File No.: STD/1674

March 2020

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

PUBLIC REPORT

1-Tetradecene, homopolymer, hydrogenated

This Assessment has been compiled in accordance with the provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by the Department of Health, and conducts the risk assessment for public health and occupational health and safety. The assessment of environmental risk is conducted by the Department of Agriculture, Water and the Environment.

This Public Report is available for viewing and downloading from the NICNAS website or available on request, free of charge, by contacting NICNAS. For requests and enquiries please contact the NICNAS Administration Coordinator at:

Street Address:	Level 7, 260 Elizabeth Street, SURRY HILLS NSW 2010, AUSTRALIA.
Postal Address:	GPO Box 58, SYDNEY NSW 2001, AUSTRALIA.
TEL:	+ 61 2 8577 8800
FAX:	+ 61 2 8577 8888
Website:	www.nicnas.gov.au

Director
NICNAS

TABLE OF CONTENTS

SUMMARY

The following details will be published in the NICNAS *Chemical Gazette:*

ASSESSMENT REFERENCE	APPLICANT(S)	CHEMICAL OR TRADE NAME	HAZARDOUS CHEMICAL	INTRODUCTION VOLUME	USE
STD/1674	Amochem Pty Ltd	1-Tetradecene, homopolymer, hydrogenated	Yes	≤ 100 tonnes per annum	Component of motor oil, automatic transmission fluid, and industrial lubricants

CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia. The hazard classification applicable to the notified chemical is presented in the following table.

Hazard Classification	*Hazard Statement*
Aspiration hazard (Category 1)	H 304 – May be fatal if swallowed and enters airways

Human Health Risk Assessment
Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

Environmental Risk Assessment
On the basis of the low hazard and the reported use pattern, the notified chemical is not considered to pose an unreasonable risk to the environment.

Recommendations

REGULATORY CONTROLS

Hazard Classification and Labelling

- The notified chemical should be classified as follows:
  - Aspiration hazard (Category 1): H 304 - May be fatal if swallowed and enters airways

  The above should be used for products/mixtures containing the notified chemical, if applicable, based on the concentration of the notified chemical present.

CONTROL MEASURES

Occupational Health and Safety

- A person conducting a business or undertaking at a workplace should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced or during reformulation:
  - Enclosed, automated processes, where possible
  - Local exhaust ventilation if aerosols or mists are generated

- A person conducting a business or undertaking at a workplace should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced, or during reformulation and use:
  - Avoid inhalation
  - Avoid contact with skin and eyes
  - Avoid ingestion/aspiration

- A person conducting a business or undertaking at a workplace should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced or during reformulation:
  - Respiratory protection, where exposure to aerosols or mists is likely

  Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the SDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* as adopted for industrial chemicals in Australia, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation should be in operation.

Public Health

- As liquid hydrocarbons are included in Schedule 5 of the SUSMP, any labelling and/or packaging requirement for products containing the notified chemical, which are available to the public, should be adhered to.

Storage

- The handling and storage of the notified chemical should be in accordance with the Safe Work Australia Code of Practice for *Managing Risks of Hazardous Chemicals in the Workplace* (SWA, 2012) or relevant State or Territory Code of Practice.

Emergency procedures

- Spills or accidental release of the notified chemical should be handled by physical containment, collection and subsequent safe disposal.

Disposal

- Where reuse or recycling are not appropriate, dispose of the notified chemical in an environmentally sound manner in accordance with relevant Commonwealth, state, territory and local government legislation.

Regulatory Obligations

Secondary Notification
This risk assessment is based on the information available at the time of notification. The Director may call for the reassessment of the chemical under secondary notification provisions based on changes in certain circumstances. Under Section 64 of the *Industrial Chemicals (Notification and Assessment) Act (1989)* the notifier, as well as any other importer or manufacturer of the notified chemical, have post-assessment regulatory obligations to notify NICNAS when any of these circumstances change. These obligations apply even when the notified chemical is listed on the Australian Inventory of Chemical Substances (AICS).

Therefore, the Director of NICNAS must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if

- additional information has become available to the person on the reproductive/developmental toxicity of the notified chemical;
- the chemical is proposed to be used in spray products

or

(2) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a component of motor oil, automatic transmission fluid, and industrial lubricants, or is likely to change significantly;
- the amount of chemical being introduced has increased, or is likely to increase, significantly;
- the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

The Director will then decide whether a reassessment (i.e. a secondary notification and assessment) is required.

Safety Data Sheet
The SDS of the notified chemical provided by the notifier was reviewed by NICNAS. The accuracy of the information on the SDS remains the responsibility of the applicant.

ASSESSMENT DETAILS

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Amochem Pty Ltd (ABN: 48 095 713 269)
34/67 Peninsula Drive
BREAKFAST POINT NSW 2137

NOTIFICATION CATEGORY
Standard: Chemical other than polymer (more than 1 tonne per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details exempt from publication include: structural formulae, molecular weight, impurities, import volume, and identity information of analogue chemicals.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Schedule data requirements are varied for hydrolysis as a function of pH, partition coefficient, adsorption/desorption, dissociation constant, flammability limits, explosive properties, oxidizing properties, and all toxicological and ecotoxicological data

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US EPA (2017)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Durasyn 164E

CAS NUMBER
1857296-89-9

CHEMICAL NAME
1-Tetradecene, homopolymer, hydrogenated

OTHER NAME(S)
Hydrogenated Tetradecene Oligomer
C14 PAO
Polyalphaolefin synthetic fluid
PAO
Synthetic hydrocarbon

MOLECULAR FORMULA
Unspecified

MOLECULAR WEIGHT
Number average molecular weight (Mn) is < 500 g/mol

ANALYTICAL DATA
Reference NMR, FT-IR, GPC, UV-vis spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
≥ 94%

ADDITIVES/ADJUVANTS
None

LOSS OF MONOMERS, OTHER REACTANTS, ADDITIVES, IMPURITIES
Under normal conditions of use, hazardous decomposition products are not expected to be produced.

DEGRADATION PRODUCTS
None

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20 ºC AND 101.3 kPa: clear oily liquid

Property	*Value*	*Data Source/Justification*
Pour Point	-40 °C	Measured
Boiling Point	358.5 - 560 °C	Measured
Density	819.8 kg/m^3 at 15.6 °C	Measured
Kinematic Viscosity	3.9 mm^2/s at 100 °C 16.39 mm^2/s at 40 °C	Measured
Vapour Pressure	< 1.33 × 10^{-3} kPa at 37.8 °C	Measured
Water Solubility	< 0.5 × 10^{-3} g/L at 20 °C	Measured
Hydrolysis as a Function of pH	Not determined	Contains no hydrolysable functionalities
Partition Coefficient (n-octanol/water)	log Pow > 6	Measured on analogue chemicals
Adsorption/Desorption	log Koc > 4.96	Calculated by the notifier based on an empirically derived relation between Koc and Pow
Dissociation Constant	Not determined	Contains no dissociable functionalities
Flash Point	221 °C	Measured
Autoignition Temperature	357 °C	Measured
Explosive Properties	Not determined	Contains no functional groups that would imply explosive properties
Oxidising Properties	Not determined	Contains no functional groups that would imply oxidising properties

DISCUSSION OF PROPERTIES
The measured viscosity provided for the notified chemical is 16.39 mm^2/s at 40 °C. According to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*, hydrocarbon substances with viscosity < 20.5 mm^2/s at 40 °C should be classified for aspiration hazard. See Section 6.2 for further details regarding the health hazard classification.

For details of tests on physical and chemical properties, refer to Appendix A.

Reactivity
The notified chemical is expected to be stable under normal conditions of use.

Physical Hazard Classification
Based on the submitted physico-chemical data depicted in the above table, the notified chemical is not recommended for hazard classification according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia.

The notified chemical has a flash point of 221 ºC which is greater than 93 °C. Based on *Australian Standard AS1940* definitions for combustible liquid, the notified chemical may be considered as a Class C2 combustible liquid if the chemical has a fire point below the boiling point.

5. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia at close to 100% concentration for the formulation of motor oils, transmission fluids, and industrial lubricants.

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	1-20	1-20	20-100	20-100	20-100

PORT OF ENTRY
Sydney

IDENTITY OF RECIPIENTS
Amochem Pty Ltd

TRANSPORTATION AND PACKAGING
The notified chemical will be imported into Australia in either 200 L drums or iso-containers. The notified chemical is expected to be primarily transported from the dockside to the customer or contract warehouse via trucks, but rail transport may be possible. The notified chemical is then stored until required for despatch to customers for reformulation. The finished lubricant products may be packaged in drums (200 L) or bottles (1 L or bigger).

USE
The notified chemical will be used as a base component of motor oil, automatic transmission fluid, and industrial lubricants at 10-98% concentration. These products will be used industrially (at ≤ 98% concentration) and by Do-It-Yourself (DIY) users (at ≤ 70% concentration).

OPERATION DESCRIPTION
Formulation of lubricants will occur at blending facilities of lubricant manufacturers.

At the blending sites, the notified chemical will be pumped via dedicated hard pipes to blending tanks. After blending with other components, the finished lubricant products containing the notified chemical at ≤ 98% concentration will be pumped via dedicated hard pipes to bulk storage tanks for subsequent packaging into 200 L drums and bottles (1 L or larger). The formulation process is expected to be largely enclosed and automated. Samples will be collected at various stages for quality control testing.

The finished lubricant products will be supplied to industrial and commercial end-users, and retail stores. They will be used industrially and in automotive applications by motor mechanics and DIY users.

6. HUMAN HEALTH IMPLICATIONS

6.1. Exposure Assessment

6.1.1. Occupational Exposure

CATEGORY OF WORKERS

Category of Worker	*Exposure Duration (hours/day)*	*Exposure Frequency (days/year)*
Formulation:		
Taking samples	5	350
Analysing samples	1	350
Maintaining equipment	3	350
Continuous blending operation	20	350
Filling packaging	10	350
Quick lube employees	8	250
Industrial oil exchangers	0.5	10-15

EXPOSURE DETAILS

Transport and storage
Transport and storage workers may come into contact with the notified chemical at ≤ 100% concentration only in the unlikely event of a spill or accidental rupture of containers.

