File No: NA/729

May 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

ChEster 306

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

ChEster 306

1. APPLICANT

Chevron Chemical Australia of 385 Bourke Street MELBOURNE VIC 3000 and Baker Hughes Inteq of 5 Stoneham Street BELMONT WA 6104 have submitted a standard notification statement in support of their application for an assessment certificate for ChEster 306.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, and molecular and structural formulae have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Name:	ChEster 306
Molecular Weight:	298
Method of Detection and Determination:	Infra Red (IR) analysis; High Performance Liquid Chromatography (HPLC).
Spectral Data:	Spectral data (^{13}C NMR, UV, GC-MS and IR spectra) for the close chemical cogeners, secondary dodecyl propanoates (SDP) and secondary octadecyl propanoates (SOP) were provided; The spectra on SDP and SOP serve to identify the principal functionalities of the notified chemical, ChEster 306.

3. PHYSICAL AND CHEMICAL PROPERTIES

The notifier indicated that the available physico-chemical data on ChEster 306 were generated from in-house investigations. In support of claims for Variation of Schedule Requirements, test reports on the physicochemical properties of two close cogeners namely, SDP (C_{12}) and SOP (C_{18}) have been provided. The cogeners lie on either side of the notified chemical in respect of the molecular weight. The tests on the cogeners were conducted in facilities that complied with OECD Principles of Good Laboratory Practice, and based on methods that complied with OECD test guidelines and or EC Directive 92/69/EEC (OECD, 1995-1996),(European Commission, 1992).

The data on SDP and SOP are accepted for this assessment as valid representation of the physicochemical properties for ChEster 306, and adequate for the assessment of environmental fate and potential hazard. The data accepted for discussion in this assessment are indicated by an asterisk (*) in the following table.

The data on SDP and SOP are also presented in support of the application for an assessment certificate for ChEster 304, which is assessed as NA/728.

The following physicochemical properties are those of ChEster 306, SDP and SOP.

	ChEster 306	SDP	SOP
Appearance at 20°C & 101.3 kPa:	clear, light yellow to brown liquid		
Boiling Point:	> 330°C (see comments below)	> 240°C* (see comments below)	Not determined
Freezing Point:	< -47°C	< -20°C	Not determined
Density:	0.86 g/mL at 15.6°C	0.852 g/mL at 20°C	Not determined
Vapour Pressure at 25°C:	<1.33 x 10^{-5} kPa	6.3 x 10^{-5} kPa*	Not determined
Vapour Density (Air = 1):	Not determined		
Kinematic Viscosity at 40°C:	4.94 x 10^{-6} m^2/sec*	Not determined	
Water Solubility at 20°C:	Not determined	32 ± 6 µg/L*	Not determined
Henry's Law Constant:	530 Pa.m^3/mole* (see comments below)		
Partition Co-efficient (n-octanol/water) log Pow:	Not determined	> 6.2*	
Adsorption/Desorption:	Log Koc>4.8 (see comments below)		
Flash Point:	Not determined	131°C	Not determined
Pour Point:	-47°C	Not determined	
Autoignition Temperature:	Not determined	226°C	358°C
Explosive Properties:	Not known to be explosive		
Reactivity/Stability:	Expected to be stable		

Comments on Physico-Chemical Properties

Physico-chemical properties of SDP and SOP may differ slightly from those of ChEster 306, however, the differences are unlikely to be great.

SDP was found to decompose above 240°C, by differential scanning calorimetry – even under nitrogen atmosphere. Consequently, the boiling point was found experimentally to be greater than 240°C under atmospheric pressure (Safepharm Laboratories Limited, 1999a).

The vapour pressure of SDP was determined using a vapour pressure balance based on the iseniscope method (Safepharm Laboratories Limited, 1999c) whereby a linear relationship is obtained from a plot of the logarithm of the equilibrium vapour pressure versus reciprocal temperature. This linear relation was determined on three separate samples of the material, and one typical result was –

Log_{10} [vapour pressure (Pa)] = -3045/ Temperature (K) + 9.06

The mean vapour pressure at 25°C from three such linear determinations gave the vapour pressure 6.3 x 10^{-2} Pa. ChEster 306 could be expected to be slightly less volatile.

Water solubility was determined for SDP at 20°C using the flask method (Safepharm Laboratories Limited, 1999a). The test was performed in triplicate, by stirring weighed aliquots of SDP into water at 30°C, and allowing to stand for at least 24 hours at 20°C. The aqueous phase was then separated by centrifugation, and the quantity of dissolved compound determined using gas chromatography (GC). For all three replicates, the water solubility was less than 6.77 x 10^{-5} g/L.

The notifier submitted a second report (Wildlife International, 1999) on water solubility for SDP; the water solubility at 20°C was 32 ± 6 µg/L. Because of the lower detection level of the instrumentation used, GC-mass spectroscopy, the water solubility determined from this method is the preferred value for assessment purposes. The water solubility of ChEster 306 is expected to be less than 32 ± 6 µg/L, as it contains an additional two methylene groups than does SDP for which the data was obtained.

The Henry's Law Constant is a measure of the degree of partitioning of a compound between the aqueous phase and the atmosphere, and is calculated according to the relation –

H = Vapour pressure (Pa) x Molecular weight (g/mole)/ Water solubility (g/m).

Taking the water solubility as 32 µg/L, the vapour pressure as 6.3 x 10^{-2} Pa and using a molecular weight of 270 g/mole, an estimate for H (at 25°C) is 530 $Pa.m^3$/mole. ChEster 306 could be expected to be less soluble in water (see above). Consequently, the Henry's Law Constant for ChEster 306 could be expected to be greater than 530 $Pa.m^3$. ChEster 306 is appreciably volatile, and the Henry's Law Constant estimate indicates that it would partition from the water phase to the atmosphere.

The ester bond of the ChEster 306 may be susceptible to hydrolysis under extreme pH, but not in the usual environmental pH region 4 to 9. The hydrophobic nature of the bulk of the molecule is also likely to hinder the close approach of water molecules to the susceptible ester linkages, further reducing the potential for hydrolytic cleavage.

The n-octanol/water partition coefficient was determined for SDP and SOP by the HPLC method (Safepharm Laboratories Limited, 1999a), (Safepharm Laboratories Limited, 1998w) where the retention time of the chemical on a C_8 column was compared with that of six reference compounds of known Log Pow. The reference compounds included benzene with the lowest value for Log Pow of 2.1 and DDT with the highest Log Pow of 6.2. The retention time of both SDP and SOP exceeded that of DDT. Consequently, the value of Log Pow is >6.2, and ChEster 306 could be expected to exceed 6.2.

No quantitative estimates for adsorption/desorption were provided, but the high values for Log Pow indicate correspondingly large values for Log Koc. (Lyman, 1982) gives a number of relations for estimation of Log Koc from values of Log Pow, all of which (as expected) give large values for this parameter. As an example, using a value for Log Pow of 6.2, their equation 4-8 –

Log Koc = 0.544 x Log Pow + 1.377,

results in a Log Koc of 4.8. Values of Log Koc in excess of 3 indicate high affinity for the organic component of soils and sediments, and low mobility in these media.

The flash point of SDP was determined using the closed cup equilibrium method (Safepharm Laboratories Limited, 1999b). The autoignition temperature for SDP and SOP was determined by heating an aliquot of the test substance in a flask and observing for any ignition (Safepharm Laboratories Limited, 1999b), (Safepharm Laboratories Limited, 1998v). ChEster 306 is not classified as a Dangerous Good for transport by road or rail but is identified in the Material Safety Data Sheet as a combustible liquid.

ChEster 306 contains no acidic or basic functionalities and dissociation constant data are not relevant.

The measured kinematic viscosity of ChEster 306 meets the criteria of aspiration hazard defined in the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

4. PURITY OF THE CHEMICAL

Degree of Purity:	100%
Toxic or Hazardous Impurities:	None
Non-hazardous Impurities (> 1% by weight):	None
Additives/Adjuvants:	None

5. USE, VOLUME AND FORMULATION

Use
ChEster 306 has been identified for use as a base fluid for invert drilling mud on offshore oil and natural gas drilling operations.

Volume and Transport
ChEster 306 will not be manufactured in Australia, but will be imported by ship in 200 L drums or 8 000 L marine isotanks. Where drums are used, they are loaded into a container (78 drums per container) prior to shipment. Over the next five years the anticipated import volume of ChEster 306 is up to 1 000 tonnes per annum. An annual import of 1 000 tonnes, (and with a specific gravity of 0.85 g/cm) equates to 1 160 000 L of ChEster 306 and would require the importation of 5 800 drums, or 145 marine isotanks per annum. The notifier indicated that imports may exceed 1 000 tonnes per annum, but could not make predictions as to possible volumes.

