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November 2001

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

KUDE-2

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Director
Chemicals Notification and Assessment

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KUDE-2

1. APPLICANT

Epson Australia Pty Ltd of 70 Gibbes Street, Chatswood, NSW 2067 (ABN 91 002 625 783) has submitted a standard notification statement in support of their application for an assessment certificate for **KUDE-2**.

2. IDENTITY OF THE CHEMICAL

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

Marketing Name: KUDE-2

3. PHYSICAL AND CHEMICAL PROPERTIES

The following physicochemical data refer to the notified chemical as a mixture of two component isomers.

Appearance at 20°C & 101.3 kPa:	Black powder
Melting Point:	> 366°C
Boiling Point:	Not determined due to high melting point.
Density:	1.48 x 10^3 kg/m^3 at 20°C
Vapour Pressure:	1.4 x 10^{-20} kPa at 25°C. See comments below.
Water Solubility:	Component 1 = 34.4 mg/L at 20°C Component 2 = 180 mg/L at 20°C See comments below.
Partition Co-efficient (n-octanol/water):	Component 1 log P_{ow} = -0.535 at 21°C Component 2 log P_{ow} < -2.22 at 21°C See comments below.

Particle Size Distribution:	10µm – 2% 20µm – 10.2% 45µm – 38.2% 75µm – 63.8% 125µm – 88.4% 212µm – 100%
Hydrolysis as a Function of pH:	$T_{1/2}$ at pH 4, 7 and 9 > 1 year at 25°C. See comments below.
Adsorption/Desorption:	Component 1 log K_{oc} < 1.77 at 45°C Component 2 log K_{oc} < 1.77 at 45°C See comments below.
Dissociation Constant:	Not determined. See comments below.
Flash Point:	Not determined
Flammability Limits:	Combustible, not flammable (Method A10, EEC)
Autoignition Temperature:	274°C (Method A16, EEC)
Explosive Properties:	Explosive when subjected to thermal strain. Not explosive when subjected to shock or friction (Method A14, EEC). See comments below.
Reactivity/Stability:	Stable. Incompatible with strong oxidisers and acids.
Surface Tension:	70.9 mN/m at 19°C

3.1 Comments on Physico-Chemical Properties

The vapour pressure (VP) of the notified chemical was determined using a VP balance system and linear regression analysis. Determination involved measuring the change in mass of the chemical placed under a vacuum when subject to temperatures between 34 and 200ºC. Five series of mass difference readings were taken at time intervals beginning at 2 minutes and ending at 6.5 hours after being placed under a vacuum. A regression slope was calculated using measurements taken during each run, excluding run 2 at which time degassing occurred. Extrapolation of the data to 25ºC was determined using the mean of each run. The VP indicates the chemical is not volatile at 25ºC (SafePharm, 1995a).

The surface tension of the notified chemical was determined using a torsion balance according to the ring method (Method A5, Commission Directive 92/69/EEC). The concentrations in the test solution were determined by HPLC. Results indicate the test substance is not surface active (ie. <60 mN/m), (SafePharm, 1995b).

The water solubility of the notified chemical was determined using the flask shaking method (Method A6, Commission Directive EEC 96/69). Following a preliminary test, the notified

chemical was added to double-distilled water at 5 times saturation concentrations, shaken at 30°C, and then left to stand at 20°C for up to 24 hours. The concentration of test material was measured by HPLC using 1 ml of sample solution added to 12.5 mL of mobile phase eluant, (potassium dihydrogen orthophosphate) and dimethylformamide (ratio 90:10), diluted to 100 mL in distilled water. Test material was compared to standard solutions prepared using mobile phase eluant, dimethylformamide, distilled water at a ratio of 22.5:2.5:75, and a nominal concentration of 10 mg/L (SafePharm, 1995b). The results show that both components are moderately soluble in water.

The partition coefficient of the notified chemical was determined using the shake-flask method (Method A8, Commission Directive EEC 92/69). Following a preliminary test to determine an approximate value, a stock partitioning mixture was prepared in n-octanol saturated water. Three sets of duplicate samples were prepared, containing 1:1, 2:1 and 1:2 ratios of octanol to water, respectively. Vials were shaken for 5 minutes then the phases were separated for measurement by HPLC analysis. The concentration of each component in the standard solutions was calculated using data provided by the sponsor, where component 1 comprises 51% and component 2 comprises 41.5% of the notified chemical. Peak areas of the pairs of standards were corrected to nominal concentrations and averaged prior to calculation of the sample concentration (SafePharm, 1995b). The P_{ow} values indicate a poor affinity to lipids.

Hydrolysis as a function of pH was determined for pH 4, 7, and 9, over a period of 5 days and maintained at 50°C, according to the methods outlined in Method C7, Commission Directive EEC 92/69). The concentrations of test material remaining after 5 days were determined using HPLC. Results showed <10% of the notified chemical underwent hydrolysis after 5 days, equating to a half-life of > 1 year (SafePharm, 1995b).

The adsorption coefficient (K_{oc}) of the notified chemical was determined using an HPLC screening method outlined in a draft "HPLC-screening method for the determination of the adsorption-coefficient on soil-comparison of different stationary phases". The method involved passing a solution containing 0.0102 g of notified chemical, dissolved in an aqueous medium (100 mL) with 0.02N potassium dihydrogen orthophosphate:acetonitrile (90:10), through an HPLC column and determining the retention times. Dead time was determined using formamide (649 mg/L). A calibration curve was constructed using the capacity factor (k), determined from the retention times of a suite of 10 reference standards, and their associated $\log_{10}K_{oc}$ values as derived from the literature (Safepharm, 1996). The Koc values for each component were determined to be <58.9.

McCall *et al*. (1980) have developed a soil mobility classification based on Koc values determined using HPLC retention times and correlated to leaching distances in soils. The resulting Koc value of the notified chemical indicates that will be highly mobile in soils.

The dissociation constant was not determined. The substance is a complex reaction mixture in which the two main components have a number of weak and strong acidic and basic groups in their structures. For example, we would expect the SO_3H to be strongly acidic with a pKa <1, CO_2H to be moderately acidic with a pKa of about 4, and phenol to be weakly acidic, with the aromatic NH_2 group comprising the basic component.

