File No: NA/486

September 1999

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Parabar 9350

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Street Address: 92 Parramatta Rd Camperdown, NSW 2050, AUSTRALIA
Postal Address: GPO Box 58, Sydney 2001, AUSTRALIA
Telephone: (61) (02) 9577-9514 FAX (61) (02) 9577-9465

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Parabar 9350

1. APPLICANT

Infineum Australia Pty Ltd of 6 Riverside Quay SOUTHBANK VIC 3006 and co-notifiers Australian Petroleum Pty Ltd, BP Australia Limited, Castrol Australia Pty Limited, Mobil Oil Australia Ltd and the Shell Company of Australia Limited have jointly submitted a standard notification statement in support of their application for an assessment certificate for Parabar 9350.

2. IDENTITY OF THE CHEMICAL

The following requests for exempt information were accepted:

chemical name;
molecular and structural formulae;
molecular weight;
spectral data;
purity;
non-hazardous impurities;
identity and percentage of additives/adjuvants;
detailed use information; and exact import volume.

Chemical Abstracts Service (CAS) Registry No.:	not assigned
Trade Name:	Parabar 9350 PDN 1164

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	viscous brown liquid with faint petroleum odour
Boiling Point:	initial 114.2°C; final 522.1°C
Specific Gravity:	0.9045 at 15.5°C
Vapour Pressure:	1.61 $x10^{-5}$ kPa at 24°C

Water Solubility:	5.755 mg/L at 20°C
Partition Co-efficient (n-octanol/water):	log P_{ow} > 6
Hydrolysis as a Function of pH:	hydrolysis of Parabar 9350 has not been determined as it does not contain hydrolysable function groups and is poorly soluble in water
Adsorption/Desorption:	see comments below
Dissociation Constant:	pK_a 6.70
Flash Point:	> 150°C
Flammability Limits:	Upper Explosive Limit = 5.0% (as for the diluent oil) Lower Explosive Limit = 1.0% (as for the diluent oil)
Autoignition Temperature:	340°C (as for the diluent oil)
Explosive Properties:	none indicated by the molecular structure
Reactivity/Stability:	stable viscous liquid at room temperature
Fat solubility:	> 1 000 g/L

Comments on Physico-Chemical Properties

Tests were performed at facilities complying with OECD Principles of Good Laboratory Practice (Organisation for Economic Co-operation and Development, 1995-1996).

The initial and final boiling points represent the boiling range temperature estimates for the notified substance.

Concentrations of the notified substance in water were determined by the total organic carbon (TOC) analysis of the equilibrated solutions. Percent carbon information and results of the TOC analysis were used to calculate the test substance concentration in water.

Hydrolysis of the notified substance was not determined. The substance does not contain any hydrolysable functional groups.

A partition coefficient test reported that the notified substance eluted several discrete chromatographic components when analysed by HPLC. The majority of these components

were estimated to have log K_{OW} values greater than 6. There was one minor component with an estimated log K_{OW} of < 1.7.

After 16 hours of equilibration testing three different soils in duplicate, the following sorption of the water-soluble fraction occurred: 0% in Freehold soil, approximately 11% in Colorado soil and approximately 24% in Snyder soil. These results did not meet the guideline for desorption determination and no further desorption testing was conducted. On the basis of these results, the notifier concluded that sorption of the water soluble components of the notified substance did not occur at any appreciable extent in these soils. The resultant K_{OC}s indicate that this fraction of the notified substance would exhibit very high mobility within soils (McCall, 1981). However, the remainder of the substance is expected to be far less mobile.

The notified substance is completely soluble in fat, indicating its potential to migrate and be stored in biological tissues.

4. PURITY OF THE CHEMICAL

Degree of Purity: 80% minimum

Toxic or Hazardous Impurities: none

5. USE, VOLUME AND FORMULATION

The notified chemical, Parabar 9350, will not be manufactured in Australia. It will be imported as cive package. The lubricating oil additive package will contain 1 to 15 % wt of the notified chemical. Over the next five years the annual import volume of the notified chemical is estimated to be greater than 1 000 metric tonnes.

6. OCCUPATIONAL EXPOSURE

Parabar 9350 will be imported in bulk vessels as a component of a lubricating oil additive package. The bulk liquid will be transported by road tanker to customer blending facilities. Lubricant processors at customer facilities will blend the additive with mineral oil and other additives in 250-25 000 L batches. Final concentration of Parabar 9350 is estimated to be approximately 2% wt of the blended lubricant. Mixed lubricant is finally dispensed into consumer size containers ranging from 2 to 200 L. The finished product is sold and transported in these containers to retail outlets, vehicle fleet operators and industrial users all over Australia

Worker exposure may occur during the following activities:

unloading the additive blend at the port for storage or road transport
transportation of the bulk additive blend to commercial customers for blending
storage sites at the importer's or oil blenders' storage tanks

blending operations at the lubricant oil blending plants
maintenance of pump, blending, and associated equipment at plants or during transport.