The quantity of drilling mud used in drilling the wells depends on drill well location. The notifier indicated that a typical oil/gas drilling platform may use 150 tonnes of ChEster 306 annually although the drilling depth and number of holes drilled are difficult to predict.

From the initial port of arrival the drums or isotanks containing ChEster 306 are delivered by truck to a storage and drilling mud blending facility. The prepared drilling mud is transported by tanker truck to docks, pumped into storage tanks on ships, then transported to the offshore platform. Up to 300 m^3 of drilling mud may be transported to the platform. The transfer of the mud from the ship to storage tanks on the platform is effected using special hoses and couplings.

Formulation
The drilling mud will be prepared at purpose built facilities (at Dampier in WA). ChEster 306 will be blended at 33-50% with water, emulsifiers, fluid loss additives, viscosity modifiers and barium sulphate[1] in high shear mixers and pumped to an onsite storage tank. While no details were provided in the submission, it is understood that the facilities at which drilling mud is prepared are provided with adequate bunds to contain spills. All spilt material would be disposed of by incineration or by other accepted methods.

Drilling Operations
During drilling operations, the mud is pumped down the drill shaft. It functions as a lubricant for the drills and a carrier fluid for removing the solid cuttings (that is, the rock removed from the bore hole). Drilling mud is pumped down the centre of the (hollow) drilling rods and is extruded through holes in the cutting head, which is of larger bore than the shaft of drilling rods. The mud then fills the annular region between the bore hole (typically 31.1 cm in diameter – (Cobby, 1999) and the drilling shaft, and as it is pushed back towards the surface carries the drill cuttings with it. The bore hole is cased and fitted with valves and plumbing on the drilling platform, the solid cuttings are separated from the fluid mud through a series of shaker and solids separation units. The cuttings are automatically discharged overboard through a pipe set a little below the sea surface, but far above the sea floor.

[1] The barium sulphate is used as a weighing agent to increase the density of the drilling fluid and control formation pressures in the wellbore during drilling operations.

While most of the drilling mud is recovered in this manner, it is inevitable that some will remain adsorbed on the surface of the cuttings and may be entrained between the particles of solid waste, and will be discarded overboard with these cuttings. All drilling fluid, other than that adsorbed to the drill cuttings, is recovered and recirculated through the drill string on a continuous basis. No whole drilling fluid is discharged overboard. At the end of the drilling phase all the drilling fluid is recovered and returned to shore for storage until required on another well. It is important to note that stringent procedures are used to ensure that there is no loss of whole drilling fluid to the environment at any stage of the drilling and transport operations. Drilling fluids adhering to the disposed cuttings may constitute up to 10% by weight of cuttings.

6. OCCUPATIONAL EXPOSURE

Number and Category of Workers

Import and Transportation: unknown;
Drill mud preparation 2 to 3 workers;
Drilling crew: approximately 20 workers per offshore platform.

Nature of Work Done

Dockside and Transport

Occupational exposure is not expected except in the event of a spill.

Drilling Mud Preparation

Using automated systems, ChEster 306 is blended with other components to produce the drilling mud as described in Section 5. Preparation of the mud takes about one to two hours depending on batch size. During preparation, potential for dermal and ocular contact to ChEster 306 at 33 to 50% exists during any sampling that may occur of the drilling mud for quality control (QC) analysis. Exposure to ChEster 306 may also occur during maintenance of equipment or in the event of a spill. Formation of aerosol and consequent inhalation exposure is expected to be negligible given the automated addition systems and the high density of the drilling muds.

Drilling

The large size of drilling equipment suggests that drill operators will have potential for exposure to high volumes of drilling mud during manipulation of the drill when the drill bit is replaced or removed from the drill hole. There is potential for skin and eye contact during these activities. Formation of aerosol and consequent inhalation exposure is expected to be negligible given the high density of the drilling mud.

Drum and Isotank Recycling

During the cleaning of drums and isotanks for recycling, workers may receive eye and skin contact to water-slop containing residual notified chemical.

Control Measures

Personal protective equipment is expected to be mandatory for drilling crews. The Material Safety Data Sheet (MSDS) for ChEster 306 recommends impervious protective clothing, safety glasses with eye shields and neoprene or nitrile gloves. In addition, an organic vapour (Type A) filter respirator is recommended where exposure to airborne material may occur.

Worker Education and Training
The notifier indicates that the pattern of use is non-dispersive, that is, workers exposed to ChEster 306 would be employees of the major international petroleum and drilling rig companies and would be well educated and trained in all aspects of drilling operation safety and chemical hazards, to achieve adequate control of exposure. Transport workers would also be educated in the occupational health and safety aspects of petroleum derived products.

7. PUBLIC EXPOSURE

It is expected that during transport and storage, the potential for exposure of the general public to the notified chemical will be low.

Onshore small spills should be cleaned up using appropriate technology such as sorbent materials or pumping before being transferred to suitable containers for recovery or disposal in accordance with local, state and federal regulations. Prompt attention to spillages will be needed to prevent spill and clean up material from entering waterways. All sources of ignition in the vicinity of the spill or released vapour should be eliminated. Where feasible and appropriate, contaminated soil should be removed.

The chemical will only be used on offshore drilling platforms, and the public will not be exposed during this operation.

Cleaning of used drums and isotanks will remove more than 95% of ChEster 306 from wastewater prior to discharge into sewers. Thus, disposal is unlikely to produce significant public exposure.

8. ENVIRONMENTAL EXPOSURE

8.1 RELEASE

The notifier indicated that very small quantities of residual compound may be left in the 200 L drums and isotanks which are subsequently steam cleaned and reconditioned. The resultant oil/water emulsion is passed to an on site waste treatment facility where the oils are separated from the water, and eventually become incorporated into a waste sludge. The waste sludge is typically incinerated.

All ChEster 306 used in drilling mud is expected to be released with the waste drill cuttings to the marine environment as described above. The drill cuttings, containing up to 10% of the notified chemical, would eventually settle to the sea floor. Depending on factors such as particle size, sea conditions, weather conditions and ocean currents, the deposition may take some time. Also, it is likely that the distribution would be disperse, and that the discarded cuttings would be spread over a wide area of the sea floor. A typical production drilling platform may be responsible for over 10 individual bore holes, each between one and four km in depth. Given that the typical diameter of a production hole is 31.1 cm, each platform is estimated to produce between 3 000 and 12 000 m^3 of rock cuttings with a weight of approximately 8 000 to 30 000 tonnes[2]. Assuming that the cuttings contain 10% of drilling

[2] In reference 8 it is mentioned that cutting piles with volumes between 10 000 and 20 000 m^3 have been documented beneath some drilling platforms.

fluid, each pile of cuttings may contain up to 3 000 tonnes of discarded fluid. Note here, that the notified chemical is one of a class of materials used in the preparation of the drilling muds. These may include internal olefins, poly alpha olefins, linear alpha olefins, esters and acetals.

Also, some of the residual fluid may remain "entrained" between particles of rock cuttings and not adsorbed to the surface of these solids. After discharge overboard this material would be expected to migrate to the sea surface, and could form a film on the surface of the water. The notifier acknowledged that while the formation of such a "slick" is possible, it would be unlikely to be observed except during extremely still weather and sea conditions. Any surface film formed from the notified chemical in this manner could be expected to slowly spread from the vicinity of the drilling rig to be eventually broken up by wind and waves. Since the compound is volatile (Henry's Law Constant around 530 $Pa.m^3mole^{-1}$), it is expected that most of the material would evaporate from the surface and enter the atmosphere.

8.2 FATE

8.2.1 Biodegradation

The chemical will be released in quantity to the sea floor. Since conditions within the marine benthic zone may be either aerobic or anaerobic, it is necessary to consider the fate of the material in both these environments.

8.2.2 Freshwater Studies - Aerobic Conditions (Safepharm Laboratories Limited, 1998h), (Safepharm Laboratories Limited, 1998u)

Test reports detailing results obtained in a carbon dioxide evolution test (Modified Sturm Test – OECD TG 301B) were provided for both SDP and SOP. SDP and SOP are close chemical cogeners of ChEster 306 and are considered valid analogues for assessing the ready biodegradability of the notified chemical. The tests on both compounds were conducted in triplicate, apparently using the same sample of activated sludge to inoculate the test samples. Two standard tests (using sodium benzoate) and two controls (no added chemicals) were run in parallel with the tests on SDP and SOP. The tests were conducted at 21± 1°C in the dark, and the test substance was initially present at a concentration of 5 mg carbon/L. After the 28 day test period the concentration had decreased by 79%, for SDP, and 98% for SOP. For SOP, the degree of degradation had exceeded 60% ten days after reaching 10%, and this substance may be classified as readily biodegradable. However, while SDP exhibited rapid biodegradation, it had not attained 60% degradation ten days after reaching the 10% point (which was around one day after commencement of the test), and may not be considered readily biodegradable.

