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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

Chemical in Ammonyx LMDO

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Director
NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Bronson and Jacobs Pty Ltd (ABN 81 000 063 249)
5 Parkview Drive, Australia Centre
Sydney Olympic Park NSW 2127

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

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:
Details of chemical identity.
Identity of impurities and adjuvants.
Spectral data.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:
Toxicological, ecotoxicological physico-chemical and biodegradation information has been supplied on an analogue of the notified chemical.

Testing was not carried out for acute inhalation toxicity, induction of germ cell damage, partition coefficient, flammability limits and dissociation constant.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
None

NOTIFICATION IN OTHER COUNTRIES
Canada (2001)

2. IDENTITY OF CHEMICAL

MARKETING NAME(S)
Ammonyx LMDO (component of this mixture)

METHODS OF DETECTION AND DETERMINATION

METHOD	Infrared (IR) Spectroscopy
Remarks	A reference spectrum was provided

3. COMPOSITION

DEGREE OF PURITY
10 % w/w in Ammonyx LMDO (produced as reaction mixture)

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
Information was supplied on hazardous impurities

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (> 1% by weight)

None

ADDITIVES/ADJUVANTS
Information was supplied on an adjuvant.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
The notified chemical will be imported into Australia as part of the mixture Ammonyx LMDO.

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

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	20	20	20	20	20

USE
Ingredient in consumer dishwashing liquids.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY
Sydney

IDENTITY OF MANUFACTURER/RECIPIENTS
Formulation sites include:
Colgate-Palmolive P/L
50 Marple Avenue
Villawood
NSW

TRANSPORTATION AND PACKAGING
Ammonyx LMDO containing the notified chemical will be imported by sea in 20 tonne isotainers and 1 tonne intermediate bulk containers (IBCs), and transported by road to the notifier's warehouse and customer sites.

5.2. Operation description

Ammonyx LMDO containing 10% of the notified chemical will be incorporated into dishwashing liquid formulations at customer sites. It is expected that the process will involve blending of the surfactant with water and other ingredients. The final dishwashing formulations containing up to 2% of the notified chemical will undergo QC procedures, and be filled into smaller containers for distribution and sale to consumers.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Truck/warehouse worker	1	1-2 h/day	10 days/year
Formulation workers	3-6	7 h/day	80 days/year
Packaging workers	12-15	7 h/day	80 days/year
QC workers	2	1- 2 h/day	80 days/year

Exposure Details
No exposure to workers is expected prior to delivery of the isotainers or IBCs at the formulation sites, as the containers would not be opened. Incidental exposure would only occur in the case of accidental spillage.

At the known formulation site, the mixture containing 10% of the notified chemical will be transferred mechanically from isotainers to storage tanks or directly into mixing tanks. The worker supervising the transfer has potential for dermal exposure during changing of hose couplings before and after the transfer step, however PPE would be worn. Transfer from IBCs would also be a mechanical process with similar exposure potential. Some dermal exposure is also possible during formulation of dishwashing products, when the notified chemical (as part of a mixture) is transferred to the semi-closed mixing tank and during routine clean-up operations. Inhalation exposure is not likely as the notified chemical has low volatility, processes are carried out below 50^{o}C, and aerosols are not generated during the processes. However there is local exhaust ventilation (LEV) on the mixing tanks. Personal protective equipment worn by all employees includes safety glasses and footwear. Gloves and aprons are also used if exposure to chemicals is likely, and in major cleaning tasks further protective clothing would also be worn

In the later stages of formulation, during transfer of batches to storage tanks and during filling of the dishwashing liquid into bottles, dermal exposure may occur to the dishwashing liquid containing up to 2% of the notified chemical. Most processes are automated with remote control, however manual changeover of hoses occurs. Each batch of the dishwashing liquid is sampled from a recycle loop in the mixing tank, and tested in the laboratories. Where dermal exposure to the product is likely, for example in sampling or cleanup of spills, gloves are worn in addition to the usual safety glasses and protective footwear.

Once the dishwashing liquid is packaged for distribution to retail outlets, no further worker exposure is expected from contact with the sealed packages. However, use of the products downstream by employees of cafes and other food preparation sites is possible, and would be similar to the pattern of public exposure. The level of PPE used in commercial dishwashing is likely to vary and would include gloves in many cases.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Environmental release of the notified chemical in the imported formulation (10% w/w) is unlikely during importation, storage and transportation. Accidental spills, leaks and catastrophic mechanical failure during a transport accident is the most likely reason for environmental release. Engineering controls (eg. Isotainer and IBC specifications), personnel training, and emergency clean-up procedures (ie. spill response instructions on Material Safety Data Sheet and label) will limit the impact on the environment of such incidents.

RELEASE OF CHEMICAL FROM USE

Manufacturing facilities

Blending and repackaging operations at manufacturing facilities are unlikely to result in environmental release of the notified chemical due to worker training, MSDS procedures for spill response, enclosed blending facilities, automated facilities and bunding. Product concentration of notified chemical will be ~1-2%. Spills of the notified chemical will be contained and disposed of by incinerator. Emptied containers will be rinsed and recycled, with rinsate (comprising <1% of notified chemical) incinerated.

After use in household and commercial cleaning products, the notified chemical will be mostly disposed of to sewer. During use, products containing the notified chemical will be diluted in water.

5.5. Disposal

The majority of the notified chemical will eventually be disposed of to sewer after use. A small proportion (1-5%) arising from spills and container rinsate may be incinerated. Residues in consumer bottles containing a low concentration of notified chemical will likely be recycled with the container or sent to landfill for disposal.

5.6. Public exposure

The EU Technical Guidance Document (ECB, 2003) lists information on consumer hand dishwashing liquids in Western Europe, based on information from the International Association for Soap, Detergents and Maintenance Products. From 3 to 10 grams of regular dishwashing liquid is used per task, and 2 to 5 grams of concentrates per task. Use frequency is 3 to 21 times per week, with typical usage 14 times per week. Duration of exposure is typically 30 minutes, ranging from 10 to 45 minutes.

The notified chemical will be incorporated in domestic dishwashing liquids at up to 2%, which will be used widely by consumers. There could be incidental dermal exposure to the dishwashing liquid itself, through splashes or contamination of the outside of the packaging. An additional form of incidental dermal exposure may be through use of the dishwashing liquid to wash hands. However, the main routine exposure is likely to be to dishwashing water containing the product. Inhalation exposure is considered unlikely either from the dishwashing liquid or from water containing it, as the chemical has low volatility and aerosols are unlikely to be formed.

Oral exposure could occur from residues of the dishwashing liquid remaining on plates and utensils, if these articles are not rinsed after washing. It is expected that residues would be low, and transfer to ingested food would be even lower. Accidental oral exposure of young children to dishwashing detergents is also possible.

It is expected that some consumers would wear gloves while washing dishes, and others would not.

6. PHYSICAL AND CHEMICAL PROPERTIES

Data in this section is from an analogue of the notified chemical unless otherwise noted.

Appearance at 20°C and 101.3 kPa Colourless to light yellow liquid with amine-like odour (Ammonyx LMDO).

Melting Point/Freezing Point Melting point < 0°C
Pour point - 4 °C

Remarks Values quoted in MSDS for Ammonyx LMDO.

Boiling Point Could not be determined.

METHOD EC Directive 92/69/EEC A.2 Boiling Temperature.
Remarks The analogue NINOX HCDO decomposes from 130°C, prior to boiling. The test authors used vapour pressure and structural data to estimate a boiling temperature of > 360°C.
TEST FACILITY Safepharm (2000a)

Density 1020 kg/m^3 at 21°C

METHOD EC Directive 92/69/EEC A.3 Relative Density.
Remarks Gas comparison pycnometer method (analogue NINOX HCDO).
TEST FACILITY Safepharm (2000a)

Vapour Pressure < 3.3x10^{-7} kPa at 25°C

METHOD EC Directive 92/69/EEC A.4 Vapour Pressure.
Remarks Vapour pressure balance method (analogue NINOX HCDO). Vapour Pressure balance measurements in the range 65-85°C were extrapolated to 25°C. Two different estimation methods were also used. The notified chemical is only very slightly volatile (Mensink *et al*., 1995).
TEST FACILITY Safepharm (2000c)

Water Solubility Miscible in all proportions at 20°C

METHOD EC Directive 92/69/EEC A.6 Water Solubility.
Remarks A preliminary and definitive test were carried out on the analogue NINOX HCDO. A modification of the Flask Method was used, the standard method being unsuitable because of the high saturation levels of the test substance. Mixtures of test substance and glass double-distilled water (41.6-89.7% w/w) were shaken at approximately 30°C for 71 h. After standing at 20°C for 24 h, the extent of dissolution was assessed visually. The mixtures of test substance and water formed either colourless viscous liquid or, at >50% w/w, a colourless gel. The water solubility is estimated in the range of 830-930 g/L at 20°C. The notified chemical is expected to be readily soluble in water.
TEST FACILITY Safepharm (2000a)

Hydrolysis as a Function of pH Hydrolytically stable.

