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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Component in OGA 574

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

Component in OGA 574

1. APPLICANT

Chevron Chemical Australia of 385 Bourke Street MELBOURNE VIC 3000 has submitted a standard notification statement in support of their application for an assessment certificate for Component in OGA 574.

2. IDENTITY OF THE CHEMICAL

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

Other Names:	CP 2474, SP 2474, polybutene amine (containing 70% the notified chemical)
Marketing Name:	OGA 574
Number-Average Molecular Weight (NAMW):	1 209
Weight-Average Molecular Weight (WAMW):	1 637
Polydispersity:	1.45
Maximum Percentage of Low Molecular Weight Species	
Molecular Weight < 500:	0%
Molecular Weight < 1 000:	24%
Method of Detection and Determination:	IR, NMR GPC (molecular weight)
Spectral Data:	Spectra of IR and NMR were provided for the identity of the notified chemical.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	Colorless to yellowish viscous liquid
Boiling Point:	Decomposes before boiling.
Specific Gravity:	0.81 g/mL at 15°C
Vapour Pressure:	$<1.33 \times 10^{-3}$ kPa
Water Solubility:	< 1 ppm
Particle size:	Not applicable as notified chemical is liquid
Partition Co-efficient (n-octanol/water):	log P_{OW}=7.1
Hydrolysis as a Function of pH:	Not determined, but expected to be stable.
Adsorption/Desorption:	Not determined, but expected adsorbed to soil strongly.
Dissociation Constant:	Will not dissociate.
Flash Point:	>189°C
Flammability Limits:	Will burn in the presence of enough heat and oxygen.
Autoignition Temperature:	>200°C
Explosive Properties:	Not known to be explosive.
Reactivity/Stability:	Will react in the presence of strong oxidising agents.

Comments on Physico-Chemical Properties

The boiling point of the notified chemical was not determined. The notifier estimates that the chemical will have a low vapour pressure.

The water solubility of the notified chemical was not determined. However, the notifier indicates with comparison to another chemical with known solubility that the polyisobutylene chain of the notified chemical will make it very insoluble in water. The chemical is expected to have a water solubility of less than 1 mg/L.

Due to the low water solubility of the notified chemical hydrolysis is unlikely in the environmental pH range of between 4 and 9. Also the notified chemical contains no functional groups that can hydrolyse.

The partition coefficient log P_{OW} of the notified chemical between n-octanol and water was estimated to be = 7.1 at 20°C by a flask shaking method using reverse phase HPLC similar to the OECD TG 107.

The determination of the adsorption/desorption coefficient of the notified chemical was not undertaken. The notified chemical is expected to be insoluble in water and will largely partition into *n*-octanol rather than water. Due to its low water solubility and surface activity, the chemical is expected to become associated with the organic component of soils and sediments. The notifier also indicates from studies of similar dispersant/detergent substances to the notified chemical that the adsorption/desorption binding coefficients are in the 40-50 000 range.

No dissociation constant data was provided for the notified chemical. At low pH the aromatic amine functionality will be protonated and may result in increased water solubility.

4. PURITY OF THE CHEMICAL

Degree of Purity: 70% in aromatic solvent

Hazardous Impurities: None

Non-hazardous Impurities (>1% by weight):

Impurity	*CAS Number*	*Weight %*
Polyisobutylene	9003-27-4	5-10

Additives/Adjuvants: C9 aromatic solvent (CAS no. 64742-95-6) is on the NOHSC *List of Designated Hazardous Substances* with R45(2) (May cause cancer, carcinogen category 2) and R65 (Harmful: May cause lung damage if swallowed), and cut-off (T%) of 0.1% (National Occupational Health and Safety Commission, 1999).

Degradation Products: Stable under normal conditions.

Loss of Monomers, Additives, Impurities: None expected.

5. USE, VOLUME AND FORMULATION

The notified chemical is intended for use as an ingredient of a deposit control detergent/ dispersant additive in unleaded petrol. The notifier claims that the generalised effects of the use of the notified chemical when formulated in a deposit control additive package and subsequently used in a petrol engine are reduced exhaust emissions, improved fuel economy, reduced engine deposits and longer engine life.

The notified chemical will not be manufactured in Australia. It will be imported into Australia in 8 000 L ISO containers. The new fuel additive will be shipped to Australia as a pre-blended fuel additive, which will contain from 10-90 % w/w of the notified chemical. Estimated import volumes for the chemical are as follows:

Year	1	2	3	4	5
Import Volume (tonnes)	100	200	300	400	500

The range of the final concentration of the notified chemical in finished petrol is expected to be 50 to 500 ppm.

6. OCCUPATIONAL EXPOSURE

As the notified chemical has low vapour pressure and is formulated as a viscous liquid, exposure via inhalation is unlikely. Dermal and ocular contact will be the main routes for occupational exposure.

