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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME

FULL PUBLIC REPORT

5-OXO-3,4-DICHLORO-1,2 DITHIOL

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Director
Chemicals Notification and Assessment

FULL PUBLIC REPORT

5-OXO-3,4-DICHLORO-1,2 DITHIOL

1. APPLICANT

Grace Dearborn, Division of WR Grace Australia Ltd of 1126 Sydney Road, Fawkner, Victoria 3060 has submitted a standard notification for the assessment of 5-oxo-3,4-dichloro-1,2 dithiol.

2. IDENTITY OF THE CHEMICAL

Chemical name: 5-oxo-3,4-dichloro-1,2 dithiol

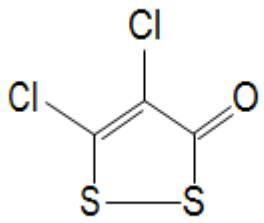
Chemical Abstracts Service (CAS) Registry No.: 1192-52-5

Other name(s): 4,5-dichloro-1,2-dithiacyclopentene-3-one
Dithiol

Trade name(s): Daracide 816-12
RYH-86
RYH-86 Ex (40% solution in methyl-carbitol)
Daracide 7816
Daracide 7802

Molecular formula: $C_3Cl_2OS_2$

Structural formula:



Molecular weight: 185.88

Method of detection and determination:

The notified chemical can be isolated by HPLC and GC and determined by infra-red and NMR spectroscopy and quantitatively determined by UV/Visible spectral analysis.

Spectral data:

IR: Major characteristic peaks were observed at 840, 965, 1162, 1510 and 1625

cm^{-1}. Overall the spectrum is consistent with the structure of the test substance.

UV: Characteristic peaks were observed at 205, 250 and 316 nm

3. PHYSICAL AND CHEMICAL PROPERTIES

Appearance at 20°C and 101.3 kPa:	Brown crystalline powder
Odour:	Not provided
Melting Point:	57-60°C
Density:	1994 kg/m^3 at 15°C
Vapour Pressure:	0.011 mmHg at 25°C 0.033 mmHg at 35°C 0.087 mmHg at 45°C 0.55 mmHg at 55°C
Water Solubility:	500 mg/L at 25°C
Partition Co-efficient (n-octanol/water) log P_{OW}:	3.6 (±0.3)
Hydrolysis as a function of pH:	Readily hydrolysed in alkaline solutions. Half-life = 54.1 days at pH 5 (25°C), 104.4 h at pH 7 (25°C), 0.9 h at pH 9 (room temperature) (1).
Flash Point:	>110°C
Flammability Limits:	Not flammable
Reactivity/Stability:	Relatively stable under acidic conditions; degrade rapidly under alkaline conditions

. Comments on physico-chemical properties

RYH-86 is claimed to be relatively soluble in water (500 mg/L), although its partition co-efficient appears somewhat high for this to be the case (log K_{OW} 3.6 ± 0.3). In other documentation accompanying the notification, the partition co-efficient was given as 2.2. The notifier has since confirmed that the partition coefficient and water solubility are 3.6 ± 0.3 and 500 mg/L, although no test methods or reports have been provided to support these results.

The tests for soil adsorption-desorption and dissociation constant were not performed. However, in additional information supplied by the company (2) they state that RYH-86 and products are expected to "bind strongly to the organic and lipophilic phases of sediments because of their strong adsorption characteristics". The EPA agrees that RYH-86 is likely to adsorb to organic material to some degree, with RYH-86 having a logK_{OW} of 3.6. The EPA also notes RYH-86 contains no functionalities that would dissociate under the expected environmental conditions of use. Aqueous photolytic degradation, and anaerobic and aerobic aquatic metabolism tests are summarised in the section on fate (below)

4. PURITY OF THE CHEMICAL

Degree of purity: >99%

Toxic or hazardous impurity/impurities:

. **Chemical name:** Sulphur
CAS No.: 7704-34-9
Weight percentage: 0.1%

Non-hazardous impurity/impurities: (> 1% by weight)

. **Chemical name:** Water
CAS No.: 7732-18-5
Weight percentage: 0.04%

Additive(s)/Adjuvant(s): None

5. INDUSTRIAL USE, FORMULATION AND IMPORT VOLUME

The notified chemical is to be used in the paper industry as a slimicide to control the growth of micro-organisms in the process water to enable reuse of this water. Such biological control is needed to prevent slime formation which adversely affects paper quality through creating weak spots, blemishes or odours in the paper. The estimated quantity of the notified chemical to be imported into Australia is up to 20 tonnes per year for the first five years. It will be formulated in Australia to a product called Daracide 7802.

6. OCCUPATIONAL EXPOSURE

The notified chemical will be imported as a brown crystalline powder in either 25 kg bags or 50 kg kegs. 10 Dock/Wharf workers will be involved in unloading and handling of shipping containers containing the notified chemical for approximately 2 hours/day for 2 days/year. 6 custom inspection officers will be exposed to the chemical during random sampling at the rate of 2 hours/day for 2 days/year. 2 truck drivers will be involved in the delivery of the containers from the receiving wharf to the formulation site.

At the formulation site 4 storemen will unload and store the pellatised drums containing the notified chemical using fork lifts for a maximum period of 30 minutes per day for 6 days per year. 2 plant operators will be exposed to the notified chemical at the rate of 6 hours/day for 15 days/year, during weighing (usually under local exhaust ventilation) and adding to the mixing vessel in a bunded area. The notified chemical is mixed with glycol and water resulting in a 10-20% aqueous solution. The work area is well ventilated, and the mixing vessels are closed and vented with dust extractors.