Explosive properties of the notified chemical when subjected to thermal strain warrant classification of the chemical as hazardous with the risk phrase R2 - Risk of explosion by

shock, friction, fire or other sources of ignition.

4. PURITY OF THE CHEMICAL

Degree of Purity: 77.1%

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

Chemical name:	Water
Weight percentage:	3 – 6%
CAS No.:	7732-18-5

Additives/Adjuvants: None

5. USE, VOLUME AND FORMULATION

The notified chemical is a component (< 5%) of liquid ink formulations for ink-jet printers. It will be imported in ready-to-use printer cartridges at the rate of 2 tonnes/year for the first year rising to 5 tonnes/year for years 2 – 5.

6. OCCUPATIONAL EXPOSURE

Import, Transport and Storage

KUDE-2 will be imported in ready to use sealed ink-jet printer cartridges in pasteboard boxes. No reformulation or repackaging will take place. Hence, occupational exposure is not expected during transport and storage except in the event of accident breakage of the boxes and cartridges.

End Use - Customer Sites

Occupational exposure to KUDE-2 will occur primarily to printer service personnel and office workers.

As the chemical is contained in a sealed cartridge, exposure predominantly via the dermal route is expected to be minimal during normal handling and replacement of printer cartridges by service technicians or printer users. Greater exposure may occur in the event of a cartridge leak or if internal printer servicing occurs requiring handling of components contaminated with ink residue. Because of the low vapour pressure of the notified chemical and low levels of aerosol formation during the printing process, inhalation exposure is expected to be negligible. Overall, the possibility for exposure would be low due to the small quantities of notified chemical present within the cartridge ink (< 5%).

Dermal exposure may occur upon handling printed matter. However, only very small quantities of notified chemical would be present per sheet of paper and it would not be available for exposure as it is fused and fixed to the printed surface.

7. PUBLIC EXPOSURE

Exposure of the public as a result of reformulation, transport and disposal of products containing the notified chemical is assessed as being negligible. The general public may make dermal contact with ink containing the notified chemical when handling printed paper. However, public exposure to the notified chemical is likely to be minimal since the notified chemical will be absorbed to the paper with the assistance of carriers in the ink formulation. Exposure of some members of the public may occur when clearing paper jams or servicing printers. However, these exposures are generally likely to be intermittent and of short duration.

8. ENVIRONMENTAL EXPOSURE

8.1 Release

Losses of the notified chemical during transport to sites of sale are not expected because the chemical is housed in sealed cartridges. These cartridges are designed to prevent release of the ink until the sealing tape is removed and the cartridges are inserted into an inkjet printer. Incidental losses during insertion, normal printer use, and replacement of the cartridge are also not expected because the chemical is held in an absorbent under negative pressure in the sealed cartridges, designed to prevent leakages.

Minimal release of the notified chemical is anticipated following disposal of the spent ink cartridges. The notifier estimates up to 5% of ink, containing less than 5% of notified chemical, may remain in spent cartridges. Most spent cartridges are likely to be sent to landfill. As such, up to 12 kg of the notified chemical may enter the environment each year at landfill sites. Due to the anticipated nationwide use, the disposal would be widespread across Australia.

Most of the notified chemical will be deposited with the ink blend onto sheets of paper during the printing process. The waste paper generated will eventually be disposed of either through recycling, landfill or incineration. As such, almost all of the notified chemical could be released into the environment, depending on paper disposal and recycling trends

8.2 Fate

Recent literature suggests that current paper recycling rates in Australia are 70-92% (Australian Environmental Review, 2001). Figures for the year 1996-1997 give a much lower (ie. 28%) average recycling rate for paper (Waste Management Industry, Australia cited in ABS, undated). If we assume the more recent figures are correct, up to 92% of the chemical could enter paper-recycling facilities.

Paper recycling is carried out in paper mills. During the recycling process, waste paper is repulped using a variety of alkalis, dispersing and wetting agents, water emulsifiable organic solvents and bleaches. These agents enhance fibre separation, ink detachment from paper fibres, pulp brightness, and the whiteness of paper (EC, 1994). It is estimated that the removal rate of ink particles from paper during the de-inking phase of recycling is 30-60% efficient for inkjet copying (EC, 1994).

The notified substance is moderately soluble in water, hence, during de-inking up to 60% of the total import volume contained in the ink blend may be associated with the aquatic compartment, and enter sewage treatment facilities following release of the effluent water from pulp mills.

In sewage treatment facilities, the notified chemical is not expected to adsorb to organic matter given its poor affinity to lipids or to break down readily because of its long half life (>1 year) and low biodegradability. In a ready biodegradation test (Closed Bottle Test, OECD TG 301D), performed using microorganisms in sewage sludge, <10% of the notified chemical was degraded over 8 days, while 19% was degraded at the end of the 28-day test period. This compared to 85% of the reference substance, sodium benzoate, degraded after 8 days and 98% degraded after 28 days, which indicates the test was viable. A toxicity control containing the notified substance and sodium benzoate, attained 31% degradation after 28 days indicating that the test material was not toxic to the microorganisms in the sewage sludge (SafePharm, 1995c).

The insoluble substances retained in the paper fibre or in the sludge will eventually be used to make recycled paper, or will be disposed to landfill with waste sludge (EC, 1994). As such, up to 40 % of the notified chemical could eventually enter the soil environment after being sent to landfill. The K_{oc} value of the notified chemical indicates it will be highly mobile in soils (McCall *et al*. 1980). Hence, any chemical entering the soil environment, either fixed to paper, residing in sludge, or released from ruptured cartridges, could potentially enter the aquatic compartment via surface runoff or percolating groundwater.

Incineration of paper containing the notified chemical is expected to destroy the chemical and result in the release of combustion products such as carbon monoxide, carbon dioxide, and oxides of nitrogen, sulphur, and phosphorus.

