File No: NA/734

May 2000

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

Z-33

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Director
Chemicals Notification and Assessment

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1. APPLICANT

Lubrizol International Inc of 28 River Street SILVERWATER, NSW 2141 has submitted a standard notification statement in support of their application for an assessment certificate for Z-33.

2. IDENTITY OF THE CHEMICAL

The chemical name, CAS number, molecular and structural formulae, molecular weight, spectral data, and details of exact import volume, use and customers have been exempted from publication in the Full Public Report and the Summary Report.

Marketing Name:	Z-33 Anglamol 88E (product containing Z-33)

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	Yellow viscous liquid
Pour Point:	-8°C
Boiling Point:	189.9°C
Specific Gravity:	0.963
Vapour Pressure:	2.1 $X10^{-11}$ kPa at 25°C
Water Solubility:	< 1.7 mg/L at 21.5°C
Fat Solubility:	Completely miscible
Partition Co-efficient (n-octanol/water):	Log P_{OW} > 6.03 (see comments below)
Hydrolysis as a Function of pH:	Not determined (see comments below)
Adsorption/Desorption:	Log K_{OC} < 1.25 to 3.69 (see comments below)

Dissociation Constant:	Not determined (see comments below)
Flash Point:	117°C
Flammability Limits:	Not determined
Autoignition Temperature:	292°C
Explosive Properties:	Does not contain any chemical groups associated with explosive properties.
Reactivity/Stability:	Not an oxidising agent
Viscosity:	6.8×10^{-6} m^2/sec at 40°C (the product containing the notified chemical)

Comments on Physico-Chemical Properties

Tests were performed according to EEC/OECD test guidelines at facilities complying with OECD Principles of Good Laboratory Practice.

Water solubility testing could not be undertaken in accordance with OECD Guideline 105. A limit value of water solubility was determined using a visual estimation method. The notified chemical was mixed with double distilled water. The mixtures (3 replicates) were shaken at 30°C for 24 h, allowed to stand at 20°C for a further 24 h and the extent of dissolution was assessed visually. Aliquots were then further diluted with 100, 1000 and 2000 mL double distilled water and mixed using shaking and ultrasonication. Further observations were then recorded. The water solubility was visually determined to be <1.7 mg/L.

Hydrolysis as a function of pH was not determined because the test was considered not technically feasible for a chemical of low water solubility. The chemical is unlikely to hydrolyse in the environmental pH range (4-9).

Partition co-efficient was determined using the HPLC Method (OECD Guideline 117). A preliminary visual assessment of the partition coefficient was made based on the approximate solubilities of the test material in n-octanol and water. In the definitive test, the retention time was greater than most hydrophobic reference standards (e.g. DDT) except for component 1 with a log P_{OW} of 6.03.

The testing laboratory also estimated the partition coefficient of the notified chemical using the KOWWIN program. From this, the log P_{OW} was estimated to lie between 3.5 and 6.8. While not clear in the report, these values appear to apply to some groups of the notified chemical.

These results indicate that the notified chemical will strongly partition to the octanol phase.

The draft OECD method of Estimation of the Adsorption Coefficient in Soil and Sewage Sludge using HPLC states that the measurement of adsorption coefficient should be carried out on substances in their ionised and un-ionised forms. However, the dissociation constants of the notified chemical are outside the environmental pH range required for this test and therefore measurement was carried out only on the ionised form. The testing laboratory also calculated the soil adsorption coefficient of the notified chemical (for components) using the PC-KOC program. These results are as follows:

For the amine component: $\log K_{OC} = 2.8$
For the acid components: $\log K_{OC} = 1.9$ and 3.9
For the model compound: $\log K_{OC} = 4.3$ and 6.2

Based on the data provided, the notified chemical will strongly sorb to sewage sludge, soil and sediments and organic material.

Dissociation constant was not determined due to the low water solubility of the notified chemical. However, dissociation of the notified chemical could be expected in the environmental pH range (4-9).

Fat solubility was also determined. The standard method specified in OECD Guideline 116 was deemed unsuitable for use with the notified chemical as the test material showed no upper limit for saturation mass fraction in standard fat. Testing was undertaken using a modified procedure which illustrated that the notified chemical is completely miscible in all proportions with standard fat at 37.0 ± 0.5°C.

4. PURITY OF THE CHEMICAL

Degree of Purity: High

Hazardous Impurities: None known

Non-hazardous Impurities (> 1% by weight): None known

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is to be used as a component for gear oil lubricants.

Z-33 will not be manufactured in Australia. It will be imported as part of a concentrate product, Anglamol 88E at between 4.5 and 12 % (w/w) in 205 Litre steel, closed head drums. Import volume for the notified chemical over the next 5 years is expected to be less than 10 tonnes per year.

Anglamol 88E will be reformulated with oil and other components to make gear lubricants. The concentration of Z-33 in the final gear oil will be 0.4 to 1.0% (w/w). After reformulation, the gear oil is packaged into containers ranging from 1 to 205 L.