METHOD EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH (NINOX HCDO analogue).

pH	*T (°C)*	$t_{½}$
4	25	>1 yr
7	25	>1 yr
9	25	>1 yr

Remarks Test solutions were analysed by GC. Test concentrations were in the range of 1.93-2.50 g/L. Based on the behaviour of the analogue, the notified chemical is expected to be stable over a range of pHs.
TEST FACILITY Safepharm (2000a)

Surface Tension 35.4 mN/m at 22°C

METHOD EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Test concentration: 1.24 g/L (Analogue NINOX HCDO). An interfacial tension balance was used. The test substance is considered to be a surface active substance (surface tension <60 mN/m).
TEST FACILITY Safepharm (2000a)

Partition Coefficient (n-octanol/water) log Pow = 4.62 at 20°C.

METHOD Estimated using KOWWIN V. 1.63 (Syracuse Research Corporation).
Remarks Being surface active and with a high water solubility, the shake flask and HPLC methods were considered inappropriate. Using EPI, a log Kow of 4.62 for the notified chemical was estimated (Environment Canada, 2001), confirming that determined similarly for the relevant fraction in NINOX HCDO.
TEST FACILITY Safepharm (2000a)

Adsorption/Desorption – screening test log K_{oc} = 1.80-3.42 (analogue NINOX HCDO)

METHOD Estimated using QSAR Equation: log Koc = 0.33 x log Pow +1.25.
Remarks Being surface active and with high water solubility, the OECD HPLC method was considered inappropriate. Using EPI, a log Koc of 5.14 was predicted for the notified chemical (Environment Canada, 2001). The notified chemical may potentially be mobile in soil; however, the cationic species is expected to be dominant resulting in strong adsorption to clay minerals.
TEST FACILITY Safepharm (2000a)

Dissociation Constant pKa = 4.7

Remarks	Estimated value based on ACD/pKa software (v. 4.56). Despite this, the substance is expected to remain ionised throughout the environmentally relevant pH range 4-9 by the notifier. The cationic species is expected to be dominant resulting in high water solubility, low volatility and strong adsorption to clay minerals.

Particle Size Not applicable as chemical is in aqueous solution.

Flash Point No flash point observed

METHOD	EC Directive 92/69/EEC A.9 Flash Point.
Remarks	Closed cup equilibrium method. The flash point test on the analogue NINOX HCDO was carried out up to 151^0C. As decomposition occurs from 129^0C (Safepharm 2000a), the test substance did not have a flash point up to its decomposition temperature. Apparent boiling occurred in the flash point test from 151^0C.
TEST FACILITY	Safepharm (2000b)

Flammability Limits Not performed

Remarks	The notifier states that the chemical has low volatility and is predicted not to possess a flash point below its boiling temperature. Therefore it not expected to form ignitable mixtures with air.

Autoignition Temperature 278 ± 5°C

METHOD	92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks	The analogue NINOX HCDO was tested.
TEST FACILITY	Safepharm (2000b)

Explosive Properties Not explosive

METHOD	EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks	The analogue NINOX HCDO was tested.
TEST FACILITY	Safepharm (2000b)

Reactivity Not expected to be reactive in use.

Remarks	MSDS for Ammonyx LMDO notes that this material reacts with acids, alkalis and oxidising agents.

7. TOXICOLOGICAL INVESTIGATIONS

All toxicity data below were based on the analogue NINOX HCDO, which is similar to the notified chemical, except in having a distribution of carbon chain lengths, rather than a carbon chain of fixed length.

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 500 to 1000 mg/kg bw	harmful
Rat, acute dermal LD50 > 2000 mg/kg bw	low toxicity
Rat, acute inhalation LC50	not performed
Rabbit, skin irritation	slightly to moderately irritating
Rabbit, eye irritation	irritating to severely irritating
Guinea pig, skin sensitisation – adjuvant test.	no evidence of sensitisation
Rat, repeat dose oral toxicity – 28 days.	NOAEL 15 mg/kg bw/day
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro chromosome aberration	non genotoxic
Genotoxicity – in vivo	not performed
Pharmacokinetic/Toxicokinetic studies	not performed

7.1. Acute toxicity – oral

TEST SUBSTANCE: NINOX HCDO 92%

METHOD: OECD TG 423 Acute Oral Toxicity – Acute Toxic Class Method.
EC Directive 96/54/EEC B.1tris Acute Oral Toxicity – Acute Toxic Class Method.

Species/Strain: Rat/Sprague-Dawley CD strain, Charles River.

Vehicle: Distilled water

Remarks - Method: Dosage was adjusted to account for 92% purity of the test substances ie actual dose level of the test substance was 2174 mg/kg bw.
A group of 3 rats was initially tested at the starting dose of 2000 mg/kg bw, (based on 100% material). Based on the results of this test, further groups were tested at a lower dose level.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3 F	2000	2/3
2	3 F	200	none
3	3 M	200	none

LD50: 500 - 1000 mg/kg bw

Signs of Toxicity: Animals dosed at 2000 mg/kg bw showed hunched posture, diarrhoea, and increased salivation, with incidents of pallor of the extremities, emaciation, lethargy, pilo-erection, decreased respiratory rate, laboured respiration, red/brown staining around the snout and tiptoe gait. The single surviving animal at 2000 mg/kg bw recovered 5 days after dosing.
No signs of toxicity were seen in animals dosed at 200 mg/kg bw and all surviving animals showed expected body weight gains.

Effects in Organs: Animals dosed at 2000 mg/kg bw that died during the study showed the following abnormalities at necropsy: haemorrhagic lungs, dark liver, dark kidneys, haemorrhagic gastric mucosa, sloughing and/or haemorrhage of the non-glandular epithelium of the stomach, and haemorrhagic small and large intestines.
No abnormalities were noted at necropsy in either the surviving animal dosed at 2000 mg/kg bw or in the animals dosed at 200 mg/kg bw.

Remarks - Results: The deaths that during the study occurred one or two days after dosing.

CONCLUSION	The notified chemical is harmful via the oral route.
TEST FACILITY	Safepharm (2000i)

7.2. Acute toxicity – dermal

TEST SUBSTANCE	NINOX HCDO 92%
METHOD	OECD TG 402 Acute Dermal Toxicity – Limit Test. EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal) – Limit Test.
Species/Strain	Rat/Sprague-Dawley CD strain Charles River.
Vehicle	None
Type of dressing	Semi-occlusive.
Remarks - Method	Dosage was adjusted to account for 92% purity of the test substances ie actual dose level of the test substance was 2174 mg/kg bw. After the 24 h contact period, the test substance was removed by wiping with cotton wool moistened with distilled water.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 M / 5 F	2000	None

LD50	> 2000 mg/kg bw based on 100% test material
Signs of Toxicity - Local	Very slight to well-defined erythema and slight oedema at the treatment site was noted in all animals, lasting in some animals for up to four days after treatment. In addition the following adverse skin effects were noted in some animals: desquamation (4 F), brown discolouration (2 M, 2 F), crust formation (5 F) and bleeding (1 M). Glossy skin was noted in six animals, starting at days 10 to 12 and persisting at day 14. All other adverse effects had cleared by the end of the 14 day observation period.
Signs of Toxicity - Systemic	None noted.
Effects in Organs	No abnormalities were noted at necropsy.
Remarks - Results	Residual test material was noted on the skin in all animals, even after removal was attempted after 24 h. In some animals the residue was evident for up to 12 days. Local effects are indicative of irritation, and may have been exacerbated because the test material was not effectively removed from the skin.
CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	Safepharm (2000j).

7.3. Acute toxicity – inhalation

Not performed

7.4. Irritation – skin

TEST SUBSTANCE	NINOX HCDO
METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White

Number of Animals	2 M, 1 F
Vehicle	None
Observation Period	14 days
Type of Dressing	Semi-occlusive.
Remarks - Method	Test substance was an off-white paste. As well as the standard 4 h test, irritation after exposure times of 3 minutes and 1 h was also evaluated.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0	2	2	2	< 7 days	0
Oedema	0	1	1.7	2	< 7 days	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	In the main test 2/3 animals also showed loss of skin flexibility/elasticity at the 48 h and 72 h observations, crust formation at the 7-day observation, and slight desquamation at the 14-day observation. When one animal was tested with 3 minute and 1 h exposure times and observed for 72 h, no adverse effects were noted.