Formulation of lubricants
Dermal and ocular exposure of workers to the notified chemical at ≤ 100% concentration may occur during quality control analysis, and cleaning and maintenance of equipment. Exposure to the notified chemical at other times is expected to be negligible given the formulation process will be largely enclosed and automated.

According to the notifier, dermal and ocular exposure to workers would be mitigated through the use of personal protective equipment (PPE), including protective clothing, impervious gloves and goggles. Inhalation exposure is not expected given the use of enclosed systems for formulation and low vapour pressure of the notified chemical.

End-use
Workers may be exposed to lubricants containing the notified chemical at ≤ 98% concentration during use, for example, at automotive car dealerships or automotive service centres during transfer, charging or top-up activities, or during plant maintenance activities at industrial sites.

Given the low vapour pressure of the notified chemical, inhalation exposure is not expected. According to the notifier, dermal and ocular exposure to workers would be mitigated through the use of PPE, including protective clothing, impervious gloves and goggles.

6.1.2. Public Exposure
Finished lubricants containing the notified chemical at ≤ 70% concentration may be sold through the retail market to DIY users to replace or top-up automotive lubricants, for example, engine and gearbox oils. Therefore, incidental dermal exposure to the notified chemical at ≤ 70% concentration may occur to DIY users. Given the low vapour pressure of the notified chemical, inhalation exposure to the notified chemical is not expected. Accidental ocular exposure may be possible.

6.2. Human Health Effects Assessment
Two studies in the table were carried out on the notified chemical. The remainder of the studies were carried out on analogue chemicals that are considered likely to have similar toxicological characteristics to the notified chemical. For full details of these studies, refer to Appendix B. Studies marked # are not included in Appendix B.

Endpoint and Result	*Test substance*	*Assessment Conclusion*
Rat, acute oral LD50 > 5,000 mg/kg bw (4 studies)	Analogue chemicals 1-4	low toxicity
Rat, acute dermal LD50 > 2,000 mg/kg bw	Durasyn 125	low toxicity
Rabbit, skin irritation (4 studies)	Analogue chemicals 1-4	slightly irritating (based on 24 hour exposure)
Rabbit, eye irritation (4 studies)	Analogue chemicals 1-4	slightly irritating
Guinea pig, skin sensitisation – adjuvant test (2 studies)	Analogue chemicals 1-2	no evidence of sensitisation
Guinea pig, skin sensitisation – adjuvant test	Analogue chemical 3	limited evidence of sensitisation
Rat, repeat dose/developmental toxicity – 91 days.	Analogue chemical 3	NOAEL = 1,000 mg/kg bw/day
Repeat dose inhalation toxicity – rat, 14 days	Notified chemical	NOAEC = 2.15 mg/L
Repeat dose inhalation toxicity – rat, 28 days	Notified chemical	NOAEC = 0.75 mg/L
Genotoxicity – bacterial reverse mutation	Analogue chemical 2	non mutagenic
Genotoxicity – *in vitro* chromosomal aberrations in human lymphocytes	Analogue chemical 5	non genotoxic
Genotoxicity – *in vitro* mammalian cell gene mutation test	Analogue chemical 5	non genotoxic
Genotoxicity – *in vivo* mouse micronucleus test	Analogue chemical 6	non genotoxic

Two-generation reproduction toxicity study – rat#	Durasyn 164X	NOEL for adult toxicity and reproductive and developmental toxicity = 1,000 mg/kg bw/day*

*Established by the study authors

Toxicokinetics, Metabolism and Distribution
Given the low molecular weight of the notified chemical (< 500 g/mol), absorption across biological membranes may occur, but would be limited by the low water solubility (< 0.5×10^{-3} g/L) and high partition coefficient (log Pow > 6). The notified chemical may also be taken up by micellular solubilisation due to its high lipophilicity.

Acute toxicity
Based on analogue data, the notified chemical has low acute oral toxicity (LD50 > 5,000 mg/kg bw) and low acute dermal toxicity (LD50 > 2,000 mg/kg bw).

An acute inhalation toxicity study according to OECD guidelines is not available for the notified chemical. As the notified chemical caused no mortality in a 14-day repeated dose inhalation study in rats (described below under repeated dose toxicity) using doses up to 5.64 mg/L, it is not considered to be classified for acute inhalation toxicity.

Irritation and Sensitisation
Some skin irritation was reported in four *in vivo* studies on analogue chemicals where the exposure time was 24 h rather than the 4 h exposure specified in the OECD Test Guideline. It is expected that the extended timeframe in these studies would have resulted in increased irritation effects. Based on these results, the notified chemical is not considered to be classified for skin irritation.

Based on *in vivo* eye irritation studies in rabbits on four analogue chemicals, the notified chemical is likely to be slightly irritating to the eyes.

Limited information is available on the potential of the notified chemical for respiratory irritation. However it cannot be ruled out, as lung and bronchial effects in the 14 day and 28 day repeated dose inhalation studies in rats were indicative of irritation and inflammation.

One of three guinea pig maximisation skin sensitisation studies carried out on analogues showed limited evidence of skin sensitisation. Responses occurred in a small percentage of the test group, were higher at 24 hours than at 48 hours after challenge and were attributed to irritation rather than sensitisation by the study authors. The two other studies were negative. Overall, the notified chemical is not considered to be sensitising to the skin.

Repeated dose toxicity
In a 90-day oral toxicity study in rats (with an in utero phase), with doses of 100, 500, 1,000 mg/kg bw/day of analogue 3, significant systemic effects were not seen in the F0 or F1 generations. A slight increase in prothrombin time in males at the highest dose (1,000 mg/kg bw/day) was not associated with other haematological changes. Minor clinical signs were attributed to the vehicle, and a NOEL of 1,000 mg/kg bw/day was established by the study authors for systemic toxicity.

The notified chemical was tested in a 28-day repeated dose inhalation study in rats with doses up to 2.35 mg/L with a 2-week recovery period. Dose related effects in organ weight and microscopic changes were seen in the respiratory system, particularly the lungs and bronchi, and did not resolve after the recovery period. Blood cell counts were also affected. The effects were interpreted as an inflammatory response to irritation, and accumulation of the test substance in the lungs, with associated effects in the local and draining lymph glands. A NOAEC of 0.75 mg/L was set based on the severity of the effects at the highest dose. Effects on the testes were not considered test substance related (see further comments under the Toxicity for Reproduction heading).

Similar effects in the respiratory system were seen in an earlier 14-day inhalation range-finding study carried out at doses up to 5.64 mg/L.

Mutagenicity
Analogue chemicals were non mutagenic or non-genotoxic in a range of studies: bacterial reverse mutation, *in vitro* chromosomal aberration test in human lymphocytes, *in vitro* mammalian cell gene mutation test using

Chinese hamster ovary cells and an *in vivo* mouse micronucleus test. Overall the notified chemical is not expected to be mutagenic or genotoxic.

Toxicity for Reproduction
A Two-Generation Reproduction oral gavage study on an analogue (Durasyn 164X) was carried out on rats according to OECD TG 416 at dose levels of 100, 300 and 1,000 mg/kg bw/day. A control group was dosed with vehicle alone (Arachis oil BP). The 'No Observed Effect Level' (NOEL) for adult toxicity and reproductive and developmental toxicity for both F0 and F1 generations and offspring was considered by the study authors to be 1,000 mg/kg bw/day.

A NOEL of 1,000 mg/kg bw/day for reproductive/developmental effects was established by the study authors in a 91-day oral combined repeated dose/developmental study (described above) on Analogue 3. Treatment-related effects on fertility, length of gestation, pregnancy status, parturition or lactation were not identified, except that one high dose female had total litter loss.

In a 28-day repeated dose inhalation study on the notified chemical (at doses of 0.249, 0.743 and 2.35 mg/L) described above under repeated dose toxicity) there were effects on the testes and epididymides. Tubular degeneration of the testes was evident microscopically in both control and test groups, with luminal debris in the epididymides. However effects on testes weight seemed to have some dose response, with statistically significant reductions in relative weights after treatment compared to the controls at the highest dose of 2.5 mg/L, and reductions at 0.743 mg/L that were not statistically significant. The study authors suggested that the effects may be related to the restraint apparatus used in the nose-only study, and a consequent period of overheating. Another possible explanation is that the build-up of the test substance in the lungs, particularly at higher doses, led to hypoxaemia that can affect the testes (Bomhard and Gelbke 2013). The cause of the effects is not conclusive.

Health Hazard Classification
Based on the available information, the notified chemical is a hazardous chemical according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS),* as adopted for industrial chemicals in Australia, based on its viscosity and chemical class. The hazard classification applicable to the notified chemical is presented in the following table.

Hazard Classification	***Hazard Statement***
Aspiration hazard (Category 1)	H 304 – May be fatal if swallowed and enters airways

6.3. Human Health Risk Characterisation
The notified chemical is classified as an aspiration hazard. Based on analogue data it is a slight skin and eye irritant, and it may have irritant effects on the respiratory tract. Adverse effects after repeated inhalation exposure were reported.

6.3.1. Occupational Health and Safety
Ingestion/aspiration is unlikely to occur in the proposed use of the chemical, except in case of an accident. There is the possibility of skin and eye irritation to lubricant blenders and end users as the lubricant contains up to 98% of notified chemical. The risk would be reduced by the controlled environment in which some of the processes occur, by safe work practices, and further reduced by the stated use of PPE by workers. Inhalation exposure and risk is likely to be low in the scenarios described, unless aerosols or mists are generated.

Under the conditions of the occupational settings described, the notified chemical is not considered to pose an unreasonable risk to the health of workers.

6.3.2. Public Health
Exposure of the public to the notified chemical will be minimal during transport, storage, blending and industrial use, except in the event of an accidental spill.

