

**Public Release Summary  
on**

**Evaluation of the new active**

**FENBUCONAZOLE**

**in the product**

**INDAR FUNGICIDE**

**Australian Pesticides and Veterinary Medicines Authority**

**November 2004**

**Canberra  
Australia**

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Dr John Paul  
Australian Pesticides and Veterinary Medicines Authority  
PO Box E 240  
KINGSTON ACT 2604

Ph: (02) 6272 3688

Fax: (02) 6272 3218

## FOREWORD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) 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 APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Office of Chemical Safety), Department of Environment and Heritage (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (Worksafe Australia) and State departments of agriculture and environment.

The APVMA 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 APVMA 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 APVMA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series*.

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the APVMA 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 APVMA. Alternatively, the reports can be viewed at the APVMA Library, 1st Floor, 22 Brisbane Avenue, Barton, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Program Manager—Pesticides Division, Australian Pesticides and Veterinary Medicines Authority, PO Box E240, Kingston ACT 2604.

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## LIST OF ABBREVIATIONS AND ACRONYMS

<b>AC</b>	active constituent
<b>ACR</b>	Acute to chronic ratio
<b>ACTH</b>	Adrenocorticotrophic hormone
<b>ADI</b>	Acceptable Daily Intake (for humans)
<b>AHMAC</b>	Australian Health Ministers Advisory Council
<b>ai</b>	active ingredient
<b>ALT</b>	Alanine aminotransferase
<b>ARfD</b>	Acute Reference Dose (for humans)
<b>AST</b>	aspartate amino transferase
<b>BBA</b>	Biologische Bundesanalstalt fur Land – und forstwirtschaft
<b>BUN</b>	blood urea nitrogen
<b>bw</b>	bodyweight
<b>CHO</b>	Chinese hamster ovary
<b>CRP</b>	Chemistry and Residues Program
<b>d</b>	day
<b>DAT</b>	Days After Treatment
<b>DM</b>	Dry Matter
<b>DT<sub>50</sub></b>	Time taken for 50% of the concentration to dissipate
<b>DT<sub>90</sub></b>	Time taken for 90% of the concentration to dissipate
<b>EA</b>	Environment Australia
<b>E<sub>b</sub>C<sub>50</sub></b>	concentration at which the biomass of 50% of the test population is impacted
<b>EC<sub>50</sub></b>	concentration at which 50% of the test population are immobilised
<b>EEC</b>	Estimated Environmental Concentration
<b>E<sub>r</sub>C<sub>50</sub></b>	concentration at which the rate of growth of 50% of the test population is impacted
<b>EUP</b>	End Use Product
<b>F<sub>0</sub></b>	original parent generation
<b>FW</b>	Fresh Weight
<b>g</b>	gram
<b>GAP</b>	Good Agricultural Practice
<b>GCP</b>	Good Clinical Practice
<b>GGT</b>	Gamma glutamyl transferase
<b>GLP</b>	Good Laboratory Practice
<b>GVP</b>	Good Veterinary Practice
<b>h</b>	hour
<b>ha</b>	hectare
<b>Hct</b>	Heamatocrit
<b>HDPE</b>	High-density polyethylene
<b>Hg</b>	Haemoglobin
<b>HGPRT</b>	hypoxanthine guanine phosphoribosyl transferase
<b>HPLC</b>	High Pressure Liquid Chromatography <i>or</i> High Performance Liquid Chromatography
<b>HPLC-UV</b>	High Performance Liquid Chromatography with Ultra-Violet Detector
<b>id</b>	intra-dermal
<b>im</b>	intra-muscular

<b>ip</b>	intraperitoneal
<b>IPM</b>	Integrated Pest Management
<b>iv</b>	intravenous
<b>in vitro</b>	outside the living body and in an artificial environment
<b>in vivo</b>	inside the living body of a plant or animal
<b>JMPR</b>	Joint FAO/WHO Meeting on Pesticide Residues
<b>Kg</b>	kilogram
<b>K<sub>oc</sub></b>	Organic carbon partitioning coefficient
<b>L</b>	Litre
<b>LC<sub>50</sub></b>	concentration that kills 50% of the test population of organisms
<b>LD<sub>50</sub></b>	dosage of chemical that kills 50% of the test population of organisms
<b>LC-MS/MS</b>	liquid chromatography, mass spectroscopy
<b>LOEC</b>	Lowest Observable Effect Concentration
<b>LOD</b>	Limit of Detection – level at which residues can be detected
<b>LOQ</b>	Limit of Quantitation – level at which residues can be quantified
<b>MCHC</b>	Mean corpuscular haemoglobin concentration
<b>MCV</b>	Mean corpuscular volume
<b>mg</b>	milligram
<b>mL</b>	millilitre
<b>MOE</b>	Margin of Exposure
<b>MRL</b>	Maximum Residue Limit
<b>MSDS</b>	Material Safety Data Sheet
<b>NDPSC</b>	National Drugs and Poisons Schedule Committee
<b>NEDI</b>	National Estimated Daily Intake
<b>NESTI</b>	National Estimated Short Term Intake
<b>Ng</b>	nanogram
<b>NHMRC</b>	National Health and Medical Research Council
<b>NOEC/NOEL</b>	No Observable Effect Concentration Level
<b>OC</b>	Organic Carbon
<b>OM</b>	Organic Matter
<b>PHED</b>	Pesticide Handlers Exposure Database
<b>PHI</b>	Pre-harvest interval
<b>po</b>	oral
<b>POEM</b>	Predictive Operator Exposure Model (UK)
<b>ppb</b>	parts per billion
<b>PPE</b>	Personal Protective Equipment
<b>ppm</b>	parts per million
<b>Q-value</b>	Quotient-value
<b>RBC</b>	Red Blood Cell Count
<b>S</b>	second
<b>sc</b>	subcutaneous
<b>SC</b>	Suspension Concentrate
<b>STMR</b>	Supervised Trial median Residue
<b>SUSDP</b>	Standard for the Uniform Scheduling of Drugs and Poisons
<b>TGA</b>	Therapeutic Goods Administration
<b>TRR</b>	Total Radioactive residues
<b>T-Value</b>	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons

<b>µg</b>	microgram
<b>vmd</b>	volume median diameter
<b>WG</b>	Water Dispersible Granule
<b>WHO</b>	World Health Organisation
<b>WHP</b>	Withholding Period

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## INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *INDAR FUNGICIDE*, which contains the new active constituent fenbuconazole. The product is proposed to be used for the control of brown rot in nectarines, and for the control of leaf spot and black sigatoka in bananas.

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

Copies of full technical evaluation reports on fenbuconazole covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request (see order form on last page). They can also be viewed at the APVMA library located at the APVMA offices, First Floor, 22 Brisbane Avenue, Barton ACT 2604.

