National Registration Authority
FOR AGRICULTURAL & VETERINARY CHEMICALS

First Floor, Industry House, National Circuit, Barton ACT
PO Box 240, Queen Victoria Terrace ACT 2600
Tel: (06) 272 5158 Fax: (06) 272 4753

Public Release Summary

DIFENOCONAZOLE

IN THE PRODUCT SCORE FOLIAR FUNGICIDE

This document is published by the National Registration Authority for Agricultural and Veterinary Chemicals.
For further information, please contact:

[redacted]

FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent Statutory Authority with responsibility for the assessment and approval of agricultural and veterinary chemical products prior to sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies including the Department of Human Services and Health (Chemical Safety Unit), the Commonwealth Environment Protection Agency (CEPA), the National Occupational Health and Safety Commission (Worksafe Australia) and State Departments of Agriculture and Health.

The NRA has a policy of encouraging openness and transparency in its activities and seeking community involvement in decision making. The publication of Public Release Summaries for all products containing new active ingredients is a part of that process.

The information and technical data required by the NRA in order 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 document "Requirements for Clearance of Agricultural and Veterinary Chemical Products" which can be obtained from the NRA.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and advisory agencies. The document has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment. The publication of more technical information to accompany Public Release Summaries is planned for the future.

As a relatively new organisation, the NRA would welcome comment on the usefulness of this document and suggestions for further improvement. Comments should be forwarded to The National Registration Manager, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box 240, Queen Victoria Terrace, Parkes, ACT, 2600.

ABBREVIATIONS AND ACRONYMS WHICH MAY BE USED IN THIS DOCUMENT

ADI	Acceptable Daily Intake (for humans)
CSU	Chemical Safety Unit (of the Department of Human Services and Health)
d	Day
EC_{50}	Concentration at which 50% of the test population of fish are immobilised
EUP	End Use Product
F_o	Original Parent Generation
h	Hour
HPLC	High Performance Liquid Chromatography
id	Intradermal
ip	Intraperitoneal
im	Intramuscular
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
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
m	Metre
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit (a legal limit)
MSDS	Material Safety Data Sheet
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration/Level
NRA	National Registration Authority for Agricultural and Veterinary Chemicals
po	Oral
ppb	parts per billion
ppm	parts per million
s	Second
sc	Subcutaneous
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TGAC	Technical Grade Active Constituent
WDG	Water Dispersible Granule
WHP	Withholding Periods

EXECUTIVE SUMMARY

Introduction

The purpose of this document is to provide a summary of the data reviewed and an outline of regulatory considerations for the proposed clearance and registration of the chemical difenoconazole in the product SCORE Foliar Fungicide as a fungicide for control of target spot on potatoes. Use in all States and Territories is proposed.

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) invites public comment before deciding whether to proceed to approve this product for use in Australia.

The NRA has completed an assessment of the data submitted by the applicant in support of this use of difenoconazole and has provided the following information for public comment:

Agricultural Aspects

Target spot (early blight) of potato can severely limit or destroy the Australian crop. SCORE Foliar Fungicide has been shown to give effective control of the disease when applied at lower application rates than conventional fungicidal treatments. The product is used in a protectant programme commencing when rows meet and before disease occurs at a rate of 300 mL/ha or 500 mL/ha.

There was no evidence of phytotoxicity to the target crop or non-target plants when used according to label directions.

Environmental Aspects

Difenoconazole is a triazole fungicide that will be applied by ground based or aerial spraying to potatoes. Residues may be expected on plant leaves, the crop itself and the soil surface. Surface water and uncultivated land may be exposed to spray drift and runoff.

Estimation of likely environmental concentrations in aquatic and terrestrial compartments indicates that difenoconazole is unlikely to pose a significant hazard to aquatic or terrestrial organisms.

Data submitted for assessment are sufficient to demonstrate that use of difenoconazole as proposed and according to good agricultural practice should not lead to significant environmental contamination or undue hazard to non-target organisms.

Public Health Aspects

Toxicology

Difenoconazole is of low acute oral, dermal and inhalational toxicity. It is a slight skin and moderate eye irritant in rabbits, but is not a skin sensitiser in guinea pigs. The formulation for SCORE Foliar Fungicide is of low acute oral, dermal and inhalational toxicity and a slight skin and eye irritant, but not a skin sensitiser.