The formulated product containing the notified chemical (Daracide 7802) will be dispatched by road to approximately 10 operational sites in 200 L polyethylene-lined steel drums or 1000 L high density polyethylene bulk containers. This operation will involve 4 workers. Daracide 7802 will be automatically pumped from the transport drums or bulk containers to a chemical dosing system which is part of a fully enclosed metering system supervised by 4 workers. The dosing will result in a concentration of 0.1 to 0.3 ppm of the notified chemical in the water.

7. PUBLIC EXPOSURE

The notified chemical will be used in industrial sites and public exposure is not expected to occur during the use of the chemical.

Due to the low application rate (0.1 - 3 ppm) and rapid hydrolysis under alkaline conditions, the level of the notified chemical in wastewater is very low. A study showed that the dithiol level in the wastewater of an overseas paper mill, when dithiol was used, was below 4.5 ppb (detection limit). The notifier claimed that the level of the notified chemical in wastewater will not exceed 10 ppb. Furthermore, dithiol will be further degraded when released into the environment. Therefore, the potential public exposure to the notified chemical through wastewater is expected to be negligible.

A study submitted by the company showed that the notified chemical was not detected (detection limit of 0.222 ppm) in fine paper or paper board manufactured using the notified chemical at the application rate of 0.8 - 1.2 ppm, although it was noted that in the study extraction recovery was very low (56.2 - 66.2% in fine paper and 1.9 - 4.1% in paper board). The paper products normally have a pH of 6 - 7.5 and are subjected to drying process at 110°C, which will sufficiently hydrolyse any residual dithiol. The company stated that at a 10 ppm application rate in white water the dithiol residue in paper products will be about 0.1 ppm. Thus, contact with paper products is not expected to result in significant public exposure to the notified chemical.

In the case of accidental spillage during transport, the public may be exposed to the notified chemical. However, the exposure will be minimal if the spills are contained and cleaned up by the recommended practices as outlined in the MSDS.

8. ENVIRONMENTAL EXPOSURE

. Use

Transport of Daracide7802 to paper mills throughout Australia would be by road. The company plans to first trial RYH-86 at a paper mill in Victoria in metropolitan Melbourne. The number of potential sites is about 10 and range from metropolitan sites in major cities, to coastal and country sites where waste water treatment and available dilution may be more limited (see Table 1).

Table 1. Qualitative breakdown of some pulp and paper mills

Site Classification					
		Large Country Town	**Country Town**	**Coastal**	**Unknown**
Number of Mills	3	1	1	3	2
Expected dilution	large	moderate	small	moderate to large	
Route	sewer	sewer	varying degree of waste treatment	varying degree of waste water treatment	
Examples	AP Petrie Qld AP Fairfield Vic Visy Coolaroo Vic	ANM Albury NSW (secondary treatment then release to Murray River	Kimberely-Clark Millicent SA (primary treatment then direct to Lake Bonney) APPM Nowra N.S.W. (primary treatment then to Shoalhaven River	APM Burnie Tas (primary treatment) AP Wesley Vale Tas (primary treatment) AP Maryvale Vic (tertiary treatment with large dilution on release)	AustTissue WA Paper Converters Qld

. Release

Daracide 7802 will be automatically pumped from the transport drums or bulk containers to a chemical dosing system, part of a fully enclosed metering system. Dosing will result in a concentration of RYH-86 of between 0.1 to 0.3 ppm.

The company states that Australian paper mills water usage ranges from 4 to 14 kL of water per tonne of paper produced. Much of the machine water is recycled into pulping, diluting stock and other processes. The company estimates that, as a result, 50-65% of the mill water could be treated with biological control agent.

Waste water, containing RYH-86 residues, will be disposed of to municipal sewer or direct to water courses or bodies. Mill discharge waste water treatment is expected to vary according to regional conditions and state regulations, and range from just primary clarification to remove settleable solids to full activated sludge treatment or municipal sewer. The company estimates that retention time will be 2 h for a low volume recycling mill prior to discharge (because of greater volume of discharge and less treatment required), to 10 d for full treatment and lagoon hold time.

Other possible releases of the polymer could occur during formulation, sampling or during dosing. These operations are done on industrial sites using appropriate equipment designed to reduce possible spills etc. This, together with the instructions on

the clean-up of spills in the MSDS, should minimise the possibility of environmental release during these processes.

. Fate

Continuous treatment of process water is needed to control the formation of slime. RYH-86 is expected to be rapidly lost, either as a result of scavenging by the biomass (1×10^6 colony forming units per mL of water by standard plate count is typical), or as a result of hydrolysis. As indicated above, RYH-86 hydrolyses rapidly under alkaline conditions. Also, the company expects process water to be neutral to alkaline, particularly for those mills that recycle water. For some fine paper manufacturing however, some machines will operate at a pH of about 6.5, although the waste water in all cases should be >7.

In response to the EPA's concerns about differences between overseas and Australian operations and conditions, the company provided the following points:

- Australian machine systems tend to be world-average, and therefore would approximate American systems.
- Many mills world-wide operate biological treatment plants for mill effluent with no reports of activated sludge biological plant problems due to added biocides.
- Warmer water is generated by the degree of re-use, rather than higher ambient temperatures; the company states that less biocide is used at higher temperatures because different bacterial species dominate.

Although RHY-86 meets several of the criteria for bioaccumulation (3) (eg 100>MW>600), its lack of a high proportion of aliphatic and aromatic C-C, C-H and C-Cl bonds, and expected lack of environmental persistence under alkaline conditions, will limit its bioaccumulation.