The notifier indicates that up to 75% of the notified chemical will be distributed to car plants and fleet operators. The remaining 25% is expected to be distributed to individual consumers (the do-it-yourself (DIY) market).

6. OCCUPATIONAL EXPOSURE

As the vapour pressure of the notified chemical is very low, skin contamination would be the main route of occupational exposure. Eye exposure is possible from splashes. Inhalation exposure may occur if oil mist is generated.

Transport and Storage
The notified chemical will be imported into Australia in steel drums. The drums would then be transported to customer sites by truck or rail. Exposure to the notified chemical during transport or storage is unlikely except in the case of accidental spillage.

Blending and Packaging
At the blending site, the concentrate product containing the notified chemical will be either decanted from drums into a trough from which it is pumped into a blend tank, or pumped directly into the blend tank. It will be formulated into gear oil products by mixing with oil and other additives. The blend facility is a fully automated closed system. The final products resulting from this blending process will contain 0.4 to 1% (w/w) Z-33. Dermal contamination from residues in pump lines and on drum bungs may occur when workers connect and disconnect the pump lines. If spills and splashes occur, eye exposure is possible. The opportunity exists for exposure when cleaning up spills or leaks and during machine maintenance. The equipment does not require cleaning after each batch as residue is left for next blend. There will be negligible occupational exposure during the fully automatic and closed blending process.

After blending, the final products containing the notified chemical will be packaged into containers ranging from 1 to 205 litres. The packaging facility is usually located near the blend operation area and equipment is automated. The only opportunity for occupational exposure during packaging would be in the event of broken packages or overflow.

Batch sizes are expected to range from 1 000 to 2 000 kg final product per batch. Each batch will involve 1 to 2 formulators for approximately 3 hours, and 2 to 3 packers for 2 to 5 hours. Blending and packaging facilities are expected to be well ventilated, and all workers will wear face shields, safety glasses, hard hats, long sleeved shirts, trousers, steel-toed shoes and cotton or neoprene gloves.

End use
The final products contain up to 1% of the notified chemical. Gear oil lubricants may be used regularly by workers in large and small facilities to top up reservoirs or, less frequently, as a complete lubricant change in gear boxes. Exposure of the hands may be significant as it is

uncommon for gloves to be worn during addition of these products to automobiles or machinery.

7. PUBLIC EXPOSURE

There is little potential for exposure of the public to the notified chemical, as it is present in the products at very low levels. Accidental exposure of the notified chemical to the skin may cause minor irritation and contact with the eye may produce irritation. The low exposure potential indicates a negligible risk to public health.

8. ENVIRONMENTAL EXPOSURE

Release

During blending of the additive concentrate containing Z-33 into lubricant products, little release is expected as the processes are conducted in fully automated, purpose constructed facilities. The notifier indicates that during the blending operations (typical blend sizes are 1 000 to 2 000 kg) the contents of the 200 L drum are decanted into a trough then pumped to a blend tank, or alternatively pumped directly to the blend tank from the drums.

Following blending, the product is repacked into containers for distribution to customers. Significant release of the blended product during repacking operations is not expected since fully automated equipment is used. The notifier speculated that any spills resulting from either the blending or repackaging operations would be contained within appropriate containment such as catch pans.

No information was provided regarding disposal of these and other spills. However, it likely spills will be soaked up with inert absorbent material. This waste is expected to be sent to an approved waste disposal facility for appropriate disposal via incineration.

Residuals left in import drums are anticipated to be small, and in typical operations involving transfer of drum contents to other vessels, approximately 1% of the total import volume may remain as residue in drums. Based on the maximum import volume, this would result in an annual release of approximately 100 kg of the notified material. The notifier did not indicate what disposal method would be employed for residues nor the fate of drums. However, the drums will be reconditioned and the residues incinerated.

The notifier has claimed to have no knowledge of the fate of wholesale/retail gear lubricant containers nor of the expected amount of residues remaining in these containers when empty. It is assumed that approximately 1% of the total import volume may remain as residue, equating to approximately 100 kg annually of the notified chemical. It is anticipated that the majority of this will be released to landfill on disposal of the containers.

During use as a component of automotive transmission oil, the notified chemical will be contained within the vehicle in an enclosed system, and release is expected to be low. The notifier has indicated that gear oil change frequencies vary considerably. For industrial trucks, the notifier has indicated that gear oil changes may occur at between 24,000 and

160,000 km depending on the wear on the truck. While no information was provided by the notifier, it is estimated that up to 1% of the annual import volume (100 kg) of the notified chemical will be released per year during gear oil changes. According to the notifier, in the majority of cases (75%), the filling of transmissions with the product would take place at properly equipped vehicle production sites or work shop sites. It is anticipated that under these circumstances, used lubricants would be drained, recovered and sent for recycling or reuse. Of the gear oils changed outside commercial workshop environments by DIY users, it is realistic to predict that up to 80% of this may be disposed of by open burning or other inappropriate disposal to soil or water (Macpherson, 1997). Based on the maximum import volume of 10 000 kg/annum, this represents a release of approximately 2 000 kg of the notified chemical per year.