Toxicity control tests were also conducted (using inoculated test media containing both sodium benzoate and the test substances at 15 mg carbon/L). The test substances did not inhibit the bacterial metabolism.

Given that the tests on both SDP and SOP were performed under identical conditions, using the same controls and standards, the significant difference between the degradation rates is to be noted, but no explanation for the differences is obvious. However, it may be concluded from these tests that ChEster 306 is likely to exhibit rapid biodegradation under aerobic conditions, but may not necessarily satisfy the criteria for ready biodegradability.

8.2.3 Freshwater Studies - Anaerobic Conditions

No test reports on anaerobic biodegradation were submitted. However, the notifier provided an article by (Steber, 1995) dealing specifically with the anaerobic degradation of drilling fluids components, two of which were unidentified fatty acid esters. The studies were conducted according to the protocol of the ECETOC screening test (ECETOC, 1988) whereby the test substance is incubated at 35°C over an extended period with sewerage digester sludge maintained under anaerobic conditions. The volume of evolved CO_2 and methane is measured periodically throughout the test period. The results indicated that after 35 days incubation under the test conditions, greater than 82 ±13% of the original carbon in the test material had been metabolised to CO_2 and methane. Consequently, it was concluded that these two esters are rapidly degraded under anaerobic conditions.

While these two tests were conducted on material containing cogeners of the components of the notified chemical, it is likely that ChEster 306 would behave in a similar manner, and exhibit degradation in an anaerobic environment.

The notifier also supplied summary data on the anaerobic biodegradation of two ester compounds presently used in drilling fluids. The two esters, 2-ethyl hexyl dodecanoate (trade name Petrofree) and 2-ethylhexyl oleate (trade name Finagreen), were degraded by 57 and 58% respectively under the test conditions. However, due to issues connected with commercial confidentiality[3], the present notifier was unable to supply details of the test method, or a detailed copy of the test report.

8.2.4 Marine Waters

The degradation (mineralisation) of chemicals in the marine environment has not been researched as extensively as has degradation in freshwater environments. No biodegradation data of the compound in seawater has been provided. However, the notifier indicated that a test that followed OECD Test Guideline 306 was currently being undertaken on ChEster 306.

It is noteworthy that a preliminary report (ECETOC, 1993) concludes that if a chemical is readily biodegradable under aerobic conditions in a freshwater environment, available evidence suggests it will also be degraded in the marine environment. The mechanisms for degradation may be aerobic or anaerobic. The rate of degradation in marine environments is likely to be substantially reduced compared to fresh water environments, primarily because of the generally lower bacterial population in marine waters and sediments. Low temperatures at the benthic interface would also decrease the rate of degradation.

In conclusion, the available literature indicates that ChEster 306 is probably susceptible to anaerobic biodegradation when released to the sea floor with waste drill cuttings. However, the rate and extent of this degradation is uncertain, and it is possible that the rate of removal from the benthic regions will be quite slow.

8.2.5 Abiotic Degradation

[3] These two compounds were tested for anaerobic degradation for Woodside Petroleum, which is an operator of drilling platforms off the WA coast. It is to be noted that the compound known as Petrofree has been assessed as a component of drilling muds by NICNAS (NA/14). Data supplied in NA/14 indicated 70-83% degradation of Petrofree in sea water using the 5 day closed bottle BOD test.

The ChEster 306 pendant ester groups are unlikely to undergo hydrolysis in the environmental pH region. Consequently, it is expected that the major pathways for abiotic degradation will be through direct or indirect photochemical mechanisms.

Hydrogen abstraction by photochemically produced hydroxy radicals is accepted as the dominant mechanism for degradation of saturated hydrocarbon molecules in the atmosphere. The OECD (OECD, 1992) gives a procedure for calculating typical rate constants for these processes. For ChEster 306 the estimated rate constant for hydrogen abstraction from the alkane portions is k_{abs} = 19.1 x 10^{-12} cm^3 molecule/sec. Assuming an ambient hydroxyl radical concentration of 5 x 10^5 radicals cm^{-3}, the estimated atmospheric half-life is around 7.2 x 10^4 sec (20 hours).

8.2.6 Bioaccumulation

The notifier offered no data or comment on the potential for bioaccumulation of ChEster 306, but provided an article by (Feitjel, 1997) of the potential for bioaccumulation. The hydrophobic nature of the chemicals indicates considerable potential for bioaccumulation (Lyman, 1982) gives a number of Quantitative Structure Activity Relations (QSARs) for estimation of bioaccumulation from known parameters such as water solubility and/or partition coefficient. Their equation 5-2 is recommended for general estimation of the bioconcentration factor (BCF) from values of Log Pow.

This equation is –

Log BCF = 0.76 x Log Pow – 0.23.

Assuming a Log Pow of 6.2, this equation gives an estimate for the BCF of 30 300. Larger values for Log Pow would increase the predicted BCF accordingly.

(Connell, 1990) indicates that compounds with a molecular weight around 350 and Log Pow around 6 may have high potential for bioaccumulation ChEster 306 has a molecular weight of 270 and Log Pow greater than 6.2. Connell, 1990 also remarks that the potential for bioaccumulation peaks when water solubility is around 2 x 10^{-6} mole/L, and drops off on either side of this value. The water solubility of the new compound is estimated to be < 32 µg/L (ie <1.2 x 10^{-7} mole/L) and consequently, while the low molecular weight and high Log Pow indicate large potential for bioaccumulation, this may be mitigated to some extent by the low water solubility.

It should be remarked here that the extent of bioaccumulation is also dependent on the rate of biodegradation, and while it is probable that after release into marine sediments, ChEster 306 will be susceptible to biodegradation, the rate of these processes is uncertain. Consequently, it must be concluded that the potential for bioaccumulation in marine organisms may be significant.

9. EVALUATION OF TOXICOLOGICAL DATA

No toxicity data were provided on ChEster 306. In support of their claim for Variation of Schedule Requirements, the notifier has submitted toxicity studies conducted on SDP and SOP, which are close cogeners of ChEster 306.

The toxicity studies conducted on SDP are: acute oral and dermal toxicity; skin and eye irritation; skin sensitisation; 90-day repeat oral dose; bacterial reverse mutation; *in vitro* chromosome aberration; and *in vivo* induction of micronuclei. Toxicity studies on SOP are limited to: acute oral and dermal toxicity; skin and eye irritation; skin sensitisation; and bacterial reverse mutation.

The notifier indicates this testing scheme was proposed by the United Kingdom competent authority to reduce the number of animals used in the testing program. The notifier claims the toxicity of ChEster 306 will be appropriately covered by the cogeners.

Tests were conducted in facilities that complied with OECD Principles of Good Laboratory Practice, and based on methods that complied with OECD test guidelines and or EC Directive 92/69/EEC (OECD, 1995-1996), (European Commission, 1992).

9.1 Toxicity Summary of SDP and SOP

End Point	***SDP***	***SOP***
Acute Oral LD_{50}	> 5 000 mg/kg	> 5 000 mg/kg
Acute Dermal LD_{50}	> 2 000 mg/kg	> 2 000 mg/kg
Skin Irritation	Slight to moderate irritant	Slight to moderate irritant
Eye Irritation	Slight irritant	Slight irritant
Skin Sensitisation	Non sensitising	Non sensitising
90-day Repeat Dose Toxicity	NOAEL: 1 000 mg/kg; NOEL: 50 mg/kg/day males, 1 000 mg/kg/day females.	Not tested
Genotoxicity:		
Ames test	Non mutagenic	Non mutagenic
Chromosome aberration, *in vitro*	Non clastogenic	Not tested
Mouse micronucleus test, *in vivo*	Non genotoxic	Not tested

9.1.1.1 Oral Toxicity (Safepharm Laboratories Limited, 1998d)

Test substance:	SDP
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Gavage, 5 000 mg/kg (dose volume of 5.90 mL/kg)
Test method:	OECD TG 401
Clinical observations:	No signs of systemic toxicity
Mortality:	Nil
Morphological findings:	No abnormalities detected
LD_{50}*:*	> 5 000 mg/kg
Result:	SDP was of very low acute oral toxicity in rats