Transport and Storage

Once received in Australia, the 8 000 L isotanks containing the notified chemical will be loaded and transported by truck to approximately 5 petrol marketeers.

Exposure of workers during transport or storage of the notified component is expected to be low except in the case of accidental spillage.

Refinery/Terminal Facility

Blending of the fuel additive package containing the notified chemical into petrol will occur at approximately 20 petrol blending terminals. At blending site, one worker will unload the isotanks. The worker will connect a flexible hose to the isotank and pump OGA 574 from the isotank to a storage tank through hard piping. In order to minimise spill or leaks, the hose is automatically pigged after the isotank is unloaded and the hose end is kept on an oily drain when not in use. During unloading of the ISO containers, there is opportunity for incidental skin and eye contact to splashes, drips and spills as hose and pipe connections are made or broken. The worker will wear protective clothing, rubber gloves, safety glasses and a hard hat.

A sampling worker will take samples of OGA 574 from the storage tank on its arrival for analysis. Exposure via skin and eye may occur during the sampling. The worker will wear eye protection, protective clothing, rubber gloves and a hard hat. Samples will be analysed by laboratory personnel.

Automatic computer controlled inline blenders are used for mixing the fuel additive package with petrol. The components for the blend are drawn directly and automatically from their storage tanks, blended then sent back to another product storage tank. Occupational exposure during blending is not expected to occur except in the case of accidental spillage.

After blending, one worker will take samples from the product storage tank for analysis. Dermal or ocular exposure may occur during the sampling. The worker will wear eye

protection, protective clothing, rubber gloves and a hard hat. Analysis will be carried out in a laboratory by a laboratory staff.

Once the final petrol is blended, distribution to petrol service stations and other commercial petrol sales outlets will occur by tank truck. Transportation workers are likely to have access to engineering controls and wear protective clothing.

Petrol Service Stations
Attendants at the petrol service stations will receive the petrol by pumping it through a hose to the storage tanks. They may add the petrol into customers' automotive fuel tanks. Some dermal exposure to the notified chemical may occur but this is expected to be at very low levels due to its low concentration in petrol (50-500 ppm). Engine mechanics may come into contact with petrol while working on the fuel system of automotive engines. Engine mechanics and petrol station attendants usually have protective clothing.

7. PUBLIC EXPOSURE

There is potential for exposure of the public to the notified chemical who pump gasoline into automotive fuel tanks. The most likely means of exposure to the notified chemical is skin and eye contact. Consumers at petrol stations seldom wear gloves or other protective equipment. However, the public exposure is expected to be low.

8. ENVIRONMENTAL EXPOSURE

Release

After importation by sea the notified chemical will be transported via road without repackaging in the closed 8 000 L isotanks; potential release would only be through accidental spills. The material safety data sheet (MSDS) details procedures to protect the environment in these cases. Once received by the customers, the isotanks are emptied via a 2 to 2.5 metre flexible hose. After the isotank is unloaded the hose is automatically pigged to the isotank. The notifier indicates that during this procedure the amount of material lost due to spills and leaks is less than 50 mL per load, which is 5 to 45 g of the notified chemical.

The empty isotanks are not cleaned in Australia, but shipped back to the USA.

The same 50 mL volume of loss due to spills and leaks is also possible when transport tankers are filled with the final blended fuel product. This loss would also occur at petrol service stations when tankers are emptied into storage tanks. In both these cases given its low percentage in fuel, the loss of notified chemical in these spills would be expected to be low.

There is no data available that takes into account the frequent minor spills (< 1 L) that would occur at petrol bowsers as customers fill their vehicles with fuel. However, given its low percentage in fuel, the loss of notified chemical in these spills would be expected to be low. The notifier also indicates that the petrol when spilled will evaporate leaving the fuel additive containing the notified chemical behind. The notified chemical will then bind strongly to the soil, concrete and asphalt and, coupled with a low water solubility, aquatic pollution should not be significant.

The intended use pattern of the notified chemical in the fuel additive is not expected to result in a significant release to the environment as it is claimed by the notifier to be destroyed by combustion within the petrol engine. The notifier indicates that small amounts may make it into the crankcase of a combustion engine in blown-by gases. Once in crankcase used oil the notified chemical will continue to act as an ashless type dispersant providing increased performance. There is no direct data to support the claim of complete combustion of the chemical to oxides of carbon, nitrogen and hydrogen when the fuel is burnt within the combustion chamber of petrol engines. The notifier states that the complete combustion of the chemical is essentially an intuitive assumption. It is noted that the chemical is made up of hydrocarbon and oxygen, the normal constituents of the petrol, and a small amount of nitrogen. The notified chemical will be a minute part of fuel and should not survive the temperatures at which the fuel is exploded within the internal combustion engine.