The risk to DIY users from manual addition of products containing the notified chemical (up to 70%) to automobiles or other machinery is not considered unreasonable as only incidental exposure is expected and the frequency of use is expected to be low. Protective gloves may not necessarily be used by DIY users during applications (up to 70% concentration), however, users may have access to the MSDS of the lubricant, which contains adequate information to warn users regarding the hazards of the lubricant.

The notified chemical is a liquid hydrocarbons. Liquid hydrocarbons are included in Schedule 5 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), with packaging/labelling requirements for products containing liquid hydrocarbons available to the public.

When used in the proposed manner, the notified chemical is not considered to pose an unreasonable risk to public health.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1. Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be imported into Australia neat for formulation of motor oils, automatic transmission fluids (ATF), and industrial lubricants. The formulation process involves blending operations in closed systems, followed by automatic filling of the formulated products into end-use containers. Any waste generated from the formulation process is expected to be recycled or disposed of by an approved waste management facility. Bulk shipments of the finished lubricants containing the notified chemical for industrial uses may be moved by truck, train, or barge. Material trapped in transfer hoses is collected or goes back into the truck, railcar, or cargo hold. Empty trucks, railcars, or cargo holds are drained and cleaned. The wastewater is collected and treated at onsite wastewater treatment plant before being discharged to the environment. Accidental spills of the notified chemical during import, transport, formulation or storage are expected to be collected for recycling or disposal of, in accordance with local government regulations.

RELEASE OF CHEMICAL FROM USE

The finished motor oils/lubricants containing the notified chemical will be available to industry, motor mechanics and public consumers. According to the notifier, about 30% of the notified chemical will be consumed during use and the remainder will be drained from the equipment or engine during oil changes. Minor accidental spills could occur during use and are expected to be collected on suitable absorbent material for disposal of, in accordance with local government regulations.

Some of the notified chemical will be used by Do-It-Yourself (DIY) users. In a recent Australian survey it was found that only 4% of households disposed of motor oil and approximately 30% of them was incorrectly disposed of (Aither, 2013). For ATF, the trend for these types of transmissions is “fill for life”, with no scheduled servicing (drain and refill). Therefore the amount of transmission fluid likely to be disposed of by DIY users will be less than that for motor oil. Therefore a small amount of used motor oils/lubricants containing the notified chemical may be incorrectly disposed by DIY users.

RELEASE OF CHEMICAL FROM DISPOSAL

Empty containers containing residues of the notified chemical will be disposed of to landfill in accordance with local government regulations. The used oil containing the notified chemical is expected to be collected and re-refined or disposed of by approved waste management contractors, in accordance with local government regulations.

7.1.2. Environmental Fate

A biodegradability study conducted on the notified chemical indicates that it is not readily biodegradable but shows inherent biodegradability (54% biodegradation after 29 days in OECD 301B test). For details of this biodegradability study, refer to Appendix C.

According to the notifier, about 30% of the notified chemical is consumed during use and the remainder will be drained from the equipment or engine during oil changes. The used oil containing the notified chemical is expected to be re-refined or disposed of by approved waste management contractors. It is likely that the notified chemical will be degraded into simpler compounds during refining. The wastewater containing the notified chemical released at site will be treated at onsite wastewater treatment plant. Based on its low solubility and high log P_{ow} (> 6), the notified chemical is expected to be removed effectively through adsorption to sludge at the treatment plant. A proportion of this may be applied to land when sludge from wastewater treatment facilities is used for soil remediation, or disposed of to landfill. Minor amounts of the notified chemical may also be disposed of to landfill as collected spills. Based on its low water solubility and high log K_{oc} (> 4.98), the notified chemical is expected to

have low mobility in soil. The notified chemical in the environment is expected to eventually degrade into water and oxides of carbon via biotic and abiotic pathways.

7.1.3. Predicted Environmental Concentration (PEC)

The predicted environmental concentration (PEC) has not been calculated. A small fraction of the notified chemical may be incorrectly disposed of by DIY users. This fraction is expected to be dispersed and not all of it will reach waterways. Therefore the concentration in the aquatic environment is expected to be limited.

7.2. Environmental Effects Assessment

The results from ecotoxicological investigations conducted on the notified chemical and its analogues are summarised in the table below. The results are presented as nominal concentrations. Details of these studies can be found in Appendix C.

Endpoint	*Test chemical*	*Result*	*Assessment Conclusion*
Acute Fish Toxicity	Analogue Chemical 1	96 h LL50 > 10,000 mg/L (WAF)	Not harmful to fish up to its water solubility limit
Acute Daphnia Toxicity	Analogue Chemical 6	48 h EL50 > 1,000 mg/L (WAF)	Not harmful to aquatic invertebrates up to its water solubility limit
Chronic Daphnia Toxicity	Analogue Chemical 1	21 d EL50 > 125 mg/L (WAF) 21 d NOEL ≥ 125 mg/L (WAF)	No adverse effect on the survival, reproduction and growth of *Daphnia magna*
	Analogue Chemical 4	21 d EL50 > 125 mg/L (WAF) 21 d NOEL ≥ 125 mg/L (WAF)	No adverse effect on the survival, reproduction and growth of *Daphnia magna*
Acute Algal Toxicity	Analogue Chemical 6	96 h EL50 > 1,000 mg/L (WAF)	Not harmful to algae up to its water solubility limit
Inhibition of Bacterial Respiration	Notified chemical	3 h IC50 > 1,000 mg/L	Not inhibitory to microbial respiration
	Analogue Chemical 1	16 h IC50 > 10,000 g/L	Not harmful to bacteria up to its water solubility limit
Sediment Reworker Toxicity	Durasyn 156	10 d LC50 > 10,000 mg/kg dry sediment 10 d NOEL ≥ 10,000 mg/kg dry sediment	Not harmful to sediment reworker *Corophium volutator*

WAF: Water Accommodated Fraction

The results above indicate the notified chemical is not expected to be harmful to aquatic organisms and sediment reworker. The notified chemical is therefore not formally classified under the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)* for acute and chronic toxicities (United Nations, 2009).

7.2.1. Predicted No-Effect Concentration

The predicted no-effect concentration (PNEC) has not been calculated as the notified chemical is not expected to be harmful to aquatic organisms up to its water solubility limit.

7.3. Environmental Risk Assessment

A Risk Quotient (PEC/PNEC) has not been calculated as the notified chemical is not expected to be harmful to aquatic organisms up to its water solubility limit, and its release to the aquatic environment is expected to be limited based on the reported use pattern. Therefore, based on the low hazard and the reported use pattern, the notified chemical is not expected to pose an unreasonable risk to the environment.

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Pour Point -40 °C

Method ASTM D-97 Standard Test Method for Pour Point of Petroleum Products
Test Facility INEOS Oligomers (2016a)

Boiling Point 358.5 - 560 °C

Method ASTM D-2887 Standard Test Method for Boiling Range Distribution of Petroleum Fractions by Gas Chromatography
Remarks GC Simulated distillation method was used. The boiling point was determined to be > 297 °C at 5.33 × 10^{-2} kPa. No attempt was made to distill the notified chemical at atmospheric pressure.
Test Facility INEOS Oligomers (2016b)

Density 819.8 kg/m^3 at 15.6 °C

Method ASTM D-4052 Standard Test Method for Density and Relative Density of Liquids by Digital Density Meter
Test Facility INEOS Oligomers (2016a)

Kinematic Viscosity 3.9 mm^2/s at 100 °C
16.39 mm^2/s at 40 °C

Method ASTM D-445 Standard Test Method for Kinematic Viscosity of Transparent and Opaque Liquids
Test Facility INEOS Oligomers (2016a)

Vapour Pressure < 1.33 × 10^{-3} kPa at 37.8 °C

Method ASTM D-2879-10 Standard Test Method for Vapour- Pressure-Temperature Relationship and Initial Decomposition Temperature of Liquids by Isoteniscope
Test Facility INEOS Oligomers (2016c)

Water Solubility < 0.5 × 10^{-3} g/L at 20 °C

Method OECD TG 105 Water Solubility
Remarks Flask Method
Test Facility ISI (2016)

Partition Coefficient (n-octanol/water) log P_{ow} > 6

Method OECD TG 117 Partition Coefficient (n-octanol/water).
Remarks HPLC Method; the test was done on five polyalphaolefins including analogue chemicals Durasyn 125 and Durasyn 156; the column temperature was maintained at 30 °C
Test Facility PTRL West (2006)

Flash Point 221 °C

Method ASTM D-92 Standard Test Method for Flash and Fire Points by Cleveland Open Cup Tester
Test Facility INEOS Oligomers (2016a)

Autoignition Temperature 357 °C

Method ASTM E-659 Standard Test Method for Auto-ignition Temperature of Liquid Chemicals
Test Facility INEOS Oligomers (2016d)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

B.1. Acute toxicity – oral

B.1.1 Analogue chemical 1

TEST SUBSTANCE	Analogue chemical 1
METHOD	Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).
Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed with a deviation. a. One male rat dosed on this acute oral study weighted 178 grams which is slightly below the specified weight range in the protocol. This deviation did not compromise any aspect of this study.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5,000	0

LD50	> 5,000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Mild depression 2. Scruffy hair coats 3. Oily and/or scruffy hair These signs persisted through the third or fourth post-dosage days after which the animals appeared grossly normal.
Effects in Organs	The gross necropsies performed at the end of the study revealed no gross pathological changes.
Remarks - Results	No deaths occurred during the observation period.
CONCLUSION	The analogue chemical is of low toxicity via the oral route.
TEST FACILITY	Hill Top Biolabs (1998a)

B.1.2 Analogue chemical 2

TEST SUBSTANCE	Analogue chemical 2
METHOD	Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).
Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5,000	0

LD50	> 5,000 mg/kg bw

Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Mild transitory depression 2. Oily and/or scruffy hair coats All animals appeared normal by the third or fourth post-dosage day.
Effects in Organs	Gross necropsies performed at the end of the study revealed in one rat: 1. Small spleen 2. Stomach lining appeared thickened and filled with clear liquid containing a bright yellow substance No other gross pathological findings were seen.
Remarks - Results	No deaths occurred during the observation period.
CONCLUSION	The analogue chemical is of low toxicity via the oral route.
TEST FACILITY	Hill Top Biolabs (1998b)