CONCLUSION The notified chemical is slightly to moderately irritating to the skin.

TEST FACILITY Safepharm (2000k)

7.5. Irritation – eye

TEST SUBSTANCE NINOX HCDO

METHOD OECD TG 405 Acute Eye Irritation/Corrosion.
EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).

Species/Strain	Rabbit/New Zealand White
Number of Animals	1
Observation Period	14 days
Remarks - Method	The protocol differed from OECD TG 405 and EC B.5 in that the results on one animal were not confirmed in a further 2 animals as recommended.

RESULTS

Lesion	*Mean Score* Animal No.*	*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1			
Conjunctiva: redness	2.3	3	< 14 days	0
Conjunctiva: chemosis	2	2	< 14 days	0
Conjunctiva: discharge	3	3	< 14 days	0
Corneal opacity	2	3	< 14 days	0
Iridial inflammation	1	1	< 7 days	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	Dulling of the cornea was noted 1h after treatment. Diffuse corneal opacity was noted at 24 h, translucent corneal opacity at 48 h, opalescent corneal opacity at 72 h and diffuse corneal opacity was apparent at 7 days. Vascularisation with localised ingrowth of vessels for 1-2 mm was

noted at the 7-day observation.
Iridial inflammation was noted 1 h after treatment, persisting to 72 h.
Conjunctival irritation was moderate at 1 h, 24h, 48 h and 7 days, and severe at 72 h.
No adverse effects were noted at the 14-day observation.

CONCLUSION The notified chemical is irritating to severely irritating to the eye.

TEST FACILITY Safepharm (2000l)

7.6. Skin sensitisation

TEST SUBSTANCE NINOX HCDO

METHOD OECD TG 406 Skin Sensitisation – Guinea Pig Maximisation Test
EC Directive 96/54/EC B.6 Skin Sensitisation - Guinea Pig Maximisation Test

Species/Strain Guinea pig/male albino Dunkin Hartley

PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: 0.1% (irritation at 0.1% cleared by 7 days)
topical: 25% (erythema at 75% minimal by 48 h)

MAIN STUDY

Number of Animals Test Group: 20 Control Group: 10

INDUCTION PHASE Induction Concentration:
intradermal: 0.1% w/w
topical: 75% w/w

Signs of Irritation Erythema (discrete or patchy to moderate and confluent) was present at the test site in all test animals 24 h after intradermal induction, reducing to discrete or patchy after 48 h. In control animals discrete or patchy erythema was observed at 24 h, but no reactions were evident after 48 h. Bleeding from the intradermal induction site was noted in some of both test and control animals at the 1 h observation.

Erythema was evident in test animals at the topical induction sites. After 1 h there was discrete or patchy to moderate and confluent erythema in all test animals, and slight oedema in some animals. This persisted to 24 h in 14 animals. In one test animal a brown scab caused by scratching was noted at 24 h. In control animals there was no erythema at 1 h or 24 h.

CHALLENGE PHASE

1st challenge topical: 2% and 5% w/w

Remarks - Method Vehicle was distilled water. Patches were occluded with overlapping aluminium foil, secured with elastic adhesive bandage wound in a double layer around the torso of each animal.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*			
		1st challenge		*2nd challenge*	
		24 h	*48 h*	*24 h*	*48 h*
Test Group	2%	0/19	0/19	-	-
	5%	019	0/19	-	-
Control Group	2%	0/10	0/10	-	-
	5%	0/10	0/10	-	-

Remarks - Results One animal in the test group was killed for humane reasons unrelated to the test, and did not undergo challenge.
Body weight gains of guinea pigs in the test group were comparable to those of the control group, over the period of the study.

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Safepharm (2000m)

7.7. Repeat dose toxicity

TEST SUBSTANCE	NINOX HCDO, 81.5% purity
METHOD	OECD TG 407 Repeated Dose 28-day Oral Toxicity Study in Rodents. EC Directive 96/54/EC B.7 Repeated Dose (28 Days) Toxicity (Oral).
Species/Strain	Rat/Sprague-Dawley Crl:CD BR, Charles River
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week Post-exposure observation period: nil
Vehicle	Distilled water
Remarks - Method	The quantity of test substance administered was adjusted to compensate for the purity of 81.5%. No recovery groups were included. No urine analysis was carried out.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day based on active ingredient*	*Mortality*
I (control)	5 M, 5 F	0	1 F
II (low dose)	5 M, 5 F	15	none
III (mid dose)	5 M, 5 F	150	none
IV (high dose)	5 M, 5 F	1000	none

Mortality and Time to Death

One high dose female died on Day 12. The death was probably treatment related, but no specific cause of death was established at necropsy.

Clinical Observations

Signs of toxicity were observed in high-dose animals from day 3, worsening and becoming more prevalent in weeks 1 and 2 before stabilising in the second half of the study. Most animal exhibited fur loss, noisy respiration, increased salivation, red/brown staining of fur, wet fur and hunched posture. Sporadic signs of diuresis, staining around the ano-genital region, tiptoe gait, gasping respiration and pallor of the extremities were also noted. The female found dead on day 12 showed substantial deterioration on day 11, with additional signs of pilo-erection, respiratory pattern changes, staining around the mouth and snout, and dehydration. No significant observations were seen in low or mid dose animals. Incidents of fur loss in these groups are common in group housed rats, and a single incident of increased salivation was attributed to the dosing procedure.

The results of weekly behavioural assessment supported the above clinical observations for high dose animals. In addition increased salivation was observed in this group. No treatment related changes in any group were noted in the functional performance tests. In sensory reactivity assessments, the only significant change noted in any group was that high dose males exhibited an enhanced startle response compared with controls.

High dose male and female rats showed a substantially reduced bodyweight gain during week 1 of the study. While body weight gain was comparable to controls in subsequent weeks, a full recovery was not apparent in high dose males, with terminal bodyweights remaining significantly lower than controls. Some variations in body weight were noted in low dose males and females but were not believed to be treatment related as they were not dose-dependent.

High dose animals also showed reduced food consumption and food efficiency (ratio of bodyweight gain to dietary intake) in week 1. This recovered in females but remained reduced in high dose males throughout the study period. Water consumption, measured from day 15, showed a sustained increase for high dose animals only.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

High dose animals showed statistically significant elevation in plasma aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT), including some readings outside the expected range for rats of this strain and age, particularly for ALAT. Some increase in ALAT and ASAT was also evident in the mid dose groups. Plasma bilirubin levels were increased in high dose groups, and were statistically significant in males. No statistically or toxicologically significant blood chemical changes were seen in low dose males or females.

High and mid dose animals exhibited haematological changes consistent with haemolytic anaemia in a dose dependent manner. Statistically significant reductions in erythrocyte count, haemoglobin, haematocrit and mean corpuscular haemoglobin concentration (MCHC) were noted, with increases in mean corpuscular volume, mean corpuscular haemoglobin (MCH) and reticulocyte count. The majority of reticulocyte values in high dose animals were outside the expected range for rats of the strain and age used. High dose animals also showed a statistically significant increase in neutrophil numbers, but not in the total leucocyte count, together with a slightly elevated prothrombin time. Low dose animals had no toxicologically or statistically significant haematological changes.

Effects in Organs

Most macroscopic changes noted at necropsy were considered non-dose related, except for thickening of the non-glandular gastric epithelium in one high-dose female. The high dose female that died on day 12 showed normal post-mortem changes and no cause of death was established.

High dose males and females showed statistically significant absolute and relative increases in spleen weight compared to controls, with many individual values outside the expected range for rats of the strain and age used. Increased spleen weight was also found in mid dose animals to a lesser extent, not always statistically significant. The following additional effects in organ weights were not considered to be toxicologically significant: increased relative testes weight at the high dose, increased relative brain weight in all male treatment groups, and reduction in absolute liver and kidney weights in high dose males. No toxicologically significant effects on organ weights were seen in the low dose group.

Several treatment-related changes were noted from histopathological examination of organs. Increased severity of splenic extramedullary haemopoiesis was noted in high and mid dose males and females. Increased pigment accumulation (probably haemosiderin) was found in the spleen in high and mid dose males and females, and in low dose females. In high dose animals an increased severity of pigment accumulation (probably haemosiderin) was also found in the kidneys. Slight hyperplasia of the urinary bladder was seen in high dose males and females. High dose animals also exhibited acanthosis and hyperkeratosis of the forestomach, in some cases associated with subepithelial inflammatory cell infiltrates, which may be attributable to ingestion and excretion of an irritant substance. There were scattered occurrences of pigment deposition (probably haemosiderin) in the liver in high dose groups, however the centrilobular hepatocyte enlargement also observed in high dose males was considered adaptation to the xenobiotic. Other morphological changes were not considered treatment related, and there were no other differences in incidence or severity between control and treatment groups that were considered toxicologically significant.

