File No: NA/210

Date: December 6, 1994

NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

DRIMARENE RED R-7B

This Assessment has been compiled in accordance with the provisions of *the Industrial Chemicals (Notification and Assessment) Act 1989,* and Regulations. This legislation is an Act of the Commonwealth of Australia. The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is administered by Worksafe Australia which also conducts the occupational health & safety assessment. The assessment of environmental hazard is conducted by the Department of the Environment, Sport, and Territories and the assessment of public health is conducted by the Department of Human Services and Health.

For the purposes of subsection 78(1) of the Act, copies of this full public report may be inspected by the public at the Library, Worksafe Australia, 92-94 Parramatta Road, Camperdown NSW 2050, between the hours of 10.00 a.m. and 12.00 noon and 2.00 p.m. and 4.00 p.m. each week day except on public holidays.

For Enquiries please contact the Administration Coordinator at:

Street Address: 92 Parramatta Rd Camperdown, NSW 2050, AUSTRALIA
Postal Address: GPO Box 58, Sydney 2001, AUSTRALIA
Telephone: (61) (02) 565-9466 **FAX (61) (02) 565-9465**

Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

DRIMARENE RED R-7B

1. APPLICANT

Sandoz Australia Pty Ltd, Chemical Division, 675 Warrigal Road, Chadstone Victoria, 3148.

2. IDENTITY OF THE CHEMICAL

- Drimarene Red R-7B has been classified as hazardous by Worksafe Australia due to its skin sensitisation and eye irritation properties. However, for commercial reasons, the identity, impurities and methods of detection and determination have been granted exemption from the Full Public Report and Summary Report. The conditions of this being permitted are:

- The descriptive generic name Monoazo Red MDO 358 Reactive dye be used to identify the substance in the MSDS,

- The relevant employee unions shall be informed of the conditions of use of Drimarene Red R-7B,

- The full chemical name shall be provided to any health professionals in the case of a legitimate need where exposure to the chemical may involve a health risk,

- The full chemical name shall be provided to those on site who are using the chemical and to those who are involved in planning for safe use, etc. in the case of a legitimate need,

- The Director of NICNAS will release the full chemical name etc in the case of a request from a medical practitioner,

- Confidentiality will expire after a 3 year period,

- That the chemical be identified as a sensitiser in the Health Effects Section of the MSDS, and that reference to its assessment by NICNAS be made on the MSDS,

- These conditions shall be published in the Chemical Gazette.

Trade names: Monoazo Red MDO 358 Reactive Dye
Drimarene Red R-7B
RED MDO 358

Molecular weight: 975

Method of detection and determination:

The active substance and organic impurities can be detected qualitatively with UV/VIS, IR and NMR spectra, and quantitatively with HPLC. Inorganic impurities can be determined by capillary electrophoresis, ion liquid chromatography and thin layer chromatography.

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa: A red solid in the form of fine granules

Odour: Not distinctive

Melting Point: > 183°C

Boiling Point: 769 °C (Calculation method)

Density: 1770 kg/m^3

Vapour Pressure: 8.7 x 10^{-24} Pa at 25°C (Calculation method)

Water Solubility: 65 g/L at 20°C (pH 2.4)

Partition Co-efficient (n-octanol/water) log $P_{o/w}$: -3.4 at 20°C (estimate)

Hydrolysis as a function of pH:

pH	Temperature [°C]	Rate Constant [$hour^{-1}$]	Half Life Time t´ [hours]
4	50		>8760.0
7	50		>8760.0
9	60	0.049	14.4
9	70	0.185	4.7
9	25	5.15	1365.0

Adsorption/Desorption: Not provided. The substance is claimed by the notifier to have low affinity to soil. This is acceptable in view of its high solubility and low partition coefficient.

Dissociation Constant pKa**:** Not provided

Flash Point: Not provided

Flammability Limits: Not highly flammable

Combustion Products: Not provided

Decomposition Temperature: > 183°C

Decomposition Products: Not provided

Autoignition Temperature: > 400°C

Explosive Properties: Non explosive when exposed to thermal or mechanical stress.

Reactivity/Stability: Stable at room temperature, does not evolve flammable gases when in contact with air or water**.**

Particle size distribution:

Size (µm)	%
<2	1.3
2-5	0.3
5-10	1.0
10-20	2.3
20-50	5.7
50-63	1.6
63-250	14.9
>250	74.1

Surface Tension: 68.4 mN/m at 20°C and 1002 mg/l (not surface active).

4. PURITY OF THE CHEMICAL

Degree of purity: 49% - 65% typically 56% this is the main component as Na -salt.

