in surface waters

Three simulation studies in surface water are available for medium-chain ethoxylates. The studies are reliable with a reliability score of 2.

Mann and Boddy (2000)
A static die-away test was conducted with nonylphenol ethoxylate with an average oligomer length of eight ethoxylate units. NPE-15, NPE-16 and NPE-17 were present in this mixture. Twelve 45 L polyethylene tubs with tight fitting lids were fillled with 40 L of lake water from a small lake within the grounds of Curtin University of Technology in Perth, Western Australia. The lake receives rainwater run-off from the university grounds during winter. Six tubs were dosed with enough surfactant to obtain nominal concentrations of 5 mg/L. The remaining six tubs were designated as controls with no added surfactant. Six tubs (three treated and three controls) were placed in a dark room at 22 ± 1°C. The remaining six tubs (three treated and three controls) were placed in a room at 22 ± 1°C with a 12 h light, 12 h dark photoperiod. The light source was two 58 W, white fluorescent tubes.

Results
Under both light and dark conditions an initial lag phase was observed of 7-9 days. Under dark conditions NPE-8 up to and including NPE-13 degraded up to 100% after 19 and under light conditions this was slower with 33 days.

Jonkers et al. (2001)
Aerobic biodegradation of NPEn was investigated in a laboratory-scale bioreactor filled with river water. The bioreactor was spiked with two different technical mixtures of NPEs (NPE-4, NPE-10) at concentration of 10 mg/L. Small amounts of octylphenol ethoxylate and decylphenol ethoxylated were present in the mixtures.

Results
After 4 days 99% of the NPEs mixtures were dissipated (primary degradation). Nonylphenol carboxylates (NPECs) were identified as the main group of metabolites. The concentration of NPECs increased until day 5 and subsequently decreased. No change in initial NP was observed during the experiment (31 days). Further degradation of NPEC-1 and NPEC-2 by a carboxylation of the alkylchain was observed in this experiment. Short-chain NPEC metabolites were still present in the bioreactor after 31 days.

Kvestak and Ahel (1995)
A study was conducted to evaluate biodegradation kinetics of NPEs in estuarine conditions by using autochthonous mixed bacterial cultures. A commercial mixture of NPEn (n= 1-18) (all analytical grade) was used in all experiments. Bacteria were sampled in a highly polluted harbour from brackish water and saline

water layers of the Krka River estuary (Croatia). Estuarine water were collected in March, September, October, and November. After transportation to the laboratory, the samples were transferred into 5-L glass containers, covered with a glass plate to minimize additional contamination, and incubated at the temperatures which corresponded to those found in the environment at the time of sampling. NPEn's were added to the media at concentrations of 0.1 and 1 mg/L. Control experiments aimed at determining possible non-biological elimination were performed under identical conditions as the main experiments except for the addition of 50 mg/L HgC12 to the media. The temperatures ranged from 13°C (March) to 22.5°C (September). Experiments were performed in the dark. Test duration was 20 days.

Results

Towards the termination of biotransformation experiments (>8 days), all higher oligomers (NPE > 5) were virtually removed from the solution (after 8 days 100% for NPE-7 to NPE 16 and 95% for NPE-6). On the other hand, an increase of absolute concentrations of the most lipophilic oligomers (NPE < 4) occurred in the later phase of the experiments, which indicates that their formation rate became greater than their degradation rate. These lower oligomers were therefore considered metabolic products of higher NPEn's (nEO > 4). Biodegedration half-lives ranged from 2.5 to 25 days at 20°C to 25° from 10 to 35 days at 18°, and increased ro 23 – 69 days at 13°C.

Additional information from literature references – simulation studies with river water

Aerobic Biodegradation of [^{14}C] 4-NPE-9 was examined and changes in the oligomer distribution and mineralization to $^{14}CO_2$ were monitored for 128 days. 87-97% of the initial NPE was degraded to metabolites other than 4-NP, NPE and NPEC after 128 days (Naylor et al., 2006). Only 0.4% 4-NP was detected (non-labelled test system), suggesting that NP is a minor metabolite under aerobic conditions in river water. After 128 days 40.5% of [^{14}C] 4-NPE-9 converted to $^{14}CO_2$ but an acclimation period of 28 days was needed.
Maki et al. (1996) conducted river water die-away tests using NPE-9.5 and reported TOC concentrations in the samples were reduced by 50% following incubations periods of 75 to 200 days. The predominant metabolite was NPEC1, with minor amounts of NPE2 and NPEC2. Quiroga et al. (1996) conducted river water die-away test using NPE-15 and reported that primary degradation reached 85 to 90% NPE-1, NPEC and nonylphenol was identified.

Biodegradation in sediment

Terneu (2004)

The degradation of NPE-n (n=2, 4, 10, and 40) was studied under aerobic and anaerobic conditions at 27°C and 10°C (Teurneu, 2004). For the batch experiments sediment samples from the bottom of a sedimentation basin of an industrial site (production of NPE-n) were used. The initial concentration of NPEn was 500 mg/L. For this dossier only the data for NPE-4 and NPE-10 are used. The theoretical calculations within 44 days for NPE-4 was 10% (27°C) and 7% (10°C) under aerobic conditions and 21% (27°C) and 0% (10°C) under anaerobic conditions. The theoretical calculations within 44 days for NPE-10 was 24% (27°C) and 197% (10°C) under aerobic conditions and 36% (27°C) and 26% (10°C) under anaerobic conditions. In general, the long-chain ethoxylates showed greater degradation than the short-chain ethoxylates. This was confirmed by screening of degrading organisms in the sediment. A higher presence of bacteria capable of 10 and 40 ethoxylate degradation was observed. The results of the sediment analysis indicate an accumulation of NP in the sediment.

Biodegradation in soil systems

One biodegradation tests in soil is available for medium-chain ethoxylates. The study is reliable with a reliability score of 2.

Dettenmaier and Doucette (2007)
Dettenmaier and Doucette conducted microcosm experiments to evaluate the mineralization of NPE-n (n= 4, 9) in a soil/biosolids (99.5:0.5 w/w) environment planted with crested wheatgrass. The microcosms were located in a greenhouse with a 18:6-h light:dark photoperiod and a day/night temperature of 20±1/16±1 °C. Three inital concentrations (6, 24, 47 mg/kg dw) of NPE-n were tested. 12-29 % of NPE-4 and 17- 28% of NPE-9 mineralized to $14CO_2$ within 150 days. No statistical difference was shown between planted and unplanted systems.

11.1.4.4 Photochemical degradation

No information available.

11.1.4.5 Summary and discussion of degradation

Ready biodegradability results show that medium chain NPEs are not readily biodegradable using the standard screening test methods (e.g. the application of the 10-day window criterion). However, significant levels of biodegradation (52 – 99%) are observed for all NPEs tested indicating they metabolize to some extent. This rate of degradation seems to rise as the number of ethoxylated group increases. The results of simulation tests with surfaces waters show rapid removal of NPEs and the formation of the more lipophilic short chain NPEs ≤ 2 as degradation products. In the majority of the studies, the metabolites did not totally disappear at the end of the assays. The abundance of a particular metabolite was very dependent on the treatment conditions. Aerobic biodegradation favors formation of NPEC-1 and NPEC-2 while anerobic biodegradations favors the formation of NPE-1 and NPE-2 finally ultimate complete breakdown (Naylor 2006). NPE-1 and NPE-2 are expected to degrade the slowest (Van Vlaardingen *et al.*, 2003) and several studies show that in solution NPE-1/NPE-2 ethoxylates compounds degrade overtime to nonylphenol (European Chemical Agency, 2013; Metcalfe *et al.*, 2001). Moreover, the dossier submitter has prepared a classification dossier where NPE-1 and NPE-2 are also considered not rapidly degradable. For purposes of classification nonylphenol, branched and linear, (n)-ethoxylated, n= ≤ 3 to < 11 are considered as not rapidly degradable.

11.2 Environmental transformation of metals or inorganic metals compounds

Not relevant for this dossier.

11.3 Environmental fate and other relevant information

Adsorption/Desorption

Information on K_{oc} and log K_{oc} was obtained from Van Vlaardingen *et al.* (2003). Data for NPE-3, NPE-9, NPE-10 and NPE-10.5 are available. In general, partitioning to soil and sediment is expected based on, Log K_{oc} values of 2.5 – 4.09 for NPE-3, 3.79 for NPE-9 and 3.58 – 3.85 for NPE-10. These K_{oc} values indicate a moderate to strong potential to absorb to organic matter.

