Public Release Summary
on

Evaluation of the new active

ZINC PYRITHIONE

in the product

INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING

National Registration Authority for Agricultural and Veterinary Chemicals

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FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies, including the Department of Health and Family Services (Chemicals and Non-prescription Drug Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (Worksafe Australia) and State departments of agriculture and environment.

The NRA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for all products containing new active ingredients and for all proposed extensions of use for existing products.

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series.*

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library Ground Floor, 22 Brisbane Avenue, Barton, ACT.

The NRA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Executive Manager—Registration, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion

PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
mg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

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INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING, which contains the active constituents zinc pyrithione and copper oxide. The product is proposed to be used to prevent fouling of commercial shipping vessels.

Although copper oxides are frequently used in antifouling paint products, the use of zinc pyrithione for this purpose is new in Australia. Zinc pyrithione is in widespread use as the active ingredient in some anti-dandruff shampoo preparations. The key focus of this PRS is on the zinc pyrithione component of the product.

Responses to this Public Release Summary will be considered prior to registration of the product. They will be taken into account by the NRA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

Written comments are invited and should be submitted by **19 November 2001,** addressed to:

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Applicant :

Akzo Nobel Pty Limited

Product details:

INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING (Ecoloflex) is a tin-free self polishing copolymer antifouling paint. It will be available in two colours, brown and dark red. The product contains 66g/L zinc pyrithione and 619g/L (brown colour) or 626g/L (dark red colour) cuprous oxide. The product will be marketed to control marine fouling on commercial ships.

The active constituent zinc pyrithione is manufactured in the USA and cuprous oxide in Norway. The product will be formulated in Australia.

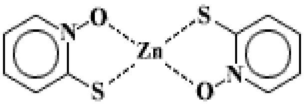
Ecoloflex is currently registered in the United Kingdom, Sweden, Malta, USA, Hong Kong and New Zealand.

CHEMISTRY AND MANUFACTURE

Active constituent

The chemical active constituent zinc pyrithione has the following properties:

Common name (ISO):	Zinc pyrithione
Chemical name:	2-pyridinethiol-1-oxide, zinc salt
CAS Registry Number:	13463-41-7
Empirical formula:	$C_{10}H_8N_2O_2S_2Zn$
Molecular weight:	317.68 g/mol
Physical form:	Powder
Colour:	Off-white to tan
Odour:	Slight amine
Melting point:	Purified substance 267°C (no visual signs of decomposition)
Octanol/water partition coefficient:	log P_{OW} = 0.90 at 25°C
Vapour pressure at 25°C:	Not measurable ($<1.0x10^{-6}$ Pa)
Structural formula:	



Formulated product

The product International Intersmooth 360 Ecoloflex Antifouling has the following properties:

Active constituents:	619 g/L cuprous oxide (brown) or 626g/L cuprous oxide (dark red), 66g/L zinc pyrithione
Formulation type:	Self polishing copolymer antifouling paint
Appearance:	Dark red or dark brown coloured liquid
Specific gravity:	1.56
Flash point:	15°C

TOXICOLOGICAL ASSESSMENT

EVALUATION OF TOXICOLOGY

The toxicological database for zinc pyrithione, which consists primarily of toxicity tests conducted using animals, is quite extensive. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Acute Studies

Zinc pyrithione showed moderate oral toxicity in rats (LD_{50} = 221 mg/kg bw) but low in monkeys (LD_{50} >1000 mg/kg bw). Acute inhalation toxicity was moderate in rats with an LC_{50} concentration in excess of 610 mg/m^3. Whilst there was no skin irritation or sensitisation observed in rabbits and guinea pigs respectively, eye administration was corrosive in rabbits resulting in frank iridial tissue destruction. In rabbits whose eyes were washed with water after a 30-sec exposure there were similar but less severe reactions although still classified as corrosive.

Toxicity studies were not supplied on Ecoloflex as a formulated paint. Studies have been supplied on International Paints Micron Optima Advanced High Strength Copper Oxide Antifouling, containing zinc pyrithione at between 39.4 and 39.6 g/kg and copper oxides at between 417 and 465 g/kg. This paint had low oral (LD_{50} >3000 mg/kg bw) and dermal (LD_{50} >2000 mg/kg bw) toxicity in rats and rabbits respectively. No dermal irritation and sensitisation was observed in rabbits and guinea pigs respectively. Using the conventional 0.1 mL application volume it was a severe irritant but by reducing both the application volume (0.01 mL) and the zinc pyrithione concentration to 1.8% (w/w) the irritation was reduced to moderate. There are significant differences in the non-active constituents of this product and Ecoloflex so these data of limited relevance.

Copper salts have a long history of use in a variety of agricultural and industrial applications and have been assessed toxicologically on a number of occasions previously. The toxicity of copper salts depends largely on the proportion of free copper ion. A lesser degree of acute toxicity is consequently seen with the more insoluble salts eg copper oxides, than those with a higher degree of aqueous solubility eg copper sulfate. Copper irritates the nerve endings in the stomach and initiates the vomiting reflex. This induction of prompt emesis in higher animals would normally limit its oral toxicity, however in a hydrocarbon solvent base this property heightens the risk of aspiration of ingested product with a consequent risk of lipid pneumonitis.

Short-Term Studies

Zinc pyrithione in gelatine capsules was orally administered to cynomolgus monkeys daily for 14 or 28 days. In the 14-day study, treatment at 10, 20, 40 or 80 mg/kg bw/day resulted in haemorrhaging of the stomach mucosa and bodyweight loss at the highest tested dose. In the 28-day study, treatment at 0, 5.5, 11 or 22 mg/kg bw, caused a death at the highest dose. Food consumption and bodyweight gain was decreased at the highest dose together with reduced haematocrit, haemoglobin concentration and erythrocyte count. An increased concentration of ketone bodies and decreased pH of the urine was also observed. These changes were either absent or had improved after a 14-day recovery period.

In a 90-day study, rats were fed zinc pyrithione in the diet at concentrations of 0, 5, 25 or 125 ppm. Clinical signs first observed during the second week at 125 ppm were a depressed respiratory rate and the onset of progressively restricted movement of the hind limbs which finally resulted in almost complete paralysis. Other changes at 125 ppm were related to severe weight loss and dehydration, resulting from the paralysis. Based on the deaths of nearly all the rats at 125 ppm (from dehydration and/or starvation) and the reduced bodyweight observed at 25 ppm in females, the NOEL for this study was 5 ppm (0.35 mg/kg bw/day for males and 0.39 mg/kg bw/day for females).

Daily dermal application of zinc pyrithione to rats at 0, 20, 100 or 1000 mg/kg bw/day for 90 days revealed slight skin irritation, bodyweight loss and reduced food intake at 1000 mg/kg bw/day. For females at 1000 mg/kg bw/day there was an increase in relative kidney weight and some had mineralisation of the kidneys. Increased leucocyte counts and reduced erythrocyte and haematocrit was also observed at the highest dose.

Whole-body exposure to an aerosol at 0, 0.5, 2.5 or 10 mg/m^3 for 6 h/day, 5 days/week over 13 weeks resulted in deaths at 2.5 and 10 mg/m^3, reduced bodyweight gain at 10 mg/m^3 and reduced creatinine at 10 mg/m^3. A dose-related increase in mean absolute lung/mainstream bronchi weight, lung/mainstream bronchi weight relative to body weight and lung/mainstream bronchi weight relative to brain weight was also observed at 2.5 and 10 mg/m^3. These weight increases were accompanied by inflammation of interstitial tissue and pulmonary artery hypertrophy.

Zinc pyrithione given to monkeys at 0, 0.5, 2 or 8 mg/kg bw/day by stomach tube for 90 days induced some vomiting at 2 and 8 mg/kg bw/day within 1-3 h on the first few treatment days. Appropriate monitoring for adverse changes failed to reveal any other effects. Hence, the NOEL for the study was 8 mg/kg bw/day.

Long-Term Study

Sodium pyrithione at 0, 0.5, 1.5 or 5 mg/kg bw/day was administered to rats by gavage in a two-year chronic and oncogenicity study. After 12 weeks at 5 mg/kg bw/day, an appreciable reduction in bodyweight gain necessitated the high dose level be reduced to 3.5 mg/kg bw/day. There was reduced bodyweight gain at 3.5 mg/kg bw/day and hind limb muscle wastage at 1.5 and 3.5 mg/kg bw/day. Nerve fibre degeneration of the spinal cord and sciatic nerve was slightly increased at 3.5 mg/kg bw/day. Fibre degeneration in the hind limb skeletal muscle was increased in all rats at 3.5 mg/kg bw/day and to a lesser extent in females at 1.5 mg/kg bw/day. There was an increase in peripheral retinal atrophy in males and females at 3.5 mg/kg bw/day and at 1.5 mg/kg bw/day in females. There was no treatment-related increase in the incidence of tumours. Therefore, under the conditions of this study, the NOEL was 0.5 mg/kg bw/day.

Reproduction and Developmental Studies

In a 2-generation reproduction study, rats were given sodium pyrithione at 0, 0.5, 1.5 or 4.5 mg/kg bw/day by gavage. Owing to an appreciable reduction in bodyweight gain the highest dose was reduced after 3 weeks to 3.5 mg/kg bw/day for the rest of the study. Rats were maintained for 2 generations, with the first litter used for breeding. In the F0 rats, salivation after dosing was seen in all treated groups, with a dose-related time of onset and severity. At 3.5 mg/kg bw/day a number of females showed hind-limb paralysis in the F0 generation; this was not seen in F1 animals. Body weight gain was statistically significantly decreased in both males and females at 3.5 mg/kg bw/day in the F0 generation, and in females at this dose in the F1 generation. Fertility was decreased at 3.5 mg/kg bw/day in the F0 generation, with the number of rats successfully mating and the number of rats pregnant decreased in comparison to controls. There was no effect on gestational length, the number of pups born or pup bodyweight seen. No effects on fertility were seen in the F1 generation. There was no increase in the incidence of fetal malformations in either generation. On postmortem examination, there was an increase in the incidence of hind-limb muscle atrophy at 3.5 mg/kg bw/day in females in both generations. On histopathological examination, there was an increase in atrophy of skeletal muscles at 3.5 mg/kg bw/day in the F0 generation, and from 1.5 mg/kg bw/day in the F1 generation. Salivation occurred in some F0 rats at 0.5 mg/kg bw/day but none in the F1 generation suggesting that this dose level is a probable NOEL.

When pregnant rats had zinc pyrithione topically applied at 0, 2.5, 7.5 or 15 mg/kg bw/day (with or without prevention from ingestion) from gestation days 6 to 15 there was a reduction in bodyweight gain at 7.5 or 15 mg/kg bw/day when ingestion was not prevented. Hind-limb paralysis among dams and reductions in fetal weight were also observed at 15 mg/kg bw/day. These effects were not seen when ingestion was prevented. With oral treatment at the same doses, bodyweight gain was reduced, paralysis occurred and fetal weight was reduced at 7.5 and 15 mg/kg bw/day. There was also an increase in skeletal variations at 15 mg/kg bw/day.

Pregnant rats given doses of 0, 0.75, 3 or 15 mg/kg bw/day by gavage on days 6–15 of gestation had treatment-related effects at 3 and 15 mg/kg bw/day. These were decreased maternal bodyweight gain, an increase in salivation immediately after dosing, increased resorptions, reduced uterine weight and increased fetal malformations. The NOEL was 0.75 mg/kg bw/day for both maternal and developmental toxicity.