Written comments should be received by the APVMA by 30 November 2004. They should be addressed to:

Dr John Paul  
Pesticides Program  
Australian Pesticides and Veterinary Medicines Authority  
PO Box E240  
KINGSTON ACT 2604

Phone: (02) 6272 3688  
Fax: (02) 6272 3218  
Email: [john.paul@apvma.gov.au](mailto:john.paul@apvma.gov.au)

### ***Applicant***

Dow AgroSciences Australia Limited

### ***Product Details***

It is proposed to register INDAR FUNGICIDE, containing fenbuconazole at 240g/L as a suspension concentrate formulation. INDAR FUNGICIDE will be imported fully formulated and packaged in 5 L and 20 L containers.

Fenbuconazole is a systemic fungicide belonging to the triazole group, with protectant and curative action. With respect to fungicide resistance, fenbuconazole is classed as a Group C Fungicide.

Application is as a foliar spray for the control of brown rot (*Monilinia spp.*) in nectarines and leaf spot or yellow sigatoka (*Mycosphaerella musicola*) and black sigatoka (*Mycosphaerella fijiensis*) in bananas.

Overseas registrations: Fenbuconazole formulations are currently registered in thirty one countries, including the USA, UK, South Korea, Phillipines and China. It is used for the control of various diseases of crops including peanuts, stone fruit, pome fruit, grapes, cucurbits, bananas and cereals.

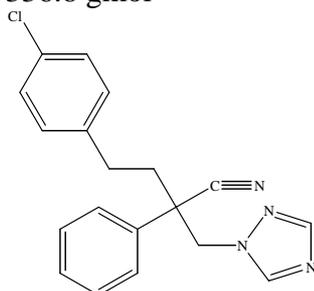
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## CHEMISTRY AND MANUFACTURE

### Active constituent

The active constituent fenbuconazole has the following properties:

Common name:	Fenbuconazole
IUPAC name:	( <i>R,S</i> )-4-(4-Chlorophenyl)-2-phenyl-2-(1 <i>H</i> -1,2,4-triazol-1-ylmethyl)butanenitrile
CAS Registry Number:	114369-43-6
Molecular formula:	C <sub>19</sub> H <sub>17</sub> ClN <sub>4</sub>
Molar mass:	336.8 gmol <sup>-1</sup>
Structure:	



Appearance:	Off-white to cream crystalline solid with a faint odour
Melting point:	125-127 °C (pure compound)
Bulk density:	0.50 g/cm <sup>3</sup> (25 °C)
Water solubility (20 °C):	Distilled water: 3.6, pH 9: 3.6, pH 4: 2.7 (all in mg/L)
Octanol/water partition coefficient:	K <sub>OW</sub> = 1700, log <sub>10</sub> K <sub>OW</sub> = 3.23 (25 °C)
Vapour pressure:	4.9×10 <sup>-6</sup> Pa (25 °C)
Safety properties:	Not an oxidising or reducing agent. Explosive when exposed to a spark or intense heat with sufficient oxygen. Combustible when at least 12% oxygen is present.
Chemical family:	Triazole
Mode of action:	Inhibition of steroid demethylation

The APVMA has evaluated the chemistry aspects of fenbuconazole (manufacturing process, quality control procedures, batch analysis results and analytical methods). The APVMA has approved the active constituent fenbuconazole.

Fenbuconazole is a new active constituent and there is no compendial specification available. On the basis of the data provided, the following Active Constituent Standard has been established for fenbuconazole:

Constituent	Specification	Level
Fenbuconazole	Fenbuconazole	Not less than 970 g/kg

Other characteristics of fenbuconazole (toxicology, environmental fate etc) are covered in subsequent sections of this Public Release Summary.

## **Formulated product**

Distinguishing name: Indar Fungicide  
Formulation type: Suspension concentrate (SC)  
Active constituent concentration: 240 g/L

## **Physical and chemical properties of the product**

Appearance: White liquid with a glycol odour  
Specific gravity: 1.05-1.08 (20 °C)  
pH: 8.0-10.0 (5% in deionised water)  
Safety properties: Not corrosive, not flammable, not a strong oxidising or reducing agent, and not classified as a dangerous good  
Storage stability: Stable for at least two years when stored under normal conditions

## **Summary of the chemistry evaluation of Indar Fungicide**

The APVMA has assessed the chemistry and manufacturing data submitted for the formulated product. The manufacturing and quality control procedures, including compliance with the release specifications, are acceptable.

The applicant provided the results of accelerated stability testing, as well as real time results for samples stored in HDPE containers (the proposed commercial packaging material). Testing of the important parameters for suspension concentrate formulations was conducted. The results indicate that the formulated product is expected to be stable for at least two years when stored under normal conditions in the proposed commercial packaging.

Based on a review of the data provided by the applicant, the APVMA is satisfied that the chemistry and manufacturing details of *Indar Fungicide* are acceptable.

# TOXICOLOGICAL ASSESSMENT

## Evaluation of toxicology

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

## Toxicokinetics and metabolism studies

Fenbuconazole was extensively absorbed in rats following oral administration of 1 mg/kg bw. Approximately 90% of <sup>14</sup>C-fenbuconazole was absorbed and peak concentrations in the whole blood and plasma occurred at 6 hours after dosing. Most of the radioactivity was excreted during the first 48 hours after treatment with the majority eliminated via the bile into the faeces. Only minor quantities of radioactivity were retained in tissues (0.5% of the dose) with the liver and/or thyroid having the highest radioactivity concentrations. Fenbuconazole underwent extensive biotransformation, which included oxidation, hydroxylation and conjugation. Thirteen metabolites were found in the excreta with the parent compound comprising approximately 10% of total radioactivity in excreta. Repeated dosing or a single high dose (100 mg/kg bw) resulted in similar kinetics. Dermal absorption of fenbuconazole was low, at up to 8% over a 24 hour period.

## Acute studies

Fenbuconazole has low oral ( $2000 < LD_{50} < 5000$  mg/kg bw), dermal ( $LD_{50} > 5000$  mg/kg bw) and inhalation toxicity ( $LC_{50} > 2100$  mg/m<sup>3</sup>) in rats. It is neither an irritant to rabbit skin and eyes, nor a skin sensitiser.

Indar Fungicide, containing 240 g/L fenbuconazole was administered to rats. The  $LD_{50}$  was greater than 5000 mg/kg bw when given orally and dermally, and the  $LC_{50}$  was greater than 2100 mg/m<sup>3</sup> by inhalation. This product was neither an irritant to rabbit skin and eyes nor a skin sensitiser in guinea pigs.

## Short-term studies

Mice received fenbuconazole at concentrations of 0, 100, 250, 500 and 1000 ppm for 2 weeks in the diet. Females at 100 ppm lost some body weight at the beginning of the study. Increased liver weights were observed at 250, 500 and 1000 ppm. The liver showed increased incidences of

hypertrophy and necrosis of hepatocytes, and periportal vacuolation mainly at 500 and 1000 ppm. Males at 500 and 1000 ppm and females at 1000 ppm also had acute inflammation in the liver and males at 1000 ppm had a higher incidence of vacuolar degeneration in the liver.

