# Nonylphenol and octylphenol ethoxylates and related compounds: Human health tier II assessment

08 March 2019

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# Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Ethanesulfonic acid, 2-[2-[2-[4-(1,1,3,3- tetramethylbutyl)phenoxy]ethoxy]ethoxy]-, sodium salt	2917-94-4
Ethanesulfonic acid, 2-[2-[4-(1,1,3,3- tetramethylbutyl)phenoxy]ethoxy]-, sodium salt	3013-94-3
Ethanol, 2-[2-[2-[2-(4- nonylphenoxy)ethoxy]ethoxy]-	7311-27-5
Poly(oxy-1,2-ethanediyl), .alpha[4-(1,1,3,3- tetramethylbutyl)phenyl]omegahydroxy-	9002-93-1
Poly(oxy-1,2-ethanediyl), .alpha (isooctylphenyl)omegahydroxy-	9004-87-9
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (nonylphenoxy)-, sodium salt	9014-90-8
Poly(oxy-1,2-ethanediyl), .alpha (dinonylphenyl)omegahydroxy-	9014-93-1
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-	9016-45-9
Poly(oxy-1,2-ethanediyl), .alpha[(1,1,3,3- tetramethylbutyl)phenyl]omegahydroxy-	9036-19-5
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (nonylphenoxy)-, ammonium salt	9051-57-4
Poly(oxy-1,2-ethanediyl), .alpha(octylphenyl)omega hydroxy-	9063-89-2



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Chemical Name in the Inventory	CAS Number
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (nonylphenoxy)-	9081-17-8
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, compound with iodine	11096-42-7
Poly(oxy-1,2-ethanediyl), .alphasulfoomega(4- nonylphenoxy)-, ammonium salt	31691-97-1
Poly(oxy-1,2-ethanediyl), .alpha(4- nonylphenyl)omegahydroxy-	26027-38-3
3,6,9,12,15,18,21,24-Octaoxahexacosan-1-ol, 26- (nonylphenoxy)-	26571-11-9
3,6,9,12-Tetraoxatetradecan-1-ol, 14-(octylphenoxy)-	27176-99-4
3,6,9,12,15-Pentaoxaheptadecan-1-ol, 17- (nonylphenoxy)-	27177-01-1
3,6,9,12,15,18,21-Heptaoxatricosan-1-ol, 23- (nonylphenoxy)-	27177-05-5
3,6,9,12,15,18,21,24,27-Nonaoxanonacosan-1-ol, 29- (nonylphenoxy)-	27177-08-8
Ethanol, 2-(nonylphenoxy)-	27986-36-3
Poly(oxy-1,2-ethanediyl), .alpha (carboxymethyl)omega(4-nonylphenoxy)-	28212-44-4
Poly(oxy-1,2-ethanediyl), .alpha (isononylphenyl)omegahydroxy-	37205-87-1
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, phosphate, sodium salt	37340-60-6
Polyethoxylated isooctyl phenol (5.6:1)	39342-50-2
Poly(oxy-1,2-ethanediyl), .alpha (dinonylphenyl)omegahydroxy-, phosphate	39464-64-7
Poly(oxy-1,2-ethanediyl), .alpha(1-oxo-2-propen-1- yl)omega(4-nonylphenoxy)-, branched	678991-31-6
Poly(oxy-1,2-ethanediyl), .alpha(4- nonylphenyl)omegahydroxy-, phosphate	51609-41-7
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, phosphate	51811-79-1
Poly(oxy-1,2-ethanediyl), .alpha(2- nonylphenyl)omegahydroxy-	51938-25-1
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, phosphate, potassium salt	52503-15-8

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Chemical Name in the Inventory	CAS Number
Poly(oxy-1,2-ethanediyl), .alpha[(1,1,3,3- tetramethylbutyl)phenyl]omegahydroxy-, phosphate	52623-95-7
Poly(oxy-1,2-ethanediyl), .alpha (carboxymethyl)omega(nonylphenoxy)-	53610-02-9
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (octylphenoxy)-, sodium salt	53879-49-5
Poly(oxy-1,2-ethanediyl), .alphaacetylomega (nonylphenoxy)-	54612-40-7
Poly(oxy-1,2-ethanediyl), .alphasulfoomega[(1,1,3,3- tetramethylbutyl)phenoxy]-, sodium salt	55348-40-8
Poly(oxy-1,2-ethanediyl), .alphasulfoomega(4- octylphenoxy)-, sodium salt	58853-83-1
Poly(oxy-1,2-ethanediyl), .alpha (phenylmethyl)omega[(1,1,3,3- tetramethylbutyl)phenoxy]-	60864-33-7
Poly(oxy-1,2-ethanediyl), .alpha (carboxymethyl)omega(diisononylphenoxy)-, sodium salt	68958-57-6
Ethanol, 2-[2-[2- (nonylphenoxy)ethoxy]ethoxy]ethoxy]-, hydrogen sulfate, ammonium salt	63351-73-5
Nonyl phenol ethoxylate blend	63496-57-1
3,6,9,12,15,18-Hexaoxaeicosan-1-ol, 20- (dinonylphenoxy)-, dihydrogen phosphate	66172-78-9
3,6,9,12,15,18-Hexaoxaeicosan-1-ol, 20- (dinonylphenoxy)-, hydrogen phosphate	66172-83-6
Poly(oxy-1,2-ethanediyl), .alpha(1,1- dimethylethyl)omega(octylphenoxy)-, branched	69279-01-2
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (isooctylphenoxy)-, sodium salt	67759-39-1
Ethanesulfonic acid, 2-[2-[2- (octylphenoxy)ethoxy]ethoxy]-,sodium salt	67923-87-9
Poly(oxy-1,2-ethanediyl), .alpha (carboxymethyl)omega(4-isooctylphenoxy)-, sodium salt	68015-73-6
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, branched, phosphates	68412-53-3
Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omega hydroxy-, branched	68412-54-4
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Chemical Name in the Inventory	CAS Number
Poly(oxy-1,2-ethanediyl), alpha -(nonylphenyl)-omega - hydroxy-, phosphate, ammonium salt	68511-21-7
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (nonylphenoxy)-, branched, ammonium salt	68649-55-8
Poly(oxy-1,2-ethanediyl), .alpha (dinonylphenyl)omegahydroxy-, branched	68891-21-4
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (nonylphenoxy)-, branched, sodium salt	68891-39-4
Poly(oxy-1,2-ethanediyl), a-(nonylphenyl)-w-hydroxy-, branched, phosphates, sodium salts	68954-84-7
Poly(oxy-1,2-ethanediyl), .alpha (carboxymethyl)omegahydroxy-, C8-18 and C18- unsaturated alkyl and (octyl or nonyl)phenyl ethers, sodium salts	68987-89-3
Poly(oxy-1,2-ethanediyl), .alpha(octylphenyl)omega hydroxy-, branched	68987-90-6
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (octylphenoxy)-, branched, sodium salt	69011-84-3
Poly(oxy-1,2-ethanediyl), .alphasulfoomega (isononylphenoxy)-, sodium salt	72580-36-0
Poly(oxy-1,2-ethanediyl), .alpha(4- nonylphenyl)omegahydroxy-branched	127087-87-0
Poly(oxy-1,2-ethanediyl), .alpha (isooctylphenyl)omegahydroxy-, phosphate	127184-51-4
Poly(oxy-1,2-ethanediyl), alpha-(3-carboxy-1-oxo-2- propenyl)omega(4-nonylphenoxy)-, (Z)-, branched	144468-71-3

# Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multitiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach

using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:www.nicnas.gov.au

#### Disclaimer

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

ACRONYMS & ABBREVIATIONS

# **Grouping Rationale**

The chemicals in this group are:

- non-ionic ethoxy ether derivatives of nonylphenol (nonylphenol ethoxylates—NPEs) or octylphenol (octylphenol ethoxylates—OPEs); and
- anionic derivatives (sulfate, phosphate, carboxylate) of NPEs or OPEs.

Whilst the surfactant properties of the chemicals in this group may vary, the systemic toxicity of the chemicals are expected to be due to the break down into NPs and OPs. The NPEs (also referred to as nonoxynols) and OPEs (octoxynols) are manufactured by the reaction of nonylphenols (NPs) or octylphenols (OPs) with ethylene oxide (EO). The NPEs belong to a general chemical category of alkylphenol ethoxylates (APE). The general formula

of NPEs is C15H24(C2H4O)n; where 'n' is the number of EO units attached to the phenol ring, and can vary from 1–120. The NPEs differ by the length of the EO chain, which also contributes to different physicochemical properties and the degree of toxicity. The NPEs are considered less toxic than NPs (Health Canada, 1999; US EPA, 2010; CIR, 2015).

The NPEs are primarily used as surfactants in a wide range of cosmetic and domestic products (~80–85 % of the production volume of APE surfactants, with the other 20 % being octylphenol ethoxylates) (CalEPA, 2010; US EPA, 2010). Among these NPEs, poly(oxy-1,2-ethanediyl), .alpha.- (nonylphenyl)-.omega.-hydroxy- (CAS No. 9016-45-9) and poly(oxy-1,2-ethanediyl), .alpha.- (nonylphenyl)-.omega.-hydroxy- (CAS No. 26027-38-3) are the main two commercial NPEs (CIR, 2015).

The OPEs are chemically very similar to the NPEs, differing by their alkyl chain length of eight carbons instead of nine. They have similar uses to NPEs and are anticipated to have similar toxicological properties, although their solubility is greater than NPEs (Env Canada, 2002). Therefore, they are included in this assessment with NPEs. The OPEs are more commonly known under the generic CAS Nos. 9036-19-5, 9002-93-1 and 9004-87-9, or as the trade name Triton X-100.

There is a lack of information on dinonylphenol ethoxylates. In the absence of information to indicate lower toxicity for this group, they will be assumed to be represented by data on nonylphenol ethoxylates. It is also probable that dinonylphenol ethoxylates are not pure substances and; therefore, contain significant levels of nonylphenol ethoxylates. Dinonylphenol ethoxylates have; therefore, been included in this assessment.

