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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

2-Naphthalenesulfonic acid, 7-amino-4-hydroxy-, coupled with diazotized 2-[(4-aminophenyl)sulfonyl]ethyl hydrogen sulfate and diazotized 2-amino-5-[[2-(sulfooxy)ethyl]sulfonyl]benzenesulfonic acid, potassium sodium salts

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NICNAS

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1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
Ciba Specialty Chemicals Pty Ltd (ABN 97 005 061 469)
235 Settlement Rd
Thomastown, VIC 3074

NOTIFICATION CATEGORY
Limited-small volume: Chemical other than polymer, (1 tonne or less per year).

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication: Spectral data, Methods of detection and determination, Purity, Identity of impurities, Identity/% weight of additives/adjuvants, Manufacture/import volume, Specific use details, Number and identity of sites of use.

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
No variation to the schedule of data requirements is claimed.

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
CEC/482, CEC/654

NOTIFICATION IN OTHER COUNTRIES
EU – 1999
KECI(Korea) - Gazette number 99-3-1270
IECSC(China) – 2003

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
2-Naphthalenesulfonic acid, 7-amino-4-hydroxy-, coupled with diazotized 2-[(4-aminophenyl)sulfonyl]ethyl hydrogen sulfate and diazotized 2-amino-5-[[2-(sulfooxy)ethyl]sulfonyl]benzenesulfonic acid, potassium sodium salts

OTHER NAME(S)
7-Amino-4-hydroxy-2-naphthalenesulfonic acid coupled with diazotized 2-[(4-aminophenyl)sulfonyl]ethyl hydrogen sulfate and diazotized 2-amino-5-[[2-(sulfooxy)ethyl]sulfonyl]benzenesulfonic acid, potassium sodium salts
Scarlet DER 8107
C.I. Reactive Brown 049
Reactive Orange DER 8068
FAT 40’571/A
FAT 40571/A

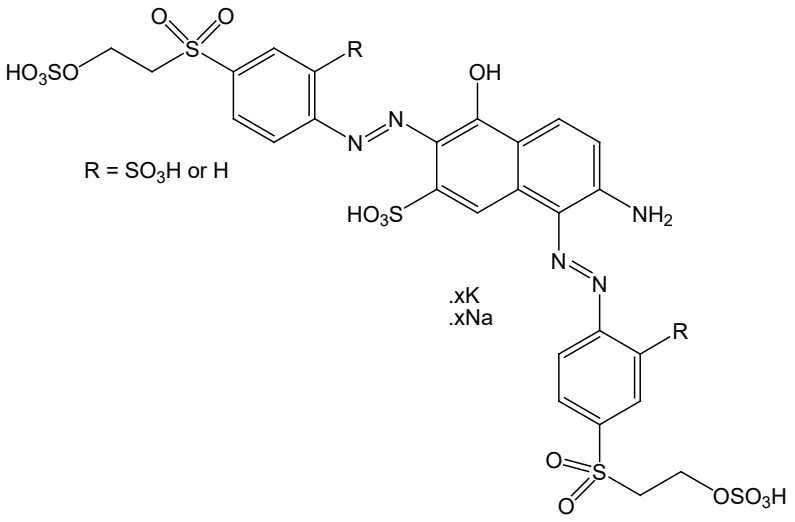
MARKETING NAME(S)
Cibacron Black C-NN HC (contains 10-30% notified chemical)

CAS NUMBER
214362-06-8

MOLECULAR FORMULA

$C_{26}H_{25}N_5O_{19}S_6.xK.xNa$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
903.89

SPECTRAL DATA

METHOD UV/Visible absorption spectra, Infrared spectra, ^{1}H-NMR spectra
Remarks Reference spectra were provided.

3. COMPOSITION

DEGREE OF PURITY
30-60%

HAZARDOUS IMPURITIES/RESIDUAL MONOMERS
The notified chemical is a complex reaction mixture with a range of impurities, some of which may be hazardous.

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Imported by sea as a component of Cibacron Black C-NN HC in 25 kg polyethylene-lined fibreboard containers.

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

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

USE
Component of textile dye used in the cold pad-batch method.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, transport and storage

PORT OF ENTRY

Melbourne.

TRANSPORTATION AND PACKAGING

The product Cibacron Black C-NN HC (containing 10-30% notified chemical) will be imported in polyethylene lined 25 kg fibreboard boxes, and transported to a warehouse. The product will be shipped to the customer's dyehouses without repackaging.

5.2. Operation description

At dyehouses in Victoria and NSW, the dye is dissolved into 10 times the weight of water. The dye is mixed with an alkali solution and dyeing occurs by passing the fabric through a pad mangle. The notified chemical is present at <1% in the final textile dye solution. Following fixation, the fabric is washed free of unfixed dye in wash off baths, and dried by hydroextraction, followed by heating to 120-140°C. Products which may be dyed include domestic textiles used for apparel, sheeting and other uses.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration*	*Exposure Frequency*
Transport drivers	1-3	30-60 mins/day	50-100 days/year
Warehouse operators	4-5	20 mins/day	100-120 days/year
Batch area operators	5-10	20 mins/day	180-240 days/year
Dye machine operators	5-10	60 mins/day	180-240 days/year

Exposure Details

Transport and warehouse workers would only be exposed to the notified chemical is the event of a spill or leak.

Workers may be exposed by inhalation/ingestion or by skin or eye contact to the product containing 10-30% notified chemical while weighing out the dye and adding it to solution. These workers will wear PPE such as gloves, overalls, goggles and a dust mask, and local extraction and general ventilation are available. Inhalation exposure and any associated ingestion would be reduced by the non-dusting form of the product containing the notified chemical.

The dyeing process is mainly automated following weighing and dissolving of the dye (containing <1% notified chemical), with the cloth driven by mechanical rollers. The system is mainly enclosed to prevent splashes and spills. Manual handling of wet cloth will occur during transport to the wash off batch on a pin chain. However the cloth will be wrapped in plastic film and thus exposure is unlikely. Dermal and possibly ocular exposure to the dilute solution may occur during some of these steps of the process. The chemical species present will change as the dye is added to the alkaline solution, as the β-sulfatoethyl-sulfonyl groups are converted to vinyl sulfone groups. The majority of residual unbound vinyl sulfone is then hydrolysed to β-hydroxyethylsulfone (USEPA 2002).

During washing and drying, the moist cloth is handled by the operator when wrapping the cloth in plastic and transferring for the hydroextraction after washing, and in starting the drying process by leading the cloth onto the pin chain. Some dermal exposure to the dilute solution is possible at these stages.

Cleaning and maintenance is performed by the machine operators. This involves flushing the holding and mixing tanks with water. During this process, workers will wear an organic vapour cartridge, gloves, safety goggles and overalls to minimise exposure.

5.4. Release

RELEASE OF CHEMICAL AT SITE

No manufacture or reprocessing of the notified substance will take place. Therefore, there will be no environmental exposure associated with this process in Australia.

Release to the environment may occur in the unlikely event of an accident during transport or storage.

