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09 September 2008

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

GTL Residual Base Oil

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

For the purposes of subsection 78(1) of the Act, this Full Public Report may be inspected at our NICNAS office by appointment only at 334-336 Illawarra Road, Marrickville NSW 2204.

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

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Director
NICNAS

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GTL Residual Base Oil

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Sasol Chevron Consulting Limited (ABN 46 096 439 404)
Level 15, QV1 Building
250 Georges Terrace
Perth WA 6000

The Shell Company of Australia Limited (ABN 46 004 610 459)
8 Redfern Road
East Hawthorn VIC 3123

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Chemical name, other names, CAS number, molecular formula, structural formula, molecular weight, spectral data, manufacture/import volume, identity of sites, identity of analogues

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Acute dermal toxicity, acute inhalation toxicity, skin irritation, eye irritation, skin sensitisation, repeat dose toxicity, genotoxicity, biodegradability, acute fish toxicity, acute *Daphnia* toxicity, and acute algal toxicity.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
US, Canada, Korea, European Union

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
GTL Residual Base Oil
FTBO Residual
F-T Residual Base Oil

MOLECULAR WEIGHT
MW < 1000 Da,

ANALYTICAL DATA
Reference NMR and IR spectra were provided.

3. COMPOSITION

The notified chemical is a complex mixture of hydrocarbons. The level of aromatic hydrocarbons is very low (≤ 1%) and benzene is essentially absent (≤ 0.1%).

4. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE AT 20°C AND 101.3 kPa: extremely pale yellow, slightly viscous liquid with petroleum odour.

Property	Value	Data Source/Justification
Pour point	< -20°C	Measured
Boiling Point	162-339°C at 102.2 kPa (possible decomposition) > 522°C	Measured Modelled
Density	833 kg/m^3 at 20°C	Measured
Vapour Pressure	1.2 x 10^{-11} kPa at 25°C	Measured
Viscosity	13 x 10^{-6} m^2/s (13 cSt) at 100°C	MSDS
Water Solubility	< 1 mg/L at 20°C	The notified chemical is a mixture of hydrocarbons. Individual components have solubilities below 0.01 mg/L.
Hydrolysis as a Function of pH	Stable	The hydrocarbon components in the notified chemical have no hydrolysable functionality.
Partition Coefficient (n-octanol/water)	log Pow > 7 at 20°C	Estimated based on the high molecular weight.
Adsorption/Desorption	Not determined	The notified chemical is a mixture of hydrophobic hydrocarbons that would be immobile in soils.
Dissociation Constant	Not determined	No dissociable functionality.
Particle Size	Not determined	Notified chemical is a liquid
Flash Point	221°C at 101.3 kPa	Measured
Flammability in air	Not determined	Based on the flash point the notified chemical is not expected to form a flammable vapour/air mixture
Autoignition Temperature	388°C	Measured
Explosive Properties	Not expected to be explosive	Estimated based on chemical structure

DISCUSSION OF PROPERTIES

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

Based on the measured flash point the notified chemical is not classified as flammable, but would be considered to be a C2 combustible liquid [NOHSC:1015(2001)].

Reactivity

The notified chemical is not expected to react with water or air, and is considered to be stable under normal use conditions.

5. INTRODUCTION AND USE INFORMATION

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

The notified chemical will be manufactured overseas from natural gas using the Fischer-Tropsch process. The notified chemical (100%) will be imported into Australia as only one grade (H).

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	500-1,000	500-1,000	500-1,000	500-1,000	500-1,000

PORT OF ENTRY

The port of entry is likely to be any major Australian port where a petroleum refinery or a major lube blending facility is located, eg Adelaide, Perth, Sydney, etc.

IDENTITY OF RECIPIENTS

Lubricant manufacturers around Australia.