B.1.3 Analogue chemical 3

TEST SUBSTANCE	Analogue chemical 3
METHOD	Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).
Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5,000	0

LD50	> 5,000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Transient mild depression 2. Oil hair coats All animals appeared normal by the fifth post-dosage day.
Effects in Organs	Gross necropsies performed at the end of the study revealed in one rat: 1. Yellow-brown spot on the stomach lining No other gross pathological findings were seen.
Remarks - Results	No deaths occurred during the observation period.
CONCLUSION	The analogue chemical is of low toxicity via the oral route.
TEST FACILITY	Hill Top Biolabs (1998c)

B.1.4 Analogue chemical 4

TEST SUBSTANCE	Analogue chemical 4
METHOD	Regulation for the Enforcement of the Federal Hazardous Substance Act (16 CFR 1500).
Species/Strain	Rat/Sprague-Dawley derived, albino rats
Vehicle	Undiluted
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	5,000	0

LD50	> 5,000 mg/kg bw
Signs of Toxicity	Clinical changes observed during the observation period are as follows: 1. Transient mild depression 2. Oily hair coats These oily hair coats were observed on the day of dosing and persisted through the third post-dosage day after which the rats appeared grossly normal.
Effects in Organs	Gross necropsies performed at the end of the study revealed no gross pathological changes.
Remarks - Results	No deaths occurred during the observation period.

CONCLUSION The analogue chemical is of low toxicity via the oral route.

TEST FACILITY Hill Top Biolabs (1998d)

B.2. Acute toxicity – dermal

TEST SUBSTANCE Durasyn 125

METHOD OECD TG 402 Acute Dermal Toxicity.
U.S. EPA Health Effects Guidelines, OPPTS 870.1200 (1998)

Species/Strain	Rat/Sprague-Dawley derived, albino
Vehicle	Undiluted
Type of dressing	Occlusive
Remarks - Method	The protocol was followed without deviation.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 per sex	2,000	0

LD50	> 2,000 mg/kg bw
Signs of Toxicity - Local	There were no signs of gross toxicity, dermal irritation, adverse pharmacological effects, or abnormal behaviour.
Signs of Toxicity - Systemic	
Effects in Organs	No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.
Remarks - Results	All animals survived, gained body weight, and appeared active and healthy during the study.

CONCLUSION The analogue chemical is of low toxicity via the dermal route.

TEST FACILITY Product Safety Laboratories (2006)

B.3. Irritation – skin

B.3.1 Analogue chemical 1

TEST SUBSTANCE Analogue chemical 1

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.

Species/Strain	Rabbit/New Zealand White
Number of Animals	6 F
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive
Remarks - Method	Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Erythema/Eschar	2	3	> 72 hours	3
Oedema	1	2	> 72 hours	1

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 3.1 out of 8 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is slightly irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988e)

B.3.2 Analogue chemical 2

TEST SUBSTANCE: Analogue chemical 2

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 6 F
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive
- Remarks - Method: Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Erythema/Eschar	0.67	3	> 72 hours	1
Oedema	0.42	2	> 24 hours	0

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results: The Primary Irritation Index was found to be 1.3 out of 8 based on erythema and oedema. No evidence of tissue damage was found.

CONCLUSION: The analogue chemical is slightly irritating to the skin.

TEST FACILITY: Hill Top Biolabs (1988f)

B.3.3 Analogue chemical 3

TEST SUBSTANCE: Analogue chemical 3

METHOD: US 16 CFR 1500 Hazardous Substances Labelling Act.
- Species/Strain: Rabbit/New Zealand White
- Number of Animals: 3 M, 3 F
- Vehicle: None
- Observation Period: 72 hours
- Type of Dressing: Semi-occlusive
- Remarks - Method: Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Erythema/Eschar	0.42	2	> 24 hours	0
Oedema	0	0	-	-

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results	The Primary Irritation Index was found to be 0.5 out of 8 based on erythema and oedema. No evidence of tissue damage was found.
CONCLUSION	The analogue chemical is slightly irritating to the skin.
TEST FACILITY	Hill Top Biolabs (1988g)

B.3.4 Analogue chemical 4

TEST SUBSTANCE	Analogue chemical 4
METHOD	US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 F, 3 M
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive
Remarks - Method	Gauze patch was applied for 24 hours. Scoring was at 24 and 72 hours only.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Erythema/Eschar	0.42	1	> 24 hours	0
Oedema	0.17	1	> 24 hours	0

*Calculated on the basis of the scores at 24 and 72 hours for ALL animals.

Remarks - Results	The Primary Irritation Index was found to be 0.5 out of 8 based on erythema and oedema. No evidence of tissue damage was found.
CONCLUSION	The analogue chemical is slightly irritating to the skin.
TEST FACILITY	Hill Top Biolabs (1988h)

B.4. Irritation – eye

B.4.1 Analogue chemical 1

TEST SUBSTANCE	Analogue chemical 1
METHOD	US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain	Rabbit/New Zealand White
Number of Animals	6 F
Observation Period	72 hours
Remarks - Method	No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Conjunctiva: redness	0.67	1	> 72 hours	1
Conjunctiva: chemosis	0.33	2	> 72 hours	1
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results	The eyes of all the rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 2.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988i)

B.4.2 Analogue chemical 2

TEST SUBSTANCE Analogue chemical 2

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain Rabbit/New Zealand White
Number of Animals 6 F
Observation Period 72 hours
Remarks - Method No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Conjunctiva: redness	0.17	1	> 72 hours	1
Conjunctiva: chemosis	0	0	-	0
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of two of the rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 1.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988j)

B.4.3 Analogue chemical 3

TEST SUBSTANCE Analogue chemical 3

METHOD US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain Rabbit/New Zealand White
Number of Animals 3 F, 3 M
Observation Period 72 hours
Remarks - Method No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Conjunctiva: redness	0.61	1	> 72 hours	1
Conjunctiva: chemosis	0.28	1	> 72 hours	1
Conjunctiva: discharge	0	0	-	
Corneal opacity	0	0	-	
Iridial inflammation	0	0	-	

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results The eyes of five rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 1.

CONCLUSION The analogue chemical is slightly irritating to the eye.

TEST FACILITY Hill Top Biolabs (1988k)

B.4.4 Analogue chemical 4

TEST SUBSTANCE	Analogue chemical 4
METHOD	US 16 CFR 1500 Hazardous Substances Labelling Act.
Species/Strain	Rabbit/New Zealand White
Number of Animals	3 F, 3 M
Observation Period	72 hours
Remarks - Method	No deviations from protocol noted.

RESULTS

Lesion	*Mean Score**	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at 72-Hour Observation Period*
Conjunctiva: redness	0.50	1	> 72 hours	1
Conjunctiva: chemosis	0.22	1	> 72 hours	1
Conjunctiva: discharge	0	0	-	0
Corneal opacity	0	0	-	0
Iridial inflammation	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for ALL animals.

Remarks - Results	The eyes of three rabbits were found to show evidence of conjunctival changes. Irritation scores in individual rabbits ranged from 0 to 1.
CONCLUSION	The analogue chemical is slightly irritating to the eye.
TEST FACILITY	Hill Top Biolabs (1988l)

B.5. Skin sensitisation

B.5.1 Analogue chemical 1

TEST SUBSTANCE	Analogue chemical 1
METHOD	Magnusson and Kligman (1969)
Species/Strain	Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: slight erythema at 0.5% topical: slight erythema at 10% in 1/4 animals.
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 20
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 10%
Signs of Irritation	None noted.
CHALLENGE PHASE	
1st challenge	topical: 10%
2nd challenge	None.
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No animals in either the control or treated groups exhibited signs of erythema.
CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the analogue chemical at 10% under the conditions of the test.
TEST FACILITY	Pharmakon Research International (1992a)

B.5.2 Analogue chemical 2

TEST SUBSTANCE	Analogue chemical 2
METHOD	Magnusson and Kligman (1969)
Species/Strain	Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: 5% topical: 100%
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 20
INDUCTION PHASE	Induction Concentration: intradermal: 5% topical: 100%
Signs of Irritation	None.
CHALLENGE PHASE	
1st challenge	topical: 100%
2nd challenge	None
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No animals in either the control or treated groups exhibited signs of erythema.

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the analogue chemical under the conditions of the test.
TEST FACILITY	Pharmakon Research International (1992b)

B.5.3 Analogue chemical 3

TEST SUBSTANCE	Analogue chemical 3
METHOD	OECD TG 406 Skin Sensitisation - Maximisation Test. EC Directive 96/54/EC B.6 Skin Sensitisation - Maximisation Test. EPA Subdivision F, Series 81-6, Dermal Sensitisation. 1984. Japanese Ministry of Agriculture Forestry and Fisheries, 59 NohSan No. 4200. 1985.
Species/Strain	Guinea pig/Dunkin-Hartley
PRELIMINARY STUDY	Maximum Non-irritating Concentration: intradermal: < 1% topical: 100%
MAIN STUDY	
Number of Animals	Test Group: 20 Control Group: 10
INDUCTION PHASE	Induction Concentration: intradermal: 10% topical: 25-100%
Signs of Irritation	Slight erythema in one control animal at the intradermal induction site. Slight erythema in most animals after topical induction.
CHALLENGE PHASE	
1st challenge	topical: 100%
2nd challenge	topical: 50%, 100%
Remarks - Method	No deviations from protocol noted.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*

Test Group	100%	2/20	1/20	1/20	0/20
	50%	-	-	0/20	0/20
Control Group	100%	0/10	0/10	0/10	0/10
	50%			0/10	0/10

Remarks - Results

Challenge
Positive responses were noted in 2/20 of the test group animals at 24 h after patch removal, lasting to 48 h after patch removal in 1 animal. There were no positive responses noted in Control group animals.