Approximately 1- 4 workers will be involved at each location with a maximum of 10 workers estimated to be involved from import to delivery. Ten to fifteen truck deliveries of bulk liquid are expected per year and would typically be completed within a few hours. All transfer and blending operations are automated with flexible pipe transfer connections to sealed containers. Dispensing to consumer containers, which are screw top sealed, is also automated. The main route of exposure to the notified chemical is expected to be dermal but as the notifier states will be minimised during these blending and transport operations due to the use of contained liquid handling systems. On completion of the blending process, containers, transfer hoses, pipelines and pumps are cleaned by flushing through with mineral base oil. Workers are to wear protective gloves, glasses and industrial clothing. Workplace ventilation, including local ventilation, is to be provided.

Workers in the automotive service industry such as mechanics and their assistants doing regular maintenance and repair work on motors are unlikely to use protective clothing apart from overalls in their daily work. Therefore, repeated dermal exposure to the low concentration of Parabar 9350 in the final lubricating oil mixture can occur for these workers.

7. PUBLIC EXPOSURE

The formulation of lubricating oil is an automated process with minimal leakage. Any waste and spills generated during the formulation process is collected and disposed of by incineration. There is low potential for public exposure to the notified chemical during formulation of lubricating oil. Lubricating oil containing the notified chemical will be available to the public through retailers. Public exposure can occur during do-it-yourself (D-I-Y) oil changes. The user may be dermally exposed to the notified chemical and its decomposition products in oils, but the dermal contact would be short and infrequent.

8. ENVIRONMENTAL EXPOSURE

Release

The notifier expects negligible environmental release of the notified substance during product manufacture. Fugitive emissions during transport and blending are considered by the notifier to be negligible due to the very low vapour pressure of the substance. If spillages occur during the blending processes, they will be contained onsite and soaked up with absorbent material, *ie* sand or soil, before being transported offsite to an approved industrial facility for disposal by incineration. The drumming or repacking of the finished lubricant product into consumer sized containers is carried out in an automated filling line. Leakage from product transfer lines is expected to be minimal. Any leakage will be collected, recycled or disposed of accordingly.

During use, the finished lubricant oils containing the notified substance are considered to be contained in the sumps of diesel and gasoline engines until the lubricant is changed. Some of the notified substance will be combusted during use. Collected spent lubricants will be reused, recycled, cleaned or burnt (for their fuel value). Release of the lubricants to the environment may occur due to engine leaks and during engine oil changes.

The empty bulk tanks will be Marpol washed (according to MARPOL[1] marine pollution requirements). The washings are placed into a "slops" tank, which is emptied by waste disposal companies. The bulk lined containers (BLC) are delivered and washed by the handling companies with appropriate washing facilities for BLC. The washed drums are mostly reused as lube drums. The waste washings may be disposed of by incineration or landfill at an industrial facility. Road tankers transport the imported additive package containing the notified substance. When delivery is completed, the tankers are washed at the company's transport wash station. Washings are sent to separator pits and disposed of according to regulations. The notifier claims that in all cases, disposal of the substance would conform to relevant local disposal regulations.

The notifier estimates that an "empty" container has approximately 1.1% unused residues. Therefore, approximately less than 10 tonnes of the notified substance may be present either for incineration as drum washings during reconditioning of the containers or for disposal as consumer container residues. Consumer containers may be recycled, however, it is unlikely that many of these containers will be disposed of to landfill.

Fate

The notified substance will be used as automotive and industrial lubricants and will share their fate. Therefore, most spent oil will be combusted (if used for fuel value) or recycled. Incineration products are expected to include oxides of carbon and sulfur, and calcium salts (in the ash). A minor component will be released to the environment from spills and leaks, but this would be widely dispersed. If the notified chemical were washed off road surfaces, the majority would adsorb to the soil and sediments adjacent to the road. However, the water-soluble components are expected to be more mobile.

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[1] MARPOL: International Convention for the Prevention of Pollution by Ships 1973/78

Collection of waste lubricants is easier to accomplish from industrial and commercial users than from the small but significant D-I-Y market (Australian and New Zealand Environment Council, 1991). The notifier estimates that greater than 10% of cars are not serviced at garages, which may lead to "used oil" not being collected. This could potentially lead to a release of used oil to the environment. It has been estimated from an ANZEC Report (Australian and New Zealand Environment Council, 1991) that 35% of oil used for automotive purposes will not be collected and could be disposed of in an inappropriate manner, such as dust suppression, vegetation control, uncontrolled burial and incomplete combustion[2].

The notified substance was found not to be readily biodegradable (calculated as the ratio of the amount of CO_2 produced to the theoretical carbon dioxide ($ThCO_2$), and expressed as a percentage). Biodegradation amounted to 9.08% at the end of the 28-day exposure to activated sludge from a domestic sewage treatment facility in the CO_2 Evolution (Modified Sturm Test) for ready biodegradability (Organisation for Economic Co-operation and Development, 1995-1996). The inherent biodegradability of the notified chemical was not measured.

The potential for bioaccumulation was not determined. Due to the partition coefficient ($\log K_{OW} > 6$), water solubility (4.506 mg/L) and high fat solubility, bioaccumulation of the substance may be perceived as an issue of concern (Connell, 1989). However, biological membranes are not permeable to chemicals of very large molecular size. Therefore, bioaccumulation of the notified substance is not expected (Australian and New Zealand Environment Council, 1991; Connell, 1989; Anliker, 1988).