Regardless of the precise chemical identities of the chemicals in this group, environmental degradation to nonyl- or octylphenols, thereby increasing the pool of these chemicals available for secondary exposure, is the main health effect which applies to all the chemicals in the group.

## Import, Manufacture and Use

## Australian

The chemical poly(oxy-1,2-ethanediyl), .alpha.-(nonylphenyl)-.omega.-hydroxy- (CAS No. 9016-45-9) is listed on the 2006 High Volume Industrial Chemicals List (HVICL) with a total reported volume of 1000–9999 tonnes.

The following Australian industrial uses were reported under previous mandatory and/or voluntary calls for information.

- domestic uses in cleaning/washing agents and additives; and
- site-limited use as surface-active agents in manufacturing other chemicals.

The chemical, poly(oxy-1,2-ethanediyl), .alpha.-sulfo-.omega.-(nonylphenoxy)-, sodium salt (CAS No. 9014-90-8) has reported uses in industrial adhesives and tapes

The chemical, poly(oxy-1,2-ethanediyl), .alpha.-(nonylphenyl)-.omega.-hydroxy- (CAS No. 26027-38-3) is reported under previous mandatory and/or voluntary calls for information with a total volume of <1 tonne per annum.

This chemical (CAS No. 26027-38-3) has reported commercial and site-limited uses, including in:

- foam suppressants and de-airing agents
- fluorescent whitening agents; and
- paper dyes, used by textile dyehouses and manufacturers.

The chemical poly(oxy-1,2-ethanediyl), .alpha.-[(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (CAS No. 9036-19-5) is reported under previous mandatory and/or voluntary calls for information with a total volume of <1000 tonnes per annum.

This chemical (CAS No. 9036-19-5) has reported domestic and/or commercial uses, including in:

- cleaners;
- paints;
- sealants and adhesives;
- resins and textile coatings;
- printing pastes; and
- mould release agents.

This chemical (CAS No. 9036-19-5) has reported non-industrial uses:

- in agricultural products;
- in contraceptive jelly; and
- as a biocide in water treatment.

The chemicals with CAS No. 68412-53-3 and CAS No 9014-90-8 have reported use as commercial use in industrial adhesivea and tapes.

No specific Australian use, import, or manufacturing information has been identified for the other chemicals in this report.

Nonylphenol and octylphenol ethoxylates have reported non-industrial uses as active constituents or excipients in agricultural and veterinary chemical products (APVMA, 2017)

Nonoxynol-9 and octoxynol-10 have reported non-industrial uses for medical purposes as spermicidal agents and in flu vaccines (TGA, 2017).

## International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the European Commission Cosmetic Ingredients and Substances (CosIng) database; the Substances and Preparations in Nordic countries (SPIN) database; the United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary; the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); and international assessments (the European Commission, 2002; OSPAR, 2006).

The NPEs (CAS Nos. 9016-45-9, 26027-38-3 and 9014-93-1) and OPE (CAS No. 9002-93-1) have reported cosmetic use as surfactants or emulsifying agents in hair products (dyes and colours, bleaches and tints, hair care products), personal cleanliness products, tonics, dressings, bath preparations, and eyeliners. The majority of uses were in rinse off products. The greatest frequency of use was reported for NPEs containing 4 and 6 EO units with reported usage decreasing from 1999 to 2015 (CIR, 2015). CAS Nos. 31691-97-1 and 39464-64-7 have reported cosmetic uses as surfactants or emulsifying agents (CosIng). The NPES and OPES (CAS Nos. 37205-87-1, 9004-87-9, 68412-54-4, 68987-90-6, 9002-93-1, 127087-87-0, 9016-45-9, 9036-19-5) are on the IFRA transparency list for use in fragrances (IFRA, 2017). The OPEs used in cosmetics are reported to contain 1–70 EO units, and at concentrations 0.0008-25 % with the majority at  $\leq 5$  % (CIR, 2004).

The chemicals in this group have reported domestic, commercial and site-limited uses as surfactants in a wide variety of products (detergents, cleaners, degreasers, dry cleaning aids, emulsifiers, wetting agents, dispersants, stabilisers, adhesives, cosmetics, paints/coatings, metal processing, and oilfield chemicals).

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The US Environmental Protection Agency (EPA) has announced the phase out of NPEs in industrial laundry detergents by 2014 (US EPA, 2010).

The chemicals have reported domestic uses, including in:

- paints, lacquers and varnishes; and
- cleaning/washing agents (in toilet waters, floor and carpet cleaners).

The chemicals have reported commercial uses, including:

- as process regulators;
- in construction materials;
- in welding and soldering agents;
- in lubricants and additives;
- as textile and leather auxiliaries (e.g. hot melts, textile printing, leather finishing);
- in wood processing; and
- for hydraulic fracturing.

The chemicals have reported site-limited uses, including:

- as flotation agents for minerals or mining products including phosphate ores; and
- as emulsifiers for emulsion polymerisation by companies producing polymers (e.g. styrene-butadiene).

The chemicals have reported non-industrial uses including in:

- agricultural sprays; and
- pharmaceutical preparations (pharmaceutical aids), NPE-9 and OPE-9 are used as spermicides.

Sulfonated and phosphorylated NPEs are used commercially as anionic detergents, lubricants and antistatic agents (Env Canada, 2002).

## Restrictions

## Australian

No known restrictions have been identified specifically for these chemicals. However

Nonoxynol-9 (NPE with 9 EO units) (CAS No. 26571-11-9) is listed in the *Poisons Standard—the Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) as' NONOXINOL 9' in Schedules 5 and 6 (SUSMP, 2017).

Schedule 6:

'NONOXINOL 9 except:

(a) when included in Schedule 5;

(b) in preparations containing 25 per cent or less of nonoxinol 9 when labelled with the statements:

IRRITANT; and

Avoid contact with eyes;

(c) in preparations containing 12.5 per cent or less of nonoxinol 9; or

(d) in preparations for human use.'

Schedule 5:

'NONOXINOL 9 in preparations containing 25 per cent or less of nonoxinol 9 except:

(a) when labelled with the statements:

#### IRRITANT; and

Avoid contact with eyes;

(b) in preparations containing 12.5 per cent or less of nonoxinol 9; or

(c) in preparations for human use.'

Schedule 6 chemicals are described as 'Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label'. Schedule 6 chemicals are labelled with 'Poison' (SUSMP, 2017).

Schedule 5 chemicals are described as 'Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.' Schedule 5 chemicals are labelled with 'Caution' (SUSMP, 2017).

The chemicals of this group are synthesised through processes which may result in 1,4-dioxane as an impurity. This impurity (listed under dioxane) is controlled through listing in the Poisons Standard (SUSMP) in Schedule 6, with schedule labelling requirements applying above 100 ppm (Appendix G).

## International

The NPEs are restricted by Annex XVII to the REACH Regulations—nonylphenol ethoxylates cannot be used in substances and preparations placed on the market for sale to the general public in individual concentrations  $\geq 0.1$  % for uses such as cleaning, textile and leather processing, cosmetic and personal care products (ECHA, 2014). An update to Annex XVII for textile articles stated that 'nonylphenol ethoxylates cannot be placed on the market after 3 February 2021 in textile articles which can be reasonably expected to be washed in water during their normal lifecycles, in concentrations  $\geq 0.01$  % by weight of that textile article or of each part of the textile article' (ECHA, 2016).

The US Environmental Protection Agency (EPA) is proposing a significant new use rule (SNUR) for 15 nonylphenols and nonylphenol ethoxylates. The NPEs with the CAS Nos. 7311-27-5, 9016-45-9, 26027-38-3, 37205-87-1 and 51938-25-1 are in the list. 'Persons subject to these SNURs would be required to notify EPA at least 90 days before they manufacture (including import) or process any of these 15 chemical substances for a significant new use. The required notification would provide EPA with the opportunity to evaluate the new uses and protect against unreasonable risks, if any, from potential new exposures to NPs and NPEs, before that activity occurs' (US EPA, 2014).

Recently, the US EPA proposed the addition of nonylphenol ethoxylates to the list of toxic chemicals subject to reporting under section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA) and section 6607 of the Pollution Prevention Act (PPA). In the proposed category of nonylphenol ethoxylates, 11 substances in this group are included. Under the proposed rule, those who manufacture, process, or use these chemicals in amounts above reporting threshold levels are required to report their environmental releases and other waste management quantities annually. Pollution prevention and recycling data for these chemicals are also required (United States Government, 2016).

The NPEs are listed on Schedule 1 of the Canadian Environmental Protection Act 1999 (the Toxic Substances List) (Government of Canada, 2013). The use of NPEs has been phased down in Canada since 2004, with most users of nonylphenols required to prepare and implement pollution prevention plans. The majority have met risk management objectives by eliminating the use of these chemicals (Environment Canada, 2014).

The OPEs under the entry of 4-(1,1,3,3-tetramethylbutyl) phenol, ethoxylated (covering well-defined substances and UVCB substances) and NPEs under the entry '4-Nonylphenol, branched and linear, ethoxylated' were included on the candidate list of substances of very high concern (SVHC) for eventual inclusion in Annex XIV (ECHA, 2012). The chemicals have subsequently been listed on Annex XIV to the REACH legislation (the Authorisation List) with the latest application date of 04/07/2019. The reason for inclusion is due to degradation to 4-tert-octylphenol and 4-nonylphenol in the environment.

Several nonylphenol ethoxylates are subject to export notification procedures and prior informed consent notification for imports under Regulation No 649/2012 of the European Parliament and of the Council. Importers and exporters of the chemical must notify relevant authorities before transportation of the substance (European Commission, 2012).

# **Existing Worker Health and Safety Controls**

## **Hazard Classification**

The chemicals are not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

## **Exposure Standards**

#### Australian

No specific exposure standards are available.

## International

No specific exposure standards are available.