Pregnant rabbits given doses of 0, 0.5, 1.5 or 3 mg/kg bw/day on days 6-18 of gestation had an increased the number of resorptions, reduced uterine weight and increased fetal malformations at 1.5 and 3 mg/kg bw/day, hence the NOEL for developmental toxicity was 0.5 mg/kg bw/day. Although food consumption was reduced at 1.5 and 3 mg/kg bw/day there was no corresponding bodyweight loss (after subtracting the weight of the gravid uterus), hence the NOEL for maternal toxicity was 1.5 mg/kg bw/day based on a clinical sign (ie. an increased incidence of red fluid in the refuse pan for does at 3 mg/kg bw/day).

Zinc pyrithione administered orally to pregnant rabbits at 5, 10 or 20 mg/kg bw/day on days 6 to 18 of gestation caused a dose-related incidence of death with no survivors at 20 mg/kg bw/day. Survivors at 5 and 10 mg/kg bw/day had reduced bodyweight gain and an increased number of resorptions. In a second study at 0, 1, 2.5 or 5 mg/kg bw/day there were no deaths but reduced bodyweight gain was observed at 2.5 and 5 mg/kg bw/day. The number of resorptions was increased at 2.5 and 5 mg/kg bw/day and the number of live fetuses at 5 mg/kg bw/day was reduced. There were no adverse effects on fetal development that could not be linked with maternal toxicity. The NOEL for both maternal and developmental toxicity was 1 mg/kg bw/day.

Genotoxicity

Zinc pyrithione was found to be negative in mutation tests in bacteria and Chinese hamster ovary cells. Similarly, no chromosomal aberration was observed in human lymphocytes incubated *in vitro* in the presence of zinc pyrithione or in lymphocytes harvested from monkeys following oral administration in a 28-day toxicity study. A mouse micronucleus assay also yielded negative results.

Human metabolite study

A study of plasma metabolites in human volunteers from a chemical factory producing pyrithiones identified 2-(methylsulfonyl)pyridine as the only metabolite in human serum and proposed that this metabolite could be used as a marker for pyrithione exposure.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

On the basis of its toxicity and likely use, the NDPSC has included zinc pyrithione in schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). Copper oxides when included in marine paints are exempted from the requirements of poisons scheduling. There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

Since the product, INTERNATIONAL INTERSMOOTH ECOLOFLEX 360 ANTIFOULING, is to be used as an antifouling paint on marine vessels, an ADI for zinc pyrithione does not need to be established.

METABOLISM AND TOXICOKINETICS ASSESSMENT

Metabolism and Toxicokinetics

An excretion study with [^{65}Zn]zinc pyrithione (ZPT) indicated that the pyrithione portion of the molecule is metabolised separately to the zinc portion with the zinc being split off in the stomach and excreted in faeces. A study with a single dose of 1 mg/kg bw [^{14}C]ZPT showed extensive absorption of the pyrithione portion and that most radioactivity (63%, 68%, 84% and 82%) was excreted in the urine during the first 24 h for rats, rabbits, dogs and monkeys, respectively with a further 10–14% excreted in the subsequent 5 days. Excretion in faeces over 6 days in this study was 3%, 20%, 6% and 6%, respectively (with the higher level in rabbits probably due to urine contamination). In the rat, 6% radioactivity remained in the carcass at 6 days after dosing (other species not tested). In another study in rats with single oral doses of 0.5 and 12.5 mg/kg bw zinc pyrithione, radioactivity recovered in the urine, faeces and carcass over 11 days was approximately 80%, 18% and 1%, respectively, with no difference between the 2 doses. The only tissues with more than 0.009% of dose at 11 days were kidney (0.01–0.02%, liver 0.05–0.09% and lungs (0.001–0.01%). A further study showed a similar pattern of excretion for intravenous and oral doses in rats.

Analysis of urinary metabolites showed a similar pattern for each species with 3 main metabolites: 2-pridinethiol-1-oxide-*S*-glucoside, 2-pridinethiol-*S*-glucuronide and 2-pridinethiol-1-oxide-*S*-glucuronide. 2-Pridinethiol-1-oxide-*S*-glucuronide was the most abundant (64%, 35%, 32% and 66% in rats, rabbits, dogs and monkeys, respectively). For rat urine, after the first day another metabolite, 2-(methylsulfonyl)pyridine, formed by the oxidation of the sulfur and reduction of the *N*-oxide of pyrithione, became more prominent. The preferred biotransformation pathway appears to involve conjugation of the 2-thiol group of the pyridine ring (with glucuronide conjugation favoured).

Dermal absorption studies in pigs showed that zinc pyrithione is very poorly absorbed through skin (<10% of dose). A maximum of 5% of the applied dose was recovered in the urine and by 48 h the levels in blood, faeces, and urine were essentially at background levels.

RESIDUES ASSESSMENT

The product is intended for application to the hulls of vessels. It is not intended for use in situations (such as aquaculture) where food for human consumption is being produced. An ADI has not been established. No detailed assessment of residues in food arising from the uses proposed for the product is considered necessary.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

The product is intended for application to the hulls of vessels. It is not intended for use in situations (such as aquaculture) where food for human consumption is being produced. No detailed assessment of overseas trade aspects of residues in food arising from the uses proposed for the product is therefore considered necessary.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING (ECOLOFLEX) is a self-polishing copolymer antifouling paint product containing zinc pyrithione and cuprous oxide.

Zinc pyrithione is not on the NOHSC *List of Designated Hazardous Substances.*
It is of moderate acute oral and inhalation toxicity in rats, and low dermal toxicity in rats. Zinc pyrithione was not a skin irritant in rabbits, nor a skin sensitiser in guinea pigs, but was corrosive to rabbit eyes.

The applicant has allocated the following risk phrases to zinc pyrithione:

R22	*Harmful if swallowed*
R23	*Toxic by inhalation*
R38	*Irritating to skin*
R41	*Risk of serious damage to eyes*

Substances containing zinc pyrithione at 10% or more are considered hazardous.

Cuprous oxide is on the NOHSC *List of Designated Hazardous Substances.* All products containing at least 25% of cuprous oxide are considered hazardous.

The following risk phrase is allocated to cuprous oxide:

R22	*Harmful if swallowed*

Ecoloflex contains a significant amount of compounds that are at least slight skin irritants and nearly 30% of the product consists of substances of moderate skin irritancy. The product also contains a high level of substances with severe to corrosive eye irritancy and the remainder of the ingredients are at least slight irritants, so the product is likely to be a severe eye irritant.

Based on the toxicological profile of the individual ingredients, the product is considered likely to have low acute oral and dermal toxicity, to be a severe eye and a moderate skin irritant and the product vapour is likely to be irritant to the respiratory tract.

The formulated paint is determined to be a hazardous substance based on its ocular effects, the amount of cuprous oxide(>25% cuprous oxide) and organic solvent.

Use and exposure

The formulated product, Ecoloflex, is intended for use on commercial/naval marine vessels, which will be painted infrequently and thus require an antifouling paint with a longer life than that of a smaller pleasure craft. Categories of workers likely to be exposed to the product are professional painters. The product is likely to be used primarily in an industrial setting, i.e. professional shipyards, and the applicant has indicated that the product will not be marketed to the general public.

Ecoloflex will mainly be applied by airless spray, though brush or roller may also be used. The main route of exposure to the product will be dermal, ocular and inhalation. During preparation and painting, workers could be directly contaminated on the skin and in the eyes by drips, splashes and spray mist. Exposure can also arise from accidental splatters during pouring and when cleaning equipment. Since Ecoloflex is capable of causing severe eye irritation, and moderate skin irritation, protective equipment such as cotton overalls, impervious footwear and eye protection are recommended to protect the eyes and the skin. As Ecoloflex contains organic solvents including xylene, Nitrile gloves are recommended. . A full facepiece respirator which has the advantage of protecting eyes and facial skin is recommended. Respirators are required to prevent inhalation exposure.

Workers will be exposed to organic solvents that are present in the product. Inhalation of these solvents may cause central nervous system effects such as headaches, dizziness, nausea and drowsiness, and in extreme cases loss of consciousness. Prolonged or frequent inhalation of solvents may result in liver or kidney damage.

Recommendations for safe use

Users should follow the instructions and Safety Directions on the product label.

Safety Directions for Ecoloflex include the following:

Full facepiece respirator with combined dust and gas cartridge (*When opening the container and using the product*).

Cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length nitrile gloves and impervious footwear (*When opening the container and using the product*).

The Personal Protective Equipment recommended should meet the relevant *Standards Australia* Standards.

Material Safety Data Sheet

Akzo Nobel Pty Limited has produced MSDS for Ecoloflex. This contains information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that their employees have ready access to it.

Conclusion

Ecoloflex can be used safely if handled in accordance with the instructions on the product label.

ENVIRONMENTAL ASSESSMENT

Environmental Fate

Hydrolysis

A study to US EPA Guidelines of hydrolysis at 25°C in the dark indicated that zinc pyrithione hydrolyses slightly in sterile buffers at pH 5, 7 and 9 and in artificial seawater solution at pH 8.2 (estimated half-lives 96-123 days extrapolated from the 30 day incubation period). Of the six metabolites detected, only which two exceeded 10% of the starting dose and were identified as pyrithione disulfide and pyrithione sulfinic acid. It may be that hydrolysis of pyrithione added as zinc pyrithione occurs at a greater rate than indicated in this study due to transchelation to copper pyrithione, which has been reported to hydrolyse with a half-life of 11.9 days at pH 9 and 19 days in sterile synthetic seawater.

Photolysis

An aqueous photolysis study based on US EPA Guidelines was provided (25°C, 12 h light:12 h dark cycles from a lamp simulating natural sunlight wavelengths). This study indicated that photolysis of zinc pyrithione in pH 9 buffer or artificial seawater at pH 8.2 occurred very rapidly (first order half-life from the first hour of incubation = ~13-18 minutes). In contrast, similarly slow degradation rates to those in the hydrolysis study were found in samples incubated in the dark (half-lives extrapolated from 30 days of incubation = 83-91 days). Several degradates were found of which four reached concentrations >10% of applied and were identified (pyridine sulfinic acid, pyridine sulfonic acid, pyridine disulfide and the pyridine/pyrithione mixed disulfide). Some degradates occurred with light exposure, but not in the dark.

An earlier scientific paper also reported rapid degradation of related pyrithione biocides (pyrithione, sodium pyrithione, pyrithione disulfide and a tertiary-butylamine pyrithione derivative, generally tested at 100 ppm) in seawater at a range of pHs exposed to sunlight. The experiments reported in this paper indicated that photodegradation was much slower if the water was deoxygenated. A more recent scientific paper has claimed that rapid photodegradation of zinc pyrithione only occurs at pH < 6, but this result is quite inconsistent with other evidence.

Aquatic metabolism & die-away studies

A series of aerobic and anaerobic aquatic metabolism studies to US EPA Guidelines were provided with zinc pyrithione and the closely related substance copper pyrithione. The latter was examined because it forms readily in natural waters and sediments through transchelation with Cu^{2+} ions. Similar reactions are possible with other heavy metals, but the Cu product evidently dominates in saltwater/marine sediment systems, possibly due to reduced availability of metal ions such as Fe^{3+} through complexation with hydroxide ions. Studies with zinc pyrithione using freshwater/river and/or saltwater/marine sediment systems at an initial concentration of 3 ppm suggested dissipation was affected by precipitation of copper pyrithione, which is much less soluble than zinc pyrithione. Hence a lower concentration of 0.05 ppm zinc pyrithione or copper pyrithione was used for later studies, which were conducted in saltwater/marine sediment systems only. The duration of incubation was 30 or 64 days in the aerobic studies and 30, 90 or 182 days in the anaerobic studies.

