Existing Chemical
Secondary Notification Assessment
NA/889S

Australian Government
Department of Health and Ageing
NICNAS

Chemical in OLOA 270

May 2008

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Preface

This assessment was carried out under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This Scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act), which came into operation on 17 July 1990.

The principal aim of NICNAS is to aid in the protection of people at work, the public and the environment from the harmful effects of industrial chemicals.

NICNAS assessments are conducted in conjunction with the Department of the Environment and Water Resources, which carries out the environmental assessment.

NICNAS has two major programs: the assessment of the health and environmental effects of new industrial chemicals prior to importation or manufacture; and the other focussing on the assessment of chemicals already in use in Australia in response to specific concerns about their health and/or environmental effects.

Chemicals that have been assessed as new or existing chemicals may require a reassessment of the risk of the chemical under the secondary notification provisions of the Act.

This assessment report has been prepared by the Director of NICNAS, in accordance with the secondary notification provisions of the Act. Under the Act manufacturers/importers of the chemical are required to notify the Director of new information and apply for assessment. New information can include an increase in quantity imported, the commencement of Australian manufacture, increased environmental exposure, and/or additional information becoming available on hazards, as is the case of OLOA 270.

Applicants for assessment are given a draft copy of the report and 28 days to advise the Director of any errors. Following the correction of any errors, the Director provides applicants and other interested parties with a copy of the draft assessment report for consideration. This is a period of public comment lasting for 28 days during which requests for variation of the report may be made. Where variations are requested the Director's decision concerning each request is made available to each respondent and to other interested parties (for a further period of 28 days). Notices in relation to public comment and decisions made appear in the *Commonwealth Chemical Gazette*.

In accordance with the Act, publication of this report revokes the declaration of this chemical for secondary assessment, therefore manufacturers and importers wishing to introduce this chemical in the future need not apply for assessment. However, manufacturers and importers need to be aware of their duty to provide any new information to NICNAS, as required under Section 64 of the Act.

For the purposes of Section 78(1) of the Act, copies of assessment reports for new and existing chemical assessments are freely available from the web (www.nicnas.gov.au).

Copies of this and other assessment reports are available on the NICNAS website. Hardcopies are available from NICNAS from the following address:

GPO Box 58, Sydney, NSW 2001, AUSTRALIA

Tel: +61 (02) 8577 8800

Freecall: 1800 638 528

Fax: +61 (02) 8577 8888

Other information about NICNAS (also available on request) includes:

- NICNAS Service Charter;
- Information sheets on NICNAS Registration;
- Information sheets on Priority Existing Chemical and New Chemicals assessment programs;
- Safety information sheets on chemicals that have been assessed as Priority Existing Chemicals;
- Details for the NICNAS Handbook for Notifiers; and
- Details for the *Commonwealth Chemical Gazette*.

More information on NICNAS can be found at the NICNAS web site:

http://www.nicnas.gov.au

Other information on the management of workplace chemicals can be found at the following web site:

http://www.ascc.gov.au

Overview and Recommendations

Overview

Background

The chemical in OLOA 270 (referred to in this report as OLOA 270) was assessed as NA/889 under the NICNAS New Chemicals program in 2001 in the standard notification category. As a result of a new study on reproductive toxicity of OLOA 270 becoming available, OLOA 270 has now been reassessed under the secondary notification provisions of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) relevant to existing chemicals, as more than five years have elapsed since the original assessment.

OLOA 270 is a dark brown viscous liquid, stable under normal conditions. It decomposes at high temperatures. The water solubility for an analogue to OLOA 270 was determined, via the shake flask method, to be 40.9 mg/L (40.9 ppm). The n-octanol/water partition coefficient for OLOA 270 was determined to be greater than 6. The high log P_{OW}, high hydrocarbon content and strong dispersant nature of OLOA 270 indicated that the material would have a large K_{OC} and adsorb strongly to the organic component of soils and sediments.

Uses

OLOA 270 is not manufactured in Australia, but is imported as part of additive packages with other lubricating oil components. Four different additive packages, containing 1%-60% OLOA 270 are imported into Australia. The packages are formulated into final lubricating oil products in Australia.

The additive packages are imported in 250 L steel drums. Import volumes of the additives have decreased over the past four years to 10-100 tonnes/year. The primary use of OLOA 270 is as an ingredient in lubricant oils used by the marine diesel engine lubricant market where its final concentration is 0.5%-15%. A small amount (<0.5%) is also used for high performance hydraulic oils for closed hydraulic systems in large construction equipment such as earth movers, road graders and power scoop shovels. Typically the hydraulic oils contain 0.1%-0.2% OLOA 270 component.

Exposure

The assessment of OLOA 270 as a new chemical in 2001 had indicated that skin and eye contact with up to 80% OLOA 270 may occur during loading and unloading storage tanks, road tankers and drums. However, new data received from the applicant indicates that a maximum of 60% of OLOA 270 is present in the additive packages. Exposure is also possible during sampling and analysis activities.

Blending of additive packages containing OLOA 270 into finished lubricant oil occurs on-line and is computer controlled, thereby excluding the potential for occupational exposure. Drum filling is automated but workers are required to connect 4-inch lines from the blending tanks to the drums and may get exposed to very small amounts of the chemical. Ship mechanics are exposed to the finished lubricant during their normal work. Transferring and using the finished

oils may lead to exposure to up to 15% OLOA 270 in the blended oil. It was reported that workers at marine terminals, lubricant blending plants and ship workers wear coveralls, gloves and eye protection. The risk to these workers is therefore expected to be low, however, there is a high concern for skin sensitisation in mechanics working on marine vessels.

OLOA 270 is not directly marketed to the public, but used as a lubricant additive, primarily for use in marine vessels. Hence direct contact with OLOA 270 by members of the public is unlikely.

Health effects

No toxicology data were provided for the chemical substance during assessment as a new chemical. All testing was conducted using the closely related structural analogue. The results obtained for the structural analogue were considered to be equivalent to those which would be obtained with OLOA 270. In this report, a new study on reproductive toxicology conducted on OLOA 270 is assessed.

The assessment conducted in 2001 indicated that OLOA 270 has very low acute oral toxicity in rats (LD50 >5000 mg/kg bw). It is not a skin irritant but a slight eye irritant and a skin sensitiser. In a 28-day repeated-dose gavage study in rats, the NOAEL was identified as 500 mg/kg bw/day based on liver toxicity with 1000 mg/kg/day in male rats. Based principally on general signs of toxicity as well as adrenal toxicity in a 90-day repeat-dose toxicity study, a NOAEL of 100 mg/kg/day was identified. No signs of developmental toxicity were observed in rats treated with up to 1000 mg/kg/day OLOA 270 in peanut oil from gestation days 6-15. Results from a reverse mutation assay in bacterial cells, a chromosome aberration assay in mammalian cells and a micronucleus study in mice were negative, indicating that OLOA 270 is not a genotoxicant.

The current data on reproductive effects provided evidence to suggest there may be an effect on fertility at 1000 mg/kg bw/day: a significant decrease in pregnancy index seen for all mating phases, along with a reduction in litter size for the F0a and F1 mating phases that was dose related and statistically significant for the latter. The NOAEL for female and male parental animals, and reproductive toxicity is 1000, 500 and 250 mg/kg bw/day respectively.

OLOA 270 is classified as a hazardous chemical under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004). OLOA 270 is also classified as a hazardous substance under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS), and would require appropriate labelling when this system is adopted in Australia. OLOA 270 is not listed in the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (FORS, 1998).

Environmental effects

Based on the blending methods and use pattern environmental exposure is expected to be minimal. Release to the environment is expected to occur only in the unlikely event of an accident during transport or an accidental leak. Any spills incurred in the blending operations are contained within concrete bunds and either reclaimed or sent to on-site waste-water treatment facilities. Aboard ship, the oil is pumped through hard piping to the engine. Containers holding residual OLOA 270 are steam-cleaned with the waste-water entering a treatment facility at the receiving terminal.

Eco-toxicological data for OLOA 270 were obtained from information provided at the earlier submission (NA/889). OLOA 270 was not expected to be toxic to fish or daphnia up to the limit of its water solubility, although some toxicity to algae was expected below this limit. The high partition coefficient and low biodegradability of OLOA 270 had indicated the potential for bioaccumulation if spilt into waterways. However, as very little of the chemical was expected to reach the aquatic compartment the risk of the chemical causing adverse effects to aquatic organisms was considered low.

Risk

Except in the event of a spill, occupational risk during transport of the imported additive package is expected to be low. Use of automated transfer systems and PPE by workers during blending is expected to result in low risk (based on information supplied to NICNAS). Occupational risk from use of products containing OLOA 270 in marine vessels is moderate due to the sensitisation effects of the chemical, however based on information supplied to NICNAS, workers in these industries generally use PPE, though it should be noted that PPE alone is not sufficient to provide protection against hazardous substances. Engineering controls to minimise exposure to lubricating fluids are unlikely to be in place in all repair workshops. Workers involved in the marine vessel repair industry are unlikely to use PPE and are expected to be repeatedly exposed to the chemical. These workers are at risk of skin sensitisation.

The public is not likely to come in contact with products containing OLOA 270 as they are not sold to the general public.

On the basis of data previously supplied, OLOA 270 is considered non-toxic to aquatic organisms up to the limit of its solubility. The chemical is unlikely to pose an environmental risk to aquatic organisms when used in marine vessels or in closed hydraulic systems in large construction equipment.

Recommendations

This section provides the recommendations arising from the secondary notification assessment of OLOA 270. Recommendations are directed principally at regulatory bodies and importers and formulators of OLOA 270 products. Implicit in these recommendations is that best practice is implemented to minimise occupational and public exposure and environmental impact.

Recommendations to National Bodies

Australian Safety and Compensation Council (ASCC)

OLOA 270 is not currently listed in the ASCC's *Hazardous Substances Information System (HSIS)*. Based on the toxic effects of OLOA 270, it is recommended that OLOA 270 be listed in the HSIS.

In accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), OLOA 270 is classified as:

R62 Possible risk of impaired fertility (Toxic to reproduction, Category 3)

R43 May cause sensitisation by skin contact

The concentration cut-offs for mixtures containing OLOA 270 are:

Risk Phrases*	Concentration Cut-off
Xi, R43	≥1%Concentration<5%
Xn, R62; R43	Concentration≥5%

*Xn=Harmful; Xi=Irritant

The following safety phrases are also recommended:

S24 **Avoid contact with skin**

S36/37 **Wear suitable protective clothing and gloves**

This classification should be reflected in the ASCC's HSIS and should be adopted by industry on publication of this report.

Recommendations to importers and States and Territories

Hazard communication – Material Safety Data Sheet

Under the *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994a) and the Commonwealth, State and Territory regulations introduced in accordance with these national model regulations, employees shall have ready access to Material Safety Data Sheets (MSDS) for hazardous substances at their workplace. MSDS provide information to those who use the hazardous substance.

It is recommended that importers of OLOA 270 review their MSDS for compliance with the *National Code of Practice for the Preparation of Material Safety Data Sheets, 2nd Edition*, paying particular attention to the hazard classification in the Recommendations above.

The MSDS should be provided to the occupational health and safety officer during the workplace assessment process and to the authorised medical practitioners responsible for health surveillance in the workplace to alert them to the potential for skin sensitisation.

A copy of the MSDS should be easily accessible to employees.

It is recommended that Sates and Territories monitor for compliance with the requirements.

Hazard communication – Labels

In accordance with the *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994b) it is recommended that importers of OLOA 270 review their labels for compliance and pay particular attention to the following:

In addition to the hazard classification risk phrases it is recommended the following safety phrases be incorporated on labels of OLOA 270 or products containing OLOA 270 in concentrations greater than or equal to 1%:

S24 Avoid contact with skin

S36/37 Wear suitable protective clothing and gloves

It is recommended that State and Territories monitor for compliance with the requirements.

Occupational controls

Overall, the risk of adverse effects from occupational use of OLOA 270 is low. However, there is a concern for skin sensitisation in mechanics working on marine vessels and workers need to wear appropriate protective equipment when handling the material. This assessment supports the recommendations in the original new chemical assessment report NA/889 and these are reproduced below. The control measures for OLOA 270 are as follows:

To minimise occupational exposure to the Chemical in OLOA 270 the following guidelines and precautions should be observed:

- Workers should receive regular instruction on good occupational hygiene practices in order to minimise personal contact, and contamination of the work environment with formulations that contain OLOA 270. In particular, contaminated clothing should be removed without delay. The affected skin area should be decontaminated with a waterless hand cleaner, mineral oil, petroleum jelly, then washed with soap and water.

- Workers should be advised of the potential for occupational dermatoses following repeated skin exposure to OLOA 270 and to report any skin changes to the occupational health and safety officer at their workplace. When an occupational skin disease occurs, work practices and opportunities for contact with the substance should be reviewed and preventive measures instigated to ensure other workers do not develop the same condition. Further guidance on preventing the occurrence of occupational skin diseases can be found in the NOHSC guide *Occupational Diseases of the Skin* (NOHSC 1990).

- Personal protective equipment (PPE) should be used on all occasions where exposure to additive packages containing OLOA 270 occurs. Chemical impervious gloves and clothing is necessary to prevent skin contact. Consideration should be given to the ambient environment, physical requirements and other substances present when selecting protective clothing and gloves. Workers should be trained in the proper fit, correct use and maintenance of their protective gear. PPE guidance in the selection, personal fit and maintenance of personal protective equipment can be obtained from:

Protective eyewear:	AS 1336 (SAA 1994); AS/NZS 1337 (SAA/SNZ 1992).
Chemical impermeable clothing:	AS 3765.2 (SAA 1990).
Impermeable gloves:	AS 2161.2 (SAA/SNZ 1998).
Occupational footwear:	AS/NZS 2210 (SAA/SNZ 1994);

- Workplace practices and control procedures consistent with provisions of State, Territory and Commonwealth legislation based on the *National Model Regulations for the Control of Workplace Hazardous Substances* must be in operation for products containing OGA 270 are determined to be hazardous.

