Prepared for
Shell QGC Pty Limited
ABN: 44 098 563 663

Hydraulic Fracturing Risk Assessment for the Tight Gas Sands Project - Tracer Update

Tracer Update

06-Feb-2024
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Client: Shell QGC Pty Limited

ABN: 44 098 563 663

Prepared by

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1.0 Background

1.1 Introduction

Shell QGC Pty Limited (Shell QGC) commissioned AECOM Australia Pty Ltd (AECOM) to complete a Hydraulic Stimulation Risk Assessment for the planned and potential future hydraulic stimulation campaigns throughout the appraisal phase of the Bowen Basin Tight Gas Sands (TGS) Project.

This assessment is an update to and should be read in conjunction with the *AECOM (2023) Hydraulic Fracturing Risk Assessments for the Tight Gas Sands Project* for a full understanding of the chemical risk assessment methodology and approach utilised in this report.

1.2 Objective

Shell QGC is proposing to use chemical water tracers (FFI) to improve the efficiency of hydraulic fracture stimulation operations. This assessment considers the hydraulic fracturing fluid recipe HVFR_A in combination with these water tracers. It is noted that HVFR_A was previously assessed in AECOM (2023), however with the addition of the new water tracers, the mass balance and concentrations have been updated in this assessment.

1.3 Approach

The method used for this updated chemical risk assessment continued to follow the guidance provided by the *Department of the Environment and Energy, Exposure Draft - Chemical Risk Assessment Guidance Manual: for chemicals associated with coal seam gas extraction, 2017* (DoEE, 2017). The methodology adopted for the chemical risk assessment is in general accordance with the following:

- National Industrial Chemicals Notification and Assessment Scheme (NICNAS), *National Assessment of Chemicals Associated with Coal Seam Gas Extraction in Australia, 2017* (herein referred to as NICNAS 2017)
- enHealth. *Environmental Health Risk Assessment, Guidelines for Assessing Human Health Risks from Environmental Hazards, 2012*
- *National Environment Protection (Assessment of Site Contamination) Measure 1999 (ASC NEPM); Schedule B4, Site-specific health risk assessment methodology, 2013.*

The chemical risk assessment comprised the following tasks:

- Hazard assessment. An evaluation of the environmental hazard of the chemical additives in the hydraulic fracturing fluid systems, based on their environmental persistence, bioaccumulation and aquatic toxicity properties. Also included was an evaluation of human health effects (i.e. genotoxicity, carcinogenicity, reproductive toxicity, oral toxicity, inhalation toxicity, dermal toxicity, chronic repeated dose toxicity).
- Exposure assessment. The exposure assessment comprised of an evaluation of surface and sub-surface exposure pathways and mass balance calculations to identify relevant exposure point concentrations of each chemical additive of the hydraulic fracturing fluid system.
- Screening and validation processes via Tier 1 and Tier 2 assessments. Determination of chemicals known to be of low concern, and identification of chemicals for further quantitative assessment.
    - Tier 1: using published information about each chemical proposed to be used in the hydraulic fracturing fluid systems.
    - Tier 2: A quantitative evaluation of the risks using toxicity values and quantitative estimates of chemical intake to provide an estimate of potential human health risk associated with the hydraulic fracturing activities, based on the identification of complete exposure pathways and hazard identification.

2.0 Hydraulic Fracture Chemical Risk Assessment Tier 1 Screen

2.1.1 Outcome of Tier 1 screen

The hydraulic fracturing fluid recipe (*HVFR_A*) will be used in combination with the water tracers for the hydraulic fracture stimulation.

Comparison of the chemicals that will be used with the assessment criteria presented in DoEE (2017) indicated that three chemicals were considered not to require a Tier 2 assessment. These chemicals (presented in **Table 1**) have been assessed under the National Assessment of Chemicals Associated with Coal Seam Gas Extraction in Australia using the adapted IMAP screening process (NICNAS 2017) and were identified to be of low concern because of low hazard.

The toxicological profile for each chemical is provided in **Appendix B**.

Table 1 Chemicals identified to be of low human health concern (Tier 1)

CAS#	Chemical
6381-77-7	Sodium erythorbate
22042-96-2	Hepta sodium phosphonate
9003-05-08	Polyacrylamide

2.1.2 Identification of human health Chemicals of Potential Concern (COPC)

Theoretical exposure point concentrations (EPCs) were calculated, based on mass balance data for the hydraulic fracture stimulation fluid systems for two flow back scenarios, where 20% and 60% of the mass of chemicals injected into the well will be present in the flowback fluid.

The theoretical concentrations for hydraulic fracture stimulation chemicals in flowback fluid are presented in **Table 2**. The determination of COPC from the theoretical datasets were based on a comparison of the estimated concentrations with human health-based screening level guidelines. Where available, the National Water Quality Management (NHMRC), Australian Drinking Water Guidelines (ADWG) 2018 (i.e. concentrations in water that are safe for all members of the population to consume every day for a lifetime) have been identified and considered in this assessment. Where these guidelines are not available, and the available published reviews have identified a suitable Total Daily Intakes (TDI) or No Observed Adverse Effect Level (NOAEL) this value has been presented and used to derive a preliminary drinking water guideline following guidance provided by the National Health and Medical Research Council (refer to AECOM 2023 for more detail).

Table 2 Theoretical concentrations of COPC in flowback fluid – Campaign Fluid System

COPC	Mass Injected in Stimulation Fluid (mg/L)	Flowback Concentration		Adopted Screening Level Guideline (mg/L)	Selected as COPC?
		20% mass recovery (mg/L)	60% mass recovery (mg/L)		
64742-47-8	Petroleum Distillates (Hydrotreated, Light)	290	871	39 (D)	Yes
14808-60-7	Crystalline silica, quartz	27	82	NA. Not toxic via oral exposure as not absorbed via GI tract	No
7647-01-0	Hydrochloric acid	225	676	NA. Acute toxicity only (irritant and corrosive)	No
111-30-8	Glutaraldehyde	46	139	0.156 (D)	Yes
67-63-0	Isopropanol	0.31	0.93	9.95 (D)	No
68551-12-2	Ethoxylated C12-C16 Alcohol	0.24	0.73	1.95 (D)	No
104-55-2	Cinnamaldehyde	0.09	0.28	7.8 (D)	No
67-56-1	Methanol	0.007	0.021	0.145 (D)	No
127087-87-0	Polyethylene glycol trimethylnonyl ether	0.90	2.69	0.2 (D)	Yes
490-97-1 499-90-1 67852-79-3 499-57-0 6185-28-0 1765-08-8 522651-44-1 17264-74-3 522651-42-9 530141-39-0 402955-41-3 522651-48-5 1604819-08-0 17264-88-9 321992-77-2	Water Tracers FFI (Sodium Benzoate)*	0.015 ^{A}	0.042 ^{A}	3.9 (D)	No
1310-73-2	Sodium hydroxide (caustic soda)	0.014	0.041	NA. Acute toxicity only (irritant and corrosive), not systemically available in body	No

**Tracers assessed using analogue chemical (refer to toxicity profiles for more information), (D) – derived (refer to individual toxicity profiles for more information); A –Total concentrations of water tracers*

2.1.3 Persistence, bioaccumulation and environmental toxicity (PBT) – Identification of environmental COPCs

A PBT evaluation was undertaken to assess the chemicals based on persistence (P), bioaccumulation (B) and toxicity (T). The PBT assessment has been conducted according to guidance developed by NICNAS and DoEE (2017). The criteria considered are presented in **Table 3**. Refer to *AECOM (2023) Hydraulic Fracturing Risk Assessments for the Tight Gas Sands Project* for further details regarding the methodology and approach for the PBT evaluation.

Table 3 PBT criteria adopted by NICNAS

Criterion	PBT criteria		
P	For PBT purposes a chemical is considered persistent in a particular media if its half-life in the media exceeds the following: Half-life ($T_{1/2}$) >2 months in water Half-life ($T_{1/2}$) >6 months in soil Half-life ($T_{1/2}$) >6 months in sediment Half-life ($T_{1/2}$) >2 days in air		
B	For PBT purposes a chemical is considered to be bioaccumulative if it has a BCF/BAF of >2000, or in its absence of any BCF/BAF measurement a log K_{ow} >4.2.		
T	For PBT purposes, in respect of aquatic toxicity, a chemical may be considered toxic under the following circumstances (corresponding to criteria for GHS chronic category 1:		
	Non-rapidly degradable substances for which there are adequate chronic toxicity data available	Chronic NOEC or EC_x (for fish)	<0.1 mg/L and/or
		Chronic NOEC or EC_x (for crustacea)	<0.1 mg/L and/or
		Chronic NOEC or EC_x (for algae or other aquatic plants)	<0.1 mg/L
	Rapidly degradable substances for which adequate chronic toxicity data are available	Chronic NOEC or EC_x (for fish)	<0.01 mg/L and/or
		Chronic NOEC or EC_x (for crustacea)	<0.01 mg/L and/or
		Chronic NOEC or EC_x (for algae or other aquatic plants)	<0.01 mg/L
	Substances for which adequate chronic toxicity data are not available (providing criteria for P and B are met)	96 h LC_{50} (for fish)	<1 mg/L and/or
		48 h EC_{50} (for crustacea)	<1 mg/L and/or
		72 or 96 ErC_{50} (for algae or other aquatic plants)	<1 mg/L
		And the substance is not rapidly degradable and/or the experimentally determined BCF is >500 (or, if absent, the log K_{ow} is >4.2	
	Toxicity to other (terrestrial) organisms	Should be considered on a case by cases basis, compared with the highly toxic classifications DotE has developed for ag/vet chemicals	
	Long term toxicity or evidence such as endocrine disruption effects	Should be considered on a case-by-case basis.	

The Australian Government criteria for PBT chemicals[1] highlights indicators and numerical thresholds for persistence, bioaccumulation and toxicity for a range of media, however it notes that *"These criteria are not directly applicable to metals and other inorganic chemicals"*.

Based on this approach, the chemicals proposed to be used in hydraulic fracture stimulation fluid have been evaluated, the outcomes of the assessment are summarised in **Table 4**.

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[1] https://www.dcceew.gov.au/sites/default/files/documents/australian-pbt-criteria.pdf

Table 4 PBT assessment of the hydraulic fracture stimulation fluid system chemicals to be used for the campaign

Substance	P/vP Criteria Fulfilled	B/vB Criteria Fulfilled	T Criteria Fulfilled?	Overall Conclusion
Methanol 67-56-1	No. Methanol is expected to be readily biodegradable.	No. The Log Kow for methanol is -0.77. Thus, methanol does not meet the screening criteria for bioaccumulation.	No. The EC50s from the acute aquatic toxicity data on methanol are >1 mg/L, hence does not meet the screening criteria for toxicity.	Not PBT
Propan-2-ol (Isopopranol) 67-63-0	No. Isopropanol is readily biodegradable and thus it does not meet the screening criteria for persistence.	Based on a measured log Kow of 0.05 and a calculated BCF of 1, isopropanol does not meet the screening criteria for bioaccumulation.	The chronic toxicity data on isopropanol show NOECs of >0.01 mg/L. Thus, isopropanol does not meet the screening criteria for toxicity.	Not PBT
Cinnamaldehyde 104-55-2	No. Based on the results of the ready biodegradability studies, cinnamaldehyde is categorised as Not Persistent.	Based on low log K values and/or expected natural metabolism and regulation of internal concentrations, the chemical is categorised as Not Bioaccumulative	Based on measured acute toxicity endpoints of greater than 1 mg/L cinnamaldehyde is categorised as Not Toxic.	Not PBT
Glutaraldehyde 111-30-8	No. Readily biodegradable and as such not persistent in the environment.	No. As the Log Pow is -0.01 (Log Pow < 4.5), it is not expected to be bioaccumulative.	No. Chronic toxicity data >1 mg/L in invertebrates, thus glutaraldehyde does not meet the screening criteria for toxicity.	Not PBT
Sodium Erythorbate 6381-77-7	No. The chemical readily biodegradable (based on modelled data).	No. The Log Pow is -3.29 (Log Pow < 4.5) which does not meet the screening criteria for bioaccumulation.	No. Based on measured acute toxicity endpoints of greater than 1 mg/L Sodium erythorbate does not meet the screening criteria for toxicity.	Not PBT
Polyacrylamide 9003-05-8	Yes. Anionic polyacrylamide is a large molecular weight, water-soluble polymer. It is not expected to be readily biodegradable; thus, it meets the screening criteria for persistence. A Tier 1 Human Health and Environmental Assessment for this chemical has been conducted by NICNAS which concluded that it was low concern to	No. Pharmacokinetic studies showed that anionic polyacrylamide was not bioavailable to rats when ingested; this is most likely due to its large size (high molecular weight) and presumed resistance to break down in the gastrointestinal tract. Anionic polyacrylamide is thus not expected to	No. The acute LC50 values in fish and invertebrates are >1 mg/L. Thus, it does not meet the criteria for toxicity.	Not BT. Potentially P.

Substance	P/vP Criteria Fulfilled	B/vB Criteria Fulfilled	T Criteria Fulfilled?	Overall Conclusion
	human health and the environment and thus required no further assessment.	be bioavailable to aquatic or terrestrial organisms. It is not expected to meet the criteria for bioaccumulation.		
Petroleum Distillates (Hydrotreated, Light) 64742-47-8	No. This chemical is expected to be biodegradable. The ready biodegradability of SHELLSOL NF a solvent naphtha (petroleum), heavy aromatics (consists predominantly of C9 aromatics 25%m/m; C10 aromatics 65%, and indanes 10%) was studied in mineral nutrient medium inoculated with activated sludge (mixed liquor suspended solids 100-101 mg/L, pH 6.9) and incubated for 28 days at 20°C. SHELLSOL NF is readily biodegrade after 28 days but not within the 10-day window.	Category members have a potential to bioaccumulate, based on calculated log BCF values for constituents that range from 2.78 to 4.06, and calculated BCF values of 598 to 11,430 L/kg wet-weight, based on the Arnot and Gobas model, that take into account biotransformation of the chemicals in fish tissue. This chemical also has a log Kow of 6.025.	Yes. The lowest acute endpoint is <1 mg/L.	Not P. Potentially B and T.
Ethoxylated C12-C16 Alcohol 68551-12-2	No. These chemicals were found to be readily biodegradable. Thus, it does not meet the screening criteria for persistence.	No. Bioaccumulation in organisms is expected to be negligible, due to biotransformation and excretion of alcohol ethoxylates.	No. The NOECs from the chronic aquatic toxicity data are >0.01 mg/L, hence does not meet the screening criteria for toxicity.	Not PBT
Hepta sodium phosphonate (22042-96-2)	Yes. Hepta sodium phosphonate and its sodium salts are not readily biodegradable.	No based on the low log Kow (-3.40), DTPMP is not bioaccumulative.	No. The NOEC from a chronic fish study on DTPMP is >0.1 mg/L.	Not BT. Potentially P
Polyethylene glycol trimethylnonyl ether (127087-87-0)	No. Based on results obtained from biodegradation studies, this chemical is categorised as Not Persistent.	No. Based on the available measured bioconcentration data, this chemical is categorised as Not Bioaccumulative.	No. Based on available acute ecotoxicity values above 1 mg/L and chronic ecotoxicity values above 0.1 mg/L, this chemical is categorised as Not Toxic.	Not PBT
Water Tracers* 490-97-1, 499-90-1, 67852-79-3, 499-57-0, 6185-28-0, 1765-08-8, 522651-44-1, 17264-74-3,	No. Sodium benzoate is readily biodegradable and as such not persistent in the environment.	Based on the log Kow of 1.88, sodium benzoate is not bioaccumulative.	The acute aquatic toxicity of sodium benzoate is > 100 mg/L for all four trophic levels. Hence the substance does not fulfil the screening criteria for toxicity.	Not PBT

Substance	P/vP Criteria Fulfilled	B/vB Criteria Fulfilled	T Criteria Fulfilled?	Overall Conclusion
522651-42-9, 530141-39-0, 402955-41-3, 522651-48-5, 1604819-08-0, 17264-88-9, 321992-77-2				

Tracers assessed using analogue chemical (refer to toxicity profiles for more information),* As illustrated in **Table 4, the organic compounds utilised in hydraulic fracture stimulation fluids are not considered to be PBT (i.e., none of the organic chemicals meet all three criteria of being persistent *and* bioaccumulative *and* toxic, refer to *AECOM (2023) Hydraulic Fracturing Risk Assessments for the Tight Gas Sands Project* for further information). As such, the compounds are expected to degrade in the sub-surface, or where these compounds are present in flowback fluid, they will subsequently readily degrade or dissociate in the environment and will not bioaccumulate in terrestrial or aquatic species.

Polyacrylamide and hepta sodium phosphonate have limited biodegradation potential however, they are not bioaccumulative and are essentially non-toxic to aquatic species. Petroleum distillates meet the screening criteria for bioaccumulation and toxicity; however, the chemical is expected to be biodegradable and adverse chronic outcomes are not evident based on its lack of persistence in the environment.

It is noted that the PBT evaluation is not directly applicable to hydrochloric acid, crystalline silica and sodium hydroxide. Crystalline silica is an inorganic substance which is ubiquitous in the environment. Sodium hydroxide is an inorganic salt. Sodium and hydroxide ions are ubiquitous and present in most water, soil and sediment. Hydrochloric acid is an inorganic salt that dissociates completely to hydrogen and chloride ions in aqueous solutions, and are present in most water, soil and sediment. Biodegradation is not applicable to these inorganic ions. Hydrogen and chloride ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. Thus, hydrochloric acid is not expected to bioaccumulate. A quantitative evaluation of the environmental risk posed by the COPCs above is presented in **Section 4.0**.

It is to be noted that some constituents used in hydraulic fracture stimulation fluid, such as sand, are solids that once injected into the well are used to prop open fractures in the TGS. These constituents are not sufficiently mobile and will not be materially extracted in flowback fluid. Hence the presence of these constituents in hydraulic fracture stimulation fluid does not warrant any further evaluation in this risk assessment.

3.0 Human Health Risk Assessment Tier 2 Screen

3.1.1 Tier 2 Screen Methodology for Human Health Risk

The fracture stimulation campaign will be carried out using the same operation, monitoring and assessment procedures as for the general campaign as described *AECOM (2023) Hydraulic Fracturing Risk Assessments for the Tight Gas Sands Project* using the fluid recipe HVFR_A and water tracers.

As such, the Tier 2 screening was based on the following information:

- Detailed operational procedures have been provided that are designed to contain the hydraulic fracture stimulation fluids within the TGS, and no connection exists between groundwater in the TGS and surface-water, aquifers utilised for the purpose of extraction (for any beneficial use), or springs (refer to AECOM 2023). As such, no further assessment is considered warranted for groundwater as there are no potentially complete exposure pathways.
- Potential risks to workers involved with the hydraulic fracture stimulation process, where the COPC are handled on and off-site (i.e., during transportation of the COPC to the site), have not been considered as detailed Health and Safety (H&S) procedures are employed to manage these exposures. It is noted that potentially complete pathways to workers would include dermal contact and incidental ingestion.
- It is noted that none of the COPC identified for consideration in this HHRA are persistent and bioaccumulative and toxic, hence secondary pathways (such as accumulation in crops and produce, and subsequent human consumption) were not quantified.
- The flowback fluid recovered during completion operations will be stored in a flowback tank where it will be held on-site for a maximum period of 3 years, after which the fluid will be trucked off-site to a disposal facility authorised to receive this waste stream.

  These flowback tanks are double lined with galvanised steel frame. Flowback tanks are inspected and monitored for leaks during the operational periods when they are used for holding fluid. The tanks are also covered with a floating cover to reduce evaporation losses.

While it is expected that the flowback tanks are not accessible to the public, exposure may occur if trespassers enter the tanks, or if there is a leak in the pipelines or flowback tank and water from this infrastructure is released to the local environment.

Based on the available information, the key receptors (and exposures that are considered significant) who may be exposed to the COPC identified on and off the site includes the following:

Trespassers

- Direct contact (ingestion and dermal contact) with COPC identified in flowback fluid contained within the flowback holding tanks. It is noted that this is a conservative scenario as the drill pad is fenced with signage and the holding tanks are covered with a floating cover to limit trespasser access.

The following **Table 5** presents an overview of the parameters selected. These parameters, as well as relevant references, are utilised in the exposure models presented **Appendix C**, the equations used to estimate exposure are also provided in **Appendix C**.

Table 5 Exposure Parameters – Trespassers

Exposure Factor	Units	Trespasser	Reference / Source
Exposure Frequency	Days/year	Assume direct contact with flowback fluid occurs over 1 day within the period that the flowback pond is on-site	Professional judgement
Exposure Duration	Year	The maximum duration of a flowback fluid on-site is 3 years.	QGC
Exposure Time Outdoors	Hours/day	Assumes adults/children get completely wet for 1 hour each time	Professional judgement
Surface Area	cm^2	20,000 cm^2 for adults, 15,900 cm^2 for children. Exposure is assumed to be equal to that of swimming, where the whole body gets wet	enHealth 2012
Body Weight	kg	78 kg for adults, 39 kg for children	enHealth 2012

3.1.2 Chemicals of Potential Concern

Exposure point concentrations (EPC) were developed for each of the hydraulic fracturing fluid systems using theoretical calculations, where it was conservatively assumed that between 20% and 60% of the mass of the chemicals injected into the well will be present in the flowback water. A summary of the chemicals that require further assessment are presented in **Table 6.**

Table 6 Chemicals requiring further assessment (Tier 2)

CAS	Chemical Name
111-30-8	Glutaraldehyde
127087-87-0	Polyethylene glycol trimethylnonyl ether
64742-47-8	Petroleum Distillates (Hydrotreated, Light)

3.1.3 Outcome of Tier 2 Screen

For the assessment of the overall potential for adverse human health effects posed by simultaneous exposure to multiple chemicals, the estimated daily intake of the chemicals by inhalation and direct (ingestion and dermal) contact were compared to acceptable risk-based intakes to calculate an individual hazard quotient (HQ) and then summed for all constituents into a hazard index (HI).

Consistent with Australian risk assessment methodologies, if the HI is less than or equal to 1, then no adverse health effects are likely associated with exposures. However, if the total HI is greater than 1, adverse health effects may be possible and therefore the assumptions inherent in the risk characterisation process warrant further evaluation.

3.1.3.1 Stimulation Fluids

A summary of the calculated risks for the trespassers that are relevant to the assessment of potential exposure to COPCs in stimulation fluid HVFR_A and the chemical tracers on-site, based on the available data is presented in **Table 7**.

Table 7 Risk associated with potential exposure to trespassers – campaign hydraulic fracture stimulation fluid system (theoretical data)

Receptor and Pathway	Non-Threshold Carcinogenic Risk	Threshold Hazard Index	Non-Threshold Carcinogenic Risk	Threshold Hazard Index
	20% Mass Return		60% Mass Return	
Hydraulic fracture stimulation fluid system - COPC associated with theoretical data				
Adult Trespassers				
Ingestion of chemicals via incidental contact with flowback fluid	NA	0.002	NA	0.006
Dermal exposure to chemicals via incidental contact with flowback fluid	NA	0.04	NA	0.1
Total Risk	NA	**0.04**	NA	**0.1**
Child Trespassers				
Ingestion of chemicals via incidental contact with flowback fluid	NA	0.004	NA	0.01
Dermal exposure to chemicals via incidental contact with flowback fluid	NA	0.06	NA	0.2
Total Risk	NA	**0.07**	NA	**0.2**

Notes:
Risk values have been rounded to two significant figures with totals rounded to one significant figure; hence, the sum of individual risks may not add up exactly to the total presented.
NA = Not Assessed as there are no non-threshold COPC in the media of concern

The following can be noted from the table above:

- The calculated risks associated with potential exposure to COPC identified in flowback fluid, where the campaign hydraulic fracture stimulation fluid and chemical tracers are used and assuming 20% or 60% mass recovery are below the target 1, hence, risks are considered to be low and acceptable.

It is to be noted that this assessment does not replace the requirement for appropriate occupational health and safety procedures and management plans. Crystalline silica is scheduled by Safe Work Australia as a chemical for which health monitoring may be required.

The Tier 2 assessment is provided in **Appendix C**, the chemical toxicological profiles are provided in **Appendix B.**

3.1.4 Conclusions

The quantification of potential risks to human health associated with the use of chemicals in well simulation activities conducted by Shell QGC within the campaign project area has involved the assessment of potential exposures to compounds used or formed in the simulation activities. Based on the conceptual site model, operational controls and management practices implemented by Shell QGC, the only potentially complete exposure pathway identified and quantified in the risk assessment was the incidental ingestion and dermal contact by trespassers at the flowback tank.

On the basis of the conservative assessment undertaken, and with consideration of the uncertainties identified AECOM (2023), in relation to potential exposures to flowback fluid from well simulation activities, no unacceptable risks to trespassers were identified.

4.0 Environmental Risk Assessment

4.1.1 General

A qualitative environmental risk assessment (ERA) was conducted to evaluate the potential for adverse environmental effects to environmental receptors that may be exposed to residual levels of hydraulic fracture stimulation fluids. The hydraulic fracture stimulation campaign will be carried out using the same hydraulic fracture stimulation design, operation, monitoring and assessment procedures as for the campaign as described in *AECOM (2023) Hydraulic Fracturing Risk Assessments for the Tight Gas Sands Project*. As such, the environmental risk assessment approach remains similar to that as described in AECOM (2023).

4.1.2 Deriving Screening Criteria

The potential COPEC in the hydraulic fracture stimulation fluid recipe were reviewed and quantitative toxicity values were identified / derived in accordance with guidance in the Environmental Risk Assessment Guidance Manual for Industrial Chemicals prepared by the Australian Environmental Agency (AEA, 2009). Detailed discussion regarding the methodology is presented in AECOM (2023), but the process essentially involves identifying a literature toxicological endpoint and associated concentration and applying a safety factor (assessment factor). **Table 8** below presents the summary of derived TRVs for the Protection of Aquatic Species or Predicted No Effect Concentration (PNECs). **Appendix C** presents the environmental reviews of the COPEC identified in the hydraulic fracture stimulation fluid and includes further details on the endpoints selected and PNEC values calculated for each potential COPEC.

Table 8 Summary of derived TRVs for protection of aquatic species (PNECs) for the Campaign Fluid System

CAS #	Chemical	Endpoint	E(L)C50 or NOEC (mg/L)	Assessment Factor	PNEC Aquatic (mg/L)
111-30-8	Glutaraldehyde	48 h acute Daphnia	2.1	10	0.21
7647-01-0	Hydrochloric Acid	Chronic Daphnia	62	10	6.2
64742-47-8	Hydrotreated light petroleum distillate	Acute Daphnia	0.018	100	0.00018
68551-12-2	Ethoxylated C12-C16 Alcohol	Chronic daphnia	0.11	10	0.011
104-55-2	Cinnamaldehyde	72 hr Algae	2	10	0.20
127087-87-0	Polyethylene glycol trimethylnonyl ether	Chronic fish	0.048	100	0.00048
22042-96-2	Hepta sodium phosphonate	Chronic fish	25.6	100	0.26
6381-77-7	Sodium erythorbate	Acute Algae	1020	100	10.2
67-63-0	Propan-2-ol	Chronic Daphnia	5000	10	500
1310-73-2	Sodium hydroxide	Chronic Daphnia	240	100	2.4
490-97-1 499-90-1 67852-79-3 499-57-0 6185-28-0 1765-08-8 522651-44-1 17264-74-3	Water Tracers (Sodium Benzoate)*	Acute fish	1000	100	10

CAS #	Chemical	Endpoint	E(L)C50 or NOEC (mg/L)	Assessment Factor	PNEC Aquatic (mg/L)
522651-42-9 530141-39-0 402955-41-3 522651-48-5 1604819-08-0 17264-88-9 321992-77-2					
14808-60-7	Crystalline silica, quartz	This chemical has been identified by NICNAS to be of low concern to the environment based on Tier I assessment under the IMAP assessment framework.			
9003-05-08	Polyacrylamide	This chemical has been identified by NICNAS to be of low concern to the environment based on Tier I assessment under the IMAP assessment framework.			
67-56-1	Methanol	This chemical has been identified by NICNAS to be of low concern to the environment based on Tier I assessment under the IMAP assessment framework.			

**Tracers assessed using analogue chemical (refer to toxicity profiles for more information),*

4.1.2.1 Tier 1 Environmental Screening Assessment

The potential for chemicals in the hydraulic fracture stimulation fluid recipe to represent a potential environmental hazard was characterised in accordance with the methodologies discussed in **Section 1.0**. If the environmental hazard quotient was less than or equal to 1.0, then the chemical was not considered to be a COPEC and was not carried forward in the assessment. A summary of the Environmental Tier 1 Screening Assessment and the identification of the COPECs are presented in **Table 9**. The hazard calculations are presented in **Appendix C**.

The source concentrations for the Tier 1 Screen were based on a theoretical data set (assuming 20% and 60% mass recovery in flowback fluid). The theoretical COPEC concentrations for the theoretical scenarios for the identified receptor group (aquatic invertebrates and fish) are presented in **Table 9**.

The environmental hazard calculations presented in **Appendix C** do not consider the significant dilution that is expected to occur where flowback fluid is discharged to a surface water body in the event of a significant spill or leak. In addition, natural attenuation processes such as sorption and biodegradation have not been considered.