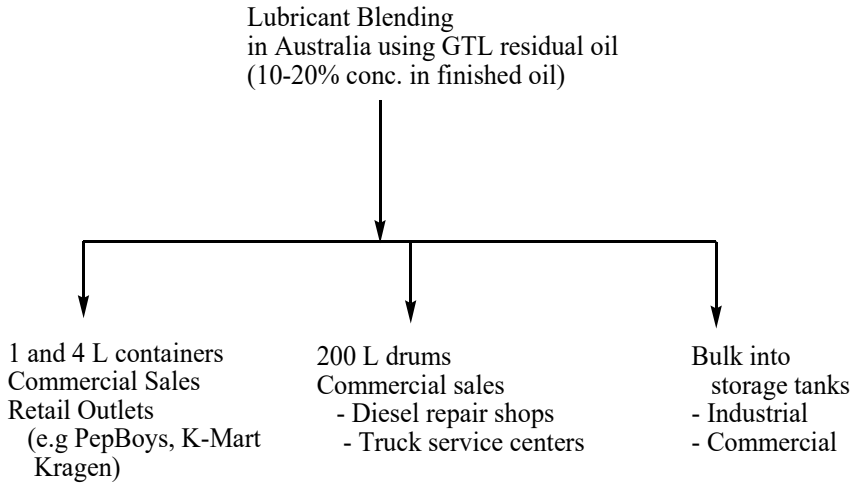
TRANSPORTATION AND PACKAGING
The notified chemical will be imported as bulk oil and transported by tank truck to formulation sites. The blended lubricant products containing the notified chemical will be packaged in 200 L drums, 20 L pails, 4 L jugs or 1 L cans, and will be transported by truck.

USE
The notified chemical will be used as a base stock for lubricants used for heavy duty diesel engine oils.

OPERATION DESCRIPTION
The notified chemical is not manufactured in Australia. It is imported as the bulk oil and transported to customer sites (lubricant reformulators).

Lubricant reformulation
At the lubricant reformulation site 10 cm hoses are connected to the tank truck and storage vessels and the notified chemical is transferred via a pumping system. An air back flush system is used to prevent spillage. The notified chemical is then transferred (usually via hard piping) to the blending vessel as required. The blending process is largely enclosed, except for sampling for quality control purposes. After blending the finished lubricant (containing 10-20% notified chemical) is transferred (usually via hard piping) to a storage tank for subsequent packaging into drums or small containers (1 and 4 L). The drumming facility uses automated weight scales to fill the drums. The operator watches (from about 3-6 feet away) to ensure the drum filling mechanism properly enters the drum before the drum is filled, and then attaches the bungs and labels. The small container packaging is a fully automated process. The operator watches (from about 3-6 feet away) to ensure the filling mechanism properly enters the container before it is filled.

End use
The finished lubricant products (10-20% notified chemical) will be used at different end use sites, as detailed in the figure below.



The small containers of lubricant will be sold to the public who will use it to top off the engine oil sump in the engine compartment of their diesel cars and trucks. The 200 L drums will be sold to workplaces such as automotive repair shops, automobile dealer service centres, service stations, and quick lubes. In these workplaces the finished lubricant product is added to engines using pneumatic delivery equipment. The bulk finished lubricants are transported in tank trucks to major diesel truck manufactures, large diesel fleets, as well as mining, agriculture and marine operations. The bulk lubricant unloading at these sites involves the connection of a 4-inch line to the truck and removal of the line after completion of the transfer. A vacuum back flush removes the lubricant from the unloading hoses, which are then capped to prevent spillage. The lubricant product is transferred from the on-site storage tank to the engines using pneumatic delivery equipment.

6. HUMAN HEALTH IMPLICATIONS

6.1 Exposure assessment

6.1.1 Occupational exposure

NUMBER AND CATEGORY OF WORKERS

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Lubricant reformulation	15	10 hours/day	240 days/year
Transport	50-100	1 hour/shipment	240 days/year
Repair Shop mechanics	5000	8 hours/day	240 days/year
Engine mechanics	2000	8 hours/day	240 days/year
Drum Cleaning	20	8 hours/day	240 days/year

EXPOSURE DETAILS

Transport

Dermal and accidental ocular exposure may occur due to drips, spills and splashes during the connection and disconnection of transfer hoses. This exposure is likely to be minimised by the engineering controls (vacuum back flush and hose caps) and the use of personal protective equipment (coveralls, gloves and safety glasses).

Lubricant Reformulation

While the blending of lubricants is a highly automated and enclosed process, there is some potential for exposure of workers involved in blending operations using the notified chemical. Dermal and accidental ocular exposure to the notified chemical (neat or 10-20% concentration) may occur due to drips, spills and splashes during quality control sampling and analysis, as well as during drum filling if worker intervention is required. This exposure is likely to be minimised by the use of personal protective equipment, including protective clothing, gloves and safety glasses. Inhalation of the notified chemical vapour is unlikely given its low volatility. Although oil mists of the notified chemical may be generated, exposure is expected to be limited due to the enclosed nature of the blending operation.

