Public Release Summary
on

Evaluation of the new active

TRITICONAZOLE

in the products

PREMIS 25FS SEED DRESSING FUNGICIDE

and

PREMIS PROFESSIONAL SEED DRESSING FUNGICIDE/INSECTICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

Canberra

Australia

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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 health.

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 *Interim Requirements for the Registration of Agricultural and Veterinary Chemical Products*.

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, Third floor, 10 National Circuit, 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.

Contents

List of Abbreviations and Acronyms

ac	active constituent
ADI	acceptable daily intake (for humans)
a.i.	active ingredient
BCF	bioconcentration factor
bw	body weight
d	day
DAT	days after treatment
DT	dissipation time
EC_{50}	concentration at which 50% of the test population are immobilised
EUP	end use product
F_O	original parent generation
GUS	groundwater ubiquity score
h	hour
HPLC	high pressure liquid chromatography *or* 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
K_{oc}	organic carbon partition 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
Log (K_{ow})	log of octanol water partition co-efficient
LOEC/LOEL	lowest observed effect concentration/level
MAT	months after treatment
µg	microgram
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
po	oral
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
s	second
sc	subcutaneous
SC	suspension concentrate
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 period

Summary

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) has before it applications to register the products Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide which contain the new active ingredient triticonazole for the control of covered smut in wheat and barley.

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide. Before determining whether to register these products for use in Australia, the NRA invites public comment. Comments should be submitted by 12 November 1997 to the NRA at the address indicated on page 1.

The NRA has assessed the data submitted by the applicant in support of the proposed use of triticonazole and provides the following information for public comment.

Two other products containing triticonazole are referred to within this publication: Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide. Although these products have been evaluated as part of the total submission to the NRA, the applicant has decided not to proceed with their registration at this stage.

Efficacy and safety aspects

Premis 25FS Seed Dressing Fungicide is a flowable concentrate containing 25g/L triticonazole and Premis Professional Seed Dressing Fungicide/ Insecticide is flowable concentrate containing 25g/L triticonazole plus 4g/L cypermethrin.

The new products have been developed for the control of covered smuts in wheat and barley which can reduce the quality and marketability of these cereals. Registration of a new active constituent to combat these diseases will provide growers with an additional means of control.

Registration is supported by Australian agricultural authorities.

Environmental aspects

Environmental fate

Triticonazole does not hydrolyse but phototransforms rapidly in aqueous solution mainly to the stable cis-isomer with a DT50 of 3.2 days (d) under artificial light (DT50 = 0.32 d when sensitised with 2% acetone).

Aerobic soil metabolism studies found half-lives of 145–816 d while triticonazole was also moderately persistent to persistent under anaerobic conditions, with 70.4% of the originally applied parent present after 100 d. Half-lives in natural sediment-water systems were 226–405 d, indicating persistence. Mobility studies in five soils found K_{OC} values of

187–570 mL/g, indicating medium to low mobility, which was confirmed with groundwater ubiquity scores (GUS) and leaching studies.

Detectable residues of triticonazole were found in the top 30 cm of soil at any of three wheat plots with 2.4–8.6% of the originally applied pesticide found 281 days after treatment (DAT). A lysimeter study found 5.2% residues at the lowest depth of 20–40 cm soil section at 15 months after treatment (MAT) while 1.7% of identified parent compound was detected at the 10–12.5 cm depth with a half-life of 284 d.

A study on treated winter wheat seeds in four European soils found first order half-lives of 105–178 d and the deepest parent residues at the 20–30 cm horizon. One metabolite peaked at 11% of the originally applied radioactivity, but was non-detectable by 1.5 yr after treatment and was not found deeper than the 10–20 cm horizon.

Animal studies

Triticonazole was practically non-toxic when administered as single oral doses to six avian species. Bobwhite quail chicks and mallard ducklings were also insensitive in 5-d dietary exposures.

Triticonazole was non-toxic to rainbow trout and bluegill sunfish up to the limit of its solubility in water. *Daphnia magna* were moderately sensitive in acute (48 h) and chronic reproductive (21 d) exposures while green alga were unaffected by 0.95 mg a.i./L and was able to grow similarly to controls when placed in clean solution. Bioconcentration is not expected to be a concern.

Two bacteria associated with the rhizospheres of wheat were unaffected by triticonazole concentrations of 0.5 mg a.i./kg soil (equivalent to 300 g a.i./ha or 7.4X higher than the maximum proposed application rate) for 21 d when compared to controls. However, application rates 8.9 and 44.4X higher caused >15% deviations over 28 d in soil nitrification processes when compared to controls in a sandy loam soil. In a sandy clay loam, this adverse effect was only observed in the lower treatment rate. Soil respiration was within 15% of controls at all times for both soils.

Environmental hazard

The environmental hazard of triticonazole will be highest to organisms living in the soil where it will be applied as a seed dressing. Its persistence in soil will result in prolonged exposure and an increased opportunity for off-site movement in sandy soils. Concentrations in surface waters are not expected to be high as phototransformation to the stable cis-isomer is rapid, however, any triticonazole leaching through sandy soil will persist in ground water. The persistence of the compound in soil may indicate significant carryover from one growing season to the next. However, the use pattern as a seed dressing and very low application rate of 40.5 g a.i./ha will serve to limit the environmental hazard.

Although limited data were submitted on the environmental chemistry, toxicology and fate of triticonazole, they were sufficient for the proposed low application rate and use pattern of the four end-use products. An assessment of the expected environmental concentrations resulting

from the registration of these products as seed dressings for wheat, barley and oats indicates that the proposed use is not expected to pose an unacceptable hazard to the environment.

Public health aspects

Toxicology

Triticonazole is the active constituent in Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide. Premis Professional Seed Dressing Fungicide/Insecticide and Real Professional Seed Dressing Fungicide/Insecticide also contain cypermethrin.

Triticonazole has low acute oral, dermal and inhalational toxicity. It is not a skin irritant or skin sensitiser and is a slight eye irritant. The formulation, Premis 25FS Seed Dressing Fungicide, also exhibited low oral, dermal, and inhalational toxicity consistent with the low toxicity of triticonazole. The formulation is a slight skin and eye irritant but is not a skin sensitiser.

Those products not directly tested—Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide—were assessed, on the basis of their individual constituents, to also have low topical and systemic toxicity. The primary hazard appears to be a slight dermal irritation (slight erythema) due to the non-active constituents of the formulations.

In repeat dose studies, the primary manifestations of triticonazole toxicity were effects on the liver and adrenals. Increased levels of liver enzymes in the blood and microscopic damage to liver and adrenal cortex cells were observed. Effects on the adrenals tended to be more pronounced during short-term studies and at interim sacrifices in chronic studies, suggesting that effects on the adrenals are temporary and do not progress into more serious lesions. They also suggest that a tolerance to these effects develops with continued exposure.

In dogs treated at high doses of 150 mg/kg bw/day, the formation of full thickness cataracts of the lenses of the eyes was observed. This effect was not seen at any other dose in dogs, was not observed at higher doses in dogs over shorter periods, and was not observed in any other species tested.

Triticonazole was not carcinogenic in mice, rats or dogs, and was not a teratogen in rats or rabbits. In a reproduction study in rats, triticonazole at 250 mg/kg bw/day reduced the fertility of adult females and caused a reduction in the number of live births and the weight of pups soon after birth. At doses which were maternally toxic, developmental delays were observed in the foetuses of rats and rabbits, characterised by delayed bone formation. Triticonazole did not damage genetic material.

Conclusion

On the basis of an assessment of the toxicology and the potential dietary intake of residues, no adverse effects on human health are expected from the proposed use of triticonazole as a component of Premis 25FS Seed Dressing Fungicide Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide.

Residues in food and trade aspects

Residues in food

The four products will be used for the control of variety of fungi and insects in cereal grains such as wheat, barley and oats. All products contain the new active ingredient, triticonazole, at concentrations of 25 g/L and 200 g/L in Premis and Real formulations, respectively. In addition, cypermethrin is used at 4 g/L as the second active in Premis and Real Professional formulations. Triticonazole is a triazole fungicide which acts as a C14 demethylation inhibitor in the sterol biosynthesis in most of the fungi.