Rechallenge
A positive response was noted in 1/20 of the test group animals challenged with 100% of the analogue chemical, at 24 h after patch removal only.
In this study, only one (5%) positive response was noted in the test group at the 48 h challenge observation. If the one response seen at challenge was a true sensitisation response, this animal would have been expected to respond in the same way at rechallenge; no such response was noted in this animal at rechallenge. It is known that the chemical is a mild irritant and is thought to be responsible for the reactions.
No clinical signs, other than skin reactions at the test sites, were noted.

CONCLUSION: There was limited evidence of reactions (50%) indicative of skin sensitisation.

TEST FACILITY: Inveresk Research (1997a)

B.6. Repeat dose toxicity: 91- day toxicity study with in utero exposure phase

TEST SUBSTANCE: Analogue chemical 3

METHOD: In-house protocol (not specified)
Species/Strain: Rat/Sprague-Dawley
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 90 days
Dose regimen: 7 days per week
Both F0 generation males and females were dosed four weeks prior to mating. For the males, dosing continued until scheduled euthanasia (at the end of the breeding period). For the females dosing continued through gestation and through lactation day 20 or until euthanasia for females without evidence of mating and/or failure to deliver. Dams that delivered and weaned their offspring were euthanised on lactation day 21. The F1 generation was dosed from Day 21 to Day 90.

Vehicle: PEG 400
Remarks - Method: Minor deviations from protocol were noted but appeared to be unlikely to affect the outcome of the study.

RESULTS

Group	*Number and Sex of Animals*		*Dose mg/kg bw/day*	*Mortality*	
	F0	F1		F0	F1
I (control)	30/sex	20/sex	0	1 female	0
II (low dose)	30/sex	20/sex	100	5 females	1 female
III (mid dose)	30/sex	20/sex	500	7 females	1 male
IV (high dose)	30/sex	20/sex	1,000	3 females	1 male

Mortality and Time to Death
F0

One control female was euthanised (moribund during an incomplete delivery) and one low dose female died accidentally. Four low dose, seven mid dose and three high dose females were euthanised post breeding day 25 after they produced no evidence of littering. One high dose female was euthanised due to total litter loss.

F1
There were no apparent test article effects on pup viability, live litter size, mean pups per litter and male to female ratio. One male in each of the mid and high dose groups and 1 low dose female were found dead on days 94, 54 and 27, respectively.

Clinical Observations
F0
A range of clinical observations was recorded as minor and likely to be due the vehicle. The study authors reported that none were attributed to the test article.

No changes in body weights or body weight gain due to treatment was found for F0 males. For the females the only observation related to treatment was a significant decrease in body weight gain for high dose females.

The only treatment related changes to food consumption were in high dose females over days 1 – 7 and 7 – 14 of lactation. These changes were statistically significant in terms of weight(g)/animal/day but not when calculated as g/kg bw/day.

There were no test article related effects on fertility, length of gestation, pregnancy status, parturition or lactation except that one high dose female had total litter loss.

F1
A number of incidental clinical findings were noted but were reported as not related to the test article. Significant increases in body weight in high dose animals were noted in males over weeks 11 and 12 and in females over weeks 3 to 4 but were reported as not ascribed to the test article. Food consumption decreased in mid dose females over weeks 6 to 7, in the low, mid and high dose groups over weeks 12 to 13 and in the low and mid dose groups over weeks 13 to 14. These changes were not considered to be biologically significant due to a lack of dose response or an abnormally increased control value.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
F1
Clinical Chemistry: No test article related changes.
Haematology: Elevated prothrombin time in high dose males; no dose related changes in females.

Effects in Organs
F0
No macroscopic changes were observed in the F0 males and female that were test article related.

F1
No test article related macroscopic or microscopic findings were noted.

Remarks – Results
Treatment of F0 rats with analogue 3 at the designated dosage levels did not produce significant organ toxicity or effects on fertility nor did the F1 pups exhibit toxic effects during the parturition and lactation phases. In the F1 rats during the 91-day toxicity phase no organ toxicity could be attributed to the test article. A significant increase in prothrombin time in high dose males was not considered to be biologically meaningful as it did not correlate with a decrease in platelets, gross necropsy or microscopic findings. The clinical signs noted were considered to be related to the vehicle and not test-substance related.

CONCLUSION
A No Observed Effect Level (NOEL) of 1,000 mg/kg bw/d was established by study authors.

TEST FACILITY Springborn Laboratories (1994)

B.7. Repeat Dose Inhalation Toxicity – Rats

TEST SUBSTANCE Notified chemical

METHOD	OECD TG 412 Repeated Dose Inhalation Toxicity: 14-day screening study for a 28-day Study
Species/Strain	Rats/Han Wistar
Route of Administration	Inhalation – exact exposure method not reported
Exposure Information	Total exposure days: 14 days Dose regimen: 5 days per week Duration of exposure: 6 hours/day Post-exposure observation period: None
Vehicle	Not reported
Remarks – Method	Only draft pathology contributing report in summary form was provided.

RESULTS

Group	*Number and Sex of Animals*	*Dose/Concentration (mg/L) Actual*	*Mortality*
Control	3 per sex	0	0
Low Dose	3 per sex	0.544	0
Mid Dose	3 per sex	2.15	0
High Dose	3 per sex	5.64	0

Mortality and Time to Death
There were no deaths during the study.

Clinical Observations
Not reported

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
Not reported

Effects in Organs
Enlargement in tracheobronchial lymph nodes was seen in all males and two females in the high dose group and one male in the mid dose group. Minimal epithelial degeneration (loss of cilia and flattening of epithelial cells) was seen at the point of tracheal bifurcation in one female in the high dose group.

Foamy alveolar macrophage accumulation in the alveoli and interstitium and occasionally within perivascular areas occurred in both sexes in the mid and high dose groups. Inflammatory cells within alveoli, primarily composed by granulocyte neutrophils, were noted in animals in the high dose group. In the high dose group, the alveolar septa and the terminal bronchioles showed minimal to slight broncholoalveolar hyperplasia of type II pneumocytes. The cellularity of BALT (bronchus-associated lymphoid tissue) was minimally increased in one male in the mid dose group and two males in the high dose group. An increased incidence/severity of inflammatory cell infiltration within perivascular/peribronchial regions, more significant in mid than higher dose group, was observed in females and account for increased background changes. In one male in the mid dose group and one female in the low dose group this change was within background limits.

Remarks – Results
No other histological changes related to treatment were noted. It is not clear whether pathology on other organs was performed

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 2.15 mg/L in this study, based on histopathology findings at the high dose tested.

TEST FACILITY Envigo (2018)

B.8. Repeat Dose Inhalation Toxicity – Rats

TEST SUBSTANCE Notified chemical

METHOD OECD TG 412 Repeated Dose Inhalation Toxicity: 28-Day Study (2009)

Species/Strain	Rats/Han Wistar
Route of Administration	Inhalation–nose only exposure
Exposure Information	Total exposure days: 28 days Dose regimen: 5 days per week Duration of exposure (inhalation): 6 hours/day Post-exposure observation period: 2 weeks
Vehicle	Air
Physical Form	Liquid aerosol

Particle Size

	MMAD (µm)	Geometric standard deviation
Low Dose	4.1	2.64
Mid Dose	3.9	2.61
High Dose	3.0	2.90

MMAD = Mass median aerodynamic diameter

The achieved MMAD values for low and mid dose groups were above the ideal size of 1 to 3 µm stated in the test guideline. The study authors considered that it was caused by agglomeration of the droplets in the exposure chamber. However, the particle size distribution showed that a large proportion of the droplets in the generated aerosol could be deposited in the lower respiratory tract.

Remarks – Method

Bronchoalveolar lavage (BAL) was performed as part of the study. A minor protocol deviation did not affect the validity of the study: the exposure chamber temperature was recorded at 30 minute intervals rather than the 60 minute intervals.

The dose levels were based on a preliminary 14-day inhalation toxicity study (0, 0.544, 2.15 and 5.64 mg/L).

RESULTS

Group	*Number and Sex of Animals*	*Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
Control	5 per sex	0	0	0/10
Low Dose	5 per sex	0.25	0.249	0/10
Mid Dose	5 per sex	0.75	0.743	0/10
High Dose	5 per sex	2.5	2.35	0/10
Control Recovery	5 per sex	0	0	0/10
High Dose Recovery	5 per sex	2.5	2.35	0/10

Mortality and Time to Death

No unscheduled deaths were recorded.

Clinical Observations

No test substance related effects were noted for clinical signs, body weights or food consumption.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Higher mean white blood cells after treatment were observed in mid and high dose females. Higher mean neutrophil counts were shown in mid and high dose females and in high dose males. Higher mean lymphocytes, eosinophils, basophils, monocytes and large unstained cells were noted in females compared with the control, mainly at the high dose. These effects were all statistically significant compared with the control mean value (about 2-3 times higher than the control means).

These changes remained even after the 2-week recovery period, although some parameters were not statistically significant.

No treatment related effects were noted for blood chemistry. Urinalysis was not conducted.

Effects in Organs

Organ weights

At the end of the 4-week treatment period, higher mean lung and bronchi weights, absolute and relative weight, were observed for mid and high dose females (up to 1.71 times higher than the control mean), and high dose males (up to 1.46 times higher than the control mean). After 2 weeks of recovery, higher mean relative lung and bronchi weights were noted for high dose males (1.49 times higher than the control mean) and females (1.67 times higher than the control mean). The relative organ weights showed statistical significance while the absolute weights did not.

Lower mean absolute (not statistically significant) and relative (statistically significant for high dose) testes weights were recorded in mid and high dose males after treatment (12.78% and 17.5% decreases for the absolute weights compared with the control mean). After the recovery period, the testes weights of treated males were 10% lower than in controls (not statistically significant) and the study authors considered that these weights were similar.

Macroscopic investigation

After 4 weeks of treatment there was enlargement of the tracheobronchial lymph node in one male and two females in the high dose group. After 2 weeks of recovery, enlargement of the tracheobronchial and mediastinal lymph nodes was seen in all treated animals.