Repeated dose studies in rats, mice and dogs identified the liver as the primary target organ for toxicity. Liver tumours developed in mice given difenoconazole at 375 mg/kg body wt/day, but since there is no evidence of genotoxicity and the tumours occurred only at doses which produced frank liver damage, it was concluded that difenoconazole does not pose a significant carcinogenic risk to humans at low levels of exposure.

High doses of difenoconazole were associated with eye cataracts in dogs and hens. Studies on other species and subsequent dog studies did not confirm this effect. Studies in rats and rabbits showed that difenoconazole does not cause reproductive disorders or birth defects. A range of studies established that difenoconazole does not damage genetic material (DNA).

Residues in Food Commodities

Residues in food products were determined at various times following treatment with a range of concentrations of the product and a maximum residue level (MRL) of *0.02 mg/kg for potatoes was established.

Based on an assessment of the toxicology and the potential dietary intake of residues, it was considered that there should be no adverse effects on human health from the use of Score Foliar Fungicide.

Occupational Health and Safety Aspects

Given the low acute toxicity of the active ingredient and the use pattern (less than 6 applications per season), the likelihood of workers experiencing acute and chronic health effects from using the product is low. The label specifies the use of appropriate protective clothing and personal hygiene to minimise any health risks when using the product.

TABLE OF CONTENTS

INTRODUCTION

The purpose of this document is to provide the public with a summary of the data reviewed and an outline of the regulatory considerations for the proposed application of the chemical difenoconazole for the control of target spot on potatoes, and to seek public comment prior to the chemical product being approved for use in Australia.

Comments should be received by 3 September 1994 and sent to:

Applicant

Ciba-Geigy Australia Limited has applied for clearance and registration of a fungicide product containing a new active constituent, difenoconazole, a new systemic triazole fungicide with broad-spectrum anti-fungal activity.

Product Details

Difenoconazole will be marketed under the trade name SCORE Foliar Fungicide as an emulsifiable concentrate formulation containing 250 g/L of active constituent.

SCORE Foliar Fungicide will be formulated locally from imported active ingredient.

Ciba-Geigy Australia Limited intends to market SCORE Foliar Fungicide in all States for the control of target spot on potatoes.

Overseas Registration Status

Products containing difenoconazole as 250 g/L EC formulations are registered in 34 countries, including the following countries: France (apples, pears, tomatoes, asparagus,grapes and sugarbeets), Greece (sugarbeets), New Zealand (brassicas, carrots, potatoes), Pakistan (apples), Paraguay (tomatoes), Romania (tomatoes, apples, pears), South Africa (beans, peanuts, apples, pears, tomatoes, potatoes, maize), Japan (sugarbeets) and Switzerland (grapes, wheat, sugarbeets, carrots, asparagus, celery, garlic, ornamentals).

Australia exports a small quantity of seed potatoes to Papua New Guinea and the islands. This trade is not likely to be affected by the use of difenoconazole. Similarly, small quantities of frozen potato products could reach overseas markets. The lack of accumulation of difenoconazole in tubers would make it unlikely that residues would remain in such products.

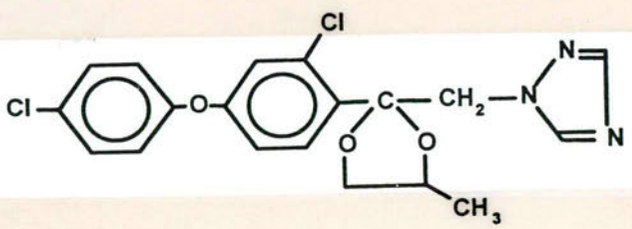
As potato crops are not subject to grazing by livestock, there is no possibility of residues in animal products for export.

PROPERTIES OF THE CHEMICAL ACTIVE INGREDIENT

The chemical active ingredient difenoconazole is manufactured in Switzerland and will be imported for formulation in Australia. Difenoconazole is a new systemic triazole fungicide with novel broad-spectrum anti-fungal activity. It significantly inhibits the development of subcuticular growth of fungal mycelium by inhibiting C-14 demethylation (DMI fungicide) and prevents the development of plant disease. It has the following properties:

Common name:	difenoconazole (proposed to ISO and approved by SAA)
Chemical name:	1-{2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-yl-methyl}-1H-1,2,4-triazole
Product name:	SCORE Foliar Fungicide
CAS registry number:	119 446-68-3
Empirical formula:	$C_{19}H_{17}Cl_2N_3O_3$
Molecular weight:	406.27
Physical form:	crystalline powder
Colour:	white to light beige
Odour:	non-specific
Melting Point:	79.4°C
Density:	1.37 g/cm^3
Octanol/water partition coefficient:	Log P_{ow} =4.2 at 25°C (OECD method)
Vapour pressure:	at 20°C 1.2 x 10^{-8} Pa
	at 30°C 9.0 x 10^{-8} Pa
	at 40°C 5.8 x 10^{-7} Pa

Structural Formula:



AGRICULTURAL ASSESSMENT

Justification for Use

In Australia, approximately 45,000 ha of potatoes are grown each year; the annual average gross value of potato production over the period 1987-1990 was $307 million. Target spot (early blight), *Alternaria solani,* can severely limit or destroy potato crops in some seasons if not treated.

SCORE Foliar Fungicide provides excellent efficacy against this disease at low application rates (75 to 125 g a.i./ha compared to a current standard treatment, chlorothalonil, which is applied at 800 to 1300 ga.i./ha) and its systemic action provides protective activity to the potatoes. It will provide growers with a longer control period leading to fewer fungicide applications and reduced costs, and will give greater reliability (due to its rainfastness) with less reliance on weather conditions for spraying.

Proposed Use Pattern

The label recommends that SCORE be used in a protectant programme commencing when rows meet and before disease occurs at 300 mL/ha or 500 mL/ha for control of target spot (early blight) of potato. The 300 mL rate is applied at 7 day intervals and the 500 mL rate at 10 to 14 day intervals. The higher rate is recommended when conditions favour high disease pressure. Use of SCORE Foliar Fungicide is limited to 6 or less applications per season and SCORE alone is not to be used for more than two consecutive applications; when necessary, an alternative fungicide or a tank mix with another protectant fungicide should be used.

Evaluation of Efficacy

Potato trials were conducted in all Australian States, under a range of different disease pressure, weather conditions and soil types. These conditions varied from season to season, and trial to trial, providing conditions ranging from extreme disease pressure to almost none over the period the trials were conducted. Data were presented for a total of 30 trials over the period 1986 to 1992. The trials consisted of replicated trials, grower trials, large scale aerial application trials and insecticide compatibility trials and were considered adequate to demonstrate that the disease control achieved was equal to or better than that of standard fungicidal treatments.

Phytotoxicity

There were no significant phytotoxic effects on the target crop when used as directed. Overseas testing of a wide range of non-target crops indicates that SCORE Foliar Fungicide would not be expected to have any adverse effects on non-target crops.

ENVIRONMENTAL ASSESSMENT

Environmental fate

SCORE will be applied as a dilute spray to potatoes, using ground based or aerial application equipment. Application rates of 75-125 g/ha of difenoconazole will be used in 20-30 L of water for aerial application and 100-500 L for ground based application. The recommended usage pattern for SCORE® involves a maximum of 6 applications per season.

Most of the applied difenoconazole is expected to be taken up by the crop, but some exposure of the soil is also likely. Also, as the crop is irrigated and spray application methods will be used, there is a potential for the contamination of surface waters due to runoff or spray drift.

Hydrolysis

Test reports indicate that no significant hydrolysis of difenoconazole occurred during 30 days at a concentration of 1 ppm in buffered solutions (pH 5, 7 and 9). Therefore, hydrolysis of the active is unlikely to occur under environmentally relevant conditions.

Photolysis

A range of unidentified polar photodegradation products formed when solutions of radiolabelled difenoconazole (2.4 ppm) were exposed to direct natural sunlight for 47 days. The extrapolated half-life of difenoconazole was about 5 months. Thus photolysis would not appear to offer a significant degradation pathway, given the characteristic turbidity of Australian surface waters.

Photolysis of radio-labelled difenoconazole (10 ppm) on the surface of soils (loam and sandy loam) using natural or artificial light led also to a number of unidentified polar degradation products, none of which exceeded 10% of applied chemical. Half-lives ranged between 1 and 10 weeks, depending on the soil and the position of the radiolabel.

Metabolism in Soils

The metabolism of difenoconazole was studied in four soils (two loams, a sandy loam and a loamy sand) which were spiked at 10 ppm and incubated for a year. Degradation was slow, with extrapolated first half-lives between 670 and 1600 days in aerobic soils. Anaerobic half-lives were in the same order.