No bioaccumulation test was carried out for the notified chemical. However, the substance is not expected to bioaccumulate given the low partition coefficient of both components of the substance.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Summary of Toxicological Investigations

Endpoint & Result	*Assessment Conclusion*
Rat, acute oral LD50 > 2000mg/kg bw	low toxicity
Rat, acute dermal LD50 > 2000mg/kg bw	low toxicity
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	severely irritating
Guinea pig, skin sensitisation - adjuvant test	strongly sensitising
Rat, Oral Repeat Dose Toxicity – 28 Days.	NOAEL = 1.5 mg/kg/day
Genotoxicity - bacterial reverse mutation	Non mutagenic

Genotoxicity – in vitro mammalian chromosome aberration test	Non genotoxic

9.2 Acute Toxicity

9.2.1 Acute Oral Toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD 401 Acute Oral Toxicity – Limit Test.
Species/Strain	Rat/ Sprague Dawley
Vehicle	Arachis oil

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 males, 5 females	2000	None

LD50	> 2000 mg/kg bw
Signs of Toxicity	Hunched posture, decreased respiratory rate, gasping, laboured and noisy respiration observed in two animals. One animal also showed lethargy and red/brown staining around the mouth.
Effects in Organs	No abnormalities detected.
CONCLUSION	The notified chemical is of low acute toxicity via the oral route.
TEST FACILITY	Safepharm Laboratories Limited, Derby, UK

9.2.2 Acute Dermal Toxicity

TEST SUBSTANCE	Notified chemical
METHOD	OECD 402 Acute Dermal Toxicity – Limit Test.
Species/Strain	Rat/Sprague Dawley
Vehicle	None
Type of dressing	Semi-occlusive

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5 males, 5 females	2000	None

LD50	> 2000 mg/kg bw
Signs of Toxicity	

- Local	None
- Systemic	None
Effects in Organs	None

CONCLUSION The notified chemical is of low acute toxicity via the dermal route.

TEST FACILITY Safepharm Laboratories Limited, Derby, UK

9.2.3 Acute Inhalation Toxicity

Not submitted

9.2.4 Skin Irritation

TEST SUBSTANCE Notified chemical

METHOD OECD 404 Acute Dermal Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	7 days
Vehicle	Distilled water
Type of Dressing	Semi-occlusive.

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	1	0	0	1	72 hours	0
Oedema	0	0	0	0	-	0

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

Remarks - Results

CONCLUSION The notified chemical is slightly irritating to skin.

TEST FACILITY Safepharm Laboratories Limited, Derby, UK

9.2.5 Eye Irritation

TEST SUBSTANCE Notified chemical

METHOD OECD 405 Acute Eye Irritation/Corrosion.

Species/Strain	Rabbit/New Zealand White
Number of Animals	3

Observation Period 21 days

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	*2*	*3*			
Conjunctiva: redness	1.7	1.3	1.7	1.7	72 hours	0
Conjunctiva: chemosis	1.3	1.0	1.3	1.3	72 hours	0
Conjunctiva: discharge	1.0	0.3	1.0		72 hours	
Corneal opacity	1.3	0.7	0.7	1.3	72 hours	0
Iridial inflammation	1.0	0.3	0.3	1.0	72 hours	0

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

Remarks - Results Corneal and iridial staining and residual test material around the eye was still observed in one animal at day 21.

CONCLUSION The notified chemical is severely irritating to the eye. Persistent staining also occurred.

TEST FACILITY Safepharm Laboratories Limited, Derby, UK

9.2.6 Skin Sensitisation

TEST SUBSTANCE Notified chemical

METHOD OECD 406 Skin Sensitisation – Magnusson and Kligman Maximisation Study

Species/Strain Guinea pig/ Dunkin Hartley Albino

PRELIMINARY STUDY Maximum non-irritating concentration:
intradermal: 10%
topical: 50%

MAIN STUDY

Number of Animals Test Group: 10 Control Group: 5

INDUCTION PHASE Induction Concentration
intradermal: 10%
topical: 50%

Signs of Irritation Blue coloured staining preventing accurate evaluation of erythema was noted at intradermal injection sites in test group animals.

CHALLENGE PHASE

1st challenge topical application: 25%
topical application: 50%

Remarks - Method Blue coloured staining was noted at the challenge sites of all test and control animals. Staining did not affect the evaluation of skin reactions.

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	25%	6/10	1/10	-	-
	50%	9/10	1/10	-	-
Control Group	25%	0/5	0/5	-	-
	50%	0/5	0/5	-	-

Remarks - Results

CONCLUSION — The notified chemical was a strong sensitiser under the conditions of the test.

TEST FACILITY — Safepharm Laboratories Limited, Derby, UK

9.2.6.1 Skin Sensitisation

The notifier provided a report of skin sensitisation study on a product HQ327B, which contains slight higher percentage (6%) of the notified chemical than in the Ink Cartridge (T026) being imported. The other 2 ingredients in HQ327B were the same as T026.

TEST SUBSTANCE — HQ327B

METHOD — OECD 406 Skin Sensitisation – Magnusson and Kligman Maximisation Study

Species/Strain — Guinea pig/ Dunkin Hartley Albino

PRELIMINARY STUDY — Maximum non-irritating concentration:
intradermal: 5%
topical: 100%

MAIN STUDY

Number of Animals — Test Group: 10 Control Group: 5

INDUCTION PHASE — Induction Concentration
intradermal: 10%
topical: 100%

Signs of Irritation — After intradermal induction, erythema could not be scored due to black staining of the skin by the test substance. Necrosis of grade 1 was observed in 3/10 animals on day 3 after intradermal induction, and intense erythema and swelling were observed in 4/10 animals after topical induction.

CHALLENGE PHASE

1st challenge — topical application: 0, 25, 50 and 100%

Remarks - Method — GLC & QA.

The duration of topical induction was 48 hours.

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	0%	0/10	0/10		
	25%	0/10	0/10		
	50%	1/10	0/10		
	100%	0/9*	1/9*		
Control Group	0%	0/5	0/5		
	25%	0/5	0/5		
	50%	0/5	0/5		
	100%	0/4*	0/4*		

* One animal in the group had black staining on the treated skin, which made scoring impossible for erythema.

Remarks - Results: Erythema was difficult to score due to black staining of the skin on 1 site of 50% challenge and 5 sites of 100% challenge at 24 hours, and 1 site of 50% challenge and 3 sites of 100% challenge at 48 hours.