Remarks – Results

The major effects of repeated oral exposure are consistent with dose-related causation of haemolytic anaemia. Toxicity was particularly evident in the high dose group, in which one death occurred. At this dose there were significant clinical signs as well as changes in haematology parameters and clinical chemistry. Histopathology revealed increased splenic extramedullary haematopoiesis and pigment deposition (probably haemosiderin) in spleen, kidneys and the liver. Some effects observed in high dose animals were also seen at the mid dose, where they were less severe. At the low dose, only increased pigment deposition in the spleen in females was observed.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 15 mg/kg bw/day in this study, based on haematology and blood chemistry changes observed at 150 mg/kg bw/day that are indicative of haemolyis, and on adverse histopathological changes at this dose, consistent with changes also occurring at 1000 mg/kg bw/day. Pigment deposition in the spleen in low dose females was slight and in isolation is not considered sufficient to alter the NOAEL.

TEST FACILITY Safepharm (2000n)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE NINOX HCDO, 77% purity

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 92/69/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100,
E. coli: WP2uvrA,

Metabolic Activation System S9 fraction from phenobarbital/β-naphthoflavone induced rat liver.

Concentration Range in Test 1 With and without metabolic activation:
a) All *Salmonella* strains 5 to 1500 µg/plate
b) *E. coli* strain: 15 to 5000 µg/plate

Vehicle Dimethyl-formamide

Remarks - Method An allowance for the purity of the test material (77%) was made in preparing dilutions.

The preliminary toxicity test was carried out on TA100 and WP2uvrA$^-$.

Based on the results of Test 1, concentration ranges were altered in Test 2 to:
TA100, TA1535, TA98 5 to 1500 µg/plate
WP2uvrA$^-$ 50 to 5000 µg/plate
TA1537 15 to 500 µg/plate

Test 3 used TA1537 only at15 to 500 µg/plate

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	≥ 500 for TA100 ≥ 1500 for WP2uvrA$^-$	≥ 500 for TA100, TA1535 and TA1537 ≥ 1500 for TA98 5000 for WP2uvrA	> 5000	Marginal positive result in TA1537 only
Test 2		≥ 200 for TA1537 ≥ 500 for TA100, TA1535 and TA98 5000 for WP2uvrA	> 5000	Negative

Test 3		≥ 200 for TA1537	> 5000	Negative
Present				
Test 1	≥ 1500 for TA100 ≥ 1500 for WP2uvrA$^-$	≥ 500 for TA100, TA1535 and TA 1537 ≥ 1500 for TA98 5000 for WP2uvrA	> 5000	Marginal positive result in TA1537 only
Test 2		≥ 500 (but 5000 for WP2uvrA)	> 5000	Negative
Test 3		500 for TA1537	> 5000	Negative

Remarks - Results: Small but statistically significant dose related increases in TA 1537 revertants were seen in Test 1 at 50 and 150 µg/plate without metabolic activation and at 150 µg/plate with metabolic activation, the highest concentrations without toxicity. All of the increases were less than twofold. These effects were not seen in Tests 2 or 3, and the effects were stated to be within the range of historical controls. Positive controls demonstrated the sensitivity of the assays and negative controls were within historical limits. No other statistically significant increases were observed. However it is noted that cytotoxicity precluded effective testing at higher concentrations.

CONCLUSION: The notified chemical was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY: Safepharm (2000o)

7.9. Genotoxicity – in vitro Chromosome aberration

TEST SUBSTANCE: NINOX HCDO, 77% purity

METHOD: OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
EC Directive 92/69/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.

Cell Type/Cell Line: Human lymphocytes
Metabolic Activation System: S9 fraction from phenobarbital/β-naphthoflavone induced rat liver.
Vehicle: Minimal Essential Media (MEM)
Remarks - Method: An allowance for the purity of the test material (77%) was made in preparing dilutions.

A preliminary test was performed to determine cytotoxicity

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*
Absent			
Test 1	0*, 9.77, 19.53, 39.06*, 78.13*, 156.25*, 234.38, 312.5	4 h	24 h
Test 2	0*, 4.89,9.77, 19.53, 39.06*, 78.13*, 117.19*	24 h	24 h
Present			
Test 1	0*, 9.77, 19.53, 39.06*, 78.13*, 156.25*, 234.38, 312.5	4 h	24 h
Test 2	0*, 19.53, 39.06*, 78.13*, 156.25*, 234.38, 312.5	4 h	24 h

*Cultures selected for metaphase analysis.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				

Test 1	> 78.13	> 78.13	>312.5	negative
Test 2	> 78.13	> 78.13	>117.19	negative
Present				
Test 1	> 78.13	> 78.13	>312.5	negative
Test 2	> 78.13	> 78.13	>312.5	negative

Remarks - Results: Positive controls demonstrated the sensitivity of the assays and negative controls were within historical limits.

CONCLUSION: The notified chemical was not clastogenic to human lymphocytes treated in vitro under the conditions of the test.

TEST FACILITY: Safepharm (2000p)

8. ENVIRONMENT

Ecological testing was carried out on the analogue NINOX HCDO, unless otherwise noted

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE: NINOX HCDO (purity not disclosed)

METHOD: OECD TG 301 D Ready Biodegradability: Closed Bottle Test.

Inoculum: Mixed population of sewage sludge microbes, Severn Trent Water plc sewage treatment plant (secondary; domestic source).

Exposure Period: 28 d

Auxiliary Solvent: None

Analytical Monitoring: Dissolved oxygen (days 0, 3, 6, 9, 12, 15, 18, 21 and 28). Oxygen meter and BOD probe. Test substance concentration was not determined.

Remarks - Method: Stock solution (1000 mg/L) was prepared by addition of test substance (100 mg) in culture medium and the volume adjusted to 100 mL. An aliquot (18 mL) of this stock solution was dispersed in a final volume of 6 L of inoculated culture medium to give the nominal test concentration of 3 mg/L. The sludge sample was allowed to settle and the supernatant filtered prior to use (1 drop/L of test material). Test containers consisted of 250-300 mL amber glass BOD bottles, and tests comprised a control, reference material (sodium benzoate 3 mg/L), test material (3 mg/L) and a toxic control (reference and test material). Degradation of the test substance was assessed by monitoring the level of oxygen consumed. Test vessels were kept in the dark at 21°C. As ThoD for the test material could not be determined, the percent degradation rate was determined based on the COD.

RESULTS

Test substance 3 mg/L (nominal)		*Sodium benzoate (3 mg/L)*	
Day	*% Degradation*	*Day*	*% Degradation*
3	15	3	61
12	56	12	75
24	58	24	79
28	60	28	80

Remarks - Results: The reference material (sodium benzoate) attained 80% degradation after 28 days, thereby confirming the suitability of the test method and culture conditions. The toxicity control attained ≥25% degradation (64%) by day

14 thereby confirming the test material (3 mg/L) was not toxic to the test organisms. Test values are not adjusted for solids content.

CONCLUSION The test material (3 mg/L) attained 60% degradation after 28 days; however, this was not attained within 10 days of reaching 10%, therefore not satisfying the test guideline protocol of readily biodegradable. The test material was not toxic to the sewage sludge microbes.

TEST FACILITY Safepharm (2000g)

8.1.2. Ready biodegradability

TEST SUBSTANCE NINOX HCDO (purity not disclosed)

METHOD OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.

Inoculum Mixed population of sewage sludge microbes, Severn Trent Water plc sewage treatment plant (secondary; domestic source).

Exposure Period 28 d

Auxiliary Solvent None

Analytical Monitoring CO_2

Remarks - Method Stock solution (1000 mg/L) was prepared by addition of test substance (1000 mg) in culture medium and the volume adjusted to 1 L. An aliquot (69.9 mL) of this stock solution was dispersed in a final volume of 3 L of inoculated culture medium to give the nominal test concentration of 23.3 mg/L (10 mg C/L). The sludge sample was triple washed by settlement and resuspension to remove excess DOC. The suspended solids (SS) content was then determined prior to use. Test containers consisted of 5 L glass culture vessels, and tests comprised a control, reference material (sodium benzoate 17.1 mg/L or 10 mg C/L), test material (23.2 mg/L) and a toxic control (reference and test material). Test vessels were sealed but received CO_2-free air (bubbled), and the CO_2 generated was captured and monitored. Degradation of the test substance was assessed by monitoring the level of CO_2 generated. Test vessels were kept in the dark at 21°C.