The chemical and additive package will not be directly marketed to the public, but pre-blended into the petrol to be sold at service stations.

Fate

If the notified chemical is released to soil in either a spill or leak from a storage tank, it is expected to bind strongly to soil due to its low water solubility and high partition coefficient of ≥7.1. If released to an aquatic environment, the chemical would tend to partition out of water and into sediment. Once adsorbed to soil/sediment, the fate of the chemical is unknown. However, the ready biodegradability of the notified chemical was examined by exposure to activated sewage sludge microorganisms at a concentration of 10 mg/L at 21°C for 28 days. Degradation of the notified chemical was assessed by the determination of carbon dioxide produced. A degradation of 9.7% was attained after 28 days, so the notified chemical cannot be considered to be readily biodegradable under the terms and conditions of the Modified Sturm Test OECD TG 301B.

The chemical is not expected to cross biological membranes, due to the low solubility and high molecular weight, and should not bioaccumulate (Connell, 1989).

The notifier provides no data concerning the effect of the notified chemical on tail pipe emissions. The notifier supplies a report published by the EPA (US EPA Office of Air and Radiation & Office of Mobile Sources, 1994) on the benefits of deposit control additives like the notified chemical in controlling tail pipe emissions and improving fuel economy. Discussions on test results provided show a statistical difference in HC, CO and NO_x emissions between test fuel with and without the fuel additive. The long term result of detergent fuel additives is to both reduce the formation of engine deposits, i.e. “keep clean”, and “clean up” existing engine deposits leading to reduced levels of tail pipe emissions.

In combination with certain detergent/dispersant additives, the notified chemical is said by the notifier to be registered and approved for use with the US EPA as a fuel additive. Deposit control additives such as OGA 499 are said to be mandated by the US 1990 Clean Air Act because of their recognised ability to control the formation of port fuel injector deposits and intake valve deposits.

9. EVALUATION OF TOXICOLOGICAL DATA

In all toxicological studies submitted, the test substance was CP 2474, which is 70% notified chemical in C9 aromatic solvent (CAS no. 64742-95-6).

9.1 Acute Toxicity

Summary of the acute toxicity of CP 2474

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	rat	LD_{50}> 5 000 mg/kg	(Glaza, 1998b)
acute dermal toxicity	rat	LD_{50}> 2 000 mg/kg	(Glaza, 1998a)
skin irritation	rabbit	Slight to moderate irritant	(Glaza, 1998c)
eye irritation	rabbit	Slight to moderate irritant	(Glaza, 1998d)
skin sensitisation	guinea pig	Not sensitising	(Morris, 1998)

9.1.1 Oral Toxicity (Glaza, 1998b)

Species/strain:	Rats/Cr1:CD(SD)BR
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Oral (gavage), single dose of 5 000 mg/kg
Test method:	Limit test, OECD TG 401
Clinical observations:	Clinical signs of red-stained face and yellow-orange-stained/wet urogenital area were observed after treatment; all animals recovered by day 4.
Mortality:	None
Morphological findings:	No treatment-related effects were observed.
Comment:	None
LD_{50}:	> 5 000 mg/kg
Result:	The test chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Glaza, 1998a)

Species/strain:	Rats/ Cr1:CD(SD)BR
Number/sex of animals:	5/sex

Observation period:	14 days
Method of administration:	A single dermal dose (2 000 mg/kg, undiluted) was applied to the intact skin on each animal's back for 24 hours under a semi-occlusive dressing.
Clinical observations:	Slight erythema was observed in one male and one female with slight edema in the one female. Other animals appeared normal throughout the study.
Test method:	Limit test, OECD TG 402
Mortality:	None
Morphological findings:	No treatment-related effects were observed.
Comment:	None
LD_{50}:	> 2 000 mg/kg
Result:	The test chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

Not performed due to high viscosity.

9.1.4 Skin Irritation (Glaza, 1998c)

Species/strain:	Rabbits/Hra:(NZW)SPF
Number/sex of animals:	4 males and 2 females
Observation period:	7 days
Method of administration:	An undiluted dose (0.5 mL) was applied on each animal's back for 4 hours under a semi-occlusive dressing.
Test method:	OECD TG 404

Draize scores (Draize, 1959):

	Time after treatment					
Animal #	***4 hours***	***1 day***	***2 days***	***3 days***	***4 days***	***7 days***
Erythema						
1	[a]2	2	2	1	1	0

2	2	1	1	1	1	0
3	2	2	1	1	1	0
4	1	1	1	1	1	0
5	1	1	0	0	0	0
6	1	1	1	1	1	0
Oedema						
1	2	2	1	1	0	0
2	2	1	1	0	0	0
3	2	2	1	1	1	0
4	2	1	1	1	1	0
5	1	0	0	0	0	0
6	1	1	1	1	0	0

[a] see Attachment 1 for Draize scales

Comment: Slight to well-defined erythema and very slight to slight oedema were observed in animals. In all cases, irritation had cleared by day 7.