Studies on a silt loam revealed that degradation of difenoconazole was significantly retarded by high concentrations, low soil temperatures, and low soil moisture content. For example, the half-life at 20°C for phenyl-labelled material at a concentration of 0.1 ppm and 60% moisture capacity was relatively short at 75 days. However, this increased to 340 days at 1 ppm, further to 602 days at 1 ppm and 10°C, and further still to 709 days at 1 ppm and 20°C but 30% moisture capacity.

Mobility in Soils

Soil mobility was investigated using conventional equilibration techniques on four soils (a clay, two sands, two silt loams, two sandy loams and a silt clay loam). Soil organic carbon adsorption coefficients (K_{oc}) calculated using the Freundlich isotherm equation are indicative of strong sorption (K_{oc} values between 1900 and 7800) with the exception of one of the sands where sorption was moderate (K_{oc} 400).

Column leaching studies were also performed on a range of soils, spiked at exaggerated rates and eluted under a range of conditions. In general, significant residues were only found in the top 2.5 cm of the columns, with little in the leachates (a maximum of 1.6%). These studies confirm the low leaching potential of difenoconazole.

Field Dissipation Studies

Summary reports for 12 studies in which difenoconazole was applied directly to bare ground at rates of 125-800 $g.ha^{-1}$ and monitored for a year indicated that the active was largely confined to the top 10 cm of soil. No half lives were calculated in any of the studies because of fluctuating measurements, but most appear to be in the order of a few months.

In contrast, full reports for two bare ground applications at the exaggerated rate of 5.6 $kg.ha^{-1}$ difenoconazole provide little evidence for significant degradation. This is consistent with the concentration dependence observed in the laboratory.

Soil Accumulation

In the absence of reliable field dissipation data, it is prudent to rely on laboratory half-lives for estimation of accumulation potential. When allowance is made for interception by the crop, it may be estimated that a program of six sprays at 125 $g.ha^{-1}$ would leave residues in the order of 0.5 ppm in the surface 5 cm soil layer. For a half-life of 1 year, soil levels would not be expected to accumulate significantly above this level. For a half-life of 3 years, accumulation would reach a plateau of about 2 ppm.

Bioaccumulation

Steady state was reached in a few days in bluegill sunfish exposed for 28 days to radiolabelled difenoconazole under flow-through conditions. The depuration half-life was in the order of a day and a whole body bioconcentration factor of about 320 was recorded. Elimination was essentially complete within a 14 day depuration period. Extensive metabolism of difenoconazole occurred in fish, leading to alcohol and ketone products from cleavage of the dioxolane ring and a range of unidentified polar metabolites. Significant bioaccumulation in fish appears unlikely.

Environmental effects

Avian Toxicity

Acute oral and dietary studies on bobwhite quail and mallard ducks indicate that difenoconazole is practically nontoxic to birds. No observable effect levels (NOEL) of 125 and 625 ppm were determined in reproduction tests on bobwhite quail and mallard ducks, respectively.

Aquatic Toxicity

Acute toxicity tests were conducted on four species of fish, two invertebrates, and oysters. Median lethal concentrations were between 0.77 and 1.1 ppm, apart from the sensitive mysid shrimp where the LC50 and NOEL were 150 and 48 ppb, respectively. The EC50 for oyster shell growth was 0.45 ppm. Results indicate moderate to high aquatic toxicity.

Effects of difenoconazole on the freshwater invertebrate *Daphnia magna* were investigated over its entire life cycle during 21 days of continuous exposure. The NOEL and LOEL (lowest observable effect level) were 5.6 and 13 ppb, respectively.

Non-target terrestrial invertebrates

Standard acute tests on earthworms and bees did not reveal any toxic effects of difenoconazole towards these organisms.

Phytotoxicity

A wide range of non-target crops was tested for phytotoxicity at recommended label rates, with no discernible effects apart from late sown winter barley seeds dressed with difenoconazole.

Prediction of environmental hazard

Hazard arising from use

Following application of SCORE Foliar Fungicide to potatoes, residues of difenoconazole would be expected on vegetation, invertebrates and the soil surface. Surface water and uncultivated land may be contaminated through spray drift and runoff, the latter less likely due to strong adsorption to and low mobility in soils.