If the conditions of use are varied from its use as a component of lubricant oil to be used in industrial engines, then further assessment may be required to assess the hazards to public health. In particular, should products become available to be added to car engines by members of the public, further consideration of the skin sensitisation effects would be required.

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Acronyms and Abbreviations

CAS	Chemical Abstracts Service
CO	Carbon monoxide
CHO	Chinese hamster ovary cells
DEW	Australian Government Department of the Environment and Water Resources
FORS	Federal Office of Road Safety
GLP	Good laboratory practice
GHS	Globally Harmonised System of Classification and Labelling of Chemicals
MSDS	Material safety data sheet
NAMW	Number average molecular weight
ND	New data
NOAEL	No-observed-adverse-effect level
ISO	International Organization for Standardization
OECD	Organisation for Economic Cooperation and Development
PMN	Premanufacture notice
PPE	Personal protective equipment
TG	Test guidelines
US EPA	United States Environment Protection Authority
US TSCA	United States Toxic Substances Control Act
WAMW	Weight-average molecular weight

Glossary

Adverse effect	Change in the morphology, physiology, growth, development, reproduction, or life span of an organism, system or (sub) population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences.
Assessment	Evaluation of appraisal of an analysis of facts and the inference of possible consequences concerning a particular object or process.
Assessment endpoint	Quantitative/qualitative expression of a specific factor with which a risk may be associated as determined through an appropriate risk assessment.
Concentration	Amount of a material or agent dissolved or contained in unit quantity in a given medium or system.
Dose	Total amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population.
Dose rate	Dose per unit time
Dose-related effect	Any effect to an organism, system or (sub) population as a result of the quantity of an agent administered to, taken up or absorbed by that organism, system or (sub) population.
Dose-response relationship	Relationship between the amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the change developed in that organism, system or (sub) population in reaction to the agent. Related Terms: *Dose-Effect Relationship, Effect Assessment, Concentration-Effect Relationship.*
Effect	Change in the state or dynamics of an organism, system or (sub) population caused by the exposure to an agent.
Exposure	Concentration or amount of a particular agent that reaches a target organism, system or (sub) population in a specific frequency for a defined duration.
Exposure assessment	Evaluation of the exposure of an organism, system or (sub) population to an agent (and its derivatives). Exposure Assessment is the third step in the process of Risk Assessment.

Exposure period	The time of continuous contact between an agent and a target.
Exposure route	The way an agent enters a target after contact (*e.g.*, by ingestion, inhalation, or dermal absorption).
Fate	Pattern of distribution of an agent, its derivatives or metabolites in an organism, system, compartment or (sub) population of concern as a result of transport, partitioning, transformation or degradation.
Hazard	Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent.
Hazard assessment	A process designed to determine the possible adverse effects of an agent or situation to which an organism, system or (sub) population could be exposed. The process includes hazard identification and hazard characterization. The process focuses on the hazard in contrast to risk assessment where exposure assessment is a distinct additional step.
Hazard characterization	The qualitative and, wherever possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. Hazard Characterisation is the second stage in the process of Hazard Assessment, and the second step in Risk Assessment. Related terms: *Dose-Effect Relationship, Effect Assessment, Dose-Response* *Relationship, Concentration -Effect Relationship.*
Hazard identification	The identification of the type and nature of adverse effects that an agent has inherent capacity to cause in an organism, system or (sub) population. Hazard identification is the first stage in hazard assessment and the first step in process of Risk Assessment.
Risk assessment	A process intended to calculate or estimate the risk to a given target organism, system or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. The Risk Assessment process includes four steps: hazard identification, hazard characterization (related term: dose-response

	assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process.
Risk characterization	The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system or (sub)population, under defined exposure conditions. Risk Characterization is the fourth step in the Risk Assessment process.
Risk management	Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Risk management comprises three elements: risk evaluation; emission and exposure control; risk monitoring.
Toxicity	Inherent property of an agent to cause an adverse biological effect.
Uptake (absorption)	The process by which an agent crosses an absorption barrier.

1. Introduction

The chemical in OLOA 270 was assessed as a new chemical under Section 23 of the *Industrial Chemicals (Notification and Assessment) Act 1989* (the Act) under the standard notification category and is now listed on the Australian Inventory of Chemical substances (AICS).

The New Chemicals Assessment Report (NA/889) was published in March 2001. No data on chemical and physical properties of OLOA 270 were provided for the assessment. All tests were conducted using a structural analogue of OLOA 270. The analogue was previously assessed by NICNAS as NA/253.

From the data provided at the time, a hazard classification was conducted in accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004). The chemical in OLOA 270 (referred to as 'OLOA 270' throughout the report) was classified as a skin sensitiser, based on positive sensitisation studies in animals and humans and the risk phrase "R43: May cause sensitisation by skin contact" was recommended for mixtures containing ≥1% OLOA 270. All the studies provided for the original assessment as a new chemical were conducted using a closely related structural analogue. Readers are refered to the New Chemicals Full Public Report on OLOA 270 available at the NICNAS website:

http://www.nicnas.gov.au/publications/car/new/na/nafullr/na0800fr/na889fr.pdf

Recommendations were made relating to engineering controls, use of personal protective equipment, safe work practices and Material Safety Data Sheet (MSDS). These recommendations were based on the intended use of OLOA 270 as a lubricating oil additive.

OLOA 270 was originally assessed for use as an ingredient in lubricants for marine diesel engines and also in high performance hydraulic oils for closed hydraulic systems in large construction equipment, such as earth movers. The use pattern remains the same.

In October 2006, additional toxicity data were supplied for OLOA 270. As five years have elapsed since the original assessment, this chemical is now being assessed as an existing chemical (Secondary Notification). The new data warrants reassessment which has been carried out under Section 68A of the Act, covering secondary notifications of existing chemicals.

Data submitted for the original assessment on use, exposure, animal and human toxicity are summarised in this report in the relevant sections. New data submitted for this assessment are discussed in detail and identified by the abbreviation ND.

13.1 Declaration and secondary notification

Declaration as a secondary notification was initiated when NICNAS received an additional study conducted on OLOA 270, that was not available during its assessment as a new chemical. The study is:

'OLOA 270: Oral Gavage Two-Generation Reproduction Study in the Rat'.

It was considered that a secondary notification for OLOA 270 was required because the additional data provided has relevance to the hazardous nature of the chemical as determined under the framework for Hazardous Substances in the Workplace.

A notice was published in the *Chemical Gazette* of 3 October 2006 requiring all persons who introduce OLOA 270 into Australia either by manufacture or import, to apply for secondary notification.

13.2 Objectives

The objectives of this assessment were to review the new data made available since the publication of the 2001 New Chemical Assessment, and where appropriate, revise the original assessment to:

- characterise the hazards of OLOA 270 to human health;
- characterise potential occupational, and public exposure to OLOA 270;
- characterise the risks of adverse effects resulting from exposure to workers, and the general public; and
- make appropriate recommendations to control exposures and/or reduce potential health and risks for workers and the general public.

No new environmental studies or use patterns were reported for OLOA 270. Hence an environmental assessment was not conducted. The environmental assessment conducted for OLOA 270 as a new chemical has been reproduced here.

13.3 International perspective

OLOA 270 was notified in Canada.

13.4 Peer review

During all stages of preparation, this report has been subject to internal peer review by NICNAS.

2. Applicant

One company applied for secondary notification assessment of this chemical. The applicant supplied additional reproductive toxicity study conducted on OLOA 270. Under Section 36 of the Act, the applicant was provided with a draft copy of the report for correction of errors and variation of content.

Applicant details are:

CHEVRON ORONITE AUSTRALIA

Level 10, 45 William Street

Melbourne, Victoria 3000

3. Chemical Identity and Composition

Name:	Long chain alkyl salicylate plus sulfurised long chain alkyl phenate, calcium salt
Chemical Name:	Confidential
Marketing name:	OLOA 270 (This name has been used throughout the report)
CAS Number:	Confidential
USA Premanufacture Notice Number (PMN):	Not available
Molecular Weight:	Confidential
Degree of purity:	Up to 60% in lubricating oil solvent
Additives/Adjuvants -	
Chemical name:	Lubricating oil solvent : petroleum distillates, hydrotreated heavy paraffinic, DMSO content <2.5%.
CAS No.:	64742-54-7
Weight percentage:	Up to 30%
Toxic properties:	Classification as a carcinogen applies when the chemical is present in mixtures at greater than 0.1% and the mixture contains >3% DMSO.
Chemical name:	Lubricating oil solvent : petroleum distillates, solvent refined heavy paraffinic, DMSO content <2.5%.
CAS No.:	64741-88-4
Weight percentage:	Up to 30%
Toxic properties:	Classification as a carcinogen applies when the chemical is present in mixtures at greater than 0.1% and the mixture contains >3% DMSO.

4. Physical and Chemical Properties

Physical and chemical data for OLOA 270 were not available for the original assessment. Physical and chemical data for a structural analogue previously assessed by NICNAS (NA/253) were used for the original assessment of OLOA 270 as a new chemical (NA/889). The data is reproduced in this report.

Appearance at 20°C & 101.3 kPa:	Dark brown viscous liquid
Boiling Point:	Decomposes before boiling
Specific Gravity:	1.093 g/mL at 15°C
Vapour Pressure:	0.49×10^{-4} KPa at 25°C (Vapour pressure is that of the refined lube oil in which this notified chemical is dissolved).
Water Solubility:	83 ppm
Partition Co-efficient (n-octanol/water):	Expected to be > 8
Hydrolysis as a Function of pH:	Does not contain hydrolysable functional groups
Adsorption/Desorption:	Expected to strongly adsorb to soil
Dissociation Constant:	Some dissociation is expected in the pH range 4 to 9
Particle Size:	Not applicable, chemical exists as a liquid
Flash Point:	> 200°C
Flammability Limits:	Will burn in the presence of sufficient heat and oxygen
Autoignition Temperature:	Not expected to auto-ignite
Explosive Properties:	Not known to be explosive
Reactivity/Stability:	Will react in the presence of strong oxidising agents. Stable to acid and base.

Comments on physico-chemical properties

In Rausina et al (1996), the water solubility of the notified chemical is stated to be 83 ppm using Semipermeable Membrane Devices (SPMDs). This value is based on the water solubility determined for oil additive detergents that are stated to be similar in structure. The stated value is consistent with the notified chemical containing long hydrophobic alkyl chains. The calcium salt of the notified chemical would be expected to be insoluble in water (as illustrated by soap binding with calcium in hard water as soap scum). The water solubility for the analogue to the

notified chemical was determined, via the shake flask method, to be 40.9 mg/L (40.9 ppm) (Robson, 1993).

Measurement of the n-octanol/water partition coefficient of the analogue chemical was attempted using an HPLC method which was briefly reported. Only 1.9% of the compound could be dissolved in acetonitrile and this had a log P_{OW} of 7.1. The insoluble material can be assumed to have a log P_{OW} >8. Based on this information, the notified chemical is expected to have a log P_{OW} > 8. The n-octanol/water partition coefficient for the notified chemical was determined by TLC to be greater than 6 (Robson, 1993).

No adsorption/desorption data were provided. However, the high log P_{OW}, high hydrocarbon content and strong dispersant nature of the notified chemical indicate that the material would have a large K_{OC} and adsorb strongly to the organic component of soils and sediments. The following results were provided for the analogue chemical (Heim, 1995).

Soil Matrix	**% OC**	**K_{oc} Adsorption**	**K_{oc} Desorption**
Loam 161	3.78	$3.14X10^4$	$4.03\ X10^4$
Silt loam 165	1.74	$6.26\ X10^4$	$1.84\ X10^5$
Sandy Loam G595	0.93	$1.72\ X10^5$	$1.10\ X10^5$

As these results are consistently around 5000 or greater it is assumed that the notified chemical would be immobile in soil. No dissociation data were provided. However, the notified chemical is a substituted phenol, which are weakly acidic (Morrison and Boyd, 1976). Therefore it is possible that some dissociation will occur in the environmental pH range of 4 to 9.

5. Manufacture, Importation and Use

No new information was provided on use during the secondary notification. The use of the chemical is as originally notified for assessment as a new chemical, however, the import volume of OLOA270 has decreased over the years.

5.1 Manufacture and importation (ND)

OLOA 270 is not manufactured in Australia. Ten to hundred tons of OLOA 270 are imported annually. The original assessment had indicated that OLOA 270 would be imported as a 70%-80% solution in a highly refined lubricating oil solvent (termed "component"), or at 10%-80% as part of an additive mixture (termed "package") with other lubricating oil components. Data provided for this secondary notification states that the "component" is no longer imported by the applicant, instead, four different additive packages are imported. The concentration of OLOA 270 in these packages ranges between 1%-60%. The packages are formulated into final lubricating oil products in Australia.

The original assessment had indicated that up to 210 tonnes of OLOA 270 would be imported each year. However, import volumes have decreased over the past four years to 10-100 tonnes/year. The additive packages containing OLOA 270 are imported in 250 L steel drums.

5.2 Formulation

The additive packages containing OLOA 270 are blended with oils to produce the final lubricating oil products. Blending into finished lubricant oil occurs on-line and is mostly computer controlled. The finished product is packaged into 200 L drums.

5.3 Use

No new use pattern data have been provided. OLOA 270 is currently used as one of the ingredients in lubricants used in marine diesel engines. The final concentration of OLOA 270 in these lubricants ranges between 0.5% and 15%. It functions as a detergent to reduce piston and crankcase deposits that can lead to wear and to control oxidation of the lubricant.