These studies indicated very rapid initial degradation in both fresh- and saltwater systems of pyrithione applied as either zinc pyrithione or copper pyrithione (DT50 = 13 minutes to 0.89 days under aerobic conditions, DT50 < 0.96 hours under anaerobic conditions). This was followed by much slower degradation, presumably of substance adsorbed to sediment (DT90 = 1.3-34 days under aerobic conditions, 2.8-20 hours under anaerobic conditions). Thus degradation in sediment under anaerobic conditions (common in sediment under natural conditions) was evidently much faster than under aerobic conditions.

A number of metabolites containing the pyrithione and/or pyridine moieties were identified in the aerobic studies at peak concentrations >10% of the applied concentration of zinc pyrithione or copper pyrithione in one or more studies. These included pyrithione sulfinic acid, pyrithione sulfonic acid, M3 and pyridine sulfonic acid (maximum recorded values respectively, 33, 46, 35, 41 and 25% of applied substance). Although pyrithione disulfide was identified in the early studies conducted at 3 ppm, it was absent in any of the other studies conducted at 0.05 ppm. With zinc pyrithione at 3 ppm, pyrithione sulfonic acid was formed to a significant extent in the marine system (peak 15% of the applied dose), but not in the freshwater system (peak ~1% of the applied dose).

The same metabolites also occurred to some extent (peaks 7-31% of the applied dose) in one or more of the anaerobic studies. However, several other metabolites reached >10% of the applied dose in one or more of the anaerobic studies, including mercaptopyridine, pyridine sulfinic acid, pyridine sulfonic acid, pyridine disulfide and the mixed (pyridine and pyrithione) disulfide (maximum recorded values respectively, 78, 57, 23, 12 and 16% of applied substance).

In most cases $^{14}CO_2$ occurred to only a limited extent (<1-2% of applied radioactivity by 30-90 days), with the exception of the freshwater/river sediment system under aerobic conditions, where $^{14}CO_2$ evolution reached ~12% of applied radioactivity after 30 days of incubation. ^{14}C residues remaining in sediment after solvent extraction reached ~12-64% of applied radioactivity in the various tests.

Danish aerobic and anaerobic aquatic metabolism studies found a similar range in metabolites, with $^{14}CO_2$ evolution reaching ~3-5% of applied radioactivity after 42 or 56 days incubation respectively, under aerobic or anaerobic conditions.

"Die-away" studies with zinc pyrithione and copper pyrithione in seawater without sediment incubated in the dark showed conversion of ~50% of applied zinc pyrithione to copper pyrithione within 24 hours, and a half-life of about 4 days for both compounds after a 2-3 day induction period. Photolysis presumably accounted for rapid initial degradation (half-life = ~25 minutes at ~10°C) in another die-away study with fresh pond water in floating containers exposed to sunlight, much faster than similar samples kept in the dark (half-life = ~7.5 h).

In a further study with river water, sewage influent and a 1:5 mixture of influent and river water the calculated half-lives were, respectively, 15 h, 7 h and 11 h, compared to 23 h for sterile influent. Evidence from this study suggested that zinc pyrithione was rapidly adsorbed onto particulate matter present in solution, rapidly removing it from ready availability in solution, after which microbial and/or chemical degradation led to rapid degradation to multiple products.

Mobility studies

Chemical and physical data indicate that zinc pyrithione is essentially non-volatile and unlikely to evaporate from soil or water.

A batch equilibrium study based on US EPA Guidelines of the adsorption and desorption of zinc pyrithione on two soils and two sediments were provided. Significant degradation of zinc pyrithione occurred during the study, hence the results apply to zinc pyrithione and its degradation products, rather than zinc pyrithione alone. The test concentrations used extended above the solubility of copper pyrithione, which may have been formed by transchelation with copper (particularly in the marine sediment tested). Freundlich adsorption and desorption coefficient values obtained from the data indicated a significant degree of adsorption (K_{ads} = ~11-99, K_{des} = 13-202). Adsorption coefficients based on organic carbon content ranged from approximately 780-2350 in the soils and ~3600-10,600 in the sediments, with the corresponding desorption values 870-3290 and 6520-21,800. Hence under the test conditions (which differed significantly between the soils and sediments), zinc pyrithione + degradation products can be classified as slightly mobile to immobile in sediment and as having low to slight mobility in the soils.

Accumulation potential in sediment
Environment Australia concludes that much of the zinc pyrithione released to the environment is likely to degrade in the water column before reaching sediment. Zinc pyrithione may transchelate to less soluble copper pyrithione, but expected concentrations in the environment are likely to remain below the solubility limit for copper pyrithione. Pyrithiones and their degradation products may adsorb to sediment, but residues reaching sediment should continue to degrade, either while still adsorbed or because of desorption and degradation in water. In many natural situations, conditions in sediment are likely to be somewhat anaerobic, favouring more rapid degradation to metabolites lacking the N-oxide. The available studies indicate that mineralisation to CO_2 occurs relatively slowly, but that some formation of residues difficult to extract from soil (hence unlikely to have biological availability and degrading more slowly) occurs and that organic volatiles may be formed under anaerobic conditions.

Bioaccumulation in aquatic organisms
The low K_{OW} (octanol:water coefficient) for zinc pyrithione suggests that this substance is unlikely to bioaccumulate; furthermore, zinc pyrithione and related pyrithiones are likely to degrade rapidly under natural conditions. This was confirmed in a bioconcentration study using carp (*Cyprinus carpio*) and ^{14}C-labelled copper pyrithione (copper pyrithione is likely to be formed from zinc pyrithione in seawater and sediment). This study indicated bioconcentration factors (BCFs) for total radioactive residues of <5 and <50 with water concentrations of 2 µg/L and 0.2 µg/L, respectively. A bioconcentration study with ^{14}C-labelled zinc pyrithione and eastern oyster (*Crassotrea virginica*) also indicated low bioaccumulation potential, with bioconcentration factors of <0.1 found with water concentrations of ~0.05 or 0.50 µg/L. Depuration of ^{14}C-zinc pyrithione residues in exposed oysters occurred relatively slowly (initial depuration half-lives 6.8 or 3.4 days, followed by much slower depuration).

Environmental Toxicity

Avian toxicity
Toxicity tests conducted to US EPA Guidelines showed that zinc pyrithione is moderately toxic to bobwhite quail (*Colinus virginianus*) with acute oral exposure (LD50 = 64 mg/kg nominal concentration) and slightly toxic with subacute dietary exposure (5 day LC50 = 1110 ppm). A similar acute oral exposure test with mallard ducks (*Anas platyrhynchos*) found zinc pyrithione was practically non-toxic (5 day LC50 > 5000 ppm). Various toxic signs were observed, in addition to effects on feed consumption and body weight gain. No Observed Effect Levels (NOELs) were <31.2 ppm (nominal) for quail with acute oral exposure and <275 ppm for both quail and mallard ducks with subacute dietary exposure.

Aquatic toxicity
As in the natural seawater environment copper pyrithione may form by transchelation from zinc pyrithione, toxicity values for copper pyrithione are also relevant. Most tests were

conducted under flow-through conditions, minimising the extent to which degradation of zinc pyrithione or copper pyrithione occurred.

Zinc pyrithione and copper pyrithione

Fish

From acute toxicity tests conducted to US EPA Guidelines, Environment Australia concludes that zinc pyrithione and copper pyrithione are very highly toxic (LC50 < 100 µg ai/L) to highly toxic (LC50 = 100-1000 µg ai/L) to fish. The 96 h LC50 to the most sensitive species tested (fathead minnow, *Pimephales promelas*) was 2.6 µg ai/L for zinc pyrithione and 4.3 µg ai/L for copper pyrithione. The 96 h LC50 to rainbow trout (*Oncorhynchus mykiss*) was 3.2 µg ai/L and to the one estuarine/marine species tested, sheepshead minnow (*Cyprinodon variegatus*), was in the range 200-590 µg/L. The 48 h LC50 to orange killifish (*Oryzias latipes*) according to Japanese guidelines was 27 µg/L. The 96 h LC50 for zinc pyrithione applied in the form of a 48% emulsion was 4 µg ai/L for fathead minnow and ranged from 8 to 34 µg ai/L for brook trout (*Salvelinus fontinalis*), golden shiner (*Notemigonas crysoleucas*), bluegill sunfish (*Lepomis macrochirus*) and channel catfish (*Ictalurus punctatus*). Most mortalities occurring with acute exposure were evident by 24-48 h after exposure commenced.

A 32 day exposure, early life stage study with zinc pyrithione and fathead minnow found a NOEC, LOEC and MATC of 1.22, 2.82 and 1.85 µg/L, respectively, based on embryo survival and mean length of surviving fish at 32 days. The 32 d LC50 to adult fish was approximately 2.48 µg/L, with little increase in toxicity beyond about 10 days and an apparently low acute:chronic toxicity ratio. Thus zinc pyrithione has high chronic toxicity to fathead minnows (NOEC < 10 µg/L). A bioconcentration study with carp (*Cuprinus carpio*) gave some indication of the chronic toxicity of copper pyrithione to this species, which appeared unaffected by up to 8 weeks exposure to copper pyrithione at ~0.2 µg ai/L.

Aquatic invertebrates

Acute toxicity tests conducted to US EPA Guidelines found that zinc pyrithione and copper pyrithione are very highly toxic to aquatic invertebrates, including the waterflea *Daphnia magna*, mysid shrimp (*Americamysis bahia*) and eastern oyster (*Crassotrea virginica*). 48 h EC50 values for zinc pyrithione to *Daphnia magna* in two separate tests were 3.6 µg ai/L and 36 µg ai/L. The 48 h EC50 value for copper pyrithione to *Daphnia magna* was 22 µg ai/L. The 96 h LC50 for zinc pyrithione to mysid shrimp was in the range 1.6-9.4 µg ai/L. The 96 h EC50 (shell growth inhibition) to eastern oyster was 22.4 µg ai/L for zinc pyrithione and 11 µg ai/L for copper pyrithione.

A 21 day chronic exposure/reproductive toxicity study with zinc pyrithione and *Daphnia magna* found a NOEC, LOEC and MATC of 2.7, 5.8 and 4.0 µg/L, respectively, based on the number of young produced and mean length of parent daphnids at 21 days. Thus zinc pyrithione has high chronic toxicity to daphnids (NOEC < 10 µg/L). The 21 d EC50 to parent daphnids was in the range 22-49 µg ai/L, with most effects becoming evident over days 2 to 6 of exposure and a low acute:chronic toxicity ratio.

A study to oil industry test guidelines indicated a 10 d LC50 of 4.4 mg/kg sediment dry weight to the burrowing amphipod *Corophium volutator* for zinc pyrithione added to sediment before exposure. This result was presumably affected by a significant degree of degradation of the originally applied zinc pyrithione.

Algae and aquatic plants
Tests to US EPA guidelines found very high toxicity of zinc pyrithione and copper pyrithione to the freshwater green alga *Selenastrum capricornutum*, with 120 h EC50s of 28 µg ai/L and 35 µg/ai/L, respectively (mean measured concentrations, static conditions). A test to US EPA Guidelines also found very high toxicity of zinc pyrithione to duckweed (*Lemna gibba*), with a 7 d EC50 of 9.6 µg ai/L (flow-through conditions).

Pyrtihione metabolites

The scientific literature suggests that the high microbiological activity of pyrithione biocides is linked to the presence of sulfur attached in the 2-position to the pyridine-N-oxide ring. Various identified metabolites of zinc pyrithione retain a sulfur atom in this position, but in some cases with loss of the oxygen to form a pyridine ring. Limited evidence indicates that much of the toxicity is lost if the N-oxide is removed, despite retention of sulfur at the 2 position (eg 2-mercaptopyridine and pyridine disulfide - see below). The acute toxicity of two major metabolites of pyrithione, pyrithione 2-sulfonic acid and pyridine 2-sulfonic acid and a transient metabolite[2,2'-dithio-bis-pyridine (pyrithione disulfide)] to various freshwater and estuarine/marine species was evaluated in tests to US EPA Guidelines. As evident below, the data clearly indicate much reduced toxicity in the 2-sulfonic acids. Similarly low toxicity is expected with the corresponding sulfinic acids, but no studies of this are available.