Organic impurities: 0.9%

Inorganic Impurities: 43.4%

Additives/Adjuvants: None

5. INDUSTRIAL USE

Drimarene Red R-7B is a cotton dye in the form of fine non dusting granules that is being introduced to replace existing dyes.

6. OCCUPATIONAL EXPOSURE

Drimarene Red R-7B will be imported in 25 kg steel drums in the range of 1-5 tonnes per year for the next 5 years. This translates to 500 kg - 2500 kg of the notified chemical being imported. It may be repacked into smaller quantities before it is distributed to approximately 10 other warehouses for its use. It will be used exclusively in commercial dyehouses.

The dye is hand weighed, dissolved in water and then pumped or gravity fed into to a closed dye bath. It is estimated that at each location one person will spend approximately one hour per day on this procedure. The only direct handling anticipated is weighing out the dye, dissolving it in water and removal of dyed fabric from the tank. As the dye is in a granular form it is claimed to be non dusting and to be easily poured out during weighing. Engineering controls are claimed not to be generally used during these processes at the dye houses.

The formulation is allegedly non dusting, thus reducing the potential exposure during repackaging, weighing, and transferring processes prior to its solubilisation in water. After it is in solution, contact via splashing remains possible prior to it entering the closed dye system. Contact with the eyes, skin and lungs are all possible during the handling of this dye.

7. PUBLIC EXPOSURE

There is a low potential for public exposure to Drimarene Red R-7B during transportation, dyeing, and disposal. The general public will be exposed to the notified chemical when present in dyed garments. Sandoz claims that the dye will become chemically bound to the substrate and will lose its "reactivity" after the dyeing process, thus resulting in negligible public exposure.

8. ENVIRONMENTAL EXPOSURE

. Release

The dye that is chemically bound to clothing fibres is not expected to adversely impact on the environment.

The notifier has indicated that the dye has an 80% level of fixation on the fibres. The unfixed residues from dyeing operations will enter the aquatic environment after discharge from the textile mills and subsequent treatment at sewage treatment plants.

. Fate

As a result of the dye's low K_{ow}, and hydrolytic stability at low pH, it is likely that quantities will remain in the aquatic phase. Furthermore, reactive dyes have been found not to strongly adsorb to sludge in model systems (1).

The dye was tested for its ready biodegradability using standard test methods. The ready biodegradability test (EEC test method C.4, closed bottle test) (2) gave a negative result (-7% and 1% for 1.0 $mg.L^{-1}$ and 3.0 $mg.L^{-1}$ respectively). As the dye is not ready biodegradable significant degradation is unlikely in sewage treatment plants (unless retained for long periods under strongly alkaline conditions).

After treatment in the sewage plant, the dye will enter either freshwater or marine environments in solution. The dye is reasonably stable to aerobic conditions but azo dyes are susceptible to reductive degradation under anaerobic conditions that are characteristic of sediments (3). The half life of this form of degradation was found to be between 2 and 16 days for several sulphonic azo dyes (4), thus no significant increase in concentration over time is expected. One possible route for the dye to enter the sediments is by precipitation of its calcium salts, as several calcium salts of sulphonic dyes are known to be insoluble (4) at modest concentrations. However, apart from precipitation as the calcium salt, the hydrophilic nature of Drimarene Red R7B should limit the affinity for soil and sediment and thus the dye should remain mainly in the aquatic compartment.

The bioaccumulation potential of the dye was not investigated due to its very low partition coefficient (log P_{OW} = -3.4), as allowed by the *Act*. This together with the high water solubility and low fat solubility indicates that bioaccumulation should not occur.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1 Summary of the acute toxicity of Drimarene Red R-7B

Test	Species	Outcome	Reference
Acute oral toxicity	Rat	LD_{50} > 2000 mg/kg	(5)
Acute dermal toxicity	Rat	LD_{50} > 2000 mg/kg	(6)
Skin Irritation	Rabbit	Non-irritant	(7)
Eye irritation	Rabbit	Severe irritant	(8)
Skin sensitisation	Guinea pig	Sensitiser	(9)

9.1.1 Oral Toxicity (5)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 401* (10).

Wistar rats (5 per sex) were administered a single dose of 2000 mg/kg Drimarene Red R-7B dissolved in water by gavage. Animals were observed for a period of 15 days after which necropsy was performed.

One male was observed to be salivating on day 1. No other clinical signs, deaths, macroscopic changes or changes in body weight were observed in any animals.