# Health Hazard Information

There are limited hazard data available for these chemicals. Data for long-chain OPEs (EO units  $\geq$ 9) are sufficient, but there are limited data for shortchain OPEs. Therefore, read-across data from other extensively studied NPEs (with specified chain lengths based on the number of EO units) are used in this assessment, where appropriate.

Most of the human and animal data available were from studies conducted using NPEs with 1–50 EO units, and for OPE with  $\geq$ 9 EO units. The NPEs and OPEs metabolise in the body and biodegrade in the environment to NPs and OPs. Therefore, toxicity of NPs and OPs was considered acceptable to derive the toxicity of the ethoxylates when there were no hazard data available on specific systemic endpoints (NICNASa; NICNASb). It is noted that compared with NPEs and OPEs, NPs and OPs are more toxic.

## **Toxicokinetics**

The metabolism of NPEs and OPEs include the shortening of the EO chain and some carboxylation of the alkyl chain by omega-oxidation. Hydrolysis of sulfate and phosphate groups is also expected. Following systemic absorption, NPEs and OPEs are expected to break down into NPs and OPs, respectively. Therefore, the toxicokinetic patterns of the ethoxylates are expected to be similar to NPs and OPs.

In an oral study in male rats, the excretion of NPE (9 EO units) was observed to be similar to NP. About 70 % of the administered dose was excreted in the faeces and 20 % in the urine, four days after administration. The primary urinary metabolites were acidic and postulated to be glucuronic acid conjugates of NP (Danish EPA, 2000).

Studies in rats have indicated that intestinal absorption decreases with increasing EO chain length. In several in vitro dermal penetration studies using cadaver skin, the dermal penetration of NPEs with EO units 2, 4 and 9 was reported to be less than 1 % over 48 hours (CIR, 2015). Absorption of OPE (9 EO units) through the vaginal wall of rabbits and rats is rapid and the chemical is excreted via the liver-bile-faeces and kidney-urine routes.

Radioactive OPE (40 EO units) was administered by stomach tube to six rats and orally to two dogs. The majority of the administered dose was excreted in the faeces (92.2 % for rats and 86.4 % for dogs). Smaller amounts were recovered in the urine (0.6–2.0 %) for both rats and dogs, and in the carcass of rats (2–4 %). Around 0.02–0.06 % of radioactivity was recovered in the liver. The authors stated that there was no storage of OPE in the liver and the amount recovered in the carcass may be indicative of metabolism. The chemical OPE-40 was concluded to be 'not absorbed to any substantial degree' (CIR, 2004).

## **Acute Toxicity**

#### Oral

The acute oral toxicity of NPEs and OPEs could range from low to moderate. The toxicity of NPEs and OPEs is considered to increase with decreasing EO units (or chain length) (Health Canada, 2002). Based on the available data (the median lethal dose (LD50) = 1300 or 1310 mg/kg bw in rats for some NPEs, and 691–1600 in rats for some OPEs), the chemicals should be classified as hazardous (see **Recommendation** section) unless data are available to indicate low acute oral toxicity (e.g. LD50 >2000 mg/kg bw in rats).

For the chemical CAS No. 9016-45-9, the oral LD50 was reported to be 1310 mg/kg bw in rats (HSDB). However, this CAS No. applies to many NPEs containing 1–120 EO units.

The following LD50s were reported for NPEs of various EO chain lengths (CIR, 1983; CIR, 2015; REACH):

- 3500–4500 mg/kg bw in rats for NPEs with EO units 2, 5, 7 or 9;
- 2000–4290 mg/kg bw in mice, guinea pigs and rabbits for an NPE with 9 EO units;
- 1300 mg/kg bw in rats for an NPE with 10 EO units; and
- other NPEs with 30 EO units were reported as 'relatively harmless' in rats but no LD50s were determined.

Reported signs of toxicity included diarrhoea, tremors, prostration and narcosis. Necropsy revealed congested lungs, gastrointestinal system and kidneys (CIR, 1983).

The following LD50s were reported for OPEs of various EO chain lengths (CIR, 2004):

- 691–1600 mg/kg bw in rats for OPEs with 9 and 13 units. Reported effects included slight to moderate weakness, diarrhoea, ataxia and
  prostration. Reddening of the gastrointestinal mucosa and fibrous tissue covering the heart or lungs were observed;
- 0.2–7.1 cc/kg (~214–7597 mg/kg bw) in rats for OPEs with 1, 3 and 5 units; and
- 2680-21200 for OPE with 16, 20 and 30 (with the highest value being for EO=30)

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The oral LD50s for OPEs of unknown chain lengths reported for other species were 3500 mg/kg bw in mice, and 6730 mg/kg bw in rabbits (Galleria Chemica).

#### Dermal

Based on the limited data available, the chemicals are expected to have low acute dermal toxicity. Dermal absorption is expected to be further reduced with increasing chain length (EO units) and; therefore, acute dermal toxicity is expected to be very low for long-chain NPEs and OPEs.

The dermal LD50 for the chemical with CAS No. 9016-45-9 was reported to be 2000 mg/kg bw in rabbits (HSDB).

Acute dermal toxicity studies conducted using six undiluted NPEs (EO units = 4–13) reported an LD50 range of 1800–4400 mg/kg bw in rabbits. Similarly to acute oral toxicity, dermal toxicity decreased as ethoxylation increased (CIR, 1983).

The dermal LD50 for OPE (9 EO units) was reported to be 5–20 cc/kg (equivalent to >5350 mg/kg) in guinea pigs (CIR, 2004).

Nonylphenols and octylphenols also have low acute dermal toxicity (NICNASa; NICNASb).

#### Inhalation

The limited data available are not sufficient to derive a conclusion on the acute inhalation toxicity of the chemicals. Animal studies for OPE (9 EO units) indicate potential respiratory irritation and lung-overload effects at high exposure.

In an acute inhalation study, male rats were exposed (whole body) to undiluted or 1 % NPEs (with 4, 7 or 9 EO units) for either four or eight hours, and observed for 14 days. The exposure concentrations were not reported. No toxic effects were observed (CIR, 1983).

In a 4-hour acute inhalation study, Sprague Dawley (SD) rats were exposed (whole body) to aerosolised detergent (containing NPE as the principal component) at concentrations of 0.50, 0.90 or 1.41 mg/L. Sub-lethal effects included eye and respiratory irrtation, hypoactivity, laboured and audible breathing, unkempt fur, and distended abdomens. At two weeks post-exposure, the animals showed body weight loss or decreased weight gain, and

perinasal encrustation. The LC50 was reported as 1.60 g/m<sup>3</sup> (CalEPA, 2010).

In a dose-response study, Syrian hamsters were exposed to OPE (9 EO units) aerosol through inhalation or bronchopulmonary lavage. The LD50s were reported to be 501 µg/g lung for inhalation, and 2060 µg/g for lavage. The reported effects were laryngeal obstruction, pulmonary oedema and acute pneumonia. Subsequent acute inhalation studies via these routes were conducted by the same authors. Syrian hamsters were administered the chemical in isotonic saline via bronchopulmonary lavage, to determine the amount of lung deposition. An LD50 of 2100 µg (estimated mean lung burden) was reported for this study. Necropsy revealed congested lungs, focal areas of peripheral atelectasis and blood-tinged fluid in the trachea and large bronchi. An LD50 of 1700 µg was reported for the inhalation study whereupon hamsters were exposed (nose-only) to OPE (9 EO units) aerosol. Reported effects included laryngeal and epiglottic oedema, haemorrhagic and mucosal ulcerations which contained neutrophils and macrophages, and obstructive asphyxia which caused death (CIR, 2004).

In an acute study, Swiss mice were exposed (nose-only) to airborne concentrations of OPE (9 EO units) up to concentrations of 38 mg/L. A concentration-related decrease in respiratory rate was reported. This chemical was classified as a sensory irritant by the author (CIR, 2004).

There were no deaths in a two week inhalation study in rats exposed to 10 mg/m<sup>3</sup> (see Repeated dose toxicity section).

## **Corrosion / Irritation**

#### Skin Irritation

Skin irritation studies in rabbits with some NPEs have shown moderate to severe irritation. The degree of irritation changes with the number of EO units (HSDB). Available data for OPEs showed moderate irritation at high concentrations. Whilst no data are available for the anionic surfactant derivatives of NPEs and OPEs these are expected to be more irritating than their non-ionic counterparts. Nonylphenols and octyphenols are classified as corrosive (NICNASa; NICNASb). Based on the available data, these chemicals should be classified as skin irritants (see **Recommendation** section), unless data are available to indicate no or minimal skin irritation.

In a skin irritation study in New Zealand White (NZW) rabbits, 11 NPEs (with EO units 2, 4, 6, 7, 9, 10, 12, 13, 15, 30 or 40) were tested undiluted by applying occlusive patches of 0.01–0.50 mL. The NPEs with EO chains ≤6 caused moderate to severe irritation (CIR, 2015; REACH).

Severe skin irritation effects were observed in animals tested with NPEs containing five or six EO units. In a skin irritation study, an NPE containing six EO units (NPE-6) was applied (occlusively, 0.5 mL) to the clipped intact and abraded skin of six rabbits. The effects (erythema and oedema) were scored at 24 and 72 hours after application. The chemical was classified as severely irritating to the skin of rabbits, with a primary irritation index (PII) of 3.0. A PII of 6.6 was reported in another skin irritation study with NPE-6 (animal species and experimental details not stated) (CIR, 1999).

In a skin irritation study, OPE (13 EO units) was applied (occlusively, 0.5 mL, concentration not stated) to the intact and abraded skin of 6 New Zealand albino rabbits. At 24 hours post-application, very slight erythema and oedema were observed. These effects were reversible by 72 hours. The chemical

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was concluded as a slight skin irritant (PII=0.50). In another study, a solution of OPE (11 EO units) at 20 % was classified as a moderate skin irritant. No details on the study are available (CIR, 2004).