9.1.1.2 Oral Toxicity (Safepharm Laboratories Limited, 1998q)

Test substance:	SOP
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Gavage, 5 000 mg/kg (dose volume of 5.90 mL/kg)
Test method:	OECD TG 401
Clinical observations:	No signs of systemic toxicity
Mortality:	Nil
Morphological findings:	No abnormalities detected
LD_{50}*:*	> 5 000 mg/kg
Result:	SOP was of very low acute oral toxicity in rats

9.1.2.1 Dermal Toxicity (Safepharm Laboratories Limited, 1998c)

Test substance:	SDP
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	5/sex
Method of administration:	A single, 24-hour semi occluded, dermal application to intact skin at 2 000 mg/kg (dose volume 2.36 mL/kg)
Observation period:	14 days. Treated sites were observed for evidence of dermal irritation approximately 30 minutes after bandage removal and on Days 3, 7, 10 and 14
Clinical observations:	No signs of systemic toxicity
Test method:	OECD TG 402
Mortality:	Nil
Morphological findings:	No abnormalities detected
Dermal responses:	No signs of skin irritation
LD_{50}:	> 2 000 mg/kg
Result:	SDP was of low dermal toxicity in rats

9.1.2.2 Dermal Toxicity (Safepharm Laboratories Limited, 1998p)

Test substance:	SOP
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	5/sex
Method of administration:	A single, 24-hour semi occluded, dermal application to intact skin at 2 000 mg/kg (dose volume 2.36 mL/kg)
Observation period:	14 days. Treated sites were observed for evidence of dermal irritation approximately 30 minutes after bandage removal and on Days 3, 7, 10 and 14
Clinical observations:	No signs of systemic toxicity
Test method:	OECD TG 402
Mortality:	Nil

Morphological findings:	No abnormalities detected
Dermal responses:	No signs of skin irritation
LD_{50}:	> 2 000 mg/kg
Result:	SOP was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

Study not conducted. Not considered to be a relevant route of exposure.

9.1.4.1 Skin Irritation (Safepharm Laboratories Limited, 1998b)

Test substance:	SDP
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	6 males
Observation period:	1, 24, 48,72 and 96 hours post exposure
Method of administration:	A single 4-hour semi occluded application of 0.5 mL of neat test substance to intact rabbit skin;
Test method:	OECD TG 404

Draize scores:

Time after treatment	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Erythema/Eschar Formation						
30 minutes	[a]2	2	2	2	2	2
24 hours	2	1	1	2	2*	2
48 hours	1	1	0	1	1	1
72 hours	1D*	0D	0D	1D*	1D	1D*
96 hours	0D*	0D	0D	1D*	0D	1D*
7 days	0D	0D	0D	0D	0D	0D
Oedema						
30 minutes	[a]1	1	1	1	2	2
24 hours	1	1	1	1	1	2
48 hours	1	0	0	1	0	1
72 hours	0	0	0	1	0	1
96 hours	0	0	0	0	0	0
7 days	0	0	0	0	0	0

[a] see Attachment 1 for Draize scales. D = desquamation. D* = moderate desquamation.

Mean group score (24, 48 & 72 hour observation): Erythema/Eschar Formation: 1.1
Oedema: 0.7

Primary Irritation Index: 2.1

Comment:
Well-defined erythema was noted at all treated skin sites at the 30 minute observation with very slight or well defined erythema at the 24 hour observation. The slight erythema persisted in two animals at the 96 hour observation with no erythema noted after 7 days. Desquamation appeared in all animals at the 72 hour observation which persisted to the 7-day observation.
Very slight or slight oedema was noted at all treated skin sites at the 30 minute observation, which persisted in two animals to the 72 hour observation with no oedema noted after 96 hours.

Result: SDP was slight to moderately irritating to the skin of rabbits

9.1.4.2 Skin Irritation (Safepharm Laboratories Limited, 1998o)

Test substance: SOP

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 6 males

Observation period: 1, 24, 48,72 and 96 hours post exposure

Method of administration: A single 4-hour semi occluded application of 0.5 mL of neat test substance to intact rabbit skin

Test method: OECD TG 404

Draize scores:

Time after treatment	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Erythema/Eschar Formation						
30 minutes	2	2	2	2	2	2
24 hours	2R	2R	2R	2R	2R	2R
48 hours	2R	1R	2	2R	1R	1
72 hours	2RLe	1LeLf	2Le	2RLe	1RLe	1Le
96 hours	?eCf	1Cf	1LeCf	1Cf	1RCf	1
7 days	0D	0D	0D	0D	0D	0D
14 days	0	0	0	0	0	0
Oedema						
30 minutes	1	2	2	2	2	2
24 hours	2	2	2	2	2	2
48 hours	2	1	1	2	1	1
72 hours	1	1	1	1	1	1
96 hours	?od	1	1	1	1	0
7 days	0	0	0	0	0	0
14 days	0	0	0	0	0	0

[a] see Attachment 1 for Draize scales.
D = slight desquamation.
Cf = crust formation.
Le = loss of skin elasticity.
R = reaction extends up to 6 cm beyond treatment site.
?0d = adverse reaction prevents accurate evaluation of oedema.
Lf = loss of skin flexibility.
?e = =adverse reactions prevent accurate evaluation of erythema.

Mean group score (24, 48 & 72 hour observation):	Erythema/Eschar Formation: 1.7 Oedema: 1.4
Primary Irritation Index:	3.3

Comment:
Erythema was noted at all treated skin sites at the 30 minute observation and persisted to the 96 hour observation;
Desquamation appeared in all animals at the 72 hour observation and persisted to the Day 7 observation;
Oedema was noted at all treated skin sites at the 24 hour observation and persisted in four animals to the 96 hour observation;
The nature of the adverse reaction noted for one animal was not described in the study report. Crust formation was noted at the treatment site of five animals at the 96 hour observation and prevented the accurate evaluation of erythema and oedema at the treatment site of one at this time. Exudate was not noted in the study report and a suggestion to the cause of the crust formation was not provided.

Result: SOP was slight to moderately irritating to the skin of rabbits

9.1.5.1 Eye Irritation (Safepharm Laboratories Limited, 1998l)

Test substance:	SDP
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	9 males
Observation period:	1, 24, 48 and 72 hours post instillation
Method of administration, Nonirrigated eyes:	A single instillation of 0.1 mL of the neat test substance into the conjunctival sac of the test eye of 6 rabbits; the contralateral eye served as the control
Method of administration, Irrigated eyes:	A single instillation of 0.1 mL of the neat test substance into the conjunctival sac of the test eye of 3 rabbits, with irrigation of the eyes after 30 seconds; the contralateral eye served as the control
Test method:	OECD TG 405

Draize scores of nonirrigated eyes:

	Time after instillation											
Animal	***1 hour***			***24 hours***			***48 hours***			***72 hours***		
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	1	1	1	0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
Cornea	*No corneal effects noted*											
Iris	*No iridial effects noted*											

[1] see Attachment 1 for Draize scales
r = redness c = chemosis d = discharge

Mean scores for nonirrigated eyes:	Corneal opacity: 0.0 Iridial lesion: 0.0 Redness of conjunctivae: 0.0 Chemosis of conjunctivae: 0.0
Comment, nonirrigated eyes:	Conjunctival redness was noted in 4 of 6 treated eyes at the and conjunctival chemosis and discharge in one treated eye at the one hour observation; treated eyes appeared normal at the 24 hour observation; no iridial or corneal effects were noted;
Comment, Irrigated eyes:	No ocular effects noted
Result:	SDP was slightly irritating to the eyes of rabbits

9.1.5.2 Eye Irritation (Safepharm Laboratories Limited, 1998n)

Test substance:	SOP
Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	6 males, 3 females
Observation period:	1, 24, 48 and 72 hours post instillation
Method of administration, nonirrigated eyes:	A single instillation of 0.1 mL of the neat test substance into the conjunctival sac of the test eye of 6 rabbits; the contralateral eye served as the control
Method of administration,	A single instillation of 0.1 mL of the neat test substance into

Irrigated eyes: the conjunctival sac of the test eye of 3 rabbits, with irrigation of the eyes after 30 seconds of treatment; the contralateral eye served as the control

Test method: OECD TG 405

Draize scores of nonirrigated eyes:

	Time after instillation											
Animal	**1 hour**			**24 hours**			**48 hours**			**72 hours**		
Conjunctiva	**r**	**c**	**d**	**r**	**c**	**d**	**r**	**c**	**d**	**r**	**c**	**d**
1	1	1	0	1	0	0	0	0	0	0	0	0
2	1	1	0	0	0	0	0	0	0	0	0	0
3	1	0	0	0	0	0	0	0	0	0	0	0
4	1	0	0	0	0	0	0	0	0	0	0	0
5	1	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
Cornea	*No corneal effects noted*											
Iris	*No iridial effects noted*											

[1] see Attachment 1 for Draize scales
r = redness c = chemosis d = discharge

Mean scores for nonirrigated eyes:
Corneal opacity: 0.0
Iridial lesion: 0.0
Redness of conjunctivae: 0.06
Chemosis of conjunctivae: 0.0

Draize scores of irrigated eyes:

	Time After Instillation											
Animal	**1 hour**			**24 hours**			**48 hours**			**72 hours**		
Conjunctiva	**r**	**c**	**d**	**r**	**c**	**d**	**r**	**c**	**d**	**r**	**c**	**d**
1F	0	0	0	0	0	0	0	0	0	0	0	0
2F	1	0	0	0	0	0	0	0	0	0	0	0
3F	0	0	0	0	0	0	0	0	0	0	0	0
Cornea	*No corneal effects noted*											
Iris	*No iridial effects noted*											

[1] see Attachment 1 for Draize scales
r = redness c = chemosis d = discharge. F = female.