No test to determine ready biodegradation was performed. However, the company has provided more advanced and comprehensive studies that report measured concentrations of RYH-86 in process and waste water (4), aqueous photolytic degradation (5,6) aerobic (7) and anaerobic (8) aquatic degradation, and measurement of RHY-86 in paper (9). Summaries of these studies will be given below.

- *Concentrations of RYH-86 in process and waste water*

The concentration of RYH-86 in process waters and the waste effluent stream was measured, when used as a slimicide during the production of board and paper at a Finnish mill (4). In determining the recovery of RYH-86 from mill waters (pH 4.9-5.1), the study found that under ideal conditions, the detection limit was 1.5 ppb, while under field sampling conditions, the detection limit was 4.0-4.5 ppb.

In total, about 12000 m^3 of process effluent water was released per day, comprising effluent water from one board machine, one paper machine and one ground-wood mechanical pulp unit. About 40 kg of Daracide was added per day, giving a possible maximum concentration in effluent waters of 0.3 mg RYH-86.L^{-1} (ie (40 kg Daracide x 10% = 4 kg of RYH-86 per 12×10^6 L). All process effluent water was treated through primary and secondary treatment, where the pH was 5-6 and temperature was 35°C in

primary clarification, but with pH increasing to 7 and the temperature ranging from 25-30°C in the activated sludge digestion and secondary clarification.

RYH-86 was recovered in process water used in the board machine during the dosing period at concentrations of about 300-400 ppb. No RYH-86 was detected in treatment plant effluent between dosing periods. Sampling after each stage of waste water treatment (which received effluent from the pulp unit, and board and paper machines) also did not detect RYH-86.

- *Aqueous photolytic degradation*

A study (5) to determine the rate of degradation of ^{14}C-RYH-86 in artificial sunlight (xenon light source) in an aqueous sterile buffer at pH 5 was performed following EPA Pesticide Assessment Guidelines (Subdivision N, Section 161-2).

The preliminary test indicated that RYH-86 had a rapid half-life when using approximately 80% of natural sunlight (equinox, 40°N latitude), with only 0.4% of radio-labelled RYH-86 found 15 min after the study. The intensity of the xenon lamp was therefore reduced to 60% of natural sunlight in the definitive test. Also, because of the rapid photolysis, the solutions of RYH-86 were irradiated until taken for sampling. Tests were performed at a room temperature of 25°C over an 11 minute period; dark controls were sampled after 635 minutes.

The main results are given in Table 2. The mean radioactivity corresponding to ^{14}C-RYH-86 decreased from 95.4% (of that applied) at the start of the test, to 39.8% at the end of the test. Dark controls had a mean total radioactivity of 103.3% (of that applied) at the end of the study. Of this, 97.1% was ^{14}C-RYH-86. A further study (6) indicated that hydrolysis was unlikely to account for the degradation products.

Table 2. Main results of photolysis study

Treatment	pH	Mean total radioactivity (%)[a]	Volatiles[b] (%)[a]		RYH-86 degradation (%)[a]		Half-life
			Start	Finish[c]	Start	Finish[c]	
Exposed	5	94.1 - 97.8	0.1	9 (3)	95.4	39.8	8.4 min
Dark	5	103.3		5 (2.9)		97.1	

a relative to time 0
b %CO_2 given in brackets
c Study period was 11 min for light exposed samples and 635 min for samples kept in dark

First order kinetics were assumed in calculating the half-life of RYH-86 using linear regression. The calculated half-life was 8.4 minutes.

- *Aerobic and Anaerobic aquatic degradation*

Studies to determine the aerobic degradation (7) and anaerobic degradation (8) of ^{14}C-RYH-86 were performed following EPA Pesticide Assessment Guidelines (Subdivision N, Section 162-4 and 162-3, respectively). The aerobic study had a test system using lake

water of pH 8.21 and sediment, while the anaerobic study had a test system using lake water and sediment (pH 7.6). Tests on both non-sterile and sterile samples in the aerobic and anaerobic studies were performed at a temperature of about 25´C in the dark, over a 32 d and 393 d period, respectively. The main results for each study are given in Table 3.

First order kinetics were assumed in calculating the half-life of RYH-86 using linear regression. The calculated half-life was 4.2 hours for non-sterile samples and 0.4 hours for sterile samples in the aerobic study. In the anaerobic study, data from Hour 0 to Day 5 was used as RYH-86 was not detected after Day 5. The calculated half-life was 1.7 d for non-sterile samples. No half-life was calculated for the sterile samples with only 7.1% of parent RYH-86 remaining after 2 h. No consistent trends in pH, Eh or dissolved oxygen appear to explain the differences in half-life between sterile and non-sterile samples in the aerobic study, although the pH was acidic at times in the non-sterile anaerobic samples, perhaps preventing as rapid hydrolysis as seen in the sterile samples.

A short study compared results of the aerobic study and the hydrolysis study, and showed that the same major product (or product complex) was formed in each. This product was then most likely metabolised by bacteria to CO_2 in the aerobic study (with bacterial contamination in the sterile samples also causing its metabolism). A similar conclusion is reached for the anaerobic study in a paper attached to the notificationan (10). This paper concludes that RYH-86 is hydrolysed through nucleophilic attack of hydroxide ion at carbonyl carbon (C-3) leading to dithiol ring opening, and giving either simple aliphatic acids such as beta-keto acid or thiol acid (shown below as I and II respectively). These simple acids could, under certain conditions and complex reaction pathways also involving the formation of 4 sulphur rings, form heterocyclic compounds which would in turn be hydrolysed through ring cleavage. Their degradation products would then undergo cleavage of the carbon-sulphur and sulphur-sulphur bonds.