It was concluded that the oral LD_{50} of Drimarene Red R-7B was > 2000 mg/kg.

9.1.2 Dermal Toxicity (6)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 402* (11).

Wistar rats (5 per sex) were administered Drimarene Red R-7B by dermal application.

On day one of the procedure the test substance was applied evenly to a portion of the shaved skin area. This was covered by a semi-occlusive dressing. Drimarene Red R-7B was diluted in water and animals received 4 ml of the substance at a dose of 2000 mg/kg. Twenty four hours after application the skin was washed and dried. The animals were then observed for a period of 15 days after which necropsy was performed.

No mortality or macroscopic abnormalities were observed during the study. The skin of all animals become slightly brown coloured. One female lost weight between days 1 and 8 of the study and the female rats in general showed low weight gain.

It was concluded that the dermal LD_{50} of Drimarene Red R-7B to rats was > 2000 mg/kg.

9.1.4 Skin Irritation (7)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 404 (12)*

New Zealand White rabbits (three males) were administered a single dose of 0.5 g of Drimarene Red R-7B moistened with water by dermal application.

On day one of the procedure the test substance was applied to a portion of the shaved area and covered with a semi-occlusive dressing.

The test substance remained on the skin for four hours after which time it was removed with lukewarm tap water. Animals were then observed at 1, 24, 48 and 72 hours and 7 days after removal of the dressing.

All animals showed skin discolouration which lasted for 1 day. No animals exhibited erythema or oedema, although this was difficult to judge on day one due to skin staining. Body weights were normal and no other clinical symptoms were observed.

Drimarene Red R-7B was concluded to be a non-irritant to the skin under the conditions of this study.

9.1.5 Eye Irritation (8)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 405 (13).*

New Zealand White rabbits (three males) were administered a single dose of 88 mg of Drimarene Red R-7B into the conjunctival sac of one eye. The other eye remained untreated and was used as a control. Animals were observed at 1, 24, 48 and 72 hours after administration of Drimarene Red R-7B. After the 24 hour observation both eyes of all animals were rinsed with 50 ml tap water in an attempt to remove the residual test substance.

Application of the test substance resulted in purple staining of the iris and conjunctival tissue of all three rabbits which persisted for 72 hours. One hour after treatment the cornea and iris of two animals could not be properly examined due to the swelling of the eyelids. In the remaining animal 50 % of the areas could be scored and opacity was not observed. Conjunctival redness could not be scored due to colouration from the test substance. Lacrimation was observed in all three animals at all time points. Discharge was absent one hour after treatment but increased to involve a considerable area around the eye in all three animals at 48 hour and 72 hour time points. Two animals were able to be scored for corneal opacity by 24 hours (approximately 50 % of the corneal and iris tissues could be observed). Both showed diffuse areas of opacity. At 72 hours, it was observed that due to opacity the details of the iris were obscured in all three animals. Remnants of Drimarene Red R-7B remained in the eyes after the rinse at 24 hours, which did not appear to remove the test substance.

No other clinical signs were observed.

Drimarene Red R-7B was concluded to be a severe eye irritant as a result of the progressive corneal injury and absence of recovery under the conditions of the study.

9.1.6 Skin Sensitisation (9)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 406 (14).*.

The test used was the guinea-pig maximisation test of Magnusson and Kligman (15).

Preliminary study

To determine the dose level for intradermal injection in the main study, 0.1 ml of a 5% solution of Drimarene Red R-7B in saline were injected into the clipped shoulder regions of one Himalayan strain guinea-pig. The resulting dermal reactions were assessed 24 and 48 hours later. Erythema and necrosis was present 24 and 48 hours after bandage removal but scoring was not possible due to purple staining of the skin.

To determine the dose level for topical induction and challenge in the main study 50% of Drimarene Red R-7B in vaseline was applied to the clipped and shaved flanks of the same guinea pig used in the previous test. Filter paper saturated with the test substance was applied to the skin under occlusive bandage. The dressings were removed after 24 hours and assessments were made 24 and 48 hours after removal of the bandage. Severe erythema was present at 24 and 48 time periods, scaliness of the skin was observed at 48 hours.

In a second preliminary experiment using an epidermal application, 0.05 ml of 50%, 25%, 10%, and 5% w/w Drimarene Red R-7B was applied occlusively to the shaved flanks of four guinea pigs using square chamber mounted on tape held in place by an elastic bandage. The bandage was removed after 24 hours and the treated sites assessed 24 and 48 hours later. Generally the animals treated with 10 - 50 % test substance had severe erythema at 24 and 48 hours, and an amount of test substance had dried to the skin. No or slight erythema was present at the 5% application level.