CONCLUSION: The test material was not a sensitiser under the conditions of the test.

TEST FACILITY: NOTOX (1995).

9.3 Repeat Dose Toxicity

TEST SUBSTANCE: Notified chemical

METHOD: OECD 407 Repeated Dose 28-day Oral Toxicity Study in Rodents.

Species/Strain: Rat/ Sprague Dawley
Route of Administration: Oral – gavage
Exposure Information: Total exposure days: 28;
Dose regimen: 7 days per week;
Post-exposure observation period: 14 days.
Vehicle: Arachis oil
Remarks - Method

RESULTS

Group	*Number & Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
Control	5 males, 5 females	0	0
Recovery control	5 males, 5 females	0	0

Low dose	5 males, 5 females	1.5	0
Intermediate dose	5 males, 5 females	15	0
High dose	5 males, 5 females	150	1
Recovery high dose	5 males, 5 females	150	0

Mortality & Time to Death

One high dose female was found deceased on day 34.

Clinical Observations

No clinical observations indicative of toxicity were made. Two high dose females showed hunched posture before dosing on day 28 but appeared normal after dosing. One of these animals died at the start of day 34. This death was deemed coincidental. Three high dose males showed isolated incidents of transitory increased salivation immediately after dosing. High dose animals all showed dark brown/black faeces and urine from day 3 onward and for several days following cessation of treatment.

High dose animals of either sex showed reduced bodyweight gain during the second half of the treatment period. This reduction gradually became more pronounced with time. The deceased high dose female showed a substantial 18% bodyweight loss. No adverse effect on bodyweight was observed during the 14-day recovery period in these animals or in intermediate or low dose animals at any stage.

All high dose animals and intermediate dose females showed slightly reduced food consumption during the second half of the treatment period. This reduction gradually became more pronounced with time. No reductions were observed during the recovery period.

Intermediate dose males and low dose males and females showed no treatment-related effects on food consumption.

Visual inspections of water consumption showed no treatment-related effects.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

Clinical Chemistry

At the end of the dosing period, high dose animals showed a statistically significant increase in plasma bilirubin and aspartate aminotransferase (ASAT) compared to controls. Most ASAT values were also above the range of historical controls. The increase was particularly marked in 3 animals whose alanine aminotransferase values were also above the range of historical controls. High dose males also showed a statistically significant reduction in total protein concentrations and slightly increased albumin/globulin ratios compared to controls. However, most of these values were within the range of historical controls.

At the end of the dosing period, high dose males also showed a statistically significant increase in plasma creatinine compared to controls but values were within the range of historical controls. High dose females showed a statistically significant reduction in total protein compared with controls at the end of the recovery period but given the absence of a similar effect in these animals at the end of the dosing period this was not considered toxicologically significant.

Haematology
High dose animals showed statistically significant increases in methaemoglobin compared to controls. Several values were also substantially above the range of historical controls. These animals also showed statistically significant reductions in haemoglobin, mean corpuscular haemoglobin concentrations and erythrocyte counts and increases in reticulocyte counts and mean corpuscular volume. High dose females showed slight reductions in haematocrit and high dose males showed statistically significant increases in platelet counts. Several high dose animals of either sex also showed abnormally high neutrophil counts although the male group mean value was not statistically significantly different from controls.

Most toxicologically significant changes were not present at the end of the recovery period. High dose males and females still showed statistically significant increases in platelet counts and methaemoglobin respectively compared to controls. However, these values were within the range of historical controls.

Intermediate and low dose animals showed no toxicologically significant changes.

Urinalysis
Measured during the final week of treatment, urine volume increased and urine specific gravity decreased significantly in all high dose animals compared to controls. Similar but non-statistically significant effects were measured for high dose males also during the recovery period. Intermediate and low dose animals showed no toxicologically significant changes.

Effects in Organs
Pathology
At the end of the dosing period, high dose animals of either sex showed statistically significant increases in relative kidney weights and absolute and relative spleen weights compared to controls. Individual spleen weights were also outside the ranges of historical controls.

High dose males also showed statistically significant reductions in absolute and relative testes weight compared to controls with values outside ranges of historical controls. These reductions in addition to increases in relative kidney weight were observed also at the end of the recovery period in these animals. Relative adrenal weights were also increased significantly in high dose males at the end of the dosing period. Relative spleen weights were still increased significantly in high dose females at the end of the recovery period.

At the end of the dosing period, high dose females showed statistically significant reductions in absolute liver and ovary weights compared to controls. However, differences were not evident in relative organ weights. Significant increases in absolute but not relative brain weight were observed also. Females from all three treatment groups showed statistically significant reductions in absolute kidney weight compared to controls at the end of the dosing period but these did not display a dose-response relationship and so were not considered of toxicological significance.

High dose females showed darkened and enlarged spleens at necropsy together with darkened livers and kidneys. Males from the same group showed similar changes to spleen and also discoloured and/or small testes. At the end of the recovery period, most high dose

animals showed darkened spleens and males showed small flaccid testes. Low dose animals showed no macroscopic abnormalities attributable to toxicity.

The high dose female animal found deceased on day 34 also showed an enlarged and darkened spleen, darkened liver, congested small intestine, darkened kidneys and fluid containing blood in thoracic and abdominal cavities.

Histopathology
Generalised hepatocyte enlargement and pigment deposits (haemosiderin) were observed in livers of intermediate and high dose animals. Changes generally receded in the recovery period. In kidneys, pigment deposits were observed in the tubular epithelium of high dose animals. Globular eosinophilic accumulations were observed in the proximal tubular epithelium of 2 high dose and one intermediate dose male animals. No recession of changes was evident in recovery animals.

Pigment deposits and increased severity of extramedullary haemopoiesis were observed in spleens of high dose animals. Splenic pigment deposition was also observed in 2 intermediate dose animals of either sex. Splenic congestion was evident also in high dose females. During the recovery period, extramedullary haemopoiesis and congestion regressed but pigment deposition remained in animals of both sexes.

Testicular atrophy was observed in all high dose male animals. This was not diminished at the end of the recovery period.

Myocarditis of notable severity was observed in 3 high dose females. This showed regression in recovery animals following cessation of treatment.