Fate

The major release of the notified chemical to the environment is expected to be via the inappropriate disposal or re-use of used oil (e.g. dust inhibition, timber treatment, dumping, open burning) by DIY consumers. Spillage of the oil may also occur during either servicing (spillage) or use (leaks). Collected used oil may be disposed of at an approved incineration facility or may be burned directly as a fuel. Marshall *et al*. (1999) reports that in Australia, approximately 75% of collected waste oils are sold as burner fuel to power stations, cement kilns, brick works and limeworks. Recovered waste oil may also be processed into diesel extender. If incinerated at high temperatures, the notified chemical in the oil will be destroyed, yielding water and oxides of carbon, nitrogen and phosphorus.

If disposed of inappropriately to soil, the notified chemical in the gear lubricant, is expected to sorb strongly to organic matter and is likely to be immobilised through association with the organic component of soils and sediments. If inappropriately disposed of to the sewer, the notified chemical is expected to ultimately sorb to sewage sludge and disposed of by incineration or sent to landfill.

Some of the notified chemical may enter stormwater drains as a result of leaks from motor vehicles. Based on the maximum import volume, this quantity is estimated at approximately 35 kg per year. A worst case Predicted Environmental Concentration (PEC) has been calculated and is presented in the Environmental Hazard Section below.

Accidental release during transport will be contained and soaked up with inert absorbent material and sent to an approved waste disposal facility for incineration.

Ready biodegradability of the notified chemical was investigated following OECD Guideline 301B (CO_2 evolution test). The test solutions included a replicated control, a standard (sodium benzoate) and the notified chemical. Each test vessel was inoculated with the prepared inoculum at a final concentration of 30 mg suspended solids/L. The CO_2 produced by degradation was collected and analysed. The test material attained 53% degradation after 28 days indicating that it is not readily biodegradable. Sodium benzoate achieved 94% degradation after 28 days confirming the suitability of the test conditions. The toxicity control attained 49% degradation after 28 days thereby confirming that the test material was not toxic to the sewage treatment micro-organisms used in the study. Despite not meeting the readily biodegradable criteria it is anticipated that the notified chemical will not be persistent and will degrade through a series of biotic and abiotic processes.

Based on its low molecular weight, insoluble nature and partition co-efficient, there is potential for the notified chemical to bioaccumulate (Connell, 1989). However, given the low percentage likely to be released to the aquatic compartment and the ability to sorb strongly to organic materials, soils and sediments this potential should be minimised in the proposed use.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Summary of the acute toxicity of Z-33

Test	*Species*	*Outcome*	*Reference*
acute oral toxicity	Rat	LD_{50} > 2000 mg/kg	(Sanders, 1998d)
acute dermal toxicity	Rat	LD_{50} > 2000 mg/kg	(Sanders, 1998b)
skin irritation	Rabbit	moderate irritant	(Sanders, 1998a)
eye irritation	Rabbit	moderate irritant	(Sanders, 1998c)
skin sensitisation	Guinea pig	non-sensitising	(Coleman, 1999)

9.1.1 Oral Toxicity (Sanders, 1998d)

Species/strain:	rat/ Sprague-Dawley CD
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	Gavage (2000 mg/kg)
Test method:	OECD TG 401
Mortality:	no deaths occurred during the study period
Clinical observations:	Hunched posture was noted in all animals up to one day after dosing; all animals had normal bodyweight gain
Morphological findings:	no abnormalities noted at necropsy
LD_{50}:	> 2000 mg/kg
Result:	the notified chemical was of very low acute oral toxicity in rats

9.1.2 Dermal Toxicity (Sanders, 1998b)

Species/strain:	rat/ Sprague-Dawley CD
Number/sex of animals:	5/sex
Observation period:	14 days
Method of administration:	2 000 mg/kg semi-occlusive dressing; test material was removed after 24 hour contact
Test method:	OECD TG 402
Mortality:	no deaths were recorded during the study period
Clinical observations:	no signs of systemic toxicity were noted during the study period; no adverse effects noted on rate of bodyweight gain
Skin reactions:	one male animal had skin irritation which included crust formation five to seven days after dosing females had very slight to well-defined erythema and crust formation one to seven days after dosing
Morphological findings:	no abnormalities noted at necropsy
LD50	> 2000 mg/kg
Result	the notified chemical was of low dermal toxicity in rats

9.1.3 Inhalation Toxicity

An inhalation study was not provided for the notified chemical.