Use

Dermal exposure to the finished lubricant products (10-20% notified chemical) may occur during commercial and industrial applications, although this will be minimised by the pneumatic delivery system and the expected use of personal protective equipment (coveralls, gloves). However, personal protective equipment may not be used in all workplaces, particularly the smaller repair shops. Inhalation exposure will be limited under normal operating conditions.

6.1.2. Public exposure

It is expected that during transport, storage, blending and industrial use, exposure of the general public to the notified chemical will be minimal, except in the event of an accidental spill.

Finished lubricants (containing 10-20% of the notified chemical) will reach the public retail market, where they will be used to replace or top-up automotive lubricants. Consequently, there is likely to be intermittent dermal exposure, with the potential for accidental eye, oral and inhalation exposure. Accidental ingestion by children is also a possibility.

6.2. Human health effects assessment

The results from toxicological investigations conducted on the notified chemical and analogue chemicals are summarised in the tables below. Analogue data is listed only for endpoints for which there were no data on the notified chemical. The analogue chemicals are petroleum-derived residual base oils, as well as petroleum-derived fractions in which the alkanes are within the defined carbon range of the notified chemical. Details of these studies can be found in Appendix B.

Notified chemical

Endpoint	*Result and Assessment Conclusion*
Rat, acute oral toxicity	oral LD50 > 5000 mg/kg bw low toxicity
Mutagenicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro micronucleus	non genotoxic

Analogue chemicals

Endpoint	*Result and Assessment Conclusion*
Rat, acute dermal toxicity	LD50 >2000 mg/kg bw low toxicity
Rat, acute inhalation toxicity	LC50 > 5 mg/L/4 hour low toxicity
Rabbit, skin irritation	non-irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation – non-adjuvant test.	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOEL = 1000 mg/kg bw/day
Genotoxicity – in vivo mouse micronucleus	non genotoxic

Toxicokinetics, metabolism and distribution
Absorption is unlikely due to the high molecular weight of the hydrocarbons in the notified chemical. After oral administration unabsorbed hydrocarbons will be excreted in the faeces.

Acute toxicity
The notified chemical was found to be of low toxicity via the oral route and, based on studies conducted on an analogue chemical, the notified chemical is expected to be of low toxicity via the dermal and inhalation routes. The notified chemical is not expected to pose a significant aspiration hazard due to the viscosity (13 cSt at 100°C).

Irritation and Sensitisation
Based on studies conducted on an analogue chemical, the notified chemical is expected to be at most slightly irritating to skin and eye, and to not be a skin sensitiser.

Repeated Dose Toxicity
A number of repeat dose studies (oral, dermal and inhalation) have been conducted on analogue chemicals of varying purities and carbon ranges. Based on the weight of evidence the notified chemical is expected to have low systemic toxicity, although adverse effects could arise with repeated inhalation exposure to significant amounts.

Mutagenicity
The notified chemical was found to be non-mutagenic to bacteria and non-clastogenic to human lymphocytes when tested in vitro. An in vivo murine micronucleus study conducted on an analogue chemical found no indication of genotoxicity, although it was not clear whether the test substance was reaching the target organ (bone marrow).

Classification
Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004).

The analogous petroleum derived residual base oil is classified as a carcinogen (category 2). However, this classification is based on the amount of aromatic hydrocarbons (including benzene), which are present as impurities due to the fact that the base oil is refined from a natural source. The notified chemical is derived from the 'Gas-to-Liquid' process, which is a synthetic process that produces aliphatic hydrocarbons. Therefore the aromatic content of the notified chemical is much lower (≤ 1%, essentially no benzene). The notified chemical is therefore considered to not require classification as a carcinogen.

6.3. Human health risk characterisation

6.3.1. Occupational health and safety

The toxicological profile does not identify any significant hazard after acute exposure and repeated or prolonged exposure will be unlikely to result in any systemic toxicity, although repeated inhalation exposure to oil mists may lead to adverse pulmonary effects. Inhalation exposure to oil mists is expected to be limited under normal operating conditions due to the enclosed processes. Dermal and accidental ocular exposure to the notified chemical may occur during transport, reformulation and use, although this is likely to be minimised by the engineering controls and personal protective equipment expected to be in use in the majority of workplaces. Therefore, the risk to workers involved in reformulation, use, transport and storage or disposal of the notified chemical is considered to be low.