Remarks – Results
Oral administration of the notified chemical induced treatment-related changes at dose levels of 15 and 150 mg/kg/day. Animals dosed at 1.5 mg/kg/day showed no toxicologically related changes.

At 150mg/kg/day, the notified chemical caused a methhaemoglobulinaemia amongst animals of both sexes and of a slightly greater extent in females. Haemolytic anaemia was also suggested by haematological and histopathological finding of haemosiderin pigment deposition particularly in the liver and kidneys. Splenic abnormalities at this dose, notably increased severity of splenic extramedullary haemopoiesis and splenic enlargement and substantially elevated splenic weights at necropsy are likely compensatory responses to anaemia. The observed macrocytosis at this dose level is further evidence of a compensatory increase in haemopoiesis. Other findings attributable to anaemia include elevated plasma bilirubin indicating of increased erythrocyte destruction and a mild thrombosis. This latter finding may not be the result of a direct toxicological insult but may be associated with automated cell counting systems scoring erythrocyte fragments as platelets.

Determinations at the end of the recovery period in these high dose animals showed reversibility of the haemolytic anaemia although haemosiderin deposits were still present in liver and kidney and also to a lesser extent in spleen. The methaemoglobulinaemia regressed completely amongst male animals. Females still showed a mild methaemoglobulinaemia but because intergroup differences were negligible this was not

considered indicative of toxicity.

Generalised hepatocyte enlargement was observed in several high dose animals at the end of the dosing period. In addition, increases in plasma ASAT and alanine aminotransferase were observed with marginal reductions in total plasma protein. These may be indicative of liver toxicity although increases in the ubiquitous ASAT could indicate tissue insult at another location. Also, the reductions in plasma protein may be directly related to the significant decreases in food consumption recorded for high dose animals. Liver effects were generally reversible after the 14-day recovery period.

Testicular atrophy, indicated by substantial reductions in absolute and relative testes weights and confirmatory macroscopic and histopathological changes at the end of the dosing period in high dose males identifies the testes as a target organ for the notified chemical. Furthermore, testicular changes showed no regression following the 14-day recovery period. Males showed small, flaccid testes of reduced weight and histopathological examination showed severe testicular atrophy.

In high dose animals, relative kidney weights were elevated slightly and urinalysis showed a diuresis and discoloured urine at the end of the dosing period. Eosinophilic globular accumulations in proximal tubular epithelium in male animals were regarded as characteristic of a typical hydrocarbon nephropathy peculiar to the male rat and absent in female rats and other laboratory species. Males continued to show mild diuresis at the end of the recovery period in the absence of urine discolouration, identifying a possible toxicologically relevant renal effect. Kidney effects were completely reversed in female rats at the end of the recovery period.

Myocarditis was observed in several high dose females at the end of the dosing period and also in the female found deceased during the recovery period (day 34). Given the low prevalence of this condition and the findings of congested small intestines and fluid containing blood in thoracic and abdominal cavities in the single deceased animal contrasting with general improvements observed in animals at the end of the recovery period, the toxicological relevance of these cardiovascular findings are unclear.

Two animals of either sex receiving an intermediate dose of notified chemical (15mg/kg/day) showed darkened spleens at necropsy at the end of the dosing period. Generalised hepatocyte enlargement with haemosiderin pigment deposition were observed also in both sexes at this dose and hydrocarbon nephropathy indicated by eosinophilic material in the renal proximal tubular epithelium was observed in male animals.

CONCLUSION
A No Observed Adverse Effect Level (NOAEL) of 1.5 mg/kg/day was assigned.

TEST FACILITY Safepharm Laboratories Limited, Derby, UK

9.4 Genotoxicity

9.4.1 Genotoxicity-Bacteria

TEST SUBSTANCE	Notified chemical
METHOD	OECD 471 Bacterial Reverse Mutation Test.
Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100; *E. coli*: WP2 uvrA
Metabolic Activation System	Aroclor-induced rat liver microsomes, S9 fraction
Concentration Range in Main Test	a) With metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate. b) Without metabolic activation: 0, 50, 150, 500, 1500, 5000 µg/plate.
Vehicle	Dimethyl sulphoxide

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	Not conducted	Not detected	Not detected	Negative
Test 2	Not conducted	Not detected	Not detected	Negative
Absent				
Test 1	No cytotoxicity	Not detected	Not detected	Negative
Test 2	No cytotoxicity	Not detected	Not detected	Negative

Remarks - Results

CONCLUSION	The notified chemical was not mutagenic to bacteria under the conditions of the test.
TEST FACILITY	Safepharm Laboratories Limited, Derby, UK

9.4.2 Genotoxicity-In Vitro

TEST SUBSTANCE	Notified chemical
METHOD	OECD 473 In vitro Mammalian Chromosomal Aberration Test.
Cell Type/Cell Line	Chinese hamster lung cells
Metabolic Activation System	Aroclor-induced rat liver microsomes, S9 fraction
Vehicle	Minimal essential media
Remarks - Method	

Metabolic Activation	*Test Substance Concentration (μg/mL)*	*Exposure Period*	*Harvest Time*
Present			
Test 1	0, 78.1, 156.3, 312.5, 625, 1250, 2500 μg/mL	4 hours	8 hours
Test 2	0, 312.5, 625, 1250, 2500, 5000 μg/mL	4 hours	8 hours
Absent			
Test 1	0, 312.5, 625, 1250, 2500, 5000 μg/mL	12 hours	0 hours
Test 2	0, 156.3, 312.5, 625, 1250, 2500, 5000 μg/mL	6, 12, 24, 48 hours	0 - 18 hours

RESULTS

Metabolic Activation	*Test Substance Concentration (μg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main test*	*Precipitation*	*Genotoxic Effect*
Present				
Test 1	> 5000	> 2500	None detected	Negative
Test 2	> 5000	> 5000	None detected	Negative
Absent				
Test 1	156.3	> 5000	None detected	Negative
Test 2	156.3	> 5000*	≥ 39 μg/mL	Negative

* 2500 μg/mL with 24 hours continuous treatment; 234.4 μg/mL with 48 hours continuous treatment

Remarks - Results	No statistically significant dose-related increases in frequencies of cells with aberrations were observed in any treatment group.
CONCLUSION	The notified chemical was not clastogenic to Chinese hamster lung cells treated in vitro under the conditions of the test.
TEST FACILITY	Safepharm Laboratories Limited, Derby, UK

9.6 Overall Assessment of Toxicological Data

The notified chemical was of low acute oral and dermal toxicity in rats with an LD_{50} > 2000mg/kg/day. A skin irritation test in rabbits showed that the chemical was slightly irritating. An eye irritation test also in rabbits showed conjunctival irritation and corneal opacity with irreversible staining of the iris and cornea.