A small amount (<0.5%) may also be added in high performance hydraulic oils used in large construction equipment (e.g. earth movers, road graders and power scoop shovels). Typically the hydraulic oils contain 0.1-0.2% OLOA 270 component.

6. Exposure

Occupational, public and environmental exposures are considered below.

6.1 Occupational exposure (ND)

Occupational exposure to OLOA 270 is likely to be different from that assessed in the original assessment (NA/889). This is due to new data being provided for the secondary notification that indicate that additve packages containing OLOA 270 are transported only in 200 L steel drums. The original assessment had indicated that OLOA 270 is imported into two marine terminals in Australia by bulk shipment, in marine isotanks or in drums.

The drums are transported by road to storage facilities or to customer blending facilities for blending with lubricating oils. According to information provided by the applicant, 1-2 workers are involved in loading/unloading of drums at the terminals and 1-4 workers are involved for each of the tasks of sampling/analysis, blending and equipment cleaning at the blending facilities. The workers typically wear personal protective equipment such as: coveralls, hard hat and safety glasses.

6.1.1 Marine terminals

Additive packages arriving in steel drums via marine vessels are transferred by road to storage facilities or to customer blending facilities for blending with lubricating oils. According to information provided by the applicant, 1-2 workers are involved in loading/unloading of drums at the terminals and the storage facilities. During transfer operations exposure to the chemical is not likely except in the event of packaging breach (leaking drums). Inhalation exposure is unlikely as OLOA 270 has low volatility.

6.1.2 Lubricant blending facility

In Australia, the additive packages are blended with oils to make the final lubricating products. There are several blending facilities. At the blending facilities, additive packages are transferred from steel drums to storage/blending tanks via a four-inch hosing which workers connect to the drums. During the process incidental skin contact to the chemical from splashes, drips and spills is likely to occur as pump lines are connected or disconnected and samples are handled. Empty drums are typically steam cleaned.

Blending into finished lubricant oil occurs on-line and is computer-controlled, thereby excluding the potential for occupational exposure. Sampling occurs from the blend tank and analysis by workers takes a few minutes. Exposure to OLOA 270 could occur during sampling and analysis. The blended lubricant is packaged into 200 L drums or transported in bulk in tanker trucks. Drum filling is an automated process and worker intervention is not required unless the filling line operation needs adjustment. However, workers are required to insert bungs and label the drums.

Table 6.1 identifies the nature of work done where occupational exposure to the notified chemical in a component, package or finished oil may occur at marine terminals or blending plants.

Table 6.1 - Potential exposure during handling of OLOA 270 products

Nature of Activity (Number of Workers)	% OLOA 270	Maximum Potential Exposure Duration
Marine Terminal		
Unloading (1)	1 - 60	2 days/year
Loading into trucks (1-2)	1 - 60	4 days/year
Blending Facility		
Unloading to storage tanks (1 - 2)	1 - 60	1 h/day; 4 days/year
Drum cleaning (1 - 2)	<1	2-3 h/day; 4 days/year
Sampling (2 - 4)	1 - 60	30 mins/day; 11 days/year
Analysis (2 - 4)	1 - 60	30 mins/day; 11 days/year
Loading into drums (1 - 2)	0.5 - 15	8 h/day; 3 days/year
Equipment cleaning (1 - 2)	<1	3 h/day; 2 days/year.
Marine vessels		
Transfering lubricant oils to marine vessels	Not known	1-2 h/day

6.1.3 Marine vessels

Ship workers may be exposed (skin and eye contact) to the finished lubricant containing OLOA 270 when transferring the lubricant oils to the ships and when cleaning the drums. Ship mechanics may be exposed to the finished lubricant during normal maintenance work or when servicing the engines. It is inevitable that mechanics will receive skin contact given the nature of the job and the scale of operations. Up to several hundred workers may be involved in these tasks.

6.1.4 Closed hydraulic systems

There is potential for exposure when oils are added to and drained from hydraulic systems. Such operations are carried out by skilled workers and are likely to occur once a year. The number of workers is not known but is estimated to be up to 40% of Australian workers involved in such activities.

6.1.5 Control measures and worker education and training

Workers at marine terminals, lubricant blending plants and ship workers wear coveralls, gloves & eye protection. For the original assessment the notifier states that inspections of their customers' sites found that the blending facilities were well ventilated, with control systems for accidental spills and wastewater treatment. OLOA 270 is mostly handled by employees of major Australian lubricant manufacturers. Workers involved in the blending activities are reported to have received training in the handling of additive packages.

6.2 Public exposure

OLOA 270 is not sold to the public. However, exposure of the public to OLOA 270 may occur in the event of an accidental spill during transport of the additive packages containing OLOA 270 or the finished oils. According to the material safety data sheets (MSDS) provided for OLOA 270, a spill should be contained with an absorbent (soil, sand or other inert material) material and sealed in properly labelled drums for disposal. Runoff should be prevented from entering drains and waterways.

OLOA 270 is blended into finished lubricant oils intended for use on large marine vessels and other heavy hydraulic equipment. The potential for public exposure is only likely in the event of an accidental or inadvertent release.

6.3 Environmental exposure

6.3.1 Release

The blending operations are performed at specially constructed sites owned and operated by petroleum companies. Up to seven sites in Australia are involved in producing the marine diesel engine lubricants and hydraulic oils. Release to the environment is expected to occur only in the unlikely event of an accident during transport or an accidental leak.

The additive packages containing OLOA 270 are delivered to and stored at the blending facilities in drums. There is minimal release of OLOA 270 during transfer from the storage containers to the blending tanks, as a special air back flush system prevents any spillage. Blending occurs in fully enclosed automated systems. Blending tanks are cleaned with lube oil, which is incinerated or recycled during subsequent blending. Any spills incurred in the blending operations are contained within concrete bunds and either reclaimed or sent to on-site waste-water treatment facilities. At the treatment facilities residual hydrocarbon based products are separated from the aqueous stream by the Australian Petroleum Industry (API) process. Before being released to the sewage system, the aqueous waste undergoes

further treatment involving pond aeration and sand filtration. The remaining oily waste is incinerated.

The empty drums containing residual OLOA 270 are steam cleaned. The resultant aqueous waste is sent to on-site waste-water treatment facilities.

At marine terminals ISO procedures are in place to minimise spills. The finished lubricant containing OLOA 270 is transferred to the ship-board storage tank by hoses from the delivery container. Aboard ship, the oil is pumped through hard piping to the engine. Containers holding residual OLOA 270 are cleaned by steam with the waste-water entering a treatment facility at the receiving terminal. The waste is treated in a similar fashion to that at blending facilities.

In both uses skilled tradesmen undertake all maintenance of the equipment so spills and leaks are kept to a minimum and cleaned up immediately. Fresh oil is added to the engines/hydraulics over time to keep levels constant and to maintain the effectiveness of the oil but generally the machinery undergoes a major service once a year.Used oil is incinerated or sent for recycling.

6.3.2 Fate

In the case of accidental release to land, the high adsorption/desorption property of OLOA 270 indicates that it is not mobile, but gets adsorbed onto and becomes strongly associated with the organic component of soils and sediments. Similarly, in the event of accidental release into the water compartment, it becomes associated with suspended organic material, and eventually gets incorporated into sediments.

Information on the capacity of OLOA 270 to undergo biodegradation is not available, however biodegradation results for the analogue chemical are available: a ready biodegradability study on the analogue according to OECD TG 301D (Closed Bottle) Method (Douglas, 1993). A piece of glass filter paper impregnated with OLOA 270 was placed into a test bottle which was then filled with activated sewage sludge bacteria inoculated inorganic nutrient medium, and sealed. The study was conducted in duplicate so that dissolved oxygen measurements could be done at 0, 5, 15 and 28 days. Sodium benzoate was used as the standard substance. After 28 days, only 12% of the analogue chemical had degraded. This indicated that it is not readily biodegradable, while the sodium benzoate reached 88% degradation.

The expected high log P_{OW} and molecular weight and low biodegradation rate of OLOA 270 indicated potential for bioaccumulation. However, direct exposure to the water compartment was considered unlikely and would limit the potential for bioaccumulation.

Incineration of waste oil containing OLOA 270 destroys the substance with evolution of water vapour and oxides of carbon and sulphur, together with production of calcium compounds that assimilates with the ash. Sludge from waste treatment plants or oil recycling facilities is also incinerated.

7. Evaluation of Animal Toxicological Data

Toxicological data submitted for the original assessment of OLOA 270 included studies on a closely related structural analogue, which had been previously assessed by NICNAS as NA/253. The data included animal studies on acute toxicity, skin irritation, eye irritation, skin sensitisation in guinea pigs, repeat dose toxicity, genotoxicity, micronucleus assay and chromosomal aberration. The results obtained for the structural analogue were considered to be equivalent to those which would be obtained with OLOA 270. For the Secondary Notification, new data (denoted by ND) was provided for reproductive/developmental toxicity conducted with OLOA 270.

Summaries of the original data and assessment of the new study are presented in the following chapters. The test chemical was administered as a 70%-80% solution in a lubricating oil solvent. The doses presented refer to the solvent mixture. All tests were performed according to OECD/EEC guidelines and in facilities that comply with GLP.

7.1 Toxicokinetics

7.1.1 In vitro skin absorption of the analogue chemical (Kreuger et al, 1995a)

Skin absorption was tested in human and rat epidermal samples. Results from human samples from this study are detailed in Section 8.1.

Dermal absorption of the chemical analogue was studied in skin sections taken from abdominal and thoracic regions of Sprague-Dawley rats. Sliced sections of rat stratum corneum, 330-370 μm thick, were mounted onto foam blocks. ^{14}C-ring labelled test chemical was applied at 10 mg/cm^2 in 6% aqueous solution of Volpo-20 in diffusion cells. Receptor fluid was sampled at 2, 4, 6, 8, 24 and 30 h after application. Radioactivity was quantified using liquid scintillation counting.

In the rat skin 0.22% and 0.5% of the applied dose was recovered in the receptor fluid 24 and 30 h after an 8-h exposure, respectively. A flux rate of 1.3 μg/cm^2/h was calculated following 30 h exposure. The mass balance was 92%-96%.

OLOA 270 is minimally absorbed through rat skin in vitro.

7.1.2 In vivo skin absorption of the analogue chemical (Kreuger et al, 1995b).

In an in vivo rat study, dermal absorption of the chemical analogue was monitored in female Sprague-Dawley rats (5 per group). ^{14}C-ring labelled test chemical was applied at 10 mg/cm^2 to dorsal skin, under a non-occlusive cell for 8 h. Animals were sampled at 8, 24 and 72 h.

Radioactivity in urine, faeces, CO_2 and body tissues was quantified using liquid scintillation.

0.4%-0.6% of the applied dose was systemically absorbed at the 8, 24 and 72 h sample times. An average absorption rate of approximately 6μg/cm^2/h was calculated. The mass balance was 86%-100%.

OLOA 270 is minimally absorbed through rat skin in vivo.

7.2 Acute toxicity

Table 7.1 - Summary of the acute toxicity of the analogue chemical

Test	Species	Outcome	Reference
acute oral toxicity	rat	LD50 >5000 mg/kg	Glaza, 1993a
acute dermal toxicity	rat	LD50 >2000 mg/kg	Glaza, 1993b
skin irritation	rabbit	Slight irritant	Glaza, 1993c
eye irritation	rabbit	Slight irritant	Glaza, 1993d
skin sensitisation	guinea pig	Skin sensitiser	numerous

7.2.1 Acute oral

In a study using the OECD Guidelines TG 401 (Limit Study), 5 male and 5 female Crl:CDBR rats were administered 5000 mg/kg undiluted test material by gavage and observed for 14 days.

No mortality was observed during the study. Soft stools were noted in 7 animals within 4 h of treatment. Dark staining of the urogenital region was observed on days 1 and 2. No other signs of toxicity or treatment-related macroscopic findings were observed. The acute oral LD50 for the chemical was determined to be > 5000 mg/kg bw. The results of the study indicated that the analogue chemical had low acute oral toxicity (Glaza, 1993a).

7.2.2 Acute dermal

In a study conducted according to OECD Guidelines TG 402 (Limit Study), the analogue of OLOA 270 was applied under occlusive dressing, to the clipped skin of 5 male and 5 female Crl:CDBR rats at a dose of 2000 mg/kg. The patch was removed after 24 h and animals observed for 14 d. No signs of local or systemic toxicity were observed and no treatment-related macroscopic findings were observed. Based on the results of the study, the dermal LD50 for the chemical was determined to be > 2000 mg/kg bw (Glaza, 1993b).

7.2.3 Acute inhalation

An inhalation study was not conducted for this viscous liquid of low volatility.

7.2.4 Skin irritation

In a study conducted according to OECD Guidelines TG 404, undiluted liquid chemical was applied to an area of intact dorsal skin of 3 male and 3 female New Zealand rabbits, and the test area covered with semi-occlusive dressing for 4 h. At

the end of the 4-h exposure period, the dressing was removed and the test site irrigated with lukewarm water. Skin reactions were assessed at 0, 24, 48, 72 and 96 h after removal of the dressing. The untreated skin of each animal was used as a control. The results were scored according to Draize method. Mean score for all six animals over the 24, 48 and 72 h periods was: Erythema = 0.1; oedema = 0. The test chemical was considered to be slightly irritating to the skin of rabbits (Glaza, 1993c).

7.2.5 Eye irritation

In a study conducted according to OECD Guidelines TG 405, three male and six female New Zealand white rabbits received 0.1 mL of undiluted test chemical in the conjunctival sac of one eye. The eyes of 3 males and 3 females remained unwashed. The eyes of another 3 females were irrigated approximately 30 seconds after instillation. Grade 1 scores for conjunctival redness and chemosis were recorded in all animals at 24 h, but this had resolved by the 48-h observation time. Zero scores were recorded for corneal and iris effects in the irrigated eyes throughout the study. Mean score for all six animals with unirrigated eyes over the 24, 48 and 72 h time points : Cornea = 0 ; Iris = 0 ; Conjunctival redness = 0.84 ; conjunctival chemosis = 0.33. The test chemical was considered slightly irritating to the eyes of rabbits (Glaza 1993d).