RELEASE OF CHEMICAL FROM USE

Nearly all of the dye containing the notified chemical will be removed from the import container liners by shaking. Less than 1 kg of the chemical per annum will remain as residue. Given the potential for recovery and reuse and the high unit cost of the dyestuff the waste due to spills is expected by the notifier to be less than 5 kg per annum. Dissolution of the dye takes place in an enclosed vat and the dye is pumped through a closed system to the dyeing machine, therefore, release of the chemical is not expected at this stage.

The dye will be used to colour cellulosic textiles by Cold-Pad Batch method. Fixation is performed at 20-30ºC with the fixation rate expected to be 85%, at least. The notified chemical adsorbed to the fabric with the dye will not be released to the environment. The rinsate, generated via fabric rinsing, contains up to 15% of the import volume of the notified chemical. This will represent a major route of environmental exposure (up to 150 kg of notified chemical per annum based on the maximum import volume). The rinsate will be discharged to the dyehouse effluent system, where cationic flocculation will be used to remove the anionic dyestuff. The treated effluent containing minor traces of the notified chemical will be disposed of to the sewer, while the sludge/solids will be disposed of to landfill.

The dye will be used in a small number of dyehouses (including some country dyehouses).

5.5. Disposal

Any solid wastes generated in the dyehouses, including container residues, will either go to landfill or be incinerated. Incineration of the notified chemical will produce water, metal salts and oxides of carbon, nitrogen and sulphur. Incineration is the preferred method of disposal due to the ready water solubility of the notified chemical.

Once bound to the fabric the notified polymer is expected to remain fixed throughout the useful life of the fabric. Hence it will share the fate of fabric and be either be disposed of in landfill or incinerated.

5.6. Public exposure

The product containing the notified chemical will be available only to industrial end users. The dyed cloth may be used for apparel, sheeting and other uses. The notified chemical is covalently linked to the cloth after the dyeing process, and there is no evidence of bleeding of the dye from dyed cloth. Public exposure to the notified chemical is not likely to be significant.

6. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20ºC and 101.3 kPa Brown-black powder.

Melting Point Could not be determined.

METHOD	OECD TG 102 Melting Point/Melting Range. EC Directive 92/69/EEC A.1 Melting/Freezing Temperature.
Remarks	No melting point detected below 400°C. At ≥320°C the test substance foams. Boiling point calculated using Meissner's method to be about 735°C.
TEST FACILITY	Ciba (1998a)

Density 1810 kg/m^3 at 20.2°C

METHOD	OECD TG 109 Density of Liquids and Solids. EC Directive 92/69/EEC A.3 Relative Density.
Remarks	Test system: gas comparison pycnometer.
TEST FACILITY	RCC (1998a)

Vapour Pressure Not determined.

METHOD	OECD TG 104 Vapour Pressure. EC Directive 92/69/EEC A.4 Vapour Pressure.

Remarks Calculated using the Modified Watson Correlation as 1.22×10^{-23} kPa at 25ºC
TEST FACILITY RCC (1998b)

Surface Tension 68.4 mN/m at 20.0°C

METHOD OECD TG 115 Surface Tension of Aqueous Solutions.
EC Directive 92/69/EEC A.5 Surface Tension.
Remarks Determined using a ring tensiometer.
Concentration: about 0.1%
Based on the criteria outlined in the OECD Guideline, the notified chemical should not be regarded as a surface active substance.
TEST FACILITY RCC (1998c)

Water Solubility >277 g/L at 20ºC

METHOD OECD TG 105 Water Solubility.
EC Directive 92/69/EEC A.6 Water Solubility.
Remarks In a preliminary test, the water solubility was determined by adding 0.1 g of the test material to a graduated test tube and adding increasing volumes of water. When the ratio of test material to water was 0.1 g to 0.1 mL of water undissolved material was observed. When 0.5 mL of water had been added it was not possible to observe test substance due to the highly coloured solution. When greater than 1 mL of water were added all the test material was observed to have dissolved. In the definitive test, ~2.0g of test material was added to 6 mL of water and shaken at 30°C for up to 72 h prior to equilibrating at 20°C for 24 h. After centrifugation the solutions were diluted and the concentration measured spectrophotometrically. The test substance is readily soluble (Mensink et al. 1995).
TEST FACILITY Ciba (1998b)

Hydrolysis as a Function of pH

METHOD OECD TG 111 Hydrolysis as a Function of pH.
EC Directive 92/69/EEC C.7 Degradation: Abiotic Degradation: Hydrolysis as a Function of pH.

pH	*T (°C)*	*$t_{½}$*
4	25ºC	>1 year
7	25ºC	2.7 days
9	25ºC	<1 day

Remarks No further testing was done at pH 4 as the test substance was stable at 50°C and at pH 9 where it was found to be very unstable with more than 50% hydrolysed after 2.4 h. In main test the hydrolysis of the test material was investigated at pH 7 at temperatures of 25 and 50°C. Both tests yielded a half-life of 64.3 h either directly or when extrapolated back to 25°C. Hence, the test material is hydrolytically stable under acidic conditions and hydrolysed in neutral and basic solutions
TEST FACILITY Ciba (1998c)

Partition Coefficient (n-octanol/water) log Pow ≤ -4.5

METHOD Ratio of octanol solubility and water solubility.
Remarks The solubility of the test material in n-octanol was determined to be 10.99 µg/L by mixing 0.6-1.0 g of the test material with 25 mL of n-octanol and analyzing the supernatant via HPLC after 24 h stirring. The water solubility was taken as 325.19 g/L (after adding 9 g of test material to 25 mL of water for 24 h and centrifuging and analysis using HPLC).
TEST FACILITY RCC (1998d)

Adsorption/Desorption – screening test
log K_{oc} = 2.82 (Speyer, loamy sand)
= 2.63 (Sissein, sandy loam)

= 2.62 (Les Barges, silt loam)

METHOD OECD TG 106 Adsorption - Desorption
Determined according to test guidelines using a procedure that measures the decrease in concentration when aqueous solutions of a chemical are in contact under laboratory conditions with three different soils common in the agricultural regions in western Europe.

Soil Type	*Organic Carbon Content (g/100 g dry soil)*	*pH*	*Koc (mL/g)*
Speyer, loamy sand	2.29	6.0	666
Sissein, sandy loam	1.57	7.1	433
Les Barges, silt loam	3.80	6.9	420

Remarks Adsorption and desorption were determined at an initial concentration of 4.95-5.02 mg/L using 0.01 M $CaCl_2$ solution with 16 hours shaking for both the adsorption and desorption (2 cycles) phases. The supernatants were analysed by UV/VIS. The notified chemical mixture can be considered have medium to high mobility in the Sissien and Les Barges soils and low to medium mobility in the Speyer soil according to McCall *et al.* (1981).
TEST FACILITY RCC (1981)

Dissociation Constant pKa (approximate)
7.2, 2.0, <0, <<-7, -7.13, -7.4

Remarks The pKa values were estimated using Taft and Hammet correlations. The notified chemical will be dissociated over the environmental pH range.
TEST FACILITY RCC (1998e)

Particle Size MMD: 23µM
<10 µM (respirable): <2.4%

METHOD OECD TG 110 Particle Size Distribution/Fibre Length and Diameter Distributions.