Positive responses were observed in a skin sensitisation study in guinea pigs indicating potential of the notified chemical to induce allergic sensitivity.

A 28-day repeat dose oral toxicity study in rats revealed significant toxicity. High dose animals (150 mg/kg/day) showed haemolytic anaemia with haemosiderin deposition in multiple organs, compensatory splenic enlargement, generalised hepatocyte enlargement,

enzyme changes and kidney weight changes and diuresis. Severe, irreversible testicular atrophy in these high dose animals indicated by substantial reductions in organ weights and confirmatory macroscopic and histopathological changes identified the testes as a target organ. Hepatocyte enlargement and haemosiderin deposits were observed also in intermediate dose animals (15 mg/kg/day). On the basis of these findings a NOAEL of 1.5 mg/kg/day was assigned.

The notified chemical was non mutagenic and non clastogenic in an in vitro bacterial reverse mutation assay and chromosome aberration assay respectively.

On the basis of the NOHSC *Approved Criteria for Classifying Hazardous Substances* (National Occupational Health and Safety Commission, 1999) the notified chemical should be classified Irritant (Xi) and Harmful (Xn) with the risk phrases R41 – Risk of serious damage to eyes; R43 – May cause sensitisation by skin contact; R48/22 – Harmful: danger of serious damage to health by prolonged exposure if swallowed and R62 – Possible risk of impaired fertility.

The notifier provided a skin sensitisation study on a product HQ327B. It contains same ingredients as T026 except a slightly high concentration (6%) of the notified chemical. The study showed that HQ327 was not found to be a skin sensitiser in guinea pigs. This result indicates that R43 (may cause sensitisation by skin contact) does not apply to the products containing the notified chemical at 6% or less.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The notifier provided ecotoxicity studies for fish, daphnia, algae and microorganisms in sewage sludge. The test results are summarised in the table below. Unless otherwise recorded, all tests were performed according to OECD/EEC Test Methods and in compliance with OECD Principles of Good Laboratory Practice.

Test	***Species***	***Results***
Acute Toxicity to fish (OECD TG 203	Rainbow Trout *Oncorhynchus mykiss*	96 h LC_{50} > 100 mg/L NOEC = 100 mg/L
Acute Immobilisation Test (OECD TG 202)	Water Flea *Daphnia Magna*	48 h EC_{50} > 100 mg/L NOEC = 100 mg/L
Algal Growth Inhibition Test (OECD TG 201)	Green Algae *Scenedesmus subspicatus*	72 h E_bC_{50} = 3 mg/L 24-48 h E_rC_{50} = 4.4 mg/L NOEC = 1 mg/L
Inhibitory Effect on Microorganisms (OECD TG 209)	Activated sewage sludge	3 h EC_{50} = 1800 mg/L

* NOEC - no observable effect concentration

Fish

A preliminary rangefinding test was carried out over 96 hours against 3 Rainbow Trout per test concentration, using nominal test concentrations of 0 (control), 1.0, 10, and 100 mg/L of the test substance. No fish mortalities were observed when exposed to these test

concentrations over the 96 hour test period (Safepharm, 1995d).

Following the rangefinding test, a definitive semi-static test was performed over a period of 96 hours against 10 Rainbow Trout (per treatment), using nominal concentrations of 0 (control) and 100 mg/L (2 replicates) of the notified chemical. The test was conducted in carbon filtered, de-chlorinated tap water, held at a temperature of 14°C, and a pH varying between 7.6 and 7.7. Dissolved oxygen was in excess of 9.9 mg/L and total hardness was 100 mg/L $CaCO_3$.

Verification of the test material concentrations by HPLC showed them to be near nominal at 0, 24 and 96 hours with no precipitation of test material observed. No mortalities or abnormal behavioural responses occurred in the 20 fish exposed to test concentrations of 100 mg/L during the definitive test. Therefore, the NOEC was determined ≥100 mg/L of the notified chemical, and the 96 hr LC_{50} was determined to be >100 mg/L.

Daphnia

A preliminary rangefinding test was performed over 48 hours against 10 daphnids per concentration using nominal concentrations of 0 (control) 0.10, 1.0, 10, and 100 mg/L of test material. The test substance (a black powder) was dispersed in reconstituted water and the volumes adjusted to give the required concentrations. Due to the colouration of the test media, the daphnids were removed from the test vessels by sieve at 24 and 48 hours and resuspended in reconstituted water, prior to observations being made of their mobility. The results showed no immobilisation of daphnids exposed to any of the test concentrations during the rangefinding test (SafePharm, 1995e).

A definitive limit test was performed over a 48 hour period against 10 daphnids per concentration using nominal test concentrations of 0 (2 controls) and 100 mg/L (4 reps) of the test substance. The test was conducted in a prepared test medium comprising reconstituted water containing selected ionic substances maintained at 21°C, and a pH varying between 7.5 and 8.1. Dissolved oxygen was in excess of 7.9 mg/L and total hardness was approximately 270 mg/L $CaCO_3$. Test concentrations were verified at 0 and 48 hours using HPLC and were found to be near nominal. The results showed no immobilisation of daphnids exposed to any of the test concentrations during the definitive test (SafePharm, 1995e).

Green Algae

An Algal Growth Inhibition test was performed to assess the effects of the notified chemical on the growth of the green alga, *Scenedesmus subspicatus.* A preliminary rangefinding test was performed against the algae over a period of 72 hours, using nominal test concentrations of 0 (control), 0.05, 0.50, 5.0, and 50 mg/L, of the notified chemical. Test results showed no effects on algal growth at test concentrations of 0.05 and 0.5 mg/L. However, growth was reduced at concentrations of 5.0 and 50 mg/L (SafePharm, 1995f).