Result: The test chemical was a slight to moderate irritant to the skin of rabbits

9.1.5 Eye Irritation (Glaza, 1998d)

Species/strain: Rabbits/Hra:(NZW)SPF

Number/sex of animals: 5 males and 1 female (group 1), 3 females (group 2).

Observation period: 7 days

Method of administration: An undiluted dose (0.1 mL) was applied into the right eye, with the left eye serving as the control.

The eyes of rabbits in group 1 remained unflushed after treatment, while the treated eyes of the group 2 rabbits were flushed with water for 1 minute starting 30 seconds after instillation.

Test method: OECD TG 405

Draize scores (Draize, 1959):

	Time after instillation														
Animal	***1 day***			***2 days***			***3 days***			***4 days***			***7 days***		
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***

Group 1	(unwashed)														
1	2	2	0	2	1	0	2	1	0	1	0	0	0	0	0
2	2	1	0	1	1	0	0	0	0	0	0	0	0	0	0
3	2	1	0	2	1	0	1	0	0	1	0	0	0	0	0
4	2	1	0	1	1	0	1	0	0	0	0	0	0	0	0
5	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
6	2	1	0	1	1	0	1	0	0	1	0	0	0	0	0
Group 2	(washed immediately after instillation)														
7	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0
8	1	1	0	1	1	0	0	0	0	0	0	0	0	0	0
9	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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

The Draize scores for cornea in both Groups 1 and 2 were zero except 1 male rabbit of Group 1 had score 1 in both degree of opacity and area of involvement at 24 hours.

The Draize scores for iris in both Groups 1 and 2 were zero.

Comment: The results of sodium fluorescein examinations at 24 and 48 hours after treatment (for possible corneal injury) were all negative in both Group 1 and 2, except 1 male from Group 1 had a 10% area positive stain retention at 24 hours after treatment.

Result: The test chemical was a slight to moderate irritant to the eyes of rabbits

9.1.6 Skin Sensitisation (Morris, 1998)

Species/strain: Guinea pigs/Hartley

Number of animals: Pilot group: 4/sex,
Test group: 10/sex,
Control group: 5/sex.

Induction procedure:

test group:
day 0 A dermal dose (0.3 mL, undiluted) was applied on the back of each animal for 6 hours using a Hill Top Chamber which was occluded with rubber dental dam pulled taut and fastened with clips.

day 7 and 14 Induction was repeated as day 0.

control group: Not treated

Challenge procedure:

day 27 A dermal dose (50% w/v in mineral oil) was applied to a skin site that had not been exposed previously for 6 hours using a Hill Top Chamber.

Test method: Buehler method, OECD TG 406

Challenge outcome:

	Test animals		***Control animals***	
Challenge concentration	***24 hours****	***48 hours****	***24 hours***	***48 hours***
50%	**0/20	0/20	0/10	0/10

* time after patch removal

** number of animals exhibiting positive response (grade 1 - slight but confluent or moderate patchy erythema).

Comment: A pilot irritation study was performed to select the test concentrations. Slight patchy erythema was observed in test group after challenge and was treated as negative response based on the similar results from the control group. Historic data of positive controls were provided to demonstrate the sensitivity of the test.

Result: The test chemical was not sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity

9.2.1 Preliminary 5-Day Oral (Gavage) Study in Rats (Knapp, 1999)

Species/strain: Rats/Cr1:CD(SD)BR

Number/sex of animals: 5/sex/group

Method of administration: Oral (gavage)

Dose: 0, 100, 300, 500, and 1 000 mg/kg/day

Study duration:: 5 consecutive days

Clinical observations: All animals survived to study termination. Clinical findings included clear matting, hair loss and soft stool, these were limited to single animals in various dose groups. No

	significant body weight changes were observed.
Comment:	None
Result:	Based on the absence of any significant clinical observations and finding, dose levels of 50, 250 and 500 mg/kg/day were selected for the 28-day oral toxicity study.

9.2.2 28-Day Oral (Gavage) Study in Rats (Knapp, 1999)

Species/strain:	Rats/Cr1:CD(SD)BR
Method of administration:	Oral (gavage)
Dose:	0, 50, 250 and 500 mg/kg/day
Test method:	OECD TG 407 and 421

Subchronic toxicity phase

Number/sex of animals:	10/sex/group, 5/sex/group comprised the recovery group
Study duration::	28 consecutive days treatment, with the recovery group having a 14-day recovery period after treatment.