Range (µm)	*Mass (%)*
<5	0.00
5-8	0.24
8-15	6.27
15-32	93.8
32-40	0.44
>40	1.16

Remarks Results obtained by sieve analysis. Note that products containing the notified chemical are imported as non-dusting granules.
TEST FACILITY RCC (1998f)

Flash Point Not determined

Flammability Limits Not “highly flammable”

METHOD EC Directive 92/69/EEC A.10 Flammability (Solids).
Remarks The notified chemical carbonised.
TEST FACILITY RCC (1998f)

Autoignition Temperature Does not autoignite.

METHOD 92/69/EEC A.15 Auto-Ignition Temperature (Liquids and Gases).
Remarks No relevant exothermic reaction observed at up to 400°C.
TEST FACILITY RCC (1998g)

Explosive Properties Evaluated as non-explosive.

METHOD	EC Directive 92/69/EEC A.14 Explosive Properties.
Remarks	The test substance was negative in tests of thermal, shock and frictional explosivity.
TEST FACILITY	ISS (1998)

Oxidizing Properties Stable.

METHOD	EC Directive 92/69/EEC A.17 Oxidizing Properties (Solids).
Remarks	The oxygen balance is negative, and the notified chemical is therefore estimated to be non-oxidising.
TEST FACILITY	RCC (1998h)

Reactivity Expected to be stable under normal environmental conditions.

7. TOXICOLOGICAL INVESTIGATIONS

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral LD50 >2000 mg/kg bw	low toxicity
Rat, acute dermal LD50 >2000 mg/kg bw	low toxicity
Rat, acute inhalation	Not provided
Rabbit, skin irritation	Slightly Irritating
Rabbit, eye irritation	severely irritating (based on persistent staining)
Guinea pig, skin sensitisation – adjuvant test	no evidence of sensitisation
Rat, repeat dose oral toxicity – 90 days.	NOAEL 200 mg/kg bw/day
Genotoxicity – bacterial reverse mutation	non mutagenic
Genotoxicity – in vitro mammalian chromosome aberration test.	genotoxic
Genotoxicity – in vivo mouse micronucleus test	non genotoxic

7.1. Acute toxicity – oral

TEST SUBSTANCE — Notified chemical

METHOD — OECD TG 401 Acute Oral Toxicity.
EC Directive 92/69/EEC B.1 Acute Toxicity (Oral).

Species/Strain	Rat / HanIbm: WIST (SPF)
Vehicle	Water
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	0

LD50	>2000 mg/kg bw
Signs of Toxicity	None.
Effects in Organs	None.
Remarks - Results	None.

CONCLUSION — The notified chemical is of low toxicity via the oral route.

TEST FACILITY — RCC (1998i)

7.2. Acute toxicity – dermal

TEST SUBSTANCE — Notified chemical

METHOD — OECD TG 402 Acute Dermal Toxicity.
EC Directive 92/69/EEC B.3 Acute Toxicity (Dermal).

Species/Strain	Rat / HanIbm: WIST (SPF)
Vehicle	Water
Type of dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	2000	0

LD50 — >2000 mg/kg bw

Signs of Toxicity - Local	Red staining of the skin occurred in all animals, and did not resolve during the test (15 days) in 3 males and 1 female. Delayed crusts were seen on the test site of 3 males and 4 females and were distributed between test days 3 and 15. Mild-moderate patchy erythema developed on day 4 in one male and did not resolve over the test period.
Signs of Toxicity - Systemic	Three female animals had a decrease in body weight during the first week.
Effects in Organs	None.
Remarks - Results	The decrease in body weight may have been an effect of the dressing rather than the notified chemical. Body weights were within the range of physiological variability known for rats of this strain and age. Some dermal irritation was seen. The red coloration on the skin was produced by the test substance, described as a dark red/brown powder. Therefore the effect is not regarded as a direct inflammatory response. However an inflammatory response was delayed to later period by developing crusts in most of the male and female animals after a 24 hour semi occlusive application. The crusts were transient in 2 males and persisting up to the end of the study in on male and in four females. The test substance is considered as irritant after a 24 hour semi occlusive application.

CONCLUSION	The notified chemical is of low toxicity via the dermal route.
TEST FACILITY	RCC (1998j)

7.3. Acute toxicity – inhalation

No test data provided.

7.4. Irritation – skin

TEST SUBSTANCE	Notified chemical
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	3
Vehicle	Test substance was moistened with water before application.
Observation Period	72 hours.
Type of Dressing	Semi-occlusive.
Remarks - Method	No significant protocol deviations.

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	0	0	0	-	0
Oedema	0	0	0	0	-	0

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

Remarks - Results	Red staining of the treated skin by the test article was observed. Erythema could not be assessed due to staining at the 1-hour and 24-hour observations. The staining persisted in all animals to the end of the observation period (72 hours).

CONCLUSION The notified chemical is slightly irritating to the skin.

TEST FACILITY RCC (1998k)

7.5. Irritation – eye

TEST SUBSTANCE Notified chemical

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 3
Observation Period 21 days
Remarks - Method No significant protocol deviations.

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 days	0
Conjunctiva: chemosis	0	0	0	1	1 hour	0
Conjunctiva: discharge	0	0	0	1	1 hour	0
Corneal opacity	0	0	0	0	-	0
Iridial inflammation	0	0	0	0	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.
[#]Could not be measured due to staining.

Remarks - Results At the end of the observation period (21 days), persistent orange staining was observed in the sclera and conjunctivae of all animals.

CONCLUSION Based on this study, the notified chemical causes irreversible colouration of the eyes, which is classified as a severe ocular lesion.

TEST FACILITY RCC (1998l)

7.6. Skin sensitisation

TEST SUBSTANCE Notified chemical

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

Species/Strain Guinea pig / HsdPoc:DH SPF
PRELIMINARY STUDY Maximum Non-irritating Concentration:
intradermal: None. Slight oedema was observed at 5, 3, and 1%. Erythema could not be evaluated due to red staining by the notified chemical.
topical: 10%. Slight erythema was observed in one guinea pig 24 hours after exposure to 15% notified chemical.
MAIN STUDY
Number of Animals Test Group: 10 Control Group: 5
INDUCTION PHASE Induction Concentration:
intradermal: 5% (day 1)
topical: 50% (day 8)
Signs of Irritation After topical application, erythema could not be measured. No test animals exhibited oedema.
CHALLENGE PHASE

1st challenge	topical: 10% (day 22)
Remarks - Method	No significant protocol deviations.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after:*	
		24 h	*48 h*
Test Group	10%	0	0
Control Group	10%	0	0

Remarks - Results None.

CONCLUSION There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.