MRLs of *0.05 mg/kg for cereal grains, *0.05 mg/kg for edible offal (mammalian), *0.05 mg/kg for eggs, *0.05 mg/kg for meat (mammalian), *0.01 mg/kg for milk, *0.05 mg/kg for poultry edible offal and *0.05 mg/kg for poultry meat were recommended based on Australian and overseas residue studies. In addition, MRLs for straw and fodder (dry) of cereal grains (*0.05 mg/kg) and forage of cereal grains (0.1 mg/kg) were also recommended. The food commodities listed above are not expected to have measurable residues of triticonazole. A harvest withholding period is not required as residues at harvest are expected to be non-quantifiable under the proposed use pattern.

Trade

The residue data for triticonazole suggest it is unlikely that residues in cereals would be a potential trade risk. For meat, edible offal and milks the MRLs have been set close to the level of quantification which means that residues should not be quantifiable and hence, are of no concern to trade.

Occupational health and safety aspects

Worksafe Australia conducted a risk assessment of Premis 25FS Seed Dressing Fungicide (2.5% triticonazole), Premis Professional Seed Dressing Fungicide/Insecticide (2.5% triticonazole and 0.4 % cypermethrin), Real Seed Dressing Fungicide (20% triticonazole) and Real Professional Seed Dressing Fungicide/Insecticide (20% triticonazole and 0.4% cypermethrin). The products, formulated as flowable concentrates, are to be used as seed treatments to control fungal diseases and insect infestations in wheat, barley and oats.

Triticonazole is not included in the National Occupational Health and Safety Commission *List of Designated Hazardous Substances*. Rhone-Poulenc Rural Australia Pty Ltd states that R 51/53 and S 60/61 phrases have been allocated to triticonazole according to the European

Union classification. These phrases do not relate to occupational health. Accordingly triticonazole is not determined to be hazardous substance.

Cypermethrin is not included in the National Occupational Health and Safety Commission *List of Designated Hazardous Substances*.

Rhone-Poulenc Rural Australia Pty Ltd has determined that none of the products are hazardous. All the products have low oral and dermal toxicity and are slight irritants. Product toxicity following long-term exposure is influenced more by triticonazole than cypermethrin.

The products will be formulated in Australia. Engineering controls, dust monitoring, biological monitoring (where appropriate) and training are in place to protect production and maintenance personnel. Transport workers, store persons and retailers will only handle the packaged product.

The products are premixed with water and mixed into seed. End users may experience skin contamination from the concentrate or premix. Mixing is an automated process, in a closed system in seed treatment plants or within an auger on farm. Treated seed does not need to be bagged or otherwise manually handled. The risk assessment indicates that workers will be adequately protected by wearing gloves when handling the concentrates and premix.

The products have low inhalation toxicity and workers do not require specific respiratory protection. However, as respiratory effects may be caused by grain dust, workers may choose to wear a disposable dust mask.

There are no occupational health and safety concerns for workers handling treated seed.

Introduction

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the chemical triticonazole as a seed dressing fungicide to control covered smut on wheat and barley.

Response to 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.

Copies of full technical reports on toxicology, occupational health and safety aspects, environmental impact and residues in food are available from the NRA on request from:

[redacted]

They can also be viewed at the NRA Library located at the NRA's offices on Level 1, Computer Associates House, 10 National Circuit, Barton ACT 2604.

Written comments should be received by the NRA by 12 November 1997. They should be sent to:

[redacted]

Applicant

Rhone-Poulenc Rural Pty Limited has applied for registration of two fungicide products containing a new active constituent, triticonazole, a triazole fungicide.

Product details

Triticonazole will be marketed under the trade names Premis 25FS Seed Dressing Fungicide, a flowable concentrate containing 25 g/L triticonazole, and Premis Professional Seed Dressing Fungicide/Insecticide, a flowable concentrate containing 25 g/L triticonazole and 4 g/L cypermethrin.

Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide will be fully formulated and packed in Australia.

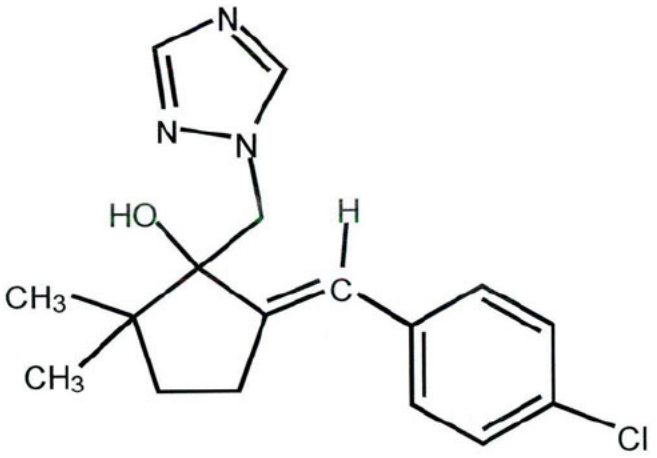
Rhone-Poulenc Rural Pty Ltd intends to market Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide in all States and Territories for the control of covered smut on wheat and barley. Triticonazole is currently registered for use in certain cereals in Argentina, Belgium, France, South Africa and Uruguay.

Chemistry and Manufacture

The chemical active constituent triticonazole is manufactured in France and has the following properties:

Common name (ISO):	triticonazole
Chemical name:	(±)-(E)-5-(4-chlorobenzylidene)-2,2-dimthyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanol (IUPAC)
	5-[(4-chlorophenyl)methylene]-2,2-dimthyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanol (CA)
Product names:	Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide.
CAS Registry Number:	131983-72-7
Empirical formula:	$C_{17}H_{20}ClN_3O$

Structural formula:



Molecular weight:	317.82
Physical form:	powder
Colour:	white to cream
Odour:	odourless at 22°C

Melting point:	139–140.5°C
Density:	1.32–1.366 g/ml
Log (K_{ow}):	3.29 at 20°C
Vapour pressure at 50°C:	<0.1 x 10-7hPa

TOXICOLOGICAL ASSESSMENT

Evaluation of toxicology

The toxicological database for triticonazole, 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 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

Triticonazole administered to rats either as a single or repeated oral dose was rapidly and extensively absorbed and metabolised, and subsequently excreted primarily in the faeces. After a single high dose to rats, absorption was more limited with up to 70 % of the dose eliminated in the faeces without absorption or change. Although the compound is widely distributed through the tissues and organs, the levels of residue were low and no indication of accumulation was observed.

Acute studies

Triticonazole has low oral (LD_{50} >2000 mg/kg), dermal (LD_{50} >2000 mg/kg), and inhalational toxicity in rats (LC_{50} >1400 mg/m^3). No mortality occurred at the dose rates tested. The compound is a slight eye irritant but not a skin irritant in rabbits and is not a skin sensitiser in guinea pigs.

Premis 25FS Seed Dressing Fungicide, containing 25 g/kg of triticonazole, has low oral (LD_{50} >2000 mg/kg), dermal (LD_{50} >2000 mg/kg), and inhalational toxicity in rats (LC_{50} > 3450 mg/m^3), and is a slight skin but not an eye irritant in rabbits and is not a skin sensitiser in guinea pigs. No mortality occurred at any of the dose rates tested.

Short-term studies

Rats were treated orally with triticonazole at 0, 10, 100 and 1000 mg/kg bw/day for 14 days. Toxicity was observed only at 1000 mg/kg bw/day. Females showed increased liver weights which correlated with the observation of prominent changes to the cellular structure of liver cells.

Beagle dogs (one male and one female in each pair) were treated orally with triticonazole in capsules, in a study to determine the maximum tolerated dose. Nervous system effects were seen at 500 mg/kg bw/day and above. A reduction in food eaten and weight gained was seen in the female from 80 mg/kg bw/day onwards and in the male from 40 mg/kg bw/day

onwards. At doses of 300 mg/kg bw/day and above an elevation of enzymes associated, in this case, with liver damage and elevated cholesterol and total protein were seen. High liver weight and pallor of the liver were also observed. The maximum tolerated dose in the beagle was considered to be 300 mg/kg bw/day.