The OPE (9 EO units) at 0.25 % was minimally irritating in a single-insult occlusive patch test of a peel-off mask product. A total of 9 rabbits were evaluated at 2 and 24 hours post application. At 2 hours, an erythema score=1 was reported for 8 rabbits, and score=2 for 1 rabbit. Oedema was not observed, and the reactions were reversible by 24 hours. The primary irritation index (PII) was 0 out of 8. The same product was non-irritating in another study in 6 rabbits. The chemical applied at 10 % w/w in distilled water to the shaved intact skin of Japanese white female rabbits up to 24 hours was slightly irritating. The maximal primary Draize skin irritation score was 0.2 out of 8.0 (CIR, 2014).

In a developmental toxicity study, Sprague-Dawley CD rats receiving dermal applications of OPE (9 EO units) at 12.5 %, 37.5 % or 100 % (equivalent to 530, 1600 and 4270 mg/kg bw/day) showed skin irritation effects. Excoriation and erythema were observed in all dose groups, and exfoliation/desquamation at the highest dose (CIR, 2004).

#### Eye Irritation

The available studies with various NPEs indicate that the level of irritation generally increases with decreasing EO chain length (HSDB). Although no data are available for OPEs with EO chain lengths >13 units, the available data for chain lengths  $\leq$ 13 units indicate eye irritation. Nonylphenols and octyphenols are classified as corrosive (NICNASa; NICNASb). Whilst no data are available for the anionic surfactant derivatives of NPEs and OPEs, these are expected to be at least as or more irritating than their non-ionic counterparts. Based on the available data, these chemicals should be classified as eye irritation, section), unless data are available to indicate no or minimal eye irritation.

In a study conducted according to the Draize method, an NPE with six EO units caused severe eye irritation in rabbits. The average scores obtained on days one and seven post-exposure were 28.8 and 16.0, respectively (maximum score=110) (CIR, 1999).

Moderate to severe eye irritation was observed in NZW rabbits instilled with 0.1 mL of NPE solution with EO chain lengths of 2–15. No eye irritation was observed when the EO chain length was  $\geq$ 30 (REACH).

Many eye irritation studies are available for OPE (9 EO units). In a Draize test, the chemical (up to 10 %) was tested in 4–6 rabbits, with observations up to 21 days. The reported scores were: severely irritating at 10 % (score=59), moderately irritating at 5 % (score=32), and minimally irritating at 1 % (score=2) (CIR, 2004).

In an eye irritation study, OPE (9 EO units) at 10 % was evaluated in six rabbits. Damage to the cornea was observed in 2 out of 3 rabbits exposed, without rinsing. Effects had not reversed 35 days after application. The eyes of the remaining 3 rabbits (with rinsing) were normal within 4 days. In another study, the undiluted chemical was instilled in 2 rabbits (one subjected to ocular rinsing), with observation up to 14 days. The unrinsed eye showed moderate to severe erythema, slight to moderate oedema, slight corneal opacity, and iridial injection. Irritation (slight pannus and slight erythema on the nictitating membrane) persisted up to 14 days. Effects observed for the rinsed eye were reversible. The chemical (concentration not stated) was moderately irritating in another study in 2 male NZW rabbits. Corneal opacity and iritis (unrinsed eyes) persisted beyond 21 days post instillation (CIR, 2004).

A skin freshener containing 0.25 % OPE (9 EO units) was classified as minimally irritating in two eye irritation studies. When tested in 6 rabbits, a Draize score of 5 was reported on day 1, but decreased to 2 by 7 days post instillation. In another study using the same procedure in 3 rabbits, the Draize scores decreased from 1 to 0 at 3 days after instillation.

Severe irritation was observed in NZW rabbits instilled with 0.1 mL (concentration not stated) of OPE (13 EO units). A solution of OPE (11 EO units) at 20 % was classified as 'very badly tolerated' but no other details are available. According to the Food and Drug Administration (FDA), the highest test concentrations that did not cause eye irritation in 3 or more, out of 5 rabbits were 15 % for OPE (1 and 3 units), 5 % for OPE (5 EO units), 0.5 % for OPE (9 EO units), and 1 % for OPE (13 EO units) (CIR, 2004).

## Observation in humans

Cosmetic formulations containing NPEs (with EO units 4, 9 or 12) at concentrations of 1.75–20 % were applied (occlusively) to the forearm and/or the inner arm of 20 subjects for 24 hours, and the patches were re-applied 10 times. Slight to mild irritation was observed (CIR, 1983).

In another skin irritation study, a gel containing 4 % NPE (with 9 EO units) was applied 11 times (occlusively) on 212 subjects. The application duration was not stated. Eleven subjects out of 804 showed some effect and the authors concluded that the product was not irritating or sensitising to the skin (CIR, 1983).

In a 24-hour human patch test study, 4 cosmetic formulations with 2 containing 2 % OPE (9 EO units), and 2 without OPE were applied on subjects (number and age range not stated). The Primary Irritation Index (PII) for the first pair of formulations with or without the chemical were 0.55 (moderately irritating) and 0.13 (minimally irritating), respectively. The PII for the second pair of formulations with or without the chemical was 0.11 (minimally irritating). The authors reported that the difference in results for the 2 formulations was due to skin penetration. One formulation contained 20 % glycol acrylic polymer which slowed down the skin penetration rate (CIR, 2004).

In another skin irritation study, 1 % OPE (9 EO units, 200 µL) was applied to the interscapular area of the back of 9 healthy female volunteers. The patches were re-applied to the same site for 4 consecutive days. The chemical was classified as a non-irritant (CIR, 2004).

## Sensitisation

## Skin Sensitisation

Based on the available data, NPEs and OPEs and their anionic surfactant derivatives are generally not considered to have skin sensitisation potential. However, there is equivocal evidence of mild contact dermatitis in human patch tests with short-chain NPEs and OPEs (see **Observation in humans** section). Ethoxylated nonylphenol acrylate (CAS No. 678991-31-6) is a potential sensitiser based on the acrylate ion (NICNASc). Nonylphenols and octylphenols are not considered to be skin sensitisers (NICNASa; NICNASb).

In a guinea pig maximisation test, five albino guinea pigs were exposed intradermally to NPE containing six EO units (NPE-6) at concentrations of 0, 1.7, 3.0, 9.0 or 27 % (w/w) during the induction phase. After seven days, undiluted NPE-6 was applied topically and the site occluded for 48 hours. The application site was later challenged topically with 2.7 % NPE-6. No dermal responses were observed after 48 hours following the challenge (CIR, 1999).

#### Observation in humans

There were a few patch tests conducted using NPEs containing different numbers of EO units (indicated as NPE-2, NPE-4 etc.), with negative results for skin sensitisation.

In three repeated predictive patch tests, test subjects (n = 102) did not show evidence of allergic contact dermatitis when patch tested with 5 % NPE-2 in mineral oil (with a three-week induction phase and 96 hours after challenge). Contact dermatitis was observed in 9/103 subjects tested with 10 % NPE-2, and 3/107 subjects tested with 10 % NPE-4 in mineral oil. When subjects testing positive were re-tested with 30 minutes of exposure to the chemical, evidence of a mild allergic response was observed in 2/7 subjects (10 % NPE-2), and 1/3 subjects of (10 % NPE-4) (CIR, 1999; CIR, 2015).

Undiluted NPE-4 was tested on the backs of volunteers (n = 25/sex) in a repeated insult patch test with an initial 48-hour treatment, followed by 14 induction patches for 24 hours each. Two weeks post treatment, the skin was challenged for 24 hours. No immediate or delayed reactions were observed following induction or challenge. The authors concluded that NPE-4 was not a primary irritant, a sensitiser, or a fatiguing agent (CIR, 2015). The other repeated patch tests conducted with NPE-9, NPE-15, and NPE-50 on volunteers did not show skin sensitisation (CIR, 2015).

In a multi-centre study in Sweden that used oxidised ethoxylated surfactants, sensitisation of 528 patients (who were previously identified as consecutive dermatitis patients with suspected allergic contact dermatitis) was investigated. The patients were patch-tested with aqueous and air-oxidised NPE-10 at a 20 % concentration, and scored according to the International Contact Dermatitis Research Group criteria. No sensitisation effects were observed with aqueous NPE-10. The oxidised chemical caused erythema in one patient on day seven, but the authors considered that it was not an allergic reaction (CIR, 2015).

Photosensitisation was observed in sun-exposed patients previously treated with a topical antiseptic preparation containing NPE-10. In a follow-up study, two patients and 32 controls were patch-tested with the antiseptic preparation and NPE-10 (undiluted, 0.2, 1.0, 2.0 %) and exposed to UV light at 24 hours post-application. The test sites were evaluated 72 hours post-application. The undiluted chemical did not cause photosensitisation reactions. In another study following the same test protocols, NPE-15 and NPE-50 were not found to be photosensitising (CIR, 2015).

Most of the tests available for OPE are for a variant with 9 EO units. A cotton twill was treated with 0.1 % of the chemical and applied to the arms of 84 men, and to the arms and legs of 122 women. The fabric was secured with adhesive tape for 6 days. After a 14-day non-treatment period, new patches were applied for 48 hours. No reactions to the chemical were observed. In another skin sensitisation test, a formulation containing 0.5 % of the chemical was applied (occlusively) to the backs of 106 subjects for 24 hours, 3 times/week for 22 days. Challenge patches were applied for 24 hours, and evaluated at 48 and 96 hours post-application. A total of 7 subjects had a score of 1 out of 5 during induction, and 1 subject had a score of 1 out of 5 during the challenge phase. The chemical at 0.5 % was concluded to not induce reactions indicative of contact sensitisation (CIR, 2004)

A foot gel containing the chemical at 8 % was applied (semi-occlusively, 0.2 mL/0.2 g) on the infrascapular region of the back of 112 subjects for 24 hours. There was a total of 9 consecutive 24 hour applications for a 3 week period. After a 10 to 14-day non-treatment period, the subjects were challenged with 0.2 mL or 0.2 g on a new test site. No adverse reactions were observed in any subjects during the induction and challenge phase. The test substance was neither a primary irritant nor a sensitiser (CIR, 2004).