9.1.4 Skin Irritation (Sanders, 1998a)

Species/strain:	Rabbit/New Zealand White
Number/sex of animals:	3 males
Observation period:	14 days
Method of administration:	0.5 ml of test material was applied under semi-occlusive conditions for 4 hours to the intact rabbit skin
Test method:	OECD TG 404

Draize scores:

Time after treatment (days)	***1 hour***	***Animal #*** ***1***	***2***	***3***	***7***	***14***
Erythema						
1	[a]2	2	2	1	0	0
2	2	2	2	1	0	0
3	2	2	2	2	0	0
Oedema						
1	2	2	2	1	0	0
2	3	2	2	1	0	0
3	2	2	2	2	0	0

[a] see Attachment 1 for Draize scales

Comment: during the observation period well-defined erythema and moderate oedema were noted

loss of elasticity was noted at one treated skin site at the 48-hour observation and at all treated skin sites at the 72-hour observation; crust formation was noted at one treated skin site with slight desquamation at two treated skin sites at the 7-day observation

all treated skin sites appeared normal at the 14-day observation

Mean score 24, 48 and 72 hour observation: erythema/eschar formation: 1.7, 1.7, 2.0; oedema formation: 1.7, 1.7, 2.0

Result: the notified chemical was moderately irritating to the skin of rabbits

9.1.5 Eye Irritation (Sanders, 1998c)

Species/strain: Rabbit/New Zealand White

Number/sex of animals: 3 males

Observation period: 7 days

Method of administration: 0.1 mL of test material was instilled into the conjunctival sac of the right eye of each animal

Test method: OECD TG 405

Draize scores of nonirrigated eyes:

	Time after instillation									
Animal	***1 hour***		***1 day***		***2 days***		***3 days***		***7 days***	
Cornea	***o***	***a***	***o***	***a***	***o***	***a***	***o***	***a***	***o***	***a***
1	[1]0	0	1	1	1	1	0	0	0	0
2	dulling	2	1	4	2	4	2 animal killed	4	-	-
3	dulling	3	1	3	1	2	1	2	0	0
Iris										
1	1		1		0		0		0	
2	1		1		1		1		-	
3	1		1		1		0		0	
Conjunctiva	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***	***r***	***c***	***d***
1	2	2	3	3	2	3	2	1	1	1	1	1	0	0	0
2	2	2	3	3	3	3	3	2	3	3	2	3	-	-	-
3	2	2	3	3	2	3	2	2	1	2	1	1	0	0	0

[1] see Attachment 1 for Draize scales
o = opacity a = area r = redness c = chemosis d = discharge

Mean scores 24, 48 and 72 hour observatiion:
corneal opacity: 0.66, 1.33, 1.0
iris lesions: 0.33, 1.0, 0.66
conjunctival redness: 2.0, 3.0, 2.33
conjunctival chemosis: 1.33, 2.33, 1.67

Comment:
over the 72 hour observation period occular readings consisted of: dulling of the normal lustre of the cornea 1 hour after treatment; diffuse corneal opacity and iridial inflammation; and severe conjunctival irritation

one animal was killed for humane reasons, immediately after the 72-hour observation, due to the severity of the reactions;

the two remaining treated eyes appeared normal at the 7-day observation

Result:	the notified chemical was a moderate irritant to the eyes of rabbits

9.1.6 Skin Sensitisation (Coleman, 1999)

Species/strain:	guinea pig/Dunkin Hartley
Number of animals:	10 control animals; 20 test animals; 10 naïve control animals (rechallenge)
Induction procedure:	intradermal induction
Test group	day 1 the dorsal skin on the scapular region of test animals received three pairs of injections as follows: (a) Freund's complete adjuvant (FCA) diluted in an equal volume of water for irrigation; (b) 0.25% test material in Alembicol D (c) 0.25% test material in a 50:50 mixture of FCA and Alembicol D day 7 a patch of filter paper saturated with 0.4 mL of test material was held in place on the skin of animals under occlusive conditions for 48 hours
Control group	control animals were treated similarly to test animals except that the test substance was omitted from the intradermal injections and topical applications
Challenge procedure:	
Test and first 10 controls	day 21 a patch of filter paper was saturated with 0.2 mL of test material (25%, v/v) in Alembicol D and applied to the anterior left flank; test material (12.5%) in Alembicol D was applied in a similar manner to the posterior site; patches were secured to sites for 24 hours; first group of 10 control animals were employed day 28 a second challenge application was made, similar to above, except that test material, 1 and 0.5% v/v was applied to left flank of all controls and test animals; in this instance, the second group of 10 control animals were employed
Test method:	OECD TG 406; Maximisation test of Magnusson and

Kligman

Comment:

Induction	<u>intradermal injection</u> test and control animals had necrosis at sites receiving FCA; slight to well-defined irritation was seen in test animals at sites receiving test material, 0.25% v/v in Alembicol D and slight to well-defined irritation was seen in control animals receiving Alembicol D <u>topical application</u> slight to well-defined erythema was seen in test animals following topical application with test material as supplied; slight erythema was seen in two control animals
Challenge	<u>first challenge</u> well-defined to moderate dermal reactions were seen in test and control animals which precluded meaningful assessment of sensitisation; a second challenge was performed using lower concentrations of test material <u>second challenge</u> no dermal reactions were seen in any of the test or control animals following the challenge
Result:	the notified chemical was non-sensitising to the skin of guinea pigs

9.2 Repeated Dose Toxicity (Jones et al., 1999)

Species/strain:	rat/Sprague Dawley
Number/sex of animals:	5/sex/group
Method of administration:	Gavage
Dose/Study duration:	0, 15, 150, 500 mg/kg/day; vehicle was arachis oil
Test method:	OECD TG 407

Clinical observations:

No deaths were observed during the course of the study.