Table 16: Estimated and experimental (log) Koc values

NPE chain length	Koc value [L/kg]	Log Koc	Remarks	Reference
NPE-3		2.5[1]	Estimated with EPI Suite	Van Vlaardingen *et al.* (2003)
NPE-3	12400	4.09[1]	Natural river sediment	John *et al.* (2000), reported in the

NPE chain length	Koc value [L/kg]	Log Koc	Remarks	Reference
				report of Van Vlaardingen *et al.* (2003)
NPE-9		3.79	Mixture in a river sediment	John *et al.* (2000), reported in the report of Van Vlaardingen *et al.* (2003)
NPE-10	3800	3.58[1]	Natural river sediment	John *et al.* (2000), reported in the report of Van Vlaardingen *et al.* (2003)
NPE-10	6100	3.85[1]	Several sediments and water concentrations	Urano *et al.* 1984, reported in the report of Van Vlaardingen *et al*, (2003)
NPE-10.5	393	2.60[1]	Grassland soils	Liu *et al.* 1992, reported in the report of Van Vlaardingen *et al*. (2003)

[1]calculated by evaluator using the K_{oc}

Volatilisation

Vapour pressure of NPE-3 is 5.24×10^{-8} Pa at 25°C (EPA, 2001, refered to in Van Vlaardingen *et al.*, 2003). The estimated vapour pressures values of 5.14×10^{-9} – 3.93×10^{-10} mmHg at 25°C for NPE-3 suggests that this medium-chain ethoxylate has a low potential to distribute into the atmospheric compartment.

Distribution modelling

No information available.

11.4 Bioaccumulation

Table 17: Summary of available information on bioaccumulation

Method	Results	Remarks*	Reference
BCF study with mussel *Mytilus edulis* Aqueous (freshwater) Method: GC-MS NPE-3	BCF: ca. 50	2 (reliable with restrictions)	Granmo *et al.* (1991)[1,2]
Field study with *Ambloplites rupestri, Lepomis macrochirus, Lepomis cyanellus, Micropterus dolomieui, Catostomus commersoni, Maxostoma macrolepidotum, Osmerus mordax* NPE-3 was measured Method: exhaustive steam distillation with concurrent liquid extraction	Bioconcentration factors not established. NP was the predominant compound, with concentrations of NPEs less than those of NP	2 (reliable with restrictions)	Keith *et al.* (2001)[2]

*Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]As summarised in the Chemical Safety Report (2015) (chapters 1 to 8) for nonylphenol, branched, ethoxylated, EC number 500-209-1.
[2]Retrieved from the open literature.

11.4.1 Estimated bioaccumulation

A log K_{ow} value of 4.48 (geometric mean) was estimated for NPE-3 by Van Vlaardingen *et al*., (2003).

Log K_{ow} values were estimated for a sub-set of NPEs (see Table 13). The following logK_{ow} values were obtained for NPE-3 (4.73 and 5.03), NPE-6 (3.91 and 4.20), NPE-7 (3.64 and 3.93) and NPE-10 (2.81 and 3.11).

11.4.2 Measured partition coefficient and bioaccumulation test data

Ahel and Giger (1993)
A study was conducted to determine the n-octanol water partition coefficient (log K_{ow}) for NPE-3, using the shake flask method and a normal-phase HPLC, according to OECD guideline 107. The log Kow of the test substance was determined to be 4.20 at 20.5°C. This method is not the most suitable experimental method to determine the log K_{ow} given the surface active propteries of the substance. Therefore potentially affecting the reliability of the result.

Granmo et al. (1991)
An accumulation study was performed with caged mussels (*Mytilus edulis*) in the unpolluted waters of a fjord on the Swedish West Coast. Mussels (40-50 mm) taken from a cultivation in an unpolluted area in the Northern part of the coast were stored in submersed tanks with a controlled dosage of wastewater from the outlet of a chemical plant of the Swedish West Coast producing surface active agents. The wastewater was distributed to the tanks in a semi-static system where the water was changed every 4 h. The concentrations of wasterwater were 100, 10 and 1%, respectively. A total of 25 specimen were used per concentration. After 50 days, the mussels were brought to the laboratory and analysed for shell growth and condition. Ten specimen per concentration were prepared and stored at -50°C for chemical analysis. Mussel dry weight was estimated. The concentrations of NP and NP ethoxylates in the frozen samples were analysed by GC-MS. Results were reported based on mussel fresh weight and fat weight. The concentrations of NP, NPE-1, NPE-2 and NPE-3 in the wastewater (100%) were equivalent to 40, 60, 40 and 50 µg/L, respectively. The study results indicated that NP and its short-chain ethoxylates bioaccumulated in mussels and that the degree of bioaccumulation was dependent on chain length, as expected based on water solubility. The average bioconcentration factor for the 100, 10 and 1% wastewater concentrations combined was between 300-400 for NP, 100 -200 for NPE-1, 50 - 100 for NPE-2 and approximately 50 for NPE-3. The authors of the REACH registration dossier assign this with a Klimisch score of 2. The overall quality and reliability of the reported BCF values could not be ascertained because essential information is missing from the study summary. Based on this, dossier submitter assigns the study a Klimisch score of 4 (non-assignable).

Keith et al (2001)
To evaluate bioaccumulation potential and identify potential related risks, concentrations of NP, NPE-1, NPE-2, and NPE-3 were determined in the tissues of fish inhabiting various waters in Michigan (USA), namely the Kalamazoo River Basin and Lake Michigan near the mouth of the Kalamazoo River. The Kalamazoo River flows through both urban and rural areas and receives secondary and tertiary WWTP effluents and industrial discharges, including those of paper manufacturing facilities. Sampling along the river was conducted up and downstream of WWTP, whenever possible. Fish were selected based on availability at sampling site, size (weight), migratory behaviour and placement in the food chain. Species analysed included rock bass

(*Ambloplites rupestris*), bluegill sunfish (*Lepomis macrochirus*), green sunfish (*Lepomis cyanellus*), smallmouth bass (*Micropterus dolomieui*), white suckers (*Catostomus commersoni*), longnose suckers (*Maxostoma macrolepidotum*) and rainbow smelt (*Osmerus mordax*). Fish were collected at three occasions between late une and early November 1999 and stored at -20°C for analysis. The digestive/excretory system was chosen for analysis, as this is the area where NP is likely to accumulate. The analysis method involved extraction of samples using exhaustive steam distillation with concurrent liquid extraction. No sampling of water was conducted. The detection limits for NP, NPE-1, NPE-2 and NPE-3 were 3.3, 16.8, 18.2 and 20.6 ng/g, respectively. Concentrations of NP among all sites and species ranged from <3.3 to 29.1 ng/g wet weight (ww) and varied little among sites. NPE-1 was detectable in some samples but at concentrations less than the method detection limit (16.8 ng/g). Concentrations of NPE-2 and NPE-3 in all samples were less than their respective minimum detection levels. Bioconcentration factors were not established. However, the study suggests the presence of nonylphenols in fish but at relatively small concentrations. NP was the predominant compound, with concentrations of NPEs less than those of NP. Fish collected near WWTP effluent discharge sites contained relatively greater concentrations than those collected from more remote areas (Keith TL et al., 2001). As BCF values could not be determined, the dossier submitter assigns the study a Klimisch score of 4 (non-assignable).

Summary

Experimentally derived BCF values for fish are not available for medium-chain NPEs. A BCF of circa 50 was obtained with *Mytilus edulis* for NPE-3. According the CLP guidance, high quality BCFs determined for non-fish species (e.g. blue mussel, oyster and/or scallop) may be used directly for classification purposes if no fish BCF is available. The quality and reliability of the reported BCF value cannot be ascertained because essential information is missing from the study summary. Therefore, the BCF value based on *Mytilus edulis* is not used for classification.

In the absence of more reliable data, experimental and predicted logKow data are considered for classification. The data shows two trends, NPEs that have log k_{ow} values above and below the log $K_{ow} \leq 4$ threshold. Experimental and predicted logK_{ow} values for NPE-3 are above 4, the lower end of the group. Predicted values for NPE-7 and NPE-10 are below 4, the upper end of the group. The logKow values for the linear and branched forms for NPE-6 were not in line with each other. The logKow values for the linear and branched forms were, 4.20 and 3.91 respectivley. As the number of ethoxylated groups increases so does the water solubility and as a result the Log Kow decreases. This is more or less in line with the predictions where the lower end of the group could be considered to have a potential to bioaccumulate and the high end of the group low potential for bioaccumulation. The threshold limit of the group seems to lie at about NPE-6. A definite conclusion on the bioaccumulation potiential of NPEs as a group is not considered possible, since the log K_{ow} values fall above and below the CLP trigger of 4.