Comment, nonirrigated eyes: Conjunctival redness was noted in 5 of 6 treated eyes at the 1 hour observation and persisted in one eye at the 24 hour observation; conjunctival chemosis was noted in two treated

	eyes at the one hour observation; all treated eyes appeared normal at the 48 hour observation; No iridial or corneal effects were noted;
Comment, Irrigated eyes:	Conjunctival redness was noted in one treated eye at the 1 hour observation; all eyes appeared normal at the 24 hour observation; No iridial or corneal effects were noted;
Result:	SOP was slightly irritating to the eyes of rabbits

9.1.6.1 Skin Sensitisation (Safepharm Laboratories Limited, 1998j)

Test substance:	SDP
Species/strain:	Guineapig/Dunkin Hartley White
Number of animals:	Females, 20 test and 10 control
Test method:	OECD TG 406 Magnusson and Kligman Maximisation Method
Induction procedure:	Intradermal Induction: Test animals: Day 1: three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region: - Freund's complete adjuvant (FCA) 1:1 in distilled water; - the test substance, diluted to 25% w/v in arachis oil; - the test substance at 25% w/v emulsified in a 50:50 mixture of FCA and distilled water; Topical Induction: Day 7 – A 48-hour semi occluded application of 0.5 mL of neat test substance to the treated area; Control animals: Treated similarly to the test animals omitting the test substance from the intradermal injections and topical application
Challenge procedure:	Test and Control animals: Day 21: A 24 hour, semi occluded application of 100% w/v and 75% w/v of test substance in arachis oil, to the right and left flank of each animal, respectively,

Number of Animals Exhibiting Positive Responses Following Challenge:

Challenge concentration	***Test animals***		***Control animals***	
	24 hours*	***48 hours****	***24 hours****	***48 hours****
100%	**2/20	1/20	0/10	0/10
75%	0/20	0/20	0/10	0/10

* time after patch removal.
** number of animals exhibiting positive responses.

Challenge Outcome: Challenge concentration of 100%: very slight erythema was noted at the challenge site of two test animals at the 24 hour observation and persisted in one animal at the 48 hour observation.
Challenge concentration of 75%: no dermal reactions were noted.
No dermal reactions were noted in control animals

Comment: Dermal reactions observed suggest irritation rather than sensitisation reactions

Result: SDP was non sensitising to guineapig skin.

9.1.6.2 Skin Sensitisation (Safepharm Laboratories Limited, 1998x)

Test substance: SOP

Species/strain: Guineapig/Dunkin Hartley White

Number of animals: Females, 20 test and 10 control

Test method: OECD TG 406 Magnusson and Kligman Maximisation Method

Induction procedure: Intradermal Induction
Test animals:
Day 1: three pairs of intradermal injections (0.1 mL) into the dorsal skin of the scapular region:

- Freund's complete adjuvant (FCA) 1:1 in distilled water;
- the test substance, diluted to 25% w/v in arachis oil;
- the test substance at 25% w/v emulsified in a 50:50 mixture of FCA and distilled water;

Topical Induction:
Day 7 – A 48-hour semi occluded application of 0.5 mL of neat test substance to the treated area;

	Control Animals: treated similarly to the test animals omitting the test substance from the intradermal injections and topical application
Challenge procedure:	Test and Control animals: Day 21: A 24 hour, semi occluded application of 100% w/v and 75% w/v of test substance in arachis oil, to the right and left flank of each animal, respectively,
Challenge Outcome:	Challenge concentration of 100%: no dermal reactions were noted in test or control animals. Challenge concentration of 75%: no dermal reactions were noted in test or control animals.
Result:	SOP was non sensitising to guineapig skin.

9.2 Repeated Dose Toxicity (Safepharm Laboratories Limited, 1998a)

Test substance:	SDP
Species/strain:	Rat/Sprague Dawley
Number/sex of animals:	10/sex/group (control and treatment groups)
Method of administration:	Oral (gavage)
Dose/Study duration:	0, 50, 250 or 1 000 mg/kg/day for 90 consecutive days
Test method:	OECD TG 408
Mortality:	Nil

Clinical observations:

No toxicologically significant clinical findings were observed in treated or control animals. Animals of the 1000 mg/kg/day group showed increase salivation soon after dosing from Day 9 onwards; this finding was also observed in one male of the 250 mg/kg/day group on Day 46. Bodyweight gain, food and water consumption were comparable to the control group. Ophthalmoscopic examination did not reveal treatment related ocular changes.

Functional Observations:

No treatment related differences were apparent between the control and treated groups, for behavioural and sensory reactivity assessments or functional performance.

Clinical Pathology:
Serum Chemistry:
Incidental, statistically significant increase in plasma cholesterol in males and total protein in females 1 000 mg/kg/day.

Haematology:
There were no toxicologically significant changes in the haematological parameters measured.

Pathology:
Organ Weights:
Significantly increased liver weights (relative to body weight) in the 1 000 mg/kg/day group males were observed.
Macroscopic:
No treatment related findings were observed.
Microscopic:
An increased incidence of centrilobular hepatocytic hypertrophy in male rats of the 250 and 1 000 mg/kg/day groups was observed, with an increase in degree in the 1 000 mg/kg/day group.

Comment:
No toxicologically significant clinical observations, neurobehavioural effects or mortality were observed at any dose level. No test substance related changes were observed in haematology parameters. Changes in total protein and cholesterol at 1 000 mg/kg/day were isolated findings and not considered biologically significant in the absence of adverse effects. Treatment related lesions (hepatocytic hypertrophy) were observed in males of the 250 and 1 000 mg/kg/day groups and relative liver weights were increased in high dose males.

Result:
Based upon treatment related adaptive changes observed in the liver of males of the 250 and 1 000 mg/kg/day groups but not in females, the No Observed Effect Level (NOEL) determined for this study is 50 mg/kg/day.

In the absence of toxicologically significant systemic toxicity, the No Observed Adverse Effect Level (NOAEL) determined for this 90 day oral toxicity study was 1 000 mg/kg/day.

9.3 Genotoxicity

9.3.1.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Safepharm Laboratories Limited, 1998m)

Test substance:	SDP
Bactria/Strains:	*Salmonella typhimurium*: TA 1535, TA 1537, TA 98, TA 100; *Escherichia coli:* WP2uvrA$^-$
Concentration range:	0, 15, 50, 150, 500, 1500 and 5000 μg/plate, each concentration was tested in triplicate, with or without metabolic activation, in two independent experiments; appropriate strain specific positive control reference substances were used
Metabolic activation system:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254
Test method:	OECD TG 471 & 472 - plate incorporation method
Comment:	Precipitation was noted at and above 1 500 μg/plate; No toxicity was observed; There were no significant increases in revertant colony numbers at any concentration, in the presence or absence of metabolic activation; Concurrent positive controls used in the test induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory
Result:	SDP was non mutagenic in the bacterial strains tested under the conditions of the test

9.3.1.2 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Safepharm Laboratories Limited, 1998y)

Test substance:	SOP
Bacteria/Strains:	*Salmonella typhimurium*: TA 1535, TA 1537, TA 98, TA 100; *Escherichia coli:* WP2uvrA$^-$
Concentration range:	0, 15, 50, 150, 500, 1500 and 5000 μg/plate, each concentration was tested in triplicate, with or without metabolic activation, in two independent experiments; appropriate strain specific positive control reference substances were used
Metabolic activation system:	Liver fraction (S9 mix) from rats pretreated with Aroclor 1254