Rats were treated with triticonazole in the diet at levels of approximately 0, 2, 1100 and 2300 mg/kg bw/day for 13 weeks. Hair loss was observed in the majority of animals at 1100 and all at 2300 mg/kg bw/day. Animals on 1100 and 2300 mg/kg bw/day ate less and gained less weight during the first 5 weeks of treatment. Evidence of a mild anaemia in males and females was seen at 1100 and 2300 mg/kg bw/day. White blood cell counts were substantially increased in females at 2300 mg/kg bw/day.

Clinical chemistry changes were minimal with the main abnormality observed consisting of increased total cholesterol levels in both sexes at 1100 and 2300 mg/kg bw/day. Increased liver and spleen weights and an abnormal shape and structure of the cells in the liver and adrenals, indicating cellular damage, were observed in both sexes on 1100 and 2300 mg/kg bw/day.

Long-term studies

Mice were treated with triticonazole in the diet at levels approximately equal to 0, 1.8, 17 and 200 mg/kg bw/day for 78 weeks with an interim sacrifice at 26 weeks. Toxicity was only observed at 200 mg/kg bw/day. Both sexes gained less weight and the weight of their livers were increased. Adrenal weights at interim sacrifice were increased in males and slightly increased in females.

At the end of the study some males had enlarged lymph nodes. A dark colouration of these nodes was observed in some males at all treatment levels and in controls but was more common at 200 mg/kg bw/day. Enlarged livers were observed in a few animals of each sex at the end of the study and microscopic abnormalities of the liver, indicating cellular damage, were found. The incidence of tumours was not increased.

Rats were treated with triticonazole in the diet at levels approximately equal to 0, 0.2, 1, 29 and 200 mg/kg bw/day for 104 weeks with some animals sacrificed at 26 and others at 53 weeks for the study of early effects. Toxicity was only observed at 200 mg/kg bw/day.

Animals of both sexes gained less weight during the first few weeks of treatment. The incidence of enlarged adrenals was increased in males and the incidence of swollen livers and enlarged ovaries were increased in females. At 53 weeks moderate hair loss was increased in females. Abnormalities of the cell nucleus (multi nucleated cells) were seen in the middle layer of the adrenal cortex in females at 26 and 53 weeks but not at 104 weeks. In females after 100 weeks of treatment, microscopic evidence of liver cell damage, and an increased incidence of macrophages in the alveoli of the lungs were seen. No evidence of carcinogenicity was observed.

Beagle dogs were treated with triticonazole in capsules at 0, 2.5, 25 and 150 mg/kg bw/day for 52 weeks. During the early phase of treatment, signs of neurotoxicity were noted at 150 mg/kg bw/day shortly after dosing, with signs of convulsion in some animals. Reddening and thickening of the ear, and patchy skin thickening of other areas of the body, were more

common, and animals in this group gained less weight during the first 13 weeks. Cataracts of the lenses of the eye (loss of lens transparency) began to appear from week 18 in animals treated at 150 mg/kg bw/day and progressed to overt cataracts by the end of the study. An increased platelet count was observed in females treated at 150 mg/kg bw/day and to a lesser extent in males at this dose.

At 25 and 150 mg/kg laboratory tests indicated probable liver damage. Increased liver and adrenal weights and decreased prostate weights in males, and increased liver, adrenal and kidney weights in females, were seen at 150 mg/kg bw/day while enlargement of the liver was noted in some animals treated at 25 and 150 mg/kg bw/day. An increased incidence of damage to the cells of the thick middle layer of the adrenal cortex was seen microscopically in animals at 150 mg/kg bw/day.

Reproduction and developmental studies

In a two-generation reproduction study, rats were treated with triticonazole technical in their diet at levels of approximately 0, 0.25, 1.3, 38 and 250 mg/kg bw/day. Toxicity and effects on reproduction were observed only at 250 mg/kg bw/day. Testes, prostate, epididymides, and adrenal weights were increased and pituitary weights decreased in parental males. Parental females gained less weight and ate less, adrenal weights were decreased and liver weights and ovary weights were increased. Microscopic abnormalities of the adrenals, liver and ovaries were seen.

The proportion of pups born alive was decreased and from the seventh day after birth, pup weights from females of the first parental generation were reduced. For the second generation of adult females, the number becoming pregnant was reduced by a third, the number of pups delivered per female was reduced by a quarter and the proportion of pups born alive was reduced by 15%. There were no treatment related malformations observed in pups.

Pregnant female rats were treated orally with triticonazole at 0, 40, 200 and 1000 mg/kg bw/day during the period of foetal development. Animals gained less weight and ate less at 1000 mg/kg bw/day. Treatment effects in foetuses were confined to an increase in the number having 14 ribs, at 1000 mg/kg bw/day. This effect is recognised to be related to delayed foetal development, as a result of maternal toxicity, rather than being a malformation, and extra ribs are usually resorbed as the pup matures.

Pregnant female rabbits were dosed orally with triticonazole at 0, 5, 25, 50 and 75 mg/kg bw/day during the period of foetal development. One animal died at 5 mg/kg bw/day, two died at 50 mg/kg bw/day and six died at 75 mg/kg bw/day. Animals treated at 50 mg/kg bw/day and above ate less and gained less weight. Embryo and foetal death were increased in animals treated at 75 mg/kg bw/day and a number of skeletal effects consistent with delayed development, as a result of maternal toxicity, were observed. At 50 mg/kg bw/day treatment related effects were limited to a delay in the calcification of the bones of the fingers and toes of the paws (metacarpals and phalanges), and an elongation of one or both of the bones forming the point of the shoulder (acromion process).

Genotoxicity

Triticonazole was not mutagenic in a bacterial mutation assay and in a gene mutation test in Chinese hamster V79 cells. The compound did not cause DNA damage in mouse bone marrow, rat hepatocytes, or in human lymphocytes. Taken together these studies do not indicate that triticonazole is a mutagenic risk to humans.

Studies on triticonazole impurities

The major impurity of synthesis had low oral and dermal toxicity in rats with an LD_{50} of > 2000 mg/kg bw/day in each case. No mortality occurred at the rates tested.

In rats treated orally with the impurity of synthesis at 0, 10, 100 and 1000 mg/kg bw/day for 14 days, toxicity was observed only at 1000 mg/kg bw/day. Increases in liver weights were observed in both sexes which correlated with the observation of prominent changes to the cellular structure of liver cells. Slight thickening of the lining of the stomach was seen in 40% of males and minimal thickening was seen in another 20% of males. The impurity of synthesis did not increase the incidence of reverse mutation in *S. typhimurium*. The toxicology of the impurity of synthesis in these studies was similar to that of triticonazole.

Public health standards

Poisons scheduling

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

The NDPSC recommended that formulations containing triticonazole be placed 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 labels.

NOEL/ADI

The most sensitive species tested was the dog with a NOEL of 2.5 mg/kg bw/day in a 12-month study.

To calculate an Acceptable Daily Intake (ADI) for humans, a safety factor is applied to the NOEL in the most sensitive species. The magnitude of the safety factor is selected to account for uncertainties in extrapolation from animal data to humans; variation within the human population; the quality of the experimental data; and the nature of the potential hazards. Using a safety factor of 100, an ADI of 0.02 mg/kg bw/day was established for triticonazole.

Residues Assessment

Potential for chemical residues in food

Triticonazole is the active constituent in Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide, and Real Professional Seed Dressing Fungicide/Insecticide for the control of certain fungi in cereal grains such as wheat, barley and oats. Cypermethrin is used as the second active in two of the products to control certain insects in storage.

These products are currently registered in France, Belgium, South Africa, Argentina, and Uruguay and registration is being sought in many other countries, including the EU countries and Canada.

Appropriate residue and metabolism studies were provided in accordance with the *Requirements for Clearance of Agricultural and Veterinary Products*, to support the use of triticonazole on cereals in Australia.

Residues in food commodities

Residue data were presented for cereal grains, from trials conducted in Australia, the UK and South Africa. Both Premis Professional and Real Professional fungicides contain cypermethrin as the second active ingredient. However, the following discussion addresses residue issues relating only to triticonazole, as seed dressing formulations containing similar levels of cypermethrin are currently registered in Australia.