Animals of either sex treated with 500 mg/kg/day had increased salivation approximately two minutes after dosing from Day 2, together with incidents of increased salivation up to one hour after dosing, noisy respiration, red/brown staining and/or wetting of the external

body surface and fur loss; these effects were not considered to be of toxicological significance.

One female treated with 500 mg/kg/day had reduced bodyweight during week one and developed noisy respiration and hunched posture from Day 13 onwards; pallor of the extremities was confined to Day 22 only.

No toxicologically significant clinical signs were detected in animals treated at 150 or 15 mg/kg/day.

Clinical chemistry/Haematology

No treatment-related changes in haematological parameters were noted.

Females treated with 500 mg/kg/day had a statistically significant increase in plasma alanine aminotransferase compared with controls; there were no other changes in the blood chemical parameters considered to be toxicologically significant.

Histopathology:

Organ weights
Animals of either sex treated with 500 mg/kg/day showed a statistically significant increase in liver weights, both absolute and relative to bodyweight, compared with controls; absolute and relative liver weights were also elevated for 150 mg/kg/day males, but were not statistically significant.

Kidney weight was affected only in male animals, being more pronounced at 500 mg/kg/day but still slightly increased at 150 mg/kg/day; no such changes were detected for 150 mg/kg/day females or for any animals at 15 mg/kg/day.

A reduction in ovary weight at 500 mg/kg/day was not considered to be treatment-related.

Necropsy
No toxicologically important macroscopically observed abnormalities were detected.

Histopathology
Treatment-related liver changes were observed; centrilobular hepatocyte enlargement was observed in all animals at 500 mg/kg/day and in one male rat at 150 mg/kg/day; overall, this finding was considered to be adaptive in nature.

Two males at 500 mg/kg/day had globular accumulation of eosinophilic material in the renal proximal tubular epithelium; this finding was attributed to excess accumulation of α_2-microglobulin, peculiar to male rats but not considered to be treatment-related in this case.

Comment: treatment-related changes were noted in animals at both 500 and 150 mg/kg/day; no such effects were demonstrated in animals treated with 15 mg/kg/day

Result:	for the notified chemical, the No Observed Effect Level (NOEL) was considered to be 15 mg/kg/day

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (Thompson, 1998)

Strains:	*Salmonella typhimurium*: TA98, TA100, TA1535, TA1537 *Escherichia coli*: WP2*uvr*A$^-$
Concentration range:	0, 0.15, 0.5, 1.5, 5, 15, 50, 150, 500, 1500 and 5000 μg/plate in vehicle (acetone)
Metabolic activation:	10% rat liver S9 fraction (Aroclor 1254-induced) in standard cofactors
Test method:	OECD TG 471 – plate incorporation method
Positive controls:	without S9 N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG): 3 μg/plate for TA100, 5 μg/plate for TA1535 and 2 μg/plate for WP2*uvr*A$^-$ 9-aminoacridine (9AA): 80 μg/plate for TA1537 4-nitroquinoline-1-oxide (4NQO): 0.2 μg/plate for TA98 with S9 2-aminoanthracene (2AA): 1 μg/plate for TA100, 2 μg/plate for TA1353 and TA1537 and 10 μg/plate for WP2*uvr*A$^-$ benzo[a]pyrene (BP): 5 μg/plate for TA98
Comment:	an oily precipitate was observed at 5000 μg/plate but this did not interfere with the scoring of the plates the test material caused a visible reduction in the growth of the bacterial lawn of all tester strains, initially at 500 and 1500 μg/plate without and with S9, respectively the test material was therefore tested up to either the maximum recommended dose of 5000 μg/plate or its toxic limit, depending on tester strain type and presence or absence of S9 no significant increases in the frequency of revertants were recorded for any of the strains, at any dose level either with or without S9; all positive controls responded appropriately
Result:	the notified chemical was considered to be non-genotoxic

under the conditions of the assay

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

Species/strain:	mouse/albino Crl:CD-1(1CR)BR
Number and sex of animals:	47/males
Doses:	0, 31.25, 62.5, 125 mg/kg in vehicle (arachis oil) cyclophosphamide was the positive control
Method of administration:	intraperitoneal injection
Test method:	OECD TG 474; EC directive 92/69/EEC
Comment:	<u>experimental design</u> one group of mice from each dose level was sacrificed 24 hours after treatment and a second group dosed at 125 mg/kg was sacrificed at 48 hours; vehicle control animals were killed at 24 and 48 hours and positive controls were killed at 48 hours after treatment; clinical signs of toxicity were evident at the highest test concentration of 125 mg/kg, including hunched posture, pilo-erection, lethargy, pallor, distended abdomen, decreased respiratory rate, laboured respiration, ptosis, ataxia and diuresis; there were three premature deaths in the 48-hour 125 mg/kg treatment group but this loss was not considered to detract from the integrity of the study; there were no statistically significant increases in the frequency of micronucleated polychromatic erythrocytes (PCEs) in any of the test material dose groups compared with concurrent vehicle controls; no adverse effects were seen in the PCE/NCE ratio; the positive control group had a marked increase in the incidence of micronucleated PCEs confirming the sensitivity of the system
Result:	the notified chemical was considered to be non-genotoxic under the conditions of the test