Rats received fenbuconazole in the diet at concentrations of 0, 100, 300, 1000 and 3000 ppm for 2 weeks. Lower body weights associated with decreased food consumption were observed at 3000 ppm. Liver weights and mixed function oxidase activity were increased in males at all dose levels and in females at 300 ppm and above. At 1000 ppm, hepatic microsomal protein concentrations were increased. The liver showed higher incidences of hypertrophy of centrilobular hepatocytes at 1000 ppm and above and vacuolation of hepatocytes in females at 3000 ppm and males at 1000 ppm and above.

Rats received fenbuconazole at 0 or 1000 mg/kg bw/day, Indar Fungicide (containing 62.5 or 250 mg fenbuconazole/kg bw/day) or a formulation blank, dermally for 4 weeks. There were no treatment-related changes in clinical chemistry, urinalysis, haematology and histopathology. Effects on the application site such as acanthosis, parakeratosis, eschar or superficial exudate, and necrosis of the epidermis were associated with the non-active constituents and/or clipping procedures rather than fenbuconazole.

Dogs received fenbuconazole at 0, 100, 1600 and 3200 ppm in the diet for 4 weeks. Two dogs (2/4) at 3200 ppm were noted to be thin. Dogs at 1600 ppm and above lost body weight probably due to a marked reduction in food consumption. No pathology changes were observed.

Dogs received fenbuconazole at 0, 200, 400, 800 or 1600 ppm for 4 weeks and 3200 ppm in the diet for 2 weeks. One dog at 1600 ppm had lower body weight gain and dogs at 3200 ppm lost body weight and had decreased food consumption. Slightly decreased WBC was also noted in this group. There were increases in alkaline phosphatase at 800 and 1600 ppm and ALT in one male dog at 3200 ppm, and decreases in cholesterol in males at 1600 ppm and above and in females at 1600 ppm. The only histopathology finding was decreased glycogen in the liver at 3200 ppm.

### **Subchronic studies**

Mice received fenbuconazole at 0, 20, 60, 180 or 540 ppm in the diet for 13 weeks. Slightly lower body weight gain was noted in 540 ppm males. Increases in AST, ALT and liver weights were observed in males at 180 ppm and above and in females at 540 ppm. Increased incidences of centrilobular hepatocellular hypertrophy were observed in males at 60 ppm and above and in females at 180 ppm and above. Periportal/perilobular hepatocellular vacuolation was increased at 540 ppm. The NOEL was 20 ppm (4.8 mg/kg bw/day) based on increased incidences of centrilobular hepatocellular hypertrophy at 60 ppm and above.

Mice received fenbuconazole at 0, 540, 1000, 3000 or 10000 ppm in the diet for 3 months. Eighteen out of 20 animals at 10000 ppm lost body weight and were either found dead or sacrificed moribund. Decreased body weight gains were observed at 3000 ppm. Decreased cholesterol (excluding females at 540) and triglycerides were observed at all dose levels. Increased ALT and decreased potassium were noted at 3000 ppm. Increases in liver weights were seen in all treated groups. Males at 1000 and 3000 ppm had slightly decreased kidney weights. There were increased incidences of centrilobular hepatocellular hypertrophy, necrosis and vacuolation in the liver at all dose levels. A NOEL was not established because of decreased triglycerides and cholesterol, and increased liver weights and histopathology findings in the liver at all doses.

Rats received fenbuconazole at 0, 20, 80, 400 or 1600 ppm in the diet for 3 months. Depressed food consumption and lower body weight gains were observed at 1600 ppm. At 1600 ppm, increased RBC, platelets, GGT and BUN were observed in females, while decreased triglycerides and increased cholesterol were noted in both sexes. Increases in liver weights were recorded at 400 and 1600 ppm. In both sexes, hepatocellular hypertrophy and vacuolation in the liver occurred in a higher incidence at 400 ppm and above. Males at 80 ppm also had increased incidences of vacuolation in the liver. A higher incidence of follicular epithelial cell hypertrophy in the thyroid was observed at 400 and 1600 ppm. Females at 400 ppm and above and males at 1600 ppm had higher incidences of hypertrophy/vacuolation in the adrenal gland. The NOEL was 20 ppm (1.3 mg/kg bw/day) based on increased incidences of vacuolation in the liver at 80 ppm and above.

Dogs received fenbuconazole at 0, 30, 100, 400 or 1600 ppm in the diet for 3 months. Body weight gains and food consumption at 1600 ppm were decreased. Increased alkaline phosphatase and ALT were observed in males at 1600 and in females at 400 ppm and above. Females at 1600 ppm had decreased RBC, albumin, globulin, cholesterol and total protein, and increased GGT and platelets, while males in this group had decreased AST and cholesterol and increased triglycerides. Increased liver weights and diffuse hepatocellular hypertrophy were observed at 400 ppm and above. Males at 1600 ppm had multifocal vacuolation in the liver, while females in this group had a higher incidence of chronic and multifocal vaginitis. The NOEL was 100 ppm (3.4 mg/kg bw/day) based on increased alkaline phosphatase, ALT, liver weights and hepatocellular hypertrophy at 400 ppm and above.

### **Chronic/carcinogenicity studies**

Mice received fenbuconazole at 0, 10, 200 (M only), 650 or 1300 (F only) ppm in the diet for 78 weeks. Lower body weight gains were seen in 650 ppm males. Elevated liver weights and higher incidences of centrilobular to mid-zonal hepatocellular enlargement and vacuolation in the liver were noted in males at 200 and 650 ppm and females at 650 ppm and above. Males at 650 ppm and females at 1300 ppm had an increased incidence of hepatocellular hyperplasia. Slightly higher incidences of hepatocellular adenoma and carcinoma were observed in females at 1300 ppm and males at 650 ppm, respectively, but the incidences were within the historical control range. The NOEL was 10 ppm (1.43 mg/kg bw/day) based on increased liver weights, hepatocellular enlargement and vacuolation in the liver at 200 ppm and above.

Rats received fenbuconazole at 0, 8, 80 or 800 ppm in the diet for two years. At 800 ppm, body weight gains were decreased, platelets and cholesterol were increased (females only), and increases in liver and thyroid/parathyroid weights and higher incidences of hepatocellular enlargement and vacuolation were observed. Additionally, males in this group had slightly higher incidences of focal mineralisation in the testis, hyperplasia in the thyroid and parathyroid glands, and follicular cell adenoma and carcinoma in the thyroid. However, the incidences of thyroid adenoma and carcinoma were within the historical control range. The NOEL was 80 ppm (3.53 mg/kg bw/day) based on decreased body weight gains, increased platelets, cholesterol, liver and thyroid/parathyroid weights, and histopathology findings in the testis, thyroid/parathyroid glands and liver at 800 ppm.