Cereal grains

Seven trials were conducted in Australia using treatment regimes of one application at rates of 3, 6, 15, 22.5, 45 and 90 g a.i./100 kg of seed (0.1 times to 3 times the maximum recommended rate). Residues in harvested cereal grains grown from treated seed were found to be below the limit of determination (<0.05 mg/kg). No residue data for processed commodities such as flour and bran were available but evidence suggests that significant residues are not likely to concentrate in processed cereal commodities.

Four trials were conducted in the UK and South Africa at application rates up to 8 times the maximum proposed rate in Australia. Residues in cereal grains at harvest were found to be below 0.01 mg/kg.

The residue data indicate that, in accordance with the recommended pattern of use, a nil withholding period is appropriate.

Metabolism studies

Metabolism studies were conducted on cereals under field trial conditions using labelled triticonazole. A maximum treatment regime of one application at a rate of 240 g a.i./100 kg of seed (8 times the maximum recommended rate) was employed.

Samples were taken at various stages of plant development and at harvest and were analysed for residues. The major residue in most components sampled was the parent compound triticonazole and hydroxylated metabolites during development and at harvest. Low residues were detected in the grain. The highest levels of radioactive residues were located in the foliage. Up to 2% of the applied dose was present in the grain and 10% in the above-ground part of the plant at harvest. Results also indicated that water soluble small molecular weight compounds were present in the residues resulting from the metabolism of triticonazole.

Animal metabolism studies were conducted in rats, hens and lactating cows. Common metabolic trends were observed in all three animal types. At all dose levels, most of the triticonazole was excreted via the faeces and urine (>80%) in all three species studied. Of the remaining residue, the most was located in the offal tissues of all animals.

The 7 day cow metabolism study indicated no detectable residues of triticonazole in the fat and muscle. The study also indicated negligible transfer of residues into milk. In the offal, the major residue was not the parent compound, but a mixture of hydroxylated metabolites and a carboxylic acid metabolite, which are common in all animal types. These compounds are formed by metabolism of the parent through processes such as ring hydroxylation, oxidation and conjugation. The parent is also detected, but at levels lower than those of the other metabolites.

Detailed descriptions of the analytical method were provided. The parent was detected directly, after extraction and solid-phase clean-up, using gas chromatography. The limits of determination ranged from 0.01 to 0.05 mg/kg.

MRL Standard

The following additions to the *MRL Standard* have been recommended:

Table 1

Compound	Food	MRL (mg/kg)
ADD:		
Triticonazole		
GC 0080	Cereal grains	*0.05
MO 0105	Edible offal (mammalian)	*0.05
PE 0112	Eggs	*0.05
MM 0095	Meat (mammalian)	*0.05
ML 0106	Milks	*0.01
PO 0111	Poultry, Edible offal of	*0.05
PM 0110	Poultry meat	*0.05

Table 3

Compound	Residue
ADD:	
Triticonazole	triticonazole

Table 4

Compound	Animal Feed Commodity	MRL (mg/kg)
ADD:		
Triticonazole		
AS 0081	Straw/fodder (dry) of cereal grains	*0.05
AF 0081	Forage of cereal grains	0.1

Withholding period statement

No harvest withholding period or withholding period for grazing and cutting for stock feed is considered necessary for triticonazole when applied as a seed treatment. The following statement has been included on the labels.

WITHHOLDING PERIOD:
WHEAT, BARLEY: NOT REQUIRED WHEN USED AS DIRECTED.

Assessment of Overseas Trade Aspects of Residues in Food

There are no MRLs established for triticonazole in major overseas markets, however, the use of triticonazole as a seed treatment is not likely to affect exports. Australian residue trials carried out at application rates up to 3 times the maximum proposed rate have shown that triticonazole residues in grain grown from treated seed were below the limit of determination. Overseas trials where rates up to 8 times the proposed rate have been used, showed residues less than 0.01 mg/kg in the harvested grain.

Plant metabolism studies indicate that small amounts of residual radioactivity in the grain results from incorporation of radioactivity into natural constituents. Therefore, no significant residues are likely to be present in the harvested grain. Furthermore, feeding of harvested grain or straw to livestock is not expected to affect livestock exports.

Metabolism studies in cows, carried out at exaggerated feed concentrations of triticonazole, indicate that triticonazole is rapidly eliminated via urine and faeces and does not accumulate in the body tissue.

Occupational Health and Safety Assessment

Triticonazole is not included in the National Occupational Health and Safety Commission *List of Designated Hazardous Substances*. Rhone-Poulenc Rural Australia Pty Ltd states that R 51/53 and S 60/61 phrases have been allocated to triticonazole according to the European Union classification. These phrases do not relate to occupational health. Accordingly, triticonazole is not determined to be hazardous substance.

Triticonazole is a white odourless powder. In experimental animals, it has low oral, dermal and inhalation toxicity. It is a slight eye irritant but not a skin irritant or a skin sensitiser. In repeat dose animal studies the main target organs are the liver and adrenal glands.

Cypermethrin is not included in the National Occupational Health and Safety Commission *List of Designated Hazardous Substances*. In experimental animals it has moderate oral toxicity and low dermal toxicity. It is a skin and eye irritant and a weak sensitiser. In humans, it can cause transient abnormal facial skin sensations if splashed onto the skin.

Four products are under consideration: Premis 25FS Seed Dressing Fungicide (2.5% triticonazole), Premis Professional Seed Dressing Fungicide/Insecticide (2.5% triticonazole and 0.4 % cypermethrin), Real Seed Dressing Fungicide (20% triticonazole) and Real Professional Seed Dressing Fungicide/Insecticide (20% triticonazole and 0.4% cypermethrin).

Rhone-Poulenc Rural Australia Pty Ltd has determined that none of the products is a hazardous substance. There are only marginal differences in product toxicity. All have low oral and dermal toxicity and are slight skin irritants. In addition, Premis Professional Seed Dressing Fungicide/Insecticide and Real Professional Seed Dressing Fungicide/Insecticide are slight eye irritants. Product toxicity following long-term exposure is influenced more by triticonazole than cypermethrin.

Products are opaque red liquids packed into 2.5, 5, 10 and 20 L containers. Container types are a selection of HDPE bottles, epon-lined metal cans or high density polyethylene bladders in fibreboard containers.

Formulation, transport and sale

The products will be formulated in Australia by Rhone-Poulenc Rural Australia Pty Ltd. Engineering controls, dust monitoring, biological monitoring (where appropriate) and training are in place to protect the production and maintenance personnel.

Transport workers, store persons and retailers will only handle the packaged product. They could only become contaminated if the packaging were breached.

Advice on safe handling of triticonazole and the products during formulation and use is contained on the material safety data sheets.

End use

All products are used in the same manner. They are mixed with wheat, barley and oat seeds to control fungal diseases and insect infestations. Seeds are treated before planting or warehousing. Each product is premixed with water before being thoroughly incorporated with the seed. Premix concentrations correspond to 0.6-7.5% triticonazole and 0.2% cypermethrin. Products are used between 75 and 150 mL per 100 kg seed, at maximum final concentrations of 0.03% triticonazole and 0.0006% cypermethrin.

Products may be used by professional seed treaters on farms and in seed treatment plants or by individual farmers. In all end-use situations, most exposure would occur when the containers are opened and the product premixed and poured. Mixing is an automated process, in a closed system in seed treatment plants or within an auger on farm. Treated seed does not need to be bagged or otherwise manually handled. Farmers would handle the product over a limited seasonal timeframe, whereas professional seed treaters may use the product over some months.

The primary route of occupational exposure will be through skin contamination when dispensing the concentrate, making up the premix and adding it to the seed. Workers may breathe in a combination of product and grain dust, if treated seed is collected in an open process and dust is generated.

The products are slight skin irritants and workers will require hand protection when handling the concentrates and premixes. No worker exposure studies were available for workers using the products. However the qualitative risk assessment indicates that workers will be adequately protected by wearing gloves when handling the concentrates and premix.

The products have low inhalation toxicity and workers do not require specific respiratory protection. However, as respiratory effects may be caused by grain dust, workers may choose to wear a disposable dust mask.

Re-handling of treated seeds

The very low concentrations of active ingredients in treated seed indicate that there are no occupational health and safety concerns for workers handling treated seed, should they need to do so.

Recommendations for safe use

Australian workers involved in formulation and packing of Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide should be protected by proper engineering controls, dust monitoring and biological monitoring (where appropriate).