RESULTS

Test substance (23.3 mg/L or 10 mg C/L)		*Sodium benzoate (17.1 mg/L)*	
Day	*% Degradation*	*Day*	*% Degradation*
0	0	0	0
1	9	1	16
5	46	5	53
9	77	9	65
13	94	13	64
28	98	28	74
29	99	29	77

Remarks - Results The control satisfied the test validation criterion. The toxicity control attained 93% degradation after 28 days, satisfying the test criterion and indicating that the test material was not toxic to the sewage microbes. The reference material attained 74% degradation after 28 days, indicating that the test conditions and inoculum were acceptable.

CONCLUSION The test material attained 98% degradation after 28 days and achieved >60% degradation within 9 days and is considered readily biodegradable under the conditions of the test.

TEST FACILITY Safepharm (2000h)

8.1.2. Bioaccumulation

Not determined

Remarks — The notified chemical has an estimated log Kow of 4.62 at 20°C and therefore may potentially bioaccumulate in aquatic organisms. The notified chemical's moderate molecular weight range suggests it may be capable of crossing biological membranes. Release of the notified chemical to sewer is likely, which may, depending on treatment processes, result in a proportion discharged in the aquatic environment; however, biodegradation is more likely to occur since it is readily biodegradable.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE — NINOX HCDO (91.7%)

METHOD — OECD TG 203 Fish, Acute Toxicity Test – freshwater/daily renewal

Species — Rainbow trout (*Oncorhynchus mykiss*), juvenile, mean length 4.6 cm, mean weight 1.20 g. Acclimated to test conditions for 14 days. Loading rate 0.60 g bodyweight/L.

Exposure Period — 96 h

Auxiliary Solvent — None

Water Hardness — 100 mg/L as $CaCO_3$

Analytical Monitoring — GC. 0 h (fresh media), 24 and 96 h (old media).

Remarks – Method — Range-finding and definitive tests were performed. Test aquaria consisted of 21 L aerated vessels. Stock solution (200 mg solids/L) was prepared by addition of test material (218 g) dissolved in dechlorinated tap water (ultrasonicated 30 mins) and the volume adjusted to 1 L. Stock solution was serially diluted to the required test concentrations. Test water parameters were monitored daily: temp. 14.0°C, dissolved oxygen ≥9.3 mg O_2/L, photoperiod 16 h light: 8 h dark; pH range 7.3-7.8. Observations of fish were made at 3, 6, 24, 48, 72 and 96 h. LC50 values and confidence limits were calculated with 48 h data using the trimmed Spearman-Karber method and with 96 h data using the geometric mean method where LC50 = √(C1 x C2), where C1 = highest concentration showing 0% mortality (0.56 mg/L) and C2 lowest concentration showing 100% mortality (1.0 mg/L).

RESULTS

Concentration mg solids/L				*No. Fish*	*Cumulative Mortality*					
Nominal	*Actual (0 h, 24 h, 96 h)*				*3 h*	*6 h*	*24 h*	*48 h*	*72 h*	*96 h*
Control	<LOQ	<LOQ	<LOQ	10 (1 rep)	0	0	0	0	0	0
0.18	0.0756/0.242	0.166	0.172	"	0	0	0	0	0	0
0.32	0.214/0.329	0.295	0.312	"	0	0	0	0	0	0
0.56	0.466	0.524	0.517	"	0	0	0	0	0	0
1.0	0.754/1.034	0.884	---	"	0	0	0	6	10	10
1.8	1.41/2.055	1.59	---	"	0	0	10	10	10	10
3.2	2.80	2.75	---	"	0	0	10	10	10	10

LC50 — 0.75 mg solids/L (nominal) at 96 hours, with 95% CI 0.56-1.0 mg/L)

NOEC — 0.56 mg solids/L (nominal) at 96 hours.

Remarks – Results — Test material contained 8.29% water, and consequently all test values were corrected for active ingredient content. Test concentrations were variable, within the range of 42-134% of nominal particularly at the start of the test. Data from 0 h were averaged to give values of 85-96% of

nominal. The variability was attributed to poor analytical procedure. Sublethal effects (swimming at bottom) were noted after 48 h at concentrations >1.0 mg/L. A stability test showed no insolubility or adherence to aquaria glass by the test substance.

CONCLUSION The test substance is very toxic to Rainbow Trout under the acute toxicity test conditions (ie. LC50 <1.0 mg/L, United Nations, 2003).

TEST FACILITY Safepharm (2000d)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE NINOX HCDO (91.7%)

METHOD OECD TG 202 Daphnia sp. Acute Immobilisation Test – freshwater/static referenced as EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia – freshwater/static.

Species	*Daphnia magna* (<24 h old)
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	250 mg/L as $CaCO_3$
Analytical Monitoring	GC. Selected samples. 0 h and 48 h.
Remarks – Method	Range-finding and definitive tests were performed. Test aquaria consisted of 250 mL aerated vessels. Stock solution (100 mg solids/L) was prepared by addition of test material (109 mg) dissolved in dechlorinated tap water (ultrasonicated 25 mins) and the volume adjusted to 1 L. Stock solution was serially diluted to the required test concentrations. Test water parameters were monitored daily: Temp. 21.0°C, dissolved oxygen ≥8.3 mg O_2/L, photoperiod 16 h light: 8 h dark; pH 7.9. Observations of daphnids were made at 24 and 48 h. EC50 values and confidence limits were calculated at 48 h by the Maximum-likelihood probit method (Finney, 1971).

RESULTS

Concentration mg solids/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
Control	<LOQ	20 (2 replicates of 10)	0	0
0.10	0.0835	"	0	0
0.18	---	"	0	0
0.32	0.314	"	0	0
0.56	---	"	0	3
1.0	0.901	"	0	15
1.8	---	"	0	17
3.2	3.10	"	2	20
5.6	---	"	7	20
10	10.0	"	16	20

EC50	6.6 mg solids/L (nominal) at 24 hours, with 95% CI of 5.5-8.3 mg/L 0.96 mg solids/L (nominal) at 48 hours, with 95% CI of 0.70-1.2 mg/L.
NOEC	0.32 mg solids/L (nominal) at 48 hours
Remarks - Results	Test material contained 8.29% water, and consequently all test values were corrected for active ingredient (solids) content. Analysis of test concentrations at 0 and 48 h were within 76-100% of nominal, and values are reported based on nominal concentrations. A stability test showed no insolubility or adherence to aquaria glass by the test substance.

CONCLUSION The test substance is very toxic to *Daphnia magna* under the acute toxicity test conditions (ie. 48-96 h EC50 <1.0 mg/L, United Nations, 2003).

TEST FACILITY Safepharm (2000e)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE NINOX HCDO (91.7%)

METHOD OECD TG 201 Alga, Growth Inhibition Test referenced as EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species	Freshwater green algae *Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	0 h Nominal : 2.0, 4.0, 8.0, 16 and 32 mg solids/L 0 h Actual: 1.50, 3.23, 6.96, 14.0 and 27.8 mg solids/L (75-87% nominal) 72 h Actual: <LOQ 0.63 mg solids/L (0% of nominal). Time-weighted mean measured: 0.76, 1.3, 2.1, 3.6 and 6.1 mg solids/L.
Auxiliary Solvent	None
Water Hardness	Not stated
Analytical Monitoring	GC. 0 and 72 h.
Remarks - Method	Three replicate flasks per test concentration. Range-finding and definitive tests were performed. Test aquaria consisted of 250 mL aerated conical flasks (continuously shaken). Stock solution (64 mg solids/L) was prepared by addition of test material (70 mg) dissolved in dechlorinated tap water (ultrasonicated 25 mins) and the volume adjusted to 1 L. Stock solution was serially diluted to the required test concentrations. Samples were collected at 0, 24, 48 and 72 h for cell density determination. Temp. 24.0°C, dissolved oxygen – not stated, photoperiod 24 H at 7000 lux. pH 8.3-7.7, declined during test). Pre-culture conditions in the log growth phase (~10^6 cells/mL) were diluted to ~10^4 cells/mL prior to use. One-way ANOVA incorporating Bartlett's Test for homogeneity of variances and Dunnett's multiple comparison procedure were used to compare test to control results.

RESULTS

Method	*Biomass EbC50 at 72 h (mg solids/L)*	*Growth ErC50 at 72 h (mg solids/L)*	*NOEC at 72 h (mg solids/L)*
Nominal	9.0	21	4.0
Time-weight mean measured conc.	2.3 (95% CI 2.1-2.5)	4.5 (95% CI 4.1-4.9)	1.3

Remarks - Results Test material contained 8.29% water, and consequently all test values were corrected for active ingredient (solids) content. Given the decline in test substance concentration during the test, a time-weighted mean measured test concentration was used to calculate the 72 h EC50 values.