Following the rangefinding test, a definitive test was performed over a period of 72 hours against green algae containing nominal cell densities of 10^4 cells/ml and using a series of nominal concentrations of 0.5, 1.0, 2.0, 4.0 and 8.0 mg/L of test material. Test temperatures were maintained at 24°C. Illumination intensities were maintained at 7000 lux. Test concentrations were verified from water samples taken from the control and each test group (R1-R3 pooled).

The results of the definitive test indicate that both the algal growth rate and the algal biomass were adversely affected by the presence of the notified chemical. During the exposure period, the pH values of the test media increased from 8.0 at 0 hours to values ranging from 8.1 to 10.4 at 72 hours. The rise in pH was concentration-dependent, with the smallest increases occurring in the test medium containing the highest test concentrations and the largest increases in the control and test medium containing the lowest test concentrations. The increases in alkalinity were considered due to the large number of cells in the log phase of growth respiring oxygen and producing carbonates and bicarbonates during respiration and photosynthesis. Increases in pH in the test media containing the lowest test concentrations were due to the greater number of viable cells present compared to media with higher concentrations.

After 72 hours, a regrowth experiment was performed, using fresh sterile culture medium to determine whether the inhibitory effects were due to the toxicity of the test substance or to a reduction in available light caused by the dark colour of the notified chemical. After 96 hours, regrowth occurred in the control and subcultures, suggesting the test material reduced algal growth by reducing the available light for photosynthesis rather than by toxic effects.

Microorganisms

A preliminary rangefinding test, Activated Sludge Respiration Inhibition Test (OECD 209), was conducted against activated sludge from domestic sewage using nominal concentrations of 100 and 1000 mg/L of the notified chemical. The test medium was prepared by dispersing the test substance directly into the test media containing synthetic sewage sludge and water. The rangefinding test resulted in 29% inhibition of respiration after 3 hours contact time. A second rangefinding test was performed using serial nominal test concentrations of 1000 and 1800 mg/L in order to identify the test concentration resulting in 50% inhibition of respiration after 3 hours. The second test resulted in 23% inhibition at 1000 mg/L and 55% inhibition at 1800 mg/L.

Following the rangefinding tests, a definitive test was conducted over an incubation period of 3 hours against activated sludge from domestic sewage using nominal concentrations of 62.5, 125, 250, 500, 1000 and 2000 mg/L of the notified chemical. The test was carried out at a temperature of 21°C, a pH of 6.9, and a dissolved oxygen concentration prior to measurement of about 6.5 mg/L.

The oxygen consumption of microorganisms exposed to the test substance was measured after 30 minutes and 3 hours incubation time and compared to that of microorganisms in a blank control and a reference substance (3,5-dichlorophenol) incubated under the same conditions. The variation in consumption between the 2 blank controls after 30 minutes was ±1% and after 3 hours was ±5%, while the EC_{50} of the reference substance was determined to be 13 mg/L, which was within the allowable range of 5-30 mg/L, therefore the test was deemed valid.

The percentage inhibition obtained for the 1000 mg/L test concentration after 3 hours contact time was 8%, lower than the inhibition obtained during the rangefinding test for the same concentration. The difference was due to daily variations in the activated sewage sludge samples collected from the sewage treatment works.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

Ultimately all of the notified chemical will be released to the environment bound to printed paper. At the end of its useful life, most of the printed paper will be either buried in landfill, incinerated, or recycled. A small amount of the chemical will enter the soil environment directly at landfill sites when spent cartridges are disposed of with normal office garbage.

Recycling trends in Australia indicate that up to 92% of paper could be recycled, suggesting a large proportion of the new chemical will enter sewage treatment plants in effluent generated from the de-inking process during paper recycling. The low octanol-water partition coefficient and moderate water solubility indicate that in sewage treatment plants the chemical will be predominantly distributed in water, where it will become diluted and dispersed.

A worst case scenario Predicted Environmental Concentration (PEC) is calculated below. In calculating the PEC value, it is assumed that:

- all of the annual imported volume of the notified chemical is deposited on paper, of which 92% is recycled;
- all recycled paper enters paper making facilities at one time, but facilities are distributed nationwide;
- 60% of ink is released into the sewer during the de-inking process, with no precipitation of soluble components occurring.

Annual Import Volume	5000 kg
Volume Fixed to Paper (100%)	5000 kg
Volume in Recycled Paper (92%)	4600 kg
Volume released to Sewage by De-inking (60%)	2760 kg
National Population	18 million
Daily Water Usage per Person 150 L	150 L
PEC	1.0 mg/L

The worst case scenario PEC of the notified chemical in aquatic environments is several orders of magnitude below the highest concentrations to which fish and *daphnia* were exposed during toxicity testing, and which had no adverse effects. Hence safety margins toward these aquatic organisms are expected to be high. The PEC is also many orders of magnitude below the concentrations able to inhibit respiration of microorganisms, and hence, is not expected to adversely affect these organisms either.

The notified chemical is moderately toxic to algae (Mensink *et al*. 1995). The worst case scenario PEC value is equivalent to the NOEC value, and three and four times lower than the concentrations able to inhibit algal biomass and algal growth by 50%, respectively. The substance was not considered biochemically toxic, but rather was able to adversely affect algal growth by reducing the amount of light available for photosynthesis.

Despite these results, the notified chemical is not expected to pose a significant threat to algae. In reality, release of the imported volume of chemical into sewage treatment facilities is not expected to occur all at once as was assumed when calculating the PEC, but would be distributed over a longer period of time, dependent on the turnover time of the printed paper. A more realistic value may be determined by dividing the import volume by 365 to reflect

release on a daily basis. In addition, upon release of treated effluent water from sewage treatment facilities to the receiving waters the notified chemical would be further diluted. These factors together would reduce the PEC value by several orders of magnitude thereby significantly increasing the safety margins toward algae and other organisms.