Table 9 Hazard Summary of COPEC for the Campaign Fluid System

CAS	Chemical	Flowback Concentration 20% mass recovery (mg/L)	Flowback Concentration 60% mass recovery (mg/L)	PNEC	HQ >1	Selected as COPEC?
111-30-8	Glutaraldehyde	46	139	0.21	Yes	Yes
7647-01-0	Hydrochloric Acid	225	676	6.2	Yes	Yes
64742-47-8	Hydrotreated light petroleum distillate	290	871	0.00018	Yes	Yes
68551-12-2	Ethoxylated C12-C16 Alcohol	0.24	0.73	0.011	Yes	Yes
104-55-2	Cinnamaldehyde	0.09	0.28	0.20	Yes	Yes

CAS	Chemical	Flowback Concentration 20% mass recovery (mg/L)	Flowback Concentration 60% mass recovery (mg/L)	PNEC	HQ >1	Selected as COPEC?
127087-87-0	Polyethylene glycol trimethylnonyl ether	0.90	2.69	0.00048	Yes	Yes
22042-96-2	Hepta sodium phosphonate	26	77	0.26	Yes	Yes
6381-77-7	Sodium erythorbate	3.1	9.3	10.2	No	No
67-63-0	Propan-2-ol	0.31	0.93	500	No	No
1310-73-2	Sodium hydroxide	0.014	0.041	2.4	No	No
490-97-1 499-90-1 67852-79-3 25832-58-0 499-57-0 6185-28-0 1765-08-8 522651-44-1 17264-74-3 3686-66-6 118537-84-1 10007-84-8 38402-11-8 855471-43-1 1938142-12-1	Water Tracers (Sodium Benzoate) *	0.014	0.042	10	No	No

**Tracers assessed using analogue chemical (refer to toxicity profiles for more information),*

4.1.3 Exposure assessment

The operational area for the campaign is considered a highly modified system that has minimal wildlife habitat to support a functioning aquatic or terrestrial ecosystem. The adjacent areas comprise unimproved pastures and remnant native vegetation, both of which are used for cattle grazing purposes. A range of surface water systems that include streams, creeks dams and rivers also exist nearby.

The security and management practices implemented by Shell QGC for the campaign are described in AECOM (2023). The flowback fluid will be contained inside a flowback tank (with at least 3 m high walls and bunded), there would be minimal opportunity for environmental receptors to interact with the flowback fluid.

As the objective of this qualitative ERA is to evaluate the potential risks from a typical gas wellfield, the selection of environmental receptors for this ERA is based on understanding that the selected environmental receptors all have an equal opportunity to be exposed to residual hydraulic fracture stimulation flowback fluid at any of the gas fields within the project area.

As such, exposure assessment was based on the following information:

- Detailed operational procedures have been provided that are designed to contain the hydraulic fracture stimulation fluids within the target formation, and no connection exists between groundwater in the target formation and surface-water, aquifers utilised for the purpose of extraction (for any beneficial use), or springs (refer to AECOM 2023). No further assessment is considered warranted for groundwater as there are no potentially complete exposure pathways.

- Due to the engineered controls and barriers that Shell QGC has implemented to contain the flowback fluid (refer to AECOM 2023); no material exposure pathway is considered to exist for terrestrial environmental receptors. The site is fenced and the flowback fluid is contained in bunded aboveground tanks, with walls of up to 3 metres in height. Terrestrial receptors identified to exist near the site and surrounds include domesticated livestock (cattle), large mammalian wildlife (kangaroos) and small mammalian wildlife (dingos). The fencing and the height of the above ground holding ponds will effectively limit their access to the flowback fluid. As such, the risk to terrestrial receptors has not been further assessed.
- The holding tanks are covered with a floating roof, limiting access for birds or bats to fly in and drink the flowback fluid or become trapped in the tank. As such, this exposure pathway is not considered to be of significance and has not been further assessed.
- It is noted that three COPEC for consideration in this ERA were either persistent, or bioaccumulative or toxic. However, none of the compounds utilised in hydraulic fracture stimulation fluids were persistent and bioaccumulative and toxic (PBT) in the environment. Polyacrylamide and hepta sodium phosphonate have limited biodegradation potential however, they are not bioaccumulative and are essentially non-toxic to aquatic species. Petroleum distillates meet the screening criteria for bioaccumulation and toxicity; however, the chemical is expected to be biodegradable and adverse chronic outcomes are not evident based on its lack of persistence in the environment.
- Whilst considered minimal, there is the potential for a release of stored hydraulic fracture stimulation flowback fluid to surface water systems located near the gas well pads in the situation of an accidental release, such as from piping, leaks, or failure of overflow system in the event of heavy rainfall. The flowback tanks are held on-site for a maximum period of 3 years, after which the fluid will be trucked off-site to a disposal facility authorised to receive this waste stream.

Based on the available information, the key receptors (and exposures that are considered significant) who may be exposed to the COPEC identified on and off the site includes the following:

Aquatic invertebrates and fish

- Direct contact (ingestion and dermal contact) with residual hydraulic fracture stimulation chemicals identified in surface water in the event of a release of stored flowback fluid.

The assessment endpoints, or environmental values selected was the survival and reproduction of aquatic invertebrates. The assessment endpoints are sensitive to the residual hydraulic fracture stimulation flowback fluid COPEC identified and have the toxicological and life history databases to support their use as representatives of the study area ecosystem.

4.1.4 Interpretation of environmental significance

The estimated environmental hazards have been qualitatively evaluated via a hazard quotient approach to determine their environmental significance for the operations evaluated in this assessment. The Tier 1 screen results show that most chemicals from the theoretical data for the campaign fluid system exceed the acceptable hazard threshold of 1.0 for aquatic receptors and were considered potential COPEC.

It is noted that the Tier 1 Screen is a conservative approach to identify potential environmental hazards associated with storage of these chemicals. In order for this hazard to result in potential environmental harm, there would need to be a significant spill or release event directly to an adjacent surface water body, with no or inadequate operational or spill management controls.

The campaign wells are located in the Condamine and Balonne rivers catchment. The southern part of ATP645 occurs within the Border Rivers and Moonie catchment. There are no springs considered to be potentially affected by TGS development located within 10 km of campaign TGS wells (OGIA, 2019).

In reviewing and considering the significance of the potentially complete exposure pathways, the following points have been considered:

- It is noted that this estimated potential risk is based on a significant spill or release event directly to an adjacent surface water body.

- The environmental risk calculations presented in this assessment do not take into account dilution that could occur where flowback fluid is discharged to a surface water body in the event of a significant spill or leak. Processes such as sorption and biodegradation have not been considered. During normal operation procedures there are no discharges to surface waterbodies.
- Furthermore, the lack of a robust aquatic toxicological database resulted in aquatic screening values for the theoretical exposure scenario COPEC to be conservative, which is expected to significantly overestimate the actual risk.

Notwithstanding this conservative approach to estimating environmental exposure levels, risk management measures are routinely implemented by Shell QGC which effectively minimise or removes the risk of accidental spills and releases of flowback fluid. These include:

1. Layout design development criteria are followed for placement of petroleum activity infrastructure, to minimise activities that require earthworks, vegetation clearing and/or placing fill (other than that is associated with the construction of linear infrastructure) in or within watercourses, wetlands, lakes, and springs.
2. Implementation of spill containment procedures during operations to prevent migration of and exposure to chemicals, and if a spill was to occur, rectification measures would be taken immediately and notification to DES of any unauthorised releases would be made. Secondary containment bunds will be added to the drill pads as a spill containment measure.
3. Routine integrity inspections are undertaken of equipment and storage tanks prior, during and post stimulation. Continuous monitoring and evaluation of well production data versus fluid storage and transfer during the production test phase.
4. Routine inspection of the flowback tank(s) and associated equipment (e.g., blender, hoses, pumps) to check for leakage of flowback fluid.
5. Flowback tank and equipment is manned during the hydraulic fracture stimulation operation and as required, fluid is transferred to vacuum truck for disposal to ensure freeboard in the tank is maintained.
6. Pre-job inspection of the flowback tank and fluid connections to confirm integrity.
7. A vacuum truck with 20,000 L capacity and a front-end loader excavator located permanently on the site, available to assist in emergency spill situations, if required.

On every wellsite included in the campaign, a Shell QGC representative inspects the site to verify controls 3 to 7 from the above list are occurring. The operational controls are routinely evaluated by Shell QGC and modifications and revisions made, where necessary.

With consideration of the above engineered controls and mitigation measures, while potential impacts to aquatic receptors could occur if releases of flowback fluid reach adjacent surface waterbodies, the likelihood that these chemicals may be discharged to an environment where a significant level of exposure may occur is considered unlikely. Therefore, it is considered that due to the engineered controls and routine implementation of existing operational management measures by Shell QGC, potential risks to aquatic environmental receptors are adequately managed.

4.1.5 Conclusions

The qualitative evaluation of potential risks to the environment associated with the use of chemicals in well simulation activities conducted by Shell QGC within the project area has involved the assessment of potential exposures to compounds used or formed in the simulation activities. On the basis no complete exposure pathways have been identified for environmental receptors, due in part to the control measures implemented by Shell QGC (described in AECOM 2023), the potential risks to the environment from the use of the hydraulic fracturing fluid (HVFR_A) with the chemical tracers are considered low and acceptable.

5.0 References

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Appendix A

Mass Balance

HVFR_A and Chemical Tracers Fluid Recipe

Chemical Name	CAS Number	Density (kg/L)	Volume of Chemical (L)	Volume Fraction (%v/v)	Chemical Mass in Fluid (kg)	Mass Fraction (% w/w)	Concentration in Injected Fluid (mg/L)	Flowback Concentration Assuming 20% Mass Recovery (mg/L)	Flowback Concentration Assuming 60% Mass Recovery (mg/L)
Petroleum Distillates (Hydrotreated, Light)	64742-47-8	0.8	11472.677	0.1664070%	9178	0.1%	1451	290	871
Quartz or Organophilic phyllosilicate (crystalline silica, quartz)	14808-60-7	2.65	327.791	0.0047540%	869	0.0%	137	27	82
Hydrochloric acid	7647-01-0	1.15	6189.145	0.0897710%	7130	0.1%	1127	225	676
Glutataldehyde	111-30-8	1.1	1383.567	0.0200680%	1467	0.0%	232	46	139
Isopropanol	67-63-0	0.79	12.492	0.0001810%	10	0.000%	1.6	0.31	0.93
Ethoxylated C12-C16 Alcohol	68551-12-2	0.9	8.517	0.0001240%	8	0.000%	1.2	0.24	0.73
Cinnamaldehyde	104-55-2	1.05	2.839	0.0000412%	3	0.000%	0.47	0.09	0.28
Sodium erythorbate	6381-77-7	1.95	49.958	0.0007250%	98	0.001%	15.4	3.09	9.26
Methanol	67-56-1	0.79	0.284	0.0000040%	0.225	0.0000%	0.04	0.01	0.02
Hepta sodium phosphonate	22042-96-2	1.945	414.957	0.0060190%	807	0.010%	128	26	77
Polyacrylamide	9003-05-08	1.189	15488.114	0.2246490%	18415	0.235%	2911	582	1747
Polyethylene glycol trimethylnonyl ether	127087-87-0	1.04	27.316	0.0003960%	28	0.00036259%	4.5	0.90	2.69
Sodium 2-fluorobenzoate	490-97-1	1.00	0.029	0.000000430%	0.029000	0.00000037%	0.004584	0.000917	0.002751
Sodium 4-fluorobenzoate	499-90-1	1.00	0.029	0.000000420%	0.029000	0.00000037%	0.004584	0.000917	0.002751
Sodium 2,3,4,5-tetrafluorobenzoate	67852-79-3	1.00	0.041	0.000000600%	0.041000	0.00000052%	0.006481	0.001296	0.003889
Sodium 3-fluorobenzoate	499-57-0	1.00	0.03	0.000000430%	0.030000	0.00000038%	0.004742	0.000948	0.002845
Sodium 2,6-difluorobenzoate	6185-28-0	1.00	0.032	0.000000460%	0.032000	0.00000041%	0.005059	0.001012	0.003035
Sodium 2,4-difluorobenzoate	1765-08-8	1.00	0.032	0.000000460%	0.032000	0.00000041%	0.005059	0.001012	0.003035
sodium 3,4-difluorobenzoate	522651-44-1	1.00	0.032	0.000000460%	0.032000	0.00000041%	0.005059	0.001012	0.003035
Sodium 2-chlorobenzoate	17264-74-3	1.00	0.031	0.000000450%	0.031000	0.00000040%	0.004900	0.000980	0.002940
Sodium 2,5-difluorobenzoate	522651-42-9	1.00	0.027	0.000000390%	0.027000	0.00000034%	0.004268	0.000854	0.002561
Sodium 3,5-difluorobenzoate	530141-39-0	1.00	0.027	0.000000390%	0.027000	0.00000034%	0.004268	0.000854	0.002561
Sodium 2,3,4-trifluorobenzoate	402955-41-3	1.00	0.028	0.000000410%	0.028000	0.00000036%	0.004426	0.000885	0.002656
Sodium 2,4,5-trifluorobenzoate	522651-48-5	1.00	0.028	0.000000410%	0.028000	0.00000036%	0.004426	0.000885	0.002656
Sodium 2,3-difluorobenzoate	1604819-08-0	1.00	0.026	0.000000380%	0.026000	0.00000033%	0.004110	0.000822	0.002466
Sodium 3-chlorobenzoate	17264-88-9	1.00	0.025	0.000000370%	0.025000	0.00000032%	0.003952	0.000790	0.002371
Sodium 2,4,6-trichlorobenzoate	321992-77-2	1.00	0.029	0.000000420%	0.029000	0.00000037%	0.004584	0.000917	0.002751
Sodium hydroxide	1310-73-2	2.13	0.201	0.000002920%	0.428130	0.00000546%	0.067679	0.013536	0.040607
Proppants									
Silicon Dioxide (quartz / sand)	14808-60-7	2.65	568471.252		1506449	19.2%			
Water									
Water in additives	7732-18-5	1	1666.627	0.024%	1666.63	0.021%			
Water	7732-18-5	1	6288843.62	91.2%	6288844	80.3%			
Total Chemical Additives			35378		38,013	0.5%			
Total Proppant			568471		1506449	19.2%			
Total Make Up Water			6290510		6290510	80.3%			

The mass balance also estimates the concentration of each chemical that will be returned to surface during the flowback of the hydraulically fractured well, based on an upper and lower estimate of 20% and 60% mass recovery

Appendix B

Toxicity Profiles

Toxicity Summary - Partially hydrolysed polyacrylamide

Chemical and Physical Properties[1,2,3,4]	
CAS number	9003-05-8
Molecular formula	$(C_3H_5NO)_x$
Molecular weight	1,000,000 to > 50,000,000 g/mol for polyacrylamide copolymers used as flocculants
Solubility in water	Water soluble
Melting point	No data available.
Boiling point	No data available.
Vapour pressure	No data available.
Henrys law constant	No data available.
Explosive potential	No data available.
Flammability potential	No data available.
Colour/Form	No data available.
Overview	Polyacrylamide polymers can exist in cationic, anionic or non-ionic forms, depending on their ionic charge. The non-ionic form of polyacrylamide is generated from the basic polymerisation of acrylamide. Anionic polyacrylamide polymer can then be formed from the hydrolysis of the acrylamide homopolymer either simultaneously during the polymerisation process or as a subsequent step. Anionic polyacrylamide polymer can also be formed from the copolymerisation of acrylamide and acrylic acid. A Tier 1 Human Health and Environmental Assessment for this chemical has been conducted by NICNAS which concluded that it was low concern to human health and the environment and thus required no further assessment.
Environmental Fate [3]	
Soil/Water/Air	No studies on the environmental fate of anionic polyacrylamide are available. As a high-molecular weight, water-soluble polymer, it is not expected to biodegrade or bioaccumulate. The environmental fate of anionic polyacrylamide will be determined primarily by adsorption. The polyanions in this group are expected to partition onto natural colloids in surface waters and in soil and are not expected to undergo long-range transport in the environment.
Human Health Toxicity Summary [1,2,4]	
Chronic Repeated Dose Toxicity	No data available.
Carcinogenicity	No data available.
Mutagenicity/ Genotoxicity	No data available.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	No data available.
Acute Toxicity	Mouse LD50 (oral): 12950 mg/kg Rabbit LD50 (oral): 11250 mg/kg Rat LD50 (oral): >1000 mg/kg
Irritation	No data available.
Sensitisation	No data available.
Health Effects Summary	Poses no unreasonable risk to human health based on Tier I assessment under the NICNAS IMAP assessment framework.

Key Study/Critical Effect for Screening Criteria	The oral acute toxicity in rats was considered the most sensitive endpoint with a LD50 of 1000 mg/kg.

Ecological Toxicity [3]

Aquatic Toxicity	Fathead minnow LC50: 810 mg/L Rainbow trout LC50: > 100 mg/L Bluegill sunfish LC50: >300 mg/L Daphnia magna LC50: 470 mg/L
Determination of PNEC aquatic	Anionic polyacrylamide has a low acute toxicity concern to aquatic organisms and thus required no further assessment.

Current Regulatory Controls

Listed as a Chemical of Concern on International Databases

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	No data available.
Australian Occupational Exposure Standards	No data available.
International Occupational Exposure Standards	No data available.
Australian Food Standards	No data available.
Australian Drinking Water Guidelines	No data available.
Aquatic Toxicity Guidelines	No data available.

PBT Assessment [3]

P/vP Criteria fulfilled?	Yes. Anionic polyacrylamide is a large molecular weight, water-soluble polymer. It is not expected to be readily biodegradable; thus, it meets the screening criteria for persistence.

B/vB criteria fulfilled?	No. Pharmacokinetic studies showed that anionic polyacrylamide was not bioavailable to rats when ingested; this is most likely due to its large size (high molecular weight) and presumed resistance to break down in the gastrointestinal tract. Anionic polyacrylamide is thus not expected to be bioavailable to aquatic or terrestrial organisms. It is not expected to meet the criteria for bioaccumulation.
T criteria fulfilled?	No. The acute LC50 values in fish and invertebrates are >1 mg/L. Thus, it does not meet the criteria for toxicity.
Overall conclusion	Not PBT
Revised	February 2022

References

1. Department of the Environment and Energy 2017, National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme
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5. HCIS, Hazardous Chemical Information System, Safe Work Australia, Retrieved February 2022: http://hcis.safeworkaustralia.gov.au/HazardousChemical.
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Toxicity Summary - Crystalline silica

Chemical and Physical Properties [1,3]	
CAS number	14808-60-7
Molecular formula	SiO_2
Molecular weight	60.09 g/mol
Solubility in water	Insoluble/negligible
Melting point	1610°C
Boiling point	2230°C
Vapour pressure	Not available
Henrys law constant	Not available
Explosive potential	Not explosive
Flammability potential	Not flammable
Colour/Form	Transparent crystals
Overview	Silica is an off-white granule that occurs naturally in various crystalline and amorphous or other non-crystalline forms. Crystalline silica is characterized by silicon dioxide (SiO2) molecules oriented in fixed, periodic patterns to form stable crystals. The primary crystalline form of silica is quartz. Other crystalline forms of silica include cristobalite, tripoli and tridymite. Particle size is a key determinate of silica toxicity, since toxicity is restricted to particles that are small enough to be deposited into the target regions of the respiratory tract. Uncalcined diatomaceous earth typically contains around 1%crystalline silica. When diatomaceous earth is subjected to pressure or is processed ("calcined") at temperatures above 1000°C some of the amorphous silica is converted to crystalline silica in the form of cristobalite. Calcined diatomaceous earth can contain anywhere from 1% to 75% cristobalite.
Environmental Fate [1,2]	
Soil/Water/Air	Crystalline Silica consists of diatomaceous earth, a naturally occurring material. Its primary component, silica, is found in common materials like quartz, sand and agate. The materials are ubiquitous and unlikely to react chemically with any other substance in the environment.
Human Health Toxicity Summary [1,2,3]	
Chronic Repeated Dose Toxicity	A number of animal studies have found that cristobalite is more toxic to the lung than quartz, and more tumorigenic (e.g., King et al. 1953; Wagner et al. 1980). However, several other authors concluded that this is not the case (Bolsaitis and Wallace 1996; Guthrie and Heaney 1995). OSHA (2013) has examined evidence on the comparative toxicity of the silica polymorphs (quartz, cristobalite, and tridymite) and found no difference in toxicity effects between cristobalite and quartz. Furthermore, no difference in toxicity between cristobalite and quartz has been observed in epidemiologic studies (NIOSH 2002). There is no information on the repeat dose oral, inhalation or dermal effect of calcined silica. However, since calcined diatomaceous earth contains varying amounts of crystalline silica in the form of cristobalite, and may also contain small amounts of quartz and tridymite, it is expected that any long-term health hazards associated with diatomaceous earth would mainly be due to the effects of crystalline silica. In humans, the most prevalent effect identified from long term exposure in occupational settings is silicosis, a diffused nodular pulmonary fibrosis (US EPA 1996).
Carcinogenicity	IARC (2012) concluded that there is sufficient evidence in humans for the carcinogenicity of inhaled crystalline silica in the form of quartz or cristobalite from occupational sources. There is sufficient evidence in experimental animals for the carcinogenicity of quartz and cristobalite.

	The IARC has also concluded that inhaled crystalline silica in the form of cristobalite or quartz from occupational sources is carcinogenic to humans (Group 1) (IARC 2012).
Mutagenicity/ Genotoxicity	Conflicting results have been reported in genotoxicity studies with crystalline quartz or cristobalite, and a direct genotoxic effect for crystalline silica has not been confirmed or ruled out. Studies on genotoxicity of calcined diatomaceous silica are not available.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	No data available.
Acute Toxicity	No data available.
Irritation	No data available. Most acute toxicity studies for quartz or cristobalite were conducted using intratracheal instillation. Single intratracheal instillation of quartz caused inflammatory effects and formation of discrete silicotic nodules in rats, mice and hamsters (IARC 2012; WHO 2000). Other effects like oxidative stress, cellular proliferation and increases in water, protein, and phospholipid content of rat lungs, apoptosis (programmed cell death) and lung cancer were also noted. In general, exposure to high concentrations of dust may cause coughing and mild, temporary irritation (CCOHS 2001).
Sensitisation	No data available. However, based on the structure and physico-chemical properties, the three forms of crystalline silica or the calcined diatomaceous silica are not expected to cause skin sensitisation.
Health Effects Summary	The substances are not skin or eye irritants but acute inhalation of dust may cause discomfort and stress as well as signs of local irritation to nasal, bronchiolar and ocular mucous membranes. Based on the evaluation of the epidemiological data it is concluded that inhalation exposure to crystalline silica results in lung cancer. This conclusion is also supported by animal studies in which inhalation and intratracheal exposure to crystalline silica resulted in lung tumours. The most common types of lung tumour observed in rats were lung adenocarcinomas.
Key Study/Critical Effect for Screening Criteria	Not applicable.
Ecological Toxicity [1,2,3]	
Aquatic Toxicity	Aquatic toxicity studies performed at saturation concentrations of synthetic amorphous silica showed no acute toxicity to fish, Daphnia, or algae, though some physical effects were observed with loading rates of greater than or equal to 10 g/L (OECD 2004). Any harmful effects to aquatic ecosystems are therefore not ecotoxicological in nature. No chronic toxicity data were identified.
Determination of PNEC aquatic	Not applicable.
Current Regulatory Controls [3]	
Listed as a Chemical of Concern on International Databases	

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	Yes
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	Yes
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No

Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	Quartz and cristobalite are listed in the Hazardous Substances Information System (HSIS) (Safe Work Australia 2014a) as hazardous substances. Calcined silica is not listed in the HSIS.
Australian Occupational Exposure Standards	Time Weighted Average (TWA) occupational exposure standard of 0.1 mg/m^3 for quartz and cristobalite are recommended in Australia (Safework Australia 2013). A Short-Term Exposure Limit (STEL) is not recommended for any of the compounds.
International Occupational Exposure Standards	TWA for quartz, cristobalite: Canada: 0.025 mg/m^3 France: 0.05 mg/m^3 Japan: 0.03 mg/m^3 Sweden: 0.05 mg/m^3 US (ACGIH): 0.025 mg/m^3 US (NIOSH): 0.05 mg/m^3 US (OSHA): 0.1 mg/m^3 US: 0.3, 0.9, 1.5, 500 mg/m^3 Temporary Emergency Exposure Limits (TEEL) (Diatomaceous silica, calcined)
Australian Food Standards	No data found.
Australian Drinking Water Guidelines	The Australian Drinking Water Guidelines state: 'To minimise an undesirable scale build up on surfaces, silica (SiO¬2) within drinking water should not exceed 80 mg/L' (National Health and Medical Research Council (NHMRC) 2001).
Aquatic Toxicity Guidelines	No data found.
PBT Assessment [3]	
P/vP Criteria fulfilled?	No. Not applicable, inorganic substance, ubiquitous in environment.
B/vB criteria fulfilled?	No. Not applicable, inorganic substance, ubiquitous in environment.
T criteria fulfilled?	No. Long term data not available (acute data >0.1 mg/L).
Overall conclusion	It is not currently possible to categorise the environmental hazards of metals and other inorganic chemicals according to standard persistence, bioaccumulation and toxicity (PBT) hazard criteria. These criteria were developed for organic chemicals and do not take into account the unique properties of inorganic substances and their behaviour in the environment (UNECE 2007; US EPA 2007). Further assessment of the environmental risks from the use of this chemical is not required as identified by DoEE

References

1. HSDB. Hazardous Substances Data Bank. Retrieved 2015, from Toxnet, Toxicology Data Network, National Library of Medicine: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
2. OECD-SIDS Initial Targeted Assessment Profile on Quartz and Cristobalite, SIAM 32, 19-21 April 2011.
3. Department of the Environment and Energy 2017, National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme

Toxicity Summary - Hepta sodium phosphonate

Chemical and Physical Properties [1,2,3]	
CAS number	22042-96-2
Molecular formula	$C_9H_{28}N_3O_{15}P_5.xNa$
Molecular weight	Not applicable. This substance is an unknow or variable-composition substance as the number of sodium counter-ions is not defined.
Solubility in water	>500 g/L at 20 °C
Density	1.3 kg/L at 20 °C
Melting point	Not applicable
Boiling point	>100 °C at 1013 hPa
Vapour pressure	2.7×10^{-11} kPa at 25 °C
Henrys law constant	No information available
Explosive potential	Non-explosive
Flammability potential	Non-flammable
Colour/Form	Liquid/aqueous solution
Overview	Hepta sodium phosphonate (DTPMP) sodium salt is a manufactured chemical used as a scale inhibitor in oilfield water systems and water desalination systems; as a scale inhibitor and bleaching agent in the textiles and paper industries; in coatings and paints in the general manufacturing and construction industry; in the manufacture and formulation of other chemicals; in cosmetics and personal care products, and in washing/cleaning products. A Tier 1 Human Health Assessment has been undertaken for this chemical by AICIS which concluded that it poses no unreasonable risk to human health, and thus required no further assessment.
Environmental Fate [1,2]	
Soil/Water/Air	The properties of DTPMP and its salts are directed by their ionisation behaviour. DTPMP can ionise by loss of a hydrogen ion up to six times. As a consequence it is a strong complexing agent, and is highly hydrophilic. Because ionisation is a rapid and reversible process, salts such as sodium and potassium salts will dissolve readily in water to give a speciation state dictated by the pH of the medium. DTPMP and its salts are adsorbed by inorganic matrices, and therefore adsorption to sewage sludge and soil is strong (measured Koc = 9748). They are not readily biodegradable in laboratory studies carried out under standard conditions. Based on the low log Kow (-3.40) and read-across from related substances, DTPMP and its salts are not expected to bioaccumulate.
Human Health Toxicity Summary [2]	
Chronic Repeated Dose Toxicity	In a 90 day study conforming to OECD guideline 408, Wistar derived rats were fed diets containing 0, 100, 1000, 10000ppm of an aqueous solution of salt of DTPMP (Central Toxicology Laboratory, 1998). Repeated exposure to 842 mg/kg bw/d (males) and 903 mg/kg bw/d (females) resulted in perturbations of iron and calcium homeostasis (in the absence of any concurrent alteration of calcium plasma levels). Changes in some blood parameters and an increase in total bone density were seen at this dose. The NOAEL for this study was therefore 83 mg/kg bw/day based on the mid dose male group.
Carcinogenicity	Hepta sodium phosphonate is not listed in the International Agency for Research on Cancer (IARC) as a carcinogen.
Mutagenicity/ Genotoxicity	The chemical is not expected to be genotoxic based on available data from in-vitro studies including bacterial and mammalian cell gene mutation assays. No genetic toxicity data is available in from in vivo systems.
Reproductive Toxicity /	No data are available for reproductive toxicity. A developmental toxicity test on SD rats exposed by gavage to doses of up to 2000 mg/kg bwt/d. Clear maternal toxicity (approximately 30% decrease in bodyweight gain, soft stools) was noted

<table>
<tr><td>Developmental Toxicity/ Teratogenicity</td><td>in pregnant SD rats given 2000 mg/kg bwt/d. A very low incidence of vertebral anomalies, but no external malformations, present in litters from high dose dams was considered evidence of an effect on the fetus. The NOAEL for maternal and foetal toxity was 1000 mg/kg bw and for teratogenicity was 2000 mg/kg bw.</td></tr>
<tr><td>Acute Toxicity</td><td>The DTPMP acid and salts are of low oral and dermal toxicity. The oral rat LD50 is 4164 mg/kg bw and the rabbit dermal LD50 >4605 mg/kg bw. The acute rat oral LD50 of the heptasodium salt lies between 5838 and 8757 mg/kg bw. The dermal LD50 values for the salts are >5838 mg/kg bw for the rat. For the octasodium salt, the oral LD50 is >3870 mg/kg bw and the dermal LD50 >860mg/kg bw for the rabbit.</td></tr>
<tr><td>Irritation</td><td>Chemical causes skin and eye irritation. Slight or mild skin and eye irritations have been reported in studies using rabbits</td></tr>
<tr><td>Sensitisation</td><td>This chemical is not expected to be a skin-sensitiser based on limited data available from tests on guinea pigs.</td></tr>
<tr><td>Health Effects Summary</td><td>DTPMP acid and salts possess properties indicating a hazard for human health (eye irritation, potential perturbations of iron and calcium homeostasis).</td></tr>
<tr><td>Key Study/Critical Effect for Screening Criteria</td><td>A Tier 1 Human Health Assessment has been undertaken for this chemical by AICIS which concluded that it poses no unreasonable risk to human health, and thus required no further assessment.</td></tr>
<tr><td colspan="2">Ecological Toxicity [2]</td></tr>
<tr><td>Aquatic Toxicity</td><td>DTPMP and its salts are of low acute toxicity to fish and aquatic invertebrates. The lowest reliable acute toxic concentrations determined for DTPMP are a 96-h LC50 for the rainbow trout, Oncorhynchus mykiss, that is in the range 180-252 mg/l and EC50 values determined in acute tests with aquatic invertebrates are all in excess of 150 mg/l.