CONCLUSION The test substance is toxic to the freshwater green alga *Scenedesmus subspicatus* under the acute toxicity test conditions (ie. 72 h EC50 1-10 mg/L, United Nations, 2003).

TEST FACILITY Safepharm (2000f)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE NINOX HCDO (purity not disclosed)

REMARKS	Readily biodegradability testing with a toxic control containing the test material at concentrations of 3 and 23.3 mg/L did not adversely affect sewage sludge microbes.
TEST FACILITY	Safepharm (2000g,h)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

If released into the aquatic environment, the notified chemical is expected to be readily soluble but will hydrolyse only very slowly and volatilisation is expected to be limited (predicted Henry's Law Constant $<10^{-19}$ atm-m^3/mol; Environment Canada, 2001). It is likely to adsorb to sediments. With an estimated log Kow of 4.62 at 20°C, bioaccumulation can occur; however biodegradation is more likely to eventuate. The test material attained ≥60% degradation in two ready biodegradability tests. In the sewerage system or aquatic environment, the notified chemical is expected to biodegrade over time.

Possible environmental exposure could result from accidental spillage/breakage of imported containers. Losses during blending/repackaging are expected to be limited due to engineering and other controls, with release most likely due to disposal of wastes to incinerator. Incineration of the notified chemical will generate water vapour and oxides of carbon and nitrogen.

The majority of the notified chemical will be discharged to sewer after use. The use pattern is expected to be widespread throughout Australia. A predicted environmental concentration (PEC) in the treated effluent, and downstream waterways, has been estimated with a sewage treatment plant (STP) model (Environment Australia, 2003). The model assumes that the notified chemical is discharged into the sewerage system and none is attenuated or biodegraded within this system. Australia has a population of ~20.1 million people, and an average value for water consumption of 200 L/person/day has been adopted for this national-level assessment (4020 ML/day for total population). Therefore the concentration of notified chemical in the Australian sewage network may be calculated on the basis of a maximum annual volume of 20 tpa.

The approximate sewerage effluent concentration under these assumptions is ~14 μg/L ($2x10^{13}$ μg per annum ÷ 365 days/year ÷ 4020 x 10^6L/day). Based on dilution factors of 1 and 10 for inland river and ocean outfall discharges of STP-treated effluents, respectively, PECs of the notified chemical in freshwater and marine surface waters may, under these assumptions, approximate 14 μg/L ($PEC_{freshwater}$) and 1.4 μg/L (PEC_{marine}), respectively.

However, based on ready biodegradability test results a proportion of the notified chemical disposed of to sewer is likely to biodegrade during the treatment process. In addition, a proportion is likely to adsorb onto particulate matter, settle with sludge, and be removed from the effluent phase.

The SIMPLETREAT model (European Commission, 2003) for modelling partitioning and losses in sewage treatment plants (STP) was used to estimate the proportions of the notified chemical partitioning into the different environmental compartments given that it passed the 10-day criterion for ready biodegradability, the estimated log Henry's Law constant is calculated as -7 and the partition coefficient (log K_{ow}) was 4.62. The results were as follows:

0% to air
8% to water
47% to sludge
45% biodegraded

The results indicate that when the notified chemical is released into the aqueous phase of a STP it is likely that some components will partition into the water compartment and others will partition to the sludge and that there will be significant removal (partly due to biodegradation). Assuming 92% of the notified chemical is removed, the above estimated freshwater and marine PECs are 1.1 μg/L and 0.11 μg/L, respectively.

Assuming STP attenuation, sewage sludge may contain ~64 mg/kg of the notified chemical. In soils, PEC values of 0.01 mg/kg and 0.64 mg/kg may be estimated for soils irrigated with treated effluent and for biosolids-applied soils, respectively. This assumes that biosolids are generated at a rate of 100 kg per ML of sewage treated, and that biosolids are applied to soil of density 1000 kg/m^3 at a rate of 10 t/ha and mixed into the soil to a depth of 10 cm. For irrigated soils, this assumes that treated effluent is applied at a rate of 1 m/ha. However, during sludge stabilisation and in soil, the notified chemical would be subjected to continuous biodegradation and the concentration in stabilised biosolids and soils is expected to be lower.

9.1.2. Environment – effects assessment

Aquatic ecotoxicity data for the analogue NINOX HCDO were available for 3 taxonomic groups (freshwater fish, cladocerans, algae). Under the test conditions, which included deionised/dechlorinated water as test media, the notified chemical was very toxic to fish and daphnids and toxic to algae under acute toxicity test conditions (ie. L(E)C50 <1-10 mg/L, United Nations, 2003). No aquatic test data were available for the notified chemical or the analogue on ecotoxicity modification in the presence of variable test water quality parameters (eg. salinity, organic carbon). The notified chemical was not toxic to sewage sludge microbes at a nominal exposure concentration of 3 mg/L and 23.3 mg/L over a 28-day period.

A predicted no effect concentration (PNEC) for freshwater organisms for the notified chemical of 7.5 µg/L has been derived by dividing the lowest acute L(E)C50 value (96 h LC50 for rainbow trout of 0.75 mg solids/L) by an assessment factor of 100 to account for interspecies sensitivity. In the absence of marine toxicity data, the $PNEC_{freshwater}$ is tentatively extrapolated to the marine environment, an approach that is supported by a preliminary review of comparative data by ECETOC (2003).

9.1.3. Environment – risk characterisation

In the event of a spill of the notified chemical into the environment, local adverse effects to organisms may potentially occur due to its high toxicity. Given the anticipated short persistence of the notified chemical in the environment, and implementation of emergency spill response clean up procedures, long lasting effects to aquatic organisms would not be expected.

The use and disposal pattern for the notified chemical is likely to be diffuse and widespread across urban and regional Australia. Risk quotient (RQ) values, where RQ = PEC/PNEC, for freshwater and marine receiving environments of 1.9 (ie. 14 ÷ 7.5) and 0.19 (ie. 1.4 ÷ 7.5), respectively, have been estimated based on a sewer disposal scenario described in Section 9.1.1 but with no attenuation capacity of the sewerage system. However, the probable biodegradation of the notified chemical in municipal STPs and partitioning to sludge is likely reduce these RQ values by up to 92%, resulting in RQ values of ~0.15 (ie. 1.1 ÷ 7.5) and ~0.015 (ie. 0.11 ÷ 7.5) for freshwater and marine environments, respectively.

There is a potential for bioaccumulation of the notified chemical but this is not likely due to the biodegradability of the notified chemical.

The sewerage system should not be adversely affected from receipt of the notified chemical as its estimated concentration in untreated wastewater is much lower than concentrations shown to have no adverse effects to sewage sludge microbes. Reuse of treated effluent or biosolids potentially containing the notified chemical is unlikely to pose an unacceptable risk to the environment (eg. <1 mg/kg soil after biosolids application assuming no biodegradation).

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

The major route of potential worker exposure to the notified chemical is dermal. Depending on the tasks performed at the formulation site or during end use of the dishwashing detergent, exposure could occur to Ammonyx LMDO containing the notified chemical at 10%, dishwashing detergent containing it at up to 2%, or washing-up water containing it at approximately 0.002%.

At the formulation site, it is expected that gloves and other PPE will be the main controls against exposure and these controls are expected to be effective in reducing exposure. Gloves would also be worn during dishwashing by some but not all workers, during enduse of the dishwashing liquid.

EASE modelling of dermal exposure at the formulation site (not taking the effect of any PPE into account) gave potential exposure estimates of up to 1.3 mg/kg/day for Ammonyx LMDO containing 10% of the notified chemical and up to 0.27 mg/kg/day for dishwashing liquid containing 2% of the notified chemical. EASE modelling (UK HSE, 2000) of exposure to workers using dishwashing liquid suggested a lower potential exposure (9µg/kg bw/day) than calculations based on those in the EU risk assessment guidance document (ECB, 2003) (133 µg/kg bw/day).

Inhalational exposure is not expected at the formulation site or during later end-use of dishwashing liquids. It could occur if processes generating aerosols occurred and EASE modelling suggests that significant exposure could be generated in this way.

Oral exposure is not expected to occur. While dishwashing residues may contaminate plates and utensils, this exposure is expected to be very low.