Test method:	OECD TG 471 & 472 - plate incorporation method
Comment:	Precipitation was noted at and above 500 µg/plate; No toxicity was observed; There were no significant increases in revertant colony numbers at any concentration, in the presence or absence of metabolic activation; Concurrent positive controls used in the test induced marked increases in the frequency of revertant colonies and the activity of the S9 fraction was found to be satisfactory
Result:	SOP was non mutagenic in the bacterial strains tested under the conditions of the test

9.3.2 Chromosomal Aberration Assay in Human Lymphocytes (Safepharm Laboratories Limited, 1998i)

Test substance:	SDP
Cells:	Human Peripheral Lymphocytes
Metabolic activation system:	liver fraction (S9 mix) from rats pretreated with Aroclor 1254

Dosing schedule:	each concentration was tested in duplicate, with or without metabolic activation, in two independent experiments,
	
	<u>Experiment 1:</u>
	without metabolic activation,
	0*, 39.06, 78.13, 156.25*, 312.5*, 625*, 1 250,2 500 5 000 µg/mL;
	treatment/harvest time = 4/20 hours;
	positive control: 750µg/mL ethylmethanesulphonate;
	
	with metabolic activation,
	0*, 39.06, 78.13, 156.25*, 312.5*, 625*, 1 250, 2 500 5 000 µg/mL,
	treatment/harvest time = 4/20 hours,
	positive control: 25µg/mL cyclophosphamide;
	
	<u>Experiment 2:</u>
	without metabolic activation,
	0*, 19.5*, 39*, 78.13*, 156.25, 312.5, and 625 µg/mL;
	treatment/harvest time = 20/20 hours;
	positive control: 500µg/mL ethylmethanesulphonate;
	
	with metabolic activation,
	0*, 19.5, 39, 78.13, 156.25*, 312.5*, and 625* µg/mL;
	treatment/harvest time: 4/20 hours,
	positive control: 25 µg/mL cyclophosphamide;

	asterisk* indicates cultures selected for metaphase analysis
Test method:	OECD TG 473
Comment:	Precipitation occurred at and above 1250 µg/mL therefore, the higher concentrations could not be used for analysis; Cytotoxicity was not observed at any concentration; The test substance did not cause any significant increases in the incidence of cells with chromosomal aberrations, polyploidy or endoreplication, at the concentrations analysed in the presence or absence of metabolic activation; Positive controls used in the test caused marked increases in the incidence of aberrant cells and the activity of the S9 fraction was found to be satisfactory
Result:	SDP was non clastogenic under the conditions of the test

9.3.3 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Safepharm Laboratories Limited, 1998k)

Test substance:	SDP
Species/strain:	mouse/Crl:CD-1 (ICR) BR
Number and sex of animals:	7 males/24 hour low, vehicle control and mid, low and high dose group; 7 males/48 hour vehicle control and high dose group; 7 males per positive control group
Doses/Method of administration:	Test substance: 500 mg/kg (low), 1 000 mg/kg (mid) or 2 000 mg/kg (high); Vehicle control: arachis oil; All administered via intraperitoneal injection at a constant volume of 10 mL/kg bw; Positive control, cyclophosphamide 50 mg/kg was administered orally;
Sampling schedule:	Vehicle control, low, mid and high dose animals were sacrificed 24 hours after dosing; Remaining animals of the vehicle control group and high dose animals were sacrificed 48 hours after dosing; Positive control group animals were sacrificed 24 hours after dosing

Clinical observations:	No mortality; No clinical signs of toxicity;
Micronuclei score:	No significant increase in micronucleated polychromatic erythrocytes (PCEs) due to treatment with test substance at either sampling time; The positive control caused a significant increase in micronucleated PCEs
Test method:	OECD TG 474
Result:	SDP did not induce a significant increase in micronucleated PCEs in bone marrow cells of the mouse *in vivo*

9.4 Overall Assessment of Toxicological Data

The cogeners, SDP and SOP, are long chain hydrocarbon (C_{12} and C_{18}, respectively) esters. ChEster 306 carries the same ester functionality but differs to SDP and SOP in hydrocarbon chain length.

Both SDP and SOP were of very low acute oral toxicity (LD_{50}>5 000 mg/kg) and low acute dermal toxicity (LD_{50}>2 000 mg/kg) in rats. On the basis of the similarities in chemical structure, ChEster 306 is very likely to share the same low order of acute oral and dermal toxicity as the analogues

Acute inhalation studies have not being conducted as the inhalation route of exposure was claimed by the notifier not to be relevant for these substances based on their low viscosity and low vapour pressure.

SDP was a slight eye irritant and a slight to moderate skin irritant in rabbits. The calculated primary irritation index (PPI) for skin was 2.1. The observed skin reactions (desquamation) in the skin irritation study appear to be representative of skin dryness due to the defatting properties associated with liquid hydrocarbon solvents. SOP demonstrated a higher degree of skin irritation (PPI of 3.3) and other skin reactions (desquamation, loss of skin flexibility/elasticity), but a lower degree of initial eye irritation. It would appear skin irritancy may be intrinsically related to hydrocarbon chain length. ChEster 306 is expected to have some irritant potential but to a lesser degree than the skin irritancy observed with SOP. Skin dryness is also expected.

In guineapigs, there was no evidence of dermal sensitisation in an adjuvant type test using SDP and SOP at challenge concentrations of 75% and 100%. ChEster 306 is not expected to be dermally sensitising based upon the sensitisation studies conducted on the analogues and the absence of functional groups commonly associated with skin sensitisers.

Oral administration of SDP to rats at dose levels of 0, 50, 250 or 1 000 mg/kg/day for 90 consecutive days revealed no toxicologically significant clinical findings, neurobehavioural effects or mortality. Haematology parameters were unaffected and isolated findings of changes in total protein and cholesterol at 1 000 mg/kg/day were not considered biologically significant in the absence of adverse effects. Treatment related lesions (hepatocytic hypertrophy) were observed in males of the 250 and 1 000 mg/kg/day groups. Based upon treatment related adaptive changes observed in the liver of males of the 250 and 1 000

mg/kg/day groups but not in females, the No Observed Effect Level (NOEL) determined for this study, is 1 000 mg/kg/day for females and 50 mg/kg/day for males. In the absence of toxicologically significant systemic toxicity, the No Observed Adverse Effect Level (NOAEL) determined for this 90 day oral toxicity study was 1 000 mg/kg/day for both males and females. Repeat dose studies were not conducted on SOP. Being structurally similar, ChEster 306 and SDP are expected to share the same metabolic fate. Therefore, the biological activity of ChEster 306 and its metabolites would be similar to that observed for SDP. No organ dysfunction or systemic toxicity is predicted for the notified chemical following repeat oral exposure.

SDP and SOP were not considered mutagenic in bacterial reverse mutation assays. No genotoxicity was observed with SDP in mammalian cells *in vivo* or *in vitro*. ChEster 306 and its metabolites are expected to display the same non genotoxic activity.

Hazard Classification
The results of the acute oral and dermal studies in rats and the skin and eye irritant studies in rabbits do not meet the thresholds for classification as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999). Based upon their low vapour pressure the cogeners are not expected to be an inhalation hazard. Signs of skin dryness were evident in the skin irritation studies for the analogues and most likely due to the defatting properties of the substances. Neither cogener showed evidence of skin sensitisation potential. Oral administration of SDP for 90 consecutive days did not reveal evidence of organ dysfunction or systemic toxicity in rats. Neither analogue was considered mutagenic.

The measured kinematic viscosity of ChEster 306 (Section 3) meets the criteria of aspiration hazard under the NOHSC *Approved Criteria for Classifying Hazardous Substances Classifying Hazardous Substances* (NOHSC, 1999) and presents an aspiration hazard, which may lead to chemical pneumonia. Therefore, ChEster 306 is classifiable as a hazardous substance, with hazard classification, Harmful (Xn) and risk phrase R65 – May Cause Lung Damage if Swallowed, assigned.

Risk phrase R66 – Repeated Exposure May Cause Skin Dryness or Cracking, has recently being adopted by the European Commission (European Commission, 1998). Although yet to be adopted by NOHSC, this risk phrase should be provisionally assigned to ChEster 306 based upon the observed defatting properties of SDP and SOP.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Ecotoxicity data was provided for freshwater species only.

The same test data is applicable to another new chemical notified by the same company, called ChEster 304 (NICNAS sequence number, NA/728). The chemical natures of the two new chemicals notified as NA/728 and NA/729 are very similar to those for the analogue substances for which data was provided, and the data is accepted for the environmental assessment. The results of these tests are summarised below.