DTPMP is of low chronic toxicity to fish (O. mykiss 60-day NOEC: 25.6 mg/l). There are no chronic data for aquatic invertebrates but an acute sub-lethal test with the oyster, Crassostrea virginica, yielded a 96-hour EC50 for effects on shell growth of 155.8 mg/l and a NOEC of 55.5 mg/l.

The toxicity of DTPMP and its salts to algae is best represented by the 95 hour ErC50 value of >10 mg/l. This value was obtained in the only test where steps were taken to counter the effects of nutrient complexation and is therefore most likely to be indicative of true toxicity. No data are available that describe the toxicity of DTPMP to terrestrial plants and invertebrates. DTPMP is of low acute toxicity to birds when administered via the dietary exposure route (Anas platyrhynchos and Colinus virginianus 14-day LC50: >454 mg/kg bw).</td></tr>
<tr><td>Determination of PNEC aquatic</td><td>An assessment factor of 100 has been applied the measured endpoint value for chronic fish (NOEC 25.6 mg/L). The PNECaquatic is 0.256 mg/L.</td></tr>
<tr><td>Listed as a Chemical of Concern on International Databases</td><td>
<table>
<tr><th>International Database</th><th>Listed?</th></tr>
<tr><td>European REACH regulation Substances of very high concern (SVHCs) according to Annex XV
https://echa.europa.eu/candidate-list-table</td><td>No</td></tr>
<tr><td>International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen
https://monographs.iarc.who.int/list-of-classifications</td><td>No</td></tr>
<tr><td>National Toxicology Program (NTP) Report on Carcinogens (RoC)
https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html</td><td>No</td></tr>
<tr><td>US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans
EU list chemicals with endocrine disruption listed in Category 1 or Category 2
https://www.epa.gov/iris</td><td>No</td></tr>
<tr><td>United States Endocrine Disrupter Screening Program
https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</td><td>No</td></tr>
<tr><td>Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin
https://wwwn.cdc.gov/TSP/index.aspx?sysid=18</td><td>No</td></tr>
<tr><td>Montreal Protocol
https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol</td><td>No</td></tr>
<tr><td>Rotterdam Convention</td><td>No</td></tr>
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http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx</td><td>No</td></tr></table></td></tr>
<tr><td>Australian Hazard Classification</td><td>This chemical is not listed as a Hazardous Chemical in Safe Work Australia HCIS.</td></tr>
<tr><td>Australian Occupational Exposure Standards</td><td>No Australian occupational exposure standards are provided by Safe Work Australia HCIS for this chemical.</td></tr>
<tr><td>International Occupational Exposure Standards</td><td>No exposure standards provided in NIOSH.</td></tr>
<tr><td>Australian Food Standards</td><td>No Australian food standards were identified in FSANZ</td></tr>
<tr><td>Australian Drinking Water Guidelines</td><td>No aesthetic or health-related guidance values were identified in the National Health and Medical Research Council (NHMRC) Australian Drinking Water Guidelines (NHMRC, 2022).</td></tr>
<tr><td>Aquatic Toxicity Guidelines</td><td>No Australian guidelines available.</td></tr>
<tr><td colspan="2">PBT Assessment [2]</td></tr>
<tr><td>P/vP Criteria fulfilled?</td><td>Yes. DTPMP and its sodium salts are not readily biodegradable.</td></tr>
<tr><td>B/vB criteria fulfilled?</td><td>No based on the low log Kow (-3.40), DTPMP is not bioaccumulative.</td></tr>
<tr><td>T criteria fulfilled?</td><td>No. The NOEC from a chronic fish study on DTPMP is >0.1 mg/L.</td></tr>
<tr><td>Overall conclusion</td><td>Not a PBT substance.</td></tr>
</table>

Notes: *AICIS – Australian Industrial Chemicals Introduction Scheme; HCIS – Hazardous Chemical Information System; NIOSH – National Institute for Occupational Safety and Health; FSANZ – Food Standards Australia New Zealand; NHMRC (2022) – National Health and Medical research Council, Australian Drinking Water Guidelines 6, 2011 (Version 3.8, Updated September 2022); ANZG – Australian and New Zealand Guidelines for Fresh and Marine Water Quality.*

References

1. ECHA, https://echa.europa.eu/registration-dossier/-/registered-dossier/14945
2. OECD (2004), SIDS Dossier on [[(phosphonomethyl)imino]bis[(ethylenenitrilo)bis(methylene)]]tetrakisphosphonic acid, sodium salt [CAS No. 22042-96-2], Phosphonic Acid Compounds Group 3, OECD HPV Chemical Programme,
3. AICIS Inventory Multi-tiered Assessment and Prioritisation (IMAP) Assessments, Tier I Human Health

Toxicity Summary - Distillates, Hydrotreated Light

Chemical and Physical Properties [1,2,3,4]	
CAS number	64742-47-8
Molecular formula	C48H94
Molecular weight	Not applicable - unknown or variable composition, complex reaction products or biological materials (UVCB)
Solubility in water	0.009 to 6.45 mg/L (at 25°C)
Melting point	-49 °C
Boiling point	146 to 299 °C
Vapour pressure	1 to 3.7 kPa at 37.8 °C
Henrys law constant	No data found.
Explosive potential	Above 66°C explosive vapour/air mixtures may be formed
Flammability potential	Combustible
Colour/Form	Liquid at room temperature
Overview	Distillates, hydrotreated light (also called deodorised kerosene) is a petroleum substance. The C_9-C_{14} Aliphatic [< 2% Aromatic] Hydrocarbon Solvents Category is comprised of complex aliphatic hydrocarbon solvents that contain >98% aliphatic constituents with carbon numbers in the range of C9-C14 and less than 2% aromatic constituents. The chemical is used as a component of a drilling fluid formulation for coal seam gas extraction.
Environmental Fate[1]	
Soil/Water/Air	Members of the C_9-C_{14} Aliphatic [≤2% aromatics] Hydrocarbon Solvents Category have the potential to volatilize from surface waters, based on Henry's Law constants (HLC) representing volatility for category members that range from 4.76 x 10^4 to 1.67 x 10^6 Pa-m^3/mole (at 25°C). In the air, category members have the potential to rapidly degrade through indirect photolytic processes mediated primarily by hydroxyl radicals (•OH) with calculated degradation half-lives ranging from 0.42 to 1.10 days or 10.8 to 26.4 hours based on a 12-hr day and an •OH concentration of 1.5 x 10^6 •OH/cm^3. These chemicals are unlikely to degrade by hydrolysis as they lack a functional group that is hydrolytically reactive.
Human Health Toxicity Summary [1,2,3]	
Chronic Repeated Dose Toxicity	In a 90-day study conducted in accordance with OECD TG 408, Sprague-Dawley rats were administered deodorized kerosene by gavage at doses of 0, 100, 500 or 1000 mg/kg bw/day (REACH 2013). Microscopic changes, such as incidence of a2µ-globulin, were seen in male kidneys. These effects are not considered relevant to humans. No other treatment-related effects were observed. No Lowest Observed Adverse Effect Level (LOAEL) or No Observed Adverse Effect Level (NOAEL) could be established in this study. Repeated dermal exposures to members of the kerosene/jet fuel category showed minimal systemic effects (API 2010). Animal data on repeat dermal toxicity of kerosene (petroleum) are summarised from REACH (2013) and presented in Table A29.2. The LOAELs and NOAELs are indicated for each study. Prolonged skin exposure to kerosene (petroleum) in rats and rabbits were consistently associated with local irritation. In rabbits only, systemic effects included changes in bodyweight and organ weights. It is expected that deodorized kerosene would have similar effects in the animals. In a 13-week study, rats (strain not specified) were exposed to deodorized kerosene vapour at concentrations of 0, 0.02, 0.048 or 0.10 mg/L for six

	hours/day, five days/week. No treatment-related effects were reported (REACH 2013).
Carcinogenicity	A study for deodorized kerosene is available in the REACH Dossier (REACH 2013) but was not reported in enough detail to be able to determine the carcinogenicity of the substance. In a study conducted similarly to OECD TG 451, B6C3F1 mice were applied 0, 250 or 500 mg/kg bw/day kerosene (petroleum) in the interscapular region (type of wrapping not specified) for 103 weeks (REACH 2013). At the end of the study, less than 10% decrease in bodyweight gain was observed at the top dose in both sexes. Mortality in females was significantly higher at the two doses compared to controls. Increased incidence and severity of chronic dermatitis was seen in all treatment groups. At the top dose, increased incidence of the following non-neoplastic lesions was reported: amyloid in the liver, kidney, adrenal cortex (males only), spleen; granulocytic hyperplasia in the bone marrow; and hyperplasia of the axillary lymph nodes (females only). The only indication of neoplastic lesions was an increased incidence of malignant lymphomas observed in treated female animals but the values were within the range of historical controls. Under the conditions of the test, kerosene (petroleum) was not carcinogenic. The LOAEL for systemic effects is 250 mg/kg bw/day. The International Agency for Research on Cancer (IARC) concluded that there is inadequate evidence for the carcinogenicity of kerosene (petroleum) in experimental animals and humans, placing the chemical in Group 3 (Not classifiable as to its carcinogenicity to humans) (IARC 1989). Deodorized kerosene is not carcinogenic, based on reading across the information available for kerosene (petroleum).
Mutagenicity/ Genotoxicity	In vitro tests reported deodorized kerosene as negative both with and without metabolic activation in Ames tests conducted in accordance with OECD TG 471 (REACH 2013; OECD 2011) and in chromosomal aberration tests conducted in accordance with OECD TG 473 (OECD 2011, 2012). In an in vivo study, deodorized kerosene was negative in a dominant lethal assay, conducted in accordance with OECD TG 478, in male Swiss mice and Long Evans rats administered 10% deodorized kerosene intraperitoneally (REACH 2013). These studies demonstrate that deodorized kerosene is not genotoxic.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	C9-C14 aliphatic (≤2% aromatic) hydrocarbon solvents and C14-C20 aliphatic (≤2% aromatic) hydrocarbon solvents are not toxic to fertility (OECD 2011, 2012). Members of the kerosene/jet fuel category are not toxic to fertility (API 2010). Sprague-Dawley rats were administered undiluted kerosene (petroleum) by gavage at doses of 0, 750, 1500 or 3000 mg/kg bw/day in males treated for 70-90 days and 0, 325, 750 or 1500 mg/kg bw/day in females treated for 21 weeks. At 750 and 1500 mg/kg bw/day, increased absolute liver weight was observed in females but with no corresponding changes in clinical chemistry or histopathology. In females only, other effects included perianal dermatitis at 1500 mg/kg bw/day and stomach hyperplasia at 750 and 1500 mg/kg bw/day. These parameters were not measured in males. In males, the study indicated dose dependent decrease in male bodyweight that was linked to nephropathy specific to male rats. Data for this effect were not provided in the study description. There were no treatment related effects on fertility in both sexes (REACH 2013). The NOAEL for systemic effects in females only was 325 mg/kg bw/day. No NOAEL can be established for fertility effects. C9-C14 aliphatic (≤2% aromatic) hydrocarbon solvents and C14-C20 aliphatic (≤2% aromatic) hydrocarbon solvents are not developmental toxicants (OECD 2011, 2012). Members of the kerosene/jet fuel category are not developmental toxicants (API 2010). In a study conducted in accordance with OECD TG 414, Sprague-Dawley rats were administered kerosene (petroleum) by gavage on gestation days (GD) 6 to 15 at doses of 0, 500, 1000, 1500 or 2000 mg/kg bw/day (REACH 2013). Bodyweight gain was decreased at 1500 and 2000 mg/kg bw/day. Foetal weight was decreased at 1500 and 2000 mg/kg bw/day which may be attributed to decreased maternal bodyweight gain. No malformations were reported. The maternal NOAEL is 1000 mg/kg bw/day.

	In another study, Sprague-Dawley rats were exposed (whole body) to kerosene (petroleum) in air at concentrations of 0, 106 or 364 ppm on GD 6-15. There were no treatment-related effects observed in the dams and offspring (REACH 2013). Deodorized kerosene is not considered a developmental toxicant, based on reading across data available for kerosene (petroleum).
Acute Toxicity	The chemicals have low acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) in rats is >2000 mg/kg bw (OECD, 2011; US EPA, 2011; OECD, 2012a; OECD, 2012b; OECD, 2012c). The chemicals have low acute toxicity based on results from animal tests following dermal exposure. The LD50 in rats and rabbits is >2000 mg/kg bw (OECD, 2011; US EPA, 2011; OECD, 2012a; OECD, 2012b; OECD, 2012c). The chemicals have low acute toxicity based on results from animal tests following inhalation exposure.
Irritation	Semi-occlusive applications of commercial grade deodorized kerosene produced slight irritation in New Zealand White and SPF rabbits in dermal irritation studies conducted in accordance with OECD TG 404. The studies reported the range of erythema and oedema scores to be 0.3-0.9 and 0.2-1.0, respectively, based on Draize scoring at 24, 48 and 72 hours. Deodorized kerosene is slightly irritating to rabbit skin. Several studies conducted similarly to OECD TG 405 showed minimal effects to the eye with the reported range of conjunctival redness score to be 0-0.2 from instillation of undiluted deodorized kerosene in the eyes of New Zealand White and SPF rabbits (OECD 2011). Deodorized kerosene is slightly irritating to rabbit eye.
Sensitisation	The C9-C14 aliphatic (≤2% aromatics) Category members do not cause skin sensitization.
Health Effects Summary	Deodorised kerosene is an aspiration hazard since it has low viscosity and is composed of aliphatic and aromatic hydrocarbons up to 10%. Deodorised kerosene has low acute oral, dermal and inhalation toxicity, and is slightly irritating to the skin and eyes. The substance is not a skin sensitiser, based on reading across data available for kerosene (petroleum). No treatment-related effects were reported in repeated oral and inhalation exposures to deodorised kerosene. Prolonged dermal exposure to kerosene (petroleum) reported local irritation in rats and rabbits, and changes in bodyweight and organ weights in rabbits. It is expected that these effects would be similar for deodorised kerosene. Based on the absence of adverse effects observed in repeat dose toxicity studies, for the purposes of quantifying the health risk to the general worker and public, the highest dose tested in the study conducted in rats (1 000 mg/kg bw/day) is used in this risk assessment. The substance is not genotoxic. It is neither a carcinogen nor a reproductive toxicant, based on reading across data available for kerosene (petroleum).
Key Study/Critical Effect for Screening Criteria	The most appropriate No-Observed-Adverse-Effect Level (NOAEL) for risk assessment is 1 000 mg/kg bw/day based on maternal toxicity (decreased bodyweight gain) at the Lowest- Observed-Adverse-Effect Level (LOAEL) of 1 500 mg/kg bw/day from a developmental toxicity study on kerosene (petroleum).
Ecological Toxicity [2]	
Aquatic Toxicity	Lowest acute endpoint for Daphnia = 0.018 mg/L (modelled)
Determination of PNEC aquatic	Based on the lowest acute endpoint for Daphnia (0.018 mg/L), an assessment factor of 100 has been applied, resulting in a PNECaquatic of 1.80E-04 mg/L.
Current Regulatory Controls [2]	
Listed as a Chemical of Concern on International Databases	

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC)	No

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<table>
<tr><td>https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html</td><td></td></tr>
<tr><td>US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans
EU list chemicals with endocrine disruption listed in Category 1 or Category 2
https://www.epa.gov/iris</td><td>No</td></tr>
<tr><td>United States Endocrine Disrupter Screening Program
https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</td><td>No</td></tr>
<tr><td>Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin
https://wwwn.cdc.gov/TSP/index.aspx?sysid=18</td><td>No</td></tr>
<tr><td>Montreal Protocol
https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol</td><td>No</td></tr>
<tr><td>Rotterdam Convention
http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals</td><td>No</td></tr>
<tr><td>Stockholm Convention
http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx</td><td>No</td></tr>
</table>
</td></tr>
<tr><td>Australian Hazard Classification</td><td>All of the chemicals are classified as hazardous, with the following risk phrase for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):
Xn; R65 (acute toxicity)

Mixtures containing the substance are classified as hazardous with the following risk phrase based on the concentration (Conc) of the substance in the mixtures:
Conc ≥10%: Xn; R65 (May cause lung damage if swallowed)</td></tr>
<tr><td>Australian Occupational Exposure Standards</td><td>No specific exposure standards are available.</td></tr>
<tr><td>International Occupational Exposure Standards</td><td>No specific exposure standards are available for this chemical.</td></tr>
<tr><td>Australian Food Standards</td><td>No data available.</td></tr>
<tr><td>Australian Drinking Water Guidelines</td><td>No data available.</td></tr>
<tr><td>Aquatic Toxicity Guidelines</td><td>Oils and greases (including petrochemicals) for freshwater production: <3006 µg/L (ANZECC 2000)</td></tr>
<tr><td colspan="2">PBT Assessment[1,2]</td></tr>
<tr><td>P/vP Criteria fulfilled?</td><td>No. This chemical is expected to be biodegradable. The ready biodegradability of SHELLSOL NF a solvent naphtha (petroleum), heavy aromatics (consists predominantly of C9 aromatics 25%m/m; C10 aromatics 65%, and indanes 10%) was studied in mineral nutrient medium inoculated with activated sludge (mixed liquor suspended solids 100-101 mg/L, pH 6.9) and incubated for 28 days at 20°C. SHELLSOL NF is readily biodegrade after 28 days but not within the 10 day window.</td></tr>
<tr><td>B/vB criteria fulfilled?</td><td>Category members have a potential to bioaccumulate, based on calculated log BCF values for constituents that range from 2.78 to 4.06, and calculated BCF values of 598 to 11,430 L/kg wet-weight, based on the Arnot and Gobas model, that take into account biotransformation of the chemicals in fish tissue. This chemical also has a log Kow of 6.025.</td></tr>
<tr><td>T criteria fulfilled?</td><td>Yes. The lowest acute endpoint is <1 mg/L.</td></tr>
<tr><td>Overall conclusion</td><td>Not PBT</td></tr>
</table>

References

1. OECD (2012) SIDS Initial Assessment Profile on C_9-C_{14} Aliphatic [≤2% aromatic] Hydrocarbon Solvents Category. Available at: http://webnet.oecd.org/HPV/UI/SIDS_Details.aspx?id=476560b6-e2b7-4466-9c52-0b278c8b71a7
2. National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2017). National assessment of chemicals associated with coal seam gas extraction in Australia. Human health hazards of chemicals associated with coal seam gas extraction in Australia.
3. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier II Assessment for Kerosene, Retrieved 2019: https://www.nicnas.gov.au
4. ECHA REACH, Distillates (petroleum), hydrotreated light, Retrieved 2017: https://echa.europa.eu/information-on-chemicals/registered-substances
5. ICSC Distillates (petroleum), hydrotreated light, Retrieved 2017: http://www.inchem.org
6. ANZECC (2000) Australian and New Zealand Guidelines for Fresh and Marine Water Quality for protection for aquatic ecosystems

Toxicity Summary - Alcohols, C12-16, ethoxylated and Decanol

Chemical and Physical Properties[1,2,3,4]	
CAS number	68551-12-2, 26183-52-8
Molecular formula	Unspecified
Molecular weight	Unspecified
Solubility in water	0.1876 - 13.18 mg/L at 25 °C (C12-14 ethoxylated, 1-2.5 EO) (CAS 68131-39-5) 1.69 - 246.7 mg/L at 25 °C (C9-11, ethoxylated (EO < 2.5) (CAS 68439-46-3) 76 - 82 µg/L @ 25 °C and pH 6.5 (CAS 26183-52-8)
Melting point	7.2 °C at 101.3 kPa (CAS 68131-39-5) -20 °C at 101.3 kPa (CAS 68439-46-3) -27 °C @ 101 kPa (CAS 26183-52-8)
Boiling point	271.11 - 516.11 °C (CAS 68131-39-5) 260 °C (CAS 68439-46-3) 224 °C @ 101 kPa (CAS 26183-52-8)
Vapour pressure	< 1 Pa at 25 °C (CAS 68131-39-5) 0.004 - 117 Pa at 20 °C (CAS 68439-46-3) 1 hPa @ 20 °C (CAS 26183-52-8)
Henrys law constant	No data available.
Explosive potential	Non explosives
Flammability potential	Non flammable
Colour/Form	Organic liquid, colourless to light yellow
Overview	The AEs in this assessment are structurally related, where the hydrophilic ethylene oxide (EO) chain is attached via an ether linkage to the hydrophobic aliphatic alcohol chain (C =6). The alkyl chain can be linear, branched, saturated or unsaturated in the AE group. Ethoxylated shorter chain alcohols (C <6) do not show the same degree of surface activity compared with longer chains, and hence they are not included in this assessment. A generic structural formula of the AE is shown below: H–(CH2)x–y–(OCH2CH2)n–OH where n = average number of ethylene oxide (EO) units x–y = range of carbon units (C =6) A simpler notation of 'Cx–yEOn' will be used to represent the corresponding AEs in this assessment. Generally, increasing the carbon chain length increases lipophilicity, whereas increasing alkoxylation increases hydrophilicity of the chemical. These trends are consistent across the linear, branched, saturated or unsaturated AEs of varying alkyl chain lengths and ethoxylation degrees (Lindner, 2010). It was demonstrated that branching of the AEs had a relatively minor impact on calculated partition coefficients (Kow), and hence their biological properties (Lindner, 2010). Further, for unsaturated AEs, as the point of unsaturation is generally remote from the carbon where the EO chain is attached, they are expected to have similar physiochemical properties to saturated AEs. The AEs in this assessment have been shown to have similarities or trends in their toxicokinetic and toxicological profiles, although the alkyl chain length (whether linear, branched, saturated or unsaturated) and ethoxylation degree vary (see Health Hazard Information section). For this AE group, SARs were reported

	between the degree of ethoxylation and the acute toxicity (direct) and skin irritation (inverse). On the basis of the analogue and chain-length category approach (i.e. by considering similarities and trends in molecular structure, physiochemical properties (Kow), uses, and hazard profiles), the AEs in this assessment are qualified to be assessed as a group. Based on such trend analyses, the available datasets for AEs ranging from C6–C18 and EO3–EO12 were considered representative of the AE category for filling data gaps (HERA, 2009; Lindner, 2010). Available data for any AEs will be applicable to group members where data are incomplete or unavailable, such as for ethoxylates of coco, tallow, and C >20 alcohols. Overall, AEs are not expected to be systemically toxic, although some short chain ethylene glycol ethers, e.g. methyl and ethyl homologues are of concern for a range of adverse health effects. They include skin and eye irritation, liver and kidney damage, bone marrow and central nervous system (CNS) depression, testicular atrophy, developmental toxicity, and immunotoxicity. For higher propyl and butyl homologues, the toxicity involves haemolysis (anaemia) with secondary effects relating to haemosiderin accumulation in the spleen, liver and kidney, and compensatory haematopoiesis in the bone marrow. Systemic toxicity was shown to decrease with increasing alkyl chain lengths and/or alkoxylation degrees (ECETOC, 2005; US EPA, 2010). The chemicals ethylene glycol hexyl ether (with a longer alkyl chain length, CAS No. 112-25-4) and diethylene glycol butyl ether (with a higher ethoxylation degree, CAS No. 112-34-5) have no evidence of systemic effects including haemolysis (ECETOC, 2005; NICNASc). Commercially available AEs are mixtures of homologues of varying carbon chain lengths and it is possible that some of the chemicals with an average alkyl chain length C =6 may also contain shorter alkyl chains C <6. It is not practical to quantify the proportion of shorter C <6 chain lengths present in such chemicals, or these shorter chain lengths may not be present at all. The available data suggest a lack of systemic toxicity for the AE chemicals with potential short alkyl chain presence; therefore, the toxicity of the chemicals in this assessment is unlikely to be significantly affected by the presence of shorter chain alkyl groups.
Environmental Fate[2,3]	
Soil/Water/Air	Alcohol ethoxylates are readily biodegradable under aerobic conditions and also anaerobically biodegradable (HERA, 2009). The main mechanism of primary biodegradation for the linear and essentially linear AE is the central cleavage of the molecule, leading to the formation of long chain alcohol and polyethylene glycol (HERA, 2009; Marcomini et al., 2000a; Marcomini et al., 2000b). Long chain alcohols themselves are readily biodegradable up to C18 (SIDS, 2006). Abiotic degradation in water, soil, sediment and air is not expected to occur because of the chemical structures of AE homologues. Neither hydrolysis under normal environmental conditions (pH range from 4 to 9) nor photolysis in the atmosphere, in water, or when absorbed to soil and sediment surfaces, is to be considered (HERA, 2009). Experimentally determined BCF-values given for pure homologues and summarized in the publication of Tolls et al. (2000) are used as read-across data for the endpoint bioaccumulation in water. It can be stated that bioaccumulation of alcohol ethoxylates is regarded to be negligible as the surfactants will be rapidly metabolised. For more detail see endpoint summary for bioaccumulation. Concerning transport and distribution of the alcohol ethoxylate mixtures a high adsorption of the substances is determined by using QSAR-models. Adsorption onto surfaces is an intrinsic property of alcohol ethoxylates and thus a high Koc-value is expected.
Human Health Toxicity Summary [1]	
Chronic Repeated Dose Toxicity	Based on the available data, the chemicals in this group are not expected to cause serious damage to health (apart from local effects) from repeated oral and dermal exposure.

	In several 90-day feeding studies in rats (similar to OECD TG 408), the reported NOAELs were between 50 and 700 mg/kg bw/day for group members (covering the range of C9–C18 and EO5–EO10). Effects observed at higher concentrations included reduced mean body weights and increases in relative liver, kidney and heart weights (SCCS, 2007; HERA 2009; CIR, 2012). Similar effects were seen in longer-term 2-year feeding studies in rats. The NOAEL for the AEs CAS No. 66455-14-9 (C12–13EO6.5 group member) and CAS No. 68951-67-7 (C14–15EO7 not listed on the Inventory) were between 50 and 190 (females) mg/kg bw/day (HERA, 2009; CIR, 2012). Repeated oral or inhalation exposure to certain short chain ethylene glycol ethers (EGEs), such as 2-butoxyethanol (ethylene glycol butyl ether, EGBE, CAS No. 111-76- 2) and its acetate (EGBEA, CAS No. 112-07-2), may cause haemolytic effects in rodents and effects on the liver, spleen and kidney. However, humans appear to be the least sensitive species for haemolytic effects (NICNAS, 1996; NICNASc; OECD, 2004; ECETOC, 2005). The AEs in this assessment are not expected to share these mechanisms of toxicity. Therefore, exposure to these AEs is not expected to cause haemolysis and associated organ toxicity in humans. In a well-reported OECD TG 411 (Subchronic 90-day Dermal Toxicity) study, Fischer rats were exposed to C9–11EO6 (CAS No. 68439-46-3) at 1, 10 or 25 % concentrations, 3 days/week. The application site was shaved and not covered. Dry, flaky skin and irritation (epidermal thickening with hyperkeratosis) were observed at >10 %. Relative kidney weights without histological lesions increased in both sexes at 25 %. The NOAEL was established at 10 %, equivalent to 80 mg/kg bw/day (HERA, 2009; CIR, 2012). In an 18-month study, C12–13EO6.5 was applied to the back of Swiss mice 3 days/week. There were no treatment-related systemic lesions at up to 270 mg/kg bw/day. No further study information was available (HERA, 2009).
Carcinogenicity	Based on the available data, chemicals in this group are not considered carcinogenic. Two AEs, CAS No. 66455-14-9 (C12–13EO6.5, group chemical) and CAS No. 68951-67-7 (C14–15EO7, not listed on the Inventory), were administered at up to 1 % in the diet to rats for 1–2 years. No treatment-related histopathological effect or increased tumour incidence were observed (HERA, 2009; CIR, 2012). There was no treatment-related lesions in mice, following 18-month dermal application of C12–13EO6.5 (HERA, 2009). The AEs are synthesised through processes which may result in 1,4-dioxane as an impurity. This impurity is classified as a Carcinogen—Category 2 (H351 Suspected of causing cancer). There are restrictions on the levels of this chemical in preparations available to consumers in Australia (SUSMP).
Mutagenicity/ Genotoxicity	Based on the data available, the chemicals in this group are not considered mutagenic or genotoxic. A broad spectrum of AEs (covering the range of C7–C22 and EO2–EO20) tested negative in multiple in vitro and in vivo tests (OECD and GLP compliant) for gene mutation and clastogenicity. In vitro, negative results were reported in bacterial reverse mutation tests in Salmonella typhimurium (TA98, TA100, TA102, TA104, TA1535, TA1537 and TA1538) and Escherichia coli (strains WP2 and WP2 uvrA pKM101), with or without metabolic activation. Negative results were also reported in chromosomal aberration tests (Chinese hamster lung V79, Chinese hamster ovary, and rat liver cells) and gene mutation tests (mouse lymphoma cells) (SCCP, 2007; HERA, 2009; CIR, 2012).