11.5 Acute aquatic hazard

Table 18: Summary of relevant information on acute aquatic toxicity

Method	Substance tested	Results (mg/L)	Remarks	KS*	Reference
Short term		$L(E)C_{50}$			
Fish					
Test guideline not mentioned Bluegill sunfish (*Lepomis macrochirus*)	NPE-4 NPE-5 NPE-9	96h LC50 = 1.3 96h LC50 = 2.4 96h LC50 = 7.9	Static, based on nominal concentations	2	Macek and Krzeminski (1975)[1]

	NPE-9.5	96h LC50 = 7.6			
Test guideline not mentioned Fathead minnow *(Pimephales promelas)*	NPE-9	96h-LC50 = 4.6	Static renewal Based on measured concentrations	2	Dorn *et al.* (1993)[1]
Aquatic invertebrates					
Test guideline not mentioned *Daphnia magna*	NPE-9	48h EC50 = 14	Static renewal Based on measured concentrations	2	Dorn *et al.* (1993)[1]
Algae					
Scenedesmus subspicatus performed according to test guideline 201	NEP-3 NPE-6	72h-E_rC50= 2.9 72h-E_rC50=13	Static, based on nominal concentrations	2	Anonymous (1994)[2]

*Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]Retrieved from the open literature.
[2]As summarized from confidential study from company.

11.5.1 Acute (short-term) toxicity to fish

Table 19: Summary of acute fish toxicity tests

Method	Substance tested	Results (mg/L)	Remarks	KS*	Reference
Fish bioassay procedure described in Japanese Industrial Standard (JIS) K0102 Medaka *(Oryzias latipes)*	NPE-3.3	48h LC50= 2.5	Static, based on nominal concentrations	4	Yoshimura (1986)[2]
Test guideline not mentioned Bluegill sunfish (*Lepomis macrochirus*)	NPE-4	96h LC50=1.3	Static, based on nominal concentrations	2	Macek and Krzeminski (1975)[2]
Test guideline not mentioned Bluegill sunfish (*Lepomis macrochirus*)	NPE-5	96h LC50=2.4	Static, based on nominal concentrations	2	Macek and Krzeminski (1975)[2]
Fish bioassay procedure described in Japanese Industrial Standard (JIS) K0102 Medaka (*Oryzias latipes*)	NPE-5	48h LC50=3.6	Static test, based on nominal concentrations	4	Yoshimura (1986)[2]
Fish bioassay procedure described in	NPE-5.4	48h LC50=6.4	Static test, based on nominal concentrations	4	Yoshimura (1986)[2]

Method	**Substance tested**	**Results (mg/L)**	**Remarks**	**KS***	**Reference**
Japanese Industrial Standard (JIS) K0102 Medaka (*Oryzias latipes*)					
Test guideline not mentioned Rainbow trout (*Oncorhynchus mykiss)*	NPE-8	96h LC50=4.7	Semi static, based on nominal concentrations	3	Anonymous (2007)[1]
Test guideline not mentioned Rainbow trout (*Oncorhynchus mykiss)*	NPE-8	96h LC50=4.7	Semi static, based on nominal concentrations	3	Calamari and Marchetti (1973)[2]
Fish bioassay procedure described in Japanese Industrial Standard (JIS) K0102 Medaka (*Oryzias latipes*)	NPE-8.4	48h LC50=11.6	Static test, based on nominal concentrations	4	Yoshimura (1986)[2]
Fish bioassay procedure described in Japanese Industrial Standard (JIS) K0102 Medaka (*Oryzias latipes*)	NPE-8.9	48h LC50=11.2	Static test, based on nominal concentrations	4	Yoshimura (1986)[2]
Test guideline not mentioned Fathead minnow *(Pimephales promelas)*	NPE-9	96h LC50=4.6	Semi static, based on nominal concentrations	2	Dorn *et al.* (1993)[2]
Test guideline not mentioned Bluegill sunfish (*Lepomis marcrochirus*)	NPE-9	96h LC50=7.9	Static, based on nominal concentrations	2	Macek and Krzeminski (1975)[2]
Test guideline not mentioned Bluegill sunfish (*Lepomis marcrochirus*)	NPE-9.5	96h LC50=7.6	Static, based on nominal concentrations	2	Macek and Krzeminski (1975)[2]
Test guideline not mentioned Harlequin fish (*Rasbora heteromorpha*)	NPE-9-10	96h LC50=8.6	Static or intermittently replaced, based on nominal concentrations	3	Reiff *et al.* (1979)[2]
Test guideline not mentioned	NPE-9-10	96h LC50=1.0	Static or intermittently replaced, based on	3	Reiff *et al.* (1979)[2]

Method	Substance tested	Results (mg/L)	Remarks	KS*	Reference
Brown trout (*Salmo solar*)			nominal concentrations		
Test guideline not mentioned Bluegill sunfish (*Lepomis marcrochirus*)	NPE-9-10	96h LC50 = 7.0 and 11.2	Static or intermittently replaced, based on nominal concentrations Results of two laboratories	3	Reiff *et al.* (1979)[2]
Test guideline not mentioned Goldfish (*Carassius aurtus*)	NPE-9-10	6h LC50=6.9	Static or intermittently replaced, based on nominal concentrations	3	Reiff *et al.* (1979)[2]
Test guideline not mentioned Cod (*Gadus morrhua* L).	NPE-10	96h LC50=2.5 (at 15-17°C); 96h LC50=6 (at 6-8°C)	Flow-through, based on nominal concentrations	3	Swedmark *et al.* (1971)[2]
Test guideline not mentioned Founder (*Pleuroneetes flesus* L.)	NPE-10	96h LC50=3 (at 15-17°C)	Flow-through, based on nominal concentrations	3	Swedmark *et al.* (1971)[2]

*Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]As summarised in the REACH Registration for nonylphenol, branched, ethoxylated, accessed on November 2015 and April 2018.
[2]Summarized from publication retrieved from open literature.

Yoshimura (1986)

In a study by Yoshimura (1986), a static acute toxicity test was carried out to determine the 48h- LC50 of NPEs. Medaka of 2cm average length and 0.2 g of average weight were placed at random in groups of 10 in glass beakers containing 2L of each concentration of samples. After the preliminary range finding test, the LC_{50} determinations were carried out by observing fish survival in single test solution prepared for each concentration. The 48-LC50 values of NPEs for medaka were determined to be 1.4 mg/L (NP), 3.0 mg/L (NPE-1), 2.5 mg/L(NPE-3.3), 3.6 mg/L (NPE-5), 6.4 mg/L (NPE-5.4), 11.6 mg/L (NPE-8.4), 11.2 mg/L (NPE-8.9), 48 mg/L (NPE-13.1), and 16.6 mg/L (NPE-110). For this dossier, the focus is only on data for NPEs 3- through 8.9. The reliability of this study is 3 because of absence in some essential information such as purity of the test substances, test concentrations, number of fish, the chemical analysis etc.

Macek and Krzeminski (1975)

Static bioassays were conducted without artificial aeration, and with a single introduction of the surfactants of NPE-4, NPE-5, NPE-9, NPE-9.5, and NPE-30 dissolved in water. Bluegill sunfish (*Lepomis macrochirus*) with mean body weight of 1 gram were held in the laboratory for at least 30 days and are in good condition. Fish were acclimated to the test conditions for 72 hours, and to the test system for at least 24 hours, prior to testing. Test solutions were prepared by adding the appropriate amount of surfactant to 15 liters of the test diluent. Ten fish were tested at each concentration, using a minimum of six concentrations per bioassay; the mass/volume ratio never exceeded 1.0 gram of fish per liter of diluent. Dissolved oxygen concentrations ranged from 9.0 mg/l initially to 5.1 mg/l at the end of the test. The recovery of nonionic surfactants from samples taken at the beginning (0 hour) of bioassays ranged from 96-106% surfactants indicating the nominal concentrations varied minimally from actual concentrations of surfactant. There were no significant differences in the concentration of surfactants between water samples taken at the beginning and end of the

static bioassays (96 hours), indicating little, if any biodegradation of these materials. In these bioassays nominal concentrations were assumed to be accurate and relatively constant. The 96h-LC50 values for NPE-4, NPE-5, NPE-9, NPE-9.5, and NPE-30 were 1.3, 2.4, 7.9, 7.6, and >1000 mg/L, respectively. For this dossier, the focus is only on data for NPEn 3-10. Ri=2

Anonymous (2007)

Effects of NPE-8 on rainbow trout were conducted in a semi-static acute toxicity test at 15^0C. Ten randomly selected rainbow trout, 12-16 cm in length were used at each concentration. Before the experiments the animals were maintained for at least 7 days in running water of the same quality as that of the dilution water used in the test. Feeding with pellets was stopped 24 h before the start of the test and then given only on alternate days in tests lasting longer than 96 h. Mortality was recorded every 3 h for the first 20 h, and then less frequently on successive days. The concentration of NPE-8 was not measured because of lack of suitable analytical method for nonionic surfactants. Under the test conditions, the 96h-LC50 for rainbow trout exposed to NPE-8 was determined to be 4.7 mg/L. The quality of this study is considered as Ri=3.