TEST FACILITY RCC (1998m)

7.7. Repeat dose toxicity

TEST SUBSTANCE Notified chemical

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 / HanIbm:WIST (SPF)
Route of Administration	Oral – gavage
Exposure Information	Total exposure days: 28 days Dose regimen: 7 days per week
Vehicle	Water
Remarks - Method	None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	5/sex	0	0
II (low dose)	5/sex	50	0
III (mid dose)	5/sex	200	0
IV (high dose)	5/sex	1000	0
V (control recovery)	5/sex	0	0
VI (high dose recovery)	5/sex	1000	0

Mortality and Time to Death
All animals survived the study period.

Clinical Observations
In animals receiving 1000 mg/kg bw/day, black faeces were recorded from day 4-28 and during days 29-32 for the recovery group. In animals receiving 200 mg/kg bw/day, dark faeces were recorded from day 7-28.

No other significant differences were observed.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis
The following haematological changes were not considered toxicologically relevant:

- Total reticulocytes increased in high-dose males (+18%, $p<0.05$). A significant change occurred in males only, although high-dose females had a non-significant increase. This may reflect very mild anemia.
- White blood cell count increased in high dose males (+25%, $p<0.05$) and decreased white blood cells in high-dose recovery males (-30%, $p<0.05$). These contradictory changes occurred in males only.
- Lymphocyte count increased in high dose males (+25%, $p<0.05$) and decreased lymphocytes in high-dose recovery males (-33%, $p<0.05$). These contradictory changes occurred in males only.

- Methemoglobin levels increased in high dose males (+133%, $p<0.05$). Change occurred in males only, and the control group had an unusually low value.
- Absolute segmented neutrophil count increased in low- and mid-dose females (+100%, $p<0.05$). Change occurred in females only, and the control group had an unusually low value.

- Other haematological changes did not indicate any dose-response relationship.

The following biochemical changes were not considered toxicologically relevant:
- Total bilirubin decreased in high-dose recovery group (-42%, $p<0.01$). There was no significant change during the main test.
- Total cholesterol decreased in high-dose males (-15%, $p<0.05$). This change occurred in males only, and there was no clear dose-response relationship.
- Gamma-glutamyl transferase decreased in high-dose males (-50%, $p<0.01$). This change occurred in males only, and there was no clear dose-response relationship.
- Total albumin increased in mid-dose (+6%, $p<0.05$) and high-dose (+7%, $p<0.01$) females. This change occurred in females only, there was no clear dose-response relationship, and there was less than 10% change.
- Total protein increased in high-dose (+5%, $p<0.05$) females. This change occurred in females only, there was no clear dose-response relationship, and there was less than 10% change.

- Other biochemical changes did not indicate any dose-response relationship.

Osmolarity of urine increased in high-dose males (+22%, $p<0.05$). This change occurred in males only and thus was not considered toxicologically relevant.

Effects in Organs

Increased kidney/body weight ratio was seen in mid-dose (+10%, $p<0.05$) and high-dose (+13%, $p<0.01$) males. In addition a slightly increased incidence and markedly increased severity of hyaline droplets was noted in the kidneys of high-dose males.

Reduced absolute liver weights were seen in low-dose (-16%, $p<0.01$) and high-dose (-13%, $p<0.05$) males. No significant differences were observed in females, no clear dose-response relationship was observed, and no microscopic changes were seen.

Other changes to organ weights did not have any dose-dependence or occurred during the recovery period only.

All macroscopic abnormalities were considered to be common findings in rats of this strain and age.

Moderate focal erosion of the nonglandular stomach, associated with moderate inflammation, slight squamous cell hyperplasia and moderate hyperkeratosis of the nonglandular stomach was noted in one female rat treated with 1000 mg/kg bw/day.

Minimal to slight interstitial fibrosis, associated with slight, multifocal alveolitis was noted in two females treated with 1000 mg/kg bw/day. In the rat with slight fibrosis, slight aggregations of brownish, pigment-laden alveolar macrophages were seen.

Remarks – Results

Black faeces were observed in groups receiving 1000 mg/kg bw/day, which cleared during the recovery period. Dark faeces were observed in animals receiving 200 mg/kg bw/day.

Changes to the kidneys were observed in males only. However there was a clear dose-response relationship to the increased kidney/body weight ratio in males receiving 200 and 1000 mg/kg bw/day. This was supported by microscopic changes to the kidneys (increased incidence and severity of hyaline droplets) observed in males receiving 1000 mg/kg bw/day. Kidney effects specific to male rats may not be relevant to humans.

Some microscopic findings were noted in the stomach and lung of females receiving 1000 mg/kg bw/day.

CONCLUSION

The No Observed Adverse Effect Level (NOAEL) was established as 200 mg/kg bw/day in this study, based on dose-dependant changes in the kidneys and microscopic changes in the stomach and lung at 1000 mg/kg bw/day.

TEST FACILITY RCC (1997n)

7.8. Genotoxicity – bacteria

TEST SUBSTANCE Notified chemical.

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure (test 1)
Pre incubation procedure (test 2)

Species/Strain	*S. typhimurium*: TA1535, TA1537, TA98, TA100 *E. coli*: WP2uvrA
Metabolic Activation System	Liver S9 fraction
Concentration Range in Main Test	a) With metabolic activation: 33.3-5000 µg/plate b) Without metabolic activation: 33.3-5000 µg/plate
Vehicle	Water.
Remarks - Method	No significant protocol deviations.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:* *Cytotoxicity in Preliminary Test*	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	None.	None.	None.	None.
Test 2	-	None.	None.	None.
Present				
Test 1	None.	None.	None.	None.
Test 2	-	5000 µg/plate (TA 90)	None.	None.

Remarks - Results Appropriate reference mutagens were used as positive controls, and showed a distinct increase of induced revertant colonies.

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

TEST FACILITY CCR (1998a)

7.9. Genotoxicity – in vitro

TEST SUBSTANCE Notified chemical

METHOD OECD TG 473 In vitro Mammalian Chromosome Aberration Test.
EC Directive 1992/69/EC B.10 Mutagenicity - In vitro Mammalian Chromosome Aberration Test.

Cell Type/Cell Line	V79 cells from Chinese hamster
Metabolic Activation System	Liver fraction S9
Vehicle	Water
Remarks - Method	A confirmatory assay was not performed. Dose levels were chosen on the basis of an initial toxicity test.

Metabolic Activation	*Test Substance Concentration (µg/mL)*	*Exposure Period*	*Harvest Time*

Absent			
Test 1	187.5, 375, 750, 1500*, 3000*, 4000* µg/mL	4 hours	18 hours
Present			
Test 1	25, 50, 100*, 200*, 300*, 400 µg/mL	4 hours	18 hours

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/mL) Resulting in:*			
	Cytotoxicity in Preliminary Test	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1	5000 µg/mL	4000 µg/mL	-	Yes (4000 µg/mL, p=0.001)
Present				
Test 1	312.5 µg/mL	300 µg/mL	-	None.

Remarks - Results

In the absence of metabolic activation test the test article induced a significant increase in the number of cells carrying structural chromosome aberrations after treatment with 4000 µg/mL.