Induction Study

Thirty female guinea-pigs of the Himalayan strain (20 test and 10 control animals) were used.

On day 1 three pairs of intra-dermal injections (0.1 ml) were made into the clipped inter-scapular region of each guinea-pig. The injected solutions were:

Freund's Complete Adjuvant (50:50) with water.
Drimarene Red R-7B diluted to 2% with saline,
Drimarene Red R-7B diluted to 4% in saline and emulsified in a 50:50 mixture with Freund's Complete Adjuvant.

Control animals received the same treatment but without the test substance.

On day 8 the clipped area between the injection sites was treated with an occlusive epidermal application of 0.5 ml of 10% Drimarene Red R-7B in vaseline in the same manner as described above for topical application in the pre-test. The bandage remained in place for 48 hours. Control animals were similarly treated but without the use of the test substance. The sites were evaluated immediately after removal of the bandages.

Challenge Study

Two weeks after the epidermal induction application, the test and control animals were challenged topically with 0.05 ml of 2%, 1%, and 0.5% w/w Drimarene Red R-7B. The test substance was applied to the left flank of each guinea pig. The techniques used were the same as those described above. The bandages remained for 24 hours and assessment was made of the skin reactions at 24 and 48 hours after removal of the bandages. After the first observation the skin sites were shaved.

Results

After epidermal induction, slight erythema was observed in two animals but generally skin reading was very difficult due to staining of the treated area.

Following challenge with 2% Drimarene Red R-7B slight (12/20 animals) to well defined (2/20 animals) erythema was observed in test animals 24 to 48 hours after removal of the bandages. No positive reactions were present in the control group. Animals challenges with 1 or 0.5% test substance demonstrated decreasing proportion of sensitisation with 9/20 and 8/20 animals respectively exhibiting sensitisation. Two control animals from each of the 1% and 0. 5% groups showed an erythema reaction.

Body weight gains in the test group were slightly higher than those observed in the control group. No toxic symptoms were observed in any animals.

In conclusion 14 animals (70%) showed skin sensitisation to the 2% concentration of Drimarene Red R-7B. Reaction to the 1% and 0.5% concentrations was less certain due to the presence of an erythema reaction of equivalent intensity in 2/5 control animals. The incidence was thus dose dependent. Drimarene Red R-7B was therefore concluded to be a strong skin sensitiser in guinea-pigs.

9.2 28 Day Repeated Dose Toxicity (16)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 407 (17).*

After a preliminary range finding study, groups of 10 rats (5 of each sex) of a Wistar derived strain were treated orally by gavage, once daily, 7 days a week for 4 weeks. Animals received 0, 50, 200 or 1000 mg/kg of Drimarene Red R-7B dissolved in distilled water at 5 ml/kg. Animals were necropsied after the 28 day treatment period was over. In a recovery study 5 animals of each sex were treated with 0 or 1000 mg/kg and allowed a 14 day recovery period prior to necropsy being performed.

Body weights and food consumption of treated animals varied slightly but this could not be ascribed to treatment. There were no changes in ophthalmic properties, haematology, or clinical chemistry among any treatment group.

One female treated with 1000 mg/kg died on day 20 of the treatment period. No clinical signs were observed in males treated with 50 mg/kg. One female given this dose exhibited salivation. Increased salivation was observed in males and females in a dose related manner. Pink discolouration of the tail occurred in some males and all females at 200 mg/kg and all animals of the main and recovery groups treated with 1000 mg/kg. A darkening of the faeces was observed in male and female animals treated with 1000 mg/kg at the end of the dose period and beginning of the recovery period. Four females (1000 mg/kg) showed laboured breathing and/or rales and two a hunched posture at 28 days, and five exhibited piloerection which persisted until the beginning of the recovery period. One male showed piloerection.

Several small haematological changes were observed in females only after 4 weeks and males and females after 6 weeks. All observed changes were present only at the 1000 mg/kg dose level. Slight but statistically significant increases were noted in males for haemoglobin and platelet count. Females showed slight increases of the red cell distribution width at 4 weeks and red blood count, haemoglobin and haeatocrit at 6 weeks. Although all of these changes are very slight the fact that they only occurred at 1000 mg/kg suggests that they may be a result of treatment rather than purely an artefact. These symptoms are typical of dehydration and suggest that the dye may be acting as a diuretic. Plasma and serum of all females treated with 200 mg/kg and 1000 mg/kg were orange or pink in colour.