7.2.6 Skin sensitisation

Five skin sensitisation studies were conducted - three testing the analogue chemical as manufactured (i.e 70%-80% in lube oil), and two testing different oil products containing lower amounts of the analogue substance (7.6%-16%).

Skin sensitisation in guineapigs, using the analogue chemical (Morris, 1993)

The test was conducted according to the OECD guideline TG 406 (Buehler) in Hartley guinea pigs. Ten male and 10 female test animals and 5 male and 5 female control animals were used. In the induction procedure 0.3 mL of 100% test chemical was applied to intact skin under occlusive dressing for 6 h on days 0, 7 and 14. Control animals received Spectrum Mineral Oil Light.

For challenge on day 28, test and control animals were treated with 0.3 mL of 0.5% test chemical in Spectrum Mineral Oil Light, applied to intact skin of a previously untreated site, under occlusive dressing for 6 h.

Challenge outcome:

Challenge concentration	*Test animals*		*Control animals*	
	*24 h**	*48 h**	*24 h*	*48 h*
0.5%	1/20**	5/20	0/10	0/10

* time after patch removal

** number of animals exhibiting responses greater than those seen in controls

All control animals showed grade +/- or 1 skin reactions at 24 and/or 48 h after challenge. Animals with grade 2 skin reactions are recorded in the table. The incidence of skin reactions in test animals was seen to increase from 24 to 48 hours post-challenge. At 48 hours, 25% of test animals showed skin reactions greater than those seen in control animals.

The test chemical is sensitising to the skin of guinea pigs.

Skin sensitisation in guineapigs, using the analogue chemical (Kreuzmann, 1993)

The test was conducted according to the OECD guideline TG 406 (Buehler) in Hartley guinea pigs. Ten male and 10 female test animals and 5 male and 5 female control animals were used. In the induction procedure 0.3 mL of 25% test chemical in Spectrum Mineral Oil Light was applied to intact skin under occlusive dressing for 6 h on days 0, 7 and 14. Control animals received Spectrum Mineral Oil Light.

For challenge on day 28, test and control animals were treated with 0.3 mL of 2.5% test chemical in Spectrum Mineral Oil Light, applied to intact skin of a previously untreated site, under occlusive dressing for 6 h.

Challenge outcome:

Challenge concentration	*Test animals*		*Control animals*	
	*24 h**	*48 h**	*24 h*	*48 h*
2.5%	2/20**	5/20	0/10	0/10

* time after patch removal

** number of animals exhibiting responses greater than those seen in controls

All control animals showed grade +/- or 1 skin reactions at 24 and/or 48 h after challenge. Animals with grade 2 skin reactions are recorded in the table. The incidence of skin reactions in test animals was seen to increase from 24 to 48 hours post-challenge. At 48 hours, 25% of test animals showed skin reactions greater than those seen in control animals. Oedema was also noted in 2 animals at 24 h after challenge and in 4 animals at 48 h after challenge.

The test chemical is sensitising to the skin of guinea pigs.

Skin sensitisation in guineapigs, using the analogue chemical (Morris, 1994a)

The test was conducted according to the OECD guideline TG 406 (Buehler) in Hartley guinea pigs. Ten male and 10 female test animals and 5 male and 5 female control animals were used. In the induction procedure 0.3 mL of 25% test chemical in Spectrum Mineral Oil Light was applied to intact skin under occlusive dressing for 6 h on days 0, 7 and 14. Control animals received Spectrum Mineral Oil Light.

For challenge on day 28, test and control animals were treated with 0.3 mL of 2.5% test chemical in Spectrum Mineral Oil Light, applied to intact skin of a previously untreated site, under occlusive dressing for 6 h. For the re-challenge on day 34, test and control animals were again treated with 0.3 mL of 2.5% test chemical in Spectrum Mineral Oil Light, applied under occlusive dressing for 6 h. Finally, a cross-challenge was done in which test and control animals were treated with 0.3

mL of 100% test chemical in Spectrum Mineral Oil Light, applied under occlusive dressing for 6 h.

Challenge outcome:

Challenge concentration	*Test animals*		*Control animals*	
	*24 h**	*48 h**	*24 h*	*48 h*
2.5%	2/20**	4/20	0/10	1/10
Rechallenge concentration				
2.5%	4/20	4/20	0/10	0/10
Cross- challenge				
100%	9/19	4/19	0/10	0/10

* time after patch removal

** number of animals exhibiting responses greater than those seen in controls

All control animals showed grade +/- or 1 skin reactions at 24 and/or 48 h after challenge and only one animal showed grade 2 reactions 48 h after challenge. Animals with skin reactions of a higher grade than the maximum observed in control animals (grade 1) are recorded in the table.

Oedema was also noted in 3 of the animals showing grade 2 reactions at rechallenge, in 8 of the animals showing grade 2 or 3 reactions at cross-challenge and in one test animal showing grade 1 skin reaction at cross-challenge. 10%, 20% and 47% of test animals showed skin reactions greater than those seen in control animals at 24 h after challenge, rechallenge and cross-challenge, respectively. The incidence of skin reactions slightly increased 48 h after challenge (4/20), but was sustained or slightly reduced 48 h following re-challenge or cross-challenge.

The test chemical was sensitising to the skin of guinea pigs.

Skin sensitisation in guineapigs, using finished oil containing 16% analogue chemical (Morris, 1994b)

The test was conducted according to the OECD guideline TG 406 (Buehler) in Hartley guinea pigs. Ten male and 10 female test animals and 5 male and 5 female control animals were used. In the induction procedure 0.3 mL of 100% finished oil (containing 16% analogue chemical), applied to intact skin, under occlusive dressing for 6 h. Control animals received Spectrum Mineral Oil Light.

For challenge on day 28, test and control animals were treated with 0.3 mL of 100% test chemical (16% analogue chemical), to intact skin of a previously untreated site, under occlusive dressing for 6 h.

Challenge outcome:

Challenge Concentration of OLOA 270	*Test animals*		*Control animals*	
	*24 h**	*48 h**	*24 h*	*48 h*
16%	11/18**	3/18**	5/10	1/10

* time after patch removal

** number of animals exhibiting responses greater than those seen in controls

All test and control animals showed grade +/- or 1 skin reactions at 24 and/or 48 h after challenge. Animals with grade 1 skin reactions are recorded in the table. The incidence of skin reactions was seen to decrease from 24 to 48 hours post-challenge in both test and control animals. By subtracting from the percentage of test animals from the percentage of control animals with grade 1 reactions at challenge, an overall sensitisation response of 11% and 6.7% was obtained 24 and 48 hours post challenge respectively. A positive result in a Buehler study is an overall skin sensitisation response of 15% or greater.

The finished oil containing 16% analogue chemical was not sensitising to the skin of guinea pigs.

Skin sensitisation in guineapigs, using finished oil containing 7.6% analogue chemical (Morris, 1996)

The test was conducted according to the OECD guideline TG 406 (Buehler) in Hartley guinea pigs. Ten male and 10 female test animals and 10 male and 10 female control animals were used. In the induction procedure 0.3 mL of 100% finished oil (containing 7.6% analogue chemical), applied to intact skin, under occlusive dressing for 6 h. Control animals received Spectrum Mineral Oil Light.

For challenge on day 28, test and control animals were treated with 0.3 mL of 100% test chemical (7.6% analogue chemical), to intact skin of a previously untreated site, under occlusive dressing for 6 h.

Challenge outcome:

Challenge concentration of OLOA 270	*Test animals*		*Control animals*	
	*24 h**	*48 h**	*24 h*	*48 h*
7.6%	0/20	1/20**	0/20	0/20
7.6%	15/20***	8/20	12/20	10/20

*time after patch removal

**number of animals exhibiting grade 2 skin response

*** number of animals exhibiting grade 1 skin responses

One test animal showed a grade 2 skin reaction (higher than that seen in control animals). 75% and 60% of test and control animals, respectively, showed grade 1 skin reactions. The incidence of skin reactions was seen to decrease from 24 to 48 hours post-challenge in both test and control animals. By subtracting the percentage of test animals from the percentage of control animals giving the same severity of

reactions at challenge, an overall response of 15% was obtained 24 hours post challenge, with a negative response seen at 48 hours. The response seen at 24 hours post challenge is the minimal incidence constituting a positive response in a Buehler study. However, the severe decrease in overall response 24 hours later would suggest that the observed skin reactions in test animals are irritant in nature. Consequently, overall, this study is not considered positive.

The finished oil containing 7.6% analogue chemical was not sensitising to the skin of guinea pigs.

7.3 Repeated-dose toxicity of the analogue chemical

7.3.1 28-day oral repeated-dose toxicity in rats

In an oral (gavage) study conducted according to OECD TG 407, 6 male and 6 female Sprague-Dawley rats per group were given 0, 100, 500 and 1000 mg/kg of the test substance for 28 consecutive days in peanut oil vehicle. An extra control and top dose group were included and allowed a 14-day recovery period.

One top-dose female died in week 2 due to gavage error. No other deaths occurred. Top-dose females showed very slight but statistically significant lower body weight gains compared to controls after the first week of dosing. However body weight gains were comparable with controls for the remainder of the study. There were no treatment-related differences in body weight gain in the top-dose males or in the lower-dose groups throughout the study. General signs of toxicity, including brown staining or matting on various body surfaces, tan staining around the mouth with increased salivation, were seen within an hour of dosing, primarily in top-dose males and females but also, usually at a lower incidence, in animals treated with 500 and 100 mg/kg/day.

Treated males showed a statistically significant decrease in reticulocyte count of 44%, 42% and 44% in 100, 500 and 1000 mg/kg/day treated groups, respectively, compared to controls. This decrease was not evident in the recovery group and due to the lack of a dose-response relationship was not considered to be of toxicological significance.

Top-dose males showed a statistically significant increase in alanine aminotransferase compared to the controls. The value was comparable with controls by the end of the recovery period.

No other treatment-related findings were observed.

A slight but statistically significant increase (18% compared to controls) in absolute liver weight was noted in top-dose males at the end of the treatment period. The increase was no longer evident at the end of the recovery period. Corresponding increases were also noted in liver weight relative to body (19%) and brain (16%) weights. Mid and top-dose females also showed statistically significant increases in liver weight, relative to body weight (10% and 18%, respectively). However increases in absolute liver weight, and relative brain weight, were not noted in females. Also, as no corresponding clinical findings were noted, the liver weight findings in females were considered to be of doubtful toxicological significance.

The only treatment-related macroscopic findings were those associated with gavage error in the female that died. No treatment-related microscopic findings were observed.

Based on liver toxicity at 1000 mg/kg/day in male rats, a No Observed Adverse Effect Level of 500 mg/kg/day was identified (Shour et al, 1993).

7.3.2 90-day repeated dose toxicity in rats

In a 90-day oral (gavage) study conducted according to OECD TG 408, groups of Sprague-Dawley rats (12/sex/group) were given 0, 100, 500 or 1000 mg/kg/day of the structural analogue of OLOA 270 (designated; control, low, mid and top-dose groups, respectively), in peanut oil, daily for 91 or 92 consecutive days, with extra control and top-dose groups given a 28 day recovery period.

Two top-dose females died in weeks 2 and 4. One low and one mid-dose male died in weeks 2 and 3 respectively. Cause of death was not determined due to excessive autolysis in these animals. Two more top-dose females died in week 6 due to gavage error.

General signs of toxicity such as increased salivation and red matting around the mouth were observed, usually 1 h after dosing, in a dose-dependant manner in all treated groups. Rales were also noted in 3 top-dose animals, one of which died. No clinical signs were seen during the recovery period.

Mean body weight gain was reduced in all male treated groups and was statistically significant in mid and top-dose males. Body weights at the end of the treatment period were 5%, 11% and 12% lower than control values in low, mid and top-dose males, respectively. The decreases were consistent with statistically significant decreases in food consumption. Similar trends were not observed for mean body weight, body weight gain or food consumption in females.

No treatment-related changes in clinical chemistry or haematology were observed.

Bilateral corneal crystals were observed at an incidence of 0/24, 2/11, 4/11 and 10/24 in control, low, mid and top-dose males, respectively, at the 13 week observation time. At the end of the recovery period, the effect was seen in 3/12 and 6/12 control and top-dose males, respectively. The effect was not seen in females and was noted to commonly occur only in Sprague-Dawley rats, particularly males and was therefore considered unlikely to be due to treatment.

Mid and top-dose females showed a statistically significant increase in adrenal weight relative to body weight (24% and 28%, respectively) at the 13-week necropsy. Mid and top-dose females also showed a statistically significant increase in relative liver weight (17% and 26%, respectively). No corresponding macro- or microscopic findings were observed in the adrenals or liver at the end of the dosing period and no changes were seen in relative organ weights at the end of the recovery period.

Mid and top-dose males showed statistically significant increases in weights of brain (11% and 11%, respectively), liver (11% and 18%, respectively) and kidney (14%, top-dose only) relative to body weight at the 13-week necropsy. Changes were not seen in absolute weights and were considered unlikely to be due to treatment. No histomorphological changes were noted in brain and liver at these

doses. Minimal interstitial infiltration of lymphocytes was noted in kidneys of 5/12 rats.

The minimal signs of clinical toxicity observed in animals at 100 mg/kg bw/day were seen only in a small number of animals and in the absence of any other signs of toxicity, and consequently are not considered biologically significant. A No Observed Adverse Effect Level of 100 mg/kg bw/day was identified in females based on clinical signs of toxicity together with a statistically significant increase in relative adrenal weight (Chengelis et al., 1995).