	In vivo, AEs (C12–C15 and EO3–EO9) did not induce chromosomal damage in Chinese hamster or Tunstall Wistar rat bone marrow cells after acute oral doses between 250 and 3400 mg/kg bw (SCCP, 2007; HERA, 2009).
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	Based on the data available, the chemicals of this group are not considered to cause reproductive or developmental toxicity. The oral NOAELs were determined at 250 mg/kg bw/day for reproductive toxicity, and >50 mg/kg bw/day for maternal and developmental toxicity. In a 2-generation study, the chemical C14–15EO7 was administered in the diet of Charles River CD rats (25/sex/group, at doses of 0, 25, 50 or 250 mg/kg bw/day). The NOAEL for reproductive toxicity was established as 250 mg/kg bw/day (or 0.5 % in diet), given no treatment related effects on fertility, gestation or viability index at this highest tested dose. The NOAEL for maternal and developmental toxicity was established as 50 mg/kg bw/day, based on reduced maternal and pup body weights and increased relative liver weights in both F1 (males and females) and F2 (males) generations at 250 mg/kg bw/day (HERA 2009; CIR, 2012). In a 2-generation study protocol using a different AE (C12EO6), the NOAEL for reproductive toxicity was set at the highest tested dose of 250 mg/kg bw/day. The NOAELs for parental (F0) and developmental toxicity were also 50 mg/kg bw/day, based on reduced body weight gains in F0 and F1 generations at 250 mg/kg bw/day (HERA, 2009; CIR 2012). In an oral developmental toxicity study, C12EO6 was administered in the diet of female rabbits at doses of 0, 50, 100 or 200 mg/kg bw/day from gestation days 2 to 16. Ataxia and a slight decrease in body weight were observed at =100 mg/kg bw/day. Nine rabbits in the control group and 31 in the treatment groups died during the study (details not available). There were no treatment related effects on corpora lutea, implantations, number of live foetuses and spontaneous abortions. No further information was available on live birth index, pup growth or developmental NOAEL. The NOAEL for maternal toxicity was reported at the lowest dose tested, i.e. 50 mg/kg bw/day (HERA, 2009; CIR, 2012). In a dermal 2-generation study, C9–11EO6 (CAS No. 68439-46-3) was applied to Fischer 344 rats (30/sex/group, at doses of 0, 10, 100 or 250 mg/kg bw/day, 3 times/week except mating periods). No effects were reported on mating, fertility or mean gestational length in both generations. No treatment-related effects on testicular weights or sperm counts were observed. There were no effects on F1 and F2 litter size, number of live pups or sex ratio. The NOAEL for reproductive and developmental toxicity was established as 250 mg/kg bw/day (HERA 2009; CIR, 2012). In 2 other dermal studies, the NOAEL values for developmental and teratogenicity of C12EO4 were reported at >240–300 mg/kg bw/day for rats and rabbits, respectively (HERA, 2009). Although certain short chain EGEs such as 2-ethoxyethanol (ethylene glycol ethyl ether, EGEE, CAS No. 110-80-5) are known reproductive toxicants, the ability of these glycol ethers to cause testicular atrophy decreases with increasing alkyl chain length, with effects not observed with chain lengths =C3 (OECD, 2004; ECETOC, 2005). In addition, no effects on reproductive organs were observed in several repeated dose toxicity studies (refer to the Repeated dose toxicity section above).
Acute Toxicity	Some of the AEs in this group are currently classified with hazard category 'Acute Toxicity – Category 4' and hazard statement 'H302 Harmful if swallowed' in the HCIS (refer to the Existing Work Health and Safety Controls section). Based on the available animal data and international reviews, the AEs in this group are expected to have low to moderate acute oral toxicity. The toxicity appears to correlate with the degree of ethoxylation (highest for EO5–EO14) and is unlikely to be greatly affected by the alkyl chain length (HERA, 2009; REACHa-h). Unless data for the specific chemical are available to indicate otherwise, moderate acute oral toxicity cannot be ruled out and hazard classification is recommended for the remaining chemicals in this group (refer to the Recommendation section).

	The oral median lethal dose (LD50) values in rats ranged from 600 mg/kg bw (C15–16EO10, C14–15EO11) to 10000 mg/kg bw (CxEO1–3, CxEO>15). The discrepancy in study results was attributable to variations in EO chain lengths and study designs. No relationship between the alkyl chain length and acute oral toxicity was observed (HERA, 2009). At necropsy, congestion of the lung, liver and kidney, haemorrhage of the gastric mucosa, and gastrointestinal irritation (e.g. stomach ulcerations) were observed, particularly after administration of a bolus dose or undiluted chemicals (HERA, 2009). Based on the available data, the AEs in this group are expected to have low acute dermal toxicity. No structural relationship was evident between the AEs and acute dermal toxicity. In rabbits, the dermal LD50s were between 2000 to 5000 mg/kg bw. In rats, the dermal LD50 values ranged from >800 mg/kg bw (C13–15EO10, C13–15EO11) to >5000 mg/kg bw. At necropsy, haemorrhage of subcutaneous tissues and hyperaemia of the small intestine were observed (SCCP, 2007; HERA, 2009). At high doses (>16000 mg/kg bw after a 24-hour dermal application), AEs caused severe skin irritation, ataxia and lung lesions in rabbits (HERA, 2009; CIR, 2012). Based on the available data, the AEs in this group are expected to have low acute inhalation toxicity. In a study compliant with OECD Test Guideline (TG) 403 (Acute Inhalation Toxicity), a single static 6-hour exposure to substantially saturated vapour (131.58 ppm) of C6EO2 (CAS No. 112-59-4) resulted in no mortality or other signs of toxicity in rats (REACHa). In a non-guideline study, a median lethal concentration (LC50) of greater than 0.22 mg/L was reported for C9–11EO5 following 4-hour inhalation as a mist in rats. Other studies reported LC50 values from 1.5 to 20.7 mg/L, indicating that acute toxic thresholds were reached when rats were exposed to undiluted AEs in the form of respirable mists or aerosols, or at concentrations exceeding the saturated vapour pressure in air. At necropsy, corneal opacity, congestion and mottling of the lung, liver and kidney and adrenals were observed (HERA, 2009).
Irritation	Inhalation of droplets and/or particles (aerodynamic diameters <10 µm) released from the aerosolised products of these surfactant chemicals may cause respiratory irritation and consequent damage to the lung through prolonged or repeated exposure (NICNASa). Some of the AEs in this group are currently classified with hazard category 'Skin Irritation – Category 2' and hazard statement 'H315 Causes skin irritation' in the HCIS (refer to the Existing Work Health and Safety Controls section). Based on the available data, this hazard classification is recommended for the remaining chemicals in the group (unless data for the specific chemical are available to indicate otherwise) (refer to the Recommendation section). Overall, the degree of irritation was reported to be dependent on the type of patch (open vs vs semi-occluded vs occluded), exposure time (4 hours to 4 weeks), single vs repeated applications, and the concentration used. The chemicals were moderately to severely irritating at 100 %, slightly to moderately irritating at 10 %, mildly irritating at 1 %, and non-irritating at 0.1–0.5 %. The severity of irritation appears to inversely correlate with the degree of ethoxylation (i.e. more severe irritation for lower ethoxylation EO1–EO3) and is unlikely to be greatly affected by the alkyl chain length (HERA, 2009). In a number of OECD TG 404 (Acute Dermal Irritation/Corrosion) compliant tests, AEs of varying chain lengths were applied undiluted to intact rabbit skin for 4 hours under fully occluded conditions. The chemicals ranged from slightly irritating (C11EO9, C12–14EO15, C13EO20), moderately irritating (C12–14EO10, C13EO6, C13EO5–6.5) to extremely irritating (C12–14EO6, C12–14EO3, C13EO3). The skin reactions from slightly irritating chemicals reversed by 6 days after exposure, and those from moderately to severely irritating chemicals

	persisted up to 14 days of the observation period. The data suggest a possible trend between irritation and degree of ethoxylation, i.e. AEs with lower EO units are likely more irritating than those with higher number of EO units (HERA, 2009). Some of the AEs in this group are currently classified with hazard category ‘Eye Damage – Category 1’ and hazard statement ‘H318 Causes serious eye damage’ in the HCIS (refer to the Existing Work Health and Safety Controls section). Based on the available data, this hazard classification is recommended for the remaining chemicals in the group (unless data are available for the specific chemical to indicate otherwise) (refer to the Recommendation section). In summary, undiluted AEs caused moderate to severe eye irritation in rabbits. The chemicals were also reported to be slightly to moderately irritating at 1–10 % and non-irritating at 0.1 %. The severity of irritation was considered concentration-dependent and appears not to correlate with ethoxylation or alkyl chain length of the AEs. Rinsing the eye immediately after application of some AEs with tap water for 20–30 seconds reduced the severity of the effects. In a number of OECD TG 405 and Good Laboratory Practice (GLP) compliant tests, the majority of undiluted AEs covering the range of C9–C19 and EO2.5–EO15 resulted in Draize eye irritation index (EII) scores of >25 to 50, and were considered moderately to severely irritating. Some chemicals caused irreversible damage to the eye, i.e. conjunctivitis and corneal opacity which persisted to the end of the observation period of 21 days. Vascularisation of the cornea was observed following exposure to undiluted AEs (C7–9EO6 and C14–15EO11; both not listed on the Inventory). Other AEs (C12–13EO2, C7–9EO12, and C14–15EO7) have reported EII scores between 0.5 and 15 (mildly irritating). Thus, there is no clear pattern between the eye irritant responses versus the alkyl or EO chain lengths. Other tests demonstrated that the irritancy of the chemicals (covering the range of C9–C18 and EO3–EO20) could be reduced by rinsing the eye immediately after instillation. Concentrations of 0.1 % were non-irritating and between 1–10 % were slightly to moderately irritating (HERA, 2009). Similar results were reported from Draize tests in albino and New Zealand White rabbits, which covered the range of C9–C15 and EO1–EO18. These chemicals (CAS No. 68439-46-3, 66455-14-9, 68131-39-5 (group members) and 68951-67-7 (not on the Inventory) were severely to extremely irritating when tested undiluted and without rinsing, slightly to moderately irritating at 10 %, and non-irritating to mildly irritating at 0.1–1 % (CIR, 2012).
Sensitisation	Based on available data, the AEs in this group are not considered skin sensitisers. Overall, AEs showed no evidence of skin sensitisation, based on 25 guinea pig maximisation tests (covering the range of C9 to C21 and EO2 to EO21), 13 non-adjuvant Buehler tests (covering the range of C9 to C15 and EO3 to EO13), and local lymph node assay (LLNA) (available for C6EO2, CAS No. 112-59-4). Most of the studies were scientifically well-conducted, and some were compliant with the OECD TG and GLP (HERA, 2009; REACHa; REACHb; REACHc; REACHe; REACHf; REACHg; REACHh).
Health Effects Summary	Undiluted AEs (covering the range of C11–C18 and EO3–EO20) were reported to cause mild skin irritation in a number of standard human occlusive patch tests (4–24 hours). In some cases, mild erythema was observed and cleared within 72 hours (HERA, 2009; CIR, 2012).
Key Study/Critical Effect for Screening Criteria	The critical human health effects of the AEs for risk characterisation are acute oral toxicity and skin and eye irritation. The irritant effects are similar to those caused by other surfactants. The severity of irritation appears to increase directly with the chemical concentration. Skin irritation, but not eye irritation, generally decreases with an increasing degrees of ethoxylation.
Ecological Toxicity[2,3]	
Aquatic Toxicity	The 96 h LC50 value for Alcohols, C9-11, ethoxylated with Oncorhynchus mykiss was 5 - 7 mg/L based on nominal concentrations. In the long-term toxicity test to Lepomis macrochirus, the NOEC (30 days) was 0.11 – 0.33 mg/L.

<table>
<tr><td></td><td>In the short–term toxicity test to Daphnia magna, the EC50 (48 h) was 2.5 mg/L.
In the long-term toxicity test to Daphnia magna, the NOEC (21 days) was 0.77 – 1.75 mg/L.
In the short–term toxicity test to Pseudokirchneriella subcapitata (green algae), the EC50 (96 h) was 1.4 mg/L.
The EC50 (3 h) for microorganisms was 140 mg/L.

In a study conducted with two different fish species (bluegill sunfish and fathead minnow) the effects of C14 -15 alcohol ethoxylates (7EO) were determined (Dorn et al., 1995, Shell). In two experiments fish were exposed for 10 d in a laboratory assay and for 30 d in an outdoor stream mesocosm. Effect parameters determined were survival and growth of juvenile bluegills and survival and reproduction of fathead minnows. In the laboratory experiment the NOEC for survival and swimming performance of bluegills and for survival of fathead minnows was 0.16 mg/L. In the stream mesocosm the NOEC for bluegill survival and growth was >0.33 mg/L and for fathead minnow survival 0.28 mg/L. There was an indication of decreased egg laying by fathead minnow in the streams at concentrations of 0.33 mg/L or greater. On the basis of the reported results a worst-case NOEC of 0.16 mg/L is assumed.

One publication is available for an alcohol ethoxylate mixture with a chain length of C12 - C13 and approximately 6.5 ethoxy groups (Gillespie et al. 1999). The 21 days flow-through chronic experiment on daphnids is conducted according to the guidelines USEPA-TSCA (U.S. EPA, 1992) and ASTM (1988) and is well documented in the paper. Nevertheless the degree of ethoxylation of the tested mixture described in the paper (6.5 EO) is higher than the degree of ethoxylation described for CAS 68131-39-5 (2.5 EO). The NOEC of 0.77 mg/L for reproduction can be used for read-across.</td></tr>
<tr><td>Determination of PNEC aquatic</td><td>A PNECaquatic of 11 µg/L was calculated using the lowest chronic endpoint of NOEC of 0.11 mg/L for Daphnia magna. An assessment factor of 10 was used.</td></tr>
<tr><th colspan="2">Current Regulatory Controls[1]</th></tr>
<tr><td>Listed as a Chemical of Concern on International Databases</td><td>
<table>
<tr><th>International Database</th><th>Listed?</th></tr>
<tr><td>European REACH regulation Substances of very high concern (SVHCs) according to Annex XV
https://echa.europa.eu/candidate-list-table</td><td>No</td></tr>
<tr><td>International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen
https://monographs.iarc.who.int/list-of-classifications</td><td>No</td></tr>
<tr><td>National Toxicology Program (NTP) Report on Carcinogens (RoC)
https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html</td><td>No</td></tr>
<tr><td>US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans
EU list chemicals with endocrine disruption listed in Category 1 or Category 2
https://www.epa.gov/iris</td><td>No</td></tr>
<tr><td>United States Endocrine Disrupter Screening Program
https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</td><td>No</td></tr>
<tr><td>Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin
https://wwwn.cdc.gov/TSP/index.aspx?sysid=18</td><td>No</td></tr>
<tr><td>Montreal Protocol
https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol</td><td>No</td></tr>
<tr><td>Rotterdam Convention
http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals</td><td>No</td></tr>
<tr><td>Stockholm Convention
http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx</td><td>No</td></tr>
</table>
</td></tr>
<tr><td>Australian Hazard Classification</td><td>Alcohols, C12-16, ethoxylated are classified as hazardous on the Hazardous Chemicals Information System (HCIS), with the hazard categories and hazard statements for human health (Safe Work Australia):
Acute Toxicity – Category 4; H302 (Harmful if swallowed)</td></tr>
</table>

	Skin Irritation – Category 2; H315 (Causes skin irritation) Eye Damage – Category 1; H318 (Causes serious eye damage)
Australian Occupational Exposure Standards	No specific exposure standards are available.
International Occupational Exposure Standards	No specific exposure standards are available.
Australian Food Standards	No data available.
Australian Drinking Water Guidelines	No data available.
Aquatic Toxicity Guidelines	Trigger values for freshwater (95% species) (ANZECC 2000): Alcohol ethoxyolated sulfate (AES) = 650 µgL^{-1} Alcohol ethoxylated surfactants (AE) = 140 µgL^{-1}
PBT Assessment	
P/vP Criteria fulfilled?	No. These chemicals were found to be readily biodegradable. Thus, it does not meet the screening criteria for persistence.
B/vB criteria fulfilled?	No. Bioaccumulation in organisms is expected to be negligible, due to biotransformation and excretion of alcohol ethoxylates.
T criteria fulfilled?	No. The NOECs from the chronic aquatic toxicity data are >0.01 mg/L, hence does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT

References

1. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier II Assessment for Ethoxylates of aliphatic alcohols (>C6), Retrieved 2020: https://www.nicnas.gov.au
2. ECHA REACH, Alcohols, C9-11 ethoxylated, < 2.5 EO, Retrieved 2020: https://echa.europa.eu/information-on-chemicals/registered-substances
3. ECHA REACH, Alcohols, C12-15 ethoxylated, Retrieved 2020: https://echa.europa.eu/information-on-chemicals/registered-substances
4. ECHA REACH, Decan-1-ol, ethoxylated, Retrieved 2020: https://echa.europa.eu/information-on-chemicals/registered-substances

Toxicity Summary - Polyethylene glycol trimethylnonyl ether

Chemical and Physical Properties [1,2]	
CAS number	127087-87-0
Molecular formula	Not applicable. This substance is an unknow or variable-composition polymer. The general formula of nonylphenol ethoxylate (NPE) chemicals is $C_{15}H_{24}(C_2H_4O)n$; where 'n' is the number of ethylene oxide (EO) units attached to the phenol ring, and can vary from 1–120.
Molecular weight	Not applicable. This substance is an unknow or variable-composition polymer as described above.
Solubility in water	1.104×10^{-3} g/L at 25 °C
Density	1.042 kg/L at 20°C
Melting point	Not applicable
Boiling point	188.6 °C at 97.77 kPa
Vapour pressure	4.86×10^{-13} kPa at 25 °C
Henrys law constant	No data available.
Explosive potential	Non-explosive
Flammability potential	Non-flammable
Colour/Form	Slightly hazy, colourless liquid
Overview	This chemical is a manufactured NPE. NPEs are primarily used as surfactants in a wide range of cosmetic, domestic and industrial products. This chemical is on the International Fragrance Association (IFRA) transparency list for use in fragrances (IFRA, 2022). It is also listed as an Organisation for Economic Co-operation and Development (OECD) High Production Volume (HPV) chemical, indicating that more than 1000 tonnes of the chemical is produced per year in at least one member country of the OECD. The chemical can be emitted into the environment in treated effluents and biosolids produced by sewage treatment plants.
Environmental Fate [3]	
Soil/Water/Air	This chemical is slightly soluble in water and has low volatility. When released into the environment, long chain NPEs may remain in water due to their high water solubility and low volatility, whereas shorter chain NPEs have lower water solubility and can adsorb to solids such as sediments and sludge. NPEs are susceptible to substantial biodegradation in the environment. Under aerobic conditions, rapid biodegradation forms nonylphenol ethoxyacetates, and under anaerobic conditions, nonylphenols (NPs) and shorter-chain NPE degradants are formed. While some degradants are much more persistent relative to their parent chemicals, they are expected to be ultimately biodegradable in the environment. The chemical is not expected to undergo long-range transport based on biodegradability, low volatility, and adsorption to soil and sediment. Although soluble in water, NPEs have a relatively short primary half-life in water.
Chronic Repeated Dose Toxicity	Based on the available data from repeated dose oral toxicity studies undertaken in rats, mice and beagle dogs these chemicals are not considered to cause serious damage to health following repeated oral exposure. No data are available for NPEs from repeated dermal or inhalation exposure.
Carcinogenicity	Based on the available data from carcinogenicity studies in rats and mice exposed to NPEs orally and intravaginally, NPEs are not considered to be carcinogenic.
Mutagenicity/ Genotoxicity	Based on the available *in vitro* genotoxicity data, NPEs are not considered to be genotoxic, with negative results obtained for NPEs in several *in vitro* assays. No *in vivo* genotoxicity data are available for NPEs.
Reproductive Toxicity /	Studies are available only for NPE-9, NPE-10, NPE-30. No data are available for other NPEs. The chemical NPE-9 is a known spermicide 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

Developmental Toxicity/ Teratogenicity	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, NPs are classified for reproductive and developmental toxicity based on animal data.
Acute Toxicity	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.
Irritation	This chemical can cause skin irritation and serious eye irritation. Moderate to severe skin and eye irritation has been reported in animal studies using rabbits and rats. Slight to mild skin irritation has been observed in humans.
Sensitisation	Based on the available data, NPEs are generally not considered to have skin sensitisation potential, however, there is evidence of mild contact dermatitis in human patch tests with short-chain NPEs.
Health Effects Summary	The critical health effects for risk characterisation are skin and eye irritation. NPEs could also cause systemic acute effects from oral exposure. However, these health effects are applicable mainly for short chain length NPEs and the effects could reduce with increasing chain lengths. Those with with ≥30 EO chains are reported to be generally non-toxic. 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. 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, particularly following secondary exposure from environmental sources.
Key Study/Critical Effect for Screening Criteria	The lowest 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.
Ecological Toxicity [2,3]	
Aquatic Toxicity	Read across from CAS 9016-45-9 (Polyoxyethylene Nonylphenol Ether) Acute: Fish: 96 h EC50 = 1.3 mg/L (Lepomis macrochirus) Invertebrates: 48 h LC50 = 1.821 mg/L (QSAR) Algae: 5 d EC50 = 37.4 mg/L (Scenedesmus opoliensis), Gallery worm: 48 h LC50 = 3.26 mg/L (Capitella capitate) Chronic: Fish: 21 d NOEC = 0.048 mg/L (Oncorhynchus mykiss) (read across from nonylphenol monoethoxylate) Invertebrates: 6 d NOEC = 1.0 mg/L (Daphnia magna) Algae: 96 h NOEC = 8.0 mg/L (Pseudokirchneriella subcapitata)
Determination of PNEC aquatic	Fish are the most sensitive taxon to toxic effects of the chemicals in this group, based on the available information. The PNEC$_{aqua}$ derived for the most toxic chemical in this group, nonylphenol monoethoxylate, is 0.48 µg/L based on the 21 d NOEC of 0.048 mg/L for Oncorhynchus mykiss. The laboratory chronic toxicity value for this fish species was divided by an assessment factor of 100 to account for both interspecies variation and the relative lack of chronic aquatic toxicity data available for chemicals in this group.
Current Regulatory Controls[4]	
Listed as a Chemical of Concern on International Databases	

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	Yes
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No

US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	This chemical is classified as hazardous in Safe Work Australia HCIS. • Hazard categories include: - Acute toxicity – Category 4 - Skin irritation – Category 2 - Eye irritation – Category 2A • Hazard statements include: - H302 (Harmful if swallowed) - H315 (Causes skin irritation) - H319 (Causes serious eye irritation)
Australian Occupational Exposure Standards	No Australian occupational exposure standards are provided by Safe Work Australia HCIS for this chemical.
International Occupational Exposure Standards	No exposure standards provided in NIOSH.
Australian Food Standards	No Australian food standards were identified in FSANZ
Australian Drinking Water Guidelines	No aesthetic or health-related guidance values were identified in the National Health and Medical Research Council (NHMRC) Australian Drinking Water Guidelines (NHMRC, 2022).
Aquatic Toxicity Guidelines	No Australian guidelines available.
PBT Assessment [3]	
P/vP Criteria fulfilled?	No. Based on results obtained from biodegradation studies, this chemical is categorised as Not Persistent.
B/vB criteria fulfilled?	No. Based on the available measured bioconcentration data, this chemical is categorised as Not Bioaccumulative.
T criteria fulfilled?	No. Based on available acute ecotoxicity values above 1 mg/L and chronic ecotoxicity values above 0.1 mg/L, this chemical is categorised as Not Toxic.
Overall conclusion	Not a PBT substance.

Notes: *HCIS – Hazardous Chemical Information System; NIOSH – National Institute for Occupational Safety and Health; FSANZ – Food Standards Australia New Zealand; NHMRC (2022) – National Health and Medical research Council, Australian Drinking Water Guidelines 6, 2011 (Version 3.8, Updated September 2022)*

References

1. AICIS (2019) Nonylphenol and octylphenol ethoxylates and related compounds: Human health Tier II assessment
2. ECHA, https://echa.europa.eu/registration-dossier/-/registered-dossier/19064
3. AICIS (2016) Nonylphenol ethoxylates and their sulfate and phosphate esters: Environment Tier II assessment
4. HCIS, Hazardous Chemical Information System, Safe Work Australia, Retrieved: http://hcis.safeworkaustralia.gov.au/HazardousChemical

Toxicity Summary - Methanol

Chemical and Physical Properties[1,3,4]	
CAS number	67-56-1
Molecular formula	CH4O
Molecular weight	32.04
Solubility in water	1,000 g/L at 20 °C
Density	0.791 kg/L
Melting point	-98 °C
Boiling point	65 °C
Vapour pressure	16.927 kPa at 25 °C
Henrys law constant	0.461 Pa m^3/mol
Explosive potential	Vapour/air mixtures are explosive
Flammability potential	Highly flammable
Colour/Form	Clear colourless liquid
Overview	Methanol occurs naturally in humans, animals and plants. The general population is exposed to methanol mainly through consumption of food and beverages and through use of consumer products such as paints, sealers and adhesives that contain methanol as a solvent. This chemical has been identified by NICNAS to be of low concern to the environment based on Tier I assessment under the NICNAS IMAP assessment framework.
Environmental Fate [1,3]	
Soil/Water/Air	Air is the main target compartment, based on a fugacity model calculation (Mackay Level III) with about 73 % of environmental methanol distributing to air and 16 % to water. Methanol is degraded in the atmosphere by photochemical, hydroxyl-radical dependent reactions. The estimated elimination half-life is calculated to be about 17-18 days with a rate constant of 0.93 x 10-2 cm3/molecule-sec. Methanol is completely miscible in water and has a low octanol/water partition coefficient. These properties are indicative of high mobility in soil.
Human Health Toxicity Summary [1,2,3]	
Chronic Repeated Dose Toxicity	Considering the no observed adverse effect level (NOAEL) available from a 90-day rat study (500 mg/kg bw/day), the chemical is not considered to cause serious damage to health by repeated oral exposure. In a 20-day inhalation study in monkeys, 3.9 mg/L (3000 mL/m3) was identified as the LOAEL (continuous exposure) where neurotoxic lesions appeared to progress in monkeys (according to NEDO 1987). This exposure concentration correlated with methanol blood levels 80 mg/L and formate levels 30 mg/L. There was no evidence of adverse effects in rats exposed to methanol up to 6.6 mg/L, six hours/day for 28 days, except local nasal irritation and increased relative spleen weights, which were observed only at the middle dose and not considered treatment-related (Andrews et al. 1987). A NOAEL could not be established in this study. In the chronic exposure studies in rats and mice, slight treatment-related decreases in body and organ weights were reported at the highest dose. These are however not considered as ‘adverse’ effects. In monkeys, slight degeneration of the inside nucleus of the thalamus was observed at 0.13 and 1.3 mg/L after seven months or more (NEDO 1987). One monkey at 0.13 mg/L and two at 1.3 mg/L showed slight but clear changes in peroneal nerves indicating damage to peripheral nerves. Some signs of fibrosis at 1.3 mg/L, which were considered

	borderline. There were mild but significant effects on heart and kidney at 0.13 and 1.3 mg/L. Histologically, a significant increase of Sudan positive granules was noted in the 1.3 mg group without pathological manifestations (e.g. fibrosis). Although the authors considered the lowest dose (0.013 mg/L) as the LOAEL, it was observed that effects at this dose were very mild and reversible and therefore not considered to be adverse effects. Based on these observations, a NOAEL of 0.013 mg/L was established in this study.
Carcinogenicity	The chemical is not likely to be a carcinogen. In a chronic inhalation study, Fisher rats and B6C3F1 mice were exposed to 0.013, 0.13, and 1.3 mg/L methanol for 24 and 18 months, respectively (NEDO 1987). No differences in survival were noted in the treatment groups compared with the control group. There was no evidence of an increase in liver tumours in rats or in the spontaneous liver tumour rate in mice. In the rats, some tumours such as papillary lung adenomas (males only), adrenal phaeochromocytomas (females only) and metastatic (transition) tumours appeared at a somewhat higher incidence in high-dose group rats after week 79 and 104 without clear dose-response relationship. However these tumour incidences were not statistically significantly different from those in the control group. In the mice, there were no appreciable differences from the control in either numbers of animals with tumours or in degree of malignancy observed. Proliferative effects on the astroglia cells were observed in monkeys continuously exposed to 0.013, 0.13 and 1.3 mg/L methanol by the inhalation route (NEDO 1987). These effects however were of a transient nature and disappeared after a six-month recovery period. There were no signs of histological degeneration.
Mutagenicity/ Genotoxicity	Methanol has been examined in numerous in vitro and in vivo test systems, including bacterial, mammalian and fungal test systems. Most in vitro studies did not demonstrate mutagenic activity. A small number of studies gave ambiguous results. All other studies produced negative results consistently. The majority of in vivo assays were negative for mutagenicity and clastogenicity (OECD 2004). Methanol was therefore concluded to be not mutagenic.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	No impairment of fertility or reproductive performance was reported in male and female rats exposed to the chemical, except at very high doses. Male mice had morphological anomalies in spermatozoa after repeated oral dosing at 1000 mg/kg bw/day (blood level > 500 to 1000 mg/L in mice) (OECD 2004). Rodent studies indicate that methanol has developmental toxicity effects. The rodent data on developmental toxicity are relevant for humans despite the known differences in methanol metabolism between the two species. However, rodents are considered adequate models for humans only at levels where formate does not accumulate (NTP 2003). Blood methanol levels associated with serious developmental effects in rodents were in the range associated with formate accumulation (1000 to 2000 mg methanol per litre of blood), which is likely to result in metabolic acidosis, and visual and clinical effects in humans (NTP 2003; OECD 2004). The limited data available in humans do not show an association between reproductive and developmental toxicity and methanol (NTP 2003). Following a review of the developmental toxicity studies, the NTP concluded that there is evidence to suggest that females with low folate levels may be more susceptible to the adverse developmental effects of methanol, but more information was necessary to clarify this issue (NTP 2003). Based on the data available, the chemical is not considered to have reproductive or developmental toxicity in humans.
Acute Toxicity	In rats, mice, rabbits and dogs, the LD50 values after single oral administration range from about 5600 to 14 400 mg/kg bw (EHC 1997). Adverse effects noted in these animals were ataxia, narcosis and coma after high methanol doses. The animals did not exhibit acidosis and ophthalmologic changes typically seen in humans at high lethal and sub-lethal doses In rhesus monkeys, no deaths were reported at doses of 1000 to 2000 mg/kg bw, while animals receiving 3000 to 8000 mg/kg bw died within two days (OECD 2004). Treated animals showed acidosis, and some exhibited semi-coma and ophthalmologic changes. Human data, however, indicate acute oral toxicity at comparatively lower doses of 300 to 1000 mg/kg bw (EHC 1997). The reported median lethal doses (LD50) for experimental animals are 7300 mg/kg bw (mouse), 5628 mg/kg bw (rat), 14 200 mg/kg bw (rabbit) and 7000 mg/kg bw (monkey). The lowest lethal dose (LDLo) for humans ranges from 143 to 428 mg/kg bw (ChemIDplus 2012).