EASE modelling of dermal exposure
EASE modelling of occupational exposure during delivery, formulation and filling (UK HSE, 2000) has indicated that inhalation exposure would be very low in the absence of aerosol formation. (However, significant inhalation exposure would occur if aerosols were to be generated). Intermittent dermal exposure (2 to 10 contacts per day) could lead to daily exposure of 0.1 to 1.0 mg/cm^2/day. If the hands were exposed, a typical area would be 800 cm^2, based on values of 840 cm^2 for men and 731 cm^2 for women (ECB, 2003). For a 60 kg worker this would be equivalent to exposure of 0.13 to 1.3 mg/kg bw/day for Ammonyx LMDO containing 10% of the notified chemical or 0.03 to 0.27 mg/kg bw/day for dishwashing liquid containing 2% of the notified chemical.

EASE modelling of dermal occupational exposure during dishwashing has indicated that extensive contact and direct handling could lead to daily exposure to 5 to 15 mg/cm^2/day of water containing dilute dishwashing liquid. If the hands and forearms were exposed (which is likely for this type of task), a typical area would be 1850 cm^2, based on values of 1980 cm^2 for men and 1723 cm^2 for women (ECB, 2003). For a 60 kg worker and assuming that 10 g of dishwashing liquid in 10 kg of water would be used in a sink, and that the notified chemical is present at 2% in the dishwashing liquid, the exposure to the notified chemical would be 3 to 9 µg/kg bw/day. The EASE estimations for this type of exposure may be an underestimation, as they cover multiple short exposures rather than prolonged exposure.

EU Technical Guidance Document method of modelling dermal exposure
An alternative method of calculating dermal occupational exposure during dishwashing is described in the EU Technical Guidance Document (ECB, 2003). Dermal exposure based on this model is estimated to be 133 µg/kg bw/day based on two washing-up sessions per day, analogous to public exposure. Details of calculations are in section 9.2.2 below.

Both method of calculation assume 100% dermal absorption, and do not take account of controls that may reduce exposure eg PPE.

9.2.2. Public health – exposure assessment

Likely routes of exposure
The notified chemical will be incorporated in domestic dishwashing liquids at up to 2%, which will be used widely by consumers. There could be incidental dermal exposure to the dishwashing liquid itself, through splashes or contamination of the outside of the packaging. An additional form of incidental dermal exposure may be through use of the dishwashing liquid to wash hands. However, the main routine exposure is likely to be to dishwashing water containing the product. If 10 g of dishwashing liquid was used with 10 kg of water, the

concentration of notified chemical in the dishwashing water would be 0.002%.

Dermal exposure is expected to be the major route of potential public exposure, through dishwashing tasks carried out by consumers. The major dermal exposure is expected to occur through contact of the hands and forearms with water containing the dishwashing liquid at low concentrations. However incidental contact with the dishwashing liquid itself could occur if product is spilt or splashed, or contaminates the outside of the package. Calculation of potential dermal exposure (ECB, 2003) gave an estimate of 133 μg/kg bw/day for an adult, based on two dishwashing tasks per day. Details of the calculation are at the end of this section (9.2.2).

Inhalation exposure is considered unlikely either from the dishwashing liquid or from water containing it, as the chemical has low volatility and aerosols are unlikely to be formed. Inhalation exposure to consumers is not expected to occur through use of dishwashing liquids. Oral exposure to residues on plates and utensils at very low levels can occur. Based on risk assessment of another surfactant (Hera, 2003) this is likely to contribute less than 1 μg/kg bw/day for an adult.

Oral exposure could occur from residues of the dishwashing liquid remaining on plates and utensils, if these articles are not rinsed after washing. It is expected that residues would be low, and transfer to ingested food would be even lower. Accidental oral exposure of young children to dishwashing detergents is also possible.

It is expected that some consumers would wear gloves while washing dishes, and others would not.

EU Technical Guidance Document method of modelling dermal exposure
The model covers dermal exposure to a substance contained in a medium.

The concentration to which skin is exposed can be calculated from the concentration of the substance in the dishwashing liquid and the concentration of dishwashing liquid in the medium (water):

$$C_{der} = \frac{C_{prod}}{D} = \frac{20}{1000} = 0.02 \text{ kg / m}^3$$

where C_{der} = dermal concentration of substance on skin [kg / m^3]

C_{prod} = concentration of substance in product before dilution [kg / m^3]
= 2% w/v or 20 kg/m^3
D = dilution factor
= 1000 if 10 g dishwashing detergent is used in 10 L of water.

The total amount to which the skin is exposed is then given by:

$$A_{der} = C_{der} \times TH_{der} \times AREA_{der} = 0.02 \times 0.001 \times 0.2$$

$$= 0.004 \times 10^{-3} \text{ kg}$$

$$= 4 \text{ mg}$$

Where A_{der} = amount of substance on skin per event [kg]

TH_{der} = thickness of product layer on skin [m]
= [assumed to be 1 mm (0.001 m)]

$AREA_{der}$ = area of contact between product and skin [m^2]
= assumed to be 2000 cm^2 (0.2 m^2) based on area of hands and forearms.

Potential uptake per kilogram body weight per day is derived as:

$$U_{der.pot} = \frac{A_{der} \times n}{BW} = \frac{0.004 \times 10^{-3} \times 2}{60} = 0.133 \times 10^{-6} \text{ kg/kg bw/day}$$

$$= 0.133 \text{ mg/kg bw/day}$$

Where $U_{der.pot}$ = amount of substance that can potentially be taken up [kg / kg_{bw} / d]

A_{der} = 0.004×10^{-3} kg as calculated above

n = mean number of events per day [d^{-1}], and is assumed to be 2.

BW = body weight [kg], and is assumed to be 60.

It should be noted that this calculation relies on an estimate of the thickness of the layer of chemical likely to be in contact with the skin during dishwashing. An estimate of 1 mm has been made.
Potential uptake is estimated in the calculation, taking no account of the degree of dermal absorption.
For the purposes of the calculation, the density of the dishwashing liquid and the dishwashing water have been assumed to be close to 1.

9.2.3. Human health – effects assessment

Toxicological test results are not available for the notified chemical. The health effects assessment is based on recent studies on a close analogue, which varies from the notified chemical in having a distribution of carbon chain lengths for an alkyl moiety, whereas the notified chemical has a fixed carbon chain length.

No test reports were submitted on the analogue for toxicokinetics, metabolism or distribution. A study on a chemical from the same general class of surfactants suggests that varying metabolic pathways may occur after oral dosing, and that metabolism in humans may more closely resemble that of rabbits than of rats. In this study, the chemical was extensively metabolised, with most of the dose eliminated in the urine or excreted as CO_2 within 24 h, and no evidence that it was excreted as the original chemical.

Based on testing of the analogue, the notified chemical has moderate acute oral toxicity and low acute dermal toxicity. No acute inhalation data were provided. The analogue was a slight to moderate skin irritant when tested on rabbits. Similar local effects were seen during acute dermal toxicity testing. Based on testing of one rabbit only, the analogue was a moderate eye irritant. It was non-sensitising in the Guinea Pig Maximisation test.

A NOAEL of 15 mg/kg bw/day for the analogue was established for repeated dose toxicity in a 28-day oral gavage study in rats. Mortality in one female was seen at the highest dose of 1000 mg/kg bw/day. Other effects at this dose included significant clinical signs, changes in haematology and clinical chemistry, and histopathological changes, the pattern of effects being consistent with haemolytic anaemic. Lesser but similar effects in the mid dose groups suggested a dose dependent effect.

Overall the results of a reverse mutation test in bacteria indicated that the analogue is non-mutagenic. However a statistically significant but non-reproducible increase in revertants was seen in one strain, and it is noted that testing at higher concentrations usually used in the test could not be done effectively because of high cytotoxicity at these concentrations. No genotoxicity was evident in an in vitro chromosome aberration test using human lymphocytes. In vivo genotoxicity testing was not performed.

No test results were submitted on the analogue for carcinogenicity or reproductive effects. No observations on human exposure were provided.

It is possible that carcinogenic nitrosamines could form in chemicals of this type, or products containing them. No information was supplied on possible formation of these impurities.

Based on the available data on the analogue, the notified chemical is classified as a hazardous substance in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2002). It is classified as harmful when swallowed, with risk phrase R22, irritating to skin, with risk phrase R38 and irritating to eyes, with risk phrase R36. However it is noted that the eye irritation classification is based on limited data, on one animal only. In these circumstances it is considered that the preliminary classification made by the notifier - risk of serious damage to eyes, risk phrase R41 – would also be acceptable as it provides an additional degree of precaution.

It is considered that the effects seen at 150 mg/kg bw/day in the 28-day repeated dose oral study and suggestive of haemolytic anaemia were not sufficient to warrant classification with risk phrase R48 (Danger of serious damage to health by prolonged exposure). At this dosage there were no clinical signs. Changes were seen in haematological parameters and blood chemistry, and histological examination showed increased extramedullary haematopoiesis in the spleen and increased pigment deposition in the spleen and liver.