A number of changes were observed in the clinical biochemistry of females treated with 200 mg/kg and both sexes treated with 1000 mg/kg Drimarene Red R-7B. After 28 days females showed a slight increase (0.49 compared to 0.34) in triglycerides at 200 and 1000 mg/kg, but this had dropped to below control after the recovery period. Total bilirubin levels of females had increased by a third in the high dose group and Alanine Aminotransferase activity had decreased in males of this group at 28 days. These parameters were normal at the end of the recovery period.

Kidney and testes relative weights were increased in high dose males at the 4 week time period. No other statistically significant changes in organ weights were observed.

Macroscopic treatment related changes were observed in the stomach and the kidney. No macroscopic changes were noted in animals treated with 50 mg/kg Drimarene Red R-7B. 2/5 males and 4/5 females treated with 200 mg/kg Drimarene Red R-7B exhibited thickening of the limiting ridge of the stomach and 3/5 males and 5/5 females showed kidney discolouration. All animals treated with 1000 mg/kg Drimarene Red R-7B exhibited these symptoms. After the recovery period discolouration was present in all animals, and stomach limiting ridge thickening in only one animal of each sex. One male had developed pelvic dilation on one side. One female had developed a red discolouration of the mandibular lymph nodes and a thymus haemorrhage, and another female presented with distended uterine horns. The deceased animal had redness in all tissues.

Microscopic treatment related changes were observed in the stomach and the kidney. All high dose animals exhibited slight to moderate hyperplasia of the keratinising epithelium of the limiting ridge of the stomach. This was also observed in some females treated with 200 mg/kg. Increased accumulations of eosinophilic inflammatory cells were noted in the submucosa of the glandular stomach in males of the 1000 mg/kg group. An increase in hyperkeratosis of the forestomach epithelium was observed in high dose males and females, and 200 mg/kg dose females. These effects were assumed by the study director to be the result of stomach irritation from Drimarene Red R-7B. After the two week recovery period the stomachs of the rats appeared to be microscopically normal. The kidneys were observed to be affected by eosinophilic inclusion body accumulations in both sexes at the high dose group, which were still present but diminished after 6 weeks.

The results of this study indicate that the kidney and stomach are the likely target organs for toxicity. Effects on the stomach were probably a result of irritant properties of the chemical. Administration of Drimarene Red R-7B to rats at 50 mg/kg or below did not cause any notable changes.

9.3 Genotoxicity

9.3.1 *Salmonella typhimurium* Reverse Mutation Assay (18)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 471 (19).*

Drimarene Red R-7B was tested in the reverse mutation assay on *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 in the presence or absence of liver microsomal S9 activation. As a result of a preliminary study the concentrations selected for the main study were 0, 33.3, 100.0, 333.3, 1000, 2500, or 5000 µg Drimarene Red R-7B /plate. Positive controls used in the absence of activation were 4-nitro-o-phenylenediamine, and sodium azide. 2-Aminoanthracene and Congo Red was used as the positive control in experiments including the liver S9 mix. All positive control substances produced marked increases in the number of revertant colonies within the anticipated range.

No significant and repeatable increases in the number of revertant colonies of bacteria were recorded for any of the strains of *S. typhimurium* used, at any dose level of the test substance, with or without metabolic activation. There was no evidence of higher mutation rates with higher plate concentrations of test substance below the statistically significant level. The test substance caused toxicity to the bacterial lawn at a concentration of 2500 µg/plate in strains TA 1537 and TA98 with and without activation and strains TA 1535 and TA 100 without activation.

The results of this study indicate that Drimarene Red R-7B is not genotoxic toward *Salmonella typhimurium*.

9.3.3 Chromosomal Aberrations in Chinese Hamster Ovary Cells (20)

The study was carried out in accordance with the *OECD Guide-lines for testing of Chemicals No: 473* (21).

Drimarene Red R-7B was investigated for its potential to cause chromosomal aberrations *in vitro* in the V79 line of cells from the Chinese Hamster.

Preliminary experiments were performed in order to determine the toxicity of Drimarene Red R-7B to the cells. Cytotoxicity was observed in the absence of liver S9 mix at 30 µg/plate and higher, and in the presence of S9 at 100 µg/ml and higher. The culture medium was used as the negative control; ethylmethanesulfonate (4.8 mM final concentration) and cyclophosphamide (3.3 µM final concentration) dissolved in nutrient medium were the positive controls utilised.