	There are limited available dermal toxicity studies in animals. In one dermal exposure study all the rats survived after application of 35 000 mg/kg bw methanol to the skin under occlusive conditions, while deaths were reported at 45 000 mg/kg bw (Eulner and Gedicke 1955). In rabbits, a dermal LD50 of 17 000 mg/kg bw was reported although no details of the study were provided (Carnegie-Mellon 1981). Limited data in monkeys indicate that the chemical is toxic via the dermal route (McCord 1931). Humans have been found to be more susceptible to methanol as compared to monkeys. Therefore, acute dermal toxicity with methanol is expected in humans (OECD 2004). The lowest reported dermal LD50 is 17 000 mg/kg bw, which was recorded in rabbits. Median lethal concentrations (LC50) of 87.5 and 128.2 mg/L were reported in rats following six and four hour inhalation exposures to methanol, respectively (BASF 1980a, 1980b). Clinical signs of toxicity were secretions from eyes and nose, laboured breathing, staggering, apathy and narcosis. A similar LC50 value (79 mg/L) was reported for mice following 2.25 hours exposure (Von Burg 1994). In cats, LC50 values after six-hour exposures ranged from 26 to 48 mg/L. A shorter duration of 4.5 hours led to an LC50 of 85.4 mg/L (Von Burg 1994). Studies in Rhesus monkeys indicated lethal concentrations (percent mortality not reported) at 13 mg/L after 18 hour exposure and 52 mg/L after one to four hour exposure (OECD 2004).
Irritation	The chemical is not a skin irritant. The chemical is a slight eye irritant in rabbits. High concentration of methanol vapours may cause irritation of the respiratory tract. In a short-term exposure study (details not available), exposure of rats to an atmosphere saturated with methanol vapours produced severe irritation of mucous membranes and milky corneal opacity (BASF 1975). All animals died after eight hours (BASF 1975).
Sensitisation	The chemical is not a skin sensitiser.
Health Effects Summary	Methanol has low acute oral, dermal and inhalation toxicity in experimental animals but moderate to high acute oral and dermal toxicity in humans. A Lowest Lethal Dose (LDLo) of 143 - 428 mg/kg bw (humans) has been reported. It is not a skin or eye irritant but is expected to be a moderate respiratory irritant, based on its effect on the mucous membrane in rats exposed to methanol vapours and on the effects observed in repeat dose inhalation studies. Tests with guinea pigs indicated that methanol is not a skin sensitiser. The critical effects to human health are acute toxicity from inhalation, skin contact and swallowing, and possible irreversible effects from acute oral exposure. No deaths were reported in Rhesus monkeys dosed at 2 000 mg/kg bw, but treated animals showed acidosis, and some exhibited semi-coma and ophthalmic changes. Human data, however, indicate acute oral toxicity and ophthalmic changes at comparatively lower doses of 300 - 1 000 mg/kg bw. Information on repeated dose toxicity by the dermal route is not available. Methanol was not genotoxic or carcinogenic. Reproductive and developmental toxicity studies did not show any significant effects of relevance to humans.
Key Study/Critical Effect for Screening Criteria	A No-Observed-Adverse-Effect-Concentration (NOAEC) of 0.013 mg/L (13 mg/m^3) is used for this risk assessment. This NOAEC is derived from a chronic inhalation study in monkeys, in which degenerative effects in the brain and slight damage to the optic and peripheral nerves were noted at 0.13 mg/L and above. Changes in peroneal nerves were also noted in higher dosed animals, indicating damage to peripheral nerves. An oral No Observed Adverse Effect Level (NOAEL) of 500 mg/kg bw/day was also established in rats in a 90-day oral study based on increased liver enzymes (enzymes not specified) and decreased absolute brain weights at the highest dose. This value is not used in this risk assessment because acute oral data indicate that humans are more sensitive to methanol toxicity than rodents.
Ecological Toxicity [2,3]	
Aquatic Toxicity	In several 96-hour studies in fish in which methanol concentrations were measured during the tests, LC50s ranged from 15,400 to 29,400 mg/L. In the chronic toxicity study to invertebrates, the NOEC was 32,000 mg/L.
Determination of PNEC aquatic	This chemical has been identified by NICNAS to be of low concern to the environment based on Tier I assessment under the NICNAS IMAP assessment framework. No further assessment is required.

Current Regulatory Controls [1,2,4]

Listed as a Chemical of Concern on International Databases

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	The chemical is classified as hazardous with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia): T; R23/24/25 (acute toxicity) T; R39/23/24/25 (irreversible effects from acute exposure) Mixtures containing the chemical are classified as hazardous based on the concentration (Conc) of the chemical in the mixtures. The risk phrases for this chemical are: Conc ≥20%: T; R23/24/25; (Toxic: Toxic by inhalation, in contact with skin and if swallowed); R39/23/24/25; (Toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed) 10% ≤Conc <20%: T; R20/21/22; (Toxic: Harmful by inhalation, in contact with skin and if swallowed); R39/23/24/25; (Toxic: danger of very serious irreversible effects through inhalation, in contact with skin and if swallowed) 3% ≤Conc <10%: Xn; R20/21/22; (Harmful: Harmful by inhalation, in contact with skin and if swallowed); R68/20/21/22; (Harmful: possible risk of irreversible effects through inhalation, in contact with skin and if swallowed).
Australian Occupational Exposure Standards	The chemical has an exposure standard of 262 mg/m³ (200 ppm) Time Weighted Average (TWA) and 328 mg/m³ (250 ppm) Short-Term Exposure Limits (STEL) (Safe Work Australia).
International Occupational Exposure Standards	The following were identified (Galleria Chemica): 250-270 mg/m³ (200 ppm) TWA in USA, Canada, Denmark, United Kingdom, Germany, France, Estonia, Greece, Hungary, South Africa, Spain, Singapore, Taiwan, Sweden, Malta, Malaysia, Latvia, Japan, Indonesia, India, Iceland, Egypt, Ireland, Mexico, Philippines and Switzerland;

	250-350 mg/m^3 (250-328 ppm) STEL in USA, Canada, United Kingdom, Greece, South Africa, Singapore, Sweden, India, Egypt and Mexico; 50 mg/m^3 TWA in Bulgaria; 100 mg/m^3 TWA and 300 mg/m^3 STEL in Poland; 133 mg/m^3 TWA in Netherlands; 25 mg/m^3 TWA and 50 mg/m^3 STEL in China; 1300 mg/m^3 (1000 ppm) STEL in France; and 1040 mg/m^3 STEL in Hungary and Switzerland.
Australian Food Standards	No Australian food standards were identified (FSANZ 2013)
Australian Drinking Water Guidelines	No aesthetic or health-related guidance values were identified for methanol in the Australian Drinking Water Guidelines (National Health and Medical Research Council (NHMRC) 2011).
Aquatic Toxicity Guidelines	No data available.
PBT Assessment[4]	
P/vP Criteria fulfilled?	No. Methanol is expected to be readily biodegradable.
B/vB criteria fulfilled?	No. The Log Kow for methanol is -0.77. Thus, methanol does not meet the screening criteria for bioaccumulation.
T criteria fulfilled?	No. The EC50s from the acute aquatic toxicity data on methanol are >1 mg/L, hence does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT

References

1. NICNAS (2017) Human Health Tier II Assessment for Methanol
2. National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2017). National assessment of chemicals associated with coal seam gas extraction in Australia. Human health hazards of chemicals associated with coal seam gas extraction in Australia.
3. OECD (2008) SIDS Initial Assessment Profile on Methanol
4. ECHA REACH, Methanol, Retrieved 2017: https://echa.europa.eu/information-on-chemicals/registered-substances

Toxicity Summary - Propan-2-ol (Isopopranol)

Chemical and Physical Properties[1,3,4,5,6]	
CAS number	67-63-0
Molecular formula	C_3H_8O
Molecular weight	60.10 g/mol
Solubility in water	100 vol% at 20 °C (miscible)
Melting point	-88.5 °C
Boiling point	82.5 °C
Vapour pressure	45.4 mm Hg at 25°C
Henrys law constant	7.52×10^{-6} atm m^3/mole
Explosive potential	Is classified as explosive. The vapours may form an explosive mixture with air.
Flammability potential	Flammable liquid and vapour.
Colour/Form	Colourless liquid with a pleasant odour.
Overview	Isopropanol (IPA) is a high production volume chemical which has wide use as an industrial solvent and as a component in numerous industrial and consumer products. It has a potential for widespread exposure to both workers and consumers. Based upon physical and chemical properties, isopropanol is not expected to persist in the environment. Aerobic biodegradation of isopropanol occurs rapidly. IPA is not expected to persist in soil due to low soil adsorption and rapid evaporation to air. In the air, isopropanol is subject to rapid oxidation by hydroxyl radical attack. IPA has a low order of toxicity to aquatic organisms and plants, and bioconcentration in aquatic organisms is not expected to occur.
Environmental Fate[1,4,5,6]	
Soil/Water/Air	Based on calculated results from a Level I fugacity model, isopropanol is expected to partition primarily to the aquatic compartment (77.7%) with the remainder to the air (22.3%) (OECD, 1977a,b). Aerobic biodegradation of isopropanol has been shown to occur rapidly under nonacclimated conditions, based on a result of 49% biodegradation from a 5-day BOD test (Bridie *et al.*, 1979). Additional biodegradation data developed using standardized test methods show that isopropanol is readily biodegradable in both freshwater and saltwater media (72 to 78% biodegradation in 20 days) (Price *et al.*, 1974). Bioconcentration of isopropanol in aquatic organisms is not expected to occur based on a measured log n-octanol/water partition coefficient (log Kow) of 0.05, a calculated bioconcentration factor of 1 for a freshwater fish, and the unlikelihood of constant, long-term exposures (OECD 1977a,b).
Human Health Toxicity Summary [1,2,3,4,5,6]	
Chronic Repeated Dose Toxicity	Considering the lowest observed adverse effect levels (LOAELs) available from a 12-week rat study (1390 mg/kg bw/day), and based on the treatment-related effects reported in various repeated dose toxicity studies, the chemical is not considered to cause serious damage to health from repeated oral exposure. Male Wistar rats were administered the chemical at concentrations of 0, 1, 2, 3, or 5 % (0, 870, 1390, 1700, or 2500 mg/kg bw/day) in drinking water for 12 weeks. The top dose was reduced to 4 % due to unpalatability after two weeks. Significantly decreased bodyweights were seen at the two highest doses and dose-related increases in relative liver and kidney weights were also significant at 1390 mg/kg bw/day and above. Relative adrenal weights were also significantly increased at the two highest doses; increased testis weight was noted only at the top dose. A dose-dependent increase of hyaline casts and hyaline droplet formation in the proximal tubules of the kidneys was also noted. The no observed adverse effect level (NOAEL) was determined to be 870 mg/kg bw/day, based on

	liver and kidney effects observed at the LOAEL of 1390 mg/kg bw/day (OECD, 2002; EFSA, 2005). In another repeated dose study, rats (strain not specified) were administered the chemical in drinking water at doses of 600 or 2300 mg/kg bw/day for males and 1000 or 3900 mg/kg bw/day for females for 27 weeks. Male rats showed decreased bodyweight gain during the first 13 weeks and increased bodyweight gain for the remainder of the treatment. Female rats showed decreased bodyweight gain throughout the dosing period. No other effects were reported. The NOAELs were 2300 and 1000 mg/kg bw/day for males and females, respectively. The LOAEL in females was 3900 mg/kg bw/day but could not be established in males (OECD, 2002). Several repeated dose inhalation studies were available in rats and mice. Considering the no observed adverse effect concentrations (NOAECs) available from these studies (500 ppm), and based on the treatment-related effects reported, the chemical is not considered to cause serious damage to health from repeated inhalation exposure. The kidney appears to be the target organ with kidney lesions and changes in urine chemistry indicative of impaired kidney function observed at doses ≥2500 ppm in animals exposed to the chemical for 78 weeks (effects not observed in 13-week studies). Transient signs of narcosis were observed for both mice and rats at doses ≥1500 ppm (OECD, 2002; REACH; US EPA, 1986). The investigation by Burleigh-Flayer et al. (1997), showed chronic kidney effects in rodents and is the only study that conducted lifetime rodent exposure to isopropanol. The kidney effects seen in this study were not reported in the 13-week studies by Burleigh-Flayer et al. (1994) which possibly indicates that longer term exposure is necessary for the development of the lesions. The increased hyaline droplets in the kidney observed in the study of Burleigh-Flayer et al. (1994) are a male rat-specific nephropathy and is not considered to be relevant to humans. The LOAEC and NOAEC established from the critical study were 2500 and 500 ppm, respectively, which are equivalent to 1275 and 255 mg/kg bw/day, respectively. Although limited information is available, it has been reported that oral intake of low doses of the chemical (2.6 or 6.4 mg/kg bw/day) by groups of eight men for six weeks had no effect on their blood cells, serum or urine and also produced no clinical symptoms (HSDB).
Carcinogenicity	Based on available data, the chemical is not considered to be carcinogenic (OECD, 2002; WHO, 1990a; EFSA, 2005; REACH). The International Agency for Research on Cancer (IARC) has concluded that there is inadequate evidence for the carcinogenicity of isopropanol in laboratory animals and humans, placing the chemical in Group 3 (Not classifiable as to its carcinogenicity to humans) (IARC, 1999). Although there are no carcinogenicity studies available for the chemical by oral exposure, studies are available for inhalation exposure in rats and mice. In a carcinogenicity study (OECD TG 451), F344 rats were exposed (whole-body) through inhalation to vapours of the chemical at concentrations of 0, 500, 2500, and 5000 ppm for six hours a day, five days a week for two years. The only neoplastic lesion found was stated to be increased frequency of interstitial (Leydig) cell adenoma of the testis (77.3, 86.7 and 94.7 % at low, mid and top dose groups, respectively). The authors did not consider the tumours to be treatment related as testicular adenomas are a common finding in aged male rats and that incidence of this spontaneous tumour reported for the control group (64.9 %) of this study was lower than the historical incidence (88 %) of control F344 rats of numerous two-year National Toxicology Program (NTP) carcinogenicity studies. In a similar carcinogenicity study, CD-1 mice were also exposed (whole-body) through inhalation to vapours of the chemical at concentrations of 0, 500, 2500, and 5000 ppm for six hours a day, five days a week for 18 months. No

	increased frequency of neoplastic changes was reported in any of the treated groups (OECD, 2002; EFSA, 2005; REACH).
Mutagenicity/ Genotoxicity	The chemical does not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were only observed secondary to maternal toxicity.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	The chemical does not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were only observed secondary to maternal toxicity. Several one or two-generation reproductive toxicity studies (rats) and developmental studies (rats and rabbits) were available. Other than a statistically significant reduction in the male mating index observed in a recent two generation study (high dose, 1000 mg//kg bw/day second generation males), there were no other effects on reproductive indices, including fertility and gestational indices and histopathology of the reproductive organs. The NOAELs for reproductive toxicity were reported as ≥500 mg/kg bw/day. A benchmark dose (BMD) assessment was conducted for the study's developmental and reproductive findings (Shipp et al., 1996). For the offspring developmental effects, BMD dosages (BMDL5) of 449 and 418 mg/kg/day were estimated for the F1 and F2 generations, respectively. Based upon the decrease in male mating index observations in the P2 males, a BMDL10 of 407 mg/kg/day was estimated for reproductive effects (OECD, 2002; EFSA, 2005; REACH). Developmental effects, including a reduction in postnatal survival and decreased foetal bodyweights, occurred only at maternally toxic doses. No accompanying malformations were observed. In a developmental toxicity study (US EPA TSCA Guidelines), pregnant Sprague Dawley (SD) rats were administered the chemical by gavage at 0, 400, 800 or 1200 mg /kg bw/day on gestational days 6–15. In the same study, pregnant New Zealand white rabbits were dosed orally with the chemical at 0, 120, 240 or 480 mg/kg bw/day during gestational days 6–18. There was no evidence of developmental toxicity in rats and rabbits at any tested dose. There was mortality of two dams (8%) at 1200 mg/kg and one dam (4%) at 800 mg/kg. Reduced maternal gestational weight gain associated with significantly reduced gravid uterine weights was noted in the higher dose group. The NOAEL for maternal toxicity in rats was reported to be 400 mg/kg bw/day. The NOAEL for developmental toxicity in rats was established as 400 mg /kg bw/day, based on significantly reduced foetal litter body weights at the 800 and 1200 mg/kg dose levels. The NOAEL for maternal toxicity in rabbits was determined to be 240 mg/kg bw/day, based on decreased maternal bodyweight and profound clinical signs (peripheral vasodilatation, cyanosis, lethargy, laboured respiration) of toxicity seen at the top dose. There was no evidence of any developmental toxicity and the NOAEL for developmental toxicity was established as the highest dose: 480 mg/kg bw/day. There was no evidence of any teratogenicity in either studies in rats and rabbits (US EPA, 1995; OECD, 2002; EFSA, 2005; HSDB; REACH).
Acute Toxicity	The chemical was of low acute toxicity in animal tests following oral exposure. The median lethal dose (LD50) in rats is greater than 2000 mg/kg bw. Observed effects included irritation and respiratory arrest while under narcosis (OECD, 2002; WHO, 1990a; HSDB). The chemical was of low acute toxicity in an animal test following dermal exposure. The median lethal dose (LD50) in rats is greater than 2000/kg mg/kg bw. Observed effects were not reported (OECD, 2002; WHO, 1990a; HSDB). The chemical was of low acute toxicity in animal tests following inhalation exposure with reported median lethal concentrations (LC50) >20 mg/L in rats (OECD, 2002; HSDB). Observed effects included severe irritation of the mucous membranes and central nervous system depression as indicated by ataxia, prostration and narcosis.

	The chemical is currently classified with the risk phrase 'Vapours may cause drowsiness and dizziness (R67)' in Australia (Safe Work Australia—HSIS). In an acute inhalation toxicity study (OECD TG 403), Fischer 344 (F344) rats were exposed (whole-body exposure) to the chemical at 500, 1500, 5000, and 10000 ppm for six hours (instead of the standard four hours). Transient concentration-related narcosis and/or central nervous system sedation was noted in the study and the motor activity was decreased at 1500 ppm (males only), 5000 ppm (both sexes). Severe central nervous system depression was seen in the 10000 ppm group. After one and six hours exposure at 10000 ppm, prostration, severe ataxia, decreased arousal, slowed or laboured respiration, decreased neuromuscular tone, hypothermia, and loss of reflex function was observed (OECD, 2002; REACH). Acute intoxication incidents in humans with the chemical have been reported (WHO, 1990b; OCED, 2002; HSDB). Ingestion and inhalation are the common routes of poisoning in humans. Acute intoxication of the chemical has a rapid onset (30–60 minutes) following ingestion, and reported symptoms included drowsiness, poor coordination, abdominal pain, cramps, nausea, vomiting and diarrhea, with unconsciousness and death following massive exposure. Inhaling high concentrations of the chemical can cause nausea, headache, light headedness, drowsiness, ataxia and deep narcosis (WHO, 1990b; OECD, 2002; HSDB).
Irritation	Isopropanol applied to the intact or abraded skin of rabbits and guinea pigs produced negligible irritation (Nixon *et al.*, 1975). Liquid isopropanol is moderately irritating to the eyes of rabbits (Griffith *et al.*, 1980; WHO, 1990). Isopropanol produced little irritation when tested on the skin of six human subjects (Bevan, 2012).The chemical is classified as hazardous with the risk phrase 'Irritating to eyes' (Xi; R36) in HSIS (Safe Work Australia). The available data support this classification (OECD, 2002; WHO, 1990a; REACH).
Sensitisation	There have been reports of isolated cases of dermal irritation and/or skin sensitization (Bevan, 2012). Except for three case reports, the positive reactions were observed on patch testing patients with contact dermatitis due to ethanol. These patients also had a positive reaction to ethanol. The chemical does not contain a structural alert for skin sensitisation (OECD Toolbox).
Health Effects Summary	The critical health effects for risk characterisation include the potential for eye irritation and intoxication symptoms following inhalation of high vapour concentrations.
Key Study/Critical Effect for Screening Criteria	The most appropriate NOAEC for risk assessment, determined from the 104-week study by Burleigh-Flayer et al. (1997), is 255 mg/kg bw/day based on kidney effects at the LOAEC of 1275 mg/kg bw/day. Uncertainty factors: 10 (interspecies variability); 10 (intraspecies variability) Oral Reference Dose = 255/100 = 2.55 mg/kg/day Drinking water = 10 mg/L
Ecological Toxicity [2,4,5]	
Aquatic Toxicity	The 96-hour LC50 in *Pimephales promelas* is 9,640 mg/L (Veith *et al.*, 1983). The 24- hour EC50 in *Daphnia magna* is >10,000 mg/L (Brinkmann and Kuehn, 1977). Chronic aquatic toxicity has also been shown to be of low concern, based on 16- and 21-day NOEC values of 141 and 30 mg/L, respectively, for the freshwater invertebrate *Daphnia magna* (Hermens *et al.*, 1985); OECD, 1977a,b). Toxicity of isopropanol to plants is expected to be low, based on a 7-day toxicity threshold value of 1,800 mg/L for freshwater algae (Bringmann and Kuehn, 1980).
Determination of PNEC aquatic	PNECaquatic: Experimental results are available for three trophic levels. Acute E(L)C50 values are available for fish (9,640 mg/L) and invertebrates (>10,000 mg/L). Results from chronic studies are available for invertebrates (16- and 21-day NOECs for Daphnia are 141 and 30 mg/L, respectively). On the basis that the data consists of a chronic study on one trophic level, an assessment factor of 100 has been applied to the lowest reported NOEC of 30 mg/L for Daphnia. The PNECaquatic is 0.3 mg/L.
Current Regulatory Controls [7]	

<table>
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<tr><td>European REACH regulation Substances of very high concern (SVHCs) according to Annex XV
https://echa.europa.eu/candidate-list-table</td><td>No</td></tr>
<tr><td>International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen
https://monographs.iarc.who.int/list-of-classifications</td><td>No</td></tr>
<tr><td>National Toxicology Program (NTP) Report on Carcinogens (RoC)
https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html</td><td>No</td></tr>
<tr><td>US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2
https://www.epa.gov/iris</td><td>No</td></tr>
<tr><td>United States Endocrine Disrupter Screening Program
https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</td><td>No</td></tr>
<tr><td>Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin
https://wwwn.cdc.gov/TSP/index.aspx?sysid=18</td><td>No</td></tr>
<tr><td>Montreal Protocol
https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol</td><td>No</td></tr>
<tr><td>Rotterdam Convention
http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals</td><td>No</td></tr>
<tr><td>Stockholm Convention
http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx</td><td>No</td></tr>
</table>
</td></tr>
<tr><td>Australian Hazard Classification</td><td>The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):
Xi; R36 (Irritation)
R67 (Vapours may cause drowsiness and dizziness)</td></tr>
<tr><td>Australian Occupational Exposure Standards</td><td>The chemical has an exposure standard of 983 mg/m^3 (400 ppm) time weighted average (TWA) and 1230 mg/m^3 (500 ppm) short-term exposure limit (STEL).</td></tr>
<tr><td>International Occupational Exposure Standards</td><td>The following exposure standards are identified (Galleria Chemica):
An exposure limit (TWA) of 245–999 mg/m^3 (100–400 ppm) in countries such as Canada, Denmark, Iceland, Germany, Norway, Sweden, Spain, Switzerland, UK, and USA.
An exposure limit (STEL) of 600–1250 mg/m^3 (250–500 ppm) in countries such as Canada, France, Spain, Sweden, Switzerland, UK, and USA.</td></tr>
<tr><td>Australian Food Standards</td><td>Isopropanol is listed in Standard 1.3.1 of the Australia New Zealand Food Standards Code and has a permitted use as a food additive at a maximum permitted level of 1000 mg/kg (Food Standards Australia New Zealand 2013).</td></tr>
<tr><td>Australian Drinking Water Guidelines</td><td>No data available</td></tr>
<tr><td>Aquatic Toxicity Guidelines</td><td>No data available</td></tr>
<tr><td colspan="2">PBT Assessment [4,5]</td></tr>
<tr><td>P/vP Criteria fulfilled?</td><td>Isopropanol is readily biodegradable and thus it does not meet the screening criteria for persistence.</td></tr>
<tr><td>B/vB criteria fulfilled?</td><td>Based on a measured log Kow of 0.05 and a calculated BCF of 1, isopropanol does not meet the screening criteria for bioaccumulation.</td></tr>
<tr><td>T criteria fulfilled?</td><td>The chronic toxicity data on isopropanol show NOECs of >0.01 mg/L. Thus, isopropanol does not meet the screening criteria for toxicity.</td></tr>
<tr><td>Overall conclusion</td><td>Not a PBT substance (based on screening data).</td></tr>
</table>

References

1. HSDB (n.d.). *Hazardous Substances Data Bank*. Retrieved 2017, from Toxnet, Toxicology Data Network, National Library of Medicine: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
2. ECHA REACH database: http://apps.echa.europa.eu/registered/registered-sub.aspx
3. IPCS Inchem, Isopropyl Alcohol, CAS#67-63-3
4. OECD (1997a). IUCLID Data Set for 2-Propanol (CAS No. 67-63-0), UNEP Publications.
5. OECD (1997b) Screening Information Dataset (SIDS) Initial Assessment Report for 2- Propanol (CAS No. 67-63-0), UNEP Publications.
6. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier II Assessment for 2-Propanol CAS Number: 67-63-0, Retrieved 2018: https://www.nicnas.gov.au
7. Safe Work Australia 2011. Workplace Exposure Standards for Airborne Contaminants.
8. Department of the Environment and Energy 2017 , National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme

Toxicity Summary - Cinnamaldehyde

Chemical and Physical Properties [1,2,3,4]	
CAS number	104-55-2
Molecular formula	C_9H_8O
Molecular weight	132.16
Solubility in water	2.11 g/L at 22 °C
Melting point	-18 °C
Boiling point	250°C
Vapour pressure	3.85 Pa at 25 °C
Henrys law constant	0.162 Pa.m^3.mol-1 at 25 °C
Explosive potential	Non-explosive
Flammability potential	Non-flammable
Colour/Form	Yellowish oily liquid with strong odour of cinnamon
Overview	Cinnamaldehyde is a plant natural product that is present in some essential oils extracted from plants. For large scale applications such as in the flavouring and fragrance industries, this chemical is synthesised.
Environmental Fate [1,3]	
Soil/Water/Air	Cinnamaldehyde is expected to remain in soil, or partition to water and sediment, when released as a result of industrial uses. It is not expected to be persistent in the environment and is expected to undergo rapid and ultimate biodegradation in water. Cinnamaldehyde is not expected to bioaccumulate in aquatic organisms. No evidence has been identified to indicate that Cinnamaldehyde biomagnify through the aquatic food chain. The atmospheric oxidation half-life of cinnamaldehyde was estimated using the level III multimedia model. It was estimated that the substance is not persistent in air medium as the half-life period of cinnamaldehyde in air is only 0.31 days. This indicates that cinnamaldehyde is rapidly phototransformed in air. The Hydrolysis rate constant of Cinnamaldehyde is estimated to be 3.36 x 10-17 cm3/molecule-sec. at half-life of 3.411 days indicating that the substance is slowly hydrolysable.
Human Health Toxicity Summary [2,4]	
Chronic Repeated Dose Toxicity	Cinnamaldehyde is 'generally regarded as safe' for use as a flavour ingredient by the US Food and Drug Administration (US FDA, 2015), reflecting the low level of concern regarding its potential for long-term toxicity via the oral route. Considering the no observed adverse effect levels (NOAELs) of 68–200 mg/kg bw/day, based on 17-week to 2-year rat studies (read across), and no toxicologically significant treatment-related effects reported in various studies, repeated oral exposure to the chemical is not considered to cause serious damage to health. Based on the limited data available, the chemical is not considered to cause serious damage to health by repeated dermal exposure.
Carcinogenicity	Based on the limited data available for cinnamaldehyde and trans-cinnamaldehyde (CAS No. 14371-10-9), the chemical is not expected to have carcinogenic potential. In a two-year carcinogenicity study, groups of F344/N rats and B6C3F1 mice (50 animals/sex/dose) were fed microencapsulated trans-cinnamaldehyde (CAS No. 14371-10-9) by daily gavage at doses of 0, 1000, 2100 or 4100 ppm (equivalent to 0, 50, 100 or 200 mg/kg bw/day). Increased incidences of preputial and prostate gland adenomas and mononuclear cell leukaemia were considered to be within the historical range in controls, or likely to represent biological variations unrelated to exposure to the chemical. No other treatment-related neoplasms or non-neoplastic lesions were reported in either species (Adams et al., 2004; NTP, 2004; REACH; US HPVIS, 2009).
Mutagenicity/ Genotoxicity	The chemical cinnamaldehyde contains an a,b-unsaturated aldehyde group, a common structural alert for genotoxicity due to the ability of the chemical to form DNA adducts. However, based on the available data, the chemical is not

	considered to be genotoxic. The chemical cinnamaldehyde and the isomer trans-cinnamaldehyde (CAS No. 14371-10-9) were negative for point mutations in almost all strains of Salmonella typhimurium in the Ames test. A positive result was found only with TA100 strain, and in only two out of eleven tests. Evidence of genotoxic activity was also observed in isolated mammalian cells. However, these results were weakly positive and observed at cytotoxic concentrations. A sex-linked recessive lethal test in Drosophila melanogaster demonstrated that systemically-available chemical (administered via injection) could enter germ cells and induce mutations; however, oral dosing did not produce the same effect. Importantly, the reported activity in in vitro and insect studies did not translate into significant genotoxic activity in mammalian systems in vivo.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	The chemical is not expected to have the potential for reproductive or developmental toxicity. Any developmental effects were only observed secondary to maternal toxicity. In a two-generation study in rats (strains not reported), cinnamaldehyde (absolute dose 2 mg—route not specified) was dosed every two days for 223 and 210 days and did not have any effects on body weight gain, reproductive ability, development or viability of offspring (NTP, 2004). Cinnamaldehyde in olive oil was administered to female SD rats via oral gavage at doses of 0, 5, 25 or 250 mg/kg bw/day on gestation days (GD) 7–17. Treatment-related, increased incidence of defective cranial ossification in all dose groups was observed. Renal abnormalities including dilated pelvis and reduced papilla and dilated ureters were observed at low and mid doses, but not at high dose. Offspring at ≥25 mg/kg bw/day had significantly increased instances of reduced ossification of the tympanic bulla. An increase in the incidence of abnormal sternebrae was also reported in the 25 mg/kg bw/day group. However, these effects were not found to be dose-related and may be attributed to a decrease in maternal weight gain that was noted in the mid- and high-dose groups. A LOAEL of 5 mg/kg bw/day for developmental toxicity was reported based on the reduced cranial ossification and kidney variations. A LOAEL of 25 mg/kg bw/day was reported for maternal toxicity based on the reduced weight gain observed in the dams (Adams et al., 2004; NTP, 2004; US HPVIS, 2009; HSDB; REACH). No signs of toxicity were reported in the dams or in the offspring of CD-1 mice after exposure to 1200 mg/kg bw/day during GD 6–13 (cinnamaldehyde) or GD 7–14 (trans-cinnamaldehyde) (NTP, 2004; US HPVIS, 2009; REACH).
Acute Toxicity	Cinnamaldehyde has low acute oral toxicity based on animal studies. The median lethal dose (LD50) in rats is >2000 mg/kg bw. Cinnamaldehyde has moderate acute dermal toxicity based on animal studies, warranting hazard classification. The dermal LD50 in rabbits was in the range of 620–1260 mg/kg bw (Bickers et al., 2005; Cocchiara et al., 2005; FFHBVC, 2005; and US HPVIS, 2009). Albino rabbits (2 animals/dose) were administered a single dose of cinnamaldehyde (0, 0.25, 0.50, 1.0, 2.0 or 4.0 mL/kg bw—equivalent to 0, 263, 525, 1050, 2100 or 4200 mg/kg bw) by application to intact and abraded skin. All animals in the 1.0 mL/kg and higher dose groups died after treatment. The LD50 was reported to be 620 mg/kg bw (Cocchiara et al., 2005; FFHPVC, 2005; US HPVIS, 2009; REACH).
Irritation	Respiratory irritation was assessed in CF-1 female mice by recording their respiratory rate following exposure to nebulised cinnamaldehyde for 1 minute, either through nose-only breathing or via a tracheal cannula. Marked respiratory depression with nose-only inhalation was observed. The ED25 (dose providing a 25 % reduction in respiratory rate) was calculated to be 241 µg/L. No significant effects were observed when inhalation was through the tracheal cannula (Cocchiara et al., 2005). Cinnamaldehyde produced severe irritation in rabbits when applied undiluted, mild irritation in mice and guinea pigs at concentrations of 3–5 %, and was non-irritating to rabbits at 1 % (Bickers et al., 2005). The US EPA considers cinnamaldehyde a strong skin irritant in guinea pigs (no study details provided) (US HPVIS, 2009). Several international agencies have concluded that cinnamaldehyde is an eye irritant (US HPVIS, 2009; REACH), and a number of notifications to the Classification and Labelling Inventory by industry in the European Union have indicated the chemical as irritating to the eyes (ECHA C&L).
Sensitisation	The chemical was considered to be a moderate to strong skin sensitiser based on the positive results in several local lymph node assays (LLNA). The EC3 value (concentration required to provoke a 3-fold increase in lymph node cell

<table>
<tr><td></td><td>proliferative activity compared with controls) was reported to be as low as 0.2 % (SCCS, 2012).</td></tr>
<tr><td>Health Effects Summary</td><td>Cinnamaldehyde is a well-recognised and frequently reported consumer contact allergen (SCCNFP, 1999; RIVM, 2009; SCCS, 2012; IFRA, 2013). It is one of eight components of the diagnostic test, the fragrance mix, used by dermatologists to determine if a patient has allergies to common chemicals used in fragrances. It is an established contact allergen in humans according to the Scientific Committee on Consumer Safety (2012), and accounts for 5–36 % of the reactions to the fragrance mix (SCCNFP, 1999).

A number of human repeat insult patch tests (HRIPTs) have been undertaken to determine the skin sensitisation potential of cinnamaldehyde in healthy volunteers, as well as groups of subjects suspected of skin allergies to fragrances (SCCNFP, 1999; NTP, 2004; Cocchiara et al., 2005). Although fewer cases of sensitisation were found when the concentration of the chemical was less than 1 %, positive allergic responses have been reported in cases where the administered concentration of cinnamaldehyde was as low as 0.2 % (Cocchiara et al., 2005). Skin irritation effects were generally predominant at concentrations above 3 % cinnamaldehyde, and often impeded the interpretation of results from the patch testing (SCCNFP, 1999; NTP, 2004).

Many cases of skin sensitisation have occurred following occupational and consumer exposure to the chemical. Workers in spice manufacturing plants, hairdressing salons and bakeries have reported cases of contact dermatitis that were traced back to cinnamaldehyde. In addition, exposure of consumers to toothpaste, cosmetics and perfumes containing the chemical as a fragrance ingredient have resulted in a number of case studies identifying cinnamaldehyde as an agent responsible for the allergic reactions (see SCCNFP, 1999; NTP, 2004; Cocchiara et al., 2005 for review).</td></tr>
<tr><td>Key Study/Critical Effect for Screening Criteria</td><td>The critical health effect for risk characterisation is skin sensitisation. Other observed health effects include systemic acute effects (acute toxicity from dermal exposure) and local effects (eye/skin/respiratory irritation).</td></tr>
<tr><td colspan="2">Ecological Toxicity [1]</td></tr>
<tr><td>Aquatic Toxicity</td><td>The following data are measured acute toxicity values for cinnamaldehyde: Danio rerio (Zebrafish) EC Directive 92/69/EEC C.1 Acute Toxicity for Fish: 96 h LC50 = 3.1 mg/L; Daphnia magna (Water flea) OECD TG 202: 48 h EC50 = 3.86 mg/L; Pseudokirchneriella subcapitata (Green algae) OECD TG 201: 72 h EC50 = 4.07 mg/L.
In the chronic toxicity study, the 72 h NOEC value of 2.0 mg/L was reported for Pseudokirchneriella subcapitata (Green algae) OECD TG 201.</td></tr>
<tr><td>Determination of PNEC aquatic</td><td>A PNECaqua = 0.2 mg/L can be calculated based on the chronic toxicity value (72 h NOEC = 2 mg/L) for green algae with the assessment factor of 10.</td></tr>
<tr><td colspan="2">Current Regulatory Controls[4]</td></tr>
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<tr><td>National Toxicology Program (NTP) Report on Carcinogens (RoC)
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<tr><td>US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2
https://www.epa.gov/iris</td><td>No</td></tr>
<tr><td>United States Endocrine Disrupter Screening Program
https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</td><td>No</td></tr>
<tr><td>Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin</td><td>No</td></tr>
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	https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	
	Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
	Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
	Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No
Australian Hazard Classification	The chemical is not listed in the Hazardous Substances Information System (HSIS) (Safe Work Australia).	
Australian Occupational Exposure Standards	No specific exposure standards are available for the chemical.	
International Occupational Exposure Standards	The US Temporary Emergency Exposure Limits (TEELs) for cinnamaldehyde are 14, 150 and 670 mg/m^3 (Galleria Chemica).	
Australian Food Standards	No data available.	
Australian Drinking Water Guidelines	No data available.	
Aquatic Toxicity Guidelines	No data available.	
PBT Assessment		
P/vP Criteria fulfilled?	Not Persistent. Based on the results of the ready biodegradability studies, cinnamaldehyde is categorised as Not Persistent.	
B/vB criteria fulfilled?	Not Bioaccumulative. Based on low log K values and/or expected natural metabolism and regulation of internal concentrations, the chemical is categorised as Not Bioaccumulative	
T criteria fulfilled?	Not Toxic. Based on measured acute toxicity endpoints of greater than 1 mg/L cinnamaldehyde is categorised as Not Toxic.	
Overall conclusion	Not PBT	

References

1. NICNAS (2017a) Environment Tier II Assessment for Cinnamic Aldehydes
2. NICNAS (2017b) Human Health Tier II assessment for 2-Propenal, 3-phenyl-
3. HSDB (n.d.). *Hazardous Substances Data Bank*. Retrieved 2015, from Toxnet, Toxicology Data Network, National Library of Medicine: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
4. ECHA REACH, Cinnamaldehyde, Retrieved 2017: https://echa.europa.eu/information-on-chemicals/registered-substances

Toxicity Summary - Glutaraldehyde

Chemical and Physical Properties [1,2,3]	
CAS number	111-30-8
Molecular formula	$C_5H_8O_2$
Molecular weight	100.11
Solubility in water	Soluble in all proportions in water and ethanol; soluble in benzene and ether.
Melting point	-14°C
Boiling point	188°C
Vapour pressure	2.03×10^{-3} kPa at 25 °C (50% solution)
Henrys law constant	0.011 Pa m^3/mol @ 25 °C
Explosive potential	Non explosive
Flammability potential	Non flammable
Colour/Form	Colourless oily liquid. In the vapour state, glutaraldehyde has a pungent odour, with an odour threshold of 0.04 ppm.
Overview	Glutaraldehyde is manufactured in Germany by BASF and in the USA by Union Carbide Corporation. It is usually sold commercially as a 45% or 50% aqueous solution. Glutaraldehyde has a wide variety of uses throughout the world with its use spread over a number of different industries. It is used primarily as a biocide but it also has wide use as a fixative, and some use as a therapeutic agent. The principal health effects of glutaraldehyde are irritation of the skin, eye and respiratory tract, skin sensitisation and occupational asthma. Exposure data indicated that, in some situations, particularly the health care industry (disinfection), x-ray film processing and the animal health industry (spray use), health concerns may arise where available control measures such as ventilation have not been implemented to minimise exposure. Due to low and intermittent exposure, the public health risk from the industrial use of glutaraldehyde is minimal. For the use of glutaraldehyde in cosmetics, a safety margin of >400 for extensive use indicated low concern.
Environmental Fate[1]	
Soil/Water/Air	Glutaraldehyde is a hydrophilic substance that will be mainly associated with the aquatic compartment, with minor amounts partitioning to the atmosphere, following release to the environment. Hydrolysis is slow, but glutaraldehyde, like other aldehydes, undergoes aerial oxidation in solution. It biodegrades rapidly in aerobic and anaerobic aquatic environments at subcidal concentrations (below 10 mg/L) and will not bioaccumulate. Tropospheric degradation is also rapid.
Human Health Toxicity Summary [1,2,3]	
Chronic Repeated Dose Toxicity	A two-year chronic study was conducted in male and female Fischer 344 rats (NICNAS 1994). Groups of 100 male and 100 female rats were administered 0, 50, 250, or 1000 ppm w/v glutaraldehyde in drinking water (4, 17 and 64 mg/kg bw/day for the males and 6, 25 and 86 mg/kg/day for the females). The mortality rate over the treatment period was 25 to 30% for males and 19 to 23% for females with no dose-related increase. The major cause of death in all rats (control and dose groups) was large granular cell lymphatic leukaemia (LGLL). Small dose-related decreases in absolute body weight and body weight gain occurred at 250 and 1000 ppm in males and at 1000 ppm in females. Dose-related decrease in urine volumes and associated increase in osmolality were observed in higher dose animals. At necropsy at 52, 78 and 104 weeks, the only statistically significant changes in organ weights were for the kidney. Relative kidney weights were increased for males and females at 52 and 78 weeks. A significant dose-related increase in kidney weight relative to final body weight occurred for males and females in the 250 and 1000 ppm groups, including an increase in absolute kidney weight for the female rats. Changes in final body

	weights and the weights of other organs were minor and / or sporadic and were unlikely to be related to glutaraldehyde exposure. The total leucocyte count was significantly increased at week 104 in males at 250 and 1000 ppm, and in females at 250 ppm only. The variation in counts was large, possibly due to the large monocyte count at 250 and 1000 ppm. Changes in clinical chemistry parameters included decreases in the activities of some enzymes at 250 and 1000 ppm and occasional decreases in total protein, globulin and phosphorous; these were probably due to reduced food consumption and body weight. Gross pathology showed evidence of gastric inflammation, particularly in rats sacrificed at the end of the study, with irritation observed as ulceration, a multifocal colour change and thickening of the mucosa (dose groups not specified). Histologic examination of the tissues revealed squamous epithelial hyperplasia and keratinised cysts and oedema. Based on the observations, a NOAEL of 4 mg/kg bw/day for males and 6 mg/kg bw/day for females was established in this study. For the purpose of human health risk assessment, the lowest NOAEL (4 mg/kg bw/day) established in the two-year chronic study in rats will be used.
Carcinogenicity	In a two-year chronic/carcinogenicity study by Van Miller et al. (2002), groups of 100 male and 100 female Fischer 344 rats were treated with 0, 50, 250, or 1000 ppm w/v glutaraldehyde in drinking water. The mean glutaraldehyde consumption for each of the three groups was 4, 17 and 64 mg/kg bw/day for the males and 6, 25 and 86 mg/kg bw/day for the females. The mortality rate during the study period was 25 to 30% for males and 19 to 23% for females and was not dose-related. Gross pathology showed evidence of gastric inflammation. The main finding of the study was an increased incidence of large granular lymphocytic leukaemia (LGLL) in the spleen and liver of male and female rats in all groups, including the control group. Treated females showed a significantly increased incidence of LGLL and analysis for dose-response trend for the severity of LLGL revealed an increased severity in females at the higher dosages (53% in spleen and 54% in liver versus respectively 20% and 23% in untreated females) while no such observation were made for the males. No other significant oncogenic effects were observed during the study. Occurrence of LGLL was seen in all groups including controls; the incidence of LGLL in the 1000 ppm group was high compared to controls but no clear dose-response relationship was evident, and LGLL mainly affected treated females whereas the incidence in treated males was within the control range (REACH 2013). Historical control data for untreated Fischer 344 rats in NTP studies also indicates that the ranges for this tumour are 10 to 72% in males and 6 to 31% in females (REACH 2013). The control data in the Van Miller et al. study fitted in with the historical control data reported from NTP studies. The variability in control data for LGLL and the wide variation reported in the literature makes a definitive conclusion difficult. Base on this study, glutaraldehyde was considered not to be carcinogenic.
Mutagenicity/ Genotoxicity	Glutaraldehyde has been extensively tested for genetic activity in vitro and in vivo, however there is disagreement in the literature regarding glutaraldehyde's genetic activity (Zeiger et al. 2005). While all in vivo genotoxicity tests with glutaraldehyde gave negative results, mixed results were reported for in vitro mutagenicity tests. Early in vitro tests were negative (Watts 1984), but some recent bacterial assays and tests in mammalian cells indicated that glutaraldehyde could be mutagenic in vitro. A series of reverse mutation assays was carried out with various Salmonella typhimurium strains, with and without metabolic activation (REACH 2013). All assays with TA 100, 1535, 1537 and 98 were negative. Some assays with TA 102 and 104 gave positive results. Tests with Escherichia coli also yielded both positive as well as negative results. Glutaraldehyde induced sister chromatid exchanges in CHO cells with and without S9 metabolic activation in one laboratory, but was negative without S9 and only weakly positive with S9 in the second laboratory (NICNAS 1994). The difference in the results was attributed to slight differences between the data evaluation systems used in the two laboratories. Glutaraldehyde was not mutagenic in any of the in vivo assays such as peripheral blood micronucleus test, rat bone marrow chromosomal aberration assay and the Drosophila melanogaster sex-linked recessive lethal test (NICNAS 1994; REACH

	2013). Chromosome aberrations in bone marrow cells were reported in only one out of eight studies using rats and mice, micronuclei were not induced in bone marrow cells of mice, and dominant lethal mutations were not induced in mice. Glutaraldehyde did not induce cell transformation in Syrian hamster embryo cells in vitro (Zeiger et al. 2005). In vivo, inhalation of glutaraldehyde induced cell proliferation in nasal tissue in rats and mice, but did not induce DNA damage at these sites. Based on these observations, it is concluded that glutaraldehyde is not a genotoxin.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	Studies on the incidence of miscarriage in pregnant women have shown no difference between those exposed to glutaraldehyde and those not exposed to the chemical. Studies in female rats and mice have resulted in embryotoxicity/foetotoxicity for glutaraldehyde, but only at doses which are maternally toxic. A number of studies have found no evidence of teratogenicity.
Acute Toxicity	Several acute oral toxicity studies with glutaraldehyde have been reported in rats and other species. In one reliable study, administration of 0.2, 0.3, 0.5, 1.0, 1.7 mL/kg bw glutaraldehyde (corresponding to 226, 339, 565, 1130 and 1921 mg/kg bw, respectively) to male/female Wistar rats by gavage gave a median lethal dose (LD50) of 226 mg/kg bw (REACH 2013). Necropsy of animals that died during the observation period revealed congestion of the lungs and the abdominal viscera. In another study in Sprague-Dawley rats, the oral LD50 was 316 mg/kg bw for males and 285 mg/kg bw for females, when 10 mL of 2.15, 3.16, 4.64, 14.7% glutaraldehyde (corresponding to 215, 316, 464 and 1470 mg/kg bw) was administered by oral gavage (REACH 2013). In a separate study using different strengths of glutaraldehyde, Ballantyne (1986) showed that the oral LD50 for glutaraldehyde in rats varied with the concentration of the glutaraldehyde used. By using different concentrations of glutaraldehyde solutions (1% to 50%) and varying the administration volume to maintain a constant dose, oral LD50 in the range 66 to 733 mg/kg bw were obtained. These studies indicate that glutaraldehyde has high acute oral toxicity. Of the 18 acute dermal toxicity studies reported in REACH (2013) dossiers, results from 14 studies indicated LD50 higher than 2000 mg/kg bw. In four other studies, LD50 ranged between 250 and 1432 mg/kg bw. These studies however did not follow international guidelines and have low reliability. Based on these studies, glutaraldehyde is considered to have low acute dermal toxicity. In a well-defined study, 10 male and 10 female Sprague-Dawley rats per dose group were exposed to glutaraldehyde as liquid aerosol at 0.22, 0.31 and 0.63 mg/L for 4 hours (REACH 2013). Exposure was followed by an observation period of 14 days. During the exposure period slight nasal discharge, snout wiping, flank respiration and irregular to intermittent respiration were reported in rats. During the post-exposure period, bloody nasal discharge, red crusts surrounding the nose, whooping or gasping respiration with rasping sounds and a tremulous gait were observed. These symptoms disappeared in the surviving animals within 5 to 9 days post-exposure. Mortalities were noted in all treated groups. The determination of the LC50 values was based on the Probit Analysis. An LC50 of 0.48 mg/L was calculated for both male and female rats. In another acute inhalation study conducted in a similar manner to the above study, Sprague-Dawley rats, 10 rats per sex per dose group, were exposed to 0.1, 0.18, 0.28, 0.39 and 0.44 mg/L glutaraldehyde as liquid aerosol for 4 hours (REACH 2013). During and after exposure, mortality and clinical signs of toxicity were recorded at regular time intervals. The LC50 in this study was established as 0.28 mg/L for females and 0.39 mg/L for males. Based on the above studies, glutaraldehyde is considered to have high acute inhalation toxicity.
Irritation	Glutaraldehyde is corrosive to the skin and eyes of rabbits at high concentrations, with signs of skin irritation evident at 2%, and eye irritation at 0.2%. Exposure to glutaraldehyde vapours in acute inhalational studies resulted in nasal irritation and respiratory difficulties. Joint irritation was seen in rabbits after intra-articular administration.
Sensitisation	The skin sensitisation effect of glutaraldehyde was demonstrated in tests with guinea pigs.
Health Effects Summary	Glutaraldehyde has high acute oral and inhalation toxicity and low to moderate acute dermal toxicity. Based on human and animal data, it is corrosive, the vapours are irritating to the respiratory tract, and it has skin and respiratory sensitisation potential. Glutaraldehyde has high repeat dose oral and inhalation toxicity, with an oral No-Observed-Adverse-Effect Level (NOAEL) of 4 mg/kg

	bw/day based on changes in liver and kidney weights and clinical chemistry parameters. Glutaraldehyde is not genotoxic or carcinogenic. It did not have any adverse effects on the reproductive system of adult rats or on the development of foetuses. The critical adverse health effects of glutaraldehyde are corrosivity, skin and respiratory tract sensitisation and acute and repeat dose oral and inhalation toxicity.
Key Study/Critical Effect for Screening Criteria	From the hazard characterisation, the critical (most sensitive) adverse health effects for repeated exposures to the chemical are changes in clinical chemistry parameters and relative organ (liver and kidney) weights. Glutaraldehyde has high repeat dose oral toxicity with an oral NOAEL of 4 mg/kg bw/day. This NOAEL is used in this human health risk assessment.

Ecological Toxicity [1,2,3,4]

Aquatic Toxicity	96 h acute Bluegill sunfish LC50 = 11.2 mg/L 48 h acute Oyster larvae LC550 = 2.1 mg/L 96 h acute Green crabs LC50 = 465 mg/L 96 h acute Grass shrimp LC50 = 41 mg/L 48 acute Daphnia magna LC50 = 0.35 mg/L 48 acute Daphnia magna LC50 = 16.3 mg/L 21 d reproduction Daphnia magna LOEC = 4.3 mg/L, NOEC = 2.1 mg/L 96 h algal growth inhibition Selenastrum capricornutum ILm = 3.9 mg/L (median inhibitory limit) 96 h algal growth inhibition Scenedesmus subspicatus EC50 = 1.0 mg/L Bacterial inhibition Sewage microbes IC50 = 25-34 mg/L In summary, the test results indicate that glutaraldehyde is slightly to moderately toxic to aquatic fauna and moderately to highly toxic to algae. In some instances, glutaraldehyde appeared to be rapidly lost from test waters in the laboratory. Such behaviour in aquatic toxicity tests generally means that their results will underestimate the inherent toxicity of a substance. However, the toxicity that will prevail under environmental conditions is likely to be lower than that recorded in the laboratory in view of the rapid degradation that would be expected to occur in natural surface waters.
Determination of PNEC aquatic	As a wide selection of species is available, applying a safety factor of 10 to the NOEC (2.1 mg/L) derived from Daphnia seems most appropriate, giving a PNEC of 2100/10 = 0.21 mg/L.

Current Regulatory Controls [1,2,4]

Listed as a Chemical of Concern on International Databases

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	Yes
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol	No

https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	Glutaraldehyde is classified as hazardous in the Hazardous Substances Information System (HSIS) with the following risk phrase (Safe Work Australia 2013): · T (Toxic); R23/25 (Toxic by inhalation and if swallowed) · C (Corrosive ; R34 (causes burns) · R42/43 (May cause sensitisation by inhalation and skin contact). Mixtures containing the chemical are classified as hazardous with the following risk phrases based on the concentration (Conc) of the chemical in the mixtures. The risk phrases for this chemical are: · Conc ≥50%: T; R23/25; R34; R42/43 (Toxic; toxic by inhalation and if swallowed; causes burns; may cause sensitisation by inhalation and skin contact) · ≥25% Conc <50%: T; R23; R22; R34; R42/43 (Toxic; toxic by inhalation, harmful if swallowed, causes burns; may cause sensitisation by inhalation and skin contact) · ≥10% Conc <25%: C; R20/22; R34; 42/43 (Corrosive; harmful by inhalation and if swallowed; causes burns; may cause sensitisation by inhalation and skin contact) · ≥2% Conc <10%: Xn; R20/22; R37/38; R41; R42/43 (Harmful; harmful by inhalation and if swallowed; irritating to respiratory system and skin; risk of serious eye damage; may cause sensitisation by inhalation and skin contact) · ≥1% Conc <2%: Xn; R36/37/38 R42/43 (Harmful; Irritating to eyes, respiratory system and skin; may cause sensitisation by inhalation and skin contact) · ≥0.5% Conc <1%: Xi; R36/37/38; R43 (Irritating; irritating to eyes, respiratory system and skin; may cause sensitisation by skin contact)
Australian Occupational Exposure Standards	The chemical has an exposure standard of 0.41 mg/m³, 0.1 ppm; Time Weighted Average (TWA).
International Occupational Exposure Standards	The following exposure standards are identified in Galleria Chemica (2013): · Occupational Exposure limit (TWA) of 0.2 mg/m3 [Canada, China, Denmark, Japan, Korea, UK] · 0.4 mg/m3 TWA [Sweden] · 0.8 mg/m3 TWA [US (NIOSH), Greece]
Australian Food Standards	No Australian food standards relating to the chemical have been identified (Food Standards Australia New Zealand 2013).
Australian Drinking Water Guidelines	No aesthetic or health-related guidance values were identified for this chemical in the Australian Drinking Water Guidelines. (National Health and Medical Research Council (NHMRC) 2011).
Aquatic Toxicity Guidelines	No data available.
PBT Assessment	
P/vP Criteria fulfilled?	No. Readily biodegradable and as such not persistent in the environment.
B/vB criteria fulfilled?	No. As the Log Pow is -0.01 (Log Pow < 4.5), it is not expected to be bioaccumulative.
T criteria fulfilled?	No. Chronic toxicity data >1 mg/L in invertebrates, thus glutaraldehyde does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT

References

1. NICNAS (1994) Priority Existing Chemical 3, Glutaraldehyde: Retrieved 2019: https://www.nicnas.gov.au

2. National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2017). National assessment of chemicals associated with coal seam gas extraction in Australia. Human health hazards of chemicals associated with coal seam gas extraction in Australia.
3. OECD (1995) SIDS Initial Assessment Profile on Glutaraldehyde
4. ECHA REACH, Glutaral, Retrieved 2019: https://echa.europa.eu/
5. Hazardous Chemical Information System (HCIS), Safe Work Australia. Retrieved 2019: http://hcis.safeworkaustralia.gov.au/
6. National Occupational Health and Safety Commission, Approved Criteria for Classifying Hazardous Substances [NOHSC:0006(1993)], AGPS, Canberra, 1993.