O=C--CH--COOH

Structure I

HS--C=C--C--OH

Structure II

Table 3. Main results of aerobic and anaerobic study

Study	pH	Mean total radioactivity (%)[a]	Volatiles (%)[a]		Radiolabel fate (%)[a]			Half-life Derivation		
			Total[b]	CO_2[b]	Phase	Start[c]	Finish[c]	% RYH-86 at start[a]	% last detectable RYH-86[a]	Half-life
Aquatic Aerobic Metabolism										
Sterile	8.21	88.5 - 104.7	27.2	27.1	Water sediment[d]	100.3 3.3	55.8 10.7	91.3	0.4 (at 0.13d)	0.4
Non-sterile	8.21	92.1 - 100	25.1	23.9	water sediment[d]	94.4	54.9	91.3	39.8 (at 0.21d)	4.2
Aquatic Anaerobic Metabolism										
Sterile	7.6	89.4 - 104.7	nd	<1%	water sediment[d]	97.5 5.5	64.2 24.9	nd		nad
Non-sterile	7.6	81.4 - 99.0	nd	<2%	water sediment[d]	90.1 6.4	57.5 23.9	54.5	4.6 (at 5 d)	1.7

a % recovered relative to time 0
b at end of study
c some minor variation in sampling times occurred compared with actual start and finish times
d pooled totals of the sediment extract and extracted sediment
nad not able to determine
nd not detected

- *Measurement of RHY-86 in paper*

A study was performed using GC/MS-SIM to determine the residual content of RYH-86 in paper (8). After adding RYH-86 to the process streams (white water) in either fine paper or paper board production, the concentration of RYH-86 in each of these process streams was 1.3 and 0.64-0.8 ppm, respectively. RYH-86 was not detected in the fine paper product or the paper board product. The detection limit was 0.222 ppm based on the paper, therefore giving a residual limit of <0.222 ppm based on the paper.

. Summary of Environmental Fate Studies

RYH-86 is relatively soluble in water, and will be used in paper manufacturing to prevent microbiological growth (slimes). The company estimates that 50-65% of the process water could be dosed with RYH-86, due to recycling of dosed process water to other water-requiring manufacturing processes.

Some RYH-86 will be taken up by the actual biomass, while some will be absorbed by the paper itself. Any residual RYH-86, and RYH-86 associated with affected biomass, is eventually expected to enter the waste water stream (depending on the degree of recycling). The pH of the waste water stream is expected to be greater than 7, even though some fine paper machines operate at pH 6.5.

A study was performed in which process water was measured to determine concentration of RYH-86 after dosing. Although RYH-86 was detected in process water at about the dose level of 300 ppm, no RYH-86 was found in treatment plant effluent between dosing periods. Sampling after each stage of waste water treatment (which

received effluent from the pulp unit, and board and paper machines) also did not detect RYH-86. The detection limit of RYH-86 under field conditions was 4.0-4.5 ppb.

Table 4. Range of half-lives determined for RYH-86 under different experimental conditions

Study		**pH**	**Half-life**
Hydrolysis		5 7 9	54.1 d 104.4 h 0.9 h
Aquatic Aerobic Metabolism		8.21	
	non-sterile sterile		4.2 h
Aquatic Anaerobic Metabolism		7.6	
	non-sterile sterile		1.7 d nd
Photolysis		5	8.4 min

nd not able to be determined - only 7.1% of parent RYH-86 recovered after 2 h

Table 4 gives the range of half-lives determined for RYH-86 under different experimental conditions. The fate of RYH-86 under alkaline conditions appears straightforward: hydrolysis and aquatic metabolism studies indicate that there is rapid degradation (ring opening) of the chemical, giving the same decomposition product (or product complex). Aquatic metabolism studies (under aerobic and anaerobic conditions) also indicate that the major degradation product is then further metabolised, but only in aerobic studies was a significant proportion of radiolabel recovered as volatiles.

Under acidic conditions, RYH-86 is quite stable, although when exposed to light, there was rapid degradation, with degradation products different to those found in the aquatic metabolism studies.

9. EVALUATION OF TOXICOLOGICAL DATA

9.1 Acute Toxicity

Table 1 Summary of the acute toxicity of 5-oxo-3,4-dichloro-1,2 dithiol

Test	**Species**	**Outcome**	**Reference**
Acute oral toxicity	Rat	LD_{50}= 361 mg/kg	(12)
Acute dermal toxicity	Rat	LD_{50}= 10936 mg/kg (m) LD_{50}= 13809 mg/kg (f)	(13)
Skin Irritation	Rabbit	Severe	(14)
Eye irritation	Rabbit	Severe	(16)
Skin sensitisation	Guinea pig	Sensitiser	(17)

9.1.1 Oral Toxicity (12)

Four groups of fasted SD derived rats (5/sex/group) were administered 178, 251, 355 or 500 mg/kg of RYH-86 in corn oil by single oral gavage and observed for 14 days. A total of 15 rats died during the 14-day observation period and all the deaths occurred within 2 days of dosing. Clinical signs of lethargy and piloerection were observed in most of the animals. Hunched posture, perianal staining and prostration were seen in the two high dose groups. The surviving animals were normal by 9 days after dosing. Necropsy performed on the dead animals showed pale or dark liver and lungs. The gastrointestinal tracts were congested and distended with liquid or gas. The acute oral LD_{50} of RYH-86 in rats was 361 mg/kg.