Two experiments were performed using cultures in the absence and presence of S9 metabolic activation. A single cell suspension of V79 was prepared from 3 day old exponentially growing stock. Cells were subsequently treated with Drimarene Red R-7B and chromosomes prepared 18 hours or 28 hours after treatment. After 48 hours (28 hour preparation interval) and 55 hours (18 h preparation interval) the cell medium of the 4 hour treatment group was replaced by serum free medium containing the test article and S9 mix. The cell medium of the 18 and 28 hour treatment group was replaced by complete medium containing different concentrations of the test article without S9 mix. Low, medium and high concentrations of Drimarene Red R-7B were used for the 18 hour fixation interval and medium and high non-toxic concentration for the 28 hour fixation interval.

Cells fixed 18 hours and 28 hours after treatment in the absence of S9 mix showed no increase in the frequency of aberrations compared to controls.

Cells fixed 18 hours after treatment and treated with 100 µg or 150 µg in the presence of S9 mix showed slight increases over the control value. Cells fixed 28 hours post treatment and treated with 30 µg or 100 µg Drimarene Red R-7B showed slight increases in cell aberrations. These changes were slight and within the range of historical control values, and not statistically significant.

Small reductions in the mitotic index were observed for both fixation intervals in the presence of S9 mix. No biological increases in the occurrence of polyploid metaphases was noted. The positive control substances both elicited a significant increase in chromosomal aberrations.

In conclusion, Drimarene Red R-7B was found not to be a clastogen in the V79 Chinese Hamster Cell line under the conditions of the study.

9.4 Overall Assessment of Toxicological Data

Drimarene Red R-7B is a chemical with low toxicity via oral (LD_{50} > 2000 mg/kg) and dermal (LD_{50} > 2000 mg/kg) routes to rats. A study performed over 28 days suggests that the target organs of Drimarene Red R-7B are the kidney and stomach. One death occurred during this study at the highest dose of 1000 mg/kg, and no abnormal observations were made at doses of 50 mg/kg or below. Drimarene Red R-7B was found to be non irritating to the rabbit skin but a severe rabbit eye irritant. It was found to cause a skin sensitising reaction to 70% of tested rabbits at a concentration of 2%. The substance did not cause point mutations to *S. typhimurium in vivo* nor was it clastogenic to the V79 cells of the Chinese hamster *in vitro*.

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

Ecotoxicity tests were performed using the ready to use formulation of the notified substance (Drimarene Red R-7B) which was tested at 56% purity. The results in Table 2 were provided by the notifier. No precipitates or other irregularities were noted in these tests and the concentrations were measured at the conclusion of tests and found to be within 2% of the nominal concentrations. These tests were performed in accordance with standard EEC test methods or OECD test guidelines, and at facilities complying with OECD principles of GLP.

Table 2 Summary of Ecotoxicity of Drimarene Red R-7B

Species	Test	Result	Ref
Carp *Cyprinus carpio*	96 hour acute EEC TG C1	NOEC < 18 $mg.L^{-1}$ LC_{50} = 24 $mg.L^{-1}$	(22)
Daphnia *Daphnia magna*	48 hour immobilisation EEC TG C2	NOEC = 10 $mg.L^{-1}$ EC_{50} = 26 $mg.L^{-1}$	(23)
Alga *Scenedesmus subspicatus*	72 hr Growth Inhibition EEC C3	NOEC = 5.6 $mg.L^{-1}$ EC_{50} = 16.3 $mg.L^{-1}$	(24)
Bacteria, from aerobic waste water	Inhibition of Microbial Activity EEC, L133	NOEC >100 $mg.L^{-1}$ EC_{50} >100 $mg.L^{-1}$	(25)

Table 2: Concentrations are nominal.

The above results show that Drimarene Red R7B is slightly toxic to fish, daphnia and alga. The dye does not affect aerobic waster water bacterial respiration at 100 $mg.L^{-1}$, indicating that it is unlikely to effect bacteria in the sewage system. Based on these results, chronic effects would not be expected at the estimated environmental concentrations, and the lack of daphnia reproduction tests is acceptable.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The notifier states that 80% of the dye is fixed in the dyeing process; 20% of the dye used could be discharged into effluent of the dye houses where it is used. The notifier has calculated the concentration of discharge for a typical dye house. The calculations presented by the company are based on a batch size of 100 kg of fabric and are as follows:

Use of Drimarene Red R7B per batch	= 2 kg
Amount of dye used per batch (56% pure)	= 1.12 kg
Fixation rate of 80%, quantity passing to effluent	= 0.224 kg
Total volume of wash waters:	=10,500 L
Effluent concentration from dye bath	=21.3 ppm
Dilution in other waste waters of the dye house @ 10:1	=2 ppm
Dilution in receiving waters @ 10:1 (Company Calculation)	=0.2 ppm

The assumptions made are very conservative, for example dilution in the dye house effluent is normally be considered at least ten times greater. The EPA therefore has extended this calculation from the dye house to include dilution in the sewage and the receiving waters for an inland rural based dye house. City based dye houses would have their effluent diluted in a at least 50 times more water than the country locations.