Birds and Mammals

Application at the highest proposed rate of 125 $g.ha^{-1}$ would leave estimated concentrations of 35 ppm on shortrange grass, and 7 ppm on forage (with similar levels likely on invertebrates). As these levels are well below no effect levels determined for birds in reproduction studies, it may be concluded that terrestrial hazard is low.

As noted above, the possibility exists that residues may accumulate in soil to levels of 2 ppm. Given that no deaths occured in earthworms exposed to levels some three hundred times higher, significant hazard to soil dwelling organisms appears unlikely.

Aquatic organisms

Application of 125 $g.ha^{-1}$ of difenoconazole to a 15 cm deep static pond would leave a concentration of about 80 ppb, which approaches the LC50 recorded for the sensitive Mysid shrimp and exceeds the no effect level for this organism. Accordingly, it must be presumed that difenoconazole is potentially hazardous to aquatic organisms.

Given that direct overspray of water is not expected, the estimated environmental concentration may be reduced by a factor of 10 to reflect indirect contamination via drift. The resultant concentration falls below the no effect level for the Mysid shrimp, and the lowest effect level for *Daphnia magna* in reproduction tests, indicating that the aquatic hazard in practice should be low.

Desirable vegetation

The hazard to non-target native vegetation should be low as limited native vegetation has been retained in agricultural areas where the fungicide will be used. Even if exposure occurs through drift, damage is unlikely due to the expected low toxicity.

Conclusions and Recommendations

Both laboratory and field studies have demonstrated the low mobility and strong binding of difenoconazole to soils. The persistence question remains slightly unclear, however, with the half-lives of a few months that were generally apparent in field dissipation studies at expected soil residue levels extending to a year or more at elevated concentrations. The possibility therefore exists that difenoconazole may accumulate in soils to some extent. However, the maximum concentration in the top 5 cm of soil is estimated at 2 ppm based on a dissipation half life of 3 years. The faster rate of dissipation expected under actual field conditions should effectively eliminate the accumulation potential. The company has agreed to notify CEPA immediately should significant soil residue levels be detected in areas where difenoconazole is used, either in Australia or overseas, and to provide any additional studies clarifying this issue as they come to hand

PUBLIC HEALTH AND SAFETY ASSESSMENT

Evaluation of Toxicology

The toxicological database for difenoconazole 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 which are high compared to likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. 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.

Toxicokinetics and Metabolism

At least 15-20% of difenoconazole was absorbed in orally dosed rats but was quickly eliminated. Excretion mainly occurred via the urine and faeces. After 7 days, only low residue levels of difenoconazole were found in the tissues.

Acute Toxicity

Difenoconazole is of low oral and inhalational toxicity in rats and low dermal toxicity in rabbits. Fatal oral doses were of the order of 1500 mg/kg body wt. It is slightly irritating to skin and moderately irritating to the eyes of rabbits, but was not a skin sensitiser in guinea pigs.

Tests done with a formulation comparable to SCORE Foliar Fungicide indicated that it would have low oral, dermal and inhalational toxicity and would be slightly irritant to the skin and eyes. The products are not considered to have skin sensitising potential.

These data confirm the low risk of acute poisoning with the formulated product, but indicate the need to prevent exposure to the skin and eyes.

Short-Term Studies

Short-term (13 weeks) dietary administration of difenoconazole to rats and mice given doses from 12 and 34 mg/kg body wt/day respectively, resulted in toxic effects on the liver. The most significant effects were increased liver weights, changes in biochemical parameters in rats indicating liver toxicity, and hepatocellular enlargement. In mice given doses at 1673 mg/kg body wt/day and above, liver toxicity was further evidenced by gross changes leading to the death of individual liver cells.

Short-term (21 days) dermal exposure to difenoconazole in rabbits at 100 mg/kg body wt/day and above resulted in dermal irritation at the application site, changes in white blood cells, increased adrenal weights and changes in the appearance of liver cells.

Long-term Studies

Long-term dietary administration of difenoconazole to rats (2 years), mice (18 months), and dogs (12 months) resulted in toxic effects on the liver from 375 and 125 mg/kg

body wt/day in mice and rats respectively, and 37 mg/kg body wt/day in dogs. The most significant effects were increased liver weights, changes in biochemical parameters indicating liver toxicity, liver cell enlargement in rats, and an increased incidence of liver adenoma and carcinoma in mice. The liver tumours occurred in mice at doses which were associated with frank hepatotoxicity and may have been secondary to the effects of the resultant cellular regeneration. Other effects attributable to treatment with difenoconazole included decreased bodyweights in all three species and in rats, some non-specific changes in haematological and biochemical parameters from 25 mg/kg body wt/day, and increased ovarian weights from 125 mg/kg body wt/day.