Undiluted OPEs with variable chain lengths (1, 3, 5, 9, and 13 EO units) were evaluated in a 48 hour skin irritation study in 50 subjects. No skin irritation was observed; however, OPE-1 was considered to have caused sensitisation in 2 subjects. No other details are available (CIR, 2004).

In a case report, a 58-year old uranium mill maintenance worker with allergic contact dermatitis used a waterless hand cleanser containing NPE-6 and 0.5 % OPE-9 in petrolatum. When patch-tested and observed up to 48 hours, the worker was allergic to NPE-6, but showed no reaction to 0.5 % OPE-9 (CIR, 2004).

## **Repeated Dose Toxicity**

Oral

Based on the available data, these chemicals are not considered to cause serious damage to health following repeated oral exposure.

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In several 90-day repeated dose oral toxicity studies (individual test protocols), NPEs containing 4, 6, 15, 20, 30 or 40 EO units were orally administered to rats in the diet at 40–5000 mg/kg bw/day (0.01–1% of the diet). Growth retardation due to poor palatability of the diets was observed with NPEs containing 4, 6, 15 and 20 EO units at ≥200 mg/kg bw/day. Increased absolute and relative liver weights were observed when animals were administered NPE-4 or NPE-6 at 200 mg/kg bw/day, but no histopathological changes were observed. No effects were observed in rats that ingested NPE-30. Slight hepatic necrosis and centrilobular granular degeneration were observed in rats administered NPE-40 at a 3 % dietary concentration (~700 mg/kg bw/day) (CIR, 1983; Danish EPA, 2000).

In 90-day studies in beagle dogs, several NPEs were administered orally in gelatine capsules at 40–1000 mg/kg bw/day. The observed effects included increased liver weights at ≥200 mg/kg bw/day (NPE-4), vomiting at doses of ≥200 mg/kg bw/day (NPE-6 and NPE-15), growth retardation at ≥640 mg/kg bw/day (NPE-9), and focal myocardial necrosis at ≥1000 mg/kg bw/day (NPE-20). No effects were observed with NPE-30 administered at doses of 200 and 1000 mg/kg bw/day (CIR, 1983; Danish EPA, 2000).

In 2-year repeated dose oral toxicity studies, NPE-4 and NPE-9 were administered to rats and dogs at doses of ~400–1000 mg/kg bw/day. In rats, reduced body weights and enlarged livers were observed at doses ≥1000 mg/kg bw/day. In dogs, reduced body weights, vomiting, and increased serum alkaline phosphatase levels were reported at the 1000 mg/kg bw/day dose. The authors concluded that these NPEs had low chronic toxicity (CIR, 1983). In another study using NPE-9 in rats, enlarged livers were accompanied by cloudy swelling and reduced polysaccharides at the 250 mg/kg bw/day dose, and focal hepatic cell necrosis at the 1250 mg/kg bw/day dose (Danish EPA, 2000).

In repeated dose oral toxicity study, mice were administered NPE-10 in the diet at doses of 0, 500, 1500 or 4500 ppm (0, 81.5, 254 or 873 mg/kg bw/day) for 104 weeks. At the highest dose, decreased body weight gain, decreased absolute liver and kidney weights, and increased relative brain, liver and kidney weights were observed. No other significant effects attributed to the chemical were observed (CIR, 2015). The no observed adverse effect level (NOAEL) for NPE-10 was determined as 254 mg/kg bw/day.

In a subchronic oral toxicity study, OPE (40 EO units) was administered orally to young albino rats (n = 15/sex) at 5 % in the diet, every day for 3 months. Mortalities occurred but were not treatment-related. There were no effects on growth and food consumption, urinary concentrations of sugar and protein and haematological parameters. No treatment-related effects were observed during histopathological examination.

The chemical was evaluated in a subsequent chronic toxicity study in albino rats (n = 30/sex) at 0.035, 0.35 or 1.5 %, every day for 3 months or 2 years. No adverse effects were observed (CIR, 2004).

In another study by the same authors, OPE (40 EO units) was administered to groups of beagle dogs at 0.35 % or 5 % in the diet for an unspecified period of time. No treatment-related effects were observed (CIR, 2004).

In a developmental toxicity study, groups of Sprague-Dawley (SD) CD rats were administered OPE (9 EO units) at 0.06 % or 0.30 % (~70 or 340 mg/kg bw/day) on gestation days (GDs) 6–16. No deaths or clinical signs were reported. Gross or microscopic examination was not conducted (CIR, 2004).

#### Dermal

No data are available for NPEs. Available data for OPEs do not indicate serious damage to health following repeated dermal exposure.

In a developmental toxicity study (also described in **Skin irritation** section), SD CD rats received dermal applications of OPE (9 EO units) at 12.5 %, 37.5 % or 100 % (equivalent to 530, 1600 and 4270 mg/kg bw/day) at 4 mL/kg on GDs 6–15. One death occurred in the highest dose group but the cause was uncertain. Effects observed at this dose included urine stains, audible respiration, perinasal encrustation and reduced body weight gain. Increased relative liver and kidney weights were considered to be due to reduced maternal weight gain. The NOAEL for maternal toxicity was 1600 mg/kg bw/day (CIR, 2004).

In another study by the US FDA, OPEs of variable chain lengths were applied to the skin of rabbits for 4 weeks (total=20 applications). The applied concentrations were 1 % for OPEs (1 and 3 EO units), and 0.1 % for OPEs (9 and 13 EO units). No 'abnormal changes were noted' during histopathologic examination (CIR, 2004).

#### Inhalation

No data are available for NPEs. Data for OPE are not sufficient to warrant hazard classification.

In a 2-week repeated dose inhalation toxicity study, SD CD rats (n = 5/sex) were exposed to *para*-tert-octylphenol ethoxylate (EO units not stated) in an inhalation chamber at 0 or 10 mg/m<sup>3</sup>, 5 days/week, 6 hours/day. No mortalities were observed. Observed lung effects included reddening, and inflammatory changes in the alveolar walls/perivascular space. Alveolar/bronchiolar epithelial hyperplasia was observed only in treated animals, and their lung-to-body weight ratios were significantly greater compared with controls.

## Genotoxicity

Based on the available in vitro genotoxicity data, NPEs and OPEs are not considered to be genotoxic. No in vivo genotoxicity data are available for NPEs.

Negative results were obtained for NPEs in several in vitro assays (CIR, 1999; CIR, 2015):

- NPE-4, NPE-9 and NPE-10 were negative in Ames tests, with or without metabolic activation;
- NPE-9 did not induce unscheduled DNA synthesis in adult rat hepatocytes at concentrations up to 25 µg/mL;
- NPE-9 did not induce malignant transformations in rat liver T51B cells or mouse IOT1/2 fibroblast cells, when cultured; and
- neither NPE-9 nor NPE-40 induced malignant transformations in mouse BALB/3T3 fibroblasts.

The following results were reported for OPE-9 in several in vitro assays (CIR, 2004):

- positive in Salmonella typhimurium TA100 when tested in combination with known mutagens. Another OPE (1 EO unit) was negative in several strains of S. typhimurium TA98, TA100, TA1535, TA1537 and TA1538 at concentrations up to 0.1 µL/plate, with or without metabolic activation;
- enhanced the induction of chromosomal aberrations by known carcinogens in Chinese hamster ovarian cells with metabolic activation. However, the chemical itself was not clastogenic;
- did not induce unscheduled DNA synthesis in rat hepatocytes (T51B cells) up to 50 µg/mL;
- negative in a mouse lymphoma thymidine kinase (TK) locus forward mutation assays and in the DNA alkaline unwinding test using L5178Y/TK cells, without metabolic activation up to 100 μL/L;
- did not cause DNA damage in rat liver cells after 2 treatments, but caused DNA breakage at 3 treatments;
- induced DNA double-strand breaks in human lung epithelial cells (A549) at 5 % concentration after cell viability was reduced to <60 %. This
  indicated that DNA double-strand breaks resulted from extragenomic damage.</li>

#### Carcinogenicity

No studies on OPEs are available. Based on the available data, NPEs are not considered to be carcinogenic.

In a carcinogenicity study, female mice (n = 50/dose) were administered NPE-10 in the diet at doses of 0, 500, 1500 or 4500 ppm (0, 81.5, 254 or 873 mg/kg bw/day) for 104 weeks. No increase in the incidence of neoplastic or non-neoplastic lesions was observed at any dose level. The authors concluded that NPE-10 was not carcinogenic (CIR, 2015).

In another carcinogenicity study, rats were administered NPE-9 intravaginally at doses of 0, 6.7 or 33.6 mg/kg bw/day, 3 times a week for 24 months. The administered doses were equivalent to 4 or 20 times the clinical dose, respectively. No significant differences (including masses or mortalities) compared with controls were observed. Positive observations (details not available) in the experimental groups at necropsy were considered to be related to ageing. The authors concluded that NPE-9 was 'neither toxic nor carcinogenic in this lifetime exposure study, even at a dose that was 20 times that recommended for humans' for use as a spermicide (CIR, 1999).

In 2-year carcinogenicity studies, NPE-4 and NPE-9 were administered orally to rats at doses of 200 and 140 mg/kg bw/day. No increase in the frequency of tumours was reported (Danish EPA, 2000).

NPEs can contain trace amounts of ethylene oxide. The International Agency for Research on Cancer (IARC) has concluded that ethylene oxide is 'probably carcinogenic to humans' (IARC, 1999; IARC 2012).

## **Reproductive and Developmental Toxicity**

Studies are available only for NPE-9, NPE-10, NPE-30, OPE-9 and OPE-40. No data are available for the other chemicals in this group. The chemical NPE-9 is a known spermicide (CIR, 2015) and the studies available using NPE-9 have reported reproductive toxicity effects in rats from doses of 50 mg/kg bw/day, when administered intravaginally. However, oral studies in rats with NPE-9 showed reproductive and developmental effects only at a dose of ≥250 mg/kg bw/day. Based on the available data and considering the routes of exposure relevant for humans (excluding spermicide use), a conclusion on the reproductive and developmental toxicity of NPEs cannot be derived. However, nonylphenols are classified for reproductive and developmental toxicity based on animal data (NICNASa).