Male rats received fenbuconazole at 0, 800 or 1600 ppm in the diet for two years. Body weight gains and T<sub>4</sub> were decreased at 1600 ppm. Slightly increased liver and thyroid/parathyroid weights and higher incidences of hepatocellular enlargement and vacuolation in the liver were observed in 800 and 1600 ppm rats. Higher incidences of follicular cell hypertrophy and adenoma in the thyroid, immature/abnormal sperm forms and hypospermia in the epididymis and reduced spermatogenesis in the testis were noted at 1600 ppm. Additionally, rats at 1600 ppm had a slightly

higher incidence of malignant lymphoma, but this change was not statistically significant. A NOEL was not established because of increased thyroid/parathyroid weights and higher incidences of hepatocellular enlargement and vacuolation at 800 ppm and above.

Dogs received fenbuconazole at 0, 15, 150 or 1200 ppm in the diet for 52 weeks. Decreased body weight gains were observed in females at 150 ppm and above and in males at 1200 ppm. Decreased neutrophils and cholesterol, and increased alkaline phosphatase were observed in 1200 ppm dogs. At 1200 ppm, males and females had decreased albumin and AST respectively, while both sexes had increased liver weights and higher incidences of hepatocyte hypertrophy and pigment in the liver. Increased hepatocyte pigment was also seen in females at 150 ppm and females at 1200 ppm had a slightly higher incidence of Kupffer cell pigment in the liver. The NOEL was 15 ppm (0.6 mg/kg bw/day) based on decreased body weight gains and increased incidences of hepatocyte pigment at 150 ppm and above.

### **Reproduction study**

Fenbuconazole at concentrations of 0, 8, 80 or 800 ppm in the diet was administered continuously to two successive generations of rats. At 800 ppm, four F0 (4/25) and three F1 (3/21) females died during gestation or parturition. Decreases in body weight and food consumption were observed in adults. There was no effect on mating or conception rate. However, increased mortality during parturition and increased dams that did not deliver or produced non-viable offspring were observed in both generations at 800 ppm. A slight increase in the length of gestation was noted in F0 dams at 800 ppm. Effects on F0 and F1 offspring at 800 ppm included an increase in stillborn pups and decreases in the total number of delivered pups, live pups/litter, viability during lactation and pup body weight gain during lactation. Liver weights were increased in adults at 800 ppm and F1 females at 80 ppm. In addition, there were slightly increased thyroid/parathyroid weights at 800 ppm. Histopathology findings included liver and thyroid hypertrophy and hepatocyte vacuolation at 800 ppm in both generations. Hypertrophy of zona glomerulosa cells and increased cortical vacuolation in the adrenal glands were also seen at 800 ppm. The NOEL was 8 ppm (0.6 mg/kg bw/day) for general toxicity based on increased liver weights observed at 80 ppm and above. The NOEL for reproduction toxicity was 80 ppm (6.3 mg/kg bw/day) based on an increase in stillborn pups and decreases in delivered pups, live pups/litter, viability during lactation and pup body weight gain at 800 ppm.

### **Developmental studies**

Mated female rats received fenbuconazole at 0, 30, 75, or 150 mg/kg bw/day by gavage on days 6 through 15 of gestation. Decreased body weight gains were observed at 75 and 150 mg/kg bw/day. Increased resorptions were recorded at 150 mg/kg bw/day. At 150 mg/kg bw/day, decreased foetal body weight, increased foetuses with developmental variations and higher incidences of rudimentary 14<sup>th</sup> ribs and partially or unossified sternbrae and pubis were evident. Foetuses at 75 mg/kg bw/day also had higher incidences of partially or unossified sternbrae. The maternal and foetal NOEL was 30 mg/kg bw/day based on lower body weight gains, and increased foetuses with partially or unossified sternbrae at 75 mg/kg bw/day and above.

Fenbuconazole was administered to presumed pregnant rabbits at doses of 0, 10, 30, or 60 mg/kg bw/day by gavage on days 7 through 19 of gestation. Two dams (2/21) at 60 mg/kg bw/day were dead or killed moribund. Food consumption was decreased at 30 mg/kg bw/day. At 60 mg/kg bw/day, 19 out of 21 does stopped eating during the last eight days of the treatment period and only one dam finally survived and produced a viable litter (ten does had completely dead or resorbed

litters and six does aborted). No treatment-related developmental toxicity was observed at 30 mg/kg bw/day and below. At 60 mg/kg bw/day, no conclusions could be made due to the limited data since only eight foetuses at this dose level were available for examination. The NOEL for maternal toxicity was 10 mg/kg bw/day based on decreased food consumption at 30 mg/kg bw/day and above. The NOEL for embryo toxicity was 30 mg/kg bw/day based on increased resorptions at 60 mg/kg bw/day.

### **Genotoxicity studies**

Fenbuconazole was not genotoxic in a battery of genotoxicity studies including the Ames test, in vitro HGPRT mutation test, chromosome aberration test in cultured mammalian cells and bone marrow in rats, unscheduled DNA synthesis in rat hepatocytes and the DNA repair test.

### **Other studies**

Female mice received diets containing fenbuconazole at 0, 20, 60, 180 or 1300 ppm or phenobarbital (positive control) at 1000 ppm for 1 or 4 weeks. Male rats were fed a diet containing 0 or 1600 ppm fenbuconazole or 1000 ppm phenobarbital for 4 weeks. Lower body weights and decreased food consumption were observed in rats at 1600 ppm. Liver weights in mice at 1300 ppm and in rats at 1600 ppm were increased. Fenbuconazole at 1300 ppm in mice caused an increase in liver cell proliferation. Higher incidences of hepatocellular hypertrophy with increased cytoplasmic eosinophilia, and increases in microsomal cytochrome P<sub>450</sub> and cytochrome b<sub>5</sub> content and cytochrome P<sub>450</sub> enzyme activity were observed in mice at 1300 ppm and rats at 1600 ppm. Mice at 180 ppm also had increased cytochrome P<sub>450</sub> and cytochrome b<sub>5</sub> concentrations. Like fenbuconazole, phenobarbital at 1000 ppm produced similar changes in the rodent liver. Western immunoblotting analysis showed that fenbuconazole induced the CYP2B form of cytochrome P<sub>450</sub> (i.e., the phenobarbital inducible form). It was noted that all of the above-mentioned liver changes induced by either fenbuconazole or phenobarbital were completely reversed after a 6-week recovery period.

Male rats received diets containing fenbuconazole at 0, 8, 800, 1600 or 3200 ppm for 4 or 13 weeks. Body weights and food consumption were decreased in rats at 1600 and 3200 ppm. Increased thyroid and liver weights and higher incidences of diffuse follicular cell hypertrophy/hyperplasia in the thyroid were observed in rats at 800 ppm and above. Increased serum TSH and decreased T<sub>4</sub> concentrations were observed at 1600 ppm and above. In addition, rats at 3200 ppm had a decrease in serum rT<sub>3</sub> concentrations. Bile flow and the ratio of <sup>125</sup>I-label in bile to plasma and the biliary clearance rate of <sup>125</sup>I-label from the plasma were increased. Similarly, the biliary excretion of <sup>125</sup>I-T<sub>4</sub> (predominantly as the glucuronide) and the activity of hepatic microsomal UDP-glucuronosyltransferase (UDP-GTF), with T<sub>4</sub> as substrate, were also increased. Except for rT<sub>3</sub>, all changes were significantly reversed after a 9-week recovery period.