9.1.2 Dermal Toxicity (13)

Four groups of NZW rabbits (6/sex/group) were dermally treated with 0, 4000, 6000 or 12000 mg/kg of RYH-86 under occlusive dressing for 24 h. The skin of 6 (3/sex) animals in each group was abraded immediately before treatment. Another group of 5/sex rabbits were similarly treated with 2000 mg/kg on the abraded skin only. The observation period was 14 days.

One male in the 2000 mg/kg group, one female in the 6000 mg/kg group, and 4 males and 2 females in the 12000 mg/kg group died within 6 days of dosing. Clinical signs included anorexia, depression and ataxia. Local irritation manifested by slight to severe erythema and oedema was observed and the severity of irritation gradually decreased during the observation period, but was still visible at termination. Necropsy of the dead animals showed congestion of most abdominal organs and the lungs. The liver was pale, mottled and friable, and the kidneys were pale or striated with dilated pelves. Microscopic examination revealed necroses of the epidermis and dermis in both intact and abraded skin. In the control group, only slight erythema at the application site was observed at 1 day after dosing.

The dermal LD_{50} values of RYH-86 in male and female rabbits were 10936 and 13809 mg/kg, respectively.

9.1.3 Inhalation Toxicity

No inhalational studies were provided.

9.1.4 Skin Irritation (14)

Six young adult male NZW rabbits were dermally treated with 500 mg RYH-86 moistened with 0.25 ml distilled water under a semi-occlusive dressing for 4 h. The skin irritation was scored using the Draize method (15).

No erythema was observed in the study. At 1 h after patch removal, severe oedema (grade 4) was seen in 5 animals and slight oedema in one animal. The oedema gradually regressed during the 7-day observation period. Very slight (grade 1) to slight (grade 2) oedema and occasional desquamation, fissuring and atonia were present on day 7. All treated skin showed yellow staining throughout the 7-day observation period. The primary irritation index was 2.7. RYH-86 was considered a severe skin irritant in rabbits.

9.1.5 Eye Irritation (16)

Nine NZW rabbits (4 male and 5 female) received 100 mg RYH-86 powder into the conjunctival sac of the left eye. The eyes of 3 rabbits (one male and two females) were washed with lukewarm water for one minute after 20 - 30 sec exposure, while the eyes of other animals were not washed. Eye irritation was scored at 24, 48 and 72 h and on days 4, 7, 10 and 14 using the Draize method (15).

Corneal opacity, iritis, conjunctival redness, chemosis and discharge were observed from 24 h through day 14 in both washed and unwashed eyes. The irritation signs were still severe by day 14 though the signs in the washed eyes were less severe than those in the unwashed eyes. The Draize scores in the unwashed eyes ranged from 34 to 47 at 24 h to 14 days, while the Draize scores in the washed eyes were between 18 and 37 at 24 h to 14 days. RYH-86 was a severe eye irritant in rabbits.

9.1.6 Skin Sensitisation (17)

The skin sensitisation potential of dithiol was studied in female albino guinea pigs using a maximisation test.

After an irritation screening test, 20 guinea pigs were intradermally injected with Freund's complete adjuvant (FCA), 0.01 %w/w of dithiol in 5 %v/v acetone in Alembicol D, and 0.01 %w/w dithiol in a 50 : 50 mixture of FCA and 5 %v/v acetone in Alembicol D. One week later, the animals were dermally applied with 0.5 %w/w dithiol in acetone for 48 h as the second induction exposure. Two weeks after induction exposure, the animals were challenged with 0.1 %w/w and 0.05 %w/w dithiol in acetone by dermal application. The skin reaction was examined at 24, 48 and 72 h after patch removal. A vehicle control group of 20 animals was similarly treated with the exception that dithiol was not used in the induction exposure.

After challenge exposure, all the test animals showed a positive reaction with grade 1-3 erythema and oedema. No reactions were observed in the vehicle control animals. It was noted that no positive controls were used in the study. Dithiol was considered a skin sensitiser in guinea pigs.

9.2 Repeated Dose Toxicity (18)

Albino rats (15/sex/group) were orally administered 0, 1.5, 3.75 or 7.5 mg/kg/day of RYH-86 in corn oil for 90 days (6 days/week) by gavage. Twenty animals (10/sex) of each group were sacrificed after 90 days dosing, and the remaining animals were allowed to recover for 58 days before necropsy.

No deaths or clinical signs of toxicity were observed in the study. Laboratory analyses including haematology, blood chemistry, urinalysis and vaginal smears did not show any treatment-related changes. Body weight gain was comparable between control and treated groups.

At necropsy, the stomach of one male in the 7.5 mg/kg/day dose group had thickened mucosal lining. No other treatment-related gross lesions or organ weight changes were detected. Microscopic examination revealed dose-related gastritis in all treated groups. The gastritis was characterised by superficial inflammatory cell infiltration. Submucosal

fibrosis and erosion of the nonglandular region of the stomach were found in 2 males and 3 females of the highest dose group. The later lesion was also observed in one control female rat.

After 58 days recovery, slight superficial inflammatory cell infiltration of the stomach mucosa was still present in a few animals of each treated group.

9.3 Genotoxicity

9.3.1 Salmonella typhimurium Reverse Mutation Assay (19,20)

Two studies were performed to detect the mutagenicity of the notified chemical in *Salmonella typhimurium*.