Toxicity Summary - Sodium hydroxide

Chemical and Physical Properties	
CAS number	1310-73-2
Molecular formula	Na-O-H
Product name	40 g/mol
Molecular weight	1.11E+06 mg/L at 20C
Solubility in water	13
Melting point	318 °C
Boiling point	1388 °C
Vapour pressure	Negligible at 25 deg C
Henrys law constant	No data found.
Explosive potential	No
Flammability potential	No
Colour/Form	Anhydrous (pure) NaOH is a solid – *refer melting point above*. However it is a hygoscopic, ionic solid, and will absorb water from air and is highly soluble
Incompatibility	Avoid contact of solid NaOH with water due to strong exothermic reaction, leather, wood, acids, organic halogen compounds or organic nitro compounds. Carbon monoxide gas can form upon contact with reducing sugars, food and beverage products in enclosed spaces. NAoH is neither explosive, flammable, nor oxidising.
Overview	Vegetable oil refining, regenerating iron exchange resins, organic fusions, peeling of fruits and vegetables in the food industry, etching and electroplating.
Environmental Fate[1]	
Soil/Water/Air	Sodium hydroxide is highly soluble, not volatile and unlikely to materially adsorb to soil and is therefore predominately found in the aquatic environment if released to the environment. NaOH will readily dissociate to be present in the environment as sodium and hydroxyl ions, both being ubiquitous in the environment. NaOH is a strong alkali, so it's dissolution in water may locally raise the pH of the affected environment. The dissolution reaction is also strongly exothermic.
Human Health Toxicity Summary [1,2,,3]	
Chronic Repeated Dose Toxicity	No animal data are available on repeated dose toxicity studies by oral or dermal routes for sodium hydroxide. In a repeat dose inhalation study, twenty seven white rats died within a month, mostly from bronchopneumonia, after being exposed twice weekly to an aerosol of unknown airborne concentration of sodium hydroxide, generated from an aqueous 40% sodium hydroxide solution (NIOSH 1975). When exposed to an aerosol generated from a 20% sodium hydroxide solution, the bronchi were dilated, the epithelial cover was thin and frequently desquamated, and the septa were dilated and cracked. A light round cell infiltration of the sub-mucus membrane tissue was also observed. Few changes occurred in a group of rats exposed to aerosols from 10% sodium hydroxide, but rats exposed to an aerosol of 5% sodium hydroxide had dilation of the bronchi and a slight degeneration of the mucus membrane and thickened strata of lymphadenoid tissue surrounding the bronchi. A NOAEL could not be established in this study. Workers exposed to 0.24 to 1.86 mg/m^3 sodium hydroxide for 2 to 15 minutes reported throat irritation and watery eyes (NIOSH 1975). Based on the observations of the irritant effects on workers exposed to 1 to 40 mg/m^3 sodium hydroxide, it was concluded that 2 mg/m^3 represented a concentration that is 'noticeably but not extensively irritant' (NIOSH 1975). Obstructive airway disease has been reported following chronic occupational exposure to sodium hydroxide mist (IPCS 1996). The patient developed cough, dyspnoea and tachypnoea after a 20-year exposure to sodium hydroxide.

Carcinogenicity	IARC Category 3 - not classifiable as to human carcinogenicity
Mutagenicity/ Genotoxicity	In vitro and vivo genetic toxicity testing reported no evidence of mutagenic activity.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	No valid studies were identified regarding reproduction toxicity after oral, dermal or inhalation exposure to NaOH. Sodium hydroxide is not expected to be systemically available to the body under normal handling and use conditions.
Acute Toxicity	Exposure to the solid or concentrated liquid can cause severe burns to the eyes, skin and gastrointestinal tract which may cause death. An oral LD50 of a 1-10% solution of NaOH in rabbits was 325 mg/kg bw (as 100% NaOH). An oral LD50 of 140 to 340 mg/kg in rats has also been reported (National Research Council 2011), however details of the study are not available. In an acute dermal study, mice were treated dermally with 50% sodium hydroxide, and the treated area was irrigated with water at various intervals (OECD 2002). The mortality of mice was 20, 40, 80 and 71% when they were irrigated at 30 minutes, one hour, two hours or not at all after the application. All animals developed rapidly progressive burns. No mortality or burns were observed when the treated area was irrigated immediately after the application. A 5% aqueous solution of sodium hydroxide produced severe necrosis when applied to the skin of rabbits for four hours (Clayton and Clayton 1993). A dermal LD50 of 1350 mg/kg has been reported in rabbits (National Research Council 2011), however details of the study are not available. Caustic dusts are irritating to the upper respiratory system. Prolonged exposure to high concentrations may cause discomfort and ulceration of nasal passages. Cases of fatality due to ingestion of liquid sodium hydroxide have been reported in humans.
Irritation	Sodium hydroxide is a corrosive irritant to skin, eyes and mucous membranes. A NaOH solution of 8% can be considered corrosive based on animal data. Human data indicate that concentrations of 0.5 to 4% were irritating.
Sensitisation	Sodium hydroxide has no skin sensitisation potential.
Health Effects Summary	An oral LD50 of 325 mg/kg in rats and a dermal LD50 of 1350 mg/kg in rabbits were reported for sodium hydroxide. Lethality has been reported in animals at oral doses of 240 mg/kg bw. Inhalational LC50 is not available. Sodium hydroxide is corrosive to skin, eyes and gastrointestinal and respiratory tracts. Based on human data, concentrations of 0.5 to 4.0% are irritating to the skin, while a concentration of 8.0% is corrosive. Sodium hydroxide is not a skin sensitiser. No animal data were available on repeated dose toxicity by oral or dermal routes for sodium hydroxide. In the single reported repeat dose inhalation study, a NOAEL could not be established. Both in vitro and in vivo genetic toxicity tests indicated no evidence of a mutagenic activity. Information is not available on reproductive and developmental toxicity and carcinogenicity of sodium hydroxide. Due to dissociation into ions which are subject to homeostatic controls in the human body, systemic effects from repeated exposures to sodium hydroxide are not expected. The critical health effect of sodium hydroxide is its corrosive effect.
Key Study/Critical Effect for Screening Criteria	No oral TRV apply. Acute toxicity only (irritant and corrosive), not systemically available in body. The Australian drinking water guideline value for pH may apply to sodium hydroxide.
Ecological Toxicity [1,2,3]	
Aquatic Toxicity	Measured acute endpoints were available for fish (196 mg/L). Measured chronic endpoint were available for Daphnia (240 mg/L)
Determination of PNEC aquatic	An assessment factor of 100 has been applied to the lowest reported NOEC of 240 mg/L for Daphnia. The PNECaquatic is 2.4 mg/L.
Current Regulatory Controls[4]	
Australian Hazard Classification	C: R35 (Corrosive, causes severe burns)

Australian Occupational Exposure Standards	Sodium hydroxide has an exposure standard of 2 mg/m³, Time Weighted Average (Safe Work Australia 2013).
International Occupational Exposure Standards	Occupational Exposure Limit (OEL) or limit values in working environment of 2 mg/m³ [Argentina, Belgium, Bulgaria, Canada, China, India, Japan and the US (NIOSH 1975)]. Occupational exposure standard: 2 mg/m³ [Korea] Occupational exposure limit values: 0.5 mg/m³ [Latvia] Short Term Exposure Limit (STEL): 2 mg/m³ [UK] US Department of Energy Temporary Emergency Exposure Limits (TEELs) = 0.5 mg/m³ (TEEL-0 and TEEL-1), 5 mg/m³ (TEEL-2) and 50 mg/m³ (TEEL-3).
Australian Food Standards	Processing aids - Generally permitted - permitted for use as acidity regulator (FSANZ 2013). Sodium hydroxide is allotted an International Numbering System (INS) of food additives number: INS 524 (Food Standards Australia New Zealand 2013).
Australian Drinking Water Guidelines	No data found. However, since sodium hydroxide readily dissociates in water into sodium and hydroxyl ions, the Australian Drinking Water Guidelines for sodium state that, based on aesthetic considerations (taste), the concentration of sodium in drinking water should not exceed 180 mg/L (National Health and Medical Research Council (NHMRC) 2011). No health-based guideline value is proposed for sodium.
Aquatic Toxicity Guidelines	No data found.
Occupational Exposure Limits	Peak limitation – 2 mg/m³
PBT Assessment	
P/vP Criteria fulfilled?	Not applicable (inorganic salt, ionic species ubiquitous in environment)
B/vB criteria fulfilled?	Not applicable. Bioaccumulation is not applicable to these inorganic ions; sodium and hydroxide ions are ubiquitous and are present in most water, soil and sediment.
T criteria fulfilled?	Not applicable. Chronic toxicity data >1 mg/L in invertebrates, thus sodium hydroxide does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT

References

1. OECD SIDS Sodium Hydroxide, UNEP Publications, March 2002
2. HSDB (n.d.). *Hazardous Substances Data Bank*. Retrieved from Toxnet, Toxicology Data Network, National Library of Medicine: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
3. European Commission (EC) Joint Research Centre (JRC) Institute for Health and Consumer Protection - European Chemical Substances Information System (ESIS), Sodium Hydroxide, Summary Risk Assessment Report, 2008
4. Safe Work Australia, Hazardous Substances System, sodium hydroxide

Toxicity Summary - Sodium Erythorbate

Chemical and Physical Properties[1,2]	
CAS number	6381-77-7
Molecular formula	C6H7NaO6
Molecular weight	199.13
Solubility in water	Soluble; 146 g/L at 20 °C and pH 6
Melting point	160 °C at 101.3 kPa
Boiling point	No data available.
Vapour pressure	No data available.
Henrys law constant	No data available.
Explosive potential	No data available.
Flammability potential	Non-flammable (100%)
Colour/Form	White, free-flowing crystals
Overview	Sodium erythorbate is a synthetic antioxidant used in food and cosmetic formulations. Foliar application of sodium erythorbate sprays and dusts are used to control young tree decline in citrus trees and to reduce ozone damage to Thompson seedless grapes. It is also used in hydraulic fracturing mixtures to prevent precipitation of metal oxides (iron control). This chemical has been identified by NICNAS to be of low concern to human health based on an initial screening approach and thus required no further assessment.
Environmental Fate[1]	
Soil/Water/Air	Limited environmental fate information is available for this chemical. Sodium erythorbate is expected to be readily biodegradable based on modelled predictions (USEPA BIOWIN).
Human Health Toxicity Summary[1]	
Chronic Repeated Dose Toxicity	Male 6-week-old F344 rats were given doses of 5% Sodium Erythorbate in feed for 168 days. Parameters of urinary excretion were investigated and the urinary bladder epithelium was examined using light and scanning electron microscopy at weeks 8, 16, and 24. The urine of rats fed Sodium Erythorbate had increased pH, elevated content of crystals and sodium, and decreased osmolality; however, no morphological alterations such as hyperplasia were detected in the mucosa. The urine values and urinary bladder mucosa were similar to controls at doses below 5 g/kg/day.
Carcinogenicity	F344/DuCrj rats of both sexes (6-week-old) were given 1.25% or 2.5% Sodium Erythorbate in drinking water for 104 weeks and untreated water for 8 additional weeks. Rats of the control group were given untreated water only. Each group consisted of 52 male and 50 female rats. Cumulative consumption of Sodium Erythorbate by male rats was 217 g/rat (1.25%) and 430 g/rat (2.5%). Consumption by females was 206 g/rat (1.25%) and 583 g/rat (2.5%). Body weight of rats given 2.5% Sodium Erythorbate was reduced by 8.5% for males and 15.5% for females at weeks 88 and 85, respectively, compared to controls. Body weight gain was normal in rats of the low dose group. All male treated and control rats (except two of the high-dose group) had testicular interstitial cell tumours. Various tumours occurred in 80% of control males, 69% of males given the low dose, and 78% of males given the high dose. A 6-18% incidence of leukaemia, pheochromocytoma, mammary fibroadenoma, and mesothelioma was observed. Of the females of the control, 1.25%, and 2.5% dose groups, 94%, 88%, and 78% had tumours, respectively. Twenty to 43% of females (all groups) had leukaemia, mammary fibroadenoma, endometrial stromal polyp and/or pituitary adenoma. Females given 2.5% Sodium Erythorbate had significantly fewer tumours than control females. The pattern of occurrence of the various

	types of tumours was similar among the groups. Sodium Erythorbate did not enhance the development of rare spontaneous tumours or transform benign tumours (e.g., solid adenoma of the thyroid) to carcinomas. The investigators concluded that Sodium Erythorbate was not carcinogenic in F344 rats.
Mutagenicity/ Genotoxicity	Sodium Erythorbate (99.8% pure; 5.0 mg/plate) was non-mutagenic in S. typhimurium strains TA92, TA94, TA98, TA100, TA1535, and TA1537 with and without S9 activation. Sodium Erythorbate (0.25 mg/mL plate) was also negative in the chromosomal aberration assay using Chinese hamster fibroblasts; Sodium Erythorbate did not induce the formation of polyploid cells after 48 hours, and caused 1 % chromosomal breaks after 24 hours.
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	Sodium erythorbate did not cause maternal or fetal toxicity when administered to female rats and mice during gestation by oral intubation at dosages up to 1,030 mg/kg/day. Developmental toxicity did not occur after pregnant rats were given up to 5% sodium erythorbate in feed during a 13-week teratogenesis study. It produced negative results in the Ames test, the host-mediated assay using S. typhimurium, chromosomal aberration tests using Chinese hamster ovary fibroblasts, the dominant lethal test using rats, and the B. subtilis rec assay.
Acute Toxicity	Sodium erythorbate powder was applied to the intact and abraded skin of six rabbits as a single 2 g/kg dose. A substantial amount of residual compound was observed 24 hours after dosing. No erythema, edema, or other signs of dermal irritation were observed at five of six test sites. One rabbit (abraded skin) had slight (1+) erythema at 24 hours that cleared by 48 hours.
Irritation	Sodium erythorbate powder did not cause signs of dermal irritation when applied to the intact and abraded skin of rabbits. Instillation of sodium erythorbate powder to the conjunctival sac of rabbits caused slight and transient reddening of the conjunctiva that cleared within 24 hours.
Sensitisation	In a dermal sensitization study (according to OECD 429) with Sodium erythorbate (5, 10, 25% w/w in propylene glycol), young adult female CBA/Ca (CBA/CaOlaHsd) mice (4/group) were tested using the local lymph node assay (LLNA). In this study, Sodium erythorbate was not considered a potential skin sensitizer.
Health Effects Summary	Sodium erythorbate did not show signs of toxicity, carcinogenicity, mutagenicity, irritation and sensitisation in the studies reported. This chemical has been identified by NICNAS to be of low concern to human health.
Key Study/Critical Effect for Screening Criteria	The Australian drinking water guideline value for sodium may apply.
Ecological Toxicity [4]	
Aquatic Toxicity	The acute toxicity of sodium erythorbate to Algae was 1020 mg/L
Determination of PNEC aquatic	A PNECaquatic of 10.2 mg/L was calculated using an assessment factor of 100.
Current Regulatory Controls[4]	
Listed as a Chemical of Concern on International Databases	

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2	No

https://www.epa.gov/iris	
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	No data available.
Australian Occupational Exposure Standards	No data available.
International Occupational Exposure Standards	No data available.
Australian Food Standards	No data available.
Australian Drinking Water Guidelines	No data available.
Aquatic Toxicity Guidelines	No data available.
PBT Assessment	
P/vP Criteria fulfilled?	No. The chemical readily biodegradable (based on modelled data).
B/vB criteria fulfilled?	No. The Log Pow is -3.29 (Log Pow < 4.5) which does not meet the screening criteria for bioaccumulation.
T criteria fulfilled?	No. Based on measured acute toxicity endpoints of greater than 1 mg/L Sodium erythorbate does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT

References

1. HSDB (n.d.). *Hazardous Substances Data Bank*. Retrieved 2015, from Toxnet, Toxicology Data Network, National Library of Medicine: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB
2. ECHA REACH, 2,3-didehydro-3-O-sodio-D-erythro-hexono-1,4-lactone, Retrieved 2019: https://echa.europa.eu/
3. Department of the Environment and Energy 2017, National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme
4. National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2017). National assessment of chemicals associated with coal seam gas extraction in Australia. Human health hazards of chemicals associated with coal seam gas extraction in Australia.

Toxicity Summary - Hydrochloric acid

Chemical and Physical Properties [1,2,3,4]	
CAS number	7647-01-0
Molecular formula	HCl
Molecular weight	36.46 g/mol
Solubility in water	Soluble
Melting point	-114.22 °C
Boiling point	-85.05°C
Vapour pressure	35,424 mm Hg at 25 deg C
Henrys law constant	2.04 x106 mol/L atm
Explosive potential	Reacts with most metals producing explosive hydrogen gas
Flammability potential	Not combustible
Colour/Form	Liquid
Overview	Hydrochloric acid has demonstrated acute oral toxicity, corrosive effects to the skin and eye, and irritant effects to the respiratory system. Following absorption, the chemical dissociates rapidly into hydrogen ions (protons) and chloride ions, which are both normal, homeostatically regulated components of the human body. Hydrochloric acid is a direct acting corrosive and irritant and adverse effects are caused at the site of contact by deposition of protons (causing pH change) rather than effects of the chloride ion. Exposure by inhalation, dermal or oral route at high concentrations has therefore been considered as inappropriate. If released to water, hydrogen chloride dissociates readily in water to chloride and hydronium ions, decreasing the pH of the water. Hydrochloric acid is one of the most widely used industrial chemicals. Uses include pickling and cleaning metals, food process, and cleaning of industrial equipment.
Environmental Fate [5,6]	
Soil/Water/Air	Hydrochloric acid is readily dissociated in water into hydrated protons and chloride ions. The increase in the concentration of hydrochloric acid in water decreases the pH in the aquatic ecosystem. Generally, the buffer capacity to maintain the pH in the aquatic ecosystem is important and the equilibrium between CO2, HCO3 - and CO3 2- in the aquatic ecosystem is mainly responsible for the buffer capacity of receiving water.

Human Health Toxicity Summary [1,2,3,4,9]	
Chronic Repeated Dose Toxicity	In a repeated dose study (non-guideline), rats were fed diets containing the chemical at 312, 625, 937 or 1250 millimoles/kg diet (180, 349, 366 or 466 mg/animal/day) for nine weeks. Water intake was high in all treatment groups. A no observed adverse effect level (NOAEL) of 625 mmol/kg diet (349 mg/kg bw) was determined based on mortalities (100 %) at 937 mmol/kg diet and above. The other effects reported include decreased body weight and food consumption, changes to blood pH and femur length at 937 mmol/kg diet and above (OECD, 2005). Based on the available data, the chemical is not considered to cause serious damage to health from repeated inhalation exposure. However, local irritation effects are expected due to the corrosivity of the chemical. Studies reporting exposure to hydrogen chloride gas are available. Rats and mice were exposed to the chemical gas (equivalent to OECD TG 413) at concentrations of 0, 10, 20 or 50 ppm (0, 15, 30 or 75 mg/m^3), six hours/day, five days/week for 90 days. Mice showed decreased body weight gain, food consumption and liver weight (in males only) at 50 ppm. Decreased body weight gain was observed in male rats at 50 ppm and food consumption was reduced in both sexes at 20 and 50 ppm. Inflammatory histopathological changes in lips or the nasal cavity were observed in mice and rats above 10 ppm. The no observed adverse effect concentration (NOAEC) for systemic toxicity was determined to be 20 ppm for rats and mice based on the reduction in body weight gain and liver weight (in male mice) (OECD, 2005).
Carcinogenicity	HCl is not classifiable as a human carcinogen. No evidence of treatment related carcinogenicity was observed either in other animal studies performed by inhalation, oral or dermal administration. In three industry-based human case studies conducted in the U.S, no association between hydrogen chloride exposure and cancers of the lung, brain, or kidney was observed. In one U.S study of steel-pickling workers an excess risk for cancer of the lung was identified in workers exposed primarily to hydrochloric acid. Under IARC definitions, HCl is not classifiable as to its carcinogenicity to humans (Group 3).
Mutagenicity/ Genotoxicity	In single studies, HCl induced mutation and chromosomal aberrations in mammalian cells and induced chromosomal aberrations in insects and in plants. It did not induce mutation in bacteria. For genetic toxicity, a negative result has been shown in the Ames test. A positive result, which is considered to be an artefact due to the low pH, has been obtained in a chromosome aberration test using Hamster ovary cells. The effects of low pH in in vitro studies are not a problem in vivo as the proton level is regulated systemically. Hydrochloric acid is not considered to be genotoxic.
Reproductive Toxicity **Developmental Toxicity/Teratogenicity**	No reliable studies have been reported regarding toxicity to reproduction and development in animals after oral, dermal or inhalation exposure to hydrogen chloride/hydrochloric acid. As protons and chloride ions are normal constituents in the body fluid of animal species, low concentrations of hydrogen chloride gas/mist or solution do not seem to cause adverse effects to animals. The cells of gastric glands secrete hydrochloric acid into the cavity of the stomach. No reliable conclusion could be drawn on the potential reproductive toxicity of hydrogen chloride/hydrochloric acid.

Acute Toxicity	Rapid evaporation of the liquid may cause frostbite. The substance is corrosive to the eyes, the skin and the respiratory tract and can cause serious skin burns and blurred/reduced vision or blindness. Inhalation of high concentrations of the gas may cause pneumonitis and lung oedema, resulting in reactive airways dysfunction syndrome. The effects may be delayed. Exposure to hydrochloric acid can produce burns on the skin and mucous membranes, with severity related to the concentration of the solution. Subsequent ulceration may occur, followed by keloid and retractile scarring. Dental decay, including yellowing, softening and breaking of teeth, and related digestive diseases have been recorded after exposures to hydrochloric acid. Mortality has been observed following ingestion of hydrochloric acid. Female rats orally administered 3.3% hydrochloric acid yielded an acute oral median lethal dose (LD50) in a range from 238 to 277 mg/kg bw (Hoechst 1966). No details of the study were available. In another study in rats, administration of a solution of undisclosed concentration induced stomach ulceration, inflammation of the intestine, discolouration of the liver and hyperaemia of the lung (Monsanto 1976). An LD50 of 700 mg/kg bw was reported. An acute dermal LD50 was established as >5010 mg/kg bw in rabbits however the dose levels administered were not reported (Monsanto 1976). Acute median lethal concentration (LC50) values of 8.3 mg/L and 3.2 mg/L were observed in rats and mice respectively after a 30 minute inhalation exposure to aerosolised hydrochloric acid (Darmer et al. 1974).
Irritation	In a skin irritation test in rabbits performed according to OECD TG 404, 37% hydrochloric acid (0.5 mL) was applied by both semi-occlusion and occlusion (Potokar 1985). The chemical was found to be corrosive under both conditions after one hour exposure. Concentrations >17% also caused corrosion in rabbits. Concentrations >3.3% caused skin irritation to rabbits after application for 5 days. Hydrochloric acid caused mild to severe eye irritation in animal studies. There were no data available for respiratory irritation however; inhalation of hydrochloric acid vapours is expected to cause irritation. In humans, the chemical was determined to be ‘irritating to skin’ (York et al. 1996).
Sensitisation	May cause dermatitis with frequent contact of aqueous solutions of hydrochloric acid.
Health Effects Summary	Hydrochloric acid has demonstrated acute oral toxicity, corrosive effects to the skin and eye, and irritant effects to the respiratory system. Hydrochloric acid is not a skin sensitiser based on the available studies. Only limited information on the repeated oral toxicity of hydrochloric acid is available. However, as the component ions are normal constituents of the human body (particularly the stomach), only localised effects are expected. No systemic effects from repeated exposures are expected. The chemical is not genotoxic. No evidence of treatment-related carcinogenicity was observed in animal studies performed by inhalation or dermal administration. In humans, no association between hydrogen chloride exposure and tumour incidence was observed. No reliable studies were identified regarding specific toxicity to reproduction and development in animals after exposure to hydrochloric acid/hydrogen chloride. Because protons and chloride ions are normal constituents in the body fluids, low concentrations of hydrochloric acid/hydrogen chloride would not be expected to cause adverse reproductive effects to animals. This conclusion is supported by the 90-day inhalation study of hydrogen chloride where no effects on the gonads of rodents were observed.

Key Study/Critical Effect for Screening Criteria	The Australian drinking water guideline value for pH may apply to hydrochloric acid. The critical health effects for risk characterisation include: - local effects (corrosivity); and - systemic acute effect (acute toxicity by the inhalation route of exposure). The critical health effects are different for gaseous hydrogen chloride, for which respiratory irritation and corrosion are critical, and aqueous solutions (hydrochloric acid) where dermal corrosion is the key effect. Due to corrosive nature of the chemical, even low concentrations of the chemical will also cause irritation to the eyes, skin and the respiratory tract.

Ecological Toxicity [1,3,4,8]

Aquatic Toxicity	The measured acute endpoint for: Algae = 0.492 mg/L Daphnia = 0.492 mg/L Fish = 4.92 mg/L The measured chronic endpoint for Daphnia is 62 mg/L
Determination of PNEC aquatic	On the basis that the data consists of short-term and long-term results from three trophic levels, an assessment factor of 10 has been applied to the lowest reported Chronic endpoint of 62 mg/L for Daphnia. The PNECaquatic is 6.2 mg/L.

Current Regulatory Controls[1,2,9]

Listed as a Chemical of Concern on International Databases

International Database	Listed?
European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://www.epa.gov/iris	No
United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No

Australian Hazard Classification	Skin corrosion – category 1B; H314 (Causes severe skin burns and eye damage) STOT SE 3; H335 (May cause respiratory irritation)
Australian Occupational Exposure Standards	There are no specific exposure standards for hydrochloric acid. However, the permissible exposure limits for hydrogen chloride gas apply (Safe Work Australia 2013): Time Weighted Average (TWA) of 7.5 mg/m^3 (5 ppm).
International Occupational Exposure Standards	The following exposure standards were identified for hydrogen chloride (Galleria Chemical 2013). TWA: 7 to 8 mg/m^3 (5 ppm) [Austria, Belgium, Denmark, EU, Hungary, Japan, Korea, Mexico, The Netherlands, New Zealand, Norway, Sweden, Turkey] 2 to 5 mg/m^3 (1-2 ppm) [Germany, Poland, Switzerland, UK]. Short Term Exposure Limit (STEL): 15 mg/m^3 (10 ppm) [Austria, Belgium, EU, Hungary]

Australian Food Standards	Hydrochloric acid is an additive permitted in accordance with Good Manufacturing Practice (GMP) in processed foods specified in Schedule 1 of the Australia New Zealand Food Standards Code – Standard 1.3.1 – Food Additives (Food Standards Australia New Zealand 2013).
Australian Drinking Water Guidelines	Hydrochloric acid is listed as an endorsed drinking water treatment chemical in the Australian Drinking Water Guidelines (National Health and Medical Research Council (NHMRC) 2011).
Aquatic Toxicity Guidelines	No data found
PBT Assessment	
P/vP Criteria fulfilled?	Hydrochloric acid is an organic salt that dissociates completely to hydrogen and chloride ions in aqueous solutions. Biodegradation is not applicable to these inorganic ions; both hydrogen and chloride ions are also ubiquitous and are present in most water, soil and sediment. Thus, the persistent criteria is not considered applicable to this inorganic salt.
B/vB criteria fulfilled?	Hydrogen and chloride ions are essential to all living organisms and their intracellular and extracellular concentrations are actively regulated. Thus, hydrochloric acid is not expected to bioaccumulate.
T criteria fulfilled?	No chronic toxicity data exist on hydrochloric acid; however, the acute EC(L)50s are >0.1 mg/L in fish, invertebrates and algae. Thus, hydrochloric acid does not meet the screening criteria for toxicity.
Overall conclusion	Not PBT. NICNAS concluded that this chemical poses no unreasonable risk to the environment based on Tier I assessment under the NICNAS IMAP assessment framework.