9.3.3 Chromosome aberration assay in human peripheral lymphocytes (Wright & Durward, 1999)

Cells:	Lymphocytes from healthy adult volunteers

Metabolic activation:	rat liver S9 fraction (Aroclor 1254-induced) with standard cofactors
Experimental design:	the notified polymer was dissolved in acetone positive controls: with S9-mix, cyclophosphamide (CP) 25 μg/ml without S9-mix, ethyl methanesulphonate (EMS) 750 and 500 μg/ml for experiments 1 and 2, respectively <u>experiment 1</u> with and without S9: treatment time 4 hours, harvest time, 20 hours test concentrations: 19.53, 39.06, 78.13*, 156.25*, 312.5*, 625, 1 250 and 2 500 μg/ml final S9 concentration: 1% <u>experiment 2</u> without S9: treatment time 20 hours, harvest time, 20 hours test concentrations: 10, 20, 40*, 80*, 160*, 320, 480 and 640 μg/ml with S9: treatment time 4 hours, harvest time, 20 hours test concentrations: 10, 20, 40, 80*, 160*, 320*, 480 and 640 μg/ml final S9 concentration: 2% * concentrations selected for metaphase analysis
Test method:	OECD TG 473; EEC Directive 92/69/EEC, method B10
Comment:	the notified chemical did not induce any significant increase in numbers of cells with chromosome aberrations in the presence and absence of metabolic activation; positive controls induced statistically significant increases in chromosome aberrations compared with vehicle controls
Result:	the notified chemical was considered to be non-clastogenic in human blood peripheral lymphocytes, under the conditions described in the report

9.4 Overall Assessment of Toxicological Data

The notified chemical, Z-33, had very low acute oral toxicity (LD_{50}>2000 mg/kg) and low dermal toxicity (LD_{50}>2000 mg/kg) in rats.

There was no evidence of skin sensitisation in a guinea pig maximisation test. A repeated

dose toxicity study established a NOEL of 15 mg/kg/day. The prime treatment-related changes noted at higher dose levels included centrilobular hepatocytic enlargement and male rat-specific kidney changes associated with accumulation of α2-microglobulin. The latter pathological findings are not considered to represent a hazard to human health.

There was no genotoxic activity associated with the notified chemical when tested for mutagenicity in the *Salmonella typhimurium/Escherichia coli* reversion assays, micronucleus induction in mice or chromosomal aberrations in human peripheral lymphocytes.

Significant findings associated with Z-33 relate to its irritant properties. Although it was a moderate irritant to the rabbit skin, it did not meet the criteria to be classified as a skin irritant, based on the mean scores of the three test animals. In an eye irritation study, severe ocular lesions of the cornea, iris and conjunctivae occurred within 72 hours after exposure and persisted for at least 24 hours, lesions were still present at the end of the 72 hour observation period, and one animal was killed for humane reasons. Based on mean scores of 3 test animals, the notified chemical would not be classified as an eye irritant. However, based on its persistence and the very severe effects seen in one of the three animals, warranting sacrifice, the notifier determines Z-33 to be a hazardous substance, a conclusion supported by this assessment. Accordingly, under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999) the notified chemical is classified as an "irritant (Xi)" and risk phrase "R41 Risk of Serious Damage to Eyes" assigned.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Species	Test	Concentrations[a] (mg/L)	Result (mg/L)
Rainbow trout *(Oncorhynchus mykiss)*	96 h acute	0, 10, 18, 32, 56, 100	56 < ELR50 < 100 NOEC = 32
Water Flea (*Daphnia magna*)	48 h acute immobilisation	0, 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56, 100	ELR50 = 16.93
Water Flea (*Daphnia magna*)	21 d chronic reproduction	0, 0.16, 0.50, 1.6, 5.0, 16.0	ELR50 = 3.36 NOEC = 5
Algae (*Scenedesmus subspicatus*)	72 h growth inhibition	5.0, 10, 20, 40, 80	ErLR50= 32 EbLR50= 16 NOEC = 5.0
Sewage Sludge	3 h respiration inhibition	100, 320, 1000, 3200, 10,000	EC50 = 2 100 NOEC = 320

Due to the low solubility of the notified chemical, test concentrations were prepared as water soluble fractions (WSF). All test material concentrations across all experiments were nominal and actual concentrations were not reported.