This increase was above the historical control range and was of the same magnitude as the increase in the positive control substance (800 µg/mL EMS). No increase was seen at 1500 or 3000 µg/mL.

The increased aberration frequencies caused by the test substance were observed only in the presence of strong toxicity indicated by reduced cell numbers.

No increase in chromosome aberrations was seen in the presence of metabolic activation. In addition, no increase in the frequency of polyploid metaphases was found.

CONCLUSION

The notified chemical was clastogenic to Chinese hamster V79 cells treated in vitro under the conditions of the test.

TEST FACILITY

CCR (1998b)

7.10. Genotoxicity – in vivo

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 474 Mammalian Erythrocyte Micronucleus Test.
EC Directive 1192/69/EC L.383 Mutagenicity - Mammalian Erythrocyte Micronucleus Test.

Species/Strain: Mouse / NMRI
Route of Administration: Oral – gavage
Vehicle: Water.
Remarks - Method: No significant protocol deviations

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Sacrifice Time hours*
I (vehicle control)	6/sex	0	24 hours
II (low dose)	6/sex	200	24 hours
III (mid dose)	6/sex	670	24 hours
IVa (high dose)	6/sex	2000	24 hours
IVb (high dose)	6/sex	2000	48 hours
V (positive control, CP)	6/sex	40	24 hours

CP=cyclophosphamide.

RESULTS	
Doses Producing Toxicity	In a pre-experiment for toxicity there were some signs of toxicity at 2000 mg/kg bw. This included reduction of spontaneous activity (persisting for 48 hours in 2/4 animals), eyelid closure and apathy.
Genotoxic Effects	The test article did not induce micronuclei as compared to corresponding vehicle controls.
Remarks - Results	The PCE/NCE ratios did not change significantly in treated animals. Therefore there is no evidence that the notified chemical reached the bone marrow. However the clinical signs observed at 2000 mg/kg bw demonstrate systemic effects. The positive control and showed a statistically significant increase of induced micronucleus frequency.
CONCLUSION	The notified chemical was not clastogenic under the conditions of this in vivo mouse micronucleus test.
TEST FACILITY	CCR (1998c)

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 A Ready Biodegradability: DOC Die-Away Test.
Inoculum	Polyvalent bacteria from aeration tank of domestic STP.
Exposure Period	28 days
Auxiliary Solvent	Unknown
Analytical Monitoring	DOC (TOC/DOC analyser Shimadzu TOC 500)
Remarks - Method	The test concentration (37.5 mg/L DOC) was made by dilution of the test stock solution (6.01 g/L DOC). The bacteria loading was 26 mg/L suspended solids. Reference substance – D(+) – Glucose (37.8 mg/L DOC) Abiotic and toxicity controls were also run. Indirect lighting and room temperature (20-22ºC) were maintained throughout the study.

RESULTS

Day	*Test substance % Degradation*	*D(+) – Glucose % Degradation*	*Toxicity control % Degradation*	*Abiotic control DOC mg/L*
0	-	-	-	39.4
1	2	51	30	-
3	6	95	50	-
7	5	96	50	-
10	6	98	50	-
14	6	98	50	-
21	6	99	51	-
28	6	99	51	36.1

Remarks - Results	The inhibition control attained >35% degradation after 14 days confirming that the test substance was not inhibitory to activated sludge bacteria under the test conditions and that the degradation of reference substance was not inhibited by the presence of the test substance. Degradation of the reference substance (>70% by day 14) confirmed the suitability of the innoculum and validity of test conditions.
CONCLUSION	Under the study conditions, the notified chemical cannot be considered to be readily biodegradable since the biodegradation level did not exceed 70% (DOC).
TEST FACILITY	Novartis (1998a)

8.2E. Inherent biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 302B Zahn-Wellens Test and Commission Directive 87/302/EEC Part C.
Inoculum	Activated sludge from a communal sewage treatment plant
Exposure Period	28 days
Auxiliary Solvent	
Analytical Monitoring	Dissolved organic carbon (DOC)

Remarks – Method

The test concentration (151 mg/L DOC) was made by dilution of the test stock solution (302 mg/L DOC).
The sludge loading was 0.46 g/L.
Reference substance – Diethylene glycol (152 mg/L DOC)
Continuous aeration ((7.1-8.6 mg/L) and agitation, indirect lighting, pH (7-7.4) and room temperature (20.6-22.3^{o}C) were maintained throughout the study.

RESULTS

Day	*Test substance % Degradation*	*Diethylene glycol % Degradation*
1	2	2
5	2	29
8	2	99
9	-	100
13	2	-
16	1	-
28	4	-

Remarks – Results

Amount of test substance removed due to adsorption is 0% (determined by the difference between DOC values at the start and after 3 hours).

Reference substance degradation (>70% after 14 days), thus indicating the viability of the culture and test conditions.

CONCLUSION

Under the study conditions, the notified chemical cannot be considered to be inherently biodegradable as the biodegradation level did not exceed 20%.

TEST FACILITY

Novartis (1998b)

8.1.2. Bioaccumulation

No bioaccumulation data were provided. However, due to its ionic nature and high water solubility it is not expected to bioaccumulate.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

TEST SUBSTANCE

Notified chemical

METHOD

OECD TG 203 Fish, Acute Toxicity Test – static conditions.
EC Directive 92/69/EEC C.1 Acute Toxicity for Fish - static conditions.

Species	Zebra fish (*Brachydanio rerio*)
Exposure Period	96 hours
Auxiliary Solvent	None
Water Hardness	142 mg $CaCO_3$/L
Analytical Monitoring	Spectrophotometric

Remarks – Method

Based on the results of a range finding test it was determined to use only one test concentration - 100 mg/L (nominal). The test concentration was made by dilution from test stock solution. A measured amount of test substance was homogenized in water by ultrasonication (2 mins) then made up to 3000 mL to form the stock solution. The concentration and stability of the test solution was determined at 0, 48 and 96 hours.

A photoperiod of 14 hours light and 10 hours dark was maintained. The

environmental test conditions during the study were acceptable: dissolved oxygen (95-98%), pH (7.9-8.4), and temperature (21.1-21.4ºC).

RESULTS

Concentration mg/L		*Number of Fish*	*Mortality (number)*			
Nominal	*Actual*		*24 h*	*48 h*	*72 h*	*96 h*
0	-	7	0	0	0	0
100	98.1-96.3%	7	0	0	0	0

LC50	>100 mg/L (nominal) at 96 hours.
NOEC	100 mg/L (nominal) at 96 hours.
Remarks – Results	No abnormal behaviour was observed during the study.

CONCLUSION — Under the study conditions, the notified chemical is very slightly toxic to fish (Mensink (1995)).

TEST FACILITY — Novartis (1998c)

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE — Notified chemical

METHOD — OECD TG 202 Daphnia sp. Acute Immobilisation Test and Reproduction Test – static conditions.
EC Directive 92/69/EEC C.2 Acute Toxicity for Daphnia - static conditions.