A small testis was seen in one high dose male after treatment, and in one control male in the recovery group.

Microscopic investigation

After 4 weeks of treatment, there were dose-related effects in the lungs and bronchi, including increased foamy alveolar macrophage aggregation, alveolar and perivascular inflammatory cell infiltrate, minimal bronchioloalveolar hyperplasia, foamy macrophage aggregation and cellularity in the bronchus-associated lymphoid tissue. There was foamy macrophage aggregation in the tracheobronchial lymph node and nasal-associated lymphoid tissue in the nasopharynx, most of which were minimal and at the high dose. No recovery in the lungs and bronchi and tracheobronchial lymph node was noted following the recovery period, with partial recovery being observed in the nasopharyngeal tissues.

There was minimal to marked tubular degeneration/atrophy of the testes in control and test males after treatment (similar incidence but higher grade as dose increased). After recovery, the effects were similar in the treated and control animals. After treatment, luminal cell debris was seen in the epididymides of high dose and control animals at similar incidence, and luminal sperm was reduced in one high dose animal. After recovery, luminal cell debris and reduced luminal sperm was also seen in one high dose animal.

Bronchoalveolar lavage

After 4 weeks of treatment, there were treatment related changes in bronchalveolar lavage, such as dose-related higher total cell counts and increased levels of some types of white blood cells, compared to controls. These effects did not fully resolved after 2-week recovery. Most of observed effects were statistically significant. There was also an increase in lactate dehydrogenase and total protein levels, in both treatment and recovery animals.

Remarks – Results

The lung findings in the high dose group were considered adverse, and effects in the tracheobronchial and mediastinal lymph nodes were considered by study authors as a secondary response. The study authors stated that these effects were possibly caused by an inflammatory reaction to an irritant effect and accumulation of the test substance in the lungs, with changes in the local and draining lymphoid tissues. The observations in the bronchoalveolar lavage fluid and haematology were considered consistent with the inhalation of poorly soluble particulate matter, being correlated with the histopathological results.

The study authors considered that minimal to marked tubular degeneration/atrophy of the testes in control and test males was potentially caused by the body temperature of animals held in restraining tubes rising for an extended period, resulting in thermal injury to the testes, due to the restraint and duration of exposure. They stated that “tubular degeneration/atrophy was associated with luminal cell debris and reduced sperm in the epididymides and correlated with the macroscopic finding of small testes observed in one male and lower than control mean body weight adjusted testes weights for males exposed to 2.35 mg/L or 0.743 mg/L.” The cause of these effects is unclear.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) was established as 0.743 mg/L in this study, based on observed higher mean lung and bronchi weights in animals at the high dose, that did not resolve after the recovery period.

TEST FACILITY Covance (2019)

B.9. Genotoxicity – bacteria

TEST SUBSTANCE Analogue chemical 2

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100; *Escherichia coli WP2uvr*A.
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction.
Concentration Range in Main Test	a) With metabolic activation: 0, 156.25, 312.5, 625, 1,250, 2,500, 5,000 µg/plate b) Without metabolic activation: 0, 156.25, 312.5, 625, 1,250, 2,500, 5,000 µg/plate
Vehicle	Sorbitan stearate and polysorbate 60.
Remarks - Method	No deviations from protocol noted.

RESULTS

Remarks - Results	No evidence of cytotoxicity was noted at any concentrations. Some precipitates were noted at 5,000 µg/plate. No toxicity was noted in a preliminary test on the basis of a consistent number of spontaneous mutant colonies in TA100 up to 5,000 µg/plate. Negative controls were within acceptable limits and positive controls demonstrated the sensitivity of the test. There were no sign of increase in revertant colonies in any test strains, with or without metabolic activation.

CONCLUSION The analogue chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY Inveresk Research (1997b)

B.10. Genotoxicity – *in vitro*

TEST SUBSTANCE Analogue chemical 5

METHOD OECD TG 473 *In vitro* Mammalian Chromosome Aberration Test.
EC Directive 92/69/EC B.10 Mutagenicity - *In vitro* Mammalian Chromosome Aberration Test.

Cell Type/Cell Line	Human lymphocytes
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction
Vehicle	Ethanol
Remarks - Method	No deviations from protocol noted.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	39, 78.1, 156.25, 312.5, 625, 1,250*, 2,500*, 5,000*	4 hr	20 hr
Test 2	625, 1,250*, 2,500*, 5,000**	4 hr	20, 44 hr
Present			
Test 1	39, 78.1, 156.25, 312.5, 625, 1,250*, 2,500*, 5,000*	4 hr	20 hr
Test 2	625, 1,250*, 2,500*, 5,000**	4 hr	20, 44 hr

*Cultures selected for metaphase analysis. ** Cultures selected for metaphase analysis at both harvest times

RESULTS

Remarks - Results	The results of the negative controls were within historical limits and the positive controls demonstrated the sensitivity of the test. In test 2 one of the positive control cultures was negative due to excessive toxicity but this did not negate the conclusions of the experiment.

CONCLUSION The analogue chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY Safepharm Laboratories Limited (1995a)

B.11. Genotoxicity – *in vitro*

TEST SUBSTANCE Analogue chemical 5

METHOD OECD TG 476 *In vitro* Mammalian Cell Gene Mutation Test.
EC Directive 2000/32/EC B.17 Mutagenicity - *In vitro* Mammalian Cell Gene Mutation Test.

Cell Type/Cell Line	Chinese Hamster Ovary cells
Metabolic Activation System	Aroclor 1254 induced rat liver S9 fraction
Vehicle	Ethanol
Remarks - Method	Two protocol deviations were described, that were considered by the study author to have no effect on the validity of the test results. The activated portion of test 1 was lost due to contamination and was repeated. In the confirmatory assay the number of cells seeded in the solvent control and all the test substance-treated cultures, except for one replicate at the highest concentration of 5,000 µg/mL, was less than 2×10^5 cells/plate.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	313, 625, 1,250, 2,500, 5,000	4 hrs	8 days	7 days
Test 2	313, 625, 1,250, 2,500, 5,000	"	"	"
Present				
Test 1	313, 625, 1,250, 2,500, 5,000	"	"	"
Test 2	313, 625, 1,250, 2,500, 5,000	"	"	"

RESULTS

Remarks - Results	The first trial exhibited no differences in relative cloning efficiencies (RCEs) without metabolic activation. Contamination of cells conducted with metabolic activation invalidated the results and therefore this portion of the study was re-initiated. An increase in the number of mutants at 625 µg/mL was observed as compared to the control with metabolic activation. During the confirmatory trial, this increase in mutants was not observed at the same dose level, but at 2500 µg/mL. As there was no dose relationship and the number of mutants fell within the historical control number for the laboratory, the test article utilised in the study was concluded to be non mutagenic.

CONCLUSION The analogue chemical was not clastogenic to Chinese hamster ovary cells treated *in vitro* under the conditions of the test.

TEST FACILITY Sitek Research Laboratories (2000)

B.12. Genotoxicity – *in vivo*

TEST SUBSTANCE	Analogue chemical 6
METHOD	OECD TG 474 Mammalian Erythrocyte Micronucleus Test. EC Directive 84/449/EC B.12 Mutagenicity - Mammalian Erythrocyte Micronucleus Test.
Species/Strain	Mouse/CD-1
Route of Administration	Oral – gavage
Vehicle	Arachis oil
Remarks - Method	No deviations from protocol noted.

Group	*Number and Sex of Animals for each sacrifice time*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	5/sex	0	24, 48, 72 hrs
II (low dose)	5/sex	1,250	24, 48, 72 hrs
III (mid dose)	5/sex	2,500	24, 48, 72 hrs
IV (high dose)	5/sex	5,000	24, 48, 72 hrs
V (positive control, CP)	5/sex	50	24 hrs

CP=cyclophosphamide.

RESULTS	
Doses Producing Toxicity	No clinical signs noted.
Genotoxic Effects	As there was no indication of toxicity at any dose level, it is not possible to confirm that the test substance reached the bone marrow.
Remarks - Results	There was no statistically significant increase in micronucleated PCEs in any test group when compared to vehicle control. There were no differences in the PCE/NCE ratio in any dose group as compared to the vehicle control. Positive control group showed a marked increase in the incidence of micronucleated polychromatic erythrocytes, confirming the test system.
CONCLUSION	The analogue chemical was not clastogenic under the conditions of this *in vivo* mouse micronucleus test.
TEST FACILITY	Safepharm Laboratories Limited (1995b)

APPENDIX C: ENVIRONMENTAL FATE AND ECOTOXICOLOGICAL INVESTIGATIONS

C.1. Environmental Fate

C.1.1. Ready Biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test
Inoculum	Activated sludge from a domestic STP
Exposure Period	29 days
Auxiliary Solvent	None
Analytical Monitoring	CO_2 by titration method
Remarks – Method	No major deviations from the test guidelines were reported. The test substance was directly added to the test medium and ultra-sonicated for 15 minutes before testing. A toxicity control was run.

RESULTS

Test Substance		*Sodium benzoate*	
Day	*% Degradation*	*Day*	*% Degradation*
2	3	2	52
14	24	14	83
21	34	21	69
29	54	29	84

Remarks – Results	All validity criteria for the test were satisfied. The toxicity control exceeded 25% biodegradation after 14 days showing that toxicity was not a factor inhibiting the biodegradability of the test substance. The test item did not satisfy the 10-day window criterion and therefore cannot be considered readily biodegradable.
CONCLUSION	The test substance is not readily biodegradable, but shows inherent biodegradability.
TEST FACILITY	Envigo (2017a)

C.2. Ecotoxicological Investigations

C.2.1. Acute Toxicity to Fish

TEST SUBSTANCE	Analogue Chemical 1
METHOD	OECD TG 203 Fish, Acute Toxicity Test - Static
Species	*Brachydanio rerio*
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	IR
Remarks – Method	A limit test was run based on screening test results. No major deviations from the test guidelines were reported. A test loading rate of 10 g/L was prepared and shaken for 24 hours. The suspension was then filtered (size not specified) and the Water Accommodated Fraction (WAF) was used for testing.