The WSFs were prepared as follows. Prior to addition of the notified chemical, dechlorinated tap water was stirred by magnetic stirrers to give a vortex depth of approximately 25% of the overall height of the water column. Appropriate amounts of the notified chemical were added to the vortex and stirred for 23 hours to give the required loading rates (see table above). Each loading rate was then allowed to stand for 1 hr prior to filtration and use. Total Organic Carbon (TOC) analysis was carried out on the test solutions (including the control).

All experiments demonstrated an increase in carbon concentration with an increase in loading rate. TOC levels were approximately half that of the nominal loading rate suggesting that a significant proportion of the notified chemical has dissolved in the water. However, in some instances the WSF gave a high carbon concentration. The testing laboratory hypothesised that these increases were due to post sampling contamination.

The fish toxicity test followed OECD Guideline 203. The experiment was designed as a semi-static system whereby test solutions were renewed daily to maintain nominal concentrations and to prevent nitrogenous waste build-up. The testing laboratory calculated the ELR50 (median effective loading rate) to be 75 mg/L using the Thompson moving average method. At 56 mg/L, sub lethal effects (swimming at the bottom) were observed from 20% of fish at 48 h, 40% at 72 h and 50% at 96 h. At 100 mg/L, 100% mortality was observed at 48 h (with zero mortality at 24 h). The steep slope of the concentration/mortality curve indicates that small changes in concentration may markedly influence toxicity. Probit analysis could not be undertaken because mortality between 0 and 100% was only observed at one concentration. This assessment concludes that the ELR50 can only be predicted to lie between 56 and 100 mg/L.

The *Daphnia magna* Acute Toxicity test followed OECD Guideline 202. The experiment was designed as a static system (i.e. test solutions were not renewed during the exposure period). The testing laboratory calculated the 48 h ELR50 for daphnia to be 16 mg/L using the Thompson moving average method. However, this method is not preferred in this assessment and the ELR50 has been re-calculated using Probit analysis as 16.93 (14.43, 19.84). The NOEC and LOEC could not be established as there were insufficient replicates to undertake non-parametric analysis. The concentration/mortality curve has a steep slope which indicates that small changes in concentration may markedly influence toxicity.

The *Daphnia magna* 21 day reproduction test also followed OECD Guideline 202. The experiment was designed as a semi static system (i.e. test solutions were renewed three times per week during the exposure period). On days 14 and 21 the numbers of young produced per adult for the control and the 0.16, 0.50, 1.6 and 5.0 mg/L loading rate WSF were tested. At the 16 mg/L loading rate WSF test group, 100% mortality occurred in the adult generation prior to maturation (and hence produced no offspring). The investigating laboratory tested for homogeneity of variance by Bartlett's test and compared using the Williams test and used the moving average method of Thompson to conclude the 21-day ELR50 was 3.5 mg/L. However, this method is not preferred. A recalculated ELR50 using Probit analysis is 3.36 (2.77, 3.60).

The Algal Inhibition Test followed OECD Guideline 201. The experiment was designed as a static system (i.e. test solutions were not renewed during the exposure period). Samples were taken at 0, 24, 48 and 72 hours and cell densities determined. The results indicate that at all concentrations except the control, both the growth and the biomass of *Scenedesmus subspicatus* were affected by the presence of the notified chemical. The authors concluded the EbLR50 and ErLR50 were 16 mg/L and 32 mg/L, respectively where EbLR50 is the loading rate that reduced biomass by 50% and ErLR50 the loading rate that reduced specific growth by 50%.

The inhibitory effect on the respiration of activated sewage sludge was investigated according to OECD Guideline 209. The test material was aerated for 3 hours in the presence of

activated sewage sludge with the addition of a synthetic sewage as a respiratory substrate. The rate of respiration was determined after 30 minutes and 3 hours contact time and compared to control data and a reference material (3,5-dichlorophenol). The notifier requested that the testing laboratory increase the maximum concentration tested from the Guideline recommended 1000 mg/L to 10,000 mg/L. The percentage inhibition was plotted against concentration and the NOEC and EC50 were derived from this graph.

These results indicate that the water soluble fraction of the notified chemical is slightly toxic to fish and algae and moderately toxic to daphnids, but not toxic to sewage micro-organisms.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The new chemical will be imported into Australia for use as a component in gear oil lubricants.

During blending, little release is expected as the processes are conducted in fully automated, purpose constructed facilities. Provided vehicles are well maintained, leakage of gear oil is considered to be unlikely. The greatest release to the environment is likely to be as a result of gear oil exchanges, particularly by the DIY market. The majority of oil used by professional workshops is expected to be collected and sent for recycling or reuse. The ultimate fate of most collected waste gear oil is burner fuel for power stations, cement kilns, brick works and limeworks where the chemical will be destroyed. Combustion products are likely to be oxides of carbon hydrogen, nitrogen and phosphorus. However, up to 80% of oil used by the DIY market may be disposed of inappropriately by open burning, or other unapproved disposal to soil or water.