Clinical observations:
No mortality occurred during the experiment. Neither bodyweight gain nor food consumption was affected during the 28-day treatment or the 14-day recovery period. The only treatment-related finding was clear matting around the mouth one hour after dosing in both male and female animals at 500 mg/kg/day, primarily during weeks 2-4 of treatment.

Clinical chemistry/Haematology
No treatment-related effects were found in hematology, serum chemistry, plasma cholinesterase levels, and urinalysis studies in any of the animals. Although, there were some individual changes such as increase in corpuscular haemoglobin concentration, decreases in globulin, total protein, uric acid and phosphorus in sera, they were not considered to be related to the treatment.

Pathology:
No treatment-related effects were found in macro- and microscopic examinations in animals with or without recovery period. Some changes such as increases in liver weight/bodyweight in 50 mg/kg/day males, and thymus weight (absolute and relative to bodyweight) in 250 mg/kg/day males, decrease in adrenal weight/bodyweight in male animals at 50 mg/kg/day, were noted. However, it was concluded that they were not related to the treatment based on the comparison with control group and other dosing groups.

Neurotoxicity phase

Number/sex of animals: 5/sex/group

Study duration: 28 consecutive days treatment

Clinical observations:
No mortality was observed during the treatment period. Both bodyweight gain and food consumption were not affected by the treatment. Clear matting around the mouth one hour following dosing in weeks 3-4 was found in all male groups (including the control group) and females at 250 and 500 mg/kg/day. The increasing incidence in 500 mg/kg/day males was considered to be treatment-related.

In a functional observational battery of tests, no remarkable differences were observed between the control and treated groups in home cage, handling, open field, sensory, neuromuscular and physiological observations. In open field observations, an increase in the mean urination count in males at 500 mg/kg/day and a decrease in the number at a normal state of arousal in males at 250 mg/kg/day were observed at week 2. However, no similar differences were seen at week 4, or in the females at higher dose levels. Motor activity was also unaffected by the treatment.

Pathology:
No treatment-related differences between the treated and control groups were found in brain weight, brain dimensions, and microscopic examinations. One female at 500 mg/kg/day had digestion chambers (graded minimal) in the sciatic nerve and one control male had a dilated myelin sheath in one lumbar ventral root fiber.

Reproduction phase

Number/sex of animals: 12/sex/group

Study duration: Animals were dosed for at least 28 days prior to mating. The males continued the treatment for a total minimum period of 70 or 71 days. The females continued the treatment until lactation day 4 for those which delivered a litter, or post-mating day 25 for those which did not deliver a litter, or 25 days after the termination of the breeding period without evidence of mating. Females were not dosed if parturition appeared to be in progress.

F_0 Clinical observations:
No mortality was observed during the treatment period. No remarkable differences were observed between the control and treated groups in both bodyweight gain and food consumption at weekly check, during gestation and lactation days. Minor changes in bodyweight and food intake were attributed to biological variation.

Similar to the findings in the subchronic and neurotoxicity studies, clear matting around the mouth one hour following dosing primarily in weeks 1-6 was found in all groups including the control group. It was demonstrated to be dose-related.

Reproductive performance in both treated and control animals was evaluated. The mating and fertility indices in F_0 males and females did not suggest any effects due to the

treatment. The mean numbers of days between pairing and coitus were comparable among the groups. Similarly, the gestation length was unaffected by treatment with the test substance.

F_0 Pathology:
One female (250 mg/kg/day) with no evidence of mating and non-pregnant was internally normal.

Seven females (3, 3 and 1 in the control, 250, 500 mg/kg/day, respectively) were mated and found non-pregnant from necropsy on post mating day 25. The 500 mg/kg/day female had clear intraluminal fluid in both uterine horns. One female from 250 mg/kg/day had dark red lungs (all lobes) and an enlarged thymus gland. One control female had white purulent contents in the cervix and uterus. No remarkable internal abnormalities were noted in the other 4 animals.

The remaining 40 females (9, 12, 8 and 11 in the control, 50, 250 and 500 mg/kg/day, respectively) were necropsied (as scheduled) on lactation day 4. Although some changes were noted in single animals and an increase in implantation sites at 250 mg/kg/day, there were no treatment-related findings compared with the control group and historical control data.

No treatment-related effects were observed at the scheduled necropsy in the 50, 250 and 500 mg/kg/day male groups.

Several statistically significant differences in organ weights were observed. The mean liver weight in 500 mg/kg/d females was increased relative to control. However, when adjusted for body weight gain, the difference was not significant. No corresponding histopathological findings in the liver were observed in high dose males and females. Differences in mean adrenal weights were observed in females at 50 and 500 mg/kg/d, and in mean kidney weights in mid-dose males. However, as these findings were not dose-related, they were attributed to biological variation.

No microscopic findings in the 50, 250 and 500 mg/kg/day groups of both sexes were considered as treatment-related when compared to the control group.