Seed treatment should be an enclosed process in treatment plants. Workers may breathe in a combination of product and grain dust, if treated seed is collected in an open process and dust is generated. Extraction or ventilation systems need to be in place in seed treatment plants to

reduce dust concentrations to acceptable levels, below the NOHSC exposure standard. Workers may choose to wear a disposable dust mask.

End users should follow the instructions and safety directions on the product labels. Safety directions include the use of personal protective equipment, namely elbow-length PVC gloves.

The personal protective equipment recommended should meet the relevant Standards Australia standard specified below:

> AS 2161-1978 Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)

Rhone-Poulenc Rural Australia Pty. Ltd has produced material safety data sheets for Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide. These should contain 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 material safety data sheets from the supplier and ensure that their employees have ready access to it.

Conclusion

Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/ Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/ Insecticide can be used safely if handled in accordance with the instructions on the product labels. Additional information is available on the material safety data sheets for triticonazole and the products.

Environmental Assessment

Environmental exposure

Premis 25FS Seed Dressing Fungicide is to be used to control flag smut, covered smut and loose smut in wheat and barley. Real Seed Dressing Fungicide is intended, in addition, to suppress stripe rust, leaf scald and powdery mildew. The Professional version of each contains cypermethrin to control various insects in these grains. The sowing rates for these grains would lead to maximum application rates of 40.5 g a.i./ha for triticonazole and 0.81 g a.i./ha for cypermethrin.

In Australia, all three grains are grown primarily in a narrow belt inland of the Great Dividing Range stretching from central Queensland through New South Wales, Victoria and southern South Australia on soils with a significant sand content. In Western Australia, the belt continues around the south-west of the State and some way north up the western side of the continent on relatively sandy soils. Wheat is usually grown in rotation with some form of pasture such as grass, clover or lucerne, with a maximum of approximately two or three years of wheat and rotation for about two years before returning to wheat.

Environmental chemistry and fate

Hydrolysis and photolysis

Triticonazole did not hydrolyse after 30 days in solutions of pH 5, 7 and 9. Rapid phototransformation, mainly to the stable cis-isomer, in aqueous solution of pH 5 occurred with a DT 50 of 3.2 days under artificial light. Phototransformation to an equilibrium with the cis-isomer was even more rapid (DT50 = 0.32 d) when sensitised with 2% acetone. When placed on dry glass, only 8.6% transformation to the isomer occurred in 14 days.

Aerobic and anaerobic metabolism

Three laboratory studies, conducted to determine the fate of triticonazole when aerobically incubated in six soils, found half-lives of 145–816 d with two main metabolites and $^{14}CO_2$. A soil anaerobic metabolism study also showed triticonazole to be moderately persistent to persistent with 70.4% of the originally applied parent present after 100 d. When incubated aerobically in natural river and pond water/sediment systems, triticonazole was persistent with half-lives of 405.1 and 226.0 d, respectively. There was a rapid dissipation from water with DT50s of 7.9–8.9 d, into sediment. Triticonazole was not readily biodegradable according to OECD test guidelines.

Mobility

An adsorption/desorption study found K_a values of 1.7–31.7 mL/g and K_{OC} values of 187–570 mL/g, indicating medium to low mobility in five soils. In these same soils, a leaching study generally found triticonazole remained in the top 18 cm of the surface except for a sand soil (96% sand) where 70.6% of the originally applied radioactivity leached through the 36 cm soil column.

Aged residues bound more strongly to soil resulting in higher proportions of radioactivity detected in the top 12 cm and less in the lower segments and leachate. The calculated GUS score of 2.69–5.03 overlaps the range for probable leachers (>2.8).

Field dissipation

Detectable residues of triticonazole were found only in the top 30 cm of soil at any of three wheat plots in France treated at 279–532 g a.i./ha (which is up to 13.1X higher than the maximum proposed rate in Australia). However, no measurement of potential lateral movement was made. While no half-life could be calculated, 2.4–8.6% of the originally applied pesticide was found 281 DAT at the 0-30 cm depth.

A lysimeter study, in which winter wheat seeds were treated at 209 g a.i./ha and planted in a sandy loam soil, found 5.2% residues at the lowest depth of 20–40 cm soil section at 15 MAT while 1.7% of identified parent compound was detected at the 10–12.5 cm depth. Environment Australia calculated the half-life of triticonazole in this study to be 283.5 d.

A study on treated winter wheat seeds in four European soils found first order half-lives of 105–178 d and the deepest parent residues at the 20–30 cm horizon. One metabolite peaked at 11% of the originally applied radioactivity, but was non-detectable by 1.5 yr after treatment and was not found deeper than the 10–20 cm horizon.

Computer modelling of dissipation and accumulation

The PELMO computer model predicted negligible concentrations of triticonazole (<0.000 µg a.i./L) below 1.1 m soil depth in the leachate of standard German soils assuming a K_{OC} of 388.4 mL/g, soil DT50 of 177 d, application rate of 10 g a.i./ha and a mean annual rainfall of 778 mm in a sandy loam soil. However, input parameters were not worst-case and did not accurately reflect the expected conditions of use in Australia. Based on a worst-case field dissipation half-life of 283.5 d, concentrations in the top 5 cm of soil could accumulate to 0.056 mg a.i./kg soil after 7 yr following a pattern of three years of annual applications (40.5 g a.i./ha) followed by two years of crop rotation during which triticonazole would not be applied, presuming no leaching outside of this depth.

Bioconcentration

When continuously exposed to 0.1 or 0.4 mg a.i./L, rainbow trout rapidly concentrated triticonazole from water and reached steady state in 24 h with a BCF of 5.7–7.1 in muscle. The BCF in viscera was more variable at 20.8–21.6 while whole fish was 11.7–12.8 after 28 d exposure. When placed in clean water, depuration was also rapid as radioactivity was non-detectable in muscle and viscera after 1 and 7 d, respectively. These BCF values indicate that triticonazole is not likely to bioconcentrate in fish tissue.

Environmental toxicology

Birds

Triticonazole was practically non-toxic to six avian species (although two were only used for preliminary screening purposes) in single oral dose exposures with LD_{50} > 2,000 mg a.i./kg bodyweight. Doses of 2,000 mg a.i./kg bodyweight caused some birds to regurgitate the

compound. Bobwhite quail chicks and mallard ducklings were also insensitive in 5-day dietary exposures where the LC_{50} was >5,380 and >5,360 mg a.i./kg food, respectively. Reduced bodyweight gains resulted in NOEC and LOEC values of 1,300 and 2,690 mg a.i./kg food, respectively for bobwhites and 1,380 and 2,700 mg a.i./kg food for mallards.

Aquatic organisms

Triticonazole was non-toxic to rainbow trout and bluegill sunfish up to the limit of its solubility in water as 96-h LC_{50} values were >8.9 mg a.i./L. *Daphnia magna* were moderately sensitive in acute exposures with a 48-h EC_{50} of 7.67 (6.36, 10.05) mg a.i./L. In a chronic reproductive study, the 21-d EC_{50} for parent daphnids was 2.37 (1.46, 3.83) mg a.i./L with the NOEC and LOEC for adverse reproductive effects of 0.092 and 0.29 mg a.i./L, respectively. The green alga *Selenastrum capricornutum* was unaffected by a concentration of 0.95 mg a.i./L and was able to grow similarly to controls when placed in clean medium.

Terrestrial invertebrates

The earthworm *Eisenia foetida* was insensitive to triticonazole as the LC_{50} value was >1,000 mg a.i./kg soil.

Soil microorganisms and processes

Populations of two bacteria, *Bacillus polymixa* and *Azospirillum brasilense* associated with the rhizospheres of wheat, were unaffected by triticonazole concentrations of 0.5 mg a.i./kg soil (equivalent to 300 g a.i./ha or 7.4X higher than the maximum proposed application rate) for 21 d when compared to controls. Triticonazole application rates of 0.36 and 1.8 kg a.i./ha, which are 8.9 and 44.4X higher than the maximum proposed application rate, caused >15% deviations in the nitrification of NH_4^+ to NO_3^- when compared to controls over 28 d in a sandy loam soil. In a sandy clay loam, this adverse effect was only observed in the lower treatment rate. Soil respiration in treated samples was within 15% of controls at all times.