10.1 Summary of Ecotoxicity Test Data for Freshwater Organisms

Test	*Acute Toxicity to Fish mg/L*	*Immobilisation of Invertebrates mg/L*	*Inhibition of Algal Growth mg/L*
	Rainbow trout *Oncorhynchus mykiss*	Water flea *Daphnia magna*	Green algae *Pseudokirchneriella subcapitata*
SDP (WAF loading 1 000 mg/L)	*LL_{50} (96 h) > 1 000 *NOEL (96 h) = 1 000	ELR_{50} (48 h) > 1 000 NOEL (48 h) =1 000	E_bLR_{50} (72 h) > 1 000 NOEL (72h) = 1 000
SOP (WAF loading 1 000 mg/L)	LL_{50} (96 h) > 1 000 NOEL (96 h) = 1 000	ELR_{50} (48 h)> 1 000 NOEL (48 h) = 1 000	E_bLR_{50} (72 h) > 1 000 NOEL (72 h) = 1 000

*In this table and the accompanying discussion, LL_{50} and ELR_{50} refer to the nominal loading of test substance used to prepare the WAF media for which 50% of the test animals died at the end of the test period. Similarly, the NOEL refers to the WAF loading below which no toxic effects are observed.

At the time of preparation of this report certain other tests on both freshwater and marine species are in progress and are to be provided for assessment when available.

10.2 Fish, Acute Toxicity Test (Safepharm Laboratories Limited, 1998f), (Safepharm Laboratories Limited, 1998s)

The acute toxicity of SDP and SOP to rainbow trout was assessed under OECD TG 303 and EC Directive 92/69/EEC (OECD, 1995-1996), (European Commission, 1992).

The range finding study was performed using Water Accommodation Fractions (WAF) of the test substance, SDP or SOP, made up in dechlorinated tap water at nominal loadings of 0 (control), 100 and 1 000 mg/L. The WAF test media were made up by stirring the requisite quantity of test substance into the water for around 24 hours, allowing to settle for approximately four hours, then siphoning off the aqueous phase containing the WAF. The WAFs prepared in this manner were clear and colourless, and devoid of undissolved material or oil droplets. The tests were conducted over a 96 hour period at a controlled temperature of 14±1°C, and the test media was replaced daily in a batchwise manner. Three fish were tested at each WAF loading. No mortalities or behavioural aberrations were observed over the 96 hour test period.

The definitive study was performed in triplicate using two controls (no test substance) and the 1 000 mg/L WAF, with ten fish in each test vessel. The pH was always between 7.6 and 7.9, the temperature was 14±1°C, water hardness around 100 mg/L as $CaCO_3$ and the dissolved oxygen levels between 8.8 and 9.8 mg/L. The water used in preparation of the test media had a total organic carbon content (exclusive of any test substance) of around 2 mg/L, and particulate matter around 0.2 mg/L. Again, no deaths or other effects were observed in the test specimens. It is concluded that the new compound is not toxic to this

species of fish, up to the limits of its water solubility. Measurements for the levels of total organic carbon in the test media indicated no discernible increase over the background level. This is in accord with the very low water solubility of the test compounds (Section 3), and indicates that the WAF of the test material is very small.

10.3 *Daphnia* sp. Acute Immobilisation Test (Safepharm Laboratories Limited, 1998e), (Safepharm Laboratories Limited, 1998r)

The acute toxicity of SDP and SOP to daphnia was assessed under OECD TG 202 and EC Directive 92/69/EEC (OECD, 1995-1996), (European Commission, 1992).

The range finding study was performed using WAF of the test substance, SDP or SOP, made up in dechlorinated tap water at nominal loadings of 0, 100 and 1 000 mg/L. The WAF test media were prepared as described in Section 10.2. The WAFs prepared in this manner were clear and colourless, and apparently devoid of undissolved material or oil droplets. The tests were conducted over a 48 hour period at a controlled temperature of 21±1°C, using 10 daphnia per test vessel. No irreversible immobilisation or any other behavioural aberrations were observed over the 48 hour test period.

A definitive study was performed using a WAF containing 1 000 mg/L of test substance. Four replicate tests were run, together with two controls with 10 daphnia per test vessel. Temperature was maintained at 21±1°C, pH was 8.0±0.1, while dissolved oxygen levels were between 8.0 and 8.2 mg/L. As with the range finding tests, no immobilisation or other effects were observed. It is concluded that the test substance is not toxic to daphnia up to the limits of its water solubility. In common with the tests on rainbow trout, the measured level of total organic carbon in the test media indicated no increase over that in the controls, reflecting the low solubility of the test chemicals.

The notifier indicated that tests of chronic toxicity against *Daphnia magna* were in progress.

10.4 Alga, Growth Inhibition (Safepharm Laboratories Limited, 1998t), (Safepharm Laboratories Limited, 1998g)

The effect of SDP and SOP on the growth of green alga was assessed under OECD TG 201 and EC Directive 92/69/EEC (OECD, 1995-1996), (European Commission, 1992).

Range finding studies on the inhibition of growth of *Pseudokirchneriella subcapitata, (formerly known as Selenastrum capricornutum*), with the WAF prepared as in Section 10.2 at nominal test substance loadings of 0, 100 and 1 000 mg/L indicated no inhibition of growth up to the highest loading. Accordingly, the definitive test was conducted using only the WAF containing 1 000 mg/L, together with controls. There were six replicates of the WAF containing medium and three replicates of the control.

The tests was performed over a 96 hour incubation period at 24±1°C. There was no inhibition in the test vessels of either the growth of algal biomass, or of the rate of biomass increase. The results of this study indicate that the E_bLR_{50} is greater than 1 000 mg/L (nominal WAF), and the NOEL is 1 000 mg/L. Both test materials are non toxic to this species of alga up to the limits of their water solubility.

10.5 Marine Organisms

No test reports on the toxicity of ChEster 306 to marine organisms were submitted. A test of sediment toxicity of the sediment reworker *Corophium volutator* (or alternate species) is in progress. The notifier indicated that no significant differences were to be expected in the toxicity of the new chemicals to marine species compared with their freshwater counterparts.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notified chemical, ChEster 306, is to be used as a component of drilling mud used on offshore drilling platforms with almost all released to the marine environment as a result of disposal with waste drill cuttings.

ChEster 306 may comprise up to 10% of the weight of the drilling waste, which is likely to form piles on the sea floor under the drilling platforms. Up to 1 000 tonnes of ChEster 306 combined with other chemicals may be released each year from drilling operations off the Australian coast. It is probable that 5 to 6 platforms may use drilling mud containing notified chemical, each of which could release around 150 tonnes of the chemical each year. A small amount (not possible to quantify) of ChEster 306 may form a "slick" on the water surface after release in calm sea conditions. This is expected to slowly evaporate and enter the atmospheric compartment where it will be degraded through reactions with hydroxyl radicals, with an initial half-life for degradation in the vicinity of 20 hours.

The ChEster 306 reaching the sea floor would become associated with benthic sediments. It is possible that 10 000 to 30 000 tonnes of drill cuttings may accumulate under a given platform, and these could contain 1 000 to 3 000 tonnes of drilling fluid, including the new ester. It is possible that this material would be spread over a relatively wide area of sea floor around each drilling platform. In respect of this point, it is relevant to note that during the operational life of a drilling platform the cuttings usually remain in a mound directly below the platform, and to some degree are "shielded" from the dispersive effects of marine storms and currents by the platform itself. However, on decommissioning of the platforms this protection is removed, allowing for much wider dispersal of the waste cuttings and the associated drilling fluid (Cobby, 1999).

Marine sediments may be either aerobic or anaerobic in nature, and while ChEster 306 is biodegradable under aerobic conditions, (ECETOC, 1993) indicates that it is also likely to be biodegradable under anaerobic conditions. However, the limited evidence and available data indicates that anaerobic degradation in benthic marine sediments may be a slow process due to factors such as low temperature and low density of bacteria. Conditions in the interior of piles of drill cuttings may not be able to sustain adequate bacterial populations (eg through lack of appropriate nutrients), so biodegradation may be a very slow process.

Under aerobic conditions, and assuming that the waste cutting pile can sustain a population of appropriate bacteria, the compounds will biodegrade to water and carbon dioxide. Under anaerobic conditions, the compound will biodegrade to water, carbon dioxide, methane, and carbon monoxide.

ChEster 306 is very hydrophobic, and while the water solubility is very low, there is potential for bioaccumulation. A BCF of 30 300 has been estimated from the n-octanol/water partition coefficient. Given that the rate of biodegradation of the material may be slow, there is potential for significant bioaccumulation in exposed organisms.

Ecotoxicology tests have established that ChEster 306 is non-toxic up to the limits of its water solubility to the fresh water water column species against which it has been tested.