Eye cataracts and associated eye changes were reported in the dog study at the two highest doses (97 and 158 mg/kg body wt/day). While a few rats in the 13-week feeding study also had eye lesions, their relationship to treatment with difenoconazole was less clear. Cataracts were not reported in the 2-year rat study at comparable doses, or in another dog study designed to study this effect.

The most sensitive species was the rat with a NOEL of 1 mg/kg body wt/day.

Reproduction and Developmental Studies

In rats, dietary administration of difenoconazole over two generations at doses up to 125 mg/kg body wt/day did not effect reproductive parameters or pup development. At the highest dose, testicular and ovarian weights were increased relative to body weight, although this could have simply been a consequence of the reduced overall growth at these doses.

There was no evidence that difenoconazole causes birth defects in rats and rabbits given oral doses during critical periods of foetal development.

Genotoxicity Studies

Difenoconazole was not mutagenic in bacterial or mammalian cells in vitro, did not induce micronuclei in Chinese hamster bone marrow or chromosomal aberrations in human lymphocytes and failed to cause unscheduled DNA synthesis in rat hepatocytes or human fibroblasts.

Other Studies

The eye damaging potential of difenoconazole was studied in chickens and dogs. In a 56-day dietary study in chickens given 450 mg/kg body wt/day difenoconazole, lesions of the lens indicative of cataract development were reported. However, in a dietary study in dogs given doses ranging from 36 to 124 mg/kg body wt/day over periods up to 127 days, there was no evidence of a treatment-related effect on the lens.

Thus, while it was confirmed that difenoconazole can produce eye lesions in susceptible species at high doses, the low potential for chronic human exposures at such high levels should result in a negligible human risk for this lesion.

Potential for Chemical Residues in Food Commodities

Australian residue studies in potatoes were conducted at Tolga in Queensland, at Orange in New South Wales and at Smeaton in Victoria. Application rates were 1.4 and 2.8 times the maximum recommended In one of the studies the withholding period was 18 days but in the other two residues were examined at 7, 14 and 21 days. At 700 mL/ha (1.4 times recommended) all samples taken at 7 days were less than 0.02 mg/kg. No residues were detected in later samples. At 1400 mL/ha some residues were detected at 7 days - up to 0.12 mg/kg. These results are supported by C-14 labelled studies which confirm that tubers do not accumulate residues of unchanged difenoconazole. It is appropriate to set the MRL for potato at *0.02 mg/kg with a withholding period of 7 days.

Studies using radiolabel C-14 in each of the phenyl and triazole rings were presented in animals and plants.

In goat, the major route of excretion was via urine and faeces. Only a small proportion of the label in tissues was parent compound Similarly, most elimination in chickens was via excreta. Metabolic pathways were similar in both animal species.

Goats were dosed in two studies in the USA. At a dose of C-14 labelled difenoconazole, equivalent to 5 ppm in the diet, the C-14 in liver was equivalent to 0.28 mg/kg while milk was 0.043 mg/kg. When the dose was equivalent to 100 ppm in feed, the level in liver was 8.5 mg/kg and milk 0.43 mg/kg. The actual parent compound was less than 10% of these amounts.

When C-14 difenoconazole was applied to wheat in the USA at 125 g ai/ha, residues were calculated from C-14 content. At 33 days after last treatment, foliage had residues of about 10 mg/kg while grain was about 1 mg/kg. At harvest, parent compound was 11% of C-label in mature stalks, 22% in hulls and 15% in grain.

In experiments in the USA, after treatment of potatoes at 125 g ai/ha, C-14 in tubers was equivalent to up to 0.14 mg/kg and tomatoes at 250 g/ha had foliage residues of about 7 mg/kg and fruit residues of 0.27 mg/kg. Metabolism was extensive and residues of parent compound were much lower. Examination of residues in soil showed that there was little penetration beyond the top 7.5 cm and that difenoconazole was metabolized rapidly in soil.