7.3.3 Combined repeat dose toxicity and reproductive screen study in rats

In a combined repeat dose toxicity and reproductive screen study conducted according to OECD TG 422, Sprague-Dawley rats (12/sex/group) were given 0, 100, 500 or 1000 mg/kg of the test substance in peanut oil vehicle by gavage. Male rats were given the test substance for at least 28 consecutive days prior to mating, during mating, and post mating for a total minimum of 70 days. Female rats received the test substance for at least 28 consecutive days prior to mating and until lactation day 4 or until post-mating day 25 for those which did not deliver a litter.

No deaths occurred in F_0 generation. Top-dose F_0 males showed a statistically significant reduction (25% compared to controls) in body weight gain during weeks 4-5. However this was not observed at any other interval and was considered to be transitory. There were no other changes in body weight or body weight gain in any F_0 dose group at any time of the study including through gestation and lactation.

General signs of toxicity, including brown staining or matting on various body surfaces, tan staining or clear matting around the mouth with increased salivation, were seen within an hour of dosing in top-dose F_0 males and females. On occasion, the signs persisted to the daily observations. Some of these clinical signs were also observed at a lower incidence in the mid-dose F_0 animals. Similar signs were also observed with low-dose F_0 females, occurring only as single incidents. An increased incidence of soft stools was noted in top-dose F_0 animals, but not in the other treatment groups. However, these effects were seen inconsistently and were not considered biologically significant.

Top–dose F_0 females showed a statistically significant increase (10% compared to controls) in absolute liver weight, although no corresponding increases were noted in liver weights relative to body or brain weight. No treatment-related micro- or macroscopic finding were observed in F_0 males or females in any treatment group. Clinical chemistry and haematology parameters were not tested.

Physical condition and body weights of pups were unaffected by treatment. No treatment-related micro- or macroscopic findings were observed in males or female pups in any treatment group.

No treatment-related changes were noted in the numbers of successful matings, pregnancies, litters delivered or stillborn and viable pups. The mean number of days between pairing and coitus, the length of gestation and the sex ratio of the pups were unaffected by treatment.

No systemic toxicity or reprotoxicity was observed in this study at 1000 mg/kg bw/day, the highest dose tested. Thus, a No Observed Adverse Effect Level of

1000 mg/kg/day, was identified for both systemic toxicity and reprotoxicity (Shour et al, 1993)

7.3.4 Developmental toxicity study in rats

In a developmental toxicity study in rats (according to OECD TG 414), female Sprague-Dawley rats (25/group) were administered by gavage 0, 100, 500 and 1000 mg/kg/day (designated; control, low, mid and top-dose groups, respectively) test chemical in peanut oil from gestation days 6-15. Hysterectomies were performed on all animals on gestation day 20.

No deaths occurred. Mid- and top-dose dams showed slight to severe hair loss (within 2 days of treatment) on the hindlimbs, ventral-abdominal area and at the base of the tail. Mid- and top-dose dams also showed tan staining around the mouth I h after treatment.

Mid- and top-dose dams showed body weight loss during gestation days 6-7. This resulted in statistically significant reductions in body weight gain on days 6-9 (both groups) and 9-12 (top-dose only). Compensatory increases in body weight gain occurred in both groups post treatment (gestation days 16-20). The decreases and increases in body weight gain reflected changes in food consumption.

No treatment-related macroscopic findings were observed in the dams and the mean gravid uterine weights were unaffected by treatment.

Intrauterine growth and survival were unaffected by treatment. There were no changes in the number of corpora lutea or implantation sites, postimplantation loss, the number of viable fetuses, foetal body weight or foetal sex ratio.

Malformations were seen in 0/373, 3/357, 2/378 and 1/345 fetuses in the 0, 100, 500 and 1000 mg/kg/day dose groups, respectively. Malformations included external, internal visceral and skeletal but did not show any consistency or dose-relationship to indicate that they were related to exposure.

No signs of developmental toxicity were observed with 1000 mg/kg/day, the highest dose tested. Mild maternal toxicity was observed at the top and mid doses (weight loss and slight to severe hair loss) and a No Observed Adverse Effect Level of 100 mg/kg/day was identified in the dams (Nemec et al, 1995).

7.4 Genotoxicity

Two in vitro studies and one in vivo study were submitted with the original application. In a bacterial (*Salmonella* and *E.coli*) gene mutation assay, conducted according to OECD TG 417, doses ranging from 33.3 to 10000 µg/plate showed no increase in the incidence of gene mutations in *Salmonella* tester strains TA 98, TA 100, TA 1535 and TA 1537 or in *E. coli* bacterial strain *WP2 uvrA*, with or without metabolic activation. There was no evidence of cytotoxicity in any of the test strains, with or without activation. Slight precipitation was observed with 333 µg/plate and above. Positive and negative controls produced results in the expected ranges. The test chemical was not mutagenic under the conditions of the test (Lawler, 1993).

In the chromosome aberration assay, Chinese hamster ovary (CHO) cells were treated with the analogue substance according to the dosing schedule given below.

There was no increase in the incidence of chromosomal damage following treatment with the chemical analogue for either the 21-or 45-h treatment, in the absence of metabolic activation. In addition, no induction of chromosomal aberration was observed after 6-h treatment with metabolic activation. Positive and negative controls produced results in the expected ranges. The test chemical was not clastogenic under the conditions of the test (Murli, 1993).

Dosing schedule for the chromosomal aberration assay in CHO cells

Metabolic Activation	Experi-ment/ Number	Test concentration (μg/mL)	Controls
-S9	1	treatment time = 21 h harvest time = 24 h test concentrations = 50*, 125*, 250*, 500*, 750, 1000 μg/mL With the 24 h harvest time, severe toxicity was evident with 500 μg/mL (with a reduction in MI > 50%) and complete toxicity with 750 and 1000 μg/mL.	Positive: : MMC Negative: PL
	2	treatment time = 45 h harvest time = 48 h test concentrations = 50*, 125*, 250*, 500, 750, 1000 μg/mL With the 48 h harvest time, severe toxicity was evident with 250 μg/mL (with a reduction in MI > 50%) and complete toxicity with 500 μg/mL and above.	
+S9	3	treatment time = 6 h harvest time = 24 h test concentrations = 10, 50*, 150*, 325*, 750*, 1500, 2250, 2290 μg/mL Severe toxicity was evident with 750 μg/mL (with a reduction in MI > 50%) and complete toxicity with 1500 μg/mL and above.	Positive: CP Negative: PL

MMC – mitomycin; PL – 10% pluronic in corn oil; CP – cyclophosphamide; * - cultures selected for metaphase analysis

In an in vivo assay conducted according to OECD TG 474, the chemical analogue was injected intra-peritoneally in ICR mice (5/sex), at doses of 1250, 2500 or 5000 mg/kg bw. There were no increases in the frequency of micronucleated cells. One low-dose animal (from 24 h sample group) was found dead approximately 15 h after treatment. All top-dose animals showed rough hair coats. Decreases in polychromatic to normochromatic cell ratio were noted in all the 48-h sample male groups which did not reach statistical significance. Positive and negative controls

produced results in the expected ranges. The test chemical was not clastogenic under the conditions of the test (Murli, 1992).

7.5 Reproductive effects (ND)

The effect of OLOA 270 on fertility was evaluated in a two generation study conducted in compliance with OECD Test Guideline 415 in Sprague Dawley Cri: CD IGS Br rats (Wood, 2002). The F0 generation consisted of groups of 28 rats per sex administered 0, 50, 250 or 1000 mg/kg bw/day OLOA 270 in corn oil by gavage during a pre-mating period of 74 days and a mating period of up to 3 weeks. Males and females from each group were randomly paired and co-habited for up to 3 weeks, resulting in the F0a generation. Females were also administered the test material during gestation and lactation. The dosing of F0 males was continued during this time.

After lactation, the F0 females and males were then paired again to re-examine their reproductive capacity. Alternative pairings to those from the F0a pairing phase were used. F0 males and females were then sacrificed on day 20 of gestation and the uterine contents of pregnant females examined and foetal external appearance and weight of the F0b offspring determined.

At least one male and female offspring from each F0a litter was retained after weaning to form the F1 generation for assessment of their reproductive capacity. Remaining F0a animals were sacrificed and selected animals assessed for sexual maturation.

F1 animals were administered OLOA 270 for a 96 day pre-mating period and up to 3 weeks for the mating period. Following evidence of mating, females were housed individually and dosed throughout gestation and lactation. Females were allowed to deliver their offsprings to produce the F2 litter. At the end of weaning F1 males and females were sacrificed.

For all F0 and all reared F1 and F2 animals, observations and weighings were performed regularly. Food consumption was also recorded in F0 and F1 animals. All live offspring were observed for physical development i.e. detachment of pinna, tooth eruption and eye opening. They were also assessed for reflexological response to various stimuli i.e. surface righting reflex, mid-air righting reflex, startle reflex and pupil reflex. Routine haematology and biochemical investigations were performed on F0 animals, and oestrus cycle assessed in F0 females prior to the initial mating phase. At necropsy organ weights were determined in F0, F0a and F1 animals. Macroscopic examination of internal and external abnormalities was undertaken in F0 and F1 animals. Additionally, microscopic examination of reproductive organs was conducted in F0 and F1 animals that received 0 or 1000 mg/kg bw/day OLOA 270. Semen assessment was also undertaken in F0 males, while macroscopic and microscopic examination of the uterus and ovaries was undertaken in F0a females.

Systemic toxicity

In parental F0 animals 8 male and 1 female deaths were observed. Mortalities in males were nearly all due to dosing trauma, while a single female receiving 1000 mg/kg bw/day was sacrificed as a result of abnormal labour. Similarly in F1 parental animals, the majority of observed mortalities in 9 males and 6 females are

attributable to dosing trauma, while 2 mortalities in females receiving 1000 mg/kg bw/day were attributable to abnormal labour.

Salivation was seen in F0 and F1 animals at 250 mg/kg bw/day and above, however, in the absence of any other signs of toxicity is considered due to a lack of palatability to the test substance rather than a toxic effect.

Compared to controls, a statistically significant decrease in overall body weight gain (16%) was seen in F0 males at 1000 mg/kg bw/day at sacrifice but not in F1 males, or female parental animals. At 1000 mg/kg bw/day food consumption was higher than controls, often statistically significant, in: F0 females during the pre-mating phase and gestation; F1 females during gestation and lactation; and F1 males during the pre-mating phase.

Statistically significant increases in relative organ weights were seen of the liver, kidney, brain, left and right testis in both F0 (17%, 22%, 10%, 5% and 9% respectively) and F1 males (13%, 17%, 8%, 9% and 10%) at 1000 mg/kg bw/day. A statistically significant increase in relative adrenal weight (22%) was also seen in F1 males at the top dose. In females statistically significant increases in relative liver weight was seen in both F0 (12%) and F1 (6%) animals at 1000 mg/kg bw/day. However, no treatment-related macroscopic or microscopic findings were seen in F0 or F1 animals at necropsy. Additionally, no treatment related effects were seen on sperm concentration, mortality or morphology in F0 males.

In F0 males, dose related statistically significant increases in haematological and biochemical parameters were only seen for activated partial thromplastin time at 250 and 1000 mg/kg bw/day (17% and 21% respectively) and alkaline phosphatase at 1000 mg/kg bw/day (30%). In F0 females, such changes were only seen in clotting time (7%) and phosphorous levels (34%) at 1000 mg/kg bw/day.

Fertility

Oestrus cycle was not affected in F0 treated females and no significant effect was seen on the mating index in parental animals. However, a decrease in the number of pregnant animals for the F0a mating phase was seen that was not dose-related (100%, 92.8%, 71.4% and 77.8% at 0, 50, 250 and 1000 mg/kg bw/day respectively). Similar results were seen for the F0b (96.4%, 82.1%, 75.0% and 80.8%) and F1 mating phase (96.4%, 96.4%, 100% and 84.0%). Additionally at 1000 mg/kg bw/day a slight reduction in mean live litter size was seen at birth in F0a offspring (13.5, 13.7, 14.5 and 12.0) that was also not dose related. Compared to controls, a dose related and statistically significant decrease was seen in the F2 live litter size at 1000 mg/kg bw/day on the day of birth (12.3 compared to 14.4 in controls) and day 1 post partum (12.2 compared to 14.2). From day 4 to day 21 post partum viability was comparable to controls.

Development

In F0a and F1 offspring (i.e. all live offspring on day 21 post partum) no clinical signs of toxicity, effects on body weight gain during lactation or effects on reflexological response were observed. Additionally, no treatment related changes were seen in the sex ratio. Compared to controls, a statistically significant increase in the time to completion of male sexual development was seen in F0a males at 250 mg/kg bw/day with a corresponding statistically significant increase in bodyweight at the time of development. In contrast although a statistically significant increase

was seen in bodyweight at the time of sexual development in F0a males at 1000 mg/kg bw/day the increase in the time for sexual development did not obtain statistical significance. No effect on sexual development was seen in F0a females. At necropsy no treatment related findings were observed in offspring that died during lactation or in the F0a generation overall, including caesarian examination of F0a females. Additionally, no treatment related effect was seen on organ weights in F0a pups.

Discussion

At 1000 mg/kg bw/day there was evidence of systemic toxicity in F0 male parental animals: a significant decrease in bodyweight gain along with changes in some haematology and biochemical parameters. Additionally in males, an increase in activated partial thromplastin time was seen at 250 mg/kg bw/day. However, this observance at 250 mg/kg bw/day is not considered toxicologically significant in the absence of other evidence of toxicity. Similarly in female parental animals (F0), the observance of changes in clotting time and phosphorous levels at 1000 mg/kg bw/day, along with changes in relative liver weight in F0 and F1 females in the absence of histopathological changes, are not considered toxicologically significant.