## **PUBLIC HEALTH STANDARDS**

### **Poisons Scheduling**

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients.

On the basis of its toxicity, the NDPSC has included fenbuconazole 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.

### **NOEL/ADI**

The Acceptable Daily Intake is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOEL obtained in the most sensitive species. This NOEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for fenbuconazole was established at 0.006 mg/kg bw/day based on a NOEL of 0.6 mg/kg bw/day in a 12-month study in dogs and 2-generation reproduction study in rats; A 100-fold safety factor was used in recognition of the extensive toxicological database available for fenbuconazole.

### **Acute Reference Dose (ARfD)**

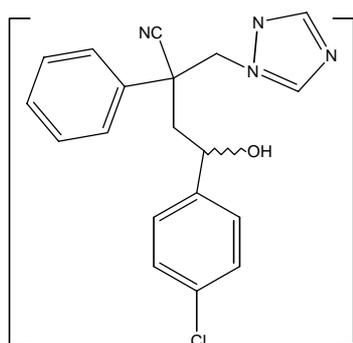
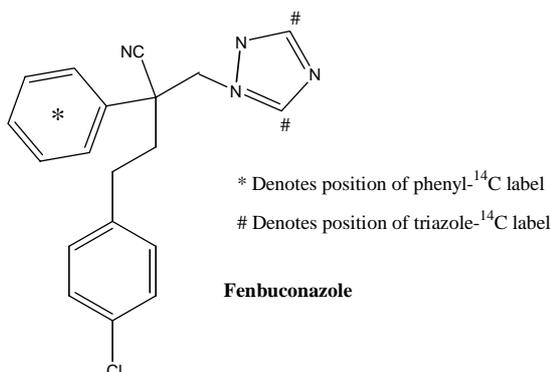
The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event. The ARfD is derived from the lowest single or short term dose which causes no effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ARfD is 0.2 mg/kg bw/day based on a NOEL of 20 mg/kg bw/day in a 4-week dog study, using a 100-fold safety factor.

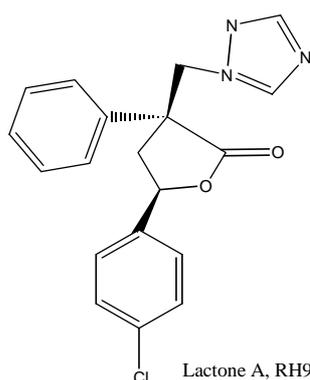
# RESIDUES ASSESSMENT

## Metabolism

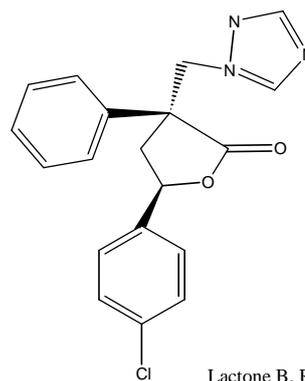
The metabolism of fenbuconazole was investigated in plants (peanuts, wheat and peaches) and animals (rats, laying hens and goats) using [phenyl-<sup>14</sup>C]-fenbuconazole and [triazole-<sup>14</sup>C]-fenbuconazole.



Benzylic alcohol, RH6648

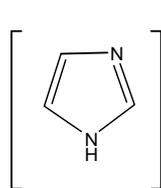


Lactone A, RH9129

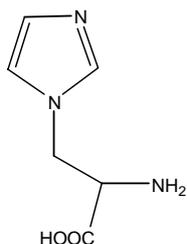


Lactone B, RH9130

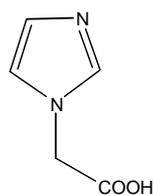
In plants, the Total Radioactive Residue (TRR) was distributed amongst the various substrates and plant tissues. In the peach study, the TRR consisted of parent (16%), lactone (4%), triazole-alanine (47%), triazole-acetic acid (7%) and sugar conjugates (4%). In the wheat and peanut studies, the parent compound formed a major proportion of the TRR, up to 65% of the fractions collected. Based upon the metabolites identified, the proposed metabolic pathway of fenbuconazole in plants consisted of three routes. The first is degradation via oxidation of the carbon next to the chlorinated phenyl ring, which forms the benzylic alcohol intermediate and the subsequent ketone and lactones A and B as metabolites. The second route identified was via oxidation or nucleophilic substitution on the carbon next to the triazole ring leading the free triazole, which undergoes transformation into triazole-alanine and triazole acetic acid. The triazole metabolic route is known to occur commonly in plants. The third route involves the hydroxylation of fenbuconazole, which leads to various conjugates, including glucuronide and malonyl-glucoside found in the crop.



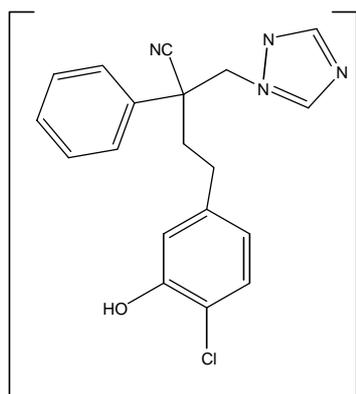
Triazole



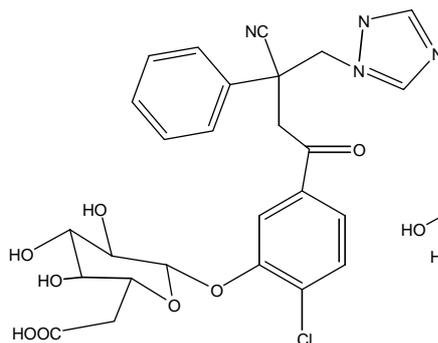
Triazole-alanine, TA



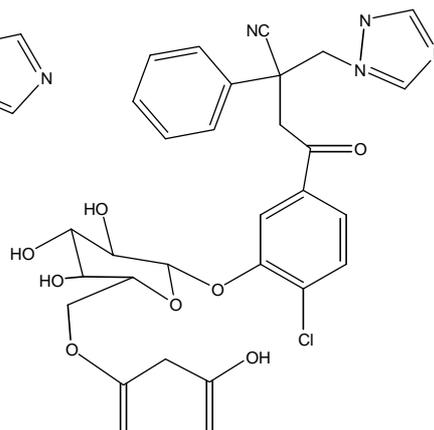
Triazole-acetic acid, TAA



Intermediate hydroxyl, RH4911



Glucuronide Conjugate



Malonyl-Glucoside Conjugate

Laying hens were fed 100 ppm of  $^{14}\text{C}$ -fenbuconazole in the diet for 7 days. Fenbuconazole was eliminated predominantly in the excreta, ~90% of the administered dose. There were small quantities found in animal tissues, the highest level present in the liver at 0.5 %, gizzard 0.3 %, abdominal egg yolk 0.3% and eggs 0.68%. Metabolites identified in tissues and eggs consisted predominately of the triazole RH3968. Other compounds identified were fenbuconazole, the lactones RH9129 and RH9130, and fenbuconazole glucuronide. Based upon the metabolites identified, metabolism of fenbuconazole in laying hens is via three oxidative pathways, similar to those observed in plants.