In one study, 5 strains (TA98, TA1538, TA1537, TA100 and TA1535) of *Salmonella typhimurium* were cultured with 0.1 - 1.6 mg/plate of RYH-86 in the absence of rat liver S9 and 2.5 - 40 mg/plate in the presence of S9. Solvent (DMSO) and positive controls were included in the study. In the positive controls, 2-aminoanthracene was used in the presence of S9 in all the strains and in the absence of S9, 2-nitrofluorene was used in strains T98 and T1538, sodium azide in strains TA100 and TA1535, and 9-aminoacridine in strain TA1537.

The revertant colonies were slightly decreased in the high dose groups (showing cytotoxicity) than in solvent control. In the low dose groups, the revertant colonies were slightly increased without dose-response relationship. The increase was within the historical control values. The positive controls produced marked increases in mutant frequency in all the test strains. Under the test condition, RYH-86 was not mutagenic in the *Salmonella typhimurium* reverse mutation assay.

In the second study, *Salmonella typhimurium* TA98, TA1538, TA1537, TA 100 and TA1535 were cultured with 0.05 - 2.5 mg/plate of RYH-86 in the absence of rat S9 and 0.5 - 50 mg/plate in the presence of S9. Solvent and positive controls were the same as those used in the first study.

Cytotoxicity was observed at the two highest dose levels. No increases in revertant colonies were observed in the treated plates, but marked increases were detected in the positive controls of all the test strains. Under the test condition, RYH-86 was not mutagenic in the *Salmonella typhimurium* reverse mutation assay.

9.3.2 Micronucleus Assay in the Bone Marrow Cells of the Mouse (21)

Out-bred CD-1 mice (15/sex/group) were orally administered 100, 200 or 400 mg/kg of RYH-86 in corn oil. A vehicle control group (15/sex) received corn oil only, and a positive control group (5/sex) received 80 mg/kg of cyclophosphamide. Bone marrow was collected from 10 animals (5/sex) from each treatment and vehicle control group at 24, 48 and 72 h after administration. Positive controls were sampled at 48 h. Two bone marrow smears from each animal were examined and 1000 polychromatic erythrocytes were scored for micronuclei.

Seven mice in the 400 mg/kg group and 3 mice in the 200 mg/kg group died within 18 h of dosing. Cytotoxicity was detected in the positive controls and in the 400 mg/kg group sampled at 48 and 72 h. Increases in micronucleus frequencies were seen in the treated groups, but the increases were not statistically significant or dose-related. The positive controls had markedly increased micronucleus frequency. RYH-86 was not considered to cause chromosomal damage in bone marrow cells of the mouse *in vivo*.

9.3.3 Unscheduled DNA Synthesis (UDS) Assay in the Rat Primary Hepatocytes (22)

Freshly prepared hepatocytes isolated from adult male Fischer 344 rats were exposed to RYH-86 at levels of 0.01 - 10.0 mg/ml for 18-20 h. The test substance was dissolved in DMSO before adding to the culture medium. 2-Acetylaminofluorene (0.1 mg/ml) in DMSO was used as a positive control and DMSO as a vehicle control.

The dose levels of 0.5 - 7.5 mg/ml produced a range of toxicity (104% - 72.4% survival) to the cultured cells and were used for analysis of nuclear labelling. Compared to the solvent control, the average nuclear grains in the treatment cultures were not significantly increased, but the positive control showed significant increase in the average nuclear grains. RYH-86 did not induce unscheduled DNA synthesis in rat hepatocytes.

9.4 Developmental study (23)

Mated female SD rats (25/dose level) were administered 0, 5, 15 or 45 mg/kg/day of RYH-86 in corn oil by oral gavage on gestation days 6-15. All animals were sacrificed on gestation day 20 and foetuses were examined.

Maternal toxicity characterised by clinical signs of rales, salivation and urine staining, reduced body weight gain and feed consumption were produced in the high dose group. Most of the high dose animals had thickened stomach mucosa. The foetuses in the high dose group were normal. No adverse effects were observed in either dams or foetuses of other treatment groups or the control group. RYH-86 was not teratogenic in rats.

9.5 Overall Assessment of Toxicological Data

Based on the toxicity studies provided by the company, 5-oxo-3,4-dichloro-1,2 dithiol was of moderate acute oral toxicity in rats and low dermal toxicity in rabbits. It was a severe skin and eye irritant in rabbits and caused corneal opacity. It was a skin sensitiser in guinea pigs. Repeated administration of 1.5 - 7.5 mg/kg/day for 3 months (6 days/week) in rats produced dose-related gastritis characterised by superficial inflammatory cell infiltration. It was not mutagenic in bacterial reverse mutation assays *in vitro*, did not cause chromosomal damage in mouse bone marrow cells *in vivo*, and did not induce unscheduled DNA synthesis in cultured rat hepatocytes. A developmental study showed that the notified chemical was not teratogenic in rats.

In accordance with Worksafe Australia's *Approved Criteria for Classifying Hazardous Substance*, the notified chemical will be classified as hazardous with respect to acute oral lethal effect, irritant effects (skin and eye) and sensitising effect (skin). However, the notified chemical would not be classified as hazardous with respect to acute dermal lethal effect, mutagenic effects nor from repeated or prolonged exposure (oral route).