The notified chemical was not readily biodegradable, however, slow biotic and abiotic processes are expected to eventually degrade the chemical in the environment. The chemical is also not expected to bioaccumulate given its low P_{ow} and high molecular weight, which would preclude any appreciable absorption across biological membrane. As such, the safety margins toward aquatic organisms are expected to be high.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Hazard Assessment

The notified chemical was of low acute oral and dermal toxicity in rats. A skin irritation test in rabbits showed that the chemical was slightly irritating. In contrast, an eye irritation test in rabbits showed conjunctival irritation and corneal opacity with irreversible staining of the iris and cornea.

Positive responses were observed in a skin sensitisation study in guinea pigs indicating potential of the notified chemical to induce allergic sensitivity.

A 28-day repeat dose oral toxicity study in rats revealed significant toxicity. High dose animals (150 mg/kg/day) showed haemolytic anaemia with haemosiderin deposition in multiple organs, compensatory splenic enlargement, generalised hepatocyte enlargement, enzyme changes and kidney weight changes and diuresis. Severe, irreversible testicular atrophy in these high dose animals indicated by substantial reductions in organ weights and confirmatory macroscopic and histopathological changes identified the testes as a target organ. Hepatocyte enlargement and haemosiderin deposits were observed also in intermediate dose animals (15 mg/kg/day). On the basis of these findings a NOAEL of 1.5 mg/kg/day was assigned.

The notified chemical was non mutagenic and non clastogenic in an in vitro bacterial reverse mutation assay and chromosome aberration assay respectively.

Given this toxicological profile, on the basis of the NOHSC *Approved Criteria for Classifying Hazardous Substances* the notified chemical should be classified Irritant (Xi) and Harmful (Xn) with the risk phrases R41 – Risk of serious damage to eyes; R43 – May cause sensitisation by skin contact; R48/22 – Harmful: danger of serious damage to health by prolonged exposure if swallowed and R62 – Possible risk of impaired fertility.

A skin sensitisation study on a product with a slightly high concentration (6%) of the notified chemical was provided. The study showed that the product was not a skin sensitiser in guinea pigs.

Occupational Health and Safety

The main exposure to KUDE-2 will be via the dermal route to service personnel who will

change printer cartridges and may come into contact with internal printer componentry that may be contaminated with ink. Office workers may also come into contact with KUDE-2 under normal circumstances during the routine replacement of spent printer cartridges or clearing paper jams. The design of the cartridge and normal installation processes should be such that contact with the notified chemical is minimal during replacement. Exposure will be minimised in these workers also by the low level of KUDE-2 (<5%) present in the ink cartridges.

Inhalation exposure to KUDE-2 is not expected due to the low vapour pressure and low level of aerosol formation during the printing process.

Despite low level of KUDE-2 in the ink, levels are above those for which a hazardous classification for the ink, on the basis of skin sensitisation, is warranted. Prolonged or repeated dermal exposure to the ink containing the notified chemical may cause allergic sensitisation. Dermal or ocular exposure may also cause local irritation. Therefore, service personnel and office workers should wear impervious gloves when contact with ink contaminated internal printer components is likely during printer servicing, when replacing spent or damaged printer cartridges or clearing paper jams.

Exposure to KUDE-2 is not expected to occur once the ink containing the chemical is bound to paper and so the health risk for workers handling printed paper would be assessed as low.

Transport and storage workers will only be exposed to KUDE-2 in the event of an accident or damage to packaging. Despite the significant toxicological profile of the notified chemical, the occupational health risk to these workers is negligible considering the low quantities (<5%) in ink jet printer cartridges and the low possibility of exposure.

Public Health

The risk to public health is expected to be low since exposures are expected to be intermittent, of short duration and involve only small amounts of ink containing a low concentration of the notified chemical.

13. RECOMMENDATIONS

Regulatory controls

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

  - R2 – Risk of explosion by shock, friction, fire or other sources of ignition;
  - R41 – Risk of serious damage to eyes;
  - R43 – May cause sensitisation by skin contact;
  - R48/22 – Harmful: danger of serious damage to health by prolonged exposure if swallowed;
  - R62 – Possible risk of impaired fertility.

- Use the following risk phrases for Ink Cartridge T026 containing the notified chemical:

  – ≥5% - <10%: R36, R62;
  – ≥10%: R41, R48/22, R62

Control Measures

Occupational Health and Safety

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical in the product Ink Cartridge T026:

  – Wear impervious gloves when servicing printers, when replacing spent or damaged printer cartridges or clearing paper jams where contact with ink residual is likely.

  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.

Storage

- The following precautions should be taken regarding storage of the notified chemical:

  – Keep containers tightly closed;
  – Keep in a cool, well ventilated place;
  – Avoid exposure to heat, sources of ignition and direct sunlight.

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(2) of the Act:
  - if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

14. MATERIAL SAFETY DATA SHEET

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

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

15. REFERENCES

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SafePharm (1995b) [Notified chemical]: (Lot Number: A013624): Determination of General Physico-chemical Properties. SPL Project Number: 370/155. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1995c) [Notified chemical]: Assessment of Ready Biodegradation; Closed Bottle Test. SPL Project Number: 370/174. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1995d) [Notified chemical]: Acute Toxicity to Rainbow Trout (*Oncorhynus mykiss*). SPL Project Number: 370/166. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1995e) [Notified chemical]: Acute Toxicity to *Daphnia Magna*. SPL Project Number: 370/167. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1995f) [Notified chemical]: Algal Inhibition Test. SPL Project Number: 370/168. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1995g) [Notified chemical]: Assessment of the Inhibitory Effects on the Respiration of Activated Sewage Sludge. SPL Project Number: 370/170. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

SafePharm (1996) [Notified chemical]: (Lot Number: A013624): Determination of Soil Adsorption Coefficient. SPL Project Number: 370/196. Safepharm Laboratories Limited, Derby, UK (Unpublished report provided by the notifier).

Attachment 1

The Draize Scale (Draize, 1959) 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 (Draize *et al*., 1944) 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

Draize, J. H., Woodward, G., Calvery, H. O. (1944) Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes, J. Pharmacol. Exp. Ther. 82 : 377-390.

Draize J. H. (1959) Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. Association of Food and Drug Officials of the US, 49 : 2-56.