[2] No figures are available for how much automotive oil was collected for re-use, but an estimate of about 35% of all oil sold is not collected and possibly disposed of in an inappropriate manner.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Parabar 9350 (PDN 1164) or analogue

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50}> 2 000mg/kg	(Oswald, 1995a)
acute dermal toxicity	rabbit	LD_{50}> 2 000mg/kg	(Oswald, 1995b)
skin irritation	rabbit	non irritant	(Oswald, 1995c)
	human	irritant	(Kenney, 1993)
eye irritation*	rabbit	slight irritant	(Plutnick, 1985)
skin sensitisation	guinea pig	moderate sensitisation	(Oswald, 1995d)
skin sensitisation	human	insufficient data to assess sensitisation	(Kenney, 1993)

*data were from an analogue product

9.1.1 **Oral Toxicity** (Oswald, 1995a)

Species/strain:	rat/Crl:CDBR
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	oral intubation
Clinical observations:	none
Mortality:	none
Morphological findings:	none
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
LD_{50}:	>2 000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in a limit test in rats

9.1.2 **Dermal Toxicity** (Oswald, 1995b)

Species/strain:	New Zealand white rabbits

Number/sex of animals: 5/sex

Observation period: 14 days

Method of administration: single dose (2 000 mg/kg) applied to a clipped area of skin (not <10% body surface); covered with gauze patch and secured with plastic sleeve; removed and washed with peanut oil at 24 hours

Clinical observations: day 1, slight to moderate/severe erythema in all animals; and slight oedema in 8 animals, day 3, slight erythema 6 animals, moderate erythema 1 animal, no oedema from this time, day 7, 4 animals slight erythema, day10, slight erythema 1 animal; day 14, no erythema, all animals gained weight over period

Mortality: none

Morphological findings: postmortem, all animals showed desquamation at application site

Draize scores (Draize, 1959):

Time after treatment (days)	***Animal***									
	1	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***
Erythema [(i)]										
1	2	2	2	2	2	2	3	2	2	2
3	1	1	1	0	1	2	0	0	1	1
7	1	0	1	0	1	0	0	0	1	0
14	0	0	0	0	0	0	0	0	0	0
Oedema										
1	1	2	1	1	0	1	1	1	0	2
3	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0

[i] see Attachment 1 for Draize scales

Test method: similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)

LD_{50}: >2 000 mg/kg

Result: the notified chemical was of low acute dermal toxicity in rabbits

9.1.3 Skin Irritation (Oswald, 1995c)

Species/strain: New Zealand white rabbits

Number/sex of animals: 6 males

Observation period: 3 days

Method of administration: 0.5 ml dose under gauze patch with semi-occlusive dressing securing to clipped backs; removed after 4 hours

Draize scores (Draize, 1959)

Time after treatment (days)	***Animal #***					
	1	***2***	***3***	***4***	***5***	***6***
Erythema [(a)]						
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
Oedema						
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0

[a] see Attachment 1 for Draize scales

Test method: similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)

Result: non irritant

9.1.4 Eye Irritation (Plutnick, 1985)

Species/strain: New Zealand white rabbits

Number/sex of animals: 6 (2 males and 4 females)

Observation period: 14 days

Method of administration: 0.1ml of analogue (see below) introduced into lower conjunctival sac of right eye of each animal; left eye served as control.

Draize scores (Draize, 1959) of unirrigated eyes:

Cornea results for all animals, at all times, were zero

Iris results for all animals, at all times, were zero

	Time after instillation														
Animal	***1 day***			***2 days***			***3 days***			***7 days***			***14 days***		
Conjunctiva [(1)]	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2	0	0	1	0	0	1	0	0	1	0	0	0	0	0
2	2	0	1	1	0	0	1	0	0	1	0	0	0	0	0
3	2	1	0	1	0	0	1	0	0	0	0	0	0	0	0
4	2	0	0	1	0	0	1	0	0	0	0	0	0	0	0
5	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0
6	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0

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

Test method: similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)

Analogue data supplied were from an analogue product, a commercial predecessor of Parabar 9350, with different calcium carbonate content; the structural variation should not alter irritant properties.

Result: slight irritant in rabbits, causing superficial changes in the conjunctiva of all animals at 24 hours; persisting as slight conjunctival redness in 5 animals at 72 hours; redness persisted in 2 animals till 7 days but disappeared at 14 days in all animals; no permanent changes recorded

9.1.5 Skin Sensitisation (Oswald, 1995d)

Species/strain: guinea pig/Hartley albino

Number of animals: 40 female (20 treated, 20 irritation control)

Induction procedure: induction by occlusive topical application
day 0; 0.4 ml applied on 1.5 inch by 1.5 inch sheer adhesive bandage to previously clipped scapular region; bandage removed at 6 hours; residual chemical removed with peanut oil.
day 7 and day 14; repeated as above

Challenge procedure: day 28: 0.4 ml was applied to previously clipped right flank by Hilltop Chamber secured by elastoplast; chamber was removed at 6 hours and remnant Parabar 9350 was removed with peanut oil after an additional 21 hours; day 35 re-challenged to left flank as above.