Studies for OPE-9 were conducted at very high doses and show developmental toxicity in rats at ≥340 mg/kg bw/day but not in mice at 800 mg/kg bw/day. The effects observed were considered common birth defects in certain strains of animals and not necessarily a manifestation of a teratogenic effect. The chemical OPE-40 did not cause reproductive toxicity in rats and dogs at dietary concentrations up to 5 %. Octylphenols are not classified for reproductive and developmental toxicity (NICNASb). Based on a weight of evidence, classification for OPES is not warranted.

In an in vivo sperm abnormality assay, male mice (n = 5/sex/dose) were injected intraperitoneally with NPE-9 in distilled water at doses of 0, 20, 40, 50 or 60 mg/kg bw/day for five days. No increase in the frequency of morphologically abnormal sperm was observed compared with controls (CIR, 1999).

In a reproductive toxicity study to evaluate embryotoxicity of NPE-9, nulliparous female Wistar rats were intravaginally administered the chemical at 5 mg/100 g bw (50 mg/kg bw) on gestation days (GD) three or seven. Ulcerative vaginitis and perivaginal oedema were observed in the dams, but were reversible by GD 15. Significant differences in the mean number of normal implantation sites and the number of resorption sites were observed in dams.

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In another study, pregnant Wistar rats were intravaginally administered NPE-9 at 25 mg/kg bw/day on GD 1–10. Increased incidences of nonpregnancies and resorptions were observed in dams administered the chemical on GD 3–6, and a significantly reduced number of live foetuses in dams was observed when the chemical was administered on GD 4, 5, and 9. The chemical NPE-9 was reported to be embryolethal and foetocidal, but not teratogenic when administered intravaginally (CIR, 2015).

In an oral developmental toxicity study, female rats were administered NPE-9 at doses up to 500 mg/kg bw/day on GD 6–15. The no observed effect level (NOEL) was determined as 50 mg/kg bw/day based on reproductive and developmental effects (increased pre-implantation losses, skeletal anomalies in the litters) observed at doses ≥250 mg/kg bw/day. The same authors conducted a dermal study in female mated rats with NPE-9 at doses of 50 or 500 mg/kg bw/day. No treatment-related effects on the skeletal or soft tissues were observed. However, an increased incidence of extra ribs was observed at 50 mg/kg bw/day (CIR, 1999).

In a developmental toxicity study, female mice were administered oral gavage doses of NPE-10 at 600 mg/kg bw/day on GD 6–13. No developmental toxicity effects were observed (CIR, 1999). Repeated subcutaneous administration of NPE-10 in female rats (from birth to day 21 after the birth of F1 offspring) at up to 80 mg/kg bw/day did not cause teratogenic effects. However, the treatment affected the growth of the offspring, e.g. decreased body weight or tendency to decrease body weight from day seven after birth (CIR, 2015).

Studies with NPE-30 have shown no treatment-related effects in female rats at oral doses up to 1000 mg/kg bw/day on GD 6–15 (HSDB).

In a developmental toxicity study, groups of Sprague-Dawley CD rats were administered OPE (9 EO units) at 0.06 % or 0.30 % (~70 and 340 mg/kg bw/day) in the diet on GDs 6–16. Statistically significant increases in skeletal variations were observed only at the highest dose. The NOAEL was determined as 70 mg/kg bw/day for developmental toxicity.

In a dermal developmental study conducted by the same authors as the oral study, female CD rats received dermal applications of OPE (9 EO units) at 12.5 %, 37.5 % or 100 % (equivalent to 530, 1600 and 4270 mg/kg bw/day) at 4 mL/kg on GDs 6–15. Clinical toxicity effects are described in the **Repeated dose toxicity** section. No effects on gestational parameters (gravid uterine weight, number of total, viable or nonviable implantations per litter, or preimplantation loss) were observed. There were prominent effects on foetal development. At the highest dose, statistically significant increases in skeletal abnormalities and increased incidences of supernumerary ribs arising from the lumber and cervical regions were observed. A statistically significant increased incidence of atelectasis was observed at ≥1600 mg/kg bw/day and a significant decreased incidence of dilated renal pelvis at 530 mg/kg bw/day. However, the authors noted that the toxicological significance of skeletal abnormalities was unclear. Increased incidences of supernumerary ribs in certain strains of animals and not necessarily a manifestation of a teratogenic effect. The maternal NOAEL was 1600 mg/kg bw/day.

The chemical OPE-9 did not cause developmental toxicity in the following studies: in female specific pathogen-free CD-1 mice administered (gavage) a dose of 800 mg/kg bw/day on GDs 6–13. The chemical OPE-9 was not embryotoxic or teratogenic in an intravaginal study in female SD COBS CD rats at doses up to 5 mg/kg bw/day on GDs 6–15 (CIR, 2004).

The chemical OPE-40 did not cause reproductive toxicity effects in male albino rats administered 5 % concentration in the diet daily for 3 months, or at dietary concentrations up to 1.4 % daily for 3 months or 2 years. In the same study, Beagle dogs administered OPE-40 up to 5 % in the diet daily for 3 months did not show an adverse effect on testes weight/body weight ratios (CIR, 2004).

Two of these chemicals (CAS Nos. 9014-90-8 and 9016-45-9) are listed in the EC Endocrine Disruptors Priority List. Poly(oxy-1,2-ethanediyl), .alpha.sulfo-.omega.-(nonylphenoxy)-, sodium salt is listed under Category 3b (i.e. no evidence of endocrine disrupting activity or no data available). Poly(oxy-1,2-ethanediyl), .alpha.-(nonylphenyl)-.omega.-hydroxy- (CAS No. 9016-45-9) is listed under Category 2, indicating at least some in vitro evidence of biological activity related to endocrine activity (EC, 2015).

Many of these chemicals are listed in the US EPA's Universe of Chemicals list for potential endocrine activity screening and testing (US EPA, 2012).

## **Other Health Effects**

#### Neurotoxicity

In a neurotoxicity study, OPE (9 EO units) was evaluated using the jejunal segments of male rats. A portion of the jejunum was removed from the peritoneal cavity and the chemical (1 % in saline) was applied to the serosal surface, every 5 minutes for 30 minutes. The tissue samples of the treated and control portions of the gut were evaluated 20 days post-application. The chemical significantly reduced the number of ganglion cells in the myenteric plexus, with a mean number of 0.47 ganglion cells/mm jejunum compared with 4.04 for the controls (CIR, 2004).

#### **Endocrine Disruption**

The metabolites, NP and OP, have measured oestrogenic activity (NICNASa, NICNASb). Assessment of NP suggested that developmental effects may derive from antiandrogenic activity (NICNASa).

# **Risk Characterisation**

## **Critical Health Effects**

The critical health effects for risk characterisation are skin and eye irritation. The chemicals could also cause systemic acute effects from oral exposure. However, these health effects are applicable mainly for short chain length NPEs and OPEs and the effects could reduce with increasing chain lengths. The chemicals with EO chains  $\geq$ 30 are reported to be generally non-toxic (CIR, 2015).

While nonoxynol-9 is toxic to reproduction and this is expected to also apply to related NPEs, the effects appear to be specific to direct spermicidal use, which is not relevant to industrial uses of the chemicals. Reproductive and developmental effects were not observed with OPEs.

Ethoxylated nonylphenol acrylate may be a potential skin sensitiser.

The NPEs biodegrade to NPs in the environment and some products containing NPEs can also contain residual amounts of NPs. Therefore, critical health effects of NPs could also be applicable for risk characterisation under those situations, particulary following secondary exposure from environmental sources. This also applies to OPEs.

# **Public Risk Characterisation**

Considering the range of cosmetics, personal care products and domestic products that may contain these chemicals, the main routes of public exposure are expected to be through the skin and inhalation, although incidental ocular and oral exposure can also occur. The Cosmetic Ingredient Review (CIR) Panel determined that cosmetic use concentrations of low molecular weight NPEs (not greater than EO = 8) should be limited to ~5 % in leave-on products (CIR, 2015). The same restriction was applied to low molecular weight OPEs (EO units  $\leq$ 8) (CIR, 2004). Whilst the chemicals may be skin and eye irritants, the chemicals are predominantly reported to be used in rinse-off products overseas. Inclusion of these chemicals in products intended for use in the eye area were limited with reported concentrations <2 % (CIR, 2004; CIR 2015).

The concentration of the impurity 1,4-dioxane is controlled through listing in the Poisons Standard (SUSMP) with labelling requirements applying at above 100 ppm (Appendix G).

Use of these chemicals is being restricted overseas. Under REACH regulations, the EU has restricted the use of these chemicals in products placed on the market for sale to the general public. These restrictions relate to environmental risks rather than direct human exposure.

Considering the breakdown of nonylphenol ethoxylates to nonylphenols in the environment, there may be potential for human exposure to nonylphenols via the environment. However, the risk to humans from nonylphenol is considered acceptable if the concentration levels are maintained in accordance with the limitations for nonylphenol set out in the Australian Guidelines for Water Recycling on the 'planned use of recycled water (treated sewage and stormwater) to augment drinking water supplies'. A maximum concentration of 2.9 µg/L has been detected for 4-nonylphenol in secondary treated sewage and a guideline value of 500 µg/L is derived for drinking water augmentation (NRMMC-EPHC-NHMRC, 2008). Detected levels of OPs in urine, overseas and Australian domestic waste water is significantly lower than NPs (OSPAR, 2006; CSIRO, 2010; CDC, 2012). Overall, the chemicals are not considered to pose an unreasonable risk to public health, although the total surfactant concentration in the products should be considered when determining label instructions.

## **Occupational Risk Characterisation**

During product formulation, dermal and ocular exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

The chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal and ocular exposure are implemented. The chemicals should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

# **NICNAS Recommendation**

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

NICNAS recommends that formulators of products containing these chemicals should take into account the total surfactant concentration in the products when determining label instructions.