Goats were orally administered  $^{14}\text{C}$ -fenbuconazole up to 100 ppm in the diet for 7 days. Fenbuconazole was primarily excreted in the faeces (67%), and to some extent, in the urine (12%). Less than 0.4% of the applied dose was found in milk and another 0.8-1.6% was found in tissues. Metabolites found in the tissues consisted of the parent, conjugates mainly the glucuronide or cleavage products such as hydroxyl fenbuconazole (RH7968), triazole and triazole-alanine. Minor metabolites were the sulfate (RH6649) and the phenol (RH1311). Based upon the metabolites found, the proposed metabolic pathway is similar to laying hens. However, it is noted that cleavage of fenbuconazole occurs to a lesser extent in goats than for hens.

### Analytical methods

The residue methods provided are capable of determining fenbuconazole and the lactone metabolites, RH9129 and RH9130 (and in some cases, metabolite RH7592) in plant matrices. Representative plant matrices are homogenised and extracted with methanol. The extract is partitioned with 10% sodium chloride and methylene chloride. The organic extract is further

purified by sequential silica gel and florisil column chromatography. For some crops, cleanup is performed using soxhlet extraction, followed by C-18 solid phase extraction (SPE).

Methodology was provided for the determination of fenbuconazole and metabolites in animal tissues, eggs and milk. The animal matrices are blended with methanol, and fat is extracted with hexane. The extracts are purified by liquid-liquid partitioning, silica gel column chromatography, and C-18 solid phase extraction (SPE) or florisil column chromatography. The purified extracts are analysed by gas chromatography using a nitrogen specific thermionic detector (NPD) or mass spectroscopy detector (MSD) operating in the selective ion mode (SIM).

Calibration of the methods is based upon the response of reference standards of known purity. The reported limit of quantification (LOQ) for all plant matrices, animal tissues, milk and eggs is 0.01 mg/kg. The efficiency of the methods was determined by measuring the recovery of analytes from fortified straw, grain, fruit and animal tissue samples. The mean recovery was within acceptable limits of 70-110%. The methods are demonstrated to be satisfactory for the determination of fenbuconazole and lactone metabolites in plant matrices, animal tissues, milk and eggs.

### **Residue definition**

The metabolism data indicate that fenbuconazole is metabolised in plant and animal tissues. The studies show that parent fenbuconazole along with the diastereomeric lactones, RH9130 and RH9129 constitute a significant proportion of the residue found. However, residue trials indicate that only 7% of the total residue corresponds to the metabolites. Because the metabolites only constitute a minor proportion of the total residue, the residue definition will be the parent fenbuconazole only. This would be aligned to the Codex definition for fenbuconazole.

The following residue definition is recommended for purposes of regulatory monitoring and dietary exposure:

**Fenbuconazole**

Fenbuconazole

### **Residues in Bananas**

Four Australian and ten USA supervised trials were provided in support of the use on bananas. When fenbuconazole is applied according to GAP, the residue levels encountered in whole fruit (ranked order) were 0.001, 0.002, 0.002, 0.0031, 0.0032, 0.0049, 0.0057, 0.01, 0.014, 0.0188, 0.019, 0.027, 0.053, 0.15, 0.18 mg/kg. The Supervised Trial Median Residue (STMR) is 0.01 mg/kg and the maximum fenbuconazole residue level encountered was 0.18 mg/kg. Data from overseas trials were conducted on bagged and unbagged bananas, and from aerial and ground application. The residue data support an MRL of 0.5 mg/kg for bananas, when Indar Fungicide is used according to label directions.

When considering dietary intake, the residue levels found in pulp (in ranked order) were: <LOD (5), 0.0024, 0.0039, 0.004, 0.01, 0.01, 0.01, 0.01, 0.01, 0.019, 0.0245, 0.03, 0.08 mg/kg (n=17, STMR=0.01 mg/kg). For chronic dietary assessment, the calculated pulp STMR of 0.01 mg/kg will be used, and for acute intake calculations, the highest residue (HR) of 0.08 mg/kg will be used.

## **Residues in Nectarines**

Four trials were conducted on nectarines in Australia during the 1997-98 growing season. When fenbuconazole was applied according to GAP, and fruit sampled at the proposed withholding period of 1 day, the residue levels in ranked order were 0.15, 0.19, 0.25, 0.41 mg/kg (n=4, STMR=0.22 mg/kg, HR=0.41 mg/kg). At 7 days after treatment, the residue levels in ranked order were: 0.13, 0.14, 0.15, 0.29 mg/kg. The decline data shows there was a slight decrease in the residue level following 1-7 days after treatment. The residue data support an MRL of 0.5 mg/kg for nectarines, when Indar Fungicide is used according to label directions.

## **Animal commodity MRLs**

Processing waste from nectarines and banana by-products, consisting of culled bananas unfit for human consumption may be used as animal feeds. They are considered fruit by-products, which can be fed to cattle, sheep and pigs up to 20% of dietary intake, and 5% for poultry. In addition, nectarine orchards may be grazed following Indar Fungicide treatment.

The estimated maximum exposure of livestock (including poultry) to fenbuconazole residues is calculated to be 0.5 ppm in the feed. In the data submission, animal transfer studies were provided for poultry and lactating cows, dosed continuously for 28 days. Residues of fenbuconazole were determined in tissues, milk and eggs. At the expected feeding level of 0.5 ppm in the diet, it is estimated that fenbuconazole residues in meat, milk and eggs will be below the limit of quantification of 0.01 mg/kg for each of these commodities. From these data, animal commodity MRLs of \*0.01 mg/kg are recommended for meat (mammalian and poultry), offal (mammalian and poultry), milk and eggs.

With respect to grazing treated nectarine orchards following Indar Fungicide treatment, the following grazing interval is recommended:

Grazing of Orchards: Do not allow livestock to graze orchards or plantations or cut fodder from treated areas for stockfeed for 4 weeks after application.

## **Processing studies**

Three processing studies were provided for fenbuconazole treatment of stone fruit. The residue level found in dried prunes were ~4× the residue level found in the corresponding fresh sample. This is closely aligned to the theoretical concentration factor of 3.4 from the loss of water in prunes [Reference: EPA Residue Chemistry Test Guidelines, OPPTS 860.1520, Processed Food/Feed, 15 August 1995].

The residue level in peeled peaches decreased by approximately 10 fold compared to the whole fruit, and similar low residue levels were found in the finished puree. These data indicate a processing factor of ~0.1 for peach puree.