Challenge outcome:

Challenge	***Test animals***		***Control animals***	
Time & concentration	***24 hours****	***48 hours***	***24 hours***	***48 hours***
28 day 100%	19/20**	15/20	Not Read	0/10
35 day 100%	20/20	15/20	1/10	Not Read

* time after patch removal
** number of animals exhibiting positive response

Test method:	modified Buehler method, similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	moderate skin sensitiser in guinea pigs

Comment

Through a reconsideration of the sensitisation effects of the notified chemical, the study author used various arguments in order to lower an apparent 70% sensitisation response to 10%, which is below the 15% cutoff for consideration as a sensitiser according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1994a). However, the following shortcomings of the test protocol do not assist in clarifying the author's argument and therefore, the arguments could not be considered:

(I) the irritant control animals in this study received no sham treatment at the time of induction but were irritated *de novo* with Parabar 9350, only at the time of challenge or re-challenge, with the same exposure to the chemical as the test animals.

(II) not all of the irritant control group were read at both challenge and re-challenge; of the twenty in this group, half were read at challenge and the other half at re-challenge.

The design of the study makes the irritant control impossible to use to investigate non-specific irritation occurring during test application and induction period. The notifier explained most of the difference between the irritant control and the treated animals as due to irritation rather than sensitisation but did not provide experimental controls to make the explanation feasible.

The report also only used 48 hour data, not 24 hour data, in the final assessments, because the author considered that allergic responses would be longer acting than irritant responses. The report stated that any result which does not show an increase in draize score between 24 and 48 hours, is caused by an irritant effect. However, if the positive sensitiser control (2-mercaptobenzothiazole, MBT) results are considered, at challenge, only 30% of the erythema scores increase at 48 hours while at 24 hours, 40% remain the same and 30% decline. If the data for MBT at re-challenge are considered, then 100% of erythema scores decline between 24 and 48 hours. These particular results are ignored in the study's considerations. The argument that a response which declines between 24 and 48 hours is caused by irritation, is totally negated by the positive sensitiser control group results at re-challenge. On this basis, the arguments in refusing to consider any animals whose results decline in the 24 to 48 hour interval are refuted and cannot be supported.

Using the methods mentioned above, the author estimated that levels of sensitisation potential were reduced from 75% to 10%. A study of the raw data shows that although the sensitisation response, ie erythema, is generally mild to moderate, all but one of the sensitised animals has increased readings over the naive irritated group at

both 28 and 35 days. Considering primary data for both 24 hour and 48 hour time points shows that only 6 animals out of 20 had a reduced response at 35 days compared to 28 days. Indeed, 9 animals showed increase response at 35 days compared to 28 days while 5 animals had response levels remaining the same. The data would appear to warrant a 70% sensitisation level. Without the use of adjuvant, only a 15% response is necessary to classify the chemical as sensitising according to NOHSC (1994a). A moderate level of sensitisation is therefore found to be shown from this data.

Human Trials (Kenney, 1993)

Subjects:	human volunteers
Number:	109 completed the study
Induction procedure:	0.1 ml applied at unknown concentration on semi-occluded patch to portion of upper arm; 9 times for 24 hours (but time of removal controlled by subject), unknown intervals between induction applications; mineral oil undiluted served as the control
Challenge procedure:	after 10-15 day rest period, challenge at naive and original site for 24 hours at 10% dilution with mineral oil for challenge, 5% for rechallenge; summary reveals read at 48 hours and 96 hours after challenge application
Test method:	adaptation of the Draize Patch Test but insufficient details to determine.
Result:	see below

Induction Response:

Sample F
Thirty-seven subjects exhibited mild to moderate erythema accompanied by oedema vesicles, papules and scabbing with the reaction spreading beyond the test area in 25 subjects at the third induction application.

Sample H
Thirty-five subjects exhibited mild to moderate erythema accompanied by papules and scabbing with reaction spreading beyond the test area in 23 subjects at the second induction application.

It is impossible to judge whether there is overlap between these two groups of respondents to Samples F and H. The total number of people irritated may be somewhere between 37 and 72 or higher (see below). Interestingly, the response begins earlier with Sample H than Sample F. Since these two are analogues, details of concentration difference or structural changes may give an insight into the irritant potential of the constituent groups of Parabar 9350.

Thirteen subjects exhibited erythema and papules (usually spreading beyond the test area to both Samples F and H) that were sufficiently severe to cause discontinuation of application of samples and referral to their own physician or a consulting dermatologist. Since the individual responses are not available it is not possible to determine whether these test subjects are included in the thirty-seven to seventy-two mentioned above or whether these numbers should be added to get the total number of irritated subjects. This study concludes that the response patterns of subjects completing all phases of the study to Samples F and H, 'are consistent with clinical irritation.'

Challenge response

Five subjects exhibited mild erythema, four with papules when tested with Sample F at the 96-hour evaluation. With Sample H, one subject at 48 hour evaluation and eleven at the 96 hour evaluation showed mild erythema with papules. Again it is impossible to estimate the overlap of these two groups.