RESULTS

Nominal Loading (mg /L WAF)	*Number of Fish*	*Mortality after 96 h*
Control	7	0

10,000	7	0

LL50 > 10,000 mg/L (WAF) (nominal concentration) at 96 hours
Remarks – Results All validity criteria for the test were satisfied. The dissolved oxygen (DO) concentration was 8.4 mg/L at 25 °C (100% saturation; USGS, 2011) during the test. The IR measurement results indicated the test substance concentration was stable during the study.

CONCLUSION The test substance is not harmful to fish up to its water solubility limit.

TEST FACILITY GmbH (1997a)

C.2.2. Acute Toxicity to Aquatic Invertebrates

TEST SUBSTANCE Analogue chemical 6

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – Static
Species *Daphnia magna*
Exposure Period 48 hours
Auxiliary Solvent None
Water Hardness 270 mg $CaCO_3$/L
Analytical Monitoring TOC
Remarks – Method No major deviations from the test guidelines were reported. A limit test was run based on a preliminary range-finding study. A loading rate of 1,000 mg/L test substance was prepared and stirred for 20 hours. The test solution was allowed to stand for 4 hours before the WAF was removed for testing. Water samples were taken for total organic carbon (TOC) analysis at 0 and 48 hours.

RESULTS

Nominal Loading Rate (mg/L WAF)	*Number of D. magna*	*Number Immobilised (48 h)*
Control	20	0
1,000	40	0

EL50 > 1,000 mg/L (WAF) at 48 hours
Remarks – Results All validity criteria for the test were satisfied. DO concentration was ≥ 7.9 mg/L at 21 °C (≥ 89% air saturation at 21 °C; USGS, 2011) during the test. TOC results were around the limit of detection so the stability of the test substance could not be confirmed.

CONCLUSION The test substance is not harmful to aquatic invertebrates up to its water solubility limit.

TEST FACILITY Safepharm (1995c)

C.2.3. Chronic Toxicity to Aquatic Invertebrates (Study 1)

TEST SUBSTANCE Analogue Chemical 1

METHOD OECD TG 211 *Daphnia magna* Reproduction Test – Semi static
Species *Daphnia magna*
Exposure Period 21 days
Auxiliary Solvent None
Water Hardness 150 - 180 mg $CaCO_3$/L
Analytical Monitoring None
Remarks – Method No major deviations from the test guidelines were reported. A loading rate of 125 mg/L was prepared daily at each renewal by adding the test

substance directly to the test water. The solution was stirred for 48 hours and allowed to settle for 1 hour. The WAF was removed from an outlet port located 2 cm from the bottom of the jar for testing.

RESULTS

Test substance loading (mg/L WAF)	Survival (% parental generation)	Mean no. offspring released by surviving *Daphnia*
Control	100	174
125	80	180

21 d NOEL	125 mg/L (WAF)
21 d EL50	> 125 mg/L (WAF)
Remarks – Results	All validity criteria for the test were satisfied. DO concentration was ≥ 7.5 mg/L at 20 °C (≥ 83% air saturation; USGS, 2011) during the test. The temperature slightly exceed the recommended maximum of 22 °C (by 2 °C) on a single day, however this is not likely to have adversely affected the test organisms. The carbon content of algal food was found to be 0.36 mg C per daphnid per day which was outside the recommended range of 0.1 – 0.2 mg C per daphnid per day but this was not considered detrimental to the health of the test organisms. Survival among daphnids exposed to the WAF (80%) was not statistically different from the control (100%).
CONCLUSION	The test substance had no adverse effects on the survival, reproduction and growth of *Daphnia magna*
TEST FACILITY	Springborn (2003a)

C.2.4. Chronic Toxicity to Aquatic Invertebrates (Study 2)

TEST SUBSTANCE	Analogue Chemical 4
METHOD	OECD TG 211 *Daphnia magna* Reproduction Test - Semi-static
Species	*Daphnia magna*
Exposure Period	21 days
Auxiliary Solvent	None
Water Hardness	148 - 172 mg $CaCO_3$/L
Analytical Monitoring	None
Remarks – Method	No major deviations from the test guidelines were reported. A loading rate of 125 mg/L was prepared daily at each renewal by adding the test substance directly to the test water. The solution was stirred for 48 hours and allowed to settle for 1 hour. The WAF was removed from an outlet port located 2 cm from the bottom of the jar for testing.

RESULTS

Test substance loading (mg/L WAF)	Survival (% parental generation)	Mean no. offspring released by surviving *Daphnia*
Control	100	174
125	80	154

21 d NOEL	125 mg/L (WAF)
21 d EL50	> 125 mg/L (WAF)
Remarks – Results	All validity criteria for the test were satisfied. DO concentration was ≥ 7.4 mg/L at 20°C (≥ 81% air saturation; USGS, 2011) during the test. The temperature slightly exceed the recommended maximum of 22 °C (by 2 °C) on a single day, however this is not likely to have adversely affected the test organisms. The carbon content of algal food was found to be 0.36

	mg C per daphnid per day which was outside the recommended range of 0.1 – 0.2 mg C per daphnid per day but this was not considered detrimental to the health of the test organisms. Survival among daphnids exposed to the WAF (80%) was not statistically different from the control (100%).
CONCLUSION	The test substance had no adverse effects on the survival, reproduction and growth of *Daphnia magna*
TEST FACILITY	Springborn (2003b)

C.2.5. Algal Growth Inhibition Test

TEST SUBSTANCE	Analogue Chemical 6
METHOD	OECD TG 201 Alga, Growth Inhibition Test
Species	*Selenastrum capricornutum*
Exposure Period	96 hours
Nominal Loading	1,000 mg/L (WAF)
Auxiliary Solvent	None
Water Hardness	Not reported
Analytical Monitoring	TOC
Remarks – Method	A limit test was run based on a preliminary range-finding test. No major deviations from the test guidelines were reported. Test solution was stirred for 20 hours, allowed to stand for 4 hours before the WAF was removed and then diluted with algal suspension to achieve a test loading of 1,000 mg/L WAF for testing. Water samples were taken for TOC analysis at 0 and 96 hours.

RESULTS

Biomass		*Growth*	
E_bL 50 (mg/L at 96 h, WAF)	*NOEL (mg/L, WAF)*	*E_rL 50 (mg/L at 96 h, WAF)*	*NOEL (mg/L, WAF)*
1,000	≥ 1,000	1,000	≥ 1,000

Remarks – Results	The validity criteria for the test were satisfied. The mean cell density in the control increased 47 times after 72 hours and 124 times after 96 hours. TOC results were around the limit of detection so the stability of the test substance could not be confirmed.
CONCLUSION	The test substance is not harmful to algae up to its water solubility limit
TEST FACILITY	Safepharm (1995d)

C.2.6. Inhibition of Microbial Activity (Study 1)

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test
Inoculum	Activated sludge from a domestic STP
Exposure Period	3 hours
Nominal Concentrations	10, 100 and 1,000 mg/L
Remarks – Method	No major deviations from the test guidelines were reported. The test substance was added to the test medium and stirred for 24 hours before testing. A reference test with 3,5-dichlorophenol was run.
RESULTS	
3 h IC50	> 1,000 mg/L
3 h NOEC	≥ 1,000 mg/L

Remarks – Results	The validity criteria for the test were satisfied. DO concentration was ≥ 63% saturation during the test. The reference item gave a 3 h IC50 of 6.9 mg/L, which was within the historical range.
CONCLUSION	The test substance does not inhibit microbial respiration
TEST FACILITY	Envigo (2017b)

C.2.7. Inhibition of Microbial Activity (Study 2)

TEST SUBSTANCE	Analogue Chemical 1
METHOD	DIN 38412, Part 8, 1991
Inoculum	*Pseudomonas putida* (laboratory stock culture)
Exposure Period	16 ± 1 hours
Nominal Concentrations	0.1, 1.0 and 10 g/L
Remarks – Method	*Pseudomonas putida* were incubated with different concentrations of the test substance for 16 ± 1 hours in a defined test medium. The retardation in the proliferation of the bacteria compared to a control solution without test substance represented the extent of the toxic effect on the test system.
RESULTS	
IC50	> 10 g/L
NOEC	≥ 10 g/L
Remarks – Results	Under the conditions of this study, no toxic effect could be observed.
CONCLUSION	The test substance does not inhibit microbial respiration.
TEST FACILITY	GmbH (1997b)

C.2.8. Sediment Reworker Toxicity Test

TEST SUBSTANCE	Durasyn 156
METHOD	PARCOM Protocol 1995 Pt A: Protocols on Methods for the Testing of Chemicals used in the Offshore Oil Industry – Static.
Species	*Corophium volutator*
Exposure Period	10 days
Nominal Concentrations	480, 1,000, 2,200, 4,800 and 10,000 mg/kg dry sediment
Remarks – Method	No major deviations from the test guidelines were reported. Eighty test organisms were each exposed to the sediment spiked with the test substance at 5 different concentrations and negative controls. All treatments were prepared and dispensed 12 to 24 hours prior to initiating the test. Treatments were kept in a dedicated environmental chamber within 14 hours light and 10 hours dark at 20 ± 1 °C with aeration. After 10 days, the final survival data were recorded. Temperature, DO, pH and salinity were measured at 24 hours intervals in each treatment.
RESULTS	
10 d LC50	> 10,000 mg/kg dry sediment
10 d NOEL	≥ 10,000 mg/kg dry sediment
Remarks – Results	Under the conditions of this study, no toxic effect could be observed.
CONCLUSION	The test substance is not harmful to the sediment worker *Corophium volutator*
TEST FACILITY	Environmental Enterprises (2015)

BIBLIOGRAPHY

Aither (2013) Third Independent Review of the Product Stewardship (Oil) Act 2000. Canberra, Australia.