F_1 Clinical observations:
Nine pups (2, 3, 1 and 3 from the control, 50, 250 and 500 mg/kg/day, respectively) were found dead at birth. Six pups (1, 4, 0 and 1 in the same respective groups) were missing and presumed to be cannibalized. The general physical condition of F_1 pups during the postnatal period was similar in all groups.

The mean live litter size, pup body weights, number of pups born and percentage of males per litter at birth and pup survival in 50, 250 and 500 mg/kg/day groups were comparable to findings in the control group.

F_1 Pathology:
No remarkable internal findings were observed in the 9 pups found dead at birth.

Malformation of unilateral microphthalmia was found in a pup in the 250 mg/kg/day group. Some individual variations including dark red eyes, haemorrhagic ring around the iris, pale

liver, non-fully developed ureters and renal papillae were observed in the animals from the treated groups and the control group. No other malformations or developmental variations were observed at any dose level.

All Studies

Comment: The increased incidence of clear matting around the mouth observed in all 3 phases of study was considered to be treatment-related at the dose level of 500 mg/kg/day. It was not considered to be a toxic effect. Minor liver weight changes were observed at 500 mg/kg/d, however, there were no corresponding histopathological findings. Other changes were noted, but did not relate to the treatment.

Result: The test chemical had a no observed effect level (NOEL) of 250 mg/kg/day based on the incidence of clear matting around the mouth, and a no observed adverse effect level (NOAEL) of 500 mg/kg/day based on the absence of systemic toxicity in all 3 phases of the study.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay (Lawlor, 1998)

Strains: *Salmonella typhimurium* TA98, TA100, TA1535 and TA1537; *Escherichia coli* WP2*uvr*A

Concentration range: 33.3, 100, 333, 1 000, 3 300 and 5 000 μg/plate in the presence and absence of S9 metabolic activation (vehicle: Pluronic F127, 25% w/w in ethanol).

Test method: OECD TG 471/472

Comment: The concentrations and vehicle were selected from results in the preliminary range-finding tests. Precipitation was observed at ≥1 000 μg/plate. Cytotoxicity was observed at 5 000 μg/plate without S9 mix in *Salmonella* strains in one of the two experiments. The positive controls had appropriate responses in the studies.

The test chemical did not cause a positive increase in the number of revertants of any the tester strains in the absence or presence of S9 mix under the test conditions.

Result: The test substance was not mutagenic in *S. typhimurium* and *E. coli* in the reverse mutation assay.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (Curry, 1998)

Species/strain:	Mouse/Cr1:CD-1(ICD)BR
Number and sex of animals:	6/males/dose group in the main test.
Doses:	24 hour harvest: 0 (vehicle), 500, 1 000 and 2 000 mg/kg; 48 hour harvest: 0 (vehicle) and 2 000 mg/kg; vehicle: peanut oil The doses were based on the results of two preliminary range-finding tests, where 2 000 mg/kg was the maximum tolerated dose.
Method of administration:	Single IP injection
Test method:	OECD TG 474
Comment:	In the main study, the test chemical did not cause clinical toxicity in treated animals and was not cytotoxic to bone marrow (no increase in ratio of polychromatic erythrocytes to normochromatic erythrocytes (PCE:NCE)). No significant increase in micronucleated PCEs occurred at any of the harvest intervals. The positive controls had appropriate responses in the studies.
Result:	The test chemical was negative in the mouse bone marrow micronucleus assay under the study conditions.

9.3.3 Chromosomal Aberration Study in Chinese Hamster Lung Cells (Murli, 1998)

Strains:	Chinese hamster lung (CHL) cells
Concentration range:	Initial trial: 8 doses in the range 7.85–1 000 μg/mL in both the absence and presence of S9 metabolic activation (6 hour treatment, 24 hour harvest). Confirmatory trial: 10 doses in the range 0.505-60.5 μg/mL (without S9, 21.8 hour treatment, 24 hour harvest or 45.8 hour treatment, 48 hour harvest); 8 doses in the range 6.06-60.5 μg/mL (with S9, 6 hour treatment, 48 hour harvest). Vehicle: test chemical was dissolved in cyclohexane and mixed 1:1 with 10% Pluronic F-68 in water.
Test method:	OECD TG 473

Comment:	*Initial trial* Precipitate was observed at ≥62.5 μg/mL. In the initial trial, cytotoxicity was observed at 15.7 and 31.3 μg/mL without S9 mix and 31.3 μg/mL with S9 mix. The assay was negative for chromosomal aberration, polyploidy and endoreduplication. *Confirmatory trial* Precipitate was observed at ≥45.4 μg/mL. Cytotoxicity was observed at 60.5 μg/mL in the 24 hour assay, 15.2 μg/mL in the 48 hour assay without S9 mix, and at 25.3 μg/mL with S9 mix. The assay was negative for chromosomal aberration, polyploidy and endoreduplication. The positive controls had appropriate responses in the studies.
Result:	The test chemical did not induce chromosomal aberrations in CHL cells with and without S9 metabolic activation under the experimental conditions.