· Dilution in sewage treatment plants for:

Rural treatment plant 5 ML per day	= 40 ppb

· In final receiving waters:

Inland waterway (3:1 dilution)	= 13 ppb
City Ocean release	= < 1 ppb

These calculations are based on no removal of Drimarene Red R7B through adsorption to sludge in the sewage treatment plant [unlikely due to its high water solubility (6.5 $g.L^{-1}$) and low partition coefficient (log P_{ow} =<-3.4)]. The calculations give expected environmental concentrations significantly below the LC^{50} for fish, daphnia and algae (see Table 2).

The dye is not expected to accumulate in the sediment nor bioaccumulate.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

Drimarene Red R-7B is a powder material with a partition coefficient of log P_{ow} = - 3.4 and a water solubility of 65 g/L, suggesting that it is unlikely to accumulate in biological tissue. It is in a granulated form that is claimed to be non dusting if used correctly and easily poured. Only 2.6% of its particles have a size less than 10 µm. The potential for inhalation and subsequent respiration is therefore limited.

The dye is handled during weighing and transferring processes when exposure to the lungs, skin and eyes is possible. Dyeing is performed in a closed system so that exposure is prevented. Protective clothing and equipment (goggles, gloves, respiratory protection) has been recommended by the notifier and exhaust ventilation is suggested by the U.S. Operating Committee of Ecological and Toxicological Association of the Dyestuffs Manufacturing Industry (26). The formulation is non dusting, thus reducing the potential for exposure during weighing and transferring processes. After it is in solution, contact via splashing remains possible prior to it entering the closed dye system.

Drimarene Red R-7B has properties that classify it as hazardous according to Worksafe Australia guidelines (27). It is a severe eye irritant with no trend towards reversibility in the rabbit and a sensitiser of the guinea pig skin. Considerable caution must therefore be taken during the use of Drimarene Red R-7B if the risk of health effects to those working with the chemical is to be acceptable.

Although there is a potential for public exposure to the notified chemical in dyed garments, it is allegedly to be chemically bound to the substrate. Therefore there should be negligible risk to public safety.

13. RECOMMENDATIONS

To minimise occupational exposure to Drimarene Red R-7B the following guidelines and precautions should be observed:

- the following personal protective equipment should be used:
  - respiratory protection conforming to Australian Standards AS 1715 (28) and AS 1716 (29);
  - chemical-type goggles conforming to Australian Standards 1336 (30) and 1337 (31);
  - impervious neoprene, PVC or nitrile gloves conforming to Australian Standard 2161 (32); and
  - protective clothing conforming to Australian Standards 3765.1 (33) or 3765.2 (34).
- good work practices should be implemented to avoid generation of dust/splashing and spillages.
- spills should be cleaned up promptly.
- good personal hygiene practices should be observed.
- a copy of the MSDS for products containing the notified chemical should be easily accessible to all employees.

14. MATERIAL SAFETY DATA SHEET

The attached Material Safety Data Sheet (MSDS) for Drimarene Red R-7B was provided in Worksafe Australia format (35).

This MSDS was provided by Sandoz Australia Pty Ltd, as part of their notification statement. It is reproduced here as a matter of public record. The accuracy of this information remains the responsibility of Sandoz Australia Pty Ltd.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989*, secondary notification of Drimarene Red R-7B shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

16. REFERENCES

1. Hobbs S, Industry Category Document: UK Dye Production and Use in the Textile Industry, UK Department of the Environment (CR36/38), July 1988.

2. RCC NOTOX Project 106706, Ready Biodegradability: Closed Bottle Test with Red MDO 358, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, November 1993.

3. Yen C-P, C; Perenich, T.A. and Baughman, G.L. Environmental Toxicology and Chemistry, 1991, 10:1009-1017.

4. Weber, E.J; Environmental Toxicology and Chemistry, 1991, 10:609-618.

5. RCC NOTOX Project 098292, Assessment of Acute Oral Toxicity with Red MDO 358 in the rat, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, July 1993

6. RCC NOTOX Project 105187, Assessment of Acute Dermal Toxicity with Red MDO 358 in the rat, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, October 1993.