Environmental hazard

The maximum proposed application rate of triticonazole of 40.5 g a.i./ha is not expected to result in residues in food that would adversely affect birds in the short term. While the chronic hazard to birds from this exposure level is unknown, triticonazole as a seed treatment is not expected to be a hazard given the extremely low acute toxicity and method of application.

The worst-case soil EEC of 0.056 mg a.i./kg soil in the top 5 cm after 7 years of rotating applications is not expected to be a hazard to earthworms. Although adverse effects on soil nitrification were observed at 0.6 mg a.i./kg soil, this concentration is 10.7 times higher than the worst-case soil EEC, and soil nitrification processes are not expected to be adversely affected by triticonazole applications over time. Also, crop rotation and cultivation practices are expected to mix residues to deeper depths and further reduce the soil EEC.

As triticonazole is applied as a seed dressing and not sprayed, the hazard to aquatic organisms is greatly reduced. It is moderately toxic to aquatic invertebrates and non-toxic to fish up to the limit of its solubility (~8.9 mg a.i./L). Algae were not adversely affected at the highest tested concentration of 0.95 mg a.i./L. Bioconcentration is low and not expected to be a hazard. It rapidly phototransforms in solution mainly to the stable cis-isomer whose toxicity

and fate are unknown but not expected to reach waters in concentrations high enough to pose a significant hazard. Planting of treated seed in a sandy soil may potentially pose a higher hazard to ground water as up to 70.6% leached in a laboratory study utilising such a column. The binding of residues to soil increases with age and may limit leaching with time. Also, the low application rate will reduce possible leaching.

Conclusions and recommendations

The proposed low application rates and use patterns of Premis 25FS Seed Dressing Fungicide, Premis Professional Seed Dressing Fungicide/Insecticide, Real Seed Dressing Fungicide and Real Professional Seed Dressing Fungicide/Insecticide for wheat and barley are not expected to pose an unacceptable hazard to the environment. The recommended modifications to the labels should be made to reduce the potential for exposure to non-target organisms and the contamination of water.

In the event that future extensions to the use pattern or an increased application rate will result in a more significant environmental exposure, Environment Australia will need to conduct a supplementary assessment which may require further data on the environmental toxicology (e.g. algae and aquatic macrophytes, terrestrial plants and nitrification processes of soil microbial populations) of triticonazole and its major metabolites (e.g. cis-isomer) in addition to several specific points.

Efficacy and Safety Assessment

Justification for use

Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide are flowable concentrates containing the new active constituent triticonazole. These products have been developed for the control of covered smut in wheat and barley which can reduce the quality and marketability of these cereals. Registration of this new active to combat these fungal diseases will provide growers with an additional means of control.

Registration is supported by Australian agricultural authorities.

Proposed use pattern

Premis 25FS Seed Dressing Fungicide, containing 25 g/L triticonazole, is proposed as a once-only seed treatment to control covered smut in wheat and barley. The proposed application rate is 100 ml of product per 100 kg seed.

Premis Professional Seed Dressing Fungicide/Insecticide, containing 25 g/L triticonazole and 4 g/L cypermethrin, is proposed as a once-only treatment to control covered smut plus several stored grain insect pests of wheat and barley. The proposed application rate is 100 ml of product per 100 kg seed. Insect pests specified include lesser grain borer, granary weevil, rice weevil, red-rust flour beetle, saw-toothed grain beetle and tropical warehouse beetle.

Evaluation of efficacy

Data presented by Rhone Poulenc Pty Limited supported claims that Premis 25FS Seed Dressing Fungicide and Premis Professional Seed Dressing Fungicide/Insecticide adequately controlled covered smut in wheat and barley. The insecticide claims for Premis Professional Seed Dressing Fungicide/Insecticide are supported by other registered seed dressings.

Trial design for the provision of controls, treatment group size and number of replicates were of an acceptable scientific standard.

The experimental conditions in relation to pest pressure were inadequate to support efficacy in most trials. Of the ten trials conducted in the wheat belt of eastern Australia, covered smut of wheat (*Tilletia laevis*) was effectively tested in two trials, and covered smut of barley (*Ustilago segetum* var. *hordei*) in two trials.

Trial data indicated that complete coverage of all grain is necessary for good control of smut. This has been emphasised on the label (see 'Labelling Requirements').

Weather conditions experienced during sowing were suitable for covered smut which favours low soil temperatures. The trials were sown over two years, with drought conditions in 1994 and wetter conditions in 1995. The trial sites ranged from southern Queensland to northeast

Victoria, indicating that possible effects on seedling emergence and vigour were observed under a wide range of weather conditions.

Soil types were consistent with soils typical of the eastern Australian wheat belt. Trials were not conducted on the Mallee, Wimmera and sandy soils typical of the Wheat Belt in areas of Victoria, South Australia and Western Australia.

The information was analysed by the standard accepted technique of ANOVA and results were adequately interpreted. The trial data is applicable to the use of the product under commercial conditions.

Efficacy data supporting claims

Covered smut or common bunt (*Tilletia* spp.) in wheat: In two experiments Premis 25FS Seed Dressing Fungicide reduced the infection of covered smut in wheat from 42% and 46% to nil, which is adequate to support the proposed claim.

Covered smut (*Ustilago segetum* var. *hordei*) in barley: In two experiments, Premis 25FS Seed Dressing Fungicide reduced the infections of covered smut in barley from 4% and 6% to nil, which is adequate to support the proposed claim.

Crop safety

Emergence data from six trials on wheat and eight trials on barley indicated that Premis 25FS Seed Dressing Fungicide had no significant effect on the emergence of barley; however, it reduced the emergence of wheat by 29% in one trial in Queensland. Emergence of the control treatment in this trial was also significantly reduced.

Premis 25FS Seed Dressing Fungicides appear as safe as other triazole fungicides. Data indicates that triazole fungicides as a group can reduce seedling emergence by reducing coleoptile length and the strength of the first true leaf. The potential for reduced seedling emergence is most likely observed when seed is sown deeper, or in warm soil, or seed has been weather damaged. The proposed product labels warns that sowing rates should be adjusted accordingly to take into account the depth of seed sown and the soil temperature.

Labelling Requirements

CAUTION

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Premis™ 25FS Seed Dressing Fungicide

Active Constituents: 25 g/L TRITICONAZOLE

GROUP C FUNGICIDE

For the control of covered smut in wheat and barley

2.5, 5, 10, 20 Litres

RHÔNE-POULENC

RHÔNE-POULENC RURAL AUSTRALIA PTY LTD
A.C.N. No 000 226 022

3 - 5 Railway Street, Baulkham Hills, N.S.W. 2153
Telephone: (02) 9842 4444 Fax: (02) 9639 6392

DIRECTIONS FOR USE

Crop	Disease/Pest	Rate per 100 kg seed	Critical comments
Wheat	Covered Smut (Bunt) (*Tilletia* spp.)	100 mL	Ensure thorough coverage of the seed. Use a minimum of 400 mL of mixture (water + product) with each 100 kg seed.
Barley	Covered Smut (*Ustilago segetum* var. *hordei*)		

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

WITHHOLDING PERIOD:
WHEAT, BARLEY: NOT REQUIRED WHEN USED AS DIRECTED.

GENERAL INSTRUCTIONS
Protection from smuts and bunts will only be achieved if all grains are treated. Therefore ensure that the application equipment is correctly set up to achieve this. In Queensland, the emergence of treated seed sown too deep or into warm soil may be affected. Sowing rates may need to be adjusted accordingly.

Mixing: Shake the container well before using. Add the required volume of Premis™ 25FS to the water whilst agitating.

Application: Slowly add the mixture to the seed and mix thoroughly ensuring thorough coverage of the seed. Wash equipment thoroughly with water after application.

Further information can be obtained from a Rhône-Poulenc Rural representative.

COMPATIBILITY
Do not mix with any other product

PROTECTION OF LIVESTOCK: DO NOT feed treated seed to animals, including poultry. Store treated seed away from feed. DO NOT allow treated seed to contaminate grain intended for animal consumption.