Pyrithione disulfide was found very highly toxic to fathead minnow, rainbow trout, *Daphnia magna* and mysid shrimp (96 h LC50 or 48 h EC50 respectively, 30 µg ai/L, 54 µg ai/L, in the range 11-18 µg ai/L, and 6.4 µg ai/L - nominal concentrations), highly toxic to eastern oyster (96 h EC50 = 160 µg/L) and the green alga *Selenastrum capricornutum* (120 h EC50 = 140 µg ai/L), and moderately toxic to the sheepshead minnow (96 h LC50 = 1100 µg ai/L). Pyrithione disulfide has itself been evaluated and/or used as a biocide. Pyrithione 2-sulfonic acid and pyridine 2-sulfonic acid were found slightly toxic (LC50 or EC50 = 10-100 mg/L) to practically non-toxic (LC50/EC50 > 100 mg/L) to the same set of species.

A scientific paper reported studies using the marine diatom *Phaeodactylum tricornutum* as a bioassay technique which indicated 2-mercaptopyridine and pyridine disulfide were toxic at about 3 ppm, about 150 times the 100% inhibitory concentration for pyrithione. Pyrithione 2-sulfonic acid was still less toxic, while pyridine and pyridine-N-oxide were non-toxic at a concentration of 100 ppm.

A 32 day exposure/early life stage study with pyridine-2-sulfonic acid and fathead minnow also indicated no toxic effects at a concentration of 10 µg/L, a value chosen to be above the maximum predicted environmental concentration. A study concluded that rapid binding to the sediment and/or transformation to metabolites considerably lowered the toxicity of zinc pyrithione to the marine copepod *Acartia tonsa*.

Mammals
Zinc pyrithione has moderate mammalian toxicity by acute oral exposure (acute oral LD50 to rats = 269 mg/kg bodyweight) and is practically non-toxic to mammals with dermal exposure (LD50 to albino rabbits > 2000 mg/kg). No information is available specifically with aquatic mammal species.

Microorganisms
Zinc pyrithione and other pyrithione derivatives including some zinc pyrithione metabolites have been tested or used as biocides in a wide range of applications because of their high

toxicity to various microorganisms, including bacteria and fungi (minimum inhibitory concentrations approximately 0.03-0.3 ppm).

Phytotoxicity

Pyrithiones such as sodium pyrithione or zinc pyrithione, or the metabolite pyrithione disulfide, may cause growth retardation of terrestrial higher plants through effects on root growth at concentrations of approximately 1-3 ppm. However, exposure of terrestrial plants to zinc pyrithione or its metabolites as a result of antifoulant use is unlikely to occur, and even in the vicinity of landfill areas, rapid degradation would limit such exposure.

Environmental hazard

Little hazard to terrestrial species is anticipated, as the use as an antifoulant on ships is not expected to result in significant contamination of the terrestrial environment. Birds consuming fish or other marine organisms are unlikely to be affected because zinc pyrithione does not bioaccumulate, hence exposure to zinc pyrithione residues would be minimal. The assessment considers the aquatic hazard from zinc pyrithione and not that from the other active ingredient in the paints, cuprous oxide, uses of which are already widely registered.

Hazard arising during application, maintenance and removal

There is a potential hazard from localised environmental exposure during paint application and during washdown or preparation of existing surfaces for repainting. However, application of the deep sea market product Intersmooth 360 Ecoloflex in commercial slipways and shipyards should facilitate control of environmental exposure during application, maintenance and removal. Waste material would presumably be collected within bunded areas of the slipways/dry-docks involved and disposed of appropriately to approved landfill facilities. Suitable general guidance for environmental precautions in the maintenance and application of vessel antifoulant coatings is provided in the Australian and New Zealand Environment and Conservation Council (ANZECC) Code of Practice for Antifouling and In-water Hull Cleaning and Maintenance. Label advice stipulates that waterways should not be contaminated with paint, dust and scrapings or used containers and some protection is also provided by relevant State and local government legislation.

Hazard from treated vessels

The potential for accumulation of zinc pyrithione in aquatic systems was modelled using a tidal prism model for a worst case harbour situation. This model assumes complete mixing due to the tide and a continuous loading of the contaminant, and estimates the steady state concentration of the test substance given the treated surface area, release rate and low and high tide volumes and extent of degradation per tidal cycle. It was assumed that this harbour was continually occupied by three vessels, each with wetted areas of ~10,000 m^2 and each treated with International Intersmooth 360 Ecoloflex according to the maker's specifications. This is a high wetted area relative to the harbour volume, well above that in busy Australian port areas, such as Swanson Dock in Victoria. A very much worst case steady state leach rate for zinc pyrithione of 5 $\mu g/cm^2/day$ (in practice, the steady state leach rate is likely to be less than 50% of this) and zinc pyrithione decay rate of 70% degradation per tidal cycle were assumed. The latter is again a worst case situation in that the likely rapid photolysis in many situations during daylight is not included, but use of this overall value allows for situations where sunlight is inhibited, eg by shading, turbidity and cloudy weather.

According to the model scenario, the steady state concentration predicted (Css) in the harbour was 0.113 µg/L. Evaluation of the hazard based on the most sensitive species in chronic/reproductive exposure tests (fathead minnow) indicates an acceptable hazard, even in this exaggerated worst case situation (chronic NOEC = 1.22 µg/L, with ratio of Css:NOEC ≈ 0.10).

Conclusions

Environment Australia concludes that zinc pyrithione released into water from painted surfaces is unlikely to accumulate in water or sediment and is not expected to result in primary poisonings of fish or other aquatic species in water or sediment, while exerting a toxic effect on treated surfaces. Application in appropriate facilities according to the Australian and New Zealand Environment and Conservation Council (ANZECC) Code of Practice for Antifouling and In-water Hull Cleaning and Maintenance and local State regulations should ensure adequate protection to the environment during application and maintenance.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Fouling organisms- such as barnacles, molluscs and algae- on ships hulls can have very significant effects on the performance and durability of a vessel. This includes increased fuel consumption and/or reduced speed. Increased fuel consumption has potential greenhouse effects and adds significantly to operating costs. Ships may need to be dry docked for cleaning more frequently and this also substantially increases operating costs. Fouling organisms may also be carried from one location to another on ships hulls and become pests in new locations.

The main products used on commercial shipping to control fouling have been organotin-based biocides, particularly tributyltin (TBT). TBT is highly toxic and has adverse impacts on the marine environment. Under *Australia's Ocean Policy,* the Commonwealth Government will be supporting the International Maritime Organisation's global ban on TBT products. It is anticipated that this will involve a ban on the application of TBT antifoulings to commercial ships from 1 January 2003.

Ecoloflex is TBT-free and is therefore an alternative to the TBT-containing products.

Efficacy

Data from trials under Australian conditions, in temperate and tropical waters, were provided. This included a series of trials using rafts and rotor tanks, patch trials on five Royal Australian Navy vessels and full hull trials on three vessels.

These trials take into account the likely differences in fouling fauna and flora across the temperate and tropical waters. The fouling data provided consisted of a series of scores. In addition, ablation rates were provided. The data were presented across all test systems including the product and these included an untreated control. The data are considered to provide a meaningful indication of the efficacy of the product. Results were directly linked to a series of clear photographs, which reinforce the data provided. The results indicate that the product will be effective for the claimed purposes.

Results from a panel trial conducted in Singapore were also submitted but these were considered to be of limited value as there was no replication and there was a wide range of scores on the various categories of fouling organisms. The paint was also applied at a greater thickness to that proposed on the label.

Safety

Safety to the marine environment is addressed in the Environmental Assessment section of this PRS. The paint is not expected to be damaging to the hull of ships, and is in use on ships painted overseas.

LABELLING REQUIREMENTS

The product will be available in two colours. The proposed labels for each colour are shown on the following pages.

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product.
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer.
Chronic	Of long duration.
Desorption	Removal of an absorbed material from a surface.
Efficacy	Production of the desired effect.
Formulation	A combination of both active and inactive constituents to form the end use product.
Genotoxicity	The ability to damage genetic material
Hydrophobic	Water repelling
Leaching	Removal of a compound by use of a solvent.
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient.
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light.
Photolysis	Breakdown of chemicals due to the action of light.
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

Suggested Further Reading

Environment Australia (1998) *Australia's Ocean Policy*, http://www.oceans.gov.au/aop/policy/aop/contents.html

National Occupational Health and Safety Commission (1994) *Control of Workplace Hazardous Substances* [NOHSC:1005(1994), 2007(1994)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1995) *Exposure Standards for Atmospheric Contaminants in the Occupational Environment*, *Guidance Note* [NOHSC:3008(1995)] and *National Exposure Standards* [NOHSC: 1003(1995)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1999a) *List of Designated Hazardous Substances* [NOHSC:10005(1999)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1999b) *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(1999)], AusInfo, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, NRA, Canberra.

NRA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of zinc pyrithione in the product International Intersmooth 360 Ecoloflex Antifouling, please fill in this form and send it, along with payment of $30 to:

David Hutchison
Agvet Chemicals Registration Section
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
David Hutchison at 02 6272 3218.

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Public Release Summary
on

Evaluation of the new active

ZINC PYRITHIONE

in the product

INTERNATIONAL
INTERSMOOTH 360 ECOLOFLEX
ANTIFOULING

National Registration Authority
for Agricultural and Veterinary Chemicals

October 2001

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FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies, including the Department of Health and Family Services (Chemicals and Non-prescription Drug Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (Worksafe Australia) and State departments of agriculture and environment.

The NRA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for all products containing new active ingredients and for all proposed extensions of use for existing products.

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series.*

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library Ground Floor, 22 Brisbane Avenue, Barton, ACT.

The NRA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Executive Manager—Registration, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT$_{50}$	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E$_b$C$_{50}$	concentration at which the biomass of 50% of the test population is impacted
EC$_{50}$	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E$_r$C$_{50}$	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K$_{oc}$	Organic carbon partitioning coefficient
L	Litre
LC$_{50}$	concentration that kills 50% of the test population of organisms
LD$_{50}$	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion

PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
μg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

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INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING, which contains the active constituents zinc pyrithione and copper oxide. The product is proposed to be used to prevent fouling of commercial shipping vessels.

Although copper oxides are frequently used in antifouling paint products, the use of zinc pyrithione for this purpose is new in Australia. Zinc pyrithione is in widespread use as the active ingredient in some anti-dandruff shampoo preparations. The key focus of this PRS is on the zinc pyrithione component of the product.

Responses to this Public Release Summary will be considered prior to registration of the product. They will be taken into account by the NRA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

Written comments are invited and should be submitted by **19 November 2001,** addressed to:

Colin Byrnes
AgVet Chemicals Evaluation Section
National Registration Authority
PO Box E240
KINGSTON ACT 2604

Phone 02 6722 4850 Fax 02 6272 3218

Applicant :

Akzo Nobel Pty Limited

Product details:

INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING (Ecoloflex) is a tin-free self polishing copolymer antifouling paint. It will be available in two colours, brown and dark red. The product contains 66g/L zinc pyrithione and 619g/L (brown colour) or 626g/L (dark red colour) cuprous oxide. The product will be marketed to control marine fouling on commercial ships.

The active constituent zinc pyrithione is manufactured in the USA and cuprous oxide in Norway. The product will be formulated in Australia.