Dose Suitability

According to the current OECD guidelines, the induction dose should be the highest to cause mild irritation, while the challenge dose should be the highest non-irritating dose (Organisation for Economic Co-operation and Development, 1992). It would appear that the induction dose is higher than the guidelines for testing skin sensitisation specify. It is unclear whether the challenge doses are suitable but it is probable that they are close. Without primary data and details of the protocol, it is impossible to accept the conclusion of the study that Parabar 9350 is not a human sensitiser. In this case the animal data, which appear to support the classification as a moderate sensitiser, would stand.

Shortcomings of the study: In brief

1. No clear statement of protocol was given. Only two statements namely, protocol amendment and protocol deviations, were supplied. The protocol was said to be found in Appendix I but this was not attached.

2. In the results section no primary data was supplied. No exact details of results for each subject were supplied.

3. The overall skin sensitisation summary identifies the test material to be analogues to Parabar 9350, prototypes differing in their 'content of minor calcium salts.' The test material was identified only in a hand written addition to the test report as Samples F and H.

4. No information of dilution was supplied but samples F and H are reportedly dispensed at 0.1 ml with an eppendorf-repeating pipette. It is believed that this task would be difficult to achieve with viscous liquid such as Parabar 9350.

5. No detail on the structural differences between the analogues and Parabar 9350 are provided to clarify classification.

9.2 Repeated Dose Toxicity (Trimmer, 1995)

Species/strain:	rats/Crl:CD.BR
Number/sex of animals:	5/sex/group: (1 control, 3 doses, 1 high dose recovery group to 42 days)
Method of administration:	topical on clipped skin on gauze and covered with a plastic wrap
Dose/Study duration::	100, 300, 1 000 mg/kg for a minimum of 6 hours per day for 28 days
Clinical observations:	no changes in body weight, food consumption, slight erythema without oedema observed sporadically in control and treated rats but with increased incidence in high dose rats, no other adverse signs.
Clinical chemistry/Haematology	no changes in haematology, serum chemistry, or clotting factors.
Histopathology:	microscopic examination revealed thickening of epidermis due to acanthosis, hyperkeratosis, sebaceous

	gland hyperplasia, and focal dermal inflammation, changes in all groups including controls, however severity increased in all treated male rats and the 300 and 1000 mg/kg treated female rats; one 1000 mg/kg male rat showed focal dermal necrosis; satellite recovery group showed similar results to control group, indicating reversibility; no other histopathological findings considered related to treatment.
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	the only treatment related toxicity was mild to moderate skin irritation and histopathological changes generally proportional to applied dose but more pronounced at high dose; all changes appeared reversible; the no observable adverse effect level (NOAEL) was determined to be 1 000 mg/kg

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Przygoda, 1995a)

Strains:	TA98, TA100, TA1535, TA1537, TA1538
Concentration range:	250, 500, 1 000, 2 500 and 5 000 μg/plate
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)

Result:	the notified chemical was not considered to be mutagenic in the bacterial strains tested in the presence or absence of metabolic activation provided by rat liver S9 fraction

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Przygoda, 1995b)

Species/strain:	mice/CD-1
Number and sex of animals:	5/5
Doses:	500, 1 000, 2 000 µg/kg
Method of administration:	oral gavage 3 treatments 24 hours apart
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	no increase in micronucleated polychromatic erythrocytes and no induced cytotoxicity

9.3.3 Chromosomal Aberration Assay in Chinese Hamster Ovary (CHO) Cells (Przygoda, 1995c)

Cell line:	CHO/WBL clone
Doses:	10, 20, 40 µg/ml final concentration (to limit of solubility in media) diluted in tetrahydrofuran for 16 and 40 hours with or without rat S9 mix
Test method:	similar to OECD guidelines (Organisation for Economic Co-operation and Development, 1995-1996)
Result:	Parabar 9350 did not induce structural chromosomal aberrations in CHO cells, in either the presence or absence of metabolic activation

9.4 Overall Assessment of Toxicological Data

Parabar 9350 shows low acute oral and dermal activity. The relevant LD_{50} for both administration routes was greater than 2 000 mg/kg. Inhalation toxicity test was not completed as the compound is a viscous liquid at room temperature with a high boiling point and low vapour pressure. The notified chemical is reported to be non-irritant on rabbit skin and a slight irritant to rabbit eyes. Irritation to the eyes was confined to the conjunctiva and though widespread was superficial and resolved in all animals at 14 days.

A test carried out in human volunteers for skin sensitisation using earlier prototypes of PDN 1164, caused at least 30 percent incidence of skin irritation. Approximately 11 percent of the treated subjects withdrew and required medical treatment as a result of skin irritation caused by two analogues of Parabar 9350. The authors conclude that the response patterns to both analogues of Parabar 9350 are consistent with clinical irritation. The results of this human dermal study would have to override the rabbit results and the level of irritancy warrants the classification of Parabar 9350 as a hazardous substance according to the NOHSC (1994a).

Dermal sensitisation in guinea pigs was mostly slight in terms of response but occurred in a large number of animals (at least 70%) and therefore the notified chemical would have to be classified as a moderate sensitiser. Any mixture in which Parabar 9350 is present at equal to or more than 1% would be classified as hazardous (NOHSC, 1994a).