Calamari and Marchetti (1973)

Calamari and marchetti (1973) conducted a toxicity test by using rainbow trout (12-16 cm) exposed to NPE-8 for 96 h in a static renewal system. NPE-8 was not measured because a suitable analytical method was lacking. Under the test conditions, the 96h-LC50 for rainbow trout exposed to NPE-8 was determined to be 4.7 mg/L. The quality of this study is considered as Ri=3.

Dorn et al. (1993)

An acute test fathead minnow *Pimephales promelas* was conducted in 96-h static renewal exposures, with daily solution replacement using five concentrations of surfactant NPE-9 and a control. NPE-9 was diluted with moderately hard dilution water (150 mg/L $CaCO_3$). Twenty randomly selected fathead minnows were used at each concentration (2 replicates). Mortality was recorded. Water samples for analysis in static renewal acute tests were collected initially and at 24-h intervals until test end. The concentration of NPE-9 was measured by using cobalt thiocyanate active substance analyses. The measured concentrations are in agreement with the nominal concentrations. Under the test conditions, the 96h-LC50 for fathead minnows exposed to NPE-9 was determined to be 4.6 mg/L. This test is considered as a valid study, Ri=2.

Reiff et al. (1979)

In an acute fish toxicity validation study on NPE 9-10, the tests were conducted in water, which was static or intermittently replaced, of hardnessess ranging from 20 to 268 mg/L expressed as CaCOa at temperatures of 15^0C or 20^0C and on 4 fish species, i.e. goldfish (*Carassius aurtus*), harlequin fish (*Rasbora heteromorpha*), golden orfe (*Idus idus*), and brown trout (*Salmo solar*). The observation times were 48 and 96h in all cases except one test which lasted 6 h. The number of fish exposed is 10 except one laboratory, which used 5 or 20 fish as alternatives. The chemical analysis was not reported. The 6h-LC_{50} for goldfish was 6.9 mg/L. The 48h-LC_{50} values were 11.3 mg/L (harlequin fish), 2.7 mg/L (brown trout), and 4.9, 7.4 and 11.3 mg/L (golden orfe, results of three different laboratories, respectively). The 96h-LC_{50} values were 8.6 mg/L (harlequin fish), 1.0 mg/L (brown trout), 7.0 and 11.2 mg/L (golden orfe, results of two laboratories). The quality of this study is considered as Ri=3.

Swedmark et al. (1971)

A 96h study was conducted to evaluate the acute toxicity of NPE-10 to the cod *Gadus morrhua* L. (30 cm long) and the flounder *Pleuroneetes flesus* L. under flow-through conditions in sea water (Swedmark et al 1971). In order to keep the concentration of the solutions constant, a standard solution of the surfactant was added to the test aquarium by means of a precision dosing pump and the sea water dispensed with siphons at a constant continuous flow. At least 5 animals/tank were usually used. Before testing, the animals were acclimatized to laboratory conditions. Acclimatization was considered complete when normal behaviour was established, usually after 3 to 7 days. The 96h-LC_{50} values for cod were 6 mg/L at temperature between 6-

8^0C and 2.5 mg/L at the temperature between 15 and 17^0C. The 96h-LC_{50} value for flounder was 3 mg/L at temperature between 15 and 17^0C. No chemical concentrations were measured. The quality of this study is considered as Ri=3.

11.5.2 Acute (short-term) toxicity to aquatic invertebrates

Table 20: Summary of crustacean toxicity tests

Method	Substance tested	Results E(L)C50 (mg/L)	Remarks	KS*	Reference**
No guideline *Daphnia magna*	NPE-9	48h EC50=14	Static renewal concentrations were measured	2	Dorn *et al.* (1993)
Conform regulation New Yersey *Mysidopsis bahia*	NPE-9	48h LC50=1.23	No detailed description	4	Patoxzka and Pulliam (1990)
No guideline *Mysidopsis bahia*	NPE-9	48h LC50=0.9-2	Static renewal Not measured	3	Hall *et al.* (1989)
No guideline Barnacle *Balanus balanoides*, stage II Nauplius larvae	NPE-10	96h LC50 = 1.5	Static Concentrations not measured	3	Swedmark *et al.* (1971)
No guideline Decapod *Leander squilla*	NPE-10	96h LC50 >10	Static Concentrations not measured	3	Swedmark *et al.* (1971)
No guideline Hermit crab *Eupagurus bernhardus*	NPE-10	96h LC50 >100	Static Concentrations not measured	3	Swedmark *et al.* (1971)
No guideline Shore crab *Careinus maenas*	NPE-10	96h LC50 >100	Static Concentrations not measured	3	Swedmark *et al.* (1971)
No guideline Spider crab *Hyas araneus*, stage I zoea larvae	NPE-10	96h LC50 = 10	Static Concentrations not measured	3	Swedmark *et al.* (1971)
Cerodaphnia dubia	NPE-10	48h EC50= 10	Static, nominal concentration	3	Isidori *et al.* (2006)
Daphnia magna	NPE-10	24h EC50 >20	Static, nominal concentration	3	Isidori *et al.* (2006)

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
** All studies were summarized from publications retrieved from open literature

Dorn et al. (1993)

Dorn et al (1993) conducted an acute test using the water flea *Daphnia magna* (Strauss) exposed to NPE-9 for 48h in static-renewal exposures with daily replacement of fresh surfactant and a control consisting of reconstituted laboratory water. Twenty neonates per concentration (4 replicates, 5 daphnia per replicate) were used. Water samples for analysis in static renewal acute tests were collected initially and at 24-h intervals until test end. Cobalt thiocyanate active substance analyses showed that nominal concentrations of NPE-9 reflected actual concentrations. The EC_{50} for *Daphnia magna* was determined to be 14 mg/L after 48 h exposure to NPE-9. The reliability of this study is considered as Ri=2.

Patoxzka and Pulliam (1990)

Patoxzka and Pulliam (1990) performed a study to evaluate the acute toxicity of NPE-9 to mysids (*Mysidopsis bahia*) after 48 h exposure. Tests were performed according to the procedure in "regulations governing laboratory certification and standards of performance, New Jersey Administrative Code, 7:18, as amended July 1984. No detailed description on the number of animals, the test concentrations and the analysis of chemicals could be found in the original paper. Under the test conditions, the LC50 for mysids was determined to be 1.23 mg/L after 48 h exposure of NPE-9. The reliability of this study is considered as Ri=4

Hall et al. (1989)

Three- to eight-day old mysids (*Mysidopsis bahia*) were used to evaluate the acute toxicities of NPE-1.5, NPE-9, NPE-15, NPE-40 and NPE-50 (Hall *et al.*, 1989). For this dossier, the focus is only on data for NPE-9. All tests were 48-hr static renewals (renewals at 24 hr) at 25 ± 1^0C under a light:dark photoperiod of 16-hr:8-hr. All mysids were 3 to 8 days old at the start of tests. Aged, natural saltwater of 25 to 28 %o salinity (25 micron filtered) was the control and dilution water in all experiments. All toxicant exposures contained two replicates of four organisms per concentration and controls contained four replicates of four organisms. With the exception of one chemical (NPE-1.5), concentrations were nominal values obtained by adding pure chemical to the saltwater. A modification of the gas chromatography following continuous distillation and extraction with octanol was used to measure NPE-1.5. *M. bahia* were fed live *Artemia* (<24-hr old) at the start of tests and after renewing solutions. Dissolved oxygen, pH, and salinity were monitored at the start, after 24-h, at renewal, and at termination of experiments. Dissolved oxygen was measured in all solutions at the start, at 24-h and 48-h of all tests. Salinity and pH were monitored only in the controls and the two highest toxicant concentrations, since changes in these parameters were not observed as a result of addition of chemicals. 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. To ensure that mysids obtained from the two suppliers were of similar and consistent sensitivity, one of the surfactants NPE-9 was used as an internal reference toxicant throughout the tests, because it is readily soluble and of high acute toxicity. Under the test conditions, the 48h-LC50 values for *Mysidopsis bahia* was determined to be 0.11 mg/L (NPE-1.5); 0.9-2 mg/L (NPE-9); 2.57 mg/L (NPE-15); >40 mg/L (NPE-40) and >4110 mg/L (NPE-50). The chemical concentrations were not measured and the study is considered as Ri=3.