For reproduction, though a significant decrease in the pregnancy index was seen at 1000 mg/kg bw/day following the F0a, F0b and F1 mating phase compared to the laboratory's historical value (97.5%), no dose response was seen for any mating phase (with all F1 animals pregnant at 250 mg/kg bw/day). However, while the absence of a dose response and lack of histological changes to male and female reproductive organs may indicate that the observed changes in pregnancy rate are unlikely to be a true effect on fertility, they were seen following all mating phases and so cannot be completely excluded as treatment related. Likewise, there was a reduction in live litter size for the F0a and F1 mating phase at 1000 mg/kg bw/day (statistically significant for the latter), the F0a reduction was not dose related. Additionally, no indication of in utero reduction of live litter size, or increase in pre or post implantation embryo loss, was seen for the F0b mating phase. However, the reduction in live litter size cannot be entirely excluded as treatment related as it was noted in both generations. The evidence for effects on sexual development at 1000 mg/kg bw/day are considered equivocal, as they were only observed in one sex (F0a males) and were not dose related or statistically significant at the top dose.

Therefore, this study provides some evidence to suggest there may be an effect on fertility at 1000 mg/kg bw/day: a significant though not dose-related decrease in pregnancy index seen for all mating phases, along with a reduction in litter size for the F0a and F1 mating phases that was dose related and statistically significant for the latter. Furthermore, though there was evidence of parental toxicity at 1000 mg/kg bw/day in males in the form of a reduction in body weight gain in F0 males only, no toxicologically significant effects were seen in females at this dose level. Therefore, overall, OLOA 270 is considered to have had a direct effect on fertility, and the NOAEL for systemic toxicity in female and male parental animals, and reproductive toxicity is 1000, 250 and 250 mg/kg bw/day respectively.

8. Evaluation of Human Toxicological Data

8.1 Toxicokinetics

Dermal absorption

In vitro skin absorption of the analogue chemical (Krueger et al, 1995a)

Skin absorption was tested in human and rat epidermal samples. Results from rat samples from this study are detailed in Section 7.1.

Dermal absorption of the chemical analogue was studied in skin sections taken from abdominal and thoracic regions of human cadavers (one black male and one caucasian female). Sliced sections of stratum corneum, 370-410 μm thick, were mounted onto foam blocks. ^{14}C-ring labelled test chemical was applied at 10 mg/cm^2 in 6% aqueous solution of Volpo-20 in diffusion cells. Receptor fluid was sampled at 2, 4, 6, 8, 24, 30, 48, 54 and 72 h after application. Radioactivity was quantified using liquid scintillation counting.

In the human skin 0.09% of the applied dose was recovered in the receptor fluid following 72 h exposure. A flux rate of 0.1μg/cm^2/h was calculated. The mass balance was 92%-96%.

OLOA 270 is minimally absorbed through human skin in vitro.

8.2 Acute toxicity

8.2.1 Skin sensitisation

Data submitted for the original new chemical assessment consisted of four human skin sensitisation studies; one using the analogue substance at 70%-80% in lube oil, and three using different finished oil products containing lower amounts of the analogue substance (5.2%–16%).

Skin sensitisation in humans using the analogue chemical (Boisits et al, 1993).

In a Repeated Insult Patch Test in Humans, 105 individuals, predominantly female, aged 21-60 years were tested for sensitivity to OLOA 270. The test chemical (100% analogue chemical) was applied under occlusive dressing to the infrascapular region of the back for 24 h, on Mondays, Wednesdays and Fridays for 6 applications. Due to skin reactions, the remaining 2 applications were made under semi-occlusive patches. Treated sites were evaluated before reapplication of test chemical.

Nineteen individuals experienced intense reactions either during the course or on completion of the induction phase of the study. Subjects with severe reactions needed medical treatment to help relieve symptoms taking up to 6 weeks in the 3 most severe cases. Due to intensity of skin reactions produced during induction, the challenge phase of the study was not conducted.

The study authors report that intense skin reactions seen in sixteen individuals during induction were considered to be sensitisation reactions. However, in the absence of a challenge phase, no reliable conclusions can be drawn from this study on the skin sensitisation potential of the test material.

Skin sensitisation in humans, using finished oil containing 16% analogue chemical (Harper et al, 1995).

In a Repeated Insult Patch Test in Humans, 89 individuals were tested for sensitivity to OLOA 270. The test chemical (100% finished oil containing 16% analogue chemical) was applied under semi-occlusive dressing to the upper arm for 24 h, on Mondays, Wednesdays and Fridays for 3 consecutive weeks. Treated sites were evaluated immediately before reapplication of test chemical.

Fourteen days after the end of the induction phase, the test chemical was applied to previously untreated sites, under semi-occlusive dressing for 24 h.

Two subjects exhibited mild erythema at the second and eighth induction visit, respectively. The responses resolved within the following two visits. One subject showed a skin reaction at the induction site immediately before the challenge application was made.

Challenge outcome: A sensitisation reaction was seen 96 hours after challenge in the subject showing a skin reaction immediately before challenge application. A confirmatory rechallenge was conducted in this subject 7 weeks after the initial challenge. A sensitisation reaction was again seen, 96 hours after challenge.

The finished oil containing 16% OLOA 270 was sensitising to the skin of humans.

Skin sensitisation in humans, using finished oils containing 7.6% analogue chemical (Buehler et al, 1997a)

In a Repeated Insult Patch Test in Humans, 24 subjects, 20 females and 4 males, aged 25-60 years were tested for sensitivity to OLOA 270. Nine repeated applications of test chemicals, 100% XF-2229 and XF-2235 (both containing 7.6% analogue chemical), were made over 3 weeks, under semi-occlusive dressing to the upper arm for 24 h each. Treated sites were evaluated before reapplication of test chemical.

Approximately 2 weeks after the end of the induction phase, the test chemicals were applied to previously untreated sites, under semi-occlusive dressing for 24 h.

Responses to both test oils were generally mild, with only transient mild erythema being observed during induction.

Challenge outcome: Responses to both test oils were generally mild, with only transient mild erythema being observed during challenge. Consequently, this study provides no robust evidence of a sensitisation reaction in any subject following challenge with the test material in either oil.

Skin sensitisation in humans, using finished oils containing 5.8% analogue chemical (Buehler et al, 1993b).

In a Repeated Insult Patch Test in Humans, 111 subjects, 85 females and 26 males, aged 21-60 years were tested for sensitivity to OLOA 270. Nine repeated applications of test chemicals, two finished oils (both containing 5.8% analogue chemical), were made over 3 weeks, under semi-occlusive dressing to the upper arm for 24 h each. Treated sites were evaluated before reapplication of test chemical.

Approximately 2 weeks after the end of the induction phase, test chemical was applied to previously untreated sites, under semi-occlusive dressing for 24 h.

Challenge outcome: There was no evidence of sensitisation reactions in any subjects following challenge with either test chemical.

Responses to both test oils were generally mild, with transient mild erythema being observed during induction and challenge phases.

The finished oils containing 5.8% OLOA 270 were not sensitising to the skin of humans.

9. Hazard Classification

This section discusses the classification of the health effects of OLOA 270 according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) which provide mandatory criteria for determining whether a workplace chemical is hazardous.

The classification for health effects is based on human data and experimental studies (animal and in vitro tests). The assessment conducted for NA/889 determined OLOA 270 to be hazardous based on the sensitisation effect of its analogue in human volunteers and classified as a skin sensitiser (R43) according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004).

The hazard classification based on the new data (ND) provided for the Secondary Notification for reproductive effects are presented below.

Classification of OLOA 270 in accordance with the Globally Harmonised System for Hazard Classification and Communications (GHS) (OECD, 2002) can be found in Appendix 1. This is provided for guidance only, is not mandatory and has no legal status at present.

9.1 Reproductive toxicity

According to the Approved Criteria, reproductive toxicity includes impairment of male and female reproductive functions or capacity, and the induction of non-heritable harmful effects on the progeny. Reproductive toxicity may be classified as effects on male or female fertility and developmental toxicity.

Fertility

Only animal data are available. The effects on fertility were investigated in a good quality oral two-generation study in the rat Section 7.5. At 1000 mg/kg (the top dose level) there was evidence of an effect on fertility: a significant though not dose-related decrease in pregnancy index seen for all mating phases, along with a reduction in litter size for the F0a and F1 mating phases. The reduction in litter size in F1 mating phase was dose related and statistically significant.

Systemic toxicity was observed only in males but these were not considered sufficient to account for the effects on fertility. Consequently, this study provides evidence of a direct effect on fertility that is not a secondary non-specific consequence of the other observed toxic effects.

The data causes a concern for human fertility and, consequently, classification as a Category 3 reproductive toxicant is warranted. In the absence of supporting evidence on the mechanism of action, site of action, chemical relationship to other known anti-fertility agents or information from humans, the data from this study is not considered to provide a strong presumption that human exposure to the chemical may result in impaired fertility i.e. Category 2 reproductive toxicant.

Classification: Based on the available animal data, OLOA 270 meets the Approved Criteria for Classifying Hazaradous Substances (NOHSC, 2004) for classification as a Category 3 reproductive toxicant, and the risk phrase R62 '*Possible risk of impaired fertility'* is applicable.

Developmental

In a developmental toxicity study in rats, no signs of developmental toxicity were observed following gavage of up to 1000 mg/kg/day of the test substance.

In addition, in an oral 2-generation study in rats there was no increase in post implantation embryo loss in the F0b mating phase. No effect on reflexological response was seen in those pups examined postnatally. While effects on time to completion of male sexual development and a corresponding increase in body weight were observed at some doses, this was not a dose dependent effect. Additionally, no effect on sexual development was seen in F0a females.

Classification: Based on the available animal data, OLOA 270 does not meet the Approved Criteria for Classifying Hazaradous Substances (NOHSC, 2004) for classification as a developmental toxicant.

10. Environmental Assessment

The following ecotoxicity studies have been previously supplied by the applicant and are included here for completeness. The tests were carried out to OECD Test Methods using a closely related structural analogue. The analogue was previously assessed by NICNAS as NA/253 and the results obtained for the structural analogue were considered to be equivalent to those which would be obtained with OLOA 270.

The following tests were carried out according to OECD Test Methods.

Species	**Test**	**Concentrations* (mg/L) (as WAF)**	**Result (mg/L) (as WAF)**
Rainbow trout *(Oncorhynchus mykiss)*	96 h acute	0 and 1000	NOEC ≥ 1000 (WAF)
Water Flea (*Daphnia magna*)	48 h acute	0 and 1000	NOEC ≥ 1000 (WAF)
Algae (*Selenastrum capricornutum*)	96 h growth	0, 62.5, 125, 250, 500 and 1000	E_RC50 > 370 E_BC50 > 340 NOEC = 250

* In the studies the water accommodated fraction (WAF) was prepared by stirring the mixtures of test chemical in water for 24 h, settling the mixtures for 1 h and siphoning off the water phase containing the WAF, while ensuring that no settled or surface floating test substance was transferred.

An acute toxicity study of the analogue chemical on rainbow trout was conducted according to OECD TG 203 (Douglas, 1993b). The study was conducted in duplicate with ten fish in each test vessel, at a 100% water accommodated fraction (WAF), ie 1000 mg/L, and a control. No mortality or sub-lethal effects were observed throughout the 96 h observation period. A no-observed effect concentration equal to or greater than 1000 mg/L (WAF) was identified.

An acute toxicity study of the analogue chemical on *Daphnia magna* was conducted according to OECD TG 202 (Douglas, 1993c). The study was conducted with a duplicate, control and in quadruplicate for the test concentration of 100% WAF, ie 1000 mg/L prepared as above, with ten daphnia in each test vessel. No immobilisation was observed throughout the 48 h observation period. A no-observed effect concentration equal to or greater than 1000 mg/L (WAF) was identified.

An algal growth inhibition study of the analogue chemical on unicellular green algae was conducted according to OECD TG 201 (Douglas, 1993d). Five concentrations (62.5, 125, 250, 500 and 1000 mg/L WAF) were tested in triplicate with one control (6 replicates). An aliquot of concentrated algal suspension was

added to each test vessel. The vessels were loosely stoppered and incubated for 72 h under a continuous illumination of 7000 lux, at 24°C and an oscillation of 100 cycles per minute. To determine growth, samples were taken at 0, 24, 28 and 72 h and the absorbance measured at 665 nm. The E_bC_{50} (72 hr) was 340 mg/L (WAF) and the E_rC_{50}(24-48 hr) was 370 mg/L (WAF). A no-observed effect concentration of 250 mg/L (WAF) was identified.

The ecotoxicity data for the analogue chemical indicated that OLOA 270 is not toxic to fish and daphnia up to the limit of its water solubility, but does show some toxicity to algae below this limit.

Release of OLOA 270 to the environment is expected only in the unlikely event of an accident during transport or an accidental leak. Very little waste is generated from lubricant formulation and use, and this waste is either incinerated or placed into landfill. Very little chemical is released from maintenance activities such as engine repair or from draining of the oil. OLOA 270 has a high log P_{OW} value and if released to the soil compartment becomes strongly associated with the organic component of soils and sediments and is not mobile in these media.

OLOA 270 is not readily biodegradable. However, when released to landfill or associated with soil, it slowly degrades through biotic and abiotic processes. This results in the formation of water, sulphides and oxides of carbon, with the calcium component associating with soil minerals. Incineration leads to water vapour and oxides of carbon and sulphur, with the calcium being assimilated into ash.

Based on the ecotoxicity data provided, OLOA 270 is not expected to be toxic to fish or daphnia up to the limit of its water solubility. Some toxicity to algae occurs below this limit. The high partition coefficient and low biodegradability of OLOA 270 indicate potential for bioaccumulation if spilt into waterways. However, very little of the chemical reaches the aquatic compartment and does not pose a hazard to aquatic organisms.