7. RCC NOTOX Project 105198, Primary Skin Irritation/Corrosion Study with Red MDO 358 in the rabbit, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, October 1993.

8. RCC NOTOX Project 105209, Acute Eye Irritation/Corrosion Study with Red MDO 358 in the rabbit, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands , November 1993.

9. RCC NOTOX Project 098303, Contact Hypersensitivity to Red MDO 358 in the albino guinea pig (maximisation test), RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, October 1993.

10. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4: Health Effects, No.401 "Acute Oral Toxicity", Paris Cedex, February 1987.

11. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4: Health Effects, No.402 "Acute Dermal Toxicity", Paris Cedex, February 1987.

12. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4: Health Effects, No.404, "Acute Dermal Irritation", Paris Cedex, May 1981.

13. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, No.405 "Acute Eye Irritation/Corrosion", Paris Cedex, February 1987.

14. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, No.406 "Skin Sensitisation", Paris Cedex, May 1981.

15. Magnusson B, and Kligman, A.M; Allergic Contact Dermatitis in the Guinea Pig, Charles G. Thomas; Springfield, Illinois, 1970.

16. RCC NOTOX Project 105211, Subacute 28-day Oral Toxicity with Red MDO 358 by Daily Gavage in the rat Followed by a 14-day Recovery Period, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, January 1994.

17. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4: Health Effects, No.407 "Repeated Dose Oral Toxicity-Rodent: 28 or 14 day Study", Paris Cedex, May 1981.

18. Project CCR 412716, *Salmonella typhimurium* Reverse Mutation Assay for Azo Dyes with Red MDO 358, CCR-Cytotest Cell Research GmbH & Co. KG, Germany, July 1993.

19. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, No.471 "*Salmonella typhimurium*, Reverse Mutation Assay", Paris Cedex, May 1983.

20. CCR Project 412727, Chromosome Aberration Assay in Chinese Hamster V79 Cells *in vitro* with Red MDO 358, CCR-Cytotest Cell Research GmbH & Co. KG, Germany, November 1993.

21. Organisation for Economic Co-Operation and Development (OECD), OECD Guidelines for Testing of Chemicals, Section 4: Health Effects No.473, "*In vitro* Mammalian Cytogenetic Test", Paris Cedex, May 1983.

22. RCC NOTOX Project 098314, 96 Hour Acute Toxicity Study in the Carp with Red MDO 358, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, July 1993.

23. RCC NOTOX Project 098325, Acute Toxicity Study in *Daphnia magna* with Red MDO 358, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, May 1993.

24. RCC NOTOX Project 105233, *Scenedesmus subsoicatus*, Fresh Water Algal Growth Inhibition Test with Red MDO 358, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, November 1993.

25. RCC NOTOX Project 105244, Activated Sludge Inhibition Test with Red MDO 358, RCC NOTOX B.V. 's-Hertogenbosch, The Netherlands, November 1993.

26. U.S. Operating Committee of Ecological and Toxicological Association of the Dyestuffs Manufacturing Industry, Guidelines for Safe Handling of Dyes, Washington, 1989.

27. Worksafe Australia, *Approved Criteria for Classifying Hazardous Substances* [NOHSC: 1008 (1994)], Australian Government Publishing Service, Canberra, March 1994.

28. Australian Standard 1715- 1991 *Selection, use and maintenance of Respiratory Protective Devices*, Standards Association of Australia Publ., Sydney, 1991.

29. Australian Standard 1716-1991 *Respiratory Protective Devices*, Standards Association of Australia Publ., Sydney, 1991.

30. Australian Standard 1336-1982 Eye Protection in the Industrial Environmental, Standards Association of Australia Publ, Sydney, 1982.

31. Australian Standard 1337-1984 Eye Protectors for Industrial Applications, Standards Association of Australia Publ, Sydney, 1984.

32. Australian Standard 2161-1978 Industrial Safety Gloves and Mittens (excluding Electrical and Medical Gloves), Standards Association of Australia Publ, Sydney, 1978.

33. Australian Standard 3765.1-1990 Clothing for Protection against Hazardous Chemicals Part 1 Protection against General or Specific Chemicals Standards Association of Australia Publ, Sydney, 1990.

34. Australian Standard 3765.2-1990 Clothing for Protection against Hazardous Chemicals Part 2 Limited Protection Against Specific Chemicals Standards Association of Australia Publ, Sydney, 1990.

35. Worksafe Australia, *National Code of Practice for the Preparation of Material Safety Data Sheets* [NOHSC:2011(1994)], Australian Government Publishing Service, Canberra, March 1994.