9.4 Overall Assessment of Toxicological Data

The toxicological studies were performed with CP 2474 which contained polybutene amine and C9 aromatic hydrocarbon solvent.

The test chemical was 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. It was a slight to moderate skin and eye irritant in rabbits. It was not a skin sensitiser in guinea pigs.

A 28-day repeat oral dose study in rats included subchronic toxicity (including 14-day recovery period), neurotoxicity and reproductive toxicity phases. The increased incidence of clear matting around the mouth one hour after dosing in both male and female animals was determined to be dose-dependent. Some minor clinical or pathological changes were noted in the study including mean liver weight changes in high dose females, however, they were attributed to biological variation. No remarkable subchronic, neurotoxic or reproductive effects were found to be related to the treatment with the test substance. CP 2474 had a NOEL of 250 mg/kg/day based on the incidence of clear matting around the mouth, and a NOAEL of 500 mg/kg/day, based on the absence of systemic toxicity in all phases of the study.

Three genotoxicity studies were provided. The test chemical was not mutagenic in the *S. typhimurium* or *E. coli* strains in an Ames assay. In a chromosome aberration assay in CHL cells, both with and without metabolic activation, and in an *in vivo* mouse bone marrow micronucleus assay, the test substance was negative. The test chemical was found to be cytotoxic in the *in vitro* studies. In particular, the chromosome aberration assay was severely hampered by high toxicity and heavy precipitation of the test material.

According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), CP 2474 is not classified as a hazardous substance.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier has supplied ecotoxicity studies that were summarised in the following table. The tests were performed in compliance with OECD/EEC Test Methods and according to OECD Principles of Good Laboratory Practices.

Ecotoxicity Test Results

Test	Species	Test concentrations (nominal) mg/L	Results (nominal) mg/L
Acute Toxicity (Static Test) (OECD TG 203)	Rainbow trout *Oncorhynchus mykiss*	60, 100, 150, 250 & 400	96 h LC_{50} = 220 96 h NOEC = 60
Acute Toxicity – Immobilisation (Static Test) (OECD TG 202)	Water Flea (*Daphnia magna*)	130, 220, 360, 600 & 1 000	48 h EC_{50} = 490 48 h NOEC = 220
Growth Inhibition Growth (μ) & Biomass (b) (Static Test) (OECD TG 201)	Green Algae (*Selenastrum capricornutum*)	17, 33, 65, 130, 250 & 500	$E\mu C_{50}$ > 500 E_bC_{50} = 200 NOEC = 65
Respiration Inhibition (OECD TG 209)	Activated Sludge -Aerobic Waste Water Bacteria	650, 1 300, 2 500, 5 000 & 10 000	***3 h EC_{50} > 10 000***

Fish
Rainbow trout were exposed to Water Accommodated Fractions (WAFs) of the notified substance at nominal loading rates of 60, 100, 150, 250 and 400 mg/L for a period of 96 hours under semi-static test conditions. WAFs were obtained by stirring the notified test material at the above nominal concentrations for 24 hours followed by standing for 4 hours prior to removal of the aqueous phase. Based on these nominal loading rate WAFs the 96 hour LC_{50} was determined to be 220 mg/L with 95% confidence limits of 93-140 mg/L. The no observed effect concentration was found to be the 60 mg/L loading rate WAF. Fish exposed to all tested WAF concentrations exhibited a change in colour, loss of equilibrium, lethargy, and immobilisation. The concentration, homogeneity and stability of the test material in the test solutions were not determined.

Aquatic Invertebrates
After 48 hours exposure of the notified chemical to *Daphnia magna* the EC_{50} was determined to be 490 mg/L. No immobilisation and no other signs of intoxication were observed in *Daphnia magna* at the WAF concentration of 220 mg/L. WAFs were made according to the method outlined above.

Algae
After 96 hours exposure of the notified chemical to green algae *Selenastrum capricornutum* the $E\mu C_{50}$ was determined to be greater than 500 mg/L and the E_bC_{50} was determined to be 200 mg/L. The no observed effect concentration at 96 hours was determined to be the 65 mg/L WAF concentration. WAFs were made according to the method outlined above.

Microorganisms
The effect of the notified chemical on the respiration of activated sewage sludge microorganisms was studied. A 3 hour EC_{50} of greater than 10 000 mg/L was determined. The notified test substance did not inhibit respiration of the activated sludge in the tested concentrations. However, insoluble test material was observed floating on the surface of the test media in all non-control test vessels throughout the study.