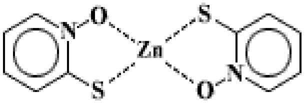
Ecoloflex is currently registered in the United Kingdom, Sweden, Malta, USA, Hong Kong and New Zealand.

CHEMISTRY AND MANUFACTURE

Active constituent

The chemical active constituent zinc pyrithione has the following properties:

Common name (ISO):	Zinc pyrithione
Chemical name:	2-pyridinethiol-1-oxide, zinc salt
CAS Registry Number:	13463-41-7
Empirical formula:	$C_{10}H_8N_2O_2S_2Zn$
Molecular weight:	317.68 g/mol
Physical form:	Powder
Colour:	Off-white to tan
Odour:	Slight amine
Melting point:	Purified substance 267°C (no visual signs of decomposition)
Octanol/water partition coefficient:	log P_{OW} = 0.90 at 25°C
Vapour pressure at 25°C:	Not measurable ($<1.0 \times 10^{-6}$ Pa)
Structural formula:	



Formulated product

The product International Intersmooth 360 Ecoloflex Antifouling has the following properties:

Active constituents:	619 g/L cuprous oxide (brown) or 626g/L cuprous oxide (dark red), 66g/L zinc pyrithione
Formulation type:	Self polishing copolymer antifouling paint
Appearance:	Dark red or dark brown coloured liquid
Specific gravity:	1.56
Flash point:	15°C

TOXICOLOGICAL ASSESSMENT

EVALUATION OF TOXICOLOGY

The toxicological database for zinc pyrithione, which consists primarily of toxicity tests conducted using animals, is quite extensive. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

Acute Studies

Zinc pyrithione showed moderate oral toxicity in rats (LD_{50} = 221 mg/kg bw) but low in monkeys (LD_{50} >1000 mg/kg bw). Acute inhalation toxicity was moderate in rats with an LC_{50} concentration in excess of 610 mg/m^3. Whilst there was no skin irritation or sensitisation observed in rabbits and guinea pigs respectively, eye administration was corrosive in rabbits resulting in frank iridial tissue destruction. In rabbits whose eyes were washed with water after a 30-sec exposure there were similar but less severe reactions although still classified as corrosive.

Toxicity studies were not supplied on Ecoloflex as a formulated paint. Studies have been supplied on International Paints Micron Optima Advanced High Strength Copper Oxide Antifouling, containing zinc pyrithione at between 39.4 and 39.6 g/kg and copper oxides at between 417 and 465 g/kg. This paint had low oral (LD_{50} >3000 mg/kg bw) and dermal (LD_{50} >2000 mg/kg bw) toxicity in rats and rabbits respectively. No dermal irritation and sensitisation was observed in rabbits and guinea pigs respectively. Using the conventional 0.1 mL application volume it was a severe irritant but by reducing both the application volume (0.01 mL) and the zinc pyrithione concentration to 1.8% (w/w) the irritation was reduced to moderate. There are significant differences in the non-active constituents of this product and Ecoloflex so these data of limited relevance.

Copper salts have a long history of use in a variety of agricultural and industrial applications and have been assessed toxicologically on a number of occasions previously. The toxicity of copper salts depends largely on the proportion of free copper ion. A lesser degree of acute toxicity is consequently seen with the more insoluble salts eg copper oxides, than those with a higher degree of aqueous solubility eg copper sulfate. Copper irritates the nerve endings in the stomach and initiates the vomiting reflex. This induction of prompt emesis in higher animals would normally limit its oral toxicity, however in a hydrocarbon solvent base this property heightens the risk of aspiration of ingested product with a consequent risk of lipid pneumonitis.

Short-Term Studies

Zinc pyrithione in gelatine capsules was orally administered to cynomolgus monkeys daily for 14 or 28 days. In the 14-day study, treatment at 10, 20, 40 or 80 mg/kg bw/day resulted in haemorrhaging of the stomach mucosa and bodyweight loss at the highest tested dose. In the 28-day study, treatment at 0, 5.5, 11 or 22 mg/kg bw, caused a death at the highest dose. Food consumption and bodyweight gain was decreased at the highest dose together with reduced haematocrit, haemoglobin concentration and erythrocyte count. An increased concentration of ketone bodies and decreased pH of the urine was also observed. These changes were either absent or had improved after a 14-day recovery period.

In a 90-day study, rats were fed zinc pyrithione in the diet at concentrations of 0, 5, 25 or 125 ppm. Clinical signs first observed during the second week at 125 ppm were a depressed respiratory rate and the onset of progressively restricted movement of the hind limbs which finally resulted in almost complete paralysis. Other changes at 125 ppm were related to severe weight loss and dehydration, resulting from the paralysis. Based on the deaths of nearly all the rats at 125 ppm (from dehydration and/or starvation) and the reduced bodyweight observed at 25 ppm in females, the NOEL for this study was 5 ppm (0.35 mg/kg bw/day for males and 0.39 mg/kg bw/day for females).

Daily dermal application of zinc pyrithione to rats at 0, 20, 100 or 1000 mg/kg bw/day for 90 days revealed slight skin irritation, bodyweight loss and reduced food intake at 1000 mg/kg bw/day. For females at 1000 mg/kg bw/day there was an increase in relative kidney weight and some had mineralisation of the kidneys. Increased leucocyte counts and reduced erythrocyte and haematocrit was also observed at the highest dose.

Whole-body exposure to an aerosol at 0, 0.5, 2.5 or 10 mg/m^3 for 6 h/day, 5 days/week over 13 weeks resulted in deaths at 2.5 and 10 mg/m^3, reduced bodyweight gain at 10 mg/m^3 and reduced creatinine at 10 mg/m^3. A dose-related increase in mean absolute lung/mainstream bronchi weight, lung/mainstream bronchi weight relative to body weight and lung/mainstream bronchi weight relative to brain weight was also observed at 2.5 and 10 mg/m^3. These weight increases were accompanied by inflammation of interstitial tissue and pulmonary artery hypertrophy.

Zinc pyrithione given to monkeys at 0, 0.5, 2 or 8 mg/kg bw/day by stomach tube for 90 days induced some vomiting at 2 and 8 mg/kg bw/day within 1-3 h on the first few treatment days. Appropriate monitoring for adverse changes failed to reveal any other effects. Hence, the NOEL for the study was 8 mg/kg bw/day.

Long-Term Study

Sodium pyrithione at 0, 0.5, 1.5 or 5 mg/kg bw/day was administered to rats by gavage in a two-year chronic and oncogenicity study. After 12 weeks at 5 mg/kg bw/day, an appreciable reduction in bodyweight gain necessitated the high dose level be reduced to 3.5 mg/kg bw/day. There was reduced bodyweight gain at 3.5 mg/kg bw/day and hind limb muscle wastage at 1.5 and 3.5 mg/kg bw/day. Nerve fibre degeneration of the spinal cord and sciatic nerve was slightly increased at 3.5 mg/kg bw/day. Fibre degeneration in the hind limb skeletal muscle was increased in all rats at 3.5 mg/kg bw/day and to a lesser extent in females at 1.5 mg/kg bw/day. There was an increase in peripheral retinal atrophy in males and females at 3.5 mg/kg bw/day and at 1.5 mg/kg bw/day in females. There was no treatment-related increase in the incidence of tumours. Therefore, under the conditions of this study, the NOEL was 0.5 mg/kg bw/day.

Reproduction and Developmental Studies

In a 2-generation reproduction study, rats were given sodium pyrithione at 0, 0.5, 1.5 or 4.5 mg/kg bw/day by gavage. Owing to an appreciable reduction in bodyweight gain the highest dose was reduced after 3 weeks to 3.5 mg/kg bw/day for the rest of the study. Rats were maintained for 2 generations, with the first litter used for breeding. In the F0 rats, salivation after dosing was seen in all treated groups, with a dose-related time of onset and severity. At 3.5 mg/kg bw/day a number of females showed hind-limb paralysis in the F0 generation; this was not seen in F1 animals. Body weight gain was statistically significantly decreased in both males and females at 3.5 mg/kg bw/day in the F0 generation, and in females at this dose in the F1 generation. Fertility was decreased at 3.5 mg/kg bw/day in the F0 generation, with the number of rats successfully mating and the number of rats pregnant decreased in comparison to controls. There was no effect on gestational length, the number of pups born or pup bodyweight seen. No effects on fertility were seen in the F1 generation. There was no increase in the incidence of fetal malformations in either generation. On postmortem examination, there was an increase in the incidence of hind-limb muscle atrophy at 3.5 mg/kg bw/day in females in both generations. On histopathological examination, there was an increase in atrophy of skeletal muscles at 3.5 mg/kg bw/day in the F0 generation, and from 1.5 mg/kg bw/day in the F1 generation. Salivation occurred in some F0 rats at 0.5 mg/kg bw/day but none in the F1 generation suggesting that this dose level is a probable NOEL.

When pregnant rats had zinc pyrithione topically applied at 0, 2.5, 7.5 or 15 mg/kg bw/day (with or without prevention from ingestion) from gestation days 6 to 15 there was a reduction in bodyweight gain at 7.5 or 15 mg/kg bw/day when ingestion was not prevented. Hind-limb paralysis among dams and reductions in fetal weight were also observed at 15 mg/kg bw/day. These effects were not seen when ingestion was prevented. With oral treatment at the same doses, bodyweight gain was reduced, paralysis occurred and fetal weight was reduced at 7.5 and 15 mg/kg bw/day. There was also an increase in skeletal variations at 15 mg/kg bw/day.

Pregnant rats given doses of 0, 0.75, 3 or 15 mg/kg bw/day by gavage on days 6–15 of gestation had treatment-related effects at 3 and 15 mg/kg bw/day. These were decreased maternal bodyweight gain, an increase in salivation immediately after dosing, increased resorptions, reduced uterine weight and increased fetal malformations. The NOEL was 0.75 mg/kg bw/day for both maternal and developmental toxicity.

Pregnant rabbits given doses of 0, 0.5, 1.5 or 3 mg/kg bw/day on days 6-18 of gestation had an increased the number of resorptions, reduced uterine weight and increased fetal malformations at 1.5 and 3 mg/kg bw/day, hence the NOEL for developmental toxicity was 0.5 mg/kg bw/day. Although food consumption was reduced at 1.5 and 3 mg/kg bw/day there was no corresponding bodyweight loss (after subtracting the weight of the gravid uterus), hence the NOEL for maternal toxicity was 1.5 mg/kg bw/day based on a clinical sign (ie. an increased incidence of red fluid in the refuse pan for does at 3 mg/kg bw/day).

Zinc pyrithione administered orally to pregnant rabbits at 5, 10 or 20 mg/kg bw/day on days 6 to 18 of gestation caused a dose-related incidence of death with no survivors at 20 mg/kg bw/day. Survivors at 5 and 10 mg/kg bw/day had reduced bodyweight gain and an increased number of resorptions. In a second study at 0, 1, 2.5 or 5 mg/kg bw/day there were no deaths but reduced bodyweight gain was observed at 2.5 and 5 mg/kg bw/day. The number of resorptions was increased at 2.5 and 5 mg/kg bw/day and the number of live fetuses at 5 mg/kg bw/day was reduced. There were no adverse effects on fetal development that could not be linked with maternal toxicity. The NOEL for both maternal and developmental toxicity was 1 mg/kg bw/day.

Genotoxicity

Zinc pyrithione was found to be negative in mutation tests in bacteria and Chinese hamster ovary cells. Similarly, no chromosomal aberration was observed in human lymphocytes incubated *in vitro* in the presence of zinc pyrithione or in lymphocytes harvested from monkeys following oral administration in a 28-day toxicity study. A mouse micronucleus assay also yielded negative results.