It is believed that low levels of nitrosamine impurities could form in mixtures containing this class of chemical. Nitrosamines are of concern for carcinogenicity, with tumours following chronic exposure confined mainly to the liver and kidney (Health Canada, 2004). A paper on control of nitrosamines in personal care products (ASCC, 2003) recommends specific control measures, including ensuring nitrosamine levels in products do not exceed 50 ppb. Analyses submitted for nitrosamines in eight batches of Ammonyx LMDO (containing the notified chemical) indicate that the levels are generally less than 50 ppb. However one sample contained 112 ppb.

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is classified as a hazardous substance, based on animal studies on a close analogue, which varied from the notified chemical in having a range of hydrocarbon chain lengths, rather than a fixed chain length. The chemical has moderate acute toxicity by the oral route, with an LD50 of 500 to 1000 mg/kg bw. Acute dermal toxicity is low, and acute inhalation toxicity testing was not performed. It is a skin and eye irritant but not a skin sensitiser.

A NOAEL of 15 mg/kg bw/day was established on the basis of a 28-day oral gavage study in rats, with the major effects being consistent with induction of haemolytic anaemia. Mutagenicity testing in bacteria and in vitro genotoxicity testing of human lymphocytes both gave negative results. No toxicokinetic data were available.

Based on known processes and methods of handling at the known formulation site, neither inhalation nor oral exposure is expected. Aerosol generation is the most likely source of inhalation exposure and is considered unlikely in the preparation of dishwashing liquids, at this or other sites. Similarly, inhalation exposure is not expected through downstream use of the dishwashing liquid by workers.

The major route of potential exposure at the formulation site and during downstream use of dishwashing detergents is dermal. The rate and extent of dermal absorption of the notified chemical is not known and it is considered that the results of the oral 28-day study in rats can be used for the risk characterisation.

The notified chemical is a skin and eye irritant and avoidance of contact is required to avoid acute adverse effects. However it is expected that irritancy would reduce at the low

concentrations used in the final dishwashing liquids.

Based on EASE estimates of potential repeated dermal exposure at the formulation site, the margin of exposure (MOE) for workers is 11.5 to 500. The exposure would be further reduced by the PPE used at the site, and by good hygiene practices.

The calculated MOE for workers using dishwashing liquid is 112 based on EU calculations, and is higher on the basis of EASE estimations.

Uncertainties in the risk assessment are related to both the health effects assessment and the exposure estimations. As repeated dose testing was not carried out by the dermal route, the NOAEL established through oral dosing has been used. The dermal absorption characteristics of the notified chemical have not been established. Exposure estimations for downstream use of dishwashing detergents have significant uncertainties about dose, concentration and frequency of use.

The possibility of formation of nitrosamines in this class of surfactant is of potential concern because dishwashing involves deliberate contact with dilute solutions of the notified chemical. The risk of carcinogenicity arising from such impurities can be minimised by precautions taken in manufacture, formulation and packaging and by monitoring levels of nitrosamines (ASCC, 2003). Available analyses of Ammonyx LMDO containing the notified chemical show reasonably low levels of nitrosamines (<50 ppb) in most batches tested, with 112 ppb in one batch. Other impurities found in surfactants of this type could have sensitising effects.

9.2.5. Public health – risk characterisation

While the notified chemical is a skin and eye irritant, these characteristics are expected to be greatly reduced at the low concentration used in the dishwashing liquids to which the public will have contact. It is expected that dishwashing would be carried out by some consumers using gloves, but in many instances skin protection would not be worn. The irritation potential of dishwashing products would be determined by both the notified chemical and the other ingredients.

There are potential risks to health from acute oral exposure eg accidental ingestion by young children. However the effects would be related to the characteristics of the total dishwashing formulation, and not the notified chemical alone. The notified chemical has only moderate acute oral toxicity (LD50 of 500 to 1000 mg/kg) and is present in dishwashing liquid at a relatively low concentration (up to 2%). At this concentration, the formulation would not be classified as hazardous substance based solely on the effects of the notified chemical. Based on the notified chemical alone, substantial quantities of dishwashing liquid would have to be ingested to cause harm.

Based on the NOAEL of 15 mg/kg bw/day set on the basis of repeated oral dosing in rats, the margin of exposure (MOE) for consumers using dishwashing liquids containing the notified chemical is 112. This is lower than the preferred MOE of 1000 for chemicals in products used by the public. There is uncertainty in the risk assessment, related to both the potential effects of the chemical and exposure scenarios. Toxicological testing by the oral route has been used as a surrogate for effects via the dermal route. The scenario used for the calculation of exposure used relatively high concentrations of dishwashing liquid. Both these factors would be expected to overestimate the risk. However it should be noted that the notified chemical is only one of several ingredients in the dishwashing liquid that could have health effects, and one of the other ingredients is expected to have a very similar toxicological profile to the notified chemical.

The possibility of formation of nitrosamines in this class of surfactant is of potential concern because dishwashing involves deliberate contact with dilute solutions of the notified chemical. The risk of carcinogenicity arising from such impurities can be minimised by precautions taken in manufacture, formulation and packaging and by monitoring levels of nitrosamines (ASCC,

2003). Available analyses of Ammonyx LMDO containing the notified chemical show reasonably low levels of nitrosamines (<50 ppb) in most batches tested, with 112 ppb in one batch. Other impurities found in surfactants of this type could have sensitising effects.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data the notified chemical is classified as hazardous under the NOHSC *Approved Criteria for Classifying Hazardous Substances*. The classification and labelling details are: R22 – Harmful if swallowed

R36 –Irritating to eyes

R38 – Irritating to skin

Classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) was not carried out, as data are only available for an analogue of the notified chemical. The GHS system is not mandated in Australia and carries no legal status.

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio, the notified chemical is not considered to pose a risk to the environment.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is No Significant Concern to public health when used in dishwashing liquids at up to 2%.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS for a mixture containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 2003). It is published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The label for a mixture containing the notified chemical provided by the notifier was in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC 1994). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS

Hazard Classification and Labelling

- The NOHSC Chemicals Standards Sub-committee should consider the following health hazard classification for the notified chemical:

- Xi: R36/38 Irritating to eyes and skin
- Xn: R22 Harmful if swallowed

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - Conc ≥ 25%: R22, R36/38
  - 20% ≥ conc < 25% R36/38

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following isolation and engineering controls to minimise occupational exposure to the notified chemical as introduced, and in the dishwashing product:
  - Measures to prevent aerosol formation at the formulation sites.
  - Measures to minimise direct handling.

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical as introduced and in the dishwashing product:
  - Good housekeeping practices to minimise spills and contamination that may lead to worker exposure.
  - Work procedures that will minimise eye and skin contact with the notified chemical at formulation sites.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical as introduced, and in the dishwashing product:
  - Protective eyewear, gloves and clothing sufficient to minimise incidental dermal exposure.

- If dishwashing liquid is marketed for occupational use, the MSDS should recommend use of gloves

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

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

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

Control of impurities

- Preventive measures should be taken by the importer of the notified chemical and marketers/formulators of dishwashing liquids to ensure control of any nitrosamine contamination and other hazardous impurities. Such measures would include where appropriate:
  - Monitoring of levels of impurities including nitrosamines in the imported mixture and dishwashing liquids, with the aim of ensuring that levels in dishwashing products do not exceed 50 ppb. Monitoring should cover any changes during storage.
  - Avoidance of nitrosating agents in formulation and handling
  - Use of suitable inhibitors
  - Packaging in nitrite-free containers.

Emergency procedures

- Spills/release of the notified chemical should be handled by absorbing the spill with liquid-binding material (eg. sand, diatomite, acid binders, universal binders, sawdust).
- Contain spill and prevent from spreading (eg. by damming-in or oil barriers).
- Do not allow notified chemical to reach sewerage system or any water course.
- Inform respective authorities in case of seepage into water course or sewerage system.

Disposal

- The notified chemical should be disposed of by either recycling (contact manufacturer) or by incineration in accordance with local jurisdiction waste management regulations.
- Emptied containers should be rinsed with water, and containers may be reused or recycled after cleaning.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Section 64(1) of the Act; if

- a) manufacturing of the notified chemical in Australia is proposed;
- b) the introduction level exceeds 50 tonnes per annum;
- c) the notified chemical is proposed for use in products other than hand dishwashing liquids; or
- d) the notified chemical is proposed for use in hand dishwashing liquids at a level greater than 2%.

Due to the predominantly aquatic disposal route for the notified chemical after use, secondary notification under a) or b) above may require the provision of a chronic Daphnia test for the notified chemical.

or

(2) Under Section 64(2) of the Act:

- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

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