Bomhard and Gelbke (2013) Hypoxaemia affects male reproduction: a case study of how to differentiate between primary and secondary hypoxic testicular toxicity due to chemical exposure. Bomhard EM, Gelbke HP. Arch Toxicol. 2013 Jul;87(7):1201-18.

Covance (2019) Notified Chemical: Toxicity Study by Inhalation Administration to Han Wistar Rats for 4 weeks Followed by a 2 Week Recovery Period (Study No. BM52ST, November, 2019). Cambridgeshire, UK, Covance CRS Limited (Unpublished report submitted by the notifier).

Bio-Research Laboratories Ltd (1994) Analogue Chemical 1: An evaluation of the acute toxicity of an inhaled nebulized aerosol formulation in the rat (safety test). Final report May 1994 Study No. 93-131 for Chevron Research and Technology Co. Richmond, CA, USA. Bio-Research Laboratories Ltd, Senneville, Montreal, Quebec 3R3, Canada (unpublished report submitted by notifier).

Envigo (2017a) Notified Chemical: Assessment of Ready Biodegradability; CO_2 Evolution Test (Study no. LX26ND, January, 2017). Derbyshire, UK, Envigo Research Limited (Unpublished report submitted by the notifier).

Envigo (2017b) Notified Chemical: Toxicity to Activated Sludge in a Respiration Inhibition Test (Study no. LM33LC, January, 2017). Derbyshire, UK, Envigo Research Limited (Unpublished report submitted by the notifier).

Envigo (2018) Notified Chemical: Pathology Contributing Report for a 14-day Inhalation Toxicity Study (Study no. HT46DY, November 2018). Derbyshire, UK, Envigo Research Limited (Unpublished report submitted by the notifier).

Environmental Enterprises (2015) Durasyn 156: Corophium volutator Acute, Static 10 – Day Sediment Reworker Test (EE USA Lab no. L-435-15, July, 2015). Louissiana, USA, Environmental Enterprises USA, INC (Unpublished report submitted by the notifier).

GmbH (1997a) Study on the Acute Toxicity towards Fish of Analogue Chemical 1 (Study no. IF-96/26782-00, February, 1997). Taunusstein, Germany, Chemical and Biological Laboratory GmbH (Unpublished report submitted by the notifier).

GmbH (1997b) Investigation of chronic bacterial toxicity of Analogue Chemical 1 (Study no. IF-96/26783-00, February, 1997). Taunusstein, Germany, Chemical and Biological Laboratory GmbH (Unpublished report submitted by the notifier).

Hill Top Biolabs, Inc. (1988a) Analogue Chemical 1: Acute Oral Toxicity in the rat. Final report April 1988 Study No. 88-3086-21 (A) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988b) Analogue Chemical 2: Acute Oral Toxicity in the rat. Final report April 1988 Study No. 88-3087-21 (A) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988c) Analogue Chemical 3: Acute Oral Toxicity in the rat. Final report April 1988 Study No. 88-3088-21 (A) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988d) Analogue Chemical 4: Acute Oral Toxicity in the rat. Final report April 1988 Study No. 88-3089-21 (A) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988e) Analogue Chemical 1: Primary Skin Irritation in Rabbits. Final report April 1988 Study No. 88-3086-21 (B) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988f) Analogue Chemical 2: Primary Skin Irritation in Rabbits. Final report April 1988 Study No. 88-3087-21 (B) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988g) Analogue Chemical 3: Primary Skin Irritation in Rabbits. Final report April 1988 Study No. 88-3088-21 (B) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988h) Analogue Chemical 4: Primary Skin Irritation in Rabbits. Final report April 1988 Study No. 88-3089-21 (B) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988i) Analogue Chemical 1: Primary Eye Irritation in Rabbits. Final report April 1988 Study No. 88-3086-21 (C) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988j) Analogue Chemical 2: Primary Eye Irritation in Rabbits. Final report April 1988 Study No. 88-3087-21 (C) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988k) Analogue Chemical 3: Primary Eye Irritation in Rabbits. Final report April 1988 Study No. 88-3088-21 (C) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

Hill Top Biolabs, Inc. (1988l) Analogue Chemical 4: Primary Eye Irritation in Rabbits. Final report April 1988 Study No. 88-3089-21 (C) for Quantum Chemical Corporation, Emery Division, Cincinnati, OH, USA. Hill Top Biolabs, Inc. Cincinnati, OH, USA (unpublished report submitted by notifier).

INEOS Oligomers (2016a) General Physical Chemical Properties for Notified Chemical (July, 2016). La Porte, Texas, INEOS Oligomers USA LLC (Unpublished report submitted by the notifier).

INEOS Oligomers (2016b) Boiling Range of Notified Chemical (July, 2016). La Porte, Texas, INEOS Oligomers USA LLC (Unpublished report submitted by the notifier).

INEOS Oligomers (2016c) Vapour Pressure of Notified Chemical (2016). La Porte, Texas, INEOS Oligomers USA LLC (Unpublished report submitted by the notifier).

INEOS Oligomers (2016d) Auto-ignition Temperature of Notified Chemical (July, 2016). La Porte, Texas, INEOS Oligomers USA LLC (Unpublished report submitted by the notifier).

Inveresk Research (1997a) Analogue Chemical 3: Magnusson-Kligman Maximisation Test in Guinea Pigs. Final report April 1997 Project No. 564969 for Amoco Corporation, Chicago, IL, USA. Inveresk Research, Tranent, Scotland (unpublished report submitted by notifier).

Inveresk Research (1997b) Analogue chemical 2: Testing for mutagenic activity. Final report March 1997 Project No. 759518 for Amoco Corporation, Chicago, IL, USA. Inveresk Research, Tranent, Scotland (unpublished report submitted by notifier).

ISI (2016) Notified Chemical: Water Solubility (Job No. 2016-18C, June, 2016). Ontario, Canada, Investigative Science Incorporated (Unpublished report submitted by the notifier).

Pharmakon Research International Inc. (1992a) Analogue Chemical 1: Magnusson-Kligman Maximisation Test in Guinea Pigs. Final report September 1992 Study No. PH 423-ET-002-92 for Ethyl Corporation, Baton Rouge, LA, USA. Pharmakon Research International Inc., Waverley, PA, USA (unpublished report submitted by notifier).

Pharmakon Research International Inc. (1992b) Analogue Chemical 2: Magnusson-Kligman Maximisation Test in Guinea Pigs. Final report September 1992 Study No. PH 423-ET-003-92 for Ethyl Corporation, Baton Rouge, LA, USA. Pharmakon Research International Inc., Waverley, PA, USA (unpublished report submitted by notifier).

Product Safety Laboratories (2006) Durasyn 125: Acute Dermal Toxicity in the rat. Final report March 2006 Study No. 18707 for Innovene, Lisle, NJ, USA. Product Safety Laboratories, East Brunswick, NJ, USA (unpublished report submitted by notifier).

PTRL West (2006) Partition Coefficient (*n*-Octanol/Water) Estimation by Liquid Chromatography of Five Polyalphaolefins (Project No. 1456 W, January, 2016). California, US, PTRL West Inc (Unpublished report submitted by the notifier).

Safepharm Laboratories Limited (1995a) Analogue Chemical 5: Chromosome aberration test in human lymphocytes *in vitro*, Final report June 1995, Project No. 703/036 for Chevron Research & Technology Company, Toxicology and Health Risk Assessment, Richmond, CA, USA. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm Laboratories Limited (1995b) Analogue Chemical 6: Micronucleus test in mouse, Final report June 1995, Project No. 703/039 for Chevron Research & Technology Company, Toxicology and Health Risk

Assessment, Richmond, CA, USA. Safepharm Laboratories Limited, Derby, UK (unpublished report submitted by notifier).

Safepharm (1995c) Analogue Chemical 6: Acute Toxicity to *Daphnia magna* (Project no. 784/012, May, 1995). Derby, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Safepharm (1995d) Analogue Chemical 6: Algal Inhibition Test (Project no. 784/013, May, 1995). Derby, UK, Safepharm Laboratories Limited (Unpublished report submitted by the notifier).

Sitek Research Laboratories (2000) Analogue Chemical 5: test for chemical induction of gene mutation at the HGPRT locus in cultured Chinese hamster ovary (CHO) cells with and without metabolic activation with a confirmatory assay, Final report April 2000, Study No. 0641-2510 for Chevron Research & Technology Co., Richmond, CA, USA. Sitek Research Laboratories, Rockville, MD, USA (unpublished report submitted by notifier).

Springborn Laboratories, Inc. (1994) Analogue Chemical 3: An oral (gavage) 90-day toxicity study in rats with an in utero exposure phase. Final Report September 1994 Study No. 3196.27 for Ethyl Corporation, Baton Rouge, LA, USA. Springborn Laboratories, Inc. Life Sciences Division, Spencerville, OH, USA (unpublished report submitted by notifier).

Springborn (2003a) Analogue Chemical 1 – Full Life – Cycle Toxicity Test with Water Fleas, *Daphnia magna,* under Static-renewal Conditions (Study no. 384.6117, February, 2003). Massachusetts, US, Springborn Smithers Laboratories (Unpublished report submitted by the notifier).

Springborn (2003b) Analogue Chemical 4 – Full Life – Cycle Toxicity Test with Water Fleas, *Daphnia magna,* under Static-renewal Conditions (Study no. 384.6118, February, 2003). Massachusetts, US, Springborn Smithers Laboratories (Unpublished report submitted by the notifier).

SWA (2012) Code of Practice: Managing Risks of Hazardous Chemicals in the Workplace, Safe Work Australia, https://www.safeworkaustralia.gov.au/doc/model-code-practice-managing-risks-hazardous-chemicals-workplace.

United Nations (2009) Globally Harmonised System of Classification and Labelling of Chemicals (GHS), 3rd revised edition. United Nations Economic Commission for Europe (UN/ECE), http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

USGS (2011) U.S. Geological Survey, Change to solubility equations for oxygen in water: Office of Water Quality Technical Memorandum 2011.03, accessed https://water.usgs.gov/software/DOTABLES/ v 3.5, 8 January 2018