The environmental risk from OLOA 270 is considered low provided the material is used as a component of marine diesel engine lubricants and in hydraulic oils.

11. Risk Characterisation

OLOA 270 is a dark brown viscous liquid that is stable under normal conditions. It is sparingly soluble in water (83 ppm) and based on the high log P_{OW}, high hydrocarbon content and strong dispersant nature, is expected to strongly adsorb to the organic component of soils and sediments. It decomposes before boiling and is combustible in the presence of sufficient heat and oxygen.

The data provided in the original assessment indicated that OLOA 270 had very low acute toxicity (LD50 >5000 mg/kg). It was not a skin irritant but slight eye irritant and a skin sensitiser.

A NOAEL of 100 mg/kg bw/d was established in a 90-day repeat dose study based on adrenal toxicity.

The chemical was negative in gene mutation assays in Salmonella *typhimurium* and E.*coli*. In a chromosome aberration assay, no increase in the incidence of chromosomal damage was noted following treatment of CHO cells with the chemical analogue. Similarly, in an in vivo assay conducted in ICR mice, the test chemical was not clastogenic under the conditions of the test. These results indicated that OLOA 270 is not genotoxic.

Based on the data provided for the Secondary Notification, OLOA 270 has reproductive toxicity effects.

OLOA 270 is classified as a hazardous substance according to the Approved Criteria for Classifying Hazaradous Substances (NOHSC, 2004).

11.1 Occupational risk

Products containing OLOA 270 are formulated prior to import into Australia. The chemical is imported in drums as part of additive packages at concentrations ranging from 1% to 60%. These additive packages are then blended to form the final lubricating oil products. Worker exposure during transport is unlikely except in the event of a spill. The MSDSs for the additive packages, supplied by the notifier, provide instructions for clean-up following a spill.

Exposure to OLOA 270 may occur during loading/unloading and sampling/analysis activities. All tasks are of short duration and infrequent and workers are reported to wear coveralls, gloves and eye protection. Exposure during blending is unlikely as this is an automated process. Whole body exposure to a mist containing OLOA 270 may occur when delivery containers are being steam cleaned. Cleaning is of intermediate duration and is infrequent and the concentration of OLOA 270 in the mist is less than 1%.

Skin and eye contact with up to 15% OLOA 270 may occur via splashes, drips or spills when transferring the finished oils to the ship and during drum cleaning operations. Duration and frequency of tasks are likely to be comparable to those at blending plants. Overall exposure is likely to be negligible as the dermal absorption of OLOA 270 is very low. Risk of adverse effects such as systemic toxicity,

reproductive toxicity or eye irritation is considered to be low. However, exposure to the liquid must be prevented to protect against skin sensitisation.

Skin exposure to the lubricating oil containing up to 15% OLOA 270 is inevitable for mechanics engaged in maintenance and conducting repair. Duration and frequency of these activities may vary. Engineering controls to minimise exposure to lubricating fluids are unlikely to be in place in all repair workshops. Workers involved in the marine vessel repair industry are reportedly unlikely to use PPE and are expected to be repeatedly exposed to the chemical. Noting that skin sensitisation has been produced in humans when exposed to finished oil containing 7.6% OLOA 270, it is possible that individuals may become sensitised to OLOA 270. Employers will need to ensure that mechanics handling OLOA 270 are given the required health effects information and have the means to avoid repeated contamination with the chemical.

Overall, risk of adverse effects occurring to workers for most of the scenarios involving exposure to OLOA 270 is low. However, concern for skin sensitisation in mechanics working on marine vessels exists and care needs to be taken.

11.2 Public

OLOA 270 is used as a lubricant additive, primarily for use in marine vessels and is not available for sale to the public. Exposure of the public to OLOA 270 is considered to be low and consequently risk of adverse effects is low.

11.3 Environmental

Based on the ecotoxicity data provided, OLOA 270 was not expected to be toxic to fish or daphnia up to the limit of its water solubility. Some toxicity to algae occurs below this limit. The high partition coefficient and low biodegradability of OLOA 270 indicate the potential for bioaccumulation if spilt into waterways. However, very little of the chemical reaches the aquatic compartment and is therefore not a hazard to aquatic organisms.

The environmental risk from OLOA 270 is considered to be low during use as a component of marine diesel engine lubricants and in hydraulic oils. Release to the environment is expected only in the unlikely event of an accident during transport or an accidental leak. It is reported that minimal waste will be generated from lubricant formulation and use, and this waste will either be incinerated or placed into landfill.

Very little release occurs from maintenance activities/engine repair, from the draining of the oil or when incinerated or sent for recycling.

The chemical has a high log P_{OW} value and if released to the soil compartment becomes strongly associated with the organic component of soils and sediments and is not expected to be mobile in these media.

OLOA 270 is not readily biodegradable. However, if released to landfill or associated with soil, it degrades through biotic and abiotic processes. This results in the formation of water, sulphides and oxides of carbon, with the calcium component associating with soil minerals. Incineration leads to water vapour and oxides of carbon and sulphur, with the calcium being assimilated into ash.

12. Discussion and Conclusions

OLOA is a dark brown viscous liquid that is stable under normal conditions and sparingly soluble in water. OLOA 270 is imported as an ingredient in 'additive packages' at concentrations ranging from 1% to 60%. The primary use of OLOA 270 is as an ingredient in lubricants used in the marine vessels. The concentration of OLOA 270 in the lubricant oils ranges from 0.5 – 15%.

New data submitted for the secondary notification indicated that OLOA 270 has reproductive toxicity.

12.1 Health hazards

Based on the new data, OLOA 270 is classified as a hazardous chemical according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004) with the following risk phrases:

- R43 May cause sensitisation by skin contact
- R62 Possible risk of impaired fertility

The concentration cut-offs for mixtures containing OLOA 270 are:

Risk Phrases*	Concentration Cut-off
Xi, R43	≥1%Concentration<5%
Xn, R62; R43	Concentration≥5%

*Xn=Harmful; Xi=Irritant

The following safety phrases are also recommended:

S24 Avoid contact with skin

S36/37 Wear suitable protective clothing and gloves

This classification should be reflected in the ASCC's HSIS and should be adopted by industry on publication of this report.

For comparison purposes, OLOA 270 is classified as a hazardous substance under the Globally Harmonised System for Hazard Classification and Labelling of Chemicals (GHS), and would require appropriate labelling when this system is adopted in Australia (Appendix A).

OLOA 270 is not listed in the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (FORS, 1998).

12.2 Occupational risk

Exposure to OLOA 270 during occupational use is expected to be very low. Additionally, OLOA 270 has very low dermal absorption. Risk of systemic toxicity from OLOA 270 is therefore likely to be low

Overall, risk of adverse effects such as systemic or reproductive toxicityoccurring in workers is considered to be low. However, there is a high concern for skin sensitisation in mechanics working on marine vessels and workers need to wear appropriate protective equipment when handling the chemical.

12.3 Public risk

Public exposure to OLOA 270 is unlikely as it is not directly marketed to the public.

12.4 Environmental risk

No new data was provided on the ecotoxicity of OLOA 270. Based on the information provided for the original assessment. OLOA 270 was not expected to be toxic to fish or daphnia up to the limit of its water solubility. Environmental risk from OLOA 270 was considered to be low.

13. Secondary Notification

Under Section 65 of the Act, the Secondary Notification of OLOA 270 may be required where an applicant or other introducer (importer) or new manufacturer of OLOA 270, becomes aware of any circumstances that may warrant a reassessment of its hazards and risks. Specific circumstances include:

a. The use of OLOA 270 has changed, or is likely to change significantly.

b. Manufacture of OLOA 270 has begun, or is likely to begin in Australia.

c. Additional information has become available on the adverse health and/or environmental effects of OLOA 270.

The Director must be notified within 28 days of the introducer becoming aware of any of the above circumstances.

Appendix 1

Classification under the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

In this report, OLOA 270 has been classified against the *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 2004) and, in the case of physicochemical hazards, the *Australian Dangerous Goods Code* (ADG Code) (FORS, 1998). However, classifications under the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (OECD, 2002) will come into force when the GHS is adopted by the Australian Government and promulgated into Commonwealth legislation. GHS documentation is available at:

http://www.unece.org/trans/danger/danger.htm

GHS classification for OLOA 270.

Health Hazard	**Classification**	**Hazard Communication**
Skin sensitisation	Category 1	 **Signal Word:** Warning **Hazard Statement:** May cause an allergic skin irritation
Toxic to reproduction	Category 2	 **Signal Word:** Warning **Hazard Statement:** Suspected of damaging fertility or the unborn child

While OLOA 270 is not readily biodegradable, the acute toxicity for all three trophic levels is greater than 100 mg/L (based on the ecotoxicity data provided for the original assessment) and it is moderately water soluble, therefore under the GHS system OLOA 270 would not be classified for environmental effects. Based on the physical and chemical data for a structural analogue, OLOA 270 is not classified for physical/chemical effects.

Appendix 2

This MSDS was provided by Chevron Oronite Australia Pty Limited. It is reproduced here as a matter of public record. The format of this MSDS is acceptable under the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 2003). However the contents require updating as outlined in Overview and Recommendations of this report. The accuracy of this information remains the responsibility of the applicant.

Material Safety Data Sheet

SECTION 1 PRODUCT AND COMPANY IDENTIFICATION

OLOA 270

Company Identification
Oronite Australia Pty. Ltd.
ACN 101 548 716
Level 10, 45 William Street
Melbourne, Victoria 3000
Australia
03) 9629 7122

Transportation Emergency Response
Asia: Chevron Emergency Information Centre +(1) 510-231-0623
Australia: Oronite Australia 1 800 009 010
Europe: Oronite SA - Gonfreville Plant (33) 2 35 25 55 00
North America: CHEMTREC (800) 424-9300 or (703) 527-3887
South America: Chevron Oronite Brasil Ltda (24 h) 55 11 4478-1200
Health Emergency
Australia: 1 800 009 010
Product Information
Product Information: 03) 9629 7122
Product Compliance: 1 510 242 4434

Contact Person/Point
Emergency Coordinator
1 800 009 010 (24hr)

SECTION 2 HAZARDS IDENTIFICATION

Classification
HAZARDOUS SUBSTANCE according to the criteria of the NOHSC.
NON-DANGEROUS GOODS according to the criteria of the Australian Dangerous Goods Code (ADG Code) for transport by Road and Rail.

Symbols: Xn – Harmful

R62; Possible risk of impaired fertility.
R43; May cause sensitization by skin contact.
R53; May cause long-term adverse effects in the aquatic environment.
S36/37; Wear suitable protective clothing and gloves.
S61; Avoid release to the environment. Refer to special instructions/safety data sheets.

IMMEDIATE HEALTH EFFECTS
Eye: Not expected to cause prolonged or significant eye irritation. If this material is heated, thermal burns may result from eye contact.
Skin: Contact with skin is not expected to cause prolonged or significant irritation**.** Contact with the skin may cause an allergic skin reaction. Symptoms may include pain, itching, discoloration, swelling, and blistering. Not expected to be harmful to internal organs if absorbed through the skin. If this material is heated, thermal burns may result from skin contact.
Ingestion: Not expected to be harmful if swallowed.
Inhalation: Not expected to be harmful if inhaled. Contains a petroleum-based mineral oil. May cause respiratory irritation or other pulmonary effects following prolonged or repeated inhalation of oil mist at airborne levels above the recommended mineral oil mist exposure limit. Symptoms of respiratory irritation may include coughing and difficulty breathing.

DELAYED OR OTHER HEALTH EFFECTS:
Reproduction and Birth Defects: Contains material that may cause adverse reproductive effects upon repeated swallowing based on animal data.
Target Organs: Contains material that may cause damage to the following organ(s) if swallowed based on animal data: Liver.
See Section 11 for additional information. Risk depends on duration and level of exposure.

SECTION 3 COMPOSITION/ INFORMATION ON INGREDIENTS

COMPONENTS	CAS NUMBER	AMOUNT
Phenol, 2(or 4)-sec-C20-30-alkyl derivatives, reaction products with carbon dioxide, dist. residues from manuf. of phenol (tetrapropenyl) derivs., phenol (tetrapropenyl) derivs. and sulfur, calcium salts	220795-16-4	72 %weight
Highly refined mineral oil (C15 - C50)	Mixture	22 %weight
Branched alkylphenol and calcium branched alkylphenol	74499-35-7 & 132752-19-3	4 %weight

Note that the remaining composition contains nonhazardous ingredients or hazardous ingredients below the relevant threshold up to 100%.

SECTION 4 FIRST AID MEASURES

Eye: No specific first-aid measures are required. As a precaution, remove contact lenses, if worn, and flush eyes with water. If heated material should splash into eyes, flush eyes immediately with fresh water for 15 minutes while holding the eyelids open. Remove contact lenses, if worn. Get immediate medical attention.
Skin: Wash skin with water immediately and remove contaminated clothing and shoes. Get medical attention if any symptoms develop. To remove the material from skin, apply a waterless hand cleaner, mineral oil, or petroleum jelly. Then wash with soap and water. Discard contaminated clothing and shoes or thoroughly clean before reuse. If the hot material gets on skin, quickly cool in water. See a doctor for extensive burns. Do not try to peel the solidified material from the skin, or use solvents or thinners to dissolve it. The use of vegetable oil or mineral oil is recommended for removal of this material from the skin.
Ingestion: If swallowed, get medical attention. Do not induce vomiting. Never give anything by mouth to an unconscious person.
Inhalation: No specific first aid measures are required. If exposed to excessive levels of material in the air, move the exposed person to fresh air. Get medical attention if coughing

or respiratory discomfort occurs.