There was no conclusive determination of clinical sensitisation of Parabar 9350 in humans based on the human study provided for the following reasons:

- The identity of the test compounds and their concentration are indefinite. Test analogues are described as prototypes only differing in the calcium content. More detailed information would be needed in any future study designed to resolve the issue of sensitisation. Dilution details are not provided. The study states that the material in Samples F and H was used as supplied, but there were no details as to the exact composition of what was supplied.

- The protocol is not specified. The technical dossier states that the protocol is detailed in Appendix I. This was not supplied in the technical dossier.

- No individual result data was supplied, leading to uncertainty in how to assess the results (see sensitiser section).

- The protocol does not fall within the general OECD guidelines as the induction dose is sufficient to cause a severe degree of irritancy. More than 10% of subjects withdrew and required medical attention. Of those that remained, 30 to 70% reported significant irritation. A primary irritancy test would have allowed for an improved protocol. As it stands

the study results can not be used to provide any information on Parabar 9350 skin sensitisation in humans.

Repeated administration of the notified chemical to rats by dermal application over 28 days induced mild to moderate skin irritation. The histopathological changes were proportional to applied dose but more pronounced at high dose; however, all changes appeared reversible. The no observable adverse effect level (NOAEL) was determined to be 1 000 mg/kg.

No mutagenicity was observed in bacteria and no increase in micronuclei occurred in mouse bone marrow cells. Similarly no clastogenicity was observed in Chinese hamster ovary cells in vitro.

Based on the human and animal studies summarised above Parabar 9350 would be classified as hazardous (NOHSC (1994a). This will warrant the Risk phrase R43, may cause sensitisation by skin contact, in any formulation containing Parabar 9350 at concentrations ≥1% and R38, irritating to skin at concentrations ≥20%.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The supplied acute algal toxicity test was conducted on CMA 604, a calcium long chain alkyl sulfonate, synthetic, high molecular weight chemical, which the notifier claims is representative of the same class as the notified substance. The precise chemical identity of this product was not supplied, as it is proprietary information not privileged to the notifier. CMA 604 is claimed to be the latest commercial predecessor of the notified substance. The notifier claims that *Environment Canada* and the United States' *Environmental Protection Agency* have both accepted this closely related material as representative of the notified substance. The algal toxicity data of CMA 604 was accepted to represent that of the notified substance.

The ecotoxicity studies presented below have been supplied by the notifier. The tests were carried out to OECD Test Methods.

Test	Species	Results (Nominal Concentrations of WAF[#])
Acute Toxicity Static system [OECD TG 203]	Rainbow trout (*Oncorhynchus mykiss*)	96 h LL_{50} > 1 000 mg/L*
Acute Immobilisation Static system [OECD TG 202]	Water flea (*Daphnia magna*)	48 h EL_{50} > 1 000 mg/L**
Growth Inhibition[†] [Wilbury Test 73-CM[Δ]]	F/W Green Algae (*Scenedesmus capricornutum*)	96 h EbC_{50} = 1 000 mg/L 96 h $E\mu C_{50}$ > 1 000 mg/L 96 h NOEC =1 000 mg/L

Water accommodated fraction - see text below; * LL_{50}: Lethal Loading; ** EL_{50}: Effect Loading; † Inhibition to CMA 604 - see text above; and Δ T.R Wilbury test protocol number 73-CM (Acute Toxicity of the Water Accommodated Fraction [WAF] of Lubricant Additive to the Freshwater Algae, *Scenedesmus capricornutum*) based on the procedures of the US EPA and OECD.

Due to the low water solubility of the notified substance, the studies were performed to determine the toxicity of the water accommodated fraction (WAF). A 1 000 mg/L treatment was prepared and stirred for 24 hours. After settling for 1 hour, the WAF was removed and used as the treatment solution. The WAF was slightly cloudy.

The notified substance can be classed as non-toxic to rainbow trout, water fleas and algae, up to its limit of solubility (the WAF).

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The main environmental exposure will be from inappropriate disposal of waste oil. A worst case scenario would be if all the uncollected oil were dumped into a sewer. Disposal of waste oil in a country centre would amount to approximately 219 mg/L per day. A major city would amount to approximately 2.19 mg/L per day, due to the much higher dilution factors expected.

It is expected that the substance will be moderately adsorbed to soil and sediment during the wastewater treatment process. The notified substance has also been shown to have a low water solubility. Therefore, the actual concentration in the effluent will be significantly less. With its anticipated use Australia wide, *ie* not concentrated in one town or city, and with good industrial and public practice, concentrations of the notified substance released to the environment are expected to be further reduced. Ecotoxicity tests showed that the substance is expected to be non-toxic to aquatic organisms up to the limit of its solubility (approximately 6 ppm).