PROTECTION OF WILDLIFE, FISH, CRUSTACEA, AND ENVIRONMENT: DO NOT feed treated seed or otherwise expose to wildlife or domestic birds. DO NOT contaminate streams, rivers or waterways with the chemical, used containers, treated seed or bags which have held treated seed.

PROTECTION OF OTHERS: When treated seed is stored, it should be kept apart from other grain or seeds, and the containers or bags should be clearly marked to show that the contents have been treated with Premis™ 25FS Seed Dressing Fungicide. DO NOT use treated seed for human consumption. DO NOT allow treated seed to contaminate food for human consumption. Bags which have held treated seed should not be used for any other purpose. Any seed not used for sowing should be destroyed.

STORAGE AND DISPOSAL: Store in the closed, original container in a dry, well-ventilated area, as cool as possible. DO NOT store for prolonged periods in direct sunlight. Triple or (preferably) pressure rinse containers before disposal. Add rinsings to the mixing tank. Do not dispose of undiluted chemical on-site. Break, crush or puncture and bury empty containers in a local authority landfill. If not available, bury the containers below 500mm in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS: Will irritate the skin. Avoid contact with skin. When opening the container and preparing the product for use wear elbow-length PVC gloves. Wash hands after use. After each day's use wash gloves.

FIRST AID: If poisoning occurs contact a doctor or Poisons Information Centre. For further information, refer to the MSDS for this product.

FUNGICIDE RESISTANCE STRATEGY: GROUP C FUNGICIDE

Premis™ 25FS Seed Dressing Fungicide is a member of the DMI group of fungicides. For fungicide resistance management the product is a Group C fungicide. Some naturally occuring individual fungi resistant to the product and other Group C fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungi population if these fungicides are used repeatedly. These resistant fungi will not be controlled by Premis™ and other Group C fungicides, thus resulting in a reduction in efficacy and possible yield loss. Since the occurance of resistant fungi is difficult to detect prior to use, Rhône-Poulenc Rural accepts no liability for any losses that may result from the failure of Premis™ to control resistant fungi.

CONDITIONS OF SALE: The product as supplied is of high quality and is believed to be suitable for the purposes for which it is recommended. The buyer or user is responsible for any misuse or negligence in the handling, storage and use of this material. This product must only be used in strict compliance with the directions given on this label. No representative of the manufacturer or seller has authority to add to or alter these conditions.

IN A TRANSPORT EMERGENCY DIAL 000, POLICE OR FIRE BRIGADE.	FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY: PHONE 1800 033 111 ALL HOURS - AUSTRALIA WIDE

(NAT)
9/97

PRODUCT ID:
LABEL ID:

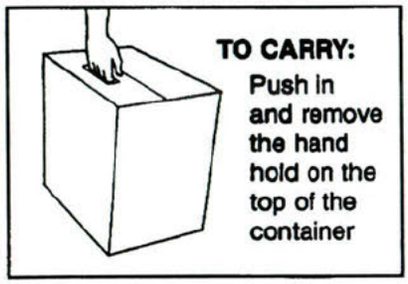
NRA Approval No.: 49025\
Batch No.
Date of manuf.:

BAR CODE

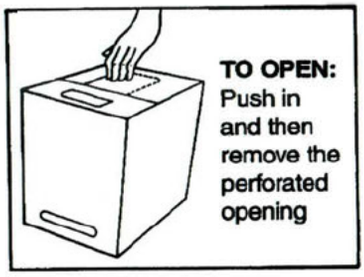
THE FOLLOWING IS FOR CUBIDOR PACKAGING ONLY

TOP OF CARTON

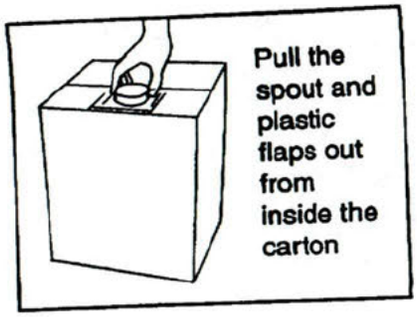
DO NOT REMOVE PLASTIC INNER CONTAINER FROM CARTON UNTIL EMPTY.



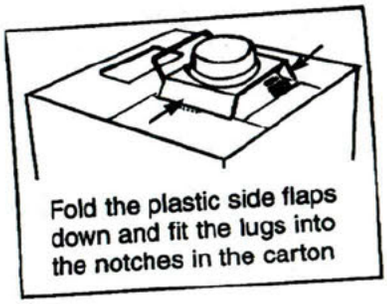
TO CARRY: Push in and remove the hand hold on the top of the container



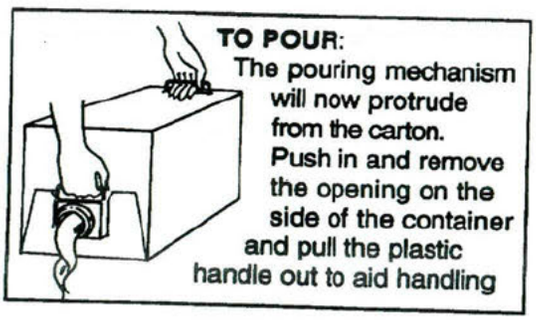
TO OPEN: Push in and then remove the perforated opening



Pull the spout and plastic flaps out from inside the carton



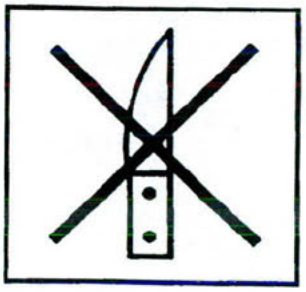
Fold the plastic side flaps down and fit the lugs into the notches in the carton



TO POUR: The pouring mechanism will now protrude from the carton. Push in and remove the opening on the side of the container and pull the plastic handle out to aid handling

SIDE OF CARTON





DO NOT TOP LOAD WHEN IN TRANSIT

CONTAINER DISPOSAL:

1. When empty, tear open carton and remove plastic inner container.
2. Triple rinse plastic inner container.
3. Break, crush or puncture, and bury empty containers in a local authority landfill.

SEE COMPLETE STORAGE AND DISPOSAL INSTRUCTIONS ELSEWHERE ON THE LABEL

TOMORROW'S TECHNOLOGY

brought to you by

RHÔNE-POULENC

TOP OF PLASTIC INNER CONTAINER

CAUTION
KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Premis™ 25FS Seed Dressing Fungicide

Active Constituents: 25 g/L TRITICONAZOLE

DO NOT REUSE THIS CONTAINER FOR ANY PURPOSE

RHÔNE-POULENC RURAL AUSTRALIA PTY LTD **A.C.N. 000 226 022**
3 - 5 Railway Street, Baulkham Hills, N.S.W. 2153
Telephone: (02) 9842 4444 Fax: (02) 9639 6392
NRA Approval No.: 49025/

CAUTION

KEEP OUT OF REACH OF CHILDREN
READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Premis™ Professional Seed Dressing Fungicide/Insecticide

Active Constituents: 25 g/L TRITICONAZOLE
4 g/L CYPERMETHRIN

GROUP C FUNGICIDE

For the control of covered smut in wheat and barley and for protection against insect pests of stored grain.

2.5, 5, 10, 20 Litres

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DIRECTIONS FOR USE

Crop	Disease/Pest	Rate per 100 kg seed	Critical comments
Wheat	Covered Smut (Bunt) (*Tilletia* spp.)	100 mL	Ensure thorough coverage of the seed. Use a minimum of 400 mL of mixture (water + product) with each 100 kg seed.
Barley	Covered Smut (*Ustilago segetum* var. *hordei*)		
Wheat, Barley	Lesser grain borer, Granary weevil, Rice weevil, Rust-red flour beetle, Saw toothed grain beetle, Tropical warehouse moth		

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

WITHHOLDING PERIOD:
WHEAT, BARLEY: NOT REQUIRED WHEN USED AS DIRECTED.

GENERAL INSTRUCTIONS
Protection from smuts and bunts will only be achieved if all grains are treated. Therefore ensure that the application equipment is correctly set up to achieve this. In Queensland, the emergence of treated seed sown too deep or into warm soil may be affected. Sowing rates may need to be adjusted accordingly.

Mixing: Shake the container well before using. Add the required volume of Premis™ to the water whilst agitating.