Following washing, residue levels decreased by approximately 1/3 –1/2 of the residue level found in unwashed fruit. It is considered that washing of fruit will remove a large proportion of the residue found on treated fruit. However, it should be noted that detectable residues of fenbuconazole may occur on washed fruit.

## **Storage stability**

Storage stability of residues has been determined for plant matrices and animal tissues. The data show that residues of fenbuconazole and metabolites are stable for a minimum of 3 months in animal tissues (muscle, kidney, liver fat), eggs and milk when maintained at  $-15\text{ }^{\circ}\text{C}$  freezer storage. Similarly, for plant matrices, a study conducted on peaches show that residue levels of fenbuconazole and metabolites, RH9129 and RH9130, remain stable after 54 months of  $-15\text{ }^{\circ}\text{C}$  freezer storage. These studies are satisfactory to confirm that results are indicative of the residue levels present at the time of sampling.

## **Spray drift**

Aerial application of Indar Fungicide may be used for banana plantations. There have been no recorded spray drift incidences from banana plantations resulting in detectable chemical residues, which have caused trade concerns.

## **Estimated dietary intake**

The chronic dietary risk is estimated by the National Estimated Daily Intake calculation encompassing all registered / temporary uses of the chemical and dietary intake data from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with the Guidelines for predicting dietary intake of pesticide residues (revised) (World Health Organisation, 1997). The NEDI of fenbuconazole is equivalent to 3 % of the ADI. It is concluded that the chronic dietary exposure is small and the risk is acceptable.

The acute dietary risk is estimated by the National Estimated Short Term Intake (NESTI) calculation, and is made in accordance with the procedures used by the JMPR. An acute reference dose (ARfD) of 0.2 mg/kg bw has been established for fenbuconazole. The acute intake of fenbuconazole was estimated for bananas, nectarines and animal commodities. The highest acute dietary intake was estimated to be 6% of the ARfD. It is concluded that the acute dietary exposure to fenbuconazole is small and the risk is acceptable.

## **Bioaccumulation potential**

The residue data indicate that fenbuconazole and metabolites do not accumulate in fat or other animal tissues.

Environmental fate data indicate that fenbuconazole does not degrade rapidly in the soil ( $t_{1/2} = 258\text{-}367$  days under aerobic conditions). However, fenbuconazole was found to bind tightly with soils, showing a low potential for soil mobility. Crop rotation studies show that following treatment at rates proposed for bananas and stone fruit, no detectable residues are expected in crops planted back 30 days after treatment. Therefore, crop rotation advice on the product label is not required.

## **Conclusion**

Assessment of the residue data supports the registration of Indar Fungicide for use on bananas and nectarines.

## Recommendations

The following amendments to the *MRL Standard* are recommended in relation to the proposed use of Indar Fungicide:

Table 1

Compound	Food	MRL (mg/kg)
ADD:		
Fenbuconazole		
FL	0327 Bananas	0.5
MO	0096 Edible offal (mammalian)	*0.01
PE	0112 Eggs	*0.01
MM	0095 Meat [mammalian]	*0.01
ML	0107 Milks	*0.01
FS	0245 Nectarine	0.5
PO	0111 Poultry, edible offal of	*0.01
PM	0110 Poultry meat	*0.01

Table 3

Compound	Residue
ADD:	
Fenbuconazole	Fenbuconazole

The above MRLs will be conveyed to Food Standards Australia New Zealand for inclusion in Schedule 1 of the Food Standards Code.

The following withholding periods are recommended in relation to the above MRLs:

**Harvest:**

Bananas, nectarines: DO NOT HARVEST FOR 1 DAY AFTER APPLICATION.

**Grazing:**

Grazing of Orchards: DO NOT ALLOW LIVESTOCK TO GRAZE ORCHARDS OR PLANTATIONS OR CUT FODDER FROM TREATED AREAS FOR STOCKFEED FOR 4 WEEKS AFTER APPLICATION

# ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

## Relevant export commodities

Harvested banana and nectarine fruit are commodities exported for trade. Annual production of bananas in Australia has been steady over the last 5 years. In 1999/2000, production was 225 Ktonne and 12.5 tonnes (<0.01%) was exported with a market value of \$50.8K. Major trade destinations for bananas include New Zealand, Indonesia and Brunei (Australian Horticultural Statistics Handbook 2000/2001). Based upon the tonnage and market value, bananas are not considered a major export commodity.

Total Australian nectarine production and exports (tonnes and \$ value) in 1999/2000 are shown below (Australian Horticultural Statistics Handbook 2000/2001):

### Major export markets for stone fruit, 1999/2000

Crop	Production (tonnes)	Exports (tonnes)	Export value (\$'000)
Nectarines	27,423	5,167	14,057

Major stone fruit markets include Southeast Asian countries (Taiwan, Singapore, Indonesia, China, Malaysia), the Middle East (UAE, Saudi Arabia) and Europe (France, UK). Based upon the tonnage and market value, nectarines are considered a major export commodity.

## Overseas registration status and MRLs

In the USA, equivalent fenbuconazole products are registered for use on bananas and stone fruits, amongst other crops. MRLs or residue tolerances for fenbuconazole have been established for bananas, stone fruit, and for animal commodities. The USEPA residue definition for fenbuconazole consists of the parent and lactone metabolites. The MRLs are time limited, and these are due to expire at the end of December 2003 or 2004. The relevant MRLs are listed in the following table:

Commodity	MRL, mg/kg	Expire Date
Banana, whole fruit	0.3	31/12/04 ‡
Stone fruit group, except plum and prune	2	31/12/04 ‡
Mammalian meat	0.01	31/12/03 †
Mammalian meat by-products	0.01	31/12/03 †
Mammalian fat	0.01	31/12/03 †

† The animal commodity tolerances have been established under Section 18 provisions.

‡ Banana and stone fruit commodities are temporary to allow USEPA to complete review of additional data for registration of fenbuconazole.

There are no overseas MRLs established for fenbuconazole in major trading partners for stone fruit commodities.

## CODEX Alimentarius Commission MRLs

Fenbuconazole was considered by the JMPR in 1997 and 2002. Codex has established MRLs for bananas, stone fruits (apricots, cherries, peach), pome fruit, cereals (barley, wheat and rye), animal commodities, animal fed commodities, and others (pecan, cucumber, grapes, melons, rape seed, squash, sunflower seed). The relevant banana and stone fruit MRLs are shown in the following table:

<b>Commodity</b>	<b>CXL, mg/kg</b>
Banana	0.05
<b>Stone fruits:</b>	
Apricots	0.5
Cherries	1
Peach	0.5
<b>Animal commodities:</b>	
Cattle meat, fat, kidney, milk	*0.05
Cattle liver	0.05
Eggs	*0.05
Poultry meat, fats, offal	*0.05

### **Potential risk to Australian export trade**

Export of treated produce containing finite (measurable) residues of fenbuconazole may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

MRLs are not established in any of Australia's major export partners for stone fruit and bananas. Residues of fenbuconazole in stone fruit and banana commodities exported to New Zealand will be covered by appropriate MRLs once they are incorporated into the Food Standards Code.