Disposal of containers with waste oil (oil residues and used oil containing the notified substance) should not result in any significant environmental exposure. Waste oil may be recycled or incinerated. Incineration of the oil for fuel value or due to container reconditioning will destroy the substance. Used or waste oil collected by industrial and commercial users that is not re-used is expected to be disposed of to

approved industrial facilities. D-I-Y consumer oil, if disposed of to domestic landfills, should remain in the containers. However, if leaks occur, there is a risk that the water-soluble components of the notified substance may become mobile since it was shown that these components exhibit high mobility within soils. However, these components are expected to be present at low concentrations and widely dispersed throughout suburban landfills in Australia. The remainder of the substance is expected to be far less mobile and remain within the landfill.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Parabar 9350 will be imported as a component of a lubricant oil additive at approximately 20% in the imported product, therefore exposure to this chemical in its pure form should not occur. In the unlikely event of an accident, transport workers would be exposed to Parabar 9350 in the oil additive mixture. The mixture will be a hazardous substance, with skin sensitisation and possibly irritant effects. The new chemical has a relatively high molecular weight (> 1 000) and low volatility; however, absorption is possible due to the fat soluble properties of the notified chemical. In the event of a spill, skin and inhalation contact should be avoided.

Since the delivery, blending and dispensing processes are automated and contained, workers on these sites will normally only be exposed to small volumes of the notified chemical. Exposure could occur at connecting hoses and during maintenance work on containers, pumps and connections but this exposure will be minimised by flushing with mineral oil on completion of processes. Toxicity studies show very low acute toxicity but topical skin effects.

The human studies reveal irritation potential for Parabar 9350 in its pure form but suggest minimal possible danger to workers if exposed for a short time. This means that blending workers will need to wear protective clothing, as well as operating with engineering controls. Sensitisation studies in guinea pigs show the notified chemical to be a moderate skin sensitiser. These studies indicate the possibility of skin sensitisation of workers repeatedly exposed to the notified chemical including those handling Parabar 9350 in the end use products. Parabar 9350 is present at a concentration above the cut-off level for classification as a skin sensitiser (NOHSC, 1994a). This will warrant the Risk phrase R43, may cause sensitisation by skin contact, in any formulation containing 1% or more of Parabar 9350.

Mechanics and associated workers performing repairs and maintenance work on motors will be repeatedly exposed to low levels of the notified chemical and any breakdown products of the lubricating oil mixtures. The concurrent exposure to solvents, detergents, physical abrasion and a range of oil products in their work environment, makes this group of workers particularly at risk to dermatological problems associated with irritants and sensitisation. Recent studies have showed an incidence of hand eczema in car mechanics varying between 15 and 46% in the previous 12 months (Meding, 1994). These values were much higher than workers in control populations who had an incidence of approximately 9%.

Studies on skin patch reactions to preparations of an oil series showed a 28% reaction rate in oil product workers with dermatological problems compared to zero in control workers who were exposed to oil products but had no skin problems. Non-exposed workers also showed no reaction (Wolf, 1996). Allergic responses to oil components are clearly an important component of current skin problems in mechanics and similar workers. These reports all confirm the difficulty for mechanics to protect their skin during their work. A high incidence of cuts, with 28% of workers reporting more than 20 cuts in the last year, was found (Moen, 1995). These studies confirm the additive nature of risk of dermal sensitisation for workers who could be repeatedly exposed to Parabar 9350.

Repeated exposure toxicity data from rats show few clinical changes macroscopically or biochemically. The skin histopathology indicates mild to moderate changes during long term and high dose exposure. All such changes appeared reversible.

None of the genotoxicity results show any effects from Parabar 9350.

Based on the above information it is considered that Parabar 9350 could pose some risk to occupational health particularly in terms of repeated and long-term skin exposure in the automobile and mechanical repair and maintenance industries. At concentrations below 1%, Parabar 9350 is unlikely to be hazardous but workers who will need to use the chemical over long periods of time will need to take precautions to minimise repeated skin exposure. Parabar 9350 is classified as hazardous according to criteria of Worksafe Australia. The Risk phrase R43, may cause sensitisation by skin contact should be used in any formulation containing Parabar 9350 at concentrations ≥1%, and R38, irritating to skin at concentrations ≥20%.

Mineral base oil is used in cleaning containers, transfer hoses, pipelines and pumps on completion of the blending process. Employers need to ensure that the exposure standard for mineral oil mist of 5 mg/m^3 time-weighted average (TWA) (National Occupational Health and Safety Commission, 1995) is not exceeded during the cleaning processes.

Public exposure can occur during DIY engine oil changes. The user may be dermally exposed to the notified chemical and its decomposition products in oil, but the dermal contact would be short and infrequent. Accidental splashing into the eye or exposure to accidental spills is not expected to have significant adverse health effects. The propose use of the notified chemical is not expected to pose a significant hazard to public health provided repeated and prolonged exposure is avoided.

13. RECOMMENDATIONS

To minimise occupational exposure to Parabar 9350 the following guidelines and precautions should be observed:

- 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 Australian Standard (AS) 2919 (Standards Australia, 1994) and AS 3765.1 (Standard Australia, 1990);

- Impermeable gloves or mittens should conform to AS 2161.2 (Standards Australia, 1998);

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

- Spillage of the notified chemical should be avoided. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal;

- Good personal hygiene should be practised to minimise the potential for ingestion;

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

There is a NOHSC exposure standard for mineral oil mist of 5 mg/m^3 (TWA). Employers are responsible for ensuring that this level is not exceeded in the workplace.