References

1. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier II Assessment for Hydrochloric acid: Retrieved 2020: https://www.nicnas.gov.au
2. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier III Assessment for Hydrochloric acid: Retrieved 2020: https://www.nicnas.gov.au
3. U.S. National Library of Medicine, Toxicology Data Network HSDB (Hazardous Substances Data Bank) http://toxnet.nlm.nih.gov/
4. OECD SIDS. (1992), *UNEP Publications 5; Hydrochloric Acid (IARC Summary & Evaluation, Volume 54*). Obtained from IPCS INCHEM http://www.inchem.org/documents/iarc/vol54/03-hydrochloric-acid.html
5. IARC (International Agency for Research on Cancer). (2011), *Agents Classified by the IARC Monographs, Volumes 1 -102.*
6. IARC (International Agency for Research on Cancer). (1992), *Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man* (Multi-volume work).
7. OECD (2002). IUCLID Data Set for Hydrogen chloride (CAS No. 7647-01-0), UNEP Publications.
8. OECD (2002). Screening Information Dataset (SIDS) Initial Assessment Report for Hydrogen chloride (CAS No. 7647-01-0), UNEP Publications.
9. Safe Work Australia Workplace Exposure Standards for Airborne Contaminants, 2013.
10. Department of the Environment and Energy 2017, National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme

References

1. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier 1 Assessment. Retrieved: https://www.nicnas.gov.au
2. ECHA REACH, Sodium Benzoate, Retrieved: https://echa.europa.eu/
3. National Center for Biotechnology Information. PubChem Database. Sodium benzoate, CID=517055, https://pubchem.ncbi.nlm.nih.gov/compound/Sodium-benzoate
4. OECD (2005) SIDS Initial Assessment Profile on Benzoates

Toxicity Summary - Water Tracers (FFI) - Sodium Benzoate used as analogue data

<table>
<tr><th colspan="2">Chemical and Physical Properties[1,2,3,4]</th></tr>
<tr><td>CAS number</td><td>Water Tracers (FFI) 15 chemicals.
<table>
<tr><td>Sodium 2-fluorobenzoate</td><td>490-97-1</td></tr>
<tr><td>Sodium 4-fluorobenzoate</td><td>499-90-1</td></tr>
<tr><td>Sodium 2,3,4,5-tetrafluorobenzoate</td><td>67852-79-3</td></tr>
<tr><td>Sodium 3-fluorobenzoate</td><td>499-57-0</td></tr>
<tr><td>Sodium 2,6-difluorobenzoate</td><td>6185-28-0</td></tr>
<tr><td>Sodium 2,4-difluorobenzoate</td><td>1765-08-8</td></tr>
<tr><td>sodium 3,4-difluorobenzoate</td><td>522651-44-1</td></tr>
<tr><td>Sodium 2-chlorobenzoate</td><td>17264-74-3</td></tr>
<tr><td>Sodium 2,5-difluorobenzoate</td><td>522651-42-9</td></tr>
<tr><td>Sodium 3,5-difluorobenzoate</td><td>530141-39-0</td></tr>
<tr><td>Sodium 2,3,4-trifluorobenzoate</td><td>402955-41-3</td></tr>
<tr><td>Sodium 2,4,5-trifluorobenzoate</td><td>522651-48-5</td></tr>
<tr><td>Sodium 2,3-difluorobenzoate</td><td>1604819-08-0</td></tr>
<tr><td>Sodium 3-chlorobenzoate</td><td>17264-88-9</td></tr>
<tr><td>Sodium 2,4,6-trichlorobenzoate</td><td>321992-77-2</td></tr>
</table></td></tr>
<tr><td>Molecular formula</td><td>C7H6O2.Na (Sodium Benzoate)</td></tr>
<tr><td>Molecular weight</td><td>144.1 g/mol</td></tr>
<tr><td>Solubility in water</td><td>556 g/L @ 20 °C</td></tr>
<tr><td>Melting point</td><td>436 °C @ 101.325 kPa</td></tr>
<tr><td>Boiling point</td><td>>450 °C to <475 °C, decomposes with no boiling</td></tr>
<tr><td>Vapour pressure</td><td>2.9X10-12 mm Hg at 25 °C (estimated)</td></tr>
<tr><td>Henrys law constant</td><td>No data available</td></tr>
<tr><td>Explosive potential</td><td>Non explosive</td></tr>
<tr><td>Flammability potential</td><td>Non flammable</td></tr>
<tr><td>Colour/Form</td><td>Solid crystalline, sweetish odour</td></tr>
<tr><td>Overview</td><td>Due to the limited toxicological information for each water tracer (sodium benzoate salts), information for Sodium Benzoate have been used as analogue data.
Sodium benzoate is an organic sodium salt resulting from the replacement of the proton from the carboxy group of benzoic acid by a sodium ion. It has a role as an antimicrobial food preservative, a drug allergen, an EC 1.13.11.33 (arachidonate 15-lipoxygenase) inhibitor, an EC 3.1.1.3 (triacylglycerol lipase) inhibitor, an algal metabolite, a human xenobiotic metabolite and a plant metabolite. It contains a benzoate.
A Tier 1 Human Health Assessment for this chemical has been conducted by NICNAS which concluded that this chemical was identified as low concern to human health.</td></tr>
<tr><th colspan="2">Environmental Fate[4]</th></tr>
<tr><td>Soil/Water/Air</td><td>For environmental effects, benzoates are all readily biodegradable, non-bioaccumulative and acute toxicity values are similar.</td></tr>
<tr><th colspan="2">Human Health Toxicity Summary [1,2,4]</th></tr>
<tr><td>Chronic Repeated Dose Toxicity</td><td>For benzoic acid repeated dose oral toxicity studies give a NOAEL of 800 mg/kg/day. For the salts values > 1000 mg/kg/day are obtained. At higher doses increased mortality, reduced weight gain, liver and kidney effects were observed.</td></tr>
</table>

	For benzyl alcohol the long-term studies indicate a NOAEL > 400 mg/kg bw/d for rats and > 200 mg/kg bw/d for mice. At higher doses effects on bodyweights, lesions in the brains, thymus, skeletal muscle and kidney were observed. It should be taken into account that administration in these studies was by gavage route, at which saturation of metabolic pathways is likely to occur. It can be concluded that benzoic acid and its salts exhibit very low repeated dose toxicity.
Carcinogenicity	Not carcinogenic in long-term carcinogenicity studies.
Mutagenicity/ Genotoxicity	Not mutagenic or genotoxic
Reproductive Toxicity / Developmental Toxicity/Teratogenicity	In rats for sodium benzoate dosed via food during the entire gestation developmental effects occurred only in the presence of marked maternal toxicity (reduced food intake and decreased body weight) (NOAEL = 1400 mg/kg bw). For hamster (NOEL: 300 mg/kg bw), rabbit (NOEL: 250 mg/kg bw) and mice (CD-1 mice, NOEL: 175 mg/kg bw) no higher doses (all by gavage) were tested and no maternal toxicity was observed. For benzyl alcohol: NOAEL= 550 mg/kg bw (gavage; CD-1 mice). LOAEL = 750 mg/kg bw (gavage mice). In this study maternal toxicity was observed e.g. increased mortality, reduced body weight and clinical toxicology.
Acute Toxicity	The compounds exhibit low acute toxicity as for the oral and dermal route. The LD50 values are > 2000 mg/kg bw except for benzyl alcohol which needs to be considered as harmful by the oral route in view of an oral LD50 of 1610 mg/kg bw. The 4 hrs inhalation exposure of benzyl alcohol or benzoic acid at 4 and 12 mg/l as aerosol/dust respectively gave no mortality, showing low acute toxicity by inhalation for these compounds.
Irritation	Sodium benzoate was not skin irritating and only slightly irritating to the eye.
Sensitisation	The available studies for benzoic acid gave no indication for a sensitizing effect in animals, however occasionally very low positive reactions were recorded with humans (dermatological patients) in patch tests. The same occurs for sodium benzoate. It has been suggested that the very low positive reactions are non-immunologic contact urticaria.
Health Effects Summary	It can be concluded that sodium benzoate exhibit very low repeated dose toxicity. This chemical has been identified by NICNAS to be of low concern to human health.
Key Study/Critical Effect for Screening Criteria	The critical health effects associated with the chemical (but not the salts) are skin, eye and respiratory tract irritation. However, no systemic effects were seen with benzoic acid. The salts are expected to exist almost entirely as the benzoate ion under normal physiological conditions and will not have the local irritant properties that arise from the acidity of benzoic acid. Therefore, it is unlikely that any systemic effects will be observed with the salts of benzoic acid. The critical lowest No Observed Adverse Effect (NOAEL) level for the purposes of risk assessment is 1000 mg/kg bw/day for the salts from the repeated chronic oral toxicity study.
Ecological Toxicity [1,2,3]	
Aquatic Toxicity	From the data (fish, daphnia, algae, bacteria) it is obvious that neutralization of the pH greatly reduces (up to one order of magnitude) the acute toxicity of benzoic acid. This is also supported by the lower toxicity observed with sodium benzoate. Under environmental relevant conditions therefore the acute toxicity of benzoic acid, sodium benzoate and potassium benzoate for all four trophic levels is > 100 mg/l. Under environmental relevant conditions the acute toxicity of benzyl alcohol for fish, daphnia and bacteria is > 100 mg/l. For algae, an EC 50 3hrs of 95 mg/l is reported. Under environmental relevant conditions, benzoic acid and its salts have very low acute toxicity whereas benzyl alcohol has low to moderate acute toxicity.
Determination of PNEC aquatic	For environmental relevant conditions and for derivation of a PNECaqua a benzylalcohol acute toxicity (LC50 96 hrs) to fish of > 100 mg/l should be used.

Current Regulatory Controls[4]		
Listed as a Chemical of Concern on International Databases	**International Database**	**Listed ?**
	European REACH regulation Substances of very high concern (SVHCs) according to Annex XV https://echa.europa.eu/candidate-list-table	No
	International Agency for Research on Cancer (IARC) as a Group 1, 2A or 2B carcinogen https://monographs.iarc.who.int/list-of-classifications	No
	National Toxicology Program (NTP) Report on Carcinogens (RoC) https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html	No
	US EPA Integrated Risk Information System (IRIS) as carcinogenic to humans, or likely / probable / possibly carcinogenic to humans https://www.epa.gov/iris	No
	EU list chemicals with endocrine disruption listed in Category 1 or Category 2 https://edlists.org/	No
	United States Endocrine Disrupter Screening Program https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and	No
	Agency for Toxic Substances and Disease Registry (ATSDR) as a neurotoxin https://wwwn.cdc.gov/TSP/index.aspx?sysid=18	No
	Montreal Protocol https://www.dcceew.gov.au/environment/protection/ozone/montreal-protocol	No
	Rotterdam Convention http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals	No
	Stockholm Convention http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx	No
Australian Hazard Classification	No data available	
Australian Occupational Exposure Standards	No data available	
International Occupational Exposure Standards	The US WEEL (Workplace Environmental Exposure Limit) Committee of the AIHA has set limits for benzyl alcohol at a value of 10-ppm (44 mg/m^3) 8hr TWA.	
Australian Food Standards	No data available	
Australian Drinking Water Guidelines	No data available	
Aquatic Toxicity Guidelines	No data available	
PBT Assessment		
P/vP Criteria fulfilled?	No. Sodium benzoate is readily biodegradable and as such not persistent in the environment.	
B/vB criteria fulfilled?	Based on the log Kow of 1.88, sodium benzoate is not bioaccumulative.	
T criteria fulfilled?	The acute aquatic toxicity of sodium benzoate is > 100 mg/L for all four trophic levels. Hence the substance does not fulfil the screening criteria for toxicity.	
Overall conclusion	Not PBT	

References

1. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). IMAP, Human Health Tier 1 Assessment. Retrieved: https://www.nicnas.gov.au
2. ECHA REACH, Sodium Benzoate, Retrieved: https://echa.europa.eu/
3. National Center for Biotechnology Information. PubChem Database. Sodium benzoate, CID=517055, https://pubchem.ncbi.nlm.nih.gov/compound/Sodium-benzoate
4. OECD (2005) SIDS Initial Assessment Profile on Benzoates

Appendix C

Exposure and Risk Calculations

Toxicity and Dermal Absorption Parameters

C = calculated from chronic value, Ch = chronic value adopted

CAS#	Chemical	Oral/Dermal Exposures Non-Threshold Slope Factor $(mg/kg/day)^{-1}$		Threshold Chronic TDI (mg/kg/day)		Dermal Permeability (cm/hr)	Reference	Drinking Water Guideline (mg/L)		NOAEL or LOAEL (mg/kg bw/d)	UF	Reference
COPC in Hydraulic Fracturing Fluid Injected into Well												
111-30-8	Glutaraldehyde			0.04	D	3.25E-04	EPI	0.2	D	4	100	NICNAS (2017)
64742-47-8	Hydrotreated light petroleum distillate			10	D	1.96	EPI	39	D	1000	100	NICNAS (2017)
127087-87-0	Polyethylene glycol trimethylnonyl ether			0.05	D	3.99E-03	EPI	0.2	D	50	1000	NICNAS (2019)

D = Derived (refer to individual Toxicity Profiles); EPI - USEPA Estimation Programs Interface (EPI) Suite

NICNAS (2017) - Department of the Environment and Energy 2017 , National assessment of chemicals associated with coal seam gas extraction in Australia, prepared by the National Industrial Chemicals Notification and Assessment Scheme

NICNAS (2019) Human Health Tier II Assessment for Nonylphenol and octylphenol ethoxylates and related compounds

Ingestion of Chemicals via Incidental Contact with Flowback Water (20% Mass Return) - HVFR_A

Adult Trespassers

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (20% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	78	Average male and female adults as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Ingestion Rate (IRw)	L/day or L/hr	0.05	Assume incidental ingestion of 50 mL
Bioavailability (B)	-	100%	Assume 100% bioavailability via ingestion of chemicals in water.
Intake Factor = IRw*ET*B*EF*ED / BW*AT	L/kg/day	**7.5E-08**	**NonThreshold**
		1.8E-06	**Threshold**

Daily Intake from Water = Concentration in Water x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data				Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor	Chronic Threshold TDI	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background)	in Water	NonThreshold	Threshold	NonThreshold Risk	Chronic Hazard Quotient
	(mg/kg-day)$^{-1}$	(mg/kg/day)		(mg/kg/day)	(mg/L)	(mg/kg/day)	(mg/kg/day)	(unitless)	(unitless)
Hydrotreated light petroleum distillate		1.00E+01		1.0E+01	290.18	2.2E-05	5.1E-04	--	5.10E-05
Glutaraldehyde		4.00E-02		4.0E-02	46.37	3.5E-06	8.1E-05	--	2.04E-03
Polyethylene glycol trimethylnonyl ether		5.00E-02		5.0E-02	0.90	6.8E-08	1.6E-06	--	3.15E-05
Total Risk (mixture)								**--**	**2.12E-03**

Dermal Exposure to Chemicals via Incidental Contact with Flowback Water (20% mass return) - HVFR_A

Adult Trespassers

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (20% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	78	Average male and female adults as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Surface Area (SAw)	cm^2	20000	Whole adult body surface area as per enHealth 2012
Exposure Time (ET)	hr/day	1	Assume adult gets completely wet for 1 hour each time
Conversion Factor (CF)	L/cm^3	1.E-03	Conversion of units
Intake Factor = SAw*ET*CF*EF*ED **BW*AT**	L-hr/(cm-kg-day)	**3.0E-05** **7.0E-04**	**NonThreshold** **Threshold**

Daily Intake from Water = Concentration in Water x Dermal Permeability x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data					Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor $(mg/kg\text{-}day)^{-1}$	Chronic Threshold TDI (mg/kg/day)	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background) (mg/kg/day)	Dermal Permeability (cm/hr)	in Water (mg/L)	NonThreshold (mg/kg/day)	Threshold (mg/kg/day)	NonThreshold Risk (unitless)	Chronic Hazard Quotient (unitless)
Hydrotreated light petroleum distillate		10.00		1.0E+01	1.96E+00	290.18	1.7E-02	4.0E-01	--	4.00E-02
Glutaraldehyde		0.04		4.0E-02	3.25E-04	46.37	4.5E-07	1.1E-05	--	2.65E-04
Polyethylene glycol trimethylnonyl ether		0.05		5.0E-02	3.99E-03	0.90	1.1E-07	2.5E-06	--	5.04E-05
								Total Risk (mixture)		**4.03E-02**

Ingestion of Chemicals via Incidental Contact with Flowback Water (20% mass return) - HVFR_A

Older Children Trespassers (5-15 yrs)

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (20% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	39	Mean body weight (from 4-7, 8-11 and 12-15 year old data) as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Ingestion Rate (IRw)	L/day or L/hr	0.05	Assume incidental ingestion of 50 mL
Bioavailability (B)	-	100%	Assume 100% bioavailability via ingestion of chemicals in water.
Intake Factor = $\frac{IRw*ET*B*EF*ED}{BW*AT}$	L/kg/day	**1.5E-07** **3.5E-06**	**NonThreshold** **Threshold**

Daily Intake from Water = Concentration in Water x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data				Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor	Chronic Threshold TDI	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background)	in Water	NonThreshold	Threshold	NonThreshold Risk	Chronic Hazard Quotient
	$(mg/kg\text{-}day)^{-1}$	(mg/kg/day)		(mg/kg/day)	(mg/L)	(mg/kg/day)	(mg/kg/day)	(unitless)	(unitless)
Hydrotreated light petroleum distillate		1.0E+01		1.0E+01	290.18	4.4E-05	1.0E-03	--	1.02E-04
Glutaraldehyde		4.0E-02		4.0E-02	46.37	7.0E-06	1.6E-04	--	4.07E-03
Polyethylene glycol trimethylnonyl ether		5.0E-02		5.0E-02	0.90	1.4E-07	3.2E-06	--	6.31E-05
							Total Risk (mixture)		**4.24E-03**

Dermal Exposure to Chemicals via Incidental Contact with Flowback Water (20% mass return) - HVFR_A

Older Children Trespassers (5-15 yrs)

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (20% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	39	Mean body weight (from 4-7, 8-11 and 12-15 year old data) as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	Averaging of exposure over 70yr lifetime as per USEPA 1989 and CSMS 1996
Averaging Time - Threshold (ATn)	days	1095	Averaging of exposure over exposure duration as per USEPA 1989 and CSMS 1996
Surface Area (SAw)	cm^2	15900	Wholebody surface area (child 11-15 yrs) as per enhealth 2012
Exposure Time (ET)	hr/day	1	Assume child gets completely wet for 1 hour each time
Conversion Factor (CF)	L/cm^3	1.E-03	Conversion of units
Intake Factor = SAw*ET*CF*EF*ED	L-hr/(cm-kg-day)	**4.8E-05**	**NonThreshold**
BW*AT		**1.1E-03**	**Threshold**

Daily Intake from Water = Concentration in Water x Dermal Permeability x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data					Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor (mg/kg-day)$^{-1}$	Chronic Threshold TDI (mg/kg/day)	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background) (mg/kg/day)	Dermal Permeability (cm/hr)	in Water (mg/L)	NonThreshold (mg/kg/day)	Threshold (mg/kg/day)	NonThreshold Risk (unitless)	Chronic Hazard Quotient (unitless)
Hydrotreated light petroleum distillate		1.0E+01		1.0E+01	2.0E+0	290.18	2.7E-02	6.4E-01	--	6.35E-02
Glutaraldehyde		4.0E-02		4.0E-02	3.3E-4	46.37	7.2E-07	1.7E-05	--	4.21E-04
Polyethylene glycol trimethylnonyl ether		5.0E-02		5.0E-02	4.0E-3	0.90	1.7E-07	4.0E-06	--	8.01E-05
								Total Risk (mixture)		**6.40E-02**

Ingestion of Chemicals via Incidental Contact with Flowback Water (60% Mass Return) - HVFR_A

Adult Trespassers

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (60% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	78	Average male and female adults as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Ingestion Rate (IRw)	L/day or L/hr	0.05	Assume incidental ingestion of 50 mL
Bioavailability (B)	-	100%	Assume 100% bioavailability via ingestion of chemicals in water.
Intake Factor = $\frac{IRw*ET*B*EF*ED}{BW*AT}$	L/kg/day	**7.5E-08**	**NonThreshold**
		1.8E-06	**Threshold**

Daily Intake from Water = Concentration in Water x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data				Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor (mg/kg-day)$^{-1}$	Chronic Threshold TDI (mg/kg/day)	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background) (mg/kg/day)	in Water (mg/L)	NonThreshold (mg/kg/day)	Threshold (mg/kg/day)	NonThreshold Risk (unitless)	Chronic Hazard Quotient (unitless)
Hydrotreated light petroleum distillate		1.00E+01		1.0E+01	870.53	6.6E-05	1.5E-03	--	1.53E-04
Glutaraldehyde		4.00E-02		4.0E-02	139.10	1.0E-05	2.4E-04	--	6.11E-03
Polyethylene glycol trimethylnonyl ether		5.00E-02		5.0E-02	2.69	2.0E-07	4.7E-06	--	9.46E-05
							Total Risk (mixture)		**6.35E-03**

Dermal Exposure to Chemicals via Incidental Contact with Flowback Water (60% mass return) - HVFR_A

Adult Trespassers

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (60% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	78	Average male and female adults as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Surface Area (SAw)	cm^2	20000	Whole adult body surface area as per enHealth 2012
Exposure Time (ET)	hr/day	1	Assume adult gets completely wet for 1 hour each time
Conversion Factor (CF)	L/cm^3	1.E-03	Conversion of units
Intake Factor = SAw*ET*CF*EF*ED	L-hr/(cm-kg-day)	**3.0E-05**	**NonThreshold**
BW*AT		**7.0E-04**	**Threshold**

Daily Intake from Water = Concentration in Water x Dermal Permeability x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data					Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor	Chronic Threshold TDI	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background)	Dermal Permeability	in Water	NonThreshold	Threshold	NonThreshold Risk	Chronic Hazard Quotient
	$(mg/kg\text{-}day)^{-1}$	(mg/kg/day)		(mg/kg/day)	(cm/hr)	(mg/L)	(mg/kg/day)	(mg/kg/day)	(unitless)	(unitless)
Hydrotreated light petroleum distillate		1.0E+01		1.0E+01	2.0E+0	870.53	5.1E-02	1.2E+00	--	1.20E-01
Glutaraldehyde		4.0E-02		4.0E-02	3.3E-4	139.10	1.4E-06	3.2E-05	--	7.94E-04
Polyethylene glycol trimethylnonyl ether		5.0E-02		5.0E-02	4.0E-3	2.69	3.2E-07	7.6E-06	--	1.51E-04
								Total Risk (mixture)		**1.21E-01**

Ingestion of Chemicals via Incidental Contact with Flowback Water (60% mass return) - HVFR_A

Older Children Trespassers (5-15 yrs)

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (60% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	39	Mean body weight (from 4-7, 8-11 and 12-15 year old data) as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	USEPA 2009
Averaging Time - Threshold (ATn)	days	1095	USEPA 2009
Ingestion Rate (IRw)	L/day or L/hr	0.05	Assume incidental ingestion of 50 mL
Bioavailability (B)	-	100%	Assume 100% bioavailability via ingestion of chemicals in water.
Intake Factor = IRw*ET*B*EF*ED **BW*AT**	L/kg/day	**1.5E-07** **3.5E-06**	**NonThreshold** **Threshold**

Daily Intake from Water = Concentration in Water x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data				Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor	Chronic Threshold TDI	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background)	in Water	NonThreshold	Threshold	NonThreshold Risk	Chronic Hazard Quotient
	$(mg/kg\text{-}day)^{-1}$	(mg/kg/day)		(mg/kg/day)	(mg/L)	(mg/kg/day)	(mg/kg/day)	(unitless)	(unitless)
Hydrotreated light petroleum distillate		1.0E+01		1.0E+01	870.53	1.3E-04	3.1E-03	--	3.06E-04
Glutaraldehyde		4.0E-02		4.0E-02	139.10	2.1E-05	4.9E-04	--	1.22E-02
Polyethylene glycol trimethylnonyl ether		5.0E-02		5.0E-02	2.69	4.1E-07	9.5E-06	--	1.89E-04
							Total Risk (mixture)		**1.27E-02**

Dermal Exposure to Chemicals via Incidental Contact with Flowback Water (60% mass return) - HVFR_A

Older Children Trespassers (5-15 yrs)

General Data/ Equations	Units	Exposure Calculations (RME) Flowback Water (60% return)	
Exposure Parameters			
Exposure Frequency (EF)	days/year	1	Assume direct contact with flowback water occurs over 1 day within the time period that the flow back pond is on-site
Exposure Duration (ED)	years	3	Maximum duration of a flow back pond on-site
Body Weight (BW)	kg	39	Mean body weight (from 4-7, 8-11 and 12-15 year old data) as per enHealth 2012
Averaging Time - NonThreshold (ATc)	days	25550	Averaging of exposure over 70yr lifetime as per USEPA 1989 and CSMS 1996
Averaging Time - Threshold (ATn)	days	1095	Averaging of exposure over exposure duration as per USEPA 1989 and CSMS 1996
Surface Area (SAw)	cm^2	15900	Wholebody surface area (child 11-15 yrs) as per enhealth 2012
Exposure Time (ET)	hr/day	1	Assume child gets completely wet for 1 hour each time
Conversion Factor (CF)	L/cm^3	1.E-03	Conversion of units
Intake Factor = SAw*ET*CF*EF*ED **BW*AT**	L-hr/(cm-kg-day)	**4.8E-05** **1.1E-03**	**NonThreshold** **Threshold**

Daily Intake from Water = Concentration in Water x Dermal Permeability x Intake Factor
NonThreshold Risk = Daily Intake for NonThreshold Effects x Slope Factor
Hazard Quotients = (Daily Intake for Threshold Effects/ADI)

Chemical	Toxicity Data					Concentration	Daily Intake		Calculated Risk	
	Non-Threshold Slope Factor $(mg/kg-day)^{-1}$	Chronic Threshold TDI (mg/kg/day)	Background Intake (% Chronic TDI)	Chronic TDI Allowable for Assessment (TDI-Background) (mg/kg/day)	Dermal Permeability (cm/hr)	in Water (mg/L)	NonThreshold (mg/kg/day)	Threshold (mg/kg/day)	NonThreshold Risk (unitless)	Chronic Hazard Quotient (unitless)
Hydrotreated light petroleum distillate		1.0E+01		1.0E+01	2.0E+0	870.53	8.2E-02	1.9E+00	--	1.91E-01
Glutaraldehyde		4.0E-02		4.0E-02	3.3E-4	139.10	2.2E-06	5.0E-05	--	1.26E-03
Polyethylene glycol trimethylnonyl ether		5.0E-02		5.0E-02	4.0E-3	2.69	5.1E-07	1.2E-05	--	2.40E-04
								Total Risk (mixture)		**1.92E-01**

Summary of Risk to Trespassers - 20 and 60% Mass Return (Theoretical) Data - HVFR_A

Exposure fo Target Chemicals

Receptor/Exposure Pathway	Calculated Non-Threshold Risk 20% Mass Return	Calculated HI 20% Mass Return	Calculated Non-Threshold Risk 60% Mass Return	Calculated HI 60% Mass Return
Adult Trespassers				
Ingestion of Chemicals via Incidental Contact with Flowback Water	--	0.002	--	0.006
Dermal Exposure to Chemicals via Incidental Contact with Flowback Water	--	0.04	--	0.1
Total Risk	--	**0.04**	--	**0.1**
Child Trespassers				
Ingestion of Chemicals via Incidental Contact with Flowback Water	--	0.004	--	0.01
Dermal Exposure to Chemicals via Incidental Contact with Flowback Water	--	0.06	--	0.2
Total Risk	--	**0.07**	--	**0.2**

Aquatic Toxicity Endpoints - Risk Calculations - HVFR_A

General Equations

$$\text{PNEC Aquatic mg/L} = \frac{\text{E(L)C50 or NOEC}}{\text{Assessment Factor}}$$

$$\text{HQ} = \frac{\text{EPC}}{\text{PNEC Aquatic}}$$

Where PNEC Aquatic = Predicted No Effects Concentration (Aquatic Receptors)
E(L)C50 = Median effective concentration
NOEC = No Observed Effect Concentration
HQ = Hazard Quotient
EPC = Exposure Point Concentration
Total HI = Hazard Index (Sum of HQ)

CAS#	Chemical	Endpoint	E(L)C50 or NOEC	Assessment Factor	PNEC Aquatic	EPC		Calculated HI	
			mg/L		mg/L	20% Mass Return mg/L	60% Mass return mg/L	20% Mass Return mg/L	60% Mass Return mg/L
111-30-8	Glutaraldehyde	48 h acute Daphnia	2.1	10	2.10E-01	46	139	220.80	662.39
7647-01-0	Hydrochloric Acid	Chronic Daphnia	62	10	6.20E+00	225	676	36.36	109.07
64742-47-8	Hydrotreated light petroleum distillate	Acute Daphnia	0.018	100	1.80E-04	290	871	1612095.29	4836285.86
68551-12-2	Ethoxylated C12-C16 Alcohol	Chronic daphnia	0.11	10	1.10E-02	0.24	0.73	22.03	66.09
104-55-2	Cinnamaldehyde	72 hr Algae	2	10	2.00E-01	0.09	0.28	0.47	1.41
127087-87-0	Polyethylene glycol trimethylnonyl ether	Chronic fish	0.048	100	4.80E-04	0.90	2.69	1871.19	5613.57
22042-96-2	Hepta sodium phosphonate	Chronic fish	25.6	100	2.56E-01	26	77	99.68	299.03
6381-77-7	Sodium erythorbate	Acute Algae	1020	100	1.02E+01	3.1	9.3	0.30	0.91
67-63-0	Propan-2-ol	Chronic Daphnia	5000	10	5.00E+02	0.31	0.93	0.001	0.002
532-32-1	FFI (Sodium Benzoate)	Acute fish	1000	100	1.00E+01	0.014	0.042	0.001	0.004
1310-73-2	Sodium hydroxide (caustic soda)	Chronic Daphnia	240	100	2.40E+00	0.014	0.041	0.006	0.017
							Total HI	**1.61E+06**	**4.84E+06**