Swedmark et al (1971)

The effects of NPE-10 were studied in crustaceans exposed to NPE-10 (Swedmark et al 1971). Larvae were all hatched in the laboratory. Static tests were made in 50 ml beakers and the beakers were immersed in a thermostat bath without illumination. Measurements and observations under the microscope were made in a small, cooled, constant-temperature aquarium. The number of adult animals per test tank was adapted to the volume of the container and the size of the animals. At least 5 animals/tank were usually used. Before testing, the animals were acclimatized to laboratory conditions. Acclimatization was considered complete

when normal behaviour was established, usually after 3 to 7 days. Mortality and survival times were continuously recorded during the tests. Experiments to determine lethal concentrations lasted 96 h. The median lethal concentration (LC 50) was obtained by graphic interpolation on the cumulative percentage mortality curve plotted against exposure time. Under the test conditions, the 96h-LC50 values for crustacean exposed to NPE10 was determined to be 1.5 mg/L (barnacle *Balanus balanoides*), 10 mg/L (decapod *Leander squilla*), >100 mg/L (shore crab, *Carcunus maenas* and hermit crab, *Eupagarus bernhardus*), >107 mg/L (spider crab *Hyas araneus*). This study is not considered valid because the chemical concentration was not measured. Ri=3.

Isidori et al. (2006)

The bioassays on *Daphnia magna* and *Cerodaphnia dubia* were performed with neonates <24 h under static conditions. Five daphnids per vessel, four replicates for each of five concentrations were exposed to NPE-10 at a temperature of 20 ^{0}C in the dark according to the ISO (International Organization for Standardization) 6341. The number of immobile daphnids was recorded after 24 h to determine the concentration able to achieve 50% immobilization. The acute test on *Ceriodaphnia dubia* was performed for 48 h of exposure of NPE-10 to young organisms, less than 24 h old. Tests were performed in 24-well plates, ten crustaceans per well (1.0 ml of test solution), three replicates per concentration, and five concentrations. Plates were incubated for 48 h in darkness at 25 ± 1 ^{0}C. The test parameter considered was mobility and the concentration found to immobilize 50% of the crustaceans in 48 h was indicated as EC50. Under the test conditions, the 24h-EC50 for Daphnia and the 48h-EC50 for Ceriodaphnia were determined to be > 20 mg/L and 10 mg/L, respectively. The test concentrations were not measured. The quality of this study is considered as Ri=3.

11.5.3 Acute (short-term) toxicity to algae or other aquatic plants

Table 21: Summary of algal acute toxicity tests

Method	Substance tested	Results EC50 (mg/L)	Remarks	KS*	Reference**
OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-3	72h-E_rC_{50} = 2.9 72h-E_bC_{50} = 2.9 72h-E_rC_{10} = 1.4 72h-NOE_bC = 1	Static, nominal concentration.	2	Anonymous (1994a)[1]
OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-6	72h-E_rC_{50} = 13 72h-E_bC_{50} = 3.7 72h-E_rC_{10} = 6.1 72h-NOE_bC = 3	Static, nominal concentration	2	Anonymous (1994b) [1]
Selenastrum capricornutum	NPE-6	3w EC_{50} >500	Static, nominal concentration	3	Nyberg (1988) [1]
Selenastrum capricornutum	NPE-9	3w EC_{50} >500	Static, nominal concentration	3	Nyberg (1988) [1]
Selenastrum capricornutum	NPE-9	96h EC_{50}= 12	Static, nominal concentration	3	Dorn *et al.* (1993) [1]

OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-9.3	72h-E_rC_{50} = >30 72h-E_bC_{50} = 30 72h-E_rC_{10} = 14.5 72h-NOE_bC = 4	Static, nominal concentration Not all validity criteria were met	3	Anonymous (1994c)[2]

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.

[1] Study summarized from publication retrieved from open literature.

[2] Summarized from confidential study from company.

Anonymous (1994a)

The toxicity of NPE-3 (purity 99.4%) to green alga (*Scenedesmus subpicatus*) was determined under GLP using OECD test guideline 201. Preparation of test solutions started with stock solutions by directly dissolving 1 g of NPE-3 into 1 L water. After shaking for 18h, the stock solution was measured photometrically at 275 nm at 0 and 72 h. The study was conducted under static conditions with an initial cell density of 2 x 10^4 cells/mL. Exponentially growing algal cultures were exposed for 72 hours to nominal concentrations of 0.25, 0.5, 1, 2 and 4 mg/L. The photoperiod (L:D) is 24:0 h, temperature 24 °C, light intensity 8000 lux, pH 8.4-8.6 at test start and 7.9-9.5 at the end of the test. A control was included in the test. Three replicates were tested for each tested concentrations. Algae were counted photometrically at 685 nm at 0, 24, 48 and 72 h.

The measured stock concentration of NPE-3 was 22 mg ai/L at 0 h and 23 mg ai/L at 72 h. Test concentrations were not further measured in the test vessels. Nominal concentrations were used to determine the effect concentrations. All validity criteria were met. The EC50 for growth rate reduction (ErC50: 0-72h) was 2.9 mg/1; 72h-ErC10 = 1.4 mg/L; 72h-EbC50 = 2.9 mg/L; 72h-NOEbC = 1 mg/L. This study is considered as Ri=2 .

Anonymous (1994b)

The toxicity of NPE-6 to green alga (*Scenedesmus subpicatus* (Chodat)) was determined under GLP using OECD test guideline 201. The test was performed with NPE-6 (purity 99.4%). Preparation of test solutions started with stock solutions by directly dissolving 1 g of NPE-6 into 1 L water. The study was conducted under static conditions with an initial cell density of 2 x 10^4 cells/mL. Exponentially growing algal cultures were exposed for 72 hours to nominal concentrations of 0.7, 1.4, 3, 6, 12 and 24 mg/L. Concentrations were measured photometrically at 275 nm at 0 and 72 h after test initation in additional test vessels without algae. The photoperiod (L:D) is 24:0 h, temperature 24 °C, light intensity 8000 lux, pH 7.9-8.3 at test start and 7.7-9.0 at the end of the test. A control was included in the test. Five replicates were tested for each tested concentrations, 8 replicates in the control. Algae were counted photometrically at 685 nm at 0, 24, 48 and 72 h.

Measured concentrations at 72 h were higher than nominal (220, 227, 128 and 148% of nominal at 3-24 mg /L). This was explained by a changed absorption level. Nominal concentrations were used to determine the effect concentrations in the original report. All validity criteria were met. The 72h EC50 for growth rate reduction was 13 mg/L; 72h-ErC10 = 6.1 mg/L; 72h-EbC50 = 3.7 mg/L; 72h-NOEbC = 3 mg/L. This study is considered as Ri=2 .

Nyberg (1988)

In a study by Nyberg (1988), the alga *Pseudokirchneriella subcapitata* was cultured in 50 ml Erlenmeyer flasks using 25 ml liquid synthetic medium in each flask. The flasks were inoculated with 0.1 ml of an algal suspension. The inoculate contained *ca* 1.5 x 10^5 cells. The surfactants were added to the cooled autoclaved

medium as stock solutions using sterile MiUipore filters to avoid any possible decomposition during sterilization. The algae were cultured at 25°C for 3 wk with gentle shaking (ll0rpm) under Airam 40W-35 white fluorescent tubes. After the growth period, at the approximate onset of the stationary phase, the cell counts in each flask were measured with a Fuchs-Rosenthal counting chamber. The 3 week EC50 values for growth were >500 mg/L for all surfactants of NPE-6, 9 and 30. The exposure period for algal species is normally 72 or 96 hour EC50 and/or aquatic plants 7 days EC50. For this dossier, the focus is only on NPE 6 and NPE 9. This study is considered as , Ri=3.

Dorn et al. (1993)
The toxicity of NPE-9 to the green algae (*Selenastrum capricornutum* (Printz)) was determined according to the principles of US EPA guideline. The study was conducted under static conditions with an initial cell density of 1 x 10^4 cells/mL. The exposure is 96 h and the photoperiod (L:D) is 24:0 h. Three replicates were tested for each tested concentrations. Chemical sampling and analysis for the algae toxicity test was not stated in the report. The following values were stated in the paper: 96h-EC50 = 12 mg/L; NOEC = 8 mg/L. The test concentrations were not measured. This study is considered as Ri=3.