10. ASSESSMENT OF ENVIRONMENTAL EFFECTS

The ecotoxicity studies were conducted using RYH-86 and a range of aquatic species. There are several problems with the interpretation of the results given in Table 5, not least of which is the tendency for test solutions to have a neutral to alkaline pH. In instances in which the actual test concentration was measured, there was significant degradation of RYH-86, even in flow-through tests (eg the actual concentration in one instance was only 7% of nominal). Actual concentrations were reported as mean concentrations for the test period, with initial rapid degradation. However, in some instances degradation continued and no generalisations could be made as to why this was so. It is also hard to generalise from one test to another, since different test conditions were used (eg with respect to pH, temperature, frequency of water change and light regime). Changes in the test solutions were often noted, with discolouration of test solutions occurring in the Golden Orfe and the green algae tests.

Table 5 Ecotoxicity test results

Species	Test	pH	Result (actual mean concentrations, unless otherwise stated)[a]
Bluegill Sunfish (*Lepomis macrochirus*)	Acute, flow through, 96 h	7.6-7.8	LC50 = 18 µg/L NOEC = 12 µg/L (nominal concentration of 100 µg/L)
Rainbow Trout (*Salmo gairdneri*)	Acute, flow through, 96 h	7.7-7.8	LC50 = 14 µg/L NOEC = <10 µg/L(nominal concentration of <13 µg/L)
Golden Orfe (*Idus idus melanotus*)	Acute, static, 48 h	not stated	LC50 = 350 µg.L-1 (nominal concentration)[b]
Water flea (Daphnia magna)	Acute, static, 24h	7.7-7.8	EC50 = 700 µg/L[c] (nominal concentration)
Water flea (*Daphnia magna*)	Acute, flow through, 48h	8.0-8.2	EC50 (24 h) = 710 µg/L EC50 (48 h) = 380 µg/L (nominal concentrations)
Water flea (Daphnia magna)	Chronic, 16 d, static renewal d	7.9-9.0	EC50 (reproduction and immobilisation) = 420 µg/L NOEC = 18 µg/L LOEC = 56 µg/L (nominal concentrations)
Green Algae (*Chlorella pyrenoidosa*)	72 h, static	3.8-8.4e	EBC50 = 13 mg/L ERC50 = 17 mg/L NOEC = 5.6 mg/L (nominal concentrations[f])

a Actual concentrations can be expected to be about 10% of nominal concentrations - see text for discussion
b Darkening of test solutions and reaching maximum at 24 h
c The test was performed using with and without acetone as the carrier, but giving the same result
d Test solutions renewed on Mondays, Wednesdays, and Fridays
e At higher concentrations, the degradation products of RYH86 appeared to cause the test solutions to become more acid
f. Results were adjusted for discolouration of test medium which was observed through the test period

Results that use nominal concentrations in Table 5 should therefore be treated with caution, while those results that report actual mean concentration (ie bluegill and trout) would tend to be more accurate. For example, in the 48 h *Daphnia magna* flow-through

test, the 48 h EC_{50} was 380 µg/L, and was calculated using nominal concentrations. However, the reported actual concentrations indicate that the EC_{50} could be as low as 6.7, but no higher than 152 µg/L. Further, 0% mortality was recorded at 24 h compared with 93% mortality at 48 h at the test concentration of 500 µg/L; at this nominal test concentration, the actual concentration was a maximum of 200µg/L, which decreased to less than the detection limit (25 µg/L) at 48 h. Although the data are limited, this raises three possibilities for this test:

- a steady state had not been reached between external media and internal body concentrations, leading to a delayed effect;
- a toxic lesion occurred as a result of exposure in the first 24 h but did not manifest itself until 24 h later; or
- the metabolites (see structures and pathways given above in Environmental Fate) of RYH-86 are more toxic than parent.

In general, the actual concentrations would best be taken as about 10% of the nominal concentrations given in Table 5, with RYH-86 appearing to be very highly toxic to aquatic fauna but only moderately toxic to aquatic green algae, although the algal species tested is considered by the US EPA to be insensitive.

11. ASSESSMENT OF ENVIRONMENTAL HAZARD

The company provided a report of a paper study on the chemical fate of RYH-86[10]. The authors concluded that RYH-86 and its decomposition products will be readily biodegraded in sewage treatment plants, river water and sea water. Their worst case scenario was based on environmental conditions expected in the United States, and gave an expected concentration of 10 ng/L in the receiving water, and 1.19 µg/L partitioned to sediment. They conclude that even if RYH-86 residues did reach receiving waters, they would be ultimately removed by anaerobic and aerobic processes in the river waters and sediments, and therefore, the residues of RYH-86 are of no concern to surface waters. This would be re-assuring if the assumptions used in the study were not dependent on rapid degradation of RYH-86 which occurs only under alkaline conditions (such as for the degradation studies they quoted and which are summarised above), that some form of treatment of waste water occurs that removes 95% of RYH-86 and its decomposition products, and that the waste water is diluted by at least 100 on mixing with the receiving water.

Greater assurance of low concentrations in waste water is given by the actual measurement of RYH-86 in process and waste water at a Finnish mill (see above). Under field sampling conditions, however, the detection limit was 4.0-4.5 µg/L. Therefore, in this study, it can not be ruled out that RYH-86 is not present in the toxic low micrograms per litre range, although this may be unlikely given the pH of the sewage treatment works and the long retention times in the treatment works.

The notifier expects that mill discharge treatments will vary from primary clarification to remove settleable solids, to full activated sludge treatment or municipal sewer. The concentration of RYH-86 that they would expect would be 0.1-0.3 ppm within the mill, and <5 ppb (ie not detected) for the sewer discharge, with a further dilution of 100 on release to the receiving water.