Human metabolite study

A study of plasma metabolites in human volunteers from a chemical factory producing pyrithiones identified 2-(methylsulfonyl)pyridine as the only metabolite in human serum and proposed that this metabolite could be used as a marker for pyrithione exposure.

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

On the basis of its toxicity and likely use, the NDPSC has included zinc pyrithione in schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). Copper oxides when included in marine paints are exempted from the requirements of poisons scheduling. There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

Since the product, INTERNATIONAL INTERSMOOTH ECOLOFLEX 360 ANTIFOULING, is to be used as an antifouling paint on marine vessels, an ADI for zinc pyrithione does not need to be established.

METABOLISM AND TOXICOKINETICS ASSESSMENT

Metabolism and Toxicokinetics

An excretion study with [^{65}Zn]zinc pyrithione (ZPT) indicated that the pyrithione portion of the molecule is metabolised separately to the zinc portion with the zinc being split off in the stomach and excreted in faeces. A study with a single dose of 1 mg/kg bw [^{14}C]ZPT showed extensive absorption of the pyrithione portion and that most radioactivity (63%, 68%, 84% and 82%) was excreted in the urine during the first 24 h for rats, rabbits, dogs and monkeys, respectively with a further 10–14% excreted in the subsequent 5 days. Excretion in faeces over 6 days in this study was 3%, 20%, 6% and 6%, respectively (with the higher level in rabbits probably due to urine contamination). In the rat, 6% radioactivity remained in the carcass at 6 days after dosing (other species not tested). In another study in rats with single oral doses of 0.5 and 12.5 mg/kg bw zinc pyrithione, radioactivity recovered in the urine, faeces and carcass over 11 days was approximately 80%, 18% and 1%, respectively, with no difference between the 2 doses. The only tissues with more than 0.009% of dose at 11 days were kidney (0.01–0.02%, liver 0.05–0.09% and lungs (0.001–0.01%). A further study showed a similar pattern of excretion for intravenous and oral doses in rats.

Analysis of urinary metabolites showed a similar pattern for each species with 3 main metabolites: 2-pridinethiol-1-oxide-*S*-glucoside, 2-pridinethiol-*S*-glucuronide and 2-pridinethiol-1-oxide-*S*-glucuronide. 2-Pridinethiol-1-oxide-*S*-glucuronide was the most abundant (64%, 35%, 32% and 66% in rats, rabbits, dogs and monkeys, respectively). For rat urine, after the first day another metabolite, 2-(methylsulfonyl)pyridine, formed by the oxidation of the sulfur and reduction of the *N*-oxide of pyrithione, became more prominent. The preferred biotransformation pathway appears to involve conjugation of the 2-thiol group of the pyridine ring (with glucuronide conjugation favoured).

Dermal absorption studies in pigs showed that zinc pyrithione is very poorly absorbed through skin (<10% of dose). A maximum of 5% of the applied dose was recovered in the urine and by 48 h the levels in blood, faeces, and urine were essentially at background levels.

RESIDUES ASSESSMENT

The product is intended for application to the hulls of vessels. It is not intended for use in situations (such as aquaculture) where food for human consumption is being produced. An ADI has not been established. No detailed assessment of residues in food arising from the uses proposed for the product is considered necessary.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

The product is intended for application to the hulls of vessels. It is not intended for use in situations (such as aquaculture) where food for human consumption is being produced. No detailed assessment of overseas trade aspects of residues in food arising from the uses proposed for the product is therefore considered necessary.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

INTERNATIONAL INTERSMOOTH 360 ECOLOFLEX ANTIFOULING (ECOLOFLEX) is a self-polishing copolymer antifouling paint product containing zinc pyrithione and cuprous oxide.

Zinc pyrithione is not on the NOHSC *List of Designated Hazardous Substances.*
It is of moderate acute oral and inhalation toxicity in rats, and low dermal toxicity in rats.
Zinc pyrithione was not a skin irritant in rabbits, nor a skin sensitiser in guinea pigs, but was corrosive to rabbit eyes.

The applicant has allocated the following risk phrases to zinc pyrithione:

R22 Harmful if swallowed
R23 Toxic by inhalation
R38 Irritating to skin
R41 Risk of serious damage to eyes

Substances containing zinc pyrithione at 10% or more are considered hazardous.

Cuprous oxide is on the NOHSC *List of Designated Hazardous Substances.* All products containing at least 25% of cuprous oxide are considered hazardous.

The following risk phrase is allocated to cuprous oxide:

R22 Harmful if swallowed

Ecoloflex contains a significant amount of compounds that are at least slight skin irritants and nearly 30% of the product consists of substances of moderate skin irritancy. The product also contains a high level of substances with severe to corrosive eye irritancy and the remainder of the ingredients are at least slight irritants, so the product is likely to be a severe eye irritant.

Based on the toxicological profile of the individual ingredients, the product is considered likely to have low acute oral and dermal toxicity, to be a severe eye and a moderate skin irritant and the product vapour is likely to be irritant to the respiratory tract.

The formulated paint is determined to be a hazardous substance based on its ocular effects, the amount of cuprous oxide(>25% cuprous oxide) and organic solvent.

Use and exposure

The formulated product, Ecoloflex, is intended for use on commercial/naval marine vessels, which will be painted infrequently and thus require an antifouling paint with a longer life than that of a smaller pleasure craft. Categories of workers likely to be exposed to the product are professional painters. The product is likely to be used primarily in an industrial setting, i.e. professional shipyards, and the applicant has indicated that the product will not be marketed to the general public.

Ecoloflex will mainly be applied by airless spray, though brush or roller may also be used. The main route of exposure to the product will be dermal, ocular and inhalation. During preparation and painting, workers could be directly contaminated on the skin and in the eyes by drips, splashes and spray mist. Exposure can also arise from accidental splatters during pouring and when cleaning equipment. Since Ecoloflex is capable of causing severe eye irritation, and moderate skin irritation, protective equipment such as cotton overalls, impervious footwear and eye protection are recommended to protect the eyes and the skin. As Ecoloflex contains organic solvents including xylene, Nitrile gloves are recommended. . A full facepiece respirator which has the advantage of protecting eyes and facial skin is recommended. Respirators are required to prevent inhalation exposure.

Workers will be exposed to organic solvents that are present in the product. Inhalation of these solvents may cause central nervous system effects such as headaches, dizziness, nausea and drowsiness, and in extreme cases loss of consciousness. Prolonged or frequent inhalation of solvents may result in liver or kidney damage.

Recommendations for safe use

Users should follow the instructions and Safety Directions on the product label.

Safety Directions for Ecoloflex include the following:

Full facepiece respirator with combined dust and gas cartridge (*When opening the container and using the product*).

Cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length nitrile gloves and impervious footwear (*When opening the container and using the product*).

The Personal Protective Equipment recommended should meet the relevant *Standards Australia* Standards.

Material Safety Data Sheet

Akzo Nobel Pty Limited has produced MSDS for Ecoloflex. This contains information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that their employees have ready access to it.

Conclusion

Ecoloflex can be used safely if handled in accordance with the instructions on the product label.

ENVIRONMENTAL ASSESSMENT

Environmental Fate

Hydrolysis

A study to US EPA Guidelines of hydrolysis at 25°C in the dark indicated that zinc pyrithione hydrolyses slightly in sterile buffers at pH 5, 7 and 9 and in artificial seawater solution at pH 8.2 (estimated half-lives 96-123 days extrapolated from the 30 day incubation period). Of the six metabolites detected, only which two exceeded 10% of the starting dose and were identified as pyrithione disulfide and pyrithione sulfinic acid. It may be that hydrolysis of pyrithione added as zinc pyrithione occurs at a greater rate than indicated in this study due to transchelation to copper pyrithione, which has been reported to hydrolyse with a half-life of 11.9 days at pH 9 and 19 days in sterile synthetic seawater.

Photolysis

An aqueous photolysis study based on US EPA Guidelines was provided (25°C, 12 h light:12 h dark cycles from a lamp simulating natural sunlight wavelengths). This study indicated that photolysis of zinc pyrithione in pH 9 buffer or artificial seawater at pH 8.2 occurred very rapidly (first order half-life from the first hour of incubation = ~13-18 minutes). In contrast, similarly slow degradation rates to those in the hydrolysis study were found in samples incubated in the dark (half-lives extrapolated from 30 days of incubation = 83-91 days). Several degradates were found of which four reached concentrations >10% of applied and were identified (pyridine sulfinic acid, pyridine sulfonic acid, pyridine disulfide and the pyridine/pyrithione mixed disulfide). Some degradates occurred with light exposure, but not in the dark.

An earlier scientific paper also reported rapid degradation of related pyrithione biocides (pyrithione, sodium pyrithione, pyrithione disulfide and a tertiary-butylamine pyrithione derivative, generally tested at 100 ppm) in seawater at a range of pHs exposed to sunlight. The experiments reported in this paper indicated that photodegradation was much slower if the water was deoxygenated. A more recent scientific paper has claimed that rapid photodegradation of zinc pyrithione only occurs at pH < 6, but this result is quite inconsistent with other evidence.

Aquatic metabolism & die-away studies

A series of aerobic and anaerobic aquatic metabolism studies to US EPA Guidelines were provided with zinc pyrithione and the closely related substance copper pyrithione. The latter was examined because it forms readily in natural waters and sediments through transchelation with Cu^{2+} ions. Similar reactions are possible with other heavy metals, but the Cu product evidently dominates in saltwater/marine sediment systems, possibly due to reduced availability of metal ions such as Fe^{3+} through complexation with hydroxide ions. Studies with zinc pyrithione using freshwater/river and/or saltwater/marine sediment systems at an initial concentration of 3 ppm suggested dissipation was affected by precipitation of copper pyrithione, which is much less soluble than zinc pyrithione. Hence a lower concentration of 0.05 ppm zinc pyrithione or copper pyrithione was used for later studies, which were conducted in saltwater/marine sediment systems only. The duration of incubation was 30 or 64 days in the aerobic studies and 30, 90 or 182 days in the anaerobic studies.

These studies indicated very rapid initial degradation in both fresh- and saltwater systems of pyrithione applied as either zinc pyrithione or copper pyrithione (DT50 = 13 minutes to 0.89 days under aerobic conditions, DT50 < 0.96 hours under anaerobic conditions). This was followed by much slower degradation, presumably of substance adsorbed to sediment (DT90 = 1.3-34 days under aerobic conditions, 2.8-20 hours under anaerobic conditions). Thus degradation in sediment under anaerobic conditions (common in sediment under natural conditions) was evidently much faster than under aerobic conditions.

A number of metabolites containing the pyrithione and/or pyridine moieties were identified in the aerobic studies at peak concentrations >10% of the applied concentration of zinc pyrithione or copper pyrithione in one or more studies. These included pyrithione sulfinic acid, pyrithione sulfonic acid, M3 and pyridine sulfonic acid (maximum recorded values respectively, 33, 46, 35, 41 and 25% of applied substance). Although pyrithione disulfide was identified in the early studies conducted at 3 ppm, it was absent in any of the other studies conducted at 0.05 ppm. With zinc pyrithione at 3 ppm, pyrithione sulfonic acid was formed to a significant extent in the marine system (peak 15% of the applied dose), but not in the freshwater system (peak ~1% of the applied dose).

The same metabolites also occurred to some extent (peaks 7-31% of the applied dose) in one or more of the anaerobic studies. However, several other metabolites reached >10% of the applied dose in one or more of the anaerobic studies, including mercaptopyridine, pyridine sulfinic acid, pyridine sulfonic acid, pyridine disulfide and the mixed (pyridine and pyrithione) disulfide (maximum recorded values respectively, 78, 57, 23, 12 and 16% of applied substance).