Anonymous (1994c)
The toxicity of NPE-9.3 to green alga (*Scenedesmus subpicatus* (Chodat)) was determined under GLP using OECD test guideline 201. The test was performed with NPE-9.3 (purity 99.7%). Preparation of test solutions started with stock solutions by directly dissolving 1 g of NPE-9.3 into 1 L water. The study was conducted under static conditions with an initial cell density of 2 x 10^4 cells/mL. Exponentially growing algal cultures were exposed for 72 hours to nominal concentrations of 1, 2, 4, 8, 16 and 32 mg/L. Concentrations were measured photometrically at 275 nm at 0 and 72 h after test initation in additional test vessels without algae. The photoperiod (L:D) is 24:0 h, temperature 24 °C, light intensity 8000 lux, pH 7.0-7.4 at test start and 8.7-9.5 at the end of the test. A control was included in the test. Five replicates were tested for each tested concentrations, 8 replicates in the control. Algae were counted photometrically at 685 nm at 0, 24, 48 and 72 h.

Measured concentrations were >80% of nominal at 0 and 72 h. The nominal concentrations were used to determine the effect concentrations. Not all validity criteria were met. The CV for day-to-day sectional growth rate in the control was 88.9% (should be <35%). The calculated values are 72h-E_rC50 = >30 mg/L; 72h-E_rC10 = 14.5 mg/L; 72h-E_bC50 = 30 mg/L; 72h-NOE_bC = 4 mg/L. This study is considered as Ri=3 since validity criteria were not met.

11.5.4 Acute (short-term) toxicity to other aquatic organisms

No experimental studies are available.

11.6 Long-term aquatic hazard

Table 22: Summary of relevant information on chronic aquatic toxicity (only valid studies included)

Method	Substance tested	Results NOEC/EC10 (mg/L)	Remarks	KS*	Reference
Fish					
Method not specified 100d exposure Medaka (*Oryzias latipes*)	NPE-4	0.114, survival 0.38, SSC[2]	Static Based on measured concentrations	2 Key study	Balch and Metcalfe (2006)[2]

Method not specified 100 d exposure Medaka (*Oryzias latipes*)	NPE-9	0.54, survival 0.54, SSC[2]	Static Based on measured concentrations	2 Key study	Balch and Metcalfe (2006)[2]
Aquatic invertebrates					
EPA guideline 7d exposure *Daphnia magna*	NPE-9	10 (mortality) >10 (growth)	Static-renewal; Based on measured concentrations	2 Key study	Dorn *et al.* (1993)[2]
Algae					
Scenedesmus subpicatus performed according to test guideline 201	NEP-3 NPE-6	72h-E_rC10 = 1.4 72h-E_rC10 = 6.1	Static, based on nominal concentrations	2	Anonymous (1994ab)[3]

*Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]As summarised in the REACH Registration for nonylphenol, branched, ethoxylated, accessed on November 2015.
[2]Summarized from the literature
[3]Summarized from confidential study from company.

11.6.1 Chronic toxicity to fish

Table 23: Summary of fish chronic toxicity tests

Method	**Substance tested**	**Results** **NOEC (mg/L)**	**Remarks**	**KS***	**Reference****
100d exposure Medaka (*Oryzias latipes*) 10, 30, 100, 300, and 1000 µg/L	NPE-4	0.114, survival 0.38, SSC > 0.38, sex ratio > 0.38, gonadal intersex	Semi-static, measured concentrations	2	Balch and Metcalfe (2006)
100 d exposure Medaka (*Oryzias latipes*) 30, 100, 300, and 1000 µg/L	NPE-9	0.54, survival 0.54, SSC > 0.54, sex ratio > 0.54, gonadal intersex	Semi-static, measured concentrations	2	Balch and Metcalfe (2006)
7 day exposure Fathead minnow (*Pimephales promelas*)	NPE-9	1-8, survival 0.4-1, growth	Semi-static, measured concentrations	4	Dorn *et al.* (1993)

42 day exposure Fathead minnow (*Pimephales promelas*)	NPE-9.5	>0.0055, SSC >0.0055, gonad histology	Flow-through, measured concentrations Test concentrations were too low to induce any toxic effects. No statistical difference in the size of SSC or effects to gonad histology	3	Miles-Richardson *et al.* (1999)
42 day exposure Fathead minnow (*Pimephales promelas*)	NPE-9.5	>0.0079, fecundity >0.0079, survival >0.0079, VTG	Flow-through, measured concentrations Test concentrations were too low to induce any toxic effects. No statistical significant-dependent relationship to NPE 9.5 exposure was established for survial, fecundity and VTG.	3	Nichols *et al.* (2001)

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the evaluator does not agree with the reliability assignment made by the dossier submitter, then this will be indicated in the study summaries below.

** All studies were summarized from publications retrieved from open literature.

VTG = vitellogenin, SSC= second sex characteristics, GSI= Gonado-somatic index

Balch and Metcalfe (2006)

A study (Balch and Metcalfe, 2006) was conducted to evaluate the effects of NP, NPE-1, NPE-4 and NPE-9 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 static conditions. The test water in individual exposure tanks was renewed every 48 h. Renewal was 100%, with the exception of the first two weeks when 15–20% of the test water was left so that the young fish did not need to be physically handled. Gentle aeration was applied to the tank water so that dissolved oxygen was at or near saturation. Survival and growth were monitored in each treatment after the first and second month of exposure by taking a digital image of the exposure tank and counting the number of fish. After counting, 20 fish were removed, euthanized and total body length and weight was measured to assess growth. Treatments that experienced greater than 20% mortality in the first month of exposure, or exceeded a total cumulative mortality of 30% prior to the termination of exposure were eliminated and not included in the analysis. NP of 1, 3, 10, 30 and 100 µg/L, NPE-1 of 10, 30, 100, and 300 µg/L, NPE-4 of 10, 30, 100, 300, and 1000 µg/L and NPE-9 of 30, 100, 300, and 1000 µg/L were tested. Each treatment was started with 150 fry to ensure at least 50 fish survived to the end of the 100-day exposure period. In addition, 40 fish from each treatment were removed and euthanized for growth measurements. None of the treatments were replicated. Fifty randomly chosen fish from each treatment were sacrificed at the end of the 100-day exposure period. Endpoints reported were secondary sex characteristics, total body

length and weight, and development of gonadal intersex (i.e. testis-ova). Gonadal tissues were examined to verify the gonadal sex of the fish and to monitor for evidence of gonadal intersex. The secondary sex characteristics were assessed according to the shape of the urogenital papilla, dorsal and anal fins and the presence or absence of papillary processes on the anal fin.

Concentrations of all test compounds declined over the period between test solution renewal. The average measured exposure concentrations determined to be 0.29, 0.87, 2.9, 8.7 and 29 µg/L for NP of 1, 3, 10, 30 and 100 µg/L; 3.5, 10.5, 35, 105 µg/L for NPE-1 of 10, 30, 100 and 300 µg/L; 3.8, 11.4, 38, 114, and 380 µg/L for NPE-4 of 10, 30, 100, 300, and 1000 µg/L; 16.2, 54, 162, and 540 µg/L for NPE-9 of 30, 100, 300, and 1000 µg/L.

Fish survival during the 100-day exposure period was greater than 70% in all treatments, except those tested at 380 µg/L of NPE-4. Survival was only 20% in the 380 µg/L of NPE-4. The NOEC values for survival are 29 µg/L for NP, 105 µg/L for NPE-1; 114 µg/L for NPE-4; 540 µg/L for NPE-9.

Exposure of medaka to all test compounds did not change sex ratios at all tested concentrations. Gonadal intersex was characterized by the presence of pre-vitellogenic oocytes within the testes of male medaka (i.e., ‘‘testis–ova’’). This condition was only observed in treatments with nonylphenol and not with any other test chemicals. A total of 18 of the 22 phenotypic male fish exposed to a concentration of 29 µg/L nonylphenol exhibited gonadal intersex. Only one of the 22 phenotypic male fish exposed to the next lower nominal concentration (8.7 µg/L) exhibited gonadal intersex. The number of pre-vitellogenic oocytes within a section of intersex gonadal tissue varied from a low of one to >20. The majority of tissues had at least five oocytes in individual sections prepared from the testis. There were significantly elevated incidences of medaka with mixed secondary sex characteristics in the two highest treatments with nonylphenol (8.7 and 29 µg/L) and in the highest treatment with NPE1 (105 µg/L) in comparison to the incidence in the acetone control treatment. A low percentage (i.e., 4%) of the fish in the clean control also exhibited mixed secondary sex characteristics. However, this likely reflects a small number of errors in assessing male and female traits. Papillary processes are normally found on the anal fin of male medaka but were not observed on the anal fins of all male medaka from the NP 29 µg/L treatment. Only 1 out of 29 males in the NPE-1 (105 µg/L) treatment had papillae on the anal fin. Papillary processes were present on the anal fins of males from all other treatments.
The NOEC values for SSC are 2.9 µg/L for NP, 35 µg/L for NPE-1; 380 µg/L for NPE-4 and 540 µg/L for NPE-9. For this dossier, the focus is only on data for NPE 3-15. This test is considered as a valid study, with reliability 2.