The analytical methodology was examined and found satisfactory . Samples of plant material were refluxed with ammonia-methanol and after addition of water and salt, residues were partitioned into hexane and then into acetonitrile. Further clean-up was by Silica Sep Pak and Phenyl Solid Phase Extraction Tube. Residues were determined by gas chromatography on silica capillary coated with cross-linked phenyl and methyl-polysiloxane (HP-17) at 280 C with nitrogen/phosphorous detector. The Limit of Determination was 0.02 mg/kg and recoveries at 0.04 mg/kg were 98$\pm$ 10%.

Examination of the analytical data shows that the significant residue is unchanged difenoconazole.

The residue and metabolism data show that when the product is used according to the approved label instructions, including the 7 day withholding period, residues would be below the limit of analytical determination ie 0.02 mg/kg. The MRL is therefore proposed at this level.

The following consequential amendments will be made to Table 1 of the MRL Standard:

Table 1

Compound	Food	MRL (mg/kg)
Difenoconazole		
	DELETE:	
	Potato	T0.1
	ADD:	
	Potato	*0.02

Note: * indicates that the MRL has been set at or about the limit of analytical determination.

The following entry will be retained in the MRL Standard:

Table 3

Compound	Residue
Difenoconazole	Difenoconazole

Trade Aspects

SCORE Foliar Fungicide is to be approved for use under Australian conditions and with due regard to local agricultural practices. Providing SCORE Foliar Fungicide is used according to label directions, residues of difenoconazole should not exceed the proposed MRL of *0.02 mg/kg.

Australia exports a small quantity of seed potatoes to Papua New Guinea and islands in the South Pacific region. Small quantities of frozen potato products could reach overseas markets.

The rapid metabolism of difenoconazole in plants makes it unlikely that residues would remain at detectable levels. The potential for trade problems arising from the use of SCORE Foliar Fungicide on potatoes is therefore considered to be low.

Public Health Standards

The Drugs and Poisons Schedule (Standing) Committee (DPSSC) of the National Health & Medical Research Council (NH&MRC) 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.

The DPSSC recommended that difenoconazole be listed in Schedule 5 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Difenoconazole and its product SCORE Foliar Fungicide have been classified as hazardous substances by Worksafe Australia.

Difenoconazole is imported into Australia for formulation. Engineering controls, safe work practices, and the proper use of personal protective equipment specified in the Material Safety Data Sheet (MSDS) and on the label should be adequate to minimise exposure.

Potential for exposure during transport, storage and retailing only exists in case of an accidental spill or a breach in the containers. The label instructions and Safe Handling Information in the MSDS are adequate to enable users to minimise exposure in these situations.

End users will handle the difenoconazole product when preparing and using the spray Given the low acute toxicity of difenoconazole and SCORE Foliar Fungicide, low chronic toxicity of the active ingredient and the use pattern (less than 6 applications recommended per season per crop), the likelihood of workers experiencing acute and chronic health effects from using the product is low.

The product label specifies the use of elbow-length PVC gloves and face shield or goggles and personal hygiene advice to enable end users to minimise any health risks when using the product.

The company has proposed the following restricted entry statement for SCORE Foliar Fungicide "do not enter sprayed areas without protective clothing until the spray dries". Worksafe Australia is not proposing any additional statement at this time.

Conclusion: Difenoconazole and its product SCORE Foliar Fungicide can be used safely with the control measures described above.

SUGGESTED FURTHER READING

Interim Requirements for Clearance of Agricultural and Veterinary Chemical Products (available from the NRA)

Code of Practice for Labelling Agricultural Chemical Products (available from the NRA)

Code of Practice for Labelling Veterinary Chemical Products (available from the NRA)

MRL Standard - Maximum residue limits in food and animal feedstuffs (NHMRC)

22-7-94

WARNING

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING

SCORE®
FOLIAR FUNGICIDE

Active Constituent: 250 g/L difenoconazole
Solvent: 500 g/L hydrocarbon liquid
Contains a DMI fungicide

CONTROLS TARGET SPOT OF POTATOES

5 LITRES Net

UN-Free. In a Transport Emergency Dial 000, Police or Fire Brigade.

CIBA-GEIGY Australia Limited, 140-150 Bungaree Road, Pendle Hill 2145

Directions for use

RESTRAINT: DO NOT apply more than 6 applications of this product per season. The effect of SCORE could be diminished if rain falls within 2 hours of application.