6.3.2. Public health

DIY enthusiasts may be exposed to the notified chemical in reformulated lubricants, but this exposure is likely to be infrequent (a few times a year). The generation of aerosols during public use of the notified chemical in reformulated products is not expected, and therefore exposure to oil mists is unlikely. Due to the low hazard identified in the toxicological profile together with low exposure, the risk of adverse health effects is considered to be low.

7. ENVIRONMENTAL IMPLICATIONS

7.1. Environmental Exposure & Fate Assessment

7.1.1 Environmental Exposure

RELEASE OF CHEMICAL AT SITE

The notified chemical will be synthesised overseas and imported into Australia. Environmental exposure to the notified chemical is expected to be limited to small amounts (a few grams) that remain on the surface of hoses used to transfer the notified chemical at lubricant blending facilities.

RELEASE OF CHEMICAL FROM USE

Small amounts of waste are expected to be produced at lubricant blending facilities. These will undergo on-site treatment as outlined below.

The notified chemical is not expected to be released during use as an engine lubricant. It will be partially combusted in the engine's combustion chamber.

RELEASE OF CHEMICAL FROM DISPOSAL

Used oil from oil changes and engine maintenance will be disposed of at used oil recycling centres. Residues in small containers used by the general public will be disposed of to landfill, where they are expected to remain immobile and degrade slowly. Residues in larger drums used by commercial establishments will be removed when the drums are cleaned, usually with steam, and discharged to on-site wastewater treatment facilities. These residues will undergo oil-water separation, pond aeration, bio-disk and sand filtration before discharge of the aqueous effluent to sewer. Residual oily waste will be incinerated or disposed of at used oil recycling centres.

There could be some illegal disposal of the notified chemical to stormwater by DIY enthusiasts who change their own engine oil. For petrol driven vehicles, this has been estimated to remain below 1% (see STD 1276). While expected to be lower for diesel engines, this value will be used for a conservative estimation of the PEC.

7.1.2 Environmental fate

As the base oils are hydrophobic hydrocarbons with long carbon chain lengths and low volatility, they are expected to partition to solid media such as soils and sediments, where they will slowly biodegrade. Aquatic and atmospheric exposures are expected to remain minimal.

No data for this fraction have been provided, but in line with the fraction notified as STD 1276, the individual components of the notified chemical are not expected to be readily biodegradable. The notified chemical should be inherently biodegradable. This conclusion is based on the established behaviour of analogue lubricant oil basestocks derived from petroleum, which have a very similar chemical composition apart from their much

higher aromatic hydrocarbon content (CONCAWE, 1997).

The notified chemical is not expected to be significantly bioaccumulated by aquatic organisms, based on the established behaviour of petroleum derived analogues, including the very low absorption of large hydrocarbon molecules through biological membranes, and the very low levels of exposure expected for dissolved residues of the notified chemical.

7.1.3 Predicted Environmental Concentration (PEC)

The notified chemical would be expected to float and spread following accidental introduction into aquatic environments, with adsorption to sediment the major fate process.

A worst case estimated PEC might be calculated if it is assumed that 1% of the notified chemical (maximum 10 tonnes) is released into stormwater drains in a single metropolitan area with a geographical footprint of 500 km^2 and an average annual rainfall of 500 mm, all of which drains to stormwater. With a maximum annual release into this localised stormwater system of 10000 kg and the annual volume of water drained from this region estimated to be approximately 250 x 10^6 m^3, the resultant PEC is approximately 40 µg/L. It should be stressed that this result is very much a worst case scenario, and that in reality releases of the chemical would be very much more diffuse than indicated here, and also at significantly reduced levels.

7.2. Environmental effects assessment

The results from ecotoxicological investigations conducted on petroleum derived analogues of the notified chemical are summarised in the table below. These acute studies were conducted on water accommodated fractions or oil in water dispersions. Results are reported as loadings rather than concentrations. The data are summarised from CONCAWE (1997) and reflect the lower solubility compared with the lighter fraction notified as STD 1276.