In most cases $^{14}CO_2$ occurred to only a limited extent (<1-2% of applied radioactivity by 30-90 days), with the exception of the freshwater/river sediment system under aerobic conditions, where $^{14}CO_2$ evolution reached ~12% of applied radioactivity after 30 days of incubation. ^{14}C residues remaining in sediment after solvent extraction reached ~12-64% of applied radioactivity in the various tests.

Danish aerobic and anaerobic aquatic metabolism studies found a similar range in metabolites, with $^{14}CO_2$ evolution reaching ~3-5% of applied radioactivity after 42 or 56 days incubation respectively, under aerobic or anaerobic conditions.

"Die-away" studies with zinc pyrithione and copper pyrithione in seawater without sediment incubated in the dark showed conversion of ~50% of applied zinc pyrithione to copper pyrithione within 24 hours, and a half-life of about 4 days for both compounds after a 2-3 day induction period. Photolysis presumably accounted for rapid initial degradation (half-life = ~25 minutes at ~10°C) in another die-away study with fresh pond water in floating containers exposed to sunlight, much faster than similar samples kept in the dark (half-life = ~7.5 h).

In a further study with river water, sewage influent and a 1:5 mixture of influent and river water the calculated half-lives were, respectively, 15 h, 7 h and 11 h, compared to 23 h for sterile influent. Evidence from this study suggested that zinc pyrithione was rapidly adsorbed onto particulate matter present in solution, rapidly removing it from ready availability in solution, after which microbial and/or chemical degradation led to rapid degradation to multiple products.

Mobility studies

Chemical and physical data indicate that zinc pyrithione is essentially non-volatile and unlikely to evaporate from soil or water.

A batch equilibrium study based on US EPA Guidelines of the adsorption and desorption of zinc pyrithione on two soils and two sediments were provided. Significant degradation of zinc pyrithione occurred during the study, hence the results apply to zinc pyrithione and its degradation products, rather than zinc pyrithione alone. The test concentrations used extended above the solubility of copper pyrithione, which may have been formed by transchelation with copper (particularly in the marine sediment tested). Freundlich adsorption and desorption coefficient values obtained from the data indicated a significant degree of adsorption (K_{ads} = ~11-99, K_{des} = 13-202). Adsorption coefficients based on organic carbon content ranged from approximately 780-2350 in the soils and ~3600-10,600 in the sediments, with the corresponding desorption values 870-3290 and 6520-21,800. Hence under the test conditions (which differed significantly between the soils and sediments), zinc pyrithione + degradation products can be classified as slightly mobile to immobile in sediment and as having low to slight mobility in the soils.

Accumulation potential in sediment
Environment Australia concludes that much of the zinc pyrithione released to the environment is likely to degrade in the water column before reaching sediment. Zinc pyrithione may transchelate to less soluble copper pyrithione, but expected concentrations in the environment are likely to remain below the solubility limit for copper pyrithione. Pyrithiones and their degradation products may adsorb to sediment, but residues reaching sediment should continue to degrade, either while still adsorbed or because of desorption and degradation in water. In many natural situations, conditions in sediment are likely to be somewhat anaerobic, favouring more rapid degradation to metabolites lacking the N-oxide. The available studies indicate that mineralisation to CO_2 occurs relatively slowly, but that some formation of residues difficult to extract from soil (hence unlikely to have biological availability and degrading more slowly) occurs and that organic volatiles may be formed under anaerobic conditions.

Bioaccumulation in aquatic organisms
The low K_{OW} (octanol:water coefficient) for zinc pyrithione suggests that this substance is unlikely to bioaccumulate; furthermore, zinc pyrithione and related pyrithiones are likely to degrade rapidly under natural conditions. This was confirmed in a bioconcentration study using carp (*Cyprinus carpio*) and ^{14}C-labelled copper pyrithione (copper pyrithione is likely to be formed from zinc pyrithione in seawater and sediment). This study indicated bioconcentration factors (BCFs) for total radioactive residues of <5 and <50 with water concentrations of 2 µg/L and 0.2 µg/L, respectively. A bioconcentration study with ^{14}C-labelled zinc pyrithione and eastern oyster (*Crassotrea virginica*) also indicated low bioaccumulation potential, with bioconcentration factors of <0.1 found with water concentrations of ~0.05 or 0.50 µg/L. Depuration of ^{14}C-zinc pyrithione residues in exposed oysters occurred relatively slowly (initial depuration half-lives 6.8 or 3.4 days, followed by much slower depuration).

Environmental Toxicity

Avian toxicity
Toxicity tests conducted to US EPA Guidelines showed that zinc pyrithione is moderately toxic to bobwhite quail (*Colinus virginianus*) with acute oral exposure (LD50 = 64 mg/kg nominal concentration) and slightly toxic with subacute dietary exposure (5 day LC50 = 1110 ppm). A similar acute oral exposure test with mallard ducks (*Anas platyrhynchos*) found zinc pyrithione was practically non-toxic (5 day LC50 > 5000 ppm). Various toxic signs were observed, in addition to effects on feed consumption and body weight gain. No Observed Effect Levels (NOELs) were <31.2 ppm (nominal) for quail with acute oral exposure and <275 ppm for both quail and mallard ducks with subacute dietary exposure.

Aquatic toxicity
As in the natural seawater environment copper pyrithione may form by transchelation from zinc pyrithione, toxicity values for copper pyrithione are also relevant. Most tests were

conducted under flow-through conditions, minimising the extent to which degradation of zinc pyrithione or copper pyrithione occurred.

Zinc pyrithione and copper pyrithione

Fish

From acute toxicity tests conducted to US EPA Guidelines, Environment Australia concludes that zinc pyrithione and copper pyrithione are very highly toxic (LC50 < 100 µg ai/L) to highly toxic (LC50 = 100-1000 µg ai/L) to fish. The 96 h LC50 to the most sensitive species tested (fathead minnow, *Pimephales promelas*) was 2.6 µg ai/L for zinc pyrithione and 4.3 µg ai/L for copper pyrithione. The 96 h LC50 to rainbow trout (*Oncorhynchus mykiss*) was 3.2 µg ai/L and to the one estuarine/marine species tested, sheepshead minnow (*Cyprinodon variegatus*), was in the range 200-590 µg/L. The 48 h LC50 to orange killifish (*Oryzias latipes*) according to Japanese guidelines was 27 µg/L. The 96 h LC50 for zinc pyrithione applied in the form of a 48% emulsion was 4 µg ai/L for fathead minnow and ranged from 8 to 34 µg ai/L for brook trout (*Salvelinus fontinalis*), golden shiner (*Notemigonas crysoleucas*), bluegill sunfish (*Lepomis macrochirus*) and channel catfish (*Ictalurus punctatus*). Most mortalities occurring with acute exposure were evident by 24-48 h after exposure commenced.

A 32 day exposure, early life stage study with zinc pyrithione and fathead minnow found a NOEC, LOEC and MATC of 1.22, 2.82 and 1.85 µg/L, respectively, based on embryo survival and mean length of surviving fish at 32 days. The 32 d LC50 to adult fish was approximately 2.48 µg/L, with little increase in toxicity beyond about 10 days and an apparently low acute:chronic toxicity ratio. Thus zinc pyrithione has high chronic toxicity to fathead minnows (NOEC < 10 µg/L). A bioconcentration study with carp (*Cuprinus carpio*) gave some indication of the chronic toxicity of copper pyrithione to this species, which appeared unaffected by up to 8 weeks exposure to copper pyrithione at ~0.2 µg ai/L.

Aquatic invertebrates

Acute toxicity tests conducted to US EPA Guidelines found that zinc pyrithione and copper pyrithione are very highly toxic to aquatic invertebrates, including the waterflea *Daphnia magna*, mysid shrimp (*Americamysis bahia*) and eastern oyster (*Crassotrea virginica*). 48 h EC50 values for zinc pyrithione to *Daphnia magna* in two separate tests were 3.6 µg ai/L and 36 µg ai/L. The 48 h EC50 value for copper pyrithione to *Daphnia magna* was 22 µg ai/L. The 96 h LC50 for zinc pyrithione to mysid shrimp was in the range 1.6-9.4 µg ai/L. The 96 h EC50 (shell growth inhibition) to eastern oyster was 22.4 µg ai/L for zinc pyrithione and 11 µg ai/L for copper pyrithione.

A 21 day chronic exposure/reproductive toxicity study with zinc pyrithione and *Daphnia magna* found a NOEC, LOEC and MATC of 2.7, 5.8 and 4.0 µg/L, respectively, based on the number of young produced and mean length of parent daphnids at 21 days. Thus zinc pyrithione has high chronic toxicity to daphnids (NOEC < 10 µg/L). The 21 d EC50 to parent daphnids was in the range 22-49 µg ai/L, with most effects becoming evident over days 2 to 6 of exposure and a low acute:chronic toxicity ratio.

A study to oil industry test guidelines indicated a 10 d LC50 of 4.4 mg/kg sediment dry weight to the burrowing amphipod *Corophium volutator* for zinc pyrithione added to sediment before exposure. This result was presumably affected by a significant degree of degradation of the originally applied zinc pyrithione.

Algae and aquatic plants
Tests to US EPA guidelines found very high toxicity of zinc pyrithione and copper pyrithione to the freshwater green alga *Selenastrum capricornutum*, with 120 h EC50s of 28 µg ai/L and 35 µg/ai/L, respectively (mean measured concentrations, static conditions). A test to US EPA Guidelines also found very high toxicity of zinc pyrithione to duckweed (*Lemna gibba*), with a 7 d EC50 of 9.6 µg ai/L (flow-through conditions).

Pyrtihione metabolites

The scientific literature suggests that the high microbiological activity of pyrithione biocides is linked to the presence of sulfur attached in the 2-position to the pyridine-N-oxide ring. Various identified metabolites of zinc pyrithione retain a sulfur atom in this position, but in some cases with loss of the oxygen to form a pyridine ring. Limited evidence indicates that much of the toxicity is lost if the N-oxide is removed, despite retention of sulfur at the 2 position (eg 2-mercaptopyridine and pyridine disulfide - see below). The acute toxicity of two major metabolites of pyrithione, pyrithione 2-sulfonic acid and pyridine 2-sulfonic acid and a transient metabolite[2,2'-dithio-bis-pyridine (pyrithione disulfide)] to various freshwater and estuarine/marine species was evaluated in tests to US EPA Guidelines. As evident below, the data clearly indicate much reduced toxicity in the 2-sulfonic acids. Similarly low toxicity is expected with the corresponding sulfinic acids, but no studies of this are available.

Pyrithione disulfide was found very highly toxic to fathead minnow, rainbow trout, *Daphnia magna* and mysid shrimp (96 h LC50 or 48 h EC50 respectively, 30 µg ai/L, 54 µg ai/L, in the range 11-18 µg ai/L, and 6.4 µg ai/L - nominal concentrations), highly toxic to eastern oyster (96 h EC50 = 160 µg/L) and the green alga *Selenastrum capricornutum* (120 h EC50 = 140 µg ai/L), and moderately toxic to the sheepshead minnow (96 h LC50 = 1100 µg ai/L). Pyrithione disulfide has itself been evaluated and/or used as a biocide. Pyrithione 2-sulfonic acid and pyridine 2-sulfonic acid were found slightly toxic (LC50 or EC50 = 10-100 mg/L) to practically non-toxic (LC50/EC50 > 100 mg/L) to the same set of species.

A scientific paper reported studies using the marine diatom *Phaeodactylum tricornutum* as a bioassay technique which indicated 2-mercaptopyridine and pyridine disulfide were toxic at about 3 ppm, about 150 times the 100% inhibitory concentration for pyrithione. Pyrithione 2-sulfonic acid was still less toxic, while pyridine and pyridine-N-oxide were non-toxic at a concentration of 100 ppm.