Dorn et al. (1993)
Dorn *et al.* (1993) conducted a fathead minnow test in 7d static renewal exposures, with daily solution replacement using six concentrations of surfactant NPE-9 and a control. Twenty randomly selected fathead minnows were used at each concentration (2 replicates). Mortality was recorded and body weight was measured. Water samples for analysis in static renewal acute tests were collected initially and at 24-h intervals until test end. The concentration of NPE-9 was measured by using cobalt thiocyanate active substance analyses. Samples of the prepared dilutions were selected from the low, medium, and high exposures for surfactant analysis. Results of all samples for each exposure concentration (time 0, 24, 48, etc.) were averaged to calculate the “measured” concentration. The 7d-LC_{50} was 2.9 mg/L; the NOEC for mortality ranged from 1 to 8 mg/L; and the NOECs for growth as measured changes in body weight ranged from 0.4 to 1 mg/L (Dorn *et al* 1993). This test is not considered as a valid study, with reliability 4 because essential information such as the life stage of fish was not reported.

Miles-Richardson et al. (1999)
Male and female sexually mature fathead minnows (*Pimephales promelas*) were exposed to nonylphenol ethoxylate (Solfonic N-95; NPE-9.5) in a flow-through system for 42 days. The technical mixture of NPEs used in this study consisted primarily of 7- to 11-carbon ethoxylate chains. Approximately 0.58% of the total

by weight consisted of NP and NPE-1 and NPE-2. NPE-9 contributed more than any other constituent of the technical mixture (10.73%). Nominal concentrations of the NPE-9.5 experiment were 0.3, 1.0, 3.0, and 10 µg/L. There were two controls, one with water only and one containing 0.00001% ethanol. The concentration of solvent was the same delivered with each test concentration. Concentrations of NP or NPE-9.5 were less than 0.01 µg/L in both the control and the solvent control. The measured concentrations of NP were 0.05, 0.16, 0.4, 1.6, and 3.4 µg/L. The measured concentrations of NPE-9.5 were 0.15, 0.43, 1.45, and 5.5 µg/L. There was no significant difference in the size, expressed as the mean, median, or range of the secondary sex characteristics or gonads among males exposed to any concentrations of NPE-9.5. No effect on the relative proportions of eggs in any of the stages of follicles were observed among any of the treatments or controls for NPE-9.5. The test concentrations were too low to induce any toxic effects. Therefore, the NOEC is ≥ 5.5 µg/L. This study is therefore considered Ri = 3 since tested concentrations were too low.

Nichols et al. (2001)

Groups of three adult male and three female fathead minnows (*Pimephales promelas*) were exposed to NPE-9.5 in a proportional flow-through system to nominal concentrations of 0, 0.3, 1, 3, and 10 µg/L for 42d (Nichols *et al.*, 2001). On the last day of exposure, fish were euthanized. Blood and tissue samples were collected. Sex determinations were made visually by gross morphology and were later confirmed by histology. Standard length and weight measurements were recorded along with observations of obvious health and morphological abnormalities. The measured concentrations were 0, 0.21, 0.65, 2.1, and 7.9 µg/L. The concentrations of NPE-9.5 tested were not overtly toxic to fathead minnows. Survival of adult fathead minnows in each concentration ranged from 67% for 2.3 µg/L to 72% for 7.9 µg/L, and to 89% for 0.0, 0.21, and 0.65 µg/L. There was no concentration-dependent relationship between survival and NPE-9.5 concentration. Fecundity (eggs/female) did not exhibit a statistically significant concentration-dependent relationship to NPE-9.5 exposure. No significant differences were observed in plasma VTG concentrations among treatments for males or females (Nichols *et al.*, 2001). The test concentrations were too low to induce any toxic effects. The NOEC is ≥ 7.9 µg/L. This study is considered Ri = 3 since tested concentrations were too low..

11.6.2 Chronic toxicity to aquatic invertebrates

Table 24: Summary of Crustacean chronic toxicity tests

Method	Substance tested	Results NOEC (mg/L)	Remarks	KS*	Reference**
EPA guideline, 7d exposure *Daphnia magna*	NPE-9	10 (mortality) >10 (growth)	Semi-static; measured concentrations	2	Dorn *et al.* (1993)
ISO/CD 20665, 7d exposure *Cerodaphnia dubia*	NPE-10	0.2, 7d-EC50, NOEC was not reported	Semi-static; nominal concentrations	3	Isidori *et al.* (2006)
Moina macrocopa, 5 d exposure	NPE-10	0.0421 (survival) <0.021 (growth and reproduction)	Semi-static; nominal concentrations	3	Hu *et al.* (2014)

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the evaluator does not agree with the reliability assignment made by the dossier submitter, then this will be indicated in the study summaries below.
** Summarized from publications retrieved from open literature.

Dorn et al. (1993)
Chronic toxicity testing was performed on the water flea *D. magna* following EPA guidelines for estimating the chronic toxicity to aquatic organisms. Daphnids were run in daily static replacement conditions for 7 d using six exposure concentrations of surfactant NPE-9 and a control. Samples of the prepared dilutions were selected from the low, medium, and high exposures for surfactant analysis. Results of all samples for each exposure concentration (time 0, 24, 48, etc.) were averaged to calculate the "measured" concentration. Cobalt thiocyanate active substance analyses showed that nominal concentrations of NPE-9 reflected actual concentrations. The 7d-LC_{50} for *Daphnia magna* was determined to be 9 mg/L. The NOECs for mortality and for growth were 10 and >10 mg/L. The reliability of this study is considered as 2.

Isidori et al. (2006)
The chronic test on *Ceriodaphnia dubia* exposed to NPE-10 was run over a period of 7 days according to the standard ISO/CD 20665 procedure and performed on young organisms, less than 24 h old at the start of exposure. In the control and in all test concentrations, the ethanol percentage was kept constant at 0.001% (v/v), that is a non-effect dose as estimated in preliminary tests. One organism, in ten replicates, was exposed to seven concentrations (two-fold dilutions) in beakers with 20 ml of an appropriate concentration of single compound in the ISO hard medium, incubated at 25^0C with a 16:8 h light: dark cycle (500 lux). Daphnids were fed at each daily renewal of the test medium with a suspension of the alga *P. subcapitata* (4 x10^8 cells/ml), food fish (5 g/l) and yeast (5 g/l). Organisms were monitored for survival, and released neonates were counted every day prior to renewals and then discharged. By comparing the number of offspring at the end of the test in the sample batch and the control, it was possible to calculate the concentration which gave rise to a 50% population growth inhibition, indicated as EC50. Under these conditions, the EC50 was 0.2 mg/L. This study is not considered valid because the chemical concentration was not measured and essential information was not reported. Ri=3.

Hu et al. (2014)
The cladoceran *Moina macrocopa* was exposed to the sublethal concentrations of NPE-10: 337, 168, 84.2, 42.1, and 21.1 µg/L. Blank control and solvents control (0.5 % acetone) were included. Each dosage group was laid ten parallels, and ten neonates (<12 h old) were respectively placed in ten 50 mL glass beakers which contained 25 mL exposure solution. During the experiment, the exposure solutions were transferred daily for maintaining the water quality. The experiment was conducted at 20 ± 1^0C on a 16 h light:8 h dark cycle and terminated after all of F0 organisms died. During this process, the survivorship, ultimate body length, breeding frequency, neonates number of every reproduction, and the total neonates number of *M. macrocopa* were recorded. Concentrations of these stock solutions were determined by HPLC equipped with UV–Vis detector. The analysis showed that the determined concentrations of NPE-10 stock solutions varied generally more or less than 5 % from the nominal concentrations. Therefore, all calculations were based on nominal concentrations. Under the experimental conditions, there is no significant difference in survival between the blank control and acetone control. After 5 days, the concentration dependent decrease in survival was observed in *M. macrocopa* exposed to NPE-10. The NOEC for survival is 42.1 µg/L. After all F0 organisms died, the ultimate body length of *M. macrocopa* showed a concentration-dependent decrease at all tested concentrations The NOEC for growth was < 21.1 µg/L. The number of neonates produced through reproduction of *M. macrocopa* was reduced after exposure to NPE-10 in a concentration dependent manner. The NOEC for growth was < 21.1 µg/L. This study is not considered valid because the chemical concentration in the test media was not measured and essential information was not reported. Ri = 3.