SECTION 5 FIRE FIGHTING MEASURES

HazChem Code: None Allocated

FIRE CLASSIFICATION (AS1940): C2 (Combustible Liquid).

EXTINGUISHING MEDIA: Use water fog, foam, dry chemical or carbon dioxide (CO2) to extinguish flames.

PROTECTION OF FIRE FIGHTERS:
Fire Fighting Instructions: This material will burn although it is not easily ignited. For fires involving this material, do not enter any enclosed or confined fire space without proper protective equipment, including self-contained breathing apparatus.
Combustion Products: Highly dependent on combustion conditions. A complex mixture of airborne solids, liquids, and gases including carbon monoxide, carbon dioxide, and unidentified organic compounds will be evolved when this material undergoes combustion. Combustion may form oxides of: Sulfur, Calcium.

SECTION 6 ACCIDENTAL RELEASE MEASURES

Protective Measures: Eliminate all sources of ignition in vicinity of spilled material.
Spill Management: Stop the source of the release if you can do it without risk. Contain release to prevent further contamination of soil, surface water or groundwater. Clean up spill as soon as possible, observing precautions in Exposure Controls/Personal Protection. Use appropriate techniques such as applying non-combustible absorbent materials or pumping. Where feasible and appropriate, remove contaminated soil. Place contaminated materials in disposable containers and dispose of in a manner consistent with applicable regulations. If heated material is spilled, allow it to cool before proceeding with disposal methods.
Reporting: Report spills to local authorities as appropriate or required.

SECTION 7 HANDLING AND STORAGE

Precautionary Measures: Do not get in eyes, on skin, or on clothing. Avoid contact of heated material with eyes, skin, and clothing. Wash thoroughly after handling.
General Handling Information: The maximum handling temperature is 90^{o}C. Avoid contaminating soil or releasing this material into sewage and drainage systems and bodies of water.
Static Hazard: Electrostatic charge may accumulate and create a hazardous condition when handling this material. To minimize this hazard, bonding and grounding may be necessary but may not, by themselves, be sufficient. Review all operations, which have the potential of generating and accumulating an electrostatic charge and/or a flammable atmosphere (including tank and container filling, splash filling, tank cleaning, sampling, gauging, switch loading, filtering, mixing, agitation, and vacuum truck operations) and use appropriate mitigating procedures. For more information, refer to OSHA Standard 29 CFR 1910.106, 'Flammable and Combustible Liquids', National Fire Protection Association (NFPA 77, 'Recommended Practice on Static Electricity', and/or the American Petroleum Institute (API) Recommended Practice 2003, 'Protection Against Ignitions Arising Out of Static, Lightning, and Stray Currents'.
General Storage Information: The maximum storage temperature is 65^{o}C.
Container Warnings: Container is not designed to contain pressure. Do not use pressure to empty container or it may rupture with explosive force. Empty containers retain product residue (solid, liquid, and/or vapor) and can be dangerous. Do not pressurize, cut, weld, braze, solder, drill, grind, or expose such containers to heat, flame, sparks, static electricity, or other sources of ignition. They may explode and cause injury or death. Empty containers should be completely drained, properly closed, and promptly returned to a drum reconditioner or disposed of properly.

SECTION 8 EXPOSURE CONTROLS/PERSONAL PROTECTION

GENERAL CONSIDERATIONS:
Consider the potential hazards of this material (see Section 3), applicable exposure limits, job activities, and other substances in the work place when designing engineering controls and selecting personal protective equipment. If engineering controls or work practices are not adequate to prevent exposure to harmful levels of this material, the personal protective equipment listed below is recommended. The user should read and understand all instructions and limitations supplied with the equipment since protection is usually provided for a limited time or under certain circumstances.

ENGINEERING CONTROLS:
Use in a well-ventilated area.

PERSONAL PROTECTIVE EQUIPMENT
Eye/Face Protection: No special eye protection is normally required. Where splashing is possible, wear safety glasses with side shields as a good safety practice. If this material is heated, wear chemical goggles or safety glasses or a face shield.
Skin Protection: Wear protective clothing to prevent skin contact. Selection of protective clothing may include gloves, apron, boots, and complete facial protection depending on operations conducted. Suggested materials for protective gloves include: Nitrile Rubber, Silver Shield, Viton. If this material is heated, wear insulated clothing to prevent skin contact if engineering controls or work practices are not adequate to prevent skin contact.
Respiratory Protection: No respiratory protection is normally required. If user operations generate an oil mist, determine if airborne concentrations are below the occupational exposure limit for mineral oil mist. If not, wear an approved respirator that provides adequate protection from the measured concentrations of this material. For air-purifying respirators use a particulate cartridge.
Use a positive pressure air-supplying respirator in circumstances where air-purifying respirators may not provide adequate protection.
Occupational Exposure Limits:

Component	Country/ Agency	TWA	STEL	Ceiling	Notation
Highly refined mineral oil (C15 - C50)	ACGIH	5 mg/m3	10 mg/m3	--	--
Highly refined mineral oil (C15 - C50)	NOHSC	5 mg/m3	--	--	--

Consult local authorities for appropriate values.

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

Attention: the data below are typical values and do not constitute a specification.

Color: Brown
Physical State: Liquid
Odor: No Data Available
Flashpoint: (Cleveland Open Cup) 180 °C (356 °F) Minimum
Autoignition: No Data Available
Flammability (Explosive) Limits: Lower: No data available
Upper: No data available
pH: Not Applicable
Vapor Pressure: 0.00017 Pa (Estimated) @ 25 °C (77°F)
Vapor Density (Air=1): No data available
Boiling Point: No Data Available
Solubility: 40.9 mg/l in water.
Freezing Point: No Data Available
Density: 1.046 kg/l @ 15°C (59°F)
Viscosity: 7200 cSt @ 40°C (104°F)
Coefficient of Therm. Expansion / °F: 0.00034

SECTION 10 STABILITY AND REACTIVITY

Chemical Stability: This material is considered stable under normal ambient and anticipated storage and handling conditions of temperature and pressure.
Conditions to Avoid: Do not heat above flash point.
Incompatibility With Other Materials: May react with strong acids or strong oxidizing agents, such as chlorates, nitrates, peroxides, etc.
Hazardous Polymerization: Hazardous polymerization will not occur.

SECTION 11 TOXICOLOGICAL INFORMATION

IMMEDIATE HEALTH EFFECTS

Eye Irritation: The eye irritation hazard is based on evaluation of data for similar materials or product components.

Skin Irritation: The skin irritation hazard is based on evaluation of data for similar materials or product components.

Skin Sensitization: The skin sensitization hazard is based on evaluation of data for similar materials or product components. This material is not expected to cause allergic skin reactions when formulated in a finished oil at the prescribed treatment rate of: 5.8 wt. %.

Acute Dermal Toxicity: The acute dermal toxicity hazard is based on evaluation of data for similar materials or product components.

Acute Oral Toxicity: The acute oral toxicity hazard is based on evaluation of data for similar materials or product components.

Acute Inhalation Toxicity: The acute inhalation toxicity hazard is based on evaluation of data for similar materials or product components.

ADDITIONAL TOXICOLOGY INFORMATION:

This product contains petroleum base oils, which may be refined by various processes including severe solvent extraction, severe hydrocracking, or severe hydrotreating. None of the oils requires a cancer warning under the OSHA Hazard Communication Standard (29 CFR 1910.1200). These oils have not been listed in the National Toxicology Program (NTP) Annual Report nor have they been classified by the International Agency for Research on Cancer (IARC) as; carcinogenic to humans (Group 1), probably carcinogenic to humans (Group 2A), or possibly carcinogenic to humans (Group 2B). These oils have not been classified by the American Conference of Governmental Industrial Hygienists (ACGIH) as: confirmed human carcinogen (A1), suspected human carcinogen (A2), or confirmed animal carcinogen with unknown relevance to humans (A3).

Contains an overbased calcium branched and linear alkyl phenate/salicylate sulfide.

Skin Absorption: In an in vitro study using radio-labeled material and human skin, absorption was 0.1µg/cm2/hr. Skin absorption was also minimal in in vitro and in vivo studies with rats.

Reproductive Toxicity: In a rat oral two-generation reproductive toxicity study at 50, 250, or 1000 mg/kg/day, parental toxicity (reduced body weights and food consumption, increased liver and kidney weights, altered hematology) occurred at >= 250 mg/kg/day. Reduced numbers of litters and reduced live litter size were observed at 1000 mg/kg/day. There were no effects on offspring viability or growth, but time to sexual maturation in males was slightly increased at >= 250 mg/kg/day.

Developmental toxicity: No adverse effects were observed in oral developmental toxicity studies in rats at 100, 500 or 1000 mg/kg/day and in rabbits at 50, 150, or 450 mg/kg/day. Maternal body weight gain was reduced in the high dose group for rats and for rabbits.

Contains a branched alkylphenol and a calcium branched alkylphenol.

Repeated Dose Toxicity: In female rats dosed orally at 5, 20, 60, 250 or 1000 mg/kg/day for 20 days, time to sexual maturation was decreased and organ weights (ovary, uterus, liver and adrenal) were altered at >= 60 mg/kg/day. In a 28-day oral

study in rats at 5, 20, 60, 180 and 300 mg/kg/day, body weight gain was decreased in males and food consumption was decreased in both sexes at >= 180 mg/kg/day. At >= 180 mg/kg/day, effects on reproductive organs in both sexes did not completely recover by 14 days post-treatment. Liver and adrenal changes occurred at >= 20 mg/kg/day. Thyroid hypertrophy occurred in males in all treated groups but did not persist through 14 days post-treatment.

Reproductive Toxicity: Based on preliminary results of a rat oral one-generation reproductive toxicity study at 0, 5, 25 and 125 mg/kg/day, parental toxicity was observed at 25 and 125 mg/kg/day in males and 125 mg/kg/day in females (reduced body weights, body weight gain). Although there were no differences in time to mating or proportion that mated, in the 125 mg/kg/day group there was an increased incidence of abnormal estrous cyclicity, and decreased fertility index, number of pups born, live litter size, postnatal survival, and pup growth. At 25 mg/kg/day, pup growth was reduced.

Developmental Toxicity: In an oral rat developmental study at 20, 100, and 300 mg/kg/day, maternal weight gains were reduced during gestation and post-dosing at 300 mg/kg/day. At 300 mg/kg/day, there were increased incidences of fetal structural effects and reduced fetal body weights.

SECTION 12 ECOLOGICAL INFORMATION

ECOTOXICITY

This material is expected to be toxic to aquatic organisms. The product has not been tested. The statement has been derived from the properties of the individual components.

MOBILITY

No data available.

PERSISTENCE AND DEGRADABILITY

May cause long-term adverse effects in the aquatic environment. The product has not been tested. The statement has been derived from the properties of the individual components.

SECTION 13 DISPOSAL CONSIDERATIONS

Use material for its intended purpose or recycle if possible. This material, if it must be discarded, may meet the criteria of a hazardous waste as defined by international, country, or local laws and regulations.

SECTION 14 TRANSPORT INFORMATION

The description shown may not apply to all shipping situations. Consult 49CFR, or appropriate Dangerous Goods Regulations, for additional description requirements (e.g., technical name) and mode-specific or quantity-specific shipping requirements.

HazChem Code: None Allocated

ADOT Shipping Description: NOT REGULATED AS DANGEROUS GOODS FOR ROAD OR RAIL TRANSPORT UNDER THE ADG CODE.

IMO/IMDG Shipping Description: NOT REGULATED AS DANGEROUS GOODS FOR ROAD OR RAIL TRANSPORT UNDER THE IMDG CODE.

ICAO/IATA Shipping Description: NOT REGULATED AS DANGEROUS GOODS FOR ROAD OR RAIL TRANSPORT UNDER ICAO

SECTION 15 REGULATORY INFORMATION

REGULATORY LISTS SEARCHED:

01-1=IARC Group 1

01-2A=IARC Group 2A
01-2B=IARC Group 2B

No components of this material were found on the regulatory lists above.

CHEMICAL INVENTORIES:

All components comply with the following chemical inventory requirements: DSL (Canada), ENCS (Japan), IECSC (China), KECI (Korea), PICCS (Philippines), TSCA (United States).

One or more components have been notified but may not be listed in the following chemical inventories: AICS (Australia). Secondary notification by the importer may be required.

One or more components is listed on ELINCS (European Union). Secondary notification by the importer may be required.

SECTION 16 OTHER INFORMATION

Poisons Schedule Number: None allocated.

REVISION STATEMENT: This revision updates the following sections of this Material Safety Data Sheet: 2.
Revision Date: October 30, 2006

ABBREVIATIONS THAT MAY HAVE BEEN USED IN THIS DOCUMENT:

TLV - Threshold Limit Value	TWA - Time Weighted Average
STEL - Short-term Exposure Limit	PEL - Permissible Exposure Limit
	CAS - Chemical Abstract Service Number
ACGIH - American Conference of Government Industrial Hygienists	IMO/IMDG - International Maritime Dangerous Goods Code
API - American Petroleum Institute	MSDS - Material Safety Data Sheet
CVX - Chevron	NFPA - National Fire Protection Association (USA)
DOT - Department of Transportation (USA)	NTP - National Toxicology Program (USA)
IARC - International Agency for Research on Cancer	OSHA - Occupational Safety and Health Administration

Prepared according to the National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011(2003)] by the Chevron Energy Technology Company, 100 Chevron Way, Richmond, California 94802.

The above information is based on the data of which we are aware and is believed to be correct as of the date hereof. Since this information may be applied under conditions beyond our control and with which we may be unfamiliar and since data made available subsequent to the date hereof may suggest modifications of the information, we do not assume any responsibility for the results of its use. This information is furnished upon condition that the person receiving it shall make his own determination of the suitability of the material for his particular purpose.

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