Application: Slowly add the mixture to the seed and mix thoroughly ensuring thorough coverage of the seed. Wash equipment thoroughly with water after application.

Further information can be obtained from a Rhône-Poulenc Rural representative.

COMPATIBILITY
Do not mix with any other product

PROTECTION OF LIVESTOCK: DO NOT feed treated seed to animals, including poultry. Store treated seed away from feed. DO NOT allow treated seed to contaminate grain intended for animal consumption.

PROTECTION OF WILDLIFE, FISH, CRUSTACEA, AND ENVIRONMENT: DO NOT feed treated seed or otherwise expose to wildlife or domestic birds. DO NOT contaminate streams, rivers, or waterways with the chemical, used containers, treated seed or bags which have held treated seed.

PROTECTION OF OTHERS: When treated seed is stored, it should be kept apart from other grain or seeds, and the containers or bags should be clearly marked to show that the contents have been treated with Premis™ Professional Seed Dressing Fungicide. DO NOT use treated seed for human consumption. DO NOT allow treated seed to contaminate food for human consumption. Bags which have held treated seed should not be used for any other purpose. Any seed not used for sowing should be destroyed.

STORAGE AND DISPOSAL: Store in the closed, original container in a dry, well-ventilated area, as cool as possible. DO NOT store for prolonged periods in direct sunlight. Triple or (preferably) pressure rinse containers before disposal. Add rinsings to the mixing tank. Do not dispose of undiluted chemical on-site. Break, crush or puncture and bury empty containers in a local authority landfill. If not available, bury the containers below 500mm in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS: Will irritate the eyes and skin. Avoid contact with eyes and skin. Facial skin contact may cause temporary facial numbness. When opening the container and preparing the product for use wear elbow-length PVC gloves. Wash hands after use. After each day's use wash gloves.

FIRST AID: If poisoning occurs contact a doctor or Poisons Information Centre. For further information, refer to the MSDS for this product.

FUNGICIDE RESISTANCE STRATEGY: **GROUP C FUNGICIDE**

Premis™ Professional Seed Dressing Fungicide/Insecticide is a member of the DMI group of fungicides. For fungicide resistance management the product is a Group C fungicide. Some naturally occuring individual fungi resistant to the product and other Group C fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungi population if these fungicides are used repeatedly. These resistant fungi will not be controlled by Premis™ and other Group C fungicides, thus resulting in a reduction in efficacy and possible yield loss. Since the occurance of resistant fungi is difficult to detect prior to use, Rhône-Poulenc Rural accepts no liability for any losses that may result from the failure of Premis™ to control resistant fungi.

CONDITIONS OF SALE: The product as supplied is of high quality and is believed to be suitable for the purposes for which it is recommended. The buyer or user is responsible for any misuse or negligence in the handling, storage and use of this material. This product must only be used in strict compliance with the directions given on this label. No representative of the manufacturer or seller has authority to add to or alter these conditions.

IN A TRANSPORT EMERGENCY DIAL 000, POLICE OR FIRE BRIGADE.	**FOR 24 HOUR SPECIALIST ADVICE IN EMERGENCY ONLY: PHONE 1800 033 111 ALL HOURS - AUSTRALIA WIDE**

(NAT)
9/97

PRODUCT ID:
LABEL ID:

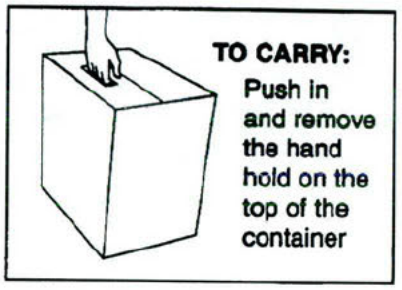
NRA Approval No.: 49024\
Batch No.:
Date of manuf.:

BAR CODE

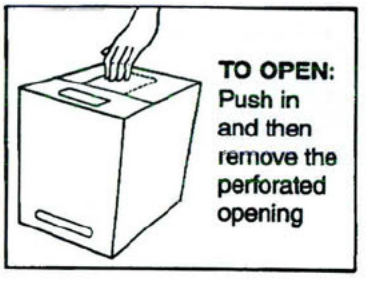
THE FOLLOWING IS FOR CUBIDOR PACKAGING ONLY

TOP OF CARTON

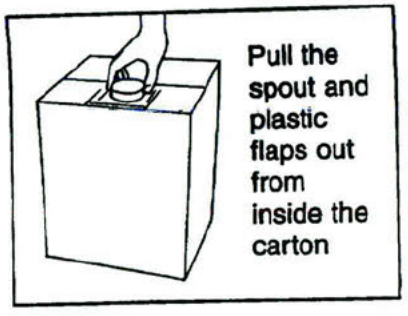
DO NOT REMOVE PLASTIC INNER CONTAINER FROM CARTON UNTIL EMPTY.



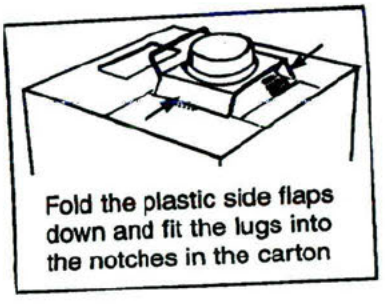
TO CARRY: Push in and remove the hand hold on the top of the container



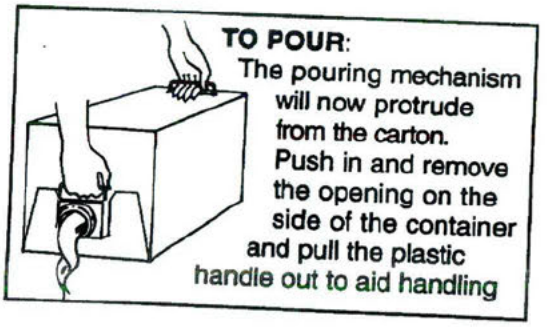
TO OPEN: Push in and then remove the perforated opening



Pull the spout and plastic flaps out from inside the carton



Fold the plastic side flaps down and fit the lugs into the notches in the carton



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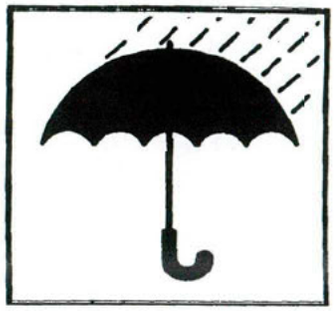

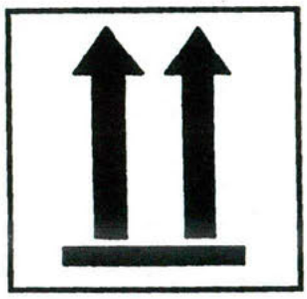

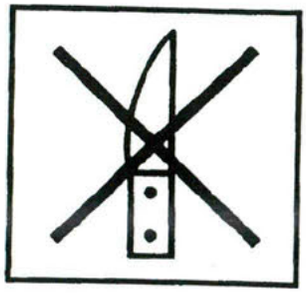

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CONTAINER DISPOSAL:		
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Glossary of Terms

Active constituent	The component of a treatment which is responsible for its biological effect.
Acute toxicity	Immediately measurable effects of a toxin on an organism.
DNA	Deoxyribonucleic acid the generic component of the chromosomes which support gene sequences.
Gene	A length of the DNA which holds the base sequences that code for the formation of a polypeptide chain (protein).
Groundwater ubiquity score	A measure of whether a compound is likely to leach through soil into groundwater.
IC_{50}	Inhibition concentration where 50% of algal cell growth is inhibited.
IPM	Integrated Pest Management. The combination of chemical and biological aspects of pest control to achieve pest management.
LC_{50}	The concentration of a substance that produces death in 50 per cent of a population of experimental organisms within a specified period. It is usually expressed as milligrams per litre (mg/L) or milligrams per kilogram (mg/kg) as a concentration in food, water or air.
LD_{50}	The dose of a substance that produces death in 50 percent of a population of experimental organisms within a specified period. It is usually expressed as milligrams per kilogram (mg/kg) of body weight.
Photolysis	Breakdown caused by light.
Schedule	The category into which a chemical is placed according to its human toxicity.

Suggested Further Reading

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 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.