Species	*Daphnia magna*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	265 mg $CaCO_3$/L
Analytical Monitoring	Spectrophotometry
Remarks - Method	Based on the results of a range finding test it was determined to use the test concentrations of 4.3, 9.4, 21, 45 and 100 mg/L (nominal). Test concentrations were made by dilution from test stock solution. A measured amount of test substance mixed with test medium and made up to a final volume of 1000 mL to form the stock solution - no homogenization was needed. The concentration and stability of the test solution was determined at 0 and 48 hours in the 100 mg/L test concentration only. A photoperiod of 14 hours light and 10 hours dark was maintained. The environmental test conditions during the study were acceptable: dissolved oxygen (95-96%), pH (7.6-8.0), and temperature (19-21ºC).

RESULTS

Concentration mg/L		*Number of D. magna*	*% Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	-	20	0	5
4.3	-	20	0	0
9.4	-	20	0	0
21	-	20	0	0
45	-	20	0	0
100	98.2-97.9%	20	0	0

LC50	>100 mg/L 48 hours
NOEC	100 mg/L at 48 hours
Remarks - Results	No abnormal behaviour was observed during the study.

CONCLUSION	Under the study conditions, the notified chemical is very slightly toxic to daphnia (Mensink *et al.* (1995)).
TEST FACILITY	Novartis (1998d)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 201 Alga, Growth Inhibition Test. EC Directive 92/69/EEC C.3 Algal Inhibition Test.
Species	*Scenedesmus subspicatus*
Exposure Period	72 hours
Concentration Range	Nominal: 4.6, 10, 22 and 100 mg/L
Auxiliary Solvent	None
Water Hardness	24 mg $CaCO_3$/L
Analytical Monitoring	
Remarks - Method	A stock solution was prepared initially to the highest test concentration by dissolving a measured amount of the test substance in water, the other test concentrations were made by dilution of aliquots of the stock solution. All test media were coloured by the test substance. The concentration and stability of the test solution was determined at 0 and 72 hours – at the start of the study 100-105% while at the end it was 69-79%. The cell density in the test vessels was $10X10^4$ cells/mL. Since the test media was coloured, the study was done in two parts. In Part A the glass dish covering the flask contained only purified water, thereby any toxicity was due to the test substance and reduced light due to the colouring of the media. In Part B, the glass dish contained the colour test media with the test substance at the same concentration but no algae, thereby determining the inhibition effect of the light quality. Each test concentration was conducted in triplicate, while there were 6 control replicates. The environmental conditions during the study were within acceptable limits: pH (7.9-8.8) and temperature (22-23°C).

RESULTS

Part A

Biomass		*Growth*	
E_bC50 *mg/L at 72 h*	*NOE_bC* *mg/L*	*E_rC50* *mg/L at 72 h*	*NOE_rC* *mg/L*
18 (15-20)	4.6	93 (86-101)	4.6

Part B

Biomass		*Growth*	
E_bC50 *mg/L at 72 h*	*NOE_bC* *mg/L*	*E_rC50* *mg/L at 72 h*	*NOE_rC* *mg/L*
23 (10-52)		147[#] (81-501)	

[#] Caution should be taken with this value as the inhibition of μ was lower than 50% up to the highest concentration.

Remarks - Results	NOEC was determined using Dunnett's multicomparison test to compare the percentage inhibition in the test group with that in the control cultures. The comparison of the growth rates in the two parts indicates that the

	growth inhibition is due to the the light absorption by the coloured test solutions. Thus concluding that the toxic effect of the test substance would occur at levels at or above 100 mg/L
CONCLUSION	Under the study conditions, the notified chemical is very slightly toxic to algae (Mensink *et al.* (1995)).
TEST FACILITY	RCC (1999)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 209 Activated Sludge, Respiration Inhibition Test. EC Directive 88/302/EEC C.11 Biodegradation: Activated Sludge Respiration Inhibition Test
Inoculum	Activated sludge from a communal sewage treatment plant
Exposure Period	3 hours
Concentration Range	Nominal: 25.6, 64, 160, 400 and 1000 mg/L
Remarks – Method	Test concentrations were made by dilution from test stock solution. Reference substance – 3,5-dichlorophenol (3.2, 10 and 32 mg/L). Sludge loading was 1.56 g/L (dry weight) Continuous aeration, pH (7.8-8.1) and room temperature (20.9-21.1^{o}C) were maintained throughout the study.
RESULTS	
IC50	>1000 mg/L
NOEC	1000 mg/L
Remarks – Results	IC50 of the reference substance was 10 mg/L, which is in the study validity criteria range of 5-30 mg/L.
CONCLUSION	Under the study conditions, the notified chemical is very slightly toxic to micro-organisms (Mensink *et al.* (1995)).
TEST FACILITY	Novartis (1998e)

8.3E. Chemical oxygen demand (COD)

TEST SUBSTANCE	Notified chemical
METHOD	DIN 38409 – H 41-1 (1980) Commission Directive 92/69/EEC Annex L 383 A, C6
Reaction Mixture	Potassium dichromate in a strong sulphuric acid medium with silver sulphate as a catalyst
Exposure Period	2 hours
Auxiliary Solvent	None
Analytical Monitoring	The residual potassium dichromate determined by titration with ferrous ammonium sulphate.
Remarks – Method	The reaction mixture was boiled with the test substance under reflux for 2 hours at 148 ± 3°C. A solution of Potassium hydrogenphthalate (at 0.17 g/L) was used as the reference item.
RESULTS	
Remarks – Results	The test was considered valid since the COD of the reference substance (194 mg O_2/L) was 198 mg O_2/L.
CONCLUSION	The COD of the test substance was 880 mg O_2/g.

TEST FACILITY	Novartis (1998f)

8.3F. Biochemical oxygen demand (BOD_5)

TEST SUBSTANCE	Notified chemical
METHOD	ISO 5815 Second Edition – 1989-08-01 – Static
Inoculum	Filtered seeding water from a communal wastewater treatment plant
Exposure Period	5 days
Auxiliary Solvent	None
Analytical Monitoring	DOC
Remarks – Method	The test substance was incubated in dark in completely filled and stoppered bottles at 19.9°C for 5 days. Eight concentrations from 6.2 to 792.1 mg/L were used. A mixture of D(+)-Glucose and L-Glutamic acid was used as the reference substance.
RESULTS	
Remarks – Results	The test was considered valid since the BOD_5 of the reference substance (183 mg O_2/L) was between 180 and 230 mg O_2/L.
CONCLUSION	The BOD_5 of the test substance was 0 mg O_2/g. This result supports the lack of ready and inherent biodegradation as reported in test results summarised under Section 8.1.
TEST FACILITY	Novartis (1998g)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

With a fixation rate of at least 85%, up to 15% of the imported volume of the notified chemical will enter the sewer in the rinsate from fabric rinsing following drying.. The high water solubility and low Kow value indicate that the test substance is not likely to adsorb to sludge. However, effluent flocculation by cationic polymer addition is expected to effectively precipitate the notified chemical. The solids containing the chemical would be disposed of through incineration or as chemical waste along with other solid waste (due to spills, leaks and container residues) from the dyehouse. Incineration is the preferred option because of the high water solubility and potential mobility of the material. Incineration of the sludge or waste containing the notified chemical will produce oxides of carbon and other main elements and metal salts in the ash.