Endpoint	*Result*	*Assessment Conclusion*
Fish Toxicity	LL50 > 5000 mg/L	Nontoxic to the limit of water solubility
Daphnia Toxicity	EL50 > 10000 mg/L	Nontoxic to the limit of water solubility
Algal Toxicity	IL50 > 1000 mg/L	Nontoxic to the limit of water solubility

The results from testing on analogue lubricant oils indicate that the notified chemical is likely to be nontoxic (to the limit of water solubility) to fish, aquatic invertebrates and algae. However, harmful effects may be expected on aquatic life from large spills of the notified chemical, as undissolved oil will cause direct physical fouling of aquatic organisms and may reduce dissolved oxygen levels in the polluted water.

7.2.1 Predicted No-Effect Concentration

Predicted No-Effect Concentration (PNEC) for the Aquatic Compartment		
Lowest median effect loading (algae)	1000	mg/L
Assessment Factor	100	
Mitigation Factor	1.00	
PNEC:	10000	µg/L

7.3. Environmental risk assessment

The risk quotient, or the ratio of the PEC to the PNEC, is 0.004, indicating a low risk to the environment under the conservative assumptions used to establish the PEC.

The notified chemical is not expected to present a risk to the environment, except when spilt in large quantities to water, as aquatic exposure is expected to be minimal, and the notified chemical is practically nontoxic to fish, aquatic invertebrates and algae.

8. CONCLUSIONS AND REGULATORY OBLIGATIONS

Hazard classification
Based on the available data the notified chemical is not classified as hazardous under the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)].

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

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

Environmental risk assessment
On the basis of the expected minimal aquatic exposure and absence of aquatic toxicity, and the reported use pattern, the notified chemical is not considered to pose a risk to the environment.

Recommendations

CONTROL MEASURES
Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Local and/or general ventilation indoor where the enclosed processes do not adequately control airborne levels

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid generation of aerosols (oil mists)

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  - Respiratory protection, if significant inhalation to oil mists is expected

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

- The notified chemical as introduced should be handled consistent with provisions of State and Territory legislation regarding the Handling of Combustible and Flammable Liquids.

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

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(2004)] workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Disposal

- The notified chemical should be disposed of by landfill.

Storage

- The notified chemical as introduced should be stored consistent with provisions of State and Territory legislation regarding the Storage of Combustible and Flammable Liquids.

Emergency procedures

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

Regulatory Obligations

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

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

(1) Under Section 64(2) of the Act; if
- the function or use of the chemical has changed from a base stock for lubricants, or is likely to change significantly;
- the amount of chemical being introduced has increased from 1,000 tonnes, or is likely to increase, significantly;
- if the chemical has begun to be manufactured in Australia;
- additional information has become available to the person as to an adverse effect of the chemical on occupational health and safety, public health, or the environment.

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

No additional secondary notification conditions are stipulated.

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

APPENDIX A: PHYSICAL AND CHEMICAL PROPERTIES

Pour Point < -20°C

Method	BS 2000: Part 15 (equivalent to ISO 3016) EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	No pour point was determined down to a temperature of -20°C
Test Facility	Safepharm Laboratories (2006a)

Boiling Point 162-339°C at 102.2 kPa (measured)
>522°C (modelled)

Method	ASTM D 86, Standard Test Method for Distillation of Petroleum Products at Atmospheric Pressure
Remarks	A theoretical value of the boiling point for the notified chemical was calculated using the proprietary modelling software SIMSCI Pro II. This value (>522°C) was considered by the notifier to fit with their knowledge of the product and process. The initial measurement of the boiling point range was determined in the SafePharm Laboratories using the distillation method according to EC Directive 92/69/EEC A.2 Boiling Temperature. In this initial test approximately 92% of the test material boiled in the range of 65.0 to 286°C. However it was considered by the test laboratory that this method was not appropriate for test materials of this nature. Therefore the boiling point range was determined at Shell Research Ltd (non-GLP) using the ASTM D 86 method. This method uses specific apparatus that controls heating rate, temperature of the condenser and temperature of the collection vessel. These parameters are very specific for a particular petroleum product type and can have a significant effect on the boiling temperatures obtained. However the value obtained from this method was also considered to be lower than expected. It is thought that this is due to decomposition (cracking) during the analysis, leading to the low boiling point fractions observed. It was noted that the notified chemical is a residual product and therefore is not distilled during manufacture. It was also noted that the ASTM D86 method is usually only considered suitable for products up to the diesel boiling point range.
Test Facility	Safepharm Laboratories (2006a)

Density 833 kg/m^3 at 20°C

Method	EC Directive 92/69/EEC A.3 Relative Density.
Remarks	The density was determined using the pycnometer method.
Test Facility	Safepharm Laboratories (2006a)

Vapour Pressure 1.2 x 10^{-11} kPa at 25°C

Method	EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks	The vapour pressure was determined using the vapour pressure balance method followed by linear regression analysis to calculate the vapour pressure at 25°C. The test material did not change in appearance under the conditions of the test.
Test Facility	Safepharm Laboratories (2006b)

Flash Point 221°C at 101.3 kPa

Method	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	The flash point was determined using the closed cup equilibrium method.
Test Facility	Safepharm Laboratories (2006b)

Autoignition Temperature 388°C

Method	EC Directive 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	No significant protocol deviations.