There are currently no available test data on toxicity against benthic or marine organisms. The drill cuttings may contain up to 10% of ChEster 306 (that is, 10^5 mg/kg), and it is conceivable that toxic levels could be exceeded in piles of drill wastes, or in the vicinity of these piles.

When used as a component of drilling mud on offshore drilling platforms, the available data indicates that ChEster 306 may present a hazard to the marine environment when it is discarded with waste drill cuttings. In particular, there are uncertainties surrounding issues of biodegradation, bioaccumulation and ecotoxicity at the likely high exposure levels. Further, it is to be noted that the physical, chemical and biological processes occurring in deposits of marine drill cuttings are not well understood, and it is only recently that appropriate techniques for examination of the spoil piles have been developed (Black, 1999). Consequently, while the present environmental hazard assessment has been based on all presently available data, it is possible that future studies may indicate other factors which should be considered in evaluating the environmental hazard of discarded organic based drilling fluids.

Subsequent to this assessment, the notified chemical in drilling fluid will be subject to state or Commonwealth legislation where environment management plans are required to be submitted by the notifier to the relevant authority for assessment of the environmental risk of each proposed drilling operation. Information to be submitted under relevant legislation should provide additional information on ecotoxicity, biodegradation and bioaccumulation properties of the drilling fluids, therefore enabling further assessment of hazard.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Based on the toxicological data for analogue substances, SDP and SOP, the notified chemical, ChEster 306, is expected to have low acute oral and dermal toxicity. ChEster 306 is not expected to cause any significant organ toxicity, neurotoxicity or reproductive or developmental effects based on the findings of a 90-day repeat oral dose study with SDP. ChEster 306 is not likely to be skin sensitising or genotoxic. However, it may cause some skin irritancy, including a skin drying effect upon repeated or prolonged exposure. The MSDS states that ChEster 306 is not expected to be harmful to internal organs if absorbed through the skin. The MSDS states contact with the eye may cause irritation, pain, reddening and impaired vision. Aspiration into the lung after oral ingestion is a potential hazard based on the measured kinematic viscosity of the analogues. On the basis of the potential aspiration hazard, ChEster 306 is considered hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999) and should carry the hazard classification Harmful (Xn) and risk phrase R65 – May Cause Lung Damage if Swallowed. Risk phrase R66 – Repeated Exposure May Cause Skin Dryness or Cracking, has recently being adopted by the European Commission (European Commission, 1998). Although yet to be adopted by the NOHSC, this risk phrase should be provisionally assigned based upon the observed skin defatting effects of SDP and SOP.

Occupational Health and Safety

Occupational exposure may occur during preparation of drilling mud, manipulation of

contaminated drill bits and associated equipment and recycling of import containers. ChEster 306 is viscous and has low vapour pressure. Consequently, inhalation is not considered a significant route of exposure under normal use conditions. Eye and skin contact is expected to be the main route of exposure. ChEster 306 has low molecular weight, low water solubility and is lipophilic. The possibility of skin absorption cannot be excluded through normal intact skin. Furthermore, skin irritation and skin dryness may compromise the skin's barrier function and subsequent exposure of damaged skin may promote skin penetration of the notified chemical.

During drilling mud preparation and use and container recycling, ChEster 306 will be handled in a manner that is automated/mechanised, intermittent and non-dispersive, with workers required to wear personal protective equipment, namely impervious protective clothing, safety glasses with eye shields and neoprene or nitrile gloves. In view of the frequency of contact, pattern of use and control measures, eye and skin contact is expected to be minimal and the risk of adverse health effects arising from the use of ChEster 306 is expected to be low. Aspiration into the lung after oral ingestion is a potential hazard; however, ingestion is not an expected route of occupational exposure.

During import and transport of ChEster 306 or prepared drilling mud, there is unlikely to be any worker exposure, except in the event of a spill. Exposure after a spill would be controlled by use of the recommended practices for spillage clean up given in the MSDS supplied by the notifier.

Public Health
Public contact will only occur following accidental exposure from a spill or with contact with water containing the notified chemical following cleaning of empty drums. Consequently, the potential for public exposure to the notified chemical during all phases of its life cycle is considered to be low. Based on the above, it is considered that ChEster 306 will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

To minimise occupational exposure to ChEster 306 the following guidelines and precautions should be observed:

- Workers should be advised of the potential for occupational dermatoses following repeated skin exposure to ChEster 306 and to report any skin changes to the occupational health and safety officer at their workplace. When an occupational skin disease occurs, the employer should review work practices and opportunities for contact with the substance and instigate preventive measures 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).

- Safety goggles should be selected and fitted in accordance with Australian Standard (AS) 1336 (Standards Australia, 1994) to comply with Australian/New Zealand Standard (AS/NZS) 1337 (Standards Australia/Standards New Zealand, 1992);

- Industrial clothing should conform to the specifications detailed in AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990);

- Impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia, 1998). The notifier recommends neoprene or nitrile gloves;

- All occupational footwear should conform to AS/NZS 2210 (Standards Australia/Standards New Zealand, 1994c);

- Where exposure to airborne material may occur an organic vapour (Type A) filter respirator should be used. Respiratory protection should conform to AS 1715 (Standards Australia/Standards New Zealand, 1994a), and AS 1716 (Standards Australia/Standards New Zealand, 1994b);

- ChEster 306 is identified as a Class 2 combustible liquid and should be stored, handled and used in accordance with AS 1940 (Standards Australia, 1993);

- Spillage of ChEster 306 should be avoided. Spillages should be cleaned up promptly with absorbents which should be put into containers for disposal;

- Good personal hygiene should be practised to minimise the potential for eye and skin contact and ingestion;

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

If the conditions of use are varied, then greater exposure of the public may occur. In such circumstances, further information may be required to assess the hazards to public health.

This assessment report be included in environmental management submissions where required under State or Commonwealth petroleum (submerged lands) legislation.

14. MATERIAL SAFETY DATA SHEET

The MSDS for ChEster 306 was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994).

This MSDS was provided by the applicant as part of the notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of the applicant.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under subsection 64(1) of the Act the notifier within 28 days, is to:

advise the Director that the following studies are available:

- ecotoxicity tests: early life stage study for fathead minnow (freshwater); chronic toxicity study for *Daphnia magna* (freshwater); and a sediment toxicity study of the marine sediment reworker *Corophium volutator*;
- biodegradation study in seawater; and
- any data on the toxicity of formulated drilling mud generated to meet the requirements of the Western Australia authorities or any other State or Commonwealth authority.

provide the Director with environmental management submissions which have been formerly approved by the relevant State or Commonwealth authority.

Secondary notification of ChEster 306 shall also be required if any of the circumstances stipulated under subsection 64(2) of the Act arise.

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Attachment 1

The Draize Scale for evaluation of skin reactions is as follows:

Erythema Formation	*Rating*	*Oedema Formation*	*Rating*
No erythema	0	No oedema	0
Very slight erythema (barely perceptible)	1	Very slight oedema (barely perceptible)	1
Well-defined erythema	2	Slight oedema (edges of area well-defined by definite raising	2
Moderate to severe erythema	3	Moderate oedema (raised approx. 1 mm)	3
Severe erythema (beet redness)	4	Severe oedema (raised more than 1 mm and extending beyond area of exposure)	4

The Draize scale for evaluation of eye reactions is as follows:

CORNEA

Opacity	*Rating*	*Area of Cornea involved*	*Rating*
No opacity	0 none	25% or less (not zero)	1
Diffuse area, details of iris clearly visible	1 slight	25% to 50%	2
Easily visible translucent areas, details of iris slightly obscure	2 mild	50% to 75%	3
Opalescent areas, no details of iris visible, size of pupil barely discernible	3 moderate	Greater than 75%	4
Opaque, iris invisible	4 severe		

CONJUNCTIVAE

Redness	*Rating*	*Chemosis*	*Rating*	*Discharge*	*Rating*
Vessels normal	0 none	No swelling	0 none	No discharge	0 none
Vessels definitely injected above normal	1 slight	Any swelling above normal	1 slight	Any amount different from normal	1 slight
More diffuse, deeper crimson red with individual vessels not easily discernible	2 mod.	Obvious swelling with partial eversion of lids	2 mild	Discharge with moistening of lids and adjacent hairs	2 mod.
		Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	3 severe
Diffuse beefy red	3 severe	Swelling with lids half-closed to completely closed	4 severe		

IRIS

Values	*Rating*
Normal	0 none
Folds above normal, congestion, swelling, circumcorneal injection, iris reacts to light	1 slight
No reaction to light, haemorrhage, gross destruction	2 severe