If the dye containing the notified chemical is disposed of to landfill the residues may be mobile. Although the notified chemical cannot be considered as readily biodegradable it would degrade very slowly via biotic and abiotic processes. Disposal to landfill, if any, will be as chemical waste, therefore, the risk of leaching to the water table is significantly reduced. The fate of the dye and the notified chemical bound to the fabrics would be the same as that of the fabrics. The fabrics may be disposed of to landfill, where the notified chemical would remain inert.

The notified chemical released to the communal sewer via the dyehouse effluent discharge will be its major environmental exposure. The dye containing the notified chemical will be used in a small number of city and country dyehouses. However, based on the typical use of the dye expected per day, worst-case predicted environmental concentration (PEC) values are estimated for two dyehouses (one discharging into a large sewage treatment works and the other into a small sewage treatment works) assuming no partitioning to sludge within the sewage treatment works.

The dye will be used in a small number (maximum 5) of dyehouses and is expected to be used in three country dyehouses.

Process or Dilution Factor	City Dye House (High volume STP discharge)	Country Dye House (Low volume STP discharge)
Typical notified chemical use expected per day	4 kg	4 kg
Quantity in wash water (at a fixation rate of 85%)	0.60 kg	0.60 kg
Typical daily volume of dye wash-water effluent	400,000 L	400,000 L
Concentration in dye wash water	1.5 mg/L	1.5 mg/L
Typical daily volume of dye house wash-water effluent	2,900,000 L	2,900,000 L
Concentration in dye house effluent	0.21 mg/L	0.21 mg/L
Dilution factor in sewage treatment plant	1:100	1:10
Concentration in effluent from sewage treatment plant	2.1 µg/L	21 µg/L
Predicted environmental concentrations (PECs) in receiving waters		
Ocean (Dilution Factor 1:10)		
PEC	0.21 µg/L	2.1 µg/L
River (Dilution Factor 1:1)		
PEC	2.1 µg/L	21 µg/L

The potential for bioaccumulation is low due to the very high water solubility, large molecular weight and the low lipid solubility and log Kow of the notified chemical.

9.1.2. Environment – effects assessment

The results of the aquatic toxicity tests are listed below. No species had an endpoint below 100 mg/L

Organism	*Duration*	*End Point*	*mg/L*
Fish	96 h	LC_{50}	>100
Daphnia	48 h	EC_{50}	>100
Algae	0-72 h	E_bC_{50}	18
		E_rC_{50}	93

A predicted no effect concentration (PNEC - aquatic ecosystems) of 0.18 mg/L has been derived by dividing the end point of 18 mg/L by a worst-case scenario uncertainty (safety) factor of 100 (as toxicity data are available for three trophic levels).

9.1.3. Environment – risk characterisation

	Location	PEC* µg/L	PNEC µg/L	Risk Quotient (RQ)*
Dyehouse 1	Ocean outfall	0.21	180	0.0012
	Inland River	2.1	180	0.012
Dyehouse 2	Ocean outfall	2.1	180	0.012
	Inland River	21	180	0.12

* The worst-case PEC and the RQ values calculated assuming the notified chemical is not removed during the wastewater treatment at the dyehouses or the STP process.

The resulting risk quotient (RQ = PEC/PNEC) values for the aquatic environment, assuming that the chemical is not removed in the dyehouse treatment facility or at communal STP, are all below 1 for both freshwater and marine water, indicating no immediate concern to the aquatic compartment. A large part of the notified chemical can be expected to be removed by flocculation in the dyehouse treatment facility and adsorbed to sludge in the STPs considerably reducing the PEC and the risk quotients.

Based on the proposed use pattern the notified chemical is not expected to pose an unacceptable risk to the health of aquatic life.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Transport and warehouse workers would only be exposed to the notified chemical in the event of a spill or leak.

Occupational exposure to the notified chemical during end-use can be divided into exposure to the powdered solid, the dye solution, and to the dyed cloth.

Workers may be exposed to solid product containing 10-30% notified chemical while weighing out the dye. Inhalation/ingestion exposure is expected to be low as the product is granular, and workers will wear dusk masks or respirators, and local extraction and general ventilation are available. Dermal exposure will be limited by PPE such as gloves, overalls and ocular exposure limited by goggles.

Workers may be exposed to dye solution during the dyeing process and while cleaning equipment. The solutions may contain varying concentrations of the notified chemical or its reaction products, all at less than 1%.

The dyeing process is mainly automated following weighing and dissolving of the dye, with the cloth driven by mechanical rollers. The system is mainly enclosed to prevent splashes and spills. Manual handling of wet cloth will occur during transport to the wash off bath on a pin chain. During washing and drying, the moist cloth is handled by the operator when transferring by pin chain for the hydroextraction. Exposure to the notified chemical is unlikely during this process

as workers will wear gloves, overalls and goggles.

Cleaning and maintenance is performed by the machine operators. This involves flushing the holding and mixing tanks with water. During this process, workers will wear an organic vapour cartridge, gloves, safety goggles and overalls to minimise exposure.

After fixation of the dye to the textile and washing off of unfixed dye, the remainder of the notified chemical will be chemically linked to the fabric and thus expected to be unavailable.

9.2.2. Public health – exposure assessment

The product containing the notified chemical will be available only to industrial end users. The dyed cloth may be used for apparel, sheeting and other uses. The notified chemical is covalently linked to the cloth after the dyeing process, and there is no evidence of bleeding of the dye from dyed cloth. Thus there will be significant exposure to the dyed product however exposure to the notified chemical is not likely to be significant.

9.2.3. Human health – effects assessment

The notified chemical has <2.4% of the particles in the respirable fraction (<10μM) and a mass median diameter of 23μM. However, the commercial form of the dye contains anti-dusting agents and has a particle size of 150-300 and thus the inspirable and respirable fractions are low. The log Pow of <–4.5 and the high MW (>500) indicate that dermal absorption would be low.

The notified chemical exhibited low acute oral and dermal toxicity. There was no evidence of sensitisation in a guinea pig maximisation test.

In a dermal irritation study, all Draize scores were 0 for erythema and oedema at all time points. Red staining of the treated skin by the test article was observed and persisted in all animals to the end of the observation period (72 hours). In the dermal toxicity test (24 hour dermal exposure) crusts developed on the application site at day 3-4 in 4 females and 3 males, and did not resolve in 4 males and 1 female. Based on this the notified chemical is considered as being irritant after a 24 hour semi occlusive application. However the notified chemical is not classified as a skin irritant under the Approved Criteria for Classifying Hazardous Substances.