11.6.3 Chronic toxicity to algae or other aquatic plants

Table 25: Summary of algae chronic toxicity tests

Method	Substance tested	Results (mg/L)	Remarks	KS*	Reference**
OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-3	72h-E_bC50 = 2.9 72h-E_bC50 = 2.9 72h-E_rC10 = 1.4 72h-NOE_bC = 1	Static, nominal concentration	2	Anonymous (1994a)[2]
OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-6	72h-E_rC50 = 13 72h-E_bC50 = 3.7 72h-E_rC10 = 6.1 72h-NOE_bC = 3	Static, nominal concentration	2	Anonymous (1994b)[2]
No test guideline provided 3 wk exposure *Selenastrum capricornutum*	NPE-6 NPE-9	E_rC_{50} >500 E_rC_{50} >500	Static; nominal concentrations	3	Nyberg (1988)[1]
US EPA guideline 96 h exposure *Selenastrum capricornutum*	NPE-9	EC_{50} = 12 NOEC = 8	Static; nominal concentrations	4	Dorn *et al.* (1993)[1]
OECD TG 201 *Scenedesmus subpicatus* (Chodat)	NPE-9.3	72h-E_rC50 = >30 72h-E_bC50 = 30 72h-E_rC10 = 14.5 72h-NOE_bC = 4	Static, nominal concentration	3	Anonymous (1994c)[2]

* Klimisch scores indicated in the REACH registration dossiers or evaluated by the dossier submitter for the publications retrieved from the open literature. If the dossier submitter does not agree with the reliability assignment made in the REACH dossier, then this will be indicated in the study summaries below.
[1]Summarized from publication retrieved from open literature.
[2]Summarized from confidential study from company.

Nyberg (1988)
In a study by Nyberg (1988), the alga *Pseudokirchneriella subcapitata* was cultured in 50 ml Erlenmeyer flasks using 25 ml liquid synthetic medium in each flask. The flasks were inoculated with 0.1 ml of an algal suspension. The inoculate contained ca 1.5 x 105 cells. The surfactants were added to the cooled autoclaved medium as stock solutions using sterile MiUipore filters to avoid any possible decomposition during sterilization. The algae were cultured at 25°C for 3 wk with gentle shaking (ll0 rpm) under Airam 40W-35 white fluorescent tubes. After the growth period, at the approximate onset of the stationary phase, the cell counts in each flask were measured with a Fuchs-Rosenthal counting chamber. The EC50 values for growth were >500 mg/L for all surfactants of NPE-6, 9 and 30. For this dossier, the focus is only on data for NPE 3-15.

Dorn et al. (1993)
The toxicity of NPE-9 to the green algae (Selenastrum capricornutum (Printz) was determined according to the principles of US EPA guideline (Dorn *et al.*, 1993). The study was conducted under static conditions with an initial cell density of 1 x 10^4 cells/mL. The exposure is 96 h. Three replicates were tested for each tested concentrations. Chemical sampling and analysis for the algae toxicity test was not stated in the report. The following values were stated in the paper: 96h-EC50=12 mg/L; NOEC = 8 mg/L. Since some essential information was not reported, this study is considered as a supporting study with reliability of 4.

Three studies of Anonymous (1994abc) are evaluated in section 11.5.3. The chronic endpoints are given in Table 25.

11.6.4 Chronic toxicity to other aquatic organisms

No data available for medium-chain NPEs.

11.7 Comparison with the CLP criteria

Valid (Ri=2) acute and chronic aquatic toxicity data are available and these are used to derive the classification for NPEs covered in this dossier.

11.7.1 Acute aquatic hazard

Valid acute aquatic toxicity data are available for all three trophic levels for NPEs. Valid fish acute toxicity data are available for NPE-4, NPE-5, NPE-9, and NPE-9.5, with the LC_{50} values ranging from 1.3 to 7.9 mg/L. A valid *Daphnia* study with 48h-EC50 of 14 mg/L is available for NPE-9. Valid studies are available for aquatic plant studies for NPE-3 and NPE-6, EC_{50} values of 2.9 and 13 mg/L, respectively. An overview of these acute toxicity data is in

Table 26.

Using Table 4.1.0 (a) of the CLP guidance, the group NPE-n (n = ≤ 3 to < 11) is not classified as acute hazard to the aquatic environment given that all valid acute toxicity values are higher than 1 mg/L.

Table 26: Summary of acute toxicity tests

Species	Valid Studies	
	96h LC50 mg/L	
Fish	NPE-4 NPE-5 NPE-9 NPE-9 NPE-9.5	1.3 2.4 4.6 7.9 7.6
	48h EC50 mg/L	
Daphnia	NPE-9	14
	E_rC50 mg/L	
Algae	NPE-3 NPE-6	2.9 13

11.7.2 Long-term aquatic hazard (including bioaccumulation potential and degradation)

For purposes of classification nonylphenol, branched and linear, (n)-ethoxylated, (n = ≤ 3 to < 11) are considered as not rapidly degradable. A definite conclusion on the bioaccumulation potiential of NPEs as a group is not considered possible, since the log Kow values fall above and below the CLP trigger of 4 (see section 10.4.1).

Valid chronic aquatic toxicity data are available for all three trophic levels for NPEs. For valid chronic fish toxicity tests, data on NPE-4 and NPE-9 are available, with NOEC values of 0.114 and 0.54 mg/L. For crustacean, valid data for NPE-9 is available with a NOEC value of 10 mg/L. For algae, valid studies are available for NPE-3 and NPE-6, with NOEC values of 1.4 and 6.1, respectively.

Table 27: Summary of chronic toxicity tests

Species	Valid Studies NOEC mg/L	
Fish	NPE-4 NPE-9	0.114 0.54
Daphnia	NPE-9	10
Algae	NPE-3 NPE-6	1.4 6.1

On the basis of the available valid data, fish is the most sensitive species with NOEC values of in the range 0.1 – 1 mg/L. According to Table 4.1.0 (b)(i) of the CLP guidance, the group nonylphenol, branched and linear, (n)-ethoxylated, (n = ≤ 3 to < 11) fulfils the criteria for classification as Category Chronic 2.

11.8 CONCLUSION ON CLASSIFICATION AND LABELLING FOR ENVIRONMENTAL HAZARDS

Aquatic Chronic 2, H411 (Toxic to aquatic life with long lasting effects) .

12 EVALUATION OF ADDITIONAL HAZARDS

12.1 Hazardous to the ozone layer

Not evaluated in this dossier.

13 ADDITIONAL LABELLING

No additional information available.

14 REFERENCES

A full reference list for selected studies are included in the confidential annex.

Anonymous	1994a	Bestimmung der biologischen Abbaubarkeit von MARLOPHEN 86 N/6 im DOC-DIE AWAY Test. Ablschlussbericht DDA-65
Anonymous	1994b	Bestimmung der biologischen Abbaubarkeit von MARLOPHEN 1028 N im DOC-DIE AWAY Test. Ablschlussbericht DDA-66
Anonymous	1994a	Bestimmung der Auswirkungen von MARLOPHEN 83 N auf das Wachstum von *Scenedesmus subspicatus* 86.81. SAG
Anonymous	1994b	Bestimmung der Auswirkungen von MARLOPHEH 86 N/6 auf das Wachstum von *Scenedesmus subspicatus* 86.81. SAG
Anonymous	1994c	Bestimmunq der Auswirkunqen von MARLOPHEN 1028 N auf das wachstum von *Scenedesmus subspicatus* 86.81. SAG
Anonymous	1999	Nonylphenol and octylphenol and their ethoxylates – determination of the biodegradability by the CO2 evolution modified sturm test.
Anonymous	2007	Toxicity of Nonylphenol, Nonylphenol Monoethoxylate, and Nonylphenol Diethoxylate and Mixtures of these Compounds to *Pimephales promelas* (Fathead Minnow) and *Ceriodaphnia dubia*. Arch Environ Contam Toxicol 53: 599–606.
Ahel M, Giger W	1993	Partitioning of alkylphenols and alkylphenol polyethoxylates between water and organic solvents. Chemosphere 26: 1471-1478
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15 ANNEXES

Information on the constituents of substance is given separately as a confidential Annex.