14. MATERIAL SAFETY DATA SHEET

The MSDS for the notified chemical was provided in accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 1994b).

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 the Act, secondary notification of the notified chemical shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

16. REFERENCES

Anliker R., Moser P. and Poppinger D. (1988), Bioaccumulation of dyestuffs and organic pigments in fish. Relationships to hydrophobicity and steric factors. *Chemosphere* vol 17(8), pp. 1631-1644.

Australian and New Zealand Environment Council (1991), Used lubricationg oil: Generation recovery and reuse in Australia. Technisearch Ltd for the Waste and Resources Committee (WRAC).

Connell DW. (1989), General characteristics of organic compounds which exhibit bioaccumulation, In: ed. Bioaccumulation of Xenobiotic Compounds. CRC Press, Boca, Raton, USA.

Gobas FAPC., Opperhuizen A. and Hutzinger O. (1986), Bioconcentration of hydrophobic chemicals in fish: relationship with membrane permeation. *Environmental Toxicology and Chemistry* vol 5, pp. 637-646.

Kenney GE. (1993), Human repeated insult patch test. Project No. 92-1341-70, Hill Top Research Inc., Deer Park, Ohio, USA.

Meding B., Barregard L. and Marcus K. (1994), Hand eczema in car mechanics. *Contact Dermatitis* vol 30, pp. 129-134.

Moen BE., Holland BE. and Torp S. (1995), A descriptive study of health problems on car mechanics hands. *Occupational Medicine* vol 45(6), pp. 318-322.

National Occupational Health and Safety Commission (1994a), Approved Criteria for Classifying Hazardous Substances [NOHSC: 1008(1994a)]. Australian Government Publishing Service (AGPS), Canberra.

National Occupational Health and Safety Commission (1994b), National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011(1994b)]. AGPS, Canberra.

National Occupational Health and Safety Commission (1995), National Exposure Standards for Atmospheric Contaminants in the Occupational Environment, [NOHSC:1003(1995)]. In: ed. Exposure Standards for Atmospheric Contaminants in the Occupational Environment: Guidance Note and National Exposure Standards. AGPS, Canberra.

Organisation for Economic Co-Operation and Development (OECD) (1995-1996) Guidelines for Testing of Chemicals CD-ROM. Paris, France.

Organisation for Economic Co-Operation and Development (OECD) (1992) Guidelines for Testing of Chemicals, No 406, Skin Sensitisation. Paris, France.

Oswald J.S. (1995a) Acute Oral Toxicity Study in the Rat. Project No. 106202, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Oswald J.S. (1995b) Acute Dermal Toxicity Study in the Rabbit. Project No. 106207, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Oswald J.S. (1995c) Primary Dermal Irritation Study in the Rabbit. Project No. 106204, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Oswald J.S. (1995d)Dermal Sensitization Study in the Guinea Pig. Project No. 106222, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Plutnick, R.T. (1985) Ocular Irritation Study in the Rabbit, Project No. 254913, Bio/dynamics Inc, East Millstone, New Jersey, USA.

Pryzygoda R.T. (1995c) *In Vitro* Chromosomal Aberration Assay in CHO Cells. Project No. 106232, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Pryzygoda R.T. (1995b) *In Vivo* Mammalian Bone Marrow Micronucleus Assay. Project No. 106230, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Pryzygoda R.T. (1995a) Microbial Mutagenesis in *Samonella* - Mammalian Microsome Plate Incorporation Assay. Project No. 106225, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA

Standards Australia (1998), Australian Standard 2161.2:1998, Occupational Protective Gloves, Part 2: General Requirements. Standards Association of Australia, Sydney.

Standards Australia (1987), Australian Standard 2919-1987, Industrial Clothing, Standards Association of Australian, Sydney.
Standards Australia (1994), Australian Standard 1336-1994, Eye Protection in the Industrial Environment, Standards Association of Australian, Sydney.

Standards Australia (1990), Australian Standard 3765.1-1990, Clothing for Protection against Hazardous Chemicals Part 1 Protection against General or Specific Chemicals, Standards Association of Australia Publications, Sydney.

Standards Australia/Standards New Zealand (1992), Australian/New Zealand Standard 1337-1992, Eye Protectors for Industrial Applications. Standards Association of Australia/Standards Association of New Zealand Publications, Sydney/Wellington.

Standards Australia/Standards New Zealand (1994), Australian/New Zealand Standard 2210-1994, Occupational Protective Footwear, Standards Association of Australia/Standards Association of New Zealand Publications, Sydney/Wellington.

Trimmer G.W. (1995) 28-Day Repeated Dose Dermal Toxicity Study in the Rat. Project No. 106210, Exxon Biomedical Sciences, Inc., East Millstone, New Jersey, USA.

Wolf R., Movshowitz M. and Brenner S. (1996) Supplemental tests in the evaluation of occupational hand dermatitis in soldiers. *International J of Dermatology* vol. 35(3), pp. 173-176.

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.
Diffuse beefy red	3 severe	Swelling with lids half-closed	3 mod.	Discharge with moistening of lids and hairs and considerable area around eye	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