In the ocular irritation assay, there was limited conjunctival chemosis and discharge at the 1-hour observation, and some conjunctival redness persisting for 7 days. These effects were not sufficient for classification. At the end of the observation period (21 days), persistent orange staining was observed in the sclera and conjunctivae of all animals. Thus the notified chemical causes irreversible colouration of the eyes, and is classed as:

- R41 Risk of serious damage to eyes.

In a 28-day repeat dose oral toxicity test, black faeces were observed in groups receiving 1000 mg/kg bw/day, which cleared during the recovery period. Dark faeces were observed in animals receiving 200 mg/kg bw/day. Changes to the kidneys were observed in males only. However there was a clear dose-response relationship to the increased kidney/body weight ratio in males receiving 200 and 1000 mg/kg bw/day. This was supported by microscopic changes to the kidneys (increased incidence and severity of hyaline droplets) observed in males receiving 1000 mg/kg bw/day. Some microscopic findings were noted in the stomach and lung of females receiving 1000 mg/kg bw/day. The No Observed Adverse Effect Level (NOAEL) was established as 200 mg/kg bw/day in this study, based on a changes in the kidneys observed at 1000 mg/kg bw/day, with lesser responses occurring at 200 mg/kg bw/day.

The notified chemical was considered to be clastogenic in an in vitro Mammalian Chromosome Aberration Test. The test article induced a significant increase in the number of cells carrying structural chromosome aberrations after treatment with 4000 μg/mL in the absence of metabolic activation. There was strong cell toxicity at this dose level. No other significant increases were seen, and a confirmatory test was not performed. This increase was above the historical control range and was of the same magnitude as the increase in the positive control substance (800 μg/mL EMS). Thus the notified chemical was clastogenic to Chinese hamster V79 cells treated

in vitro under the conditions of the test.

The notified chemical was not considered mutagenic in an Ames test, or in an in vivo Mammalian Erythrocyte Micronucleus Test.

Classification as a mutagenic substance requires a positive result in an in vivo mutagenic assay. Thus, the chemical is not classed as a mutagen even though the in vitro mouse micronucleus test gave a positive result. Additionally, analysis of the chemical structure reveals chemical moieties that are of concern with respect to mutagenicity and oncogenicity (detailed below).

The USEPA Categories of Concern lists the vinyl sulfone group, and its typical precursors as potential health risks, with oncogenicity and mutagenicity concerns. The notified chemical contains ß-sulfatoethyl-sulfonyl groups, which have been identified as precursors to vinyl sulfone. Therefore inhalation or ingestion of the powdered dye or water-dye solution may pose a potential health risks, and strict controls need to be put in place to minimise the risk of such exposure. The reactive vinyl sulfone group is used to attach the dye to the fabric, and it is not expected that dye fixed to the fabric would contain vinyl sulfone groups or their precursors.

Another potential risk posed by azo dyes such as the notified chemical is the potential carcinogenicity of aromatic amines produced by cleavage of the azo bond *in vivo*. The notified azo dye is not to expected to be reductively cleaved to release one or more of the aromatic amines listed in either the Appendix to EC Directive 76/769/EEC: (http://europa.eu.int/comm/enterprise/chemicals/legislation/markrestr/consolid_1976L0769_en.pdf) or the annexes of the European Union SCCNFP/0495/01, Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers concerning ``The Safety Review of the Use of Certain Azo-Dyes in Cosmetic Products," 2/27/02. http://europa.eu.int/comm/food/fs/sc/sccp/out155_en.pdf (prepared in the context of Directive 76/768/EEC).

Based on the available data, the notified chemical is classified as a hazardous substance for eye irritation in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 2004).

9.2.4. Occupational health and safety – risk characterisation

The notified chemical is classified as a severe eye irritant (may cause serious damage to eyes). Additionally there are concerns about the mutagenicity and oncogenicity of reaction products and some impurities of the notified chemical, some of which will be present in the dye solution. Also the effects seen in the acute dermal toxicity study cannot be discounted as the chemical is considered as a skin irritant after a 24 hour semi occlusive application.

Exposure of workers to the notified chemical is not expected to occur in the presence of the engineering and PPE controls described. The imported dye is in powder form, however potential inhalation or ingestion exposure would be reduced by the non-dusting form of the product. Dermal or ocular exposure during handling of the solid dye and to dye solutions could occur during preparation, dyeing and equipment cleaning, but would be reduced by engineering and PPE controls. Contact with dry dyed textiles should not lead to exposure to the notified chemical as it will be chemical bonded to the textiles and not available.

Where dermal contact occurs, the low Kow of the notified chemical suggests that it would not be absorbed through the skin.

In addition, exposure is likely to be avoided due to the staining properties of the dye.

Overall, the risk to occupational health and safety is low, providing that sufficient safety precautions are taken to minimise exposure.

9.2.5. Public health – risk characterisation

The notified chemical is classified as hazardous. However, the notified chemical will not be available to the public in a form where exposure is likely. Articles that have been dyed with the notified chemical will be available to the public, however the notified chemical is covalently

linked to the cloth after the dyeing process, and excess dye is washed off.

The risk to public health is low based on low exposure to the notified chemical.

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:

- R41 Risk of serious damage to eyes.

and

As a comparison only, the classification of notified chemical using the Globally Harmonised System for the Classification and Labelling of Chemicals (GHS) (United Nations 2003) is presented below. This system is not mandated in Australia and carries no legal status but is presented for information purposes. Based on the data provided, the notified chemical would have a Chronic IV classification on environmental grounds and a Category 1 Hazard – Irreversible Effects on the Eye based on health effects.

10.2. Environmental risk assessment

On the basis of the PEC/PNEC ratio, the chemical is not considered to pose a risk to the environment based on its reported use pattern.

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 Negligible Concern to public health when used as a textile dye for commercial use only.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the imported product 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 the imported product 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:
  - R41 Risk of serious damage to eyes.

- Use the following risk phrases for products/mixtures containing the notified chemical:
  - ≥ 5 < 10%: Xi: R36 Irritating to eyes.
  - ≥ 10 < 20%: Xi: R41 Risk of serious damage to eyes.
  - ≥20%: Xi: R41 Risk of serious damage to eyes..

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical as introduced:
  - Local exhaust ventilation where there is potential exposure to solid product.
  - Isolation controls where feasible.

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:
  As introduced:
  - Dusk masks or respirators capable of removing all product particles
  - Gloves, overalls and goggles.
  In dye solutions:
  - Gloves, overalls and goggles

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

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid exposure to eyes and skin.
  - Clean spills immediately, taking care to avoid dust formation.
  - Avoid inhalation of dust.

- 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.

Environment

Disposal

- The notified chemical waste and contaminated packaging should be disposed of as chemical waste to an approved waste disposal facility in accordance with official regulations. Incineration is recommended.

Emergency procedures

- Spills should be handled by dampening powder and scooping into marked containers for disposal as chemical waste in accordance with official regulations.

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
  - the importation volume exceeds one tonne per annum notified chemical; or
  - health and/or environmental data becomes available on potential degradation products; or
  - any further information regarding genotoxic potential becomes available.

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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