It is difficult to estimate the Predicted Environmental Concentration (PEC) of released lubricant additives because of the diverse disposal routes. However, a worst case estimated PEC may be calculated if the following assumptions are made. That is, all lubricants containing the new chemical are used in a single metropolitan area of 500 square kilometres, the average annual rainfall is 50 cm and 25 % of total import volume (total DIY sales) is eventually washed (in used oil) into the stormwater channels. Under these conditions, the maximum annual release into this localised stormwater system would be around 2.5 tonnes. The annual volume of water drained from this region would be approximately 250×10^6 m^3, and the resultant PEC is approximately 10 μg/L. The safety factor (using daphnia as the most sensitive organism) is calculated to be 336. It is pertinent to note that this result is an extreme worst case scenario, and that in reality releases of the chemical would be at lower levels and more diffuse than indicated here.

Any accidental spillage to the terrestrial environment would be expected to sorb strongly to soils, and is only expected to reach the aquatic compartment by erosion and transport of contaminated soil particles. If accidentally released to the aquatic compartment, the notified chemical is expected to degrade by biotic and abiotic processes. Based on its low molecular weight, insoluble nature and partition co-efficient, there is potential for the notified chemical to bioaccumulate. However, given the low percentage likely to be released to the aquatic environment and the chemical's ability to sorb strongly to organic materials, soils and sediments this potential should be reduced.

Based on the nominal concentrations tested, the notified chemical is considered to be slightly toxic to fish and algae and moderately toxic to daphnids up to its level of solubility.

When used in the manner stated, the notified chemical is unlikely to present a hazard to the environment.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical had very low acute oral and low dermal toxicity in rats. It was a moderate skin and eye irritant in rabbits, but not a skin sensitiser in guinea pigs. In a 28 day repeat dose oral study in rats, the NOEL was established at 15 mg/kg/day. The notified chemical was not mutagenic in bacteria in a reverse mutation assay, or in a micronucleus assay in bone marrow cells in mice. It was not clastogenic in human peripheral lymphocytes. According to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), the notified chemical is classified as hazardous based on its eye irritant effects. The risk phrases R41 (Risk of serious damage to eyes) is assigned for the notified chemical, with a cut-off concentration of ≥5% for any products containing the notified chemical.

The imported product, Anglamol 88E is classified as a hazardous substance based on the concentration of the notified chemical (4.5-12%) in the product according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999).

Occupational Health & Safety
Workers handling the notified chemical in the imported product will be exposed to a hazardous substance, causing severe eye effects.

The risk of eye or skin irritation in transport or storage workers is considered to be low given that exposure may only occur in the event of accidental spillage.

The risk of eye or skin irritation in workers involved in formulating the final products is limited to exposure to residues in piping and on drum bungs and couplings as the notified chemical is pumped to a blending vessel. When the chemical is transferred by decanting, there may be a risk of eye or skin irritation from drips and spills. There may also be a risk of eye or skin irritation should exposure occur during clean up of spills. Following blending, package filling is accomplished in a closed system. The system does not require cleanup after each batch. The risk of eye or skin irritation to workers involved in these operations or to maintenance workers should be negligible given that the concentration of the notified chemical in the blend is less than 1%. The risk of systemic toxicity is also judged to be low. Given the frequency of handling by workers, the engineering controls and use of safety eyewear, gloves and protective clothes and the low concentration of chemical in the final products, the health risk for formulators and packers would be low. The MSDS for the notified chemical and the imported product recommend using nitrile or neoprene gloves.

End use of the formulated products, namely, addition or changing of gear oils may result in frequent exposure. However, the risk of adverse health effects in end use workers is considered to be low given the low levels of the notified chemical in the products.

Public Health
There is negligible potential for public exposure to the notified chemical arising from its use as a component for gear oil lubricants. There will be public contact with the notified chemical when incorporated into products, but the low exposure indicates a negligible risk to public health. Based on the above information, it is considered that the notified chemical will not pose a significant hazard to public health when used in the proposed manner.

13. RECOMMENDATIONS

Occupational Health and Safety
To minimise occupational exposure to Z-33 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 AS 2919 (Standards Australia, 1987) and AS 3765.1 (Standards Australia, 1990); impermeable gloves should conform to AS/NZS 2161.2 (Standards Australia/Standards New Zealand, 1998) (nitrile or neoprene gloves are recommended in the MSDS); 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.

The following regulatory action is recommended:

- Nomination of the notified chemical to the National Occupational Health and Safety Commission for consideration for inclusion in the NOHSC List of Designated Hazardous Substances.

If products containing the notified chemical are hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999), then workplace practices and control procedures consistent with State and territory hazardous substances regulations must be in operation.

Public Health
To minimise public exposure to Z-33 the following guidelines and precautions should be observed:

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

14. MATERIAL SAFETY DATA SHEET

The MSDS for Z-33 and for a final product Anglamol 88E containing the notified chemical were 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 were provided by the applicant as part of the notification statement. They are 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.
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