Test Facility Safepharm Laboratories (2006b)

APPENDIX B: TOXICOLOGICAL INVESTIGATIONS

Choice of analogue data

For endpoints where information was available on the notified chemical only this data was considered. Analogue 1 was considered to be the most suitable analogue as it represented the species with the lowest molecular weights in the notified chemical. Therefore for endpoints where data was available on Analogue 1 no other analogue data was considered. However, for endpoints where no information was available either on the notified chemical or Analogue 1, data for lower molecular weight analogues were considered, along with data from the CONCAWE product dossier (1997) for lubricating oil base stocks (petroleum derived distillates).

B.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 420 Acute Oral Toxicity: Fixed Dose Procedure. EC Directive 2004/73/EC B.1 bis Acute Oral Toxicity – Fixed Dose Procedure
Species/Strain	Rat/ Sprague-Dawley CD
Vehicle	None, test substance administered as supplied
Remarks - Method	No significant protocol deviations. Five females were dosed at 5000 mg/kg bw.
RESULTS	
LD50	> 5000 mg/kg bw
Signs of Toxicity	There were no mortalities or clinical observations indicating systemic toxicity, and all animals showed the expected gains in bodyweight over the study period.
Effects in Organs	No abnormalities were noted at necropsy.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Safepharm Laboratories (2007a)

B.2. Acute toxicity – dermal

A study conducted on Analogue 1 (a petroleum derived fraction consisting of hydrocarbons at the lower end of the molecular weight range of the notified chemical) was conducted in accordance with OECD TG 402 Acute Dermal Toxicity, and was GLP compliant. No signs of local or systemic toxicity were observed at any point and so the LD50 was considered to be > 2000 mg/kg bw (Safepharm Laboratories, 1995a).

B.3. Acute toxicity – inhalation

A study conducted on Analogue 1 was conducted in accordance with OECD TG 403 Acute Inhalation Toxicity, and was GLP compliant. This study was limit dose (5 mg/L) using nose-only, four hour exposure. No deaths occurred and so the LD50 is considered to be > 5 mg/L (Safepharm Laboratories, 1995b).

B.4. Irritation – skin

A study conducted on Analogue 1 was conducted in accordance with OECD TG 404 Acute Dermal Irritation/Corrosion, and was GLP compliant. After a four hour exposure no skin reactions were observed in any of the 6 animals tested (Safepharm Laboratories, 1995c).

B.5. Irritation – eye

A study conducted on Analogue 1 was conducted in accordance with OECD TG 405 Acute Eye Irritation/Corrosion, and was GLP compliant. Conjunctival redness was observed in 1/6 animals 1 hour after treatment. No other ocular effects were observed during the study period (Safepharm Laboratories, 1995d).

B.6. Skin sensitisation

A non-adjuvant study (Buehler test) on Analogue 1 was conducted in guinea pigs and was GLP compliant. After challenge with undiluted test material the incidence of skin reactions (only slight, patchy erythema) was comparable between the control and test groups, indicating that sensitisation had not been induced (Hill Top Biolabs, 1995).

B.7. Repeat dose toxicity

Repeat dose studies (28 day, oral gavage, Sprague-Dawley rats) have been conducted on Analogues 2 and 3 (petroleum derived alkanes with molecular weights lower than that found in the notified chemical). These studies were conducted in accordance with OECD TG 407 and were GLP compliant. Both studies were limit dose studies and no treatment-related effects were observed. The NOEL for each analogue was determined to be 1000 mg/kg bw/day (Safepharm Laboratories, 1995e-f).