## **Regulatory Control**

Public Health

Products containing the chemicals should be labelled in accordance with state and territory legislation (SUSMP, 2017).

## Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. The CAS number represents chemicals with a range of ethoxylate units. This hazard classification should be applicable for chemicals with EO chains <30 and only when specific hazard data are not available for the specific lengths. If empirical data become available for a specific chemical under the CAS description indicating that a lower (or higher) classification is appropriate, these may be used to amend the default classification for that chemical. This assessment does not consider classification of physical and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS) <sup>a</sup>	GHS Classification (HCIS) <sup>b</sup>
Acute Toxicity	Not Applicable	Harmful if swallowed - Cat. 4 (H302)
Irritation / Corrosivity	Not Applicable	Causes serious eye irritation - Cat. 2A (H319) Causes skin irritation - Cat. 2 (H315)

<sup>a</sup> Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

<sup>b</sup> Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

\* Existing Hazard Classification. No change recommended to this classification

## Advice for consumers

Products containing the chemicals should be used according to the instructions on the label.

## Advice for industry

#### **Control measures**

Control measures to minimise the risk from dermal and ocular exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

#### Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals*—Code of practice and Labelling of workplace hazardous chemicals—Code of practice, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

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Last Update 08 March 2019

# **Chemical Identities**

Chemical Name in the Inventory and Synonyms Ethanesulfonic acid, 2-[2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethoxy]-, sodium salt entsufon sodium

04/2020	IMAP Group Assessment Report sodium octoxynol-2 ethane sulfonate
CAS Number	2917-94-4
Structural Formula	
Molecular Formula	C20H34O6S.Na
Molecular Weight	424.53

Chemical Name in the Inventory and Synonyms	Ethanesulfonic acid, 2-[2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]-, sodium salt sodium octylphenoxyethoxyethyl sulfonate nonylphenoxyethoxyethanolsulfonate,sodium salt
CAS Number	3013-94-3
Structural Formula	





Chemical Name in the Inventory and Synonyms	Ethanol, 2-[2-[2-[2-(4-nonylphenoxy)ethoxy]ethoxy]- tetraethylene glycol mono(4-nonylphenyl) ether nonoxynol-4
CAS Number	7311-27-5
Structural Formula	

04/2020	
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Molecular Formula	C23H40O5
Molecular Weight	396.56

Chemical Name in the	Poly(oxy-1,2-ethanediyl), .alpha[4-(1,1,3,3-tetramethylbutyl)phenyl]omegahydroxy- polyethylene glycol octylphenol ether
Inventory and Synonyms	octoxynol-9 Triton X-100
CAS Number	9002-93-1
Structural Formula	

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/04/2020	IMAP Group Assessment Report
Molecular Formula	(C2H4O)nC14H22O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(isooctylphenyl)omegahydroxy- octoxynol-7 PEG-7 octylphenyl ether ethoxylated isooctylphenol
CAS Number	9004-87-9
Structural Formula	



Molecular Formula	(C2H4O)nC14H22O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(nonylphenoxy)-, sodium salt nonyl phenol ethoxy sulfate, sodium salt sodium salt of sulfated nonylphenoxypoly(ethyleneoxy)ethanol
CAS Number	9014-90-8
Structural Formula	No Structural Diagram Available

Molecular Formula	(C2H4O)nC15H24O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(dinonylphenyl)omegahydroxy- polyethylene glycol dinonylphenyl ether dinonylphenol polyoxyethylene nonyl nonoxynol-5 nonyl nonoxynol-10
CAS Number	9014-93-1
Structural Formula	No Structural Diagram Available
Molecular Formula	(C2H4O)nC24H42O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy- 2-(nonylphenyl)omegahydroxypoly(oxy-1,2-ethanediyl) ethoxylated nonylphenol polyethylene glycol nonyl phenyl ether nonylphenol, ethylene oxide, condensate nonoxynols(generic)
CAS Number	9016-45-9
Structural Formula	





Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha[(1,1,3,3-tetramethylbutyl)phenyl]omegahydroxy- alpha[(1,1,3,3-tetramethylbutyl)phenyl polyethylene glycol octylphenyl ether ethoxylated octyl phenol octylphenoxypoly(ethoxyethanol) glycols, polyethylene, mono((1,1,3,3-tetramethylbutyl)phenyl) ether
CAS Number	9036-19-5
Structural Formula	



Chemical Name in the Inventory and Synonyms	<b>Poly(oxy-1,2-ethanediyl), .alphasulfoomega(nonylphenoxy)-, ammonium salt</b> ammonium nonoxynol-4 sulfate poly(oxyethylene) nonylphenyl ether ammonium sulfate polyethylene glycol nonylphenyl ether ammonium bisulfate
CAS Number	9051-57-4
Structural Formula	



Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(octylphenyl)omegahydroxy- Triton X 100 octoxynol-3
CAS Number	9063-89-2
Structural Formula	No Structural Diagram Available

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Molecular Formula	(C2H4O)nC14H22O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	<b>Poly(oxy-1,2-ethanediyl), .alphasulfoomega(nonylphenoxy)-</b> poly(oxy-1,2-ethanediyl), alpha-sulfo-omega-(nonylphenoxy)- nonylphenol polyoxyethylene sulfuric acid alpha-sulfo-omega-(nonylphenoxy)-poly(oxy-1,2-ethanediyl)
CAS Number	9081-17-8
Structural Formula	No Structural Diagram Available
Molecular Formula	(C2H4O)nC15H24O4S
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, compound with iodine nonylphenol ethoxylate-iodine complex
CAS Number	11096-42-7
Structural Formula	



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Molecular Formula	(C2H4O)nC15H24O.xI2
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(4-nonylphenoxy)-, ammonium salt p-nonylphenol, ethoxylate, sulfate, ammonium salt
CAS Number	31691-97-1
Structural Formula	

04/2020	
Molecular Formula	(C2H4O)nC15H24O4S.H3N
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(4-nonylphenyl)omegahydroxy- polyoxyethylated p-nonylphenol nonoxynol-5, -6 glycols, polyethylene, mono(p-nonylphenyl) ether poly(oxy-1,2-ethanediyl), alpha-(4-nonylphenyl)-mega-hydroxy-
CAS Number	26027-38-3
Structural Formula	



Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15,18,21,24-Octaoxahexacosan-1-ol, 26-(nonylphenoxy)-</b> nonylphenol octa(oxyethylene)ethanol nonoxynol-9 nonaethylene glycol nonylphenyl ether
CAS Number	26571-11-9
Structural Formula	

Molecular Formula	C33H60O10
Molecular Weight	616.83

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12-Tetraoxatetradecan-1-ol, 14-(octylphenoxy)-</b> (octylphenoxy)tetra(ethyleneoxy)ethanol octoxynol-5
CAS Number	27176-99-4
Structural Formula	No Structural Diagram Available

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Molecular Formula	
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15-Pentaoxaheptadecan-1-ol, 17-(nonylphenoxy)-</b> ethanol, 2-[2-[2-[2-[2-[2-(nonylphenyl)ethoxy nonylphenoxydiglycol nonoxynol-6 nonylphenol hexaethoxylate nonylphenol polyethylene glycol ether
CAS Number	27177-01-1
Structural Formula	
Molecular Formula	C27H48O7
Molecular Weight	484.67

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15,18,21-Heptaoxatricosan-1-ol, 23-(nonylphenoxy)-</b> nonylphenol octaethoxylate nonoxynol-8 PEG-8 nonyl phenyl ether
CAS Number	27177-05-5
CAS Number	27177-05-5

Structural Formula	_~~~~
Molecular Formula	C31H56O9
Molecular Weight	572.77

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15,18,21,24,27-Nonaoxanonacosan-1-ol, 29-(nonylphenoxy)-</b> nonylphenol decaethylene glycol ether nonylphenol decaethoxylate nonylphenolnona(oxyethylene) ethanol nonoxynol-10
CAS Number	27177-08-8
Structural Formula	



Chemical Name in the Inventory and Synonyms	Ethanol, 2-(nonylphenoxy)- nonylphenol monoethoxylate terics 2-(nonylphenoxy)ethanol
CAS Number	27986-36-3
Structural Formula	
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Molecular Formula	C17H28O2
Molecular Weight	264.41

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(carboxymethyl)omega(4-nonylphenoxy)- nonoxynol-5 carboxylic acid PEG-5 Nonylphenyl ether carboxylic acid
CAS Number	28212-44-4
Structural Formula	No Structural Diagram Available

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Molecular Formula	(C2H4O)nC17H26O3
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(isononylphenyl)omegahydroxy- isononylphenol ethoxylate nonoxynol-1 polyethylene glycol isononylphenol ether
CAS Number	37205-87-1
Structural Formula	No Structural Diagram Available
Molecular Formula	(C2H4O)nC15H24O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, phosphate, sodium salt alcohol ethoxylate, phosphate ester, sodium salt ethoxylated nonylphenol, polyphosphates, sodium salt nonylphenol, ethoxylated, phosphated, sodium salt
CAS Number	37340-60-6
Structural Formula	

Molecular Formula	(C2H4O)nC15H24O.xH3O4P.xNa
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Polyethoxylated isooctyl phenol (5.6:1) Citowett
CAS Number	39342-50-2
Structural Formula	No Structural Diagram Available

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Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(dinonylphenyl)omegahydroxy-, phosphate Wayfos M 60 nonyl nonoxynol-7 phosphate dinonylphenol ethoxylated phosphate
CAS Number	39464-64-7
Structural Formula	
Molecular Formula	(C2H4O)nC24H42O.xH3O4P
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(1-oxo-2-propen-1-yl)omega(4-nonylphenoxy)-, branched polyethylene glycol, mono(nonylphenyl)ester, acrylate ethoxylated nonylphenol acrylate
CAS Number	678991-31-6