Conclusion
The ecotoxicity data for the notified substance suggests that it is practically non-toxic to fish, aquatic invertebrates, algae and microorganisms. However, the studies on fish, daphnia and algae all use WAFs which could very well have much lower test substance concentrations, due to low water solubility, than the nominal ones provided. This is confirmed by Total Organic Carbon Analyses carried out by the notifier for the fish and daphnia studies. The results indicate that on average only 1-3 mg/L of the notified component is found within any given WAF irrespective of the starting nominal concentration. The test substance is, therefore, likely to be at least slightly toxic to fish, algae and possibly daphnia.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The intended use pattern of the notified chemical in the fuel additive is not expected to result in a significant release to the environment as it is claimed to be completely destroyed by combustion within the petrol engine, resulting in oxides of carbon, nitrogen and hydrogen. In the event of spills, the MSDS of the additive package containing the chemical contains information on procedures to enable clean up operators to reduce release to the environment.

There is no direct data to support the claim of complete combustion of the chemical to oxides of carbon and hydrogen when the fuel is burnt within the combustion chamber of petrol engines. However, it is evident that the chemical and other constituents of petrol also made up of hydrocarbon and oxygen, will be a minute part will not survive the temperatures at which the fuel is exploded within the internal combustion engine.

Given the above, environmental exposure and the overall environmental hazard is expected to be low.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Toxicological studies were provided with a test chemical containing 70% notified chemical in C9 aromatic solvent. It had low acute oral and dermal toxicity, was a slight to moderate skin and eye irritant but not a skin sensitiser. It did not exhibit evidence of systemic toxicity, neurotoxicity or reproductive toxicity in a combined oral repeated dose rat study (with a

NOAEL of 500 mg/kg/day). It was not mutagenic or genotoxic in bacteria, Chinese hamster lung cells or mouse bone marrow cells. On the data available, the test chemical is not a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999).

Occupational Health and Safety
Dermal and ocular contamination will be the main routes for occupational exposure to the notified chemical. Inhalation will be a minor route of exposure given the high viscosity and low vapour pressure of the notified chemical. Skin absorption is unlikely due to the high molecular weight of the chemical.

The transfer and blending operations at the refinery/terminal facilities are largely enclosed and automatically operated. However, workers at the storage sites could be contaminated with the notified component when connecting and disconnecting hoses and during sampling for laboratory analysis. There is therefore the potential for skin and eye irritancy during these operations. Repeated or prolonged contact to OGA 574 may cause dermatitis. This risk of these effects is expected to diminish in the final petrol mix due to the low concentration of notified chemical added (50-500 ppm). Workers at these sites will need to wear appropriate protective equipment to minimise exposure the chemicals they handle. Under these circumstances, the risk of adverse health risks arising from possible exposure to the notified chemical is expected to be low for these workers.

The health risk in transport workers is considered to be low given that exposure may only occur in the event of accidental spillage. Transportation workers are likely to have access to engineering controls and wear protective clothing to eliminate exposure. Since petrol products are classified as dangerous goods class 3, personal protective and safety equipment such as chemically resistant gloves or gauntlets, and electric torch should be carried on road vehicles according to the ADG code.

Engine mechanics and petrol station attendants will handle petrol products containing low concentrations of the notified chemical. Some skin or eye exposure may occur but expected to be at low levels. Therefore, the health risk is low.

Public Health
There is potential for public exposure to the notified chemical arising from its use as a fuel additive in gasoline, but the low exposure indicates a negligible risk to public health.

13. RECOMMENDATIONS

To minimise occupational exposure to OGA 474, the following guidelines and precautions should be observed:

- Workers should be advised of the potential of occupational dermatoses following repeated skin exposure to the notified chemical and to report any skin changes to the occupational health and safety officer at their workplace. When an occupational skin disease occurs, work practices and opportunities for contact with the substance should be reviewed and preventive measures instigated to ensure other workers do not develop the same condition. Further guideline on preventing the occurrence of

occupational skin disease can be found in the NOHSC guide *Occupational Diseases of the Skin* (National Occupational Health and Safety Commission, 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, 1978);
- 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 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;

If the conditions of use are varied, such as the concentration in petrol is increased, greater exposure of the public may occur. In such circumstances, secondary notification may be required to assess the hazards to public health.

The notified chemical will need to be tested to ensure that it will meet the upcoming criteria in the Australian Standard, *Evaluation of Devices and Additives which Claim to Improve Vehicle Performance*, to be AS 4430.2.

14. MATERIAL SAFETY DATA SHEET

The MSDS for OGA 574 was provided in a format consistent with the *National Code of Practice for the Preparation of Material Safety Data Sheets* (National Occupational Health and Safety Commission, 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 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.

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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