Crop	Disease Controlled	State/ Territory	Rate per ha	Withholding Period	Critical Comments
Potatoes	Target Spot / Early Blight (*Alternaria solani*)	All States, ACT, NT	300 mL or 500 mL	7 days	**This use is subject to an AVCARE anti-resistance strategy.** Use in a protectant programme commencing when rows meet and before disease occurs. Limit the use of DMI fungicides to periods when conditions favour disease development. Apply the 300mL rate at 7 day intervals and the 500mL rate at 10 to 14 day intervals. Use the 500mL rate when conditions favour high disease pressure. Do not apply more than two consecutive sprays of SCORE alone. Alternate or tank mix with a registered protectant fungicide. Good crop hygiene will aid disease control. SCORE does not control late blight, *Phytophthora infestans*. If this disease is a problem, mix SCORE with an appropriate fungicide for control of this disease and observe the spray interval for that product.

NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION

WITHHOLDING PERIOD:

POTATOES - DO NOT APPLY LATER THAN 7 DAYS BEFORE HARVEST.

RE-ENTRY PERIOD: DO NOT ENTER SPRAYED AREAS WITHOUT PROTECTIVE CLOTHING UNTIL SPRAY DRIES

Batch No.	
Date of Manufacture	

General Instructions

Mixing
Add the required amount of Score directly to the spray tank and mix well.

Application
Thorough coverage is essential for effective results. For aerial application use 20-30 L water/ha. For ground application, use at least 100 L water/ha.

Compatibility
This product is compatible with Nuvacron® 400, Azodrin*, Gesapon®, Monitor*, Nitofol*, Metasystox*, Rogor*, Supracide®, Lorsban*, Pirimor*, Thiodan*, Ambush*, Dominex*, Ridomil® MZ formulations, Bravo*, Benlate*, Sumisclex*, Rovral*, Ronilan*, Dithane* M45, Kendon High K, urea, EC formulations of synthetic pyrethroids and organophosphate insecticides and formulations of copper oxychloride.

Protection of Livestock
Low hazard to bees. May be applied to plants any time.

Protection of Wildlife, Fish, Crustacea and Environment
Toxic to fish and aquatic invertebrates. Do not contaminate dams, waterways, or drains with the product or its containers.

Storage and Disposal
Store in closed original container in a dry, well ventilated place as cool as possible. Do not store in direct sunlight. Do not reuse container.
When empty, triple or (preferably) pressure rinse the container adding rinsate to the spray tank. Destroy empty containers by breaking, crushing, puncturing or shredding them where applicable. Dispose of the containers at a local authority landfill that does not burn its refuse. If there is no local authority lanfill readily available in your area, bury the containers at a depth of 500 mm or more at a licensed/approved disposal site. In some States wastes can only be buried at a licensed landfill. Do not burn empty containers or product.

Material Safety Data Sheet
If additional hazard information is required refer to the Material Safety Data Sheet.
For a copy phone 1 800 02 5931.

Re-entry Period
Do not enter treated areas without protective clothing until spray has dried.

SAFETY DIRECTIONS
Harmful if swallowed. Will irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container and preparing spray wear elbow-length PVC gloves and face shield or goggles. If product gets in eyes, wash it out immediately with water. Wash hands after use. After each day's use, wash gloves and face shield or goggles and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre.

RESISTANCE STRATEGY
To reduce the development of fungicide resistant strains it may be necessary to tank mix, or alternate this product with a registered fungicide from a different chemical group. Consult a company representative and refer to Critical Comments for specific instructions.

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY

This product as supplied is of a high grade and believed to be suitable for any purpose for which it is expressly recommended and must be used in accordance with the directions for use given on the label. No responsibility is accepted in respect of this product, save those non-excludable conditions implied by any Federal or State legislation or law of a Territory.

The Manufacturer excludes all liability for damage resulting from improper storage or use of the product, weather and soil conditions, plant types, resistance, spraying technology and other application. Such factors may influence the effect of the product and the user shall bear all risk in this respect.

Recommendations for product usage are based on the latest level of expertise of the manufacturer and should be observed by all users of the product. The manufacturer limits its liability in accordance with section 74L of the Trade Practices Act, provided that this limitation shall not apply if the reseller establishes that reliance on it would not be fair and reasonable. Nothing in this clause shall exclude, restrict or modify any non-excludable condition, warranty, right or liability implied by any Federal or State law.