The CONCAWE product dossier (1997) summarises the results from a number of repeat dose studies conducted on petroleum derived base oils of varying viscosity and refining history. In the majority of feeding studies on highly refined mineral oils, which are likely to be the most relevant to the notified chemical due to the low impurity (including aromatics) content, these oils were found to be of low systemic toxicity after chronic exposure. Adverse systemic effects (microgranulomas/granulomas in liver and lymph nodes) were seen in some of the studies conducted in rats. These effects were mainly observed for low viscosity oils and appeared to be species specific (most severe in Fischer 344 rats compared to Sprague-Dawley rats, and absent in Long Evans rats and dogs). In recent reports it has been concluded that the relevance of these effects to humans is questionable, as they are morphologically different from the changes observed in the lymph nodes and livers of humans exposed to mineral oils (Carlton et al, 2001).

The CONCAWE product dossier (1997) also summarises the results of several sub-acute and sub-chronic studies via the dermal and inhalation route. In the dermal studies systemic effects were rarely seen, with only one oil showing liver effects. The studies conducted on the more highly refined oils showed no systemic effects. The summaries of the inhalation studies showed adverse effects from high doses of the less refined oils, while effects seen in studies conducted on more highly refined oils showed primarily an increase in wet lung weight.

B.8. Genotoxicity – bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 471 Bacterial Reverse Mutation Test. EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria. Plate incorporation procedure
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	S9 fraction derived from phenobarbitone/β-naphthoflavone induced rat liver
Concentration Range in Main Test	a) With metabolic activation: 15-5000 µg/plate b) Without metabolic activation: 15-5000 µg/plate
Vehicle	Tetrahydrofuran
Remarks - Method	No significant protocol deviations. GLP compliant. In a preliminary toxicity study the notified chemical was found to be non-toxic to the strains of bacteria used (TA100 and WP2uvrA) up to a dose of 5000 µg/plate.
RESULTS	
Remarks - Results	The oily precipitate which formed at and above 1500 µg/plate did not prevent scoring of the revertant colonies. No significant increases in the frequency of revertant colonies were recorded for any of the bacterial strains at any dose level, either with or without metabolic activation. The positive control chemicals induced marked increases in the frequency of revertant colonies, thereby confirming the validity of the test system.

CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safepharm Laboratories (2006c)

B.9. Genotoxicity – in vitro

TEST SUBSTANCE	Notified chemical
METHOD	Modified Draft OECD TG 487 In vitro Micronucleus Test in Human Lymphocytes.
Species	Human
Cell Type	Lymphocytes
Metabolic Activation System	S9 fraction derived from phenobarbitone/β-naphthoflavone induced rat liver
Vehicle	Acetone
Remarks - Method	The method from Draft OECD TG 487 was modified to more closely resemble the OECD TG 473 for the chromosome aberration test. In particular the exposure groups from OECD TG 473 were adopted in preference to those suggested in the draft OECD TG 487. In a preliminary toxicity study the test material induced no evidence of toxicity in any of the exposure groups. The maximum dose level for the main study was therefore set at 2500 μg/mL based on the maximum practical dose achievable.

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Expression Time*	*Selection Time*
Absent				
Test 1	0*, 312.5, 625*, 1250*, 2500*	4 h	20 h	48 h
Test 2	0*, 78.13, 156.25, 312.5, 625*, 1250*, 2500*	20 h	20 h	48 h
Present				
Test 1	0*, 312.5, 625*, 1250*, 2500*	4 h	20 h	48 h
Test 2	0*, 78.13, 156.25, 312.5, 625*, 1250*, 2500*	4 h	20 h	48 h

*Cultures selected for binucleate analysis.

RESULTS	
Remarks - Results	The notified chemical did not induce any statistically significant increases in the frequency of cells with micronuclei, in either the absence or presence of metabolic activation. The positive control chemicals induced statistically significant increase in the frequency of cells with micronuclei, thereby confirming the validity of the test system.
CONCLUSION	The notified chemical was not clastogenic or aneugenic to human lymphocytes treated in vitro under the conditions of the test.
TEST FACILITY	Safepharm Laboratories (2006d)

B.10. Genotoxicity – in vivo

A murine bone marrow micronucleus study conducted on Analogue 1 was conducted in accordance with OECD TG 474 and was GLP compliant. Analogue 1 did not induce a toxicologically significant increase in the incidence of micronucleated polychromatic erythrocytes when tested up to the maximum recommended dose of 5000 mg/kg bw. However there was no indication in this study as to whether the test substance was reaching the bone marrow (Safepharm Laboratories, 1995g).

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