A 32 day exposure/early life stage study with pyridine-2-sulfonic acid and fathead minnow also indicated no toxic effects at a concentration of 10 µg/L, a value chosen to be above the maximum predicted environmental concentration. A study concluded that rapid binding to the sediment and/or transformation to metabolites considerably lowered the toxicity of zinc pyrithione to the marine copepod *Acartia tonsa*.

Mammals
Zinc pyrithione has moderate mammalian toxicity by acute oral exposure (acute oral LD50 to rats = 269 mg/kg bodyweight) and is practically non-toxic to mammals with dermal exposure (LD50 to albino rabbits > 2000 mg/kg). No information is available specifically with aquatic mammal species.

Microorganisms
Zinc pyrithione and other pyrithione derivatives including some zinc pyrithione metabolites have been tested or used as biocides in a wide range of applications because of their high

toxicity to various microorganisms, including bacteria and fungi (minimum inhibitory concentrations approximately 0.03-0.3 ppm).

Phytotoxicity

Pyrithiones such as sodium pyrithione or zinc pyrithione, or the metabolite pyrithione disulfide, may cause growth retardation of terrestrial higher plants through effects on root growth at concentrations of approximately 1-3 ppm. However, exposure of terrestrial plants to zinc pyrithione or its metabolites as a result of antifoulant use is unlikely to occur, and even in the vicinity of landfill areas, rapid degradation would limit such exposure.

Environmental hazard

Little hazard to terrestrial species is anticipated, as the use as an antifoulant on ships is not expected to result in significant contamination of the terrestrial environment. Birds consuming fish or other marine organisms are unlikely to be affected because zinc pyrithione does not bioaccumulate, hence exposure to zinc pyrithione residues would be minimal. The assessment considers the aquatic hazard from zinc pyrithione and not that from the other active ingredient in the paints, cuprous oxide, uses of which are already widely registered.

Hazard arising during application, maintenance and removal

There is a potential hazard from localised environmental exposure during paint application and during washdown or preparation of existing surfaces for repainting. However, application of the deep sea market product Intersmooth 360 Ecoloflex in commercial slipways and shipyards should facilitate control of environmental exposure during application, maintenance and removal. Waste material would presumably be collected within bunded areas of the slipways/dry-docks involved and disposed of appropriately to approved landfill facilities. Suitable general guidance for environmental precautions in the maintenance and application of vessel antifoulant coatings is provided in the Australian and New Zealand Environment and Conservation Council (ANZECC) Code of Practice for Antifouling and In-water Hull Cleaning and Maintenance. Label advice stipulates that waterways should not be contaminated with paint, dust and scrapings or used containers and some protection is also provided by relevant State and local government legislation.

Hazard from treated vessels

The potential for accumulation of zinc pyrithione in aquatic systems was modelled using a tidal prism model for a worst case harbour situation. This model assumes complete mixing due to the tide and a continuous loading of the contaminant, and estimates the steady state concentration of the test substance given the treated surface area, release rate and low and high tide volumes and extent of degradation per tidal cycle. It was assumed that this harbour was continually occupied by three vessels, each with wetted areas of ~10,000 m^2 and each treated with International Intersmooth 360 Ecoloflex according to the maker's specifications. This is a high wetted area relative to the harbour volume, well above that in busy Australian port areas, such as Swanson Dock in Victoria. A very much worst case steady state leach rate for zinc pyrithione of 5 $\mu g/cm^2/day$ (in practice, the steady state leach rate is likely to be less than 50% of this) and zinc pyrithione decay rate of 70% degradation per tidal cycle were assumed. The latter is again a worst case situation in that the likely rapid photolysis in many situations during daylight is not included, but use of this overall value allows for situations where sunlight is inhibited, eg by shading, turbidity and cloudy weather.

According to the model scenario, the steady state concentration predicted (Css) in the harbour was 0.113 $\mu g/L$. Evaluation of the hazard based on the most sensitive species in chronic/reproductive exposure tests (fathead minnow) indicates an acceptable hazard, even in this exaggerated worst case situation (chronic NOEC = 1.22 µg/L, with ratio of Css:NOEC ≈ 0.10).

Conclusions

Environment Australia concludes that zinc pyrithione released into water from painted surfaces is unlikely to accumulate in water or sediment and is not expected to result in primary poisonings of fish or other aquatic species in water or sediment, while exerting a toxic effect on treated surfaces. Application in appropriate facilities according to the Australian and New Zealand Environment and Conservation Council (ANZECC) Code of Practice for Antifouling and In-water Hull Cleaning and Maintenance and local State regulations should ensure adequate protection to the environment during application and maintenance.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Fouling organisms- such as barnacles, molluscs and algae- on ships hulls can have very significant effects on the performance and durability of a vessel. This includes increased fuel consumption and/or reduced speed. Increased fuel consumption has potential greenhouse effects and adds significantly to operating costs. Ships may need to be dry docked for cleaning more frequently and this also substantially increases operating costs. Fouling organisms may also be carried from one location to another on ships hulls and become pests in new locations.

The main products used on commercial shipping to control fouling have been organotin-based biocides, particularly tributyltin (TBT). TBT is highly toxic and has adverse impacts on the marine environment. Under *Australia's Ocean Policy,* the Commonwealth Government will be supporting the International Maritime Organisation's global ban on TBT products. It is anticipated that this will involve a ban on the application of TBT antifoulings to commercial ships from 1 January 2003.

Ecoloflex is TBT-free and is therefore an alternative to the TBT-containing products.

Efficacy

Data from trials under Australian conditions, in temperate and tropical waters, were provided. This included a series of trials using rafts and rotor tanks, patch trials on five Royal Australian Navy vessels and full hull trials on three vessels.

These trials take into account the likely differences in fouling fauna and flora across the temperate and tropical waters. The fouling data provided consisted of a series of scores. In addition, ablation rates were provided. The data were presented across all test systems including the product and these included an untreated control. The data are considered to provide a meaningful indication of the efficacy of the product. Results were directly linked to a series of clear photographs, which reinforce the data provided. The results indicate that the product will be effective for the claimed purposes.

Results from a panel trial conducted in Singapore were also submitted but these were considered to be of limited value as there was no replication and there was a wide range of scores on the various categories of fouling organisms. The paint was also applied at a greater thickness to that proposed on the label.

Safety

Safety to the marine environment is addressed in the Environmental Assessment section of this PRS. The paint is not expected to be damaging to the hull of ships, and is in use on ships painted overseas.

LABELLING REQUIREMENTS

The product will be available in two colours. The proposed labels for each colour are shown on the following pages.

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product.
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer.
Chronic	Of long duration.
Desorption	Removal of an absorbed material from a surface.
Efficacy	Production of the desired effect.
Formulation	A combination of both active and inactive constituents to form the end use product.
Genotoxicity	The ability to damage genetic material
Hydrophobic	Water repelling
Leaching	Removal of a compound by use of a solvent.
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient.
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light.
Photolysis	Breakdown of chemicals due to the action of light.
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

Suggested Further Reading

Environment Australia (1998) *Australia's Ocean Policy*, http://www.oceans.gov.au/aop/policy/aop/contents.html

National Occupational Health and Safety Commission (1994) *Control of Workplace Hazardous Substances* [NOHSC:1005(1994), 2007(1994)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1995) *Exposure Standards for Atmospheric Contaminants in the Occupational Environment*, *Guidance Note* [NOHSC:3008(1995)] and *National Exposure Standards* [NOHSC: 1003(1995)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1999a) *List of Designated Hazardous Substances* [NOHSC:10005(1999)], AusInfo, Canberra.

National Occupational Health and Safety Commission (1999b) *Approved Criteria for Classifying Hazardous Substances* [NOHSC:1008(1999)], AusInfo, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, NRA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, NRA, Canberra.

NRA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of zinc pyrithione in the product International Intersmooth 360 Ecoloflex Antifouling, please fill in this form and send it, along with payment of $30 to:

David Hutchison
Agvet Chemicals Registration Section
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
David Hutchison at 02 6272 3218.

Name (Mr, Mrs, Ms, Dr)____
Position ____
Company/organisation ____
Address ____
Contact phone number (___) ____________________________________

I enclose payment by cheque, money order or credit card for $__________

Make cheques payable to ‘National Registration Authority’.

___ Bankcard ___ Visa ___ Mastercard ___ Amex

Card number ______/______/______/______ Expiry date ...../....../......

Signature__________________________________ Date ______________

POISON
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTION BEFORE OPENING OR USING

International

INTERSMOOTH 360

ECOLOFLEX ANTIFOULING

ACTIVE CONSTITUENTS	66g/L ZINC PYRITHIONE 626g/L CUPROUS OXIDE

CAN I.D

SQ

PAINT
U.N. NO 1263

BEA 369 DARK RED 20 LITRES

MIX THOROUGHLY BEFORE USE PPA 3/5

IN A TRANSPORT EMERGENCY
DIAL 000 POLICE OR FIRE BRIGADE

USE AS AN ANTIFOULING PAINT TO CONTROL MARINE GROWTH ON COMMERCIAL/NAVAL VESSELS

NRA APPROVAL NO xxxxxx

388035

BARCODES

DIRECTIONS FOR USE/APPLICATION AT NEWBUILDING

The anticorrosive coating should be dry and free from all contamination (oil, grease, salt, etc) and overcoated within the specified over-coating time.

APPLICATION AT MAINTENANCE DOCKING

The existing coatings should be dry and free of marine fouling and all other contamination (oil, grease, salt, etc). Fresh water should be used for washing down. Damaged and corroded areas should be touched up with anticorrosive paint. If the existing antifouling will not provide a suitable substrate, a barrier coating of anticorrosive should be applied before over-coating with antifouling.

PRODUCT APPLICATION: Airless Spray at 4.8 square meters per litre

AIRLESS SPRAY: Tip range 0.66 – 0.79mm (26 – 31 thou)
Total output pressure 2100kPa 9210kg/square centimetre

THINNING: Not recommended. If necessary use up to 5% International GTA007 Thinner.

CLEAN UP: Use International GTA007 Thinner.

Please refer to the detailed product data sheet for full instructions on use.

not to be used for any purpose or in any manner contrary to this label unless authorised under appropriate legislation.

Protection of wildlife, fish, crustacea and environment

AS THIS PRODUCT IS AN ANTIFOULING PAINT IT CONTAINS CERTAIN ACTIVE MATERIALS WHICH, IF USED INCORRECTLY CAN HAVE A DETRIMENTAL EFFECT ON MARINE LIFE. DO NOT CONTAMINATE WATERWAYS WITH PAINT, DUST AND SCRAPINGS OR WITH USED CONTAINERS.

STORAGE AND DISPOSAL

STORE IN ORIGINAL CONTAINER, TIGHTLY CLOSED IN COOL, DRY PLACE. DO NOT STORE FOR PROLONGED PERIODS IN DIRECT SUNLIGHT. STORE IN A LOCKED ROOM OR PLACE AWAY FROM

POISON
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTION BEFORE OPENING OR USING

International

INTERSMOOTH 360

ECOLOFLEX ANTIFOULING

ACTIVE CONSTITUENTS	66g/L ZINC PYRITHIONE 619g/L CUPROUS OXIDE

CAN I.D

SQ

BARCODES

PAINT
U.N. NO 1263

BEA 368 BROWN 20 LITRES

MIX THOROUGHLY BEFORE USE PPA 3/5

IN A TRANSPORT EMERGENCY
DIAL 000 POLICE OR FIRE BRIGADE

USE AS AN ANTIFOULING PAINT TO CONTROL MARINE GROWTH ON COMMERCIAL/NAVAL VESSELS

NRA APPROVAL NO xxxxxx

388035

DIRECTIONS FOR USE/APPLICATION AT NEWBUILDING

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