Given the above information, the EPA considers the worst case to be:

Concentration of RYH-86 entering receiving water	5 ppb
Concentration in receiving waters (ocean, 10:1 dilution)	0.5 ppb
Concentration in receiving waters (river, 2:1 dilution)	2.5 ppb

If Daracide 7802 was supplied to mills at sites given in Table 1, the above worst case concentrations would be applicable for 2 mills with outfalls to ocean (AP Wesley Vale) or a bay (APM, Burnie, to Bell Bay) and 2 "country" mills with an outfall in a country area and limited available dilution (Kimberley-Clark, Millicent, to Lake Bonney, and APPM, Nowra, to Shoalhaven River).

There is enough evidence that under alkaline conditions and exposure to sunlight, RYH-86 will rapidly degrade with a half-life of a few hours to a few minutes. Further, with its $\log K_{OW}$ of 3.6, it is likely that some RYH-86 will partition to the humic fraction of sediments as indicated above. However, given that toxicity was observed within an order of magnitude of the worst case concentration of 2.5 ppb, and with ecotoxicity test results again highly affected by the alkaline pH of the test system, there appears to be some potential hazard of RYH-86 to the aquatic fauna in receiving waters. This is particularly so in those instances (as indicated in the calculation of the worst case concentration above) where there is inadequate treatment of the waste water, and the receiving water is acid to neutral and gives low dilution.

The notifier has indicated that they are part of a Responsible Care program and are willing to voluntarily apply restrictions on the sale of products containing RYH-86. The EPA therefore strongly recommends that the notifier only sells products containing RYH-86 to those mills that have secondary treatment works, or release to municipal sewer, or can guarantee that the waste water stream has a pH > 7. Of the above sites, particular caution should be paid to the Kimberley-Clark mill at Millicent in South Australia, and the APPM mill at Nowra in New South Wales.

The MSDS has a caution that it is harmful to aquatic life. However, both the label and the MSDS should clearly state that:

> *The chemical is dangerous to aquatic life. To avoid environmental impact the product must be released as part of the waste water stream to secondary treatment plants or municipal sewer, or as part of a waste water stream which on mixing with the receiving water has a pH of 7.*

Please consult the company prior to use.

12. ASSESSMENT OF PUBLIC AND OCCUPATIONAL HEALTH AND SAFETY EFFECTS

The notified chemical is expected to exibit moderate and low toxicities by the oral and dermal routes respectively. It is not expected to exibit serious effects on repeated or prolonged exposure. It is likely to be a severe skin and eye irritant and is unlikely to be genotoxic. However, the notified chemical is likely to exhibit skin sensitisation and respiratory sensitisation.

Exposure during weighing out of the notified chemical is expected to be low due to its non-dusty form and the fact that local exhaust ventilation is generally used in the formulation site. During mixing with glycol and water, dermal exposure will be minimal, as a result of the mixing vessel being closed and the area, vented with dust extractors.

The risk of respiratory sensitisation and eye irritation during weighing out of the notified chemical is expected to be low as a result of its non-dusty form and the use of local exhaust ventilation. There would also appear to be a low risk of dermal sensitisation, skin and eye irritation to the notified chemical during mixing due to the enclosed nature of the process. The exposure to the notified chemical at the operational sites is considered to be low due to the use of automated dosing and enclosed metering systems.

The notified chemical will be used in industrial sites and public exposure is not expected to occur during the use of dithiol. Because the application rate of dithiol is low and it is readily hydrolysed under alkaline conditions, public exposure to dithiol through wastewater and paper products is expected to be negligible. Although analyses for the hydrolysis products in wastewater or paper products were not conducted, the hydrolysis products are not known to be significantly toxic.

13. RECOMMENDATIONS

To minimise occupational exposure to 5-oxo-3,4-dichloro-1,2 dithiol the following guidelines and precautions should be observed:

. local exhaust ventilation should be employed, a respirator conforms to Australian/New Zealand Standard AS/NZS 1715 (25) and goggles (AS 1336, AS 1337) (26,27) during weighing out and dissolution of the of the chemical in solvents. During these operations care should be taken not to generate dust.

. during all operations in which contact with the dissolved notified chemical is possible, personal protective equipment which conforms to and is used in accordance with Australian Standard (AS) for eye protection (AS 1336, AS 1337) (26,27), impermeable gloves (AS 2161) (28), protective clothing (AS 2919) (29) and footwear (AS/NZ 2210) (30) should be worn;

. good work practices should be implemented to avaoid spillages and splashing;

. good housekeeping and maintenance should be practised. Spillages should be cleaned up promptly with absorbents which should then be put into containers for disposal in accordance with Local or State government regulations;

. the workplace should be well ventilated;

. good personal hygiene should be observed; and

. a copy of the Material Safety Data Sheet (MSDS) should be accessible to employees.

14. MATERIAL SAFETY DATA SHEET

The attached Material Safety Data Sheet (MSDS) for 5-oxo-3,4-dichloro-1,2 dithiol was provided in Worksafe Australia format (31).

This MSDS was provided by Grace Dearborn, Division of WR Grace Australia 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 Grace Dearborn, Division of WR Grace Australia Ltd.

15. REQUIREMENTS FOR SECONDARY NOTIFICATION

Under the *Industrial Chemicals (Notification and Assessment) Act 1989*, secondary notification of 5-oxo-3,4-dichloro-1,2 dithiol shall be required if any of the circumstances stipulated under subsection 64(2) of the Act arise. No other specific conditions are prescribed.

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[1] This Guidance Note, to which an MSDS must conform in accordance with the *Act,* has been superseded by Worksafe Australia's National Code of Practice for the Preparation of Material Safety Data Sheets (March 1994) published by the Australian Government Publishing Service.