Structural Formula

## No Structural

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(4-nonylphenyl)omegahydroxy-, phosphate p-nonylphenol ethoxy ether phosphate 4-nonylphenol ethoxylated phosphate ester nonoxynol-10 phosphate
CAS Number	51609-41-7
Structural Formula	

Molecular Formula	(C2H4O)nC15H24O.xH3O4P
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, phosphate ethoxylated nonylphenol phosphate nonylphenol, ethoxylated and phosphated phosphoric ester of poly(oxyethylene) nonylphenol ether polyethylene glycol, nonylphenyl ether, phosphate
CAS Number	51811-79-1
Structural Formula	
Molecular Formula	(C2H4O)nC15H24O.xH3O4P
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(2-nonylphenyl)omegahydroxy-
CAS Number	51938-25-1

Structural Formula	IMAP Group Assessment Report
Molecular Formula	(C2H4O)nC15H24O
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, phosphate, potassium salt ethoxylated nonylphenol, polyphosphates, potassium salt nonylphenol, ethoxylated, phosphated, potassium salt phosphated, ethoxylated nonylphenol, potassium salt polyethylene glycol, nonylphenol ether, phosphate, potassium salt
CAS Number	52503-15-8
Structural Formula	

Molecular Formula	(C2H4O)nC15H24O.xH3O4P.xK
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha[(1,1,3,3-tetramethylbutyl)phenyl]omegahydroxy-, phosphate tert-octylphenol, ethoxylated and phosphated polyethylene glycol (1,1,3,3-tetramethylbutyl)phenyl ether phosphate
CAS Number	52623-95-7
Structural Formula	



Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(carboxymethyl)omega(nonylphenoxy)- polyethylene glycol carboxymethyl nonylphenyl ether nonoxynol-8 carboxylic acid PEG-10 nonylphenyl ether carboxylic acid sodium laureth-11 carboxylate
CAS Number	53610-02-9
Structural Formula	



)4/2020	IMAP Group Assessment Report
Molecular Formula	(C2H4O)nC17H26O3
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(octylphenoxy)-, sodium salt
CAS Number	53879-49-5
Structural Formula	No Structural Diagram Available

Molecular Formula	(C2H4O)nC14H22O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphaacetylomega(nonylphenoxy)- polyethylene glycol, acetate, nonylphenyl ether nonylphenol polyethyleneglycol acetate
CAS Number	54612-40-7
Structural Formula	
Molecular Formula	(C2H4O)nC17H26O2
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega[(1,1,3,3-tetramethylbutyl)phenoxy]-, sodium salt Triton X-200 sodium alkyl aryl ether sulfate
CAS Number	55348-40-8

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Structural Formula	$\begin{bmatrix} \mathbf{n} \mathbf{x}^{T} \end{bmatrix} \xrightarrow{\mathbf{n}} \mathbf{n} \mathbf{n} \mathbf{n} \mathbf{n} \mathbf{n} \mathbf{n} n$
Molecular Formula	(C2H4O)nC14H22O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(4-octylphenoxy)-, sodium salt sodium octylphenoxy ether sulfate
CAS Number	58853-83-1
Structural Formula	No Structural Diagram Available

Molecular Formula	(C2H4O)nC14H22O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(phenylmethyl)omega[(1,1,3,3- tetramethylbutyl)phenoxy]- polyethylene glycol benzyl (1,1,3,3-tetramethylbutyl)phenyl ether poly(oxy-1,2-ethanediyl), alpha-(phenylmethyl)-omega-((1,1,3,3-tetramethylbutyl)phenoxy)-
CAS Number	60864-33-7
Structural Formula	$\begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} \\ \end{array} \\ \begin{array}{c} \end{array} \\ \end{array} $
Molecular Formula	(C2H4O)nC21H28O
Molecular Weight	Unspecified

Chemical Name in the	Poly(oxy-1,2-ethanediyl), .alpha(carboxymethyl)omega(diisononylphenoxy)-, sodium
Inventory and Synonyms	salt
CAS Number	68958-57-6



Chemical Name in the Inventory and Synonyms	Ethanol, 2-[2-[2-[2-(nonylphenoxy)ethoxy]ethoxy]ethoxy]-, hydrogen sulfate, ammonium salt nonylphenoxytri(ethyleneoxy)ethylammonium sulfate
CAS Number	63351-73-5
Structural Formula	





Chemical Name in the Inventory and Synonyms	Nonyl phenol ethoxylate blend nonionic ethylene oxide derivative TERIC 200
CAS Number	63496-57-1
Structural Formula	No Structural Diagram Available

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Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15,18-Hexaoxaeicosan-1-ol, 20-(dinonylphenoxy)-, dihydrogen phosphate</b> (dinonylphenol hepta(oxyethylene)) dihydrogen phosphate nonyl nonoxynol-7 phosphate
CAS Number	66172-78-9
Structural Formula	
Molecular Formula	C38H71O11P
Molecular Weight	734.94

Chemical Name in the Inventory and Synonyms	<b>3,6,9,12,15,18-Hexaoxaeicosan-1-ol, 20-(dinonylphenoxy)-, hydrogen phosphate</b> di(dinonylphenol hepta(oxyethylene))hydrogen phosphate nonyl nonoxynol-7 phosphate PEG-7 dinonyl phenyl ether phosphate
CAS Number	66172-83-6

Structural Formula	
Molecular Formula	C76H139O18P
Molecular Weight	1371.89

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(1,1-dimethylethyl)omega(octylphenoxy)-, branched (C8) branched alkylphenol, ethoxylated, tert-butyl ether
CAS Number	69279-01-2
Structural Formula	No Structural Diagram Available

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Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(isooctylphenoxy)-, sodium salt Isooctylphenol, ethoxylated, sulfated, sodium salt
CAS Number	67759-39-1
Structural Formula	No Structural Diagram Available
Molecular Formula	(C2H4O)nC14H22O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Ethanesulfonic acid, 2-[2-[2-(octylphenoxy)ethoxy]ethoxy]-,sodium salt 2-(2-(octylphenoxy)ethoxy)ethoxy)ethanesulfonic acid, sodium salt
CAS Number	67923-87-9
Structural Formula	



Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(carboxymethyl)omega(4-isooctylphenoxy)-, sodium salt p-isooctylphenoxypoly(ethyleneoxy)acetic acid, sodium salt
CAS Number	68015-73-6
Structural Formula	



Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, branched, phosphates (C9) branched alkylphenol, ethoxylate, phosphorate
CAS Number	68412-53-3
Structural Formula	No Structural Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(nonylphenyl)omegahydroxy-, branched (C9) branched alkylphenol, ethoxylate
CAS Number	68412-54-4
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), alpha -(nonylphenyl)-omega -hydroxy-, phosphate, ammonium salt
CAS Number	68511-21-7
Structural Formula	





Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(nonylphenoxy)-, branched, ammonium salt (C9) branched alkyl phenol ethoxylate sulfuric acid ammonium salt SDA 23-101-01 polyethylene glycol branched-nonylphenyl ether sulfate ammonium salt
CAS Number	68649-55-8
Structural Formula	No Structural Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(dinonylphenyl)omegahydroxy-, branched (C9) branched dialkylphenol ethoxylate
CAS Number	68891-21-4
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(nonylphenoxy)-, branched, sodium salt (C9) branched alkylphenol ethoxylate sulfuric acid, sodium salt SDA 23-101-04 sodium C9-branched alkylphenol ether sulfate
CAS Number	68891-39-4
Structural Formula	No Structural Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), a-(nonylphenyl)-w-hydroxy-, branched, phosphates, sodium salts polyoxyethylene NP branched ether phosphate sodium salt
CAS Number	68954-84-7
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(carboxymethyl)omegahydroxy-, C8-18 and C18- unsaturated alkyl and (octyl or nonyl)phenyl ethers, sodium salts
CAS Number	68987-89-3
Structural Formula	

## No Structural

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(octylphenyl)omegahydroxy-, branched (C8) branched alkyl phenol ethoxylate octylphenol ethoxylated branched
CAS Number	68987-90-6
Structural Formula	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(octylphenoxy)-, branched, sodium salt poly(oxy-1,2-ethanediyl), .alphasulfoomega(octylphenoxy)-, branched, sodium salt SDA 22-101-04 C8 branched alkylphenol ethoxylate sulfuric acid, sodium salt
CAS Number	69011-84-3

## No Structural

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alphasulfoomega(isononylphenoxy)-, sodium salt polyethylene glycol, isononylphenyl ether, sulfate, sodium salt
CAS Number	72580-36-0
Structural Formula	

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	D1—(C <sub>9</sub> H <sub>19</sub> )
	O O O D1 OH $O O D1$
	• Na
Molecular Formula	(C2H4O)nC15H24O4S.Na
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(4-nonylphenyl)omegahydroxy-branched polyethylene glycol mono(branched p-nonylphenyl) ether poly(oxy-1,2-ethanediyl), alpha-(4-nonylphenyl)-omega-hydroxy-, branched nonylphenol, 4-, branched, ethoxylated
CAS Number	127087-87-0
Structural Formula	

Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	Poly(oxy-1,2-ethanediyl), .alpha(isooctylphenyl)omegahydroxy-, phosphate poly(oxy-1,2-ethanediyl), a-(3-carboxy-1-oxo-2-propenyl)-?-(4-nonylphenoxy)-, (Z)-, branched poly(oxy-1,2-ethanediyl), a-[(2Z)-3-carboxy-1-oxo-2-propenyl]-?-(4-nonylphenoxy)-, branched
CAS Number	127184-51-4
Structural Formula	No Structural Diagram Available
Molecular Formula	(C2H4O)nC14H22O.xH3O4P
Molecular Weight	Unspecified

Chemical Name in the	Poly(oxy-1,2-ethanediyl), alpha-(3-carboxy-1-oxo-2-propenyl)omega(4-nonylphenoxy)-,
Inventory and Synonyms	(Z)-, branched
CAS Number	144468-71-3

# No Structural

### Diagram Available

Molecular Formula	Unspecified
Molecular Weight	Unspecified

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