The volume of banana exports is considered minor. As a minor trade commodity, there is unlikely to be any prejudice to trade when Indar Fungicide is used on bananas.

Measurable residues of fenbuconazole are likely to occur on nectarines from the use of Indar Fungicide. The export value and volume of nectarines is considered major, and therefore, there is a theoretical risk to Australian trade when treated produce is exported to markets that do not have MRLs in place. However, the Australian MRL of 0.5 mg/kg is comparable to the Codex MRLs of 0.5 mg/kg for apricots and peaches, and 1 mg/kg for cherries. It is also comparable to the USA tolerance for stone fruit (except plums and prunes) of 2 mg/kg.

When processed waste and culled bananas are used for stock feed, or treated nectarine orchards are grazed by animals, residues in meat, meat products, eggs and milk will not be detectable. In order to ensure safe grazing in orchards, a 4 week grazing interval is stated on the product label.

# OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

## Health hazards

Fenbuconazole is not on the NOHSC *List of Designated Hazardous Substances*. Based on the available information NOHSC has classified fenbuconazole as hazardous substance according to the NOHSC *Approved Criteria for Classifying Hazardous Substances*. NOHSC has classified Indar Fungicide as hazardous according to the NOHSC *Approved Criteria for Classifying Hazardous Substances*.

Fenbuconazole will be manufactured overseas. It has low oral, dermal and inhalation toxicity. It is neither a skin and eyes irritant in rabbits, nor a skin sensitiser in guinea pigs.

Indar Fungicide will be manufactured overseas. It has low oral, dermal and inhalation toxicity. It is neither a skin and eyes irritant in rabbits, nor a skin sensitiser in guinea pigs.

## Formulation, packaging, transport, storage and retailing

Fenbuconazole will be imported fully formulated. The product will be packed into either 1 L or 5 L HDPE containers using an automated, closed filling system.

Packers will be exposed to the EUP during the process of charging the filling tanks and packing. The applicant states that packers are trained and utilise appropriate protective clothing. Transport workers, store persons and retailers will handle packaged product and could only become contaminated if packaging were breached.

Advice on safe handling of the active or product during routine transport and storage is provided in the Material Safety Data Sheet (MSDS) for Indar Fungicide.

## Use and exposure

Indar Fungicide is to be used for the control of certain diseases in bananas and stonefruit. It will be applied using air assisted ground sprayers in bananas and stone fruit, aircraft application may be used in bananas. The maximum application rate is 0.420 L/ha and suggested spray volumes are between 500 and 1500 L/ha for ground spraying and 20 L/ha for aircraft.

The main routes of exposure are dermal, inhalation and ocular. Categories of workers that can be exposed to the product are mixer/loaders, ground applicators, clean-up personnel and re-entry workers.

There are no available worker exposure data on Indar Fungicide. NOHSC used the UK Predictive Operator Exposure Model (POEM) and Pesticide Handlers Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate applicator exposure to Indar Fungicide.

These estimates in conjunction with toxicology data demonstrated that the use of protective clothing, and gloves during mixing/loading and, application are necessary to protect workers.

## **Entry into treated areas**

Workers entering treated areas can be exposed to product residues and degradation products during crop management activities and harvesting.

Using the US Occupational Post-Application Risk Assessment Calculator (US Policy 003.1) and based on the toxicity profile and use pattern of Indar Fungicide, NOHSC recommend restricted entry until the spray has dried.

## **Recommendations for safe use**

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of cotton overalls buttoned to the neck and wrist, a washable hat and elbow-length PVC gloves when mixing / loading and using the prepared spray for ground application.

The PPE recommended should meet the relevant *Standards-Australia*.

## **Re-entry statement**

NOHSC recommends the following re-entry statement on the product label:

“Do not allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.”

## **Conclusion**

NOHSC supports the registration of fenbuconazole in Indar Fungicide at 240 g/L as a suspension concentrate, for use on bananas and stone fruit.

Indar Fungicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available in the Indar Fungicide MSDS.

## **ENVIRONMENTAL ASSESSMENT**

### **Environmental exposure**

Indar Fungicide is to be applied as a foliar spray at an application rate of 15 mL EUP/100 L water (dilute spraying) or 40 mL EUP/100 L water (concentrate spraying), equivalent to 72-90 g a.i./ha for stone fruit given a maximum spray volume of 2,000-2,500 L/ha for dilute spraying. For brown rot control in fully fruiting trees in modern commercial orchards, the company advises an application rate of 65 g a.i./ha is the most appropriate. The company confirms that ground spraying only and not aerial spraying is proposed for this use pattern.

For protection against the fruit phase of brown rot, the label indicates Indar Fungicide should be applied as two sprays at 3 weeks and 1 week before harvest, but in the case of susceptible varieties or favourable disease conditions, additional sprays before or during harvest may be required. Therefore, at least eight sprays are possible but to minimise resistance development, no more than two consecutive sprays of Indar Fungicide or other Group C fungicide should be made. The company indicated that it is unlikely that more than two Indar Fungicide sprays would be applied in a season given the expected total number of sprays (five to nine per season), range of products on the market and grower awareness of resistance management.

For bananas, a maximum of 420 mL EUP per ha should be used per application, equivalent to 101 g a.i./ha, to protect against leaf spot (also called yellow sigatoka) and black sigatoka. In tropical areas, a 14-21 d schedule should be followed whereas in subtropical areas, the schedule should be 21-28 d. The label advises ground application by misting or airblast machines to provide thorough coverage of all foliage, or aerial application in a minimum total volume of 20 L/ha. As these application methods normally produce very small droplet sizes to allow them to be suspended in the air, the company specified that fine to medium sprays from ground misters are most appropriate.

For resistance management in tropical areas, two to three consecutive applications of Indar Fungicide are recommended before changing to a fungicide of another group with no more than six Group C sprays in any 12 month period and no spraying in July, August and September. According to this schedule, a maximum of five Indar Fungicide applications could be made per year. For subtropical areas, at least two consecutive sprays should be applied with no more than five Group C fungicides in any 12 month period. However, the company has indicated that it is unlikely that >3 sprays of Indar Fungicide would be made in any one season due to the range of products on the market and resistance management strategies.

### **Environmental chemistry and fate**

- Abiotic transformation

Fenbuconazole does not hydrolyse appreciably at pH 5-9. After 30 d irradiation, fenbuconazole did not photolyse in sterile water, but photodegraded slowly with a DT50 of 87 d in a natural pond water and 79 d on a sandy loam soil surface.

- Biotic transformation

Biodegradation in two aerobic soils was relatively slow with DT50 values of 258-440 d with the lactone diastereomers RH-9129 and RH-9130 together peaking at 14% of the originally applied radioactivity and the triazole RH-0118 reaching the same amount. About 21-37% of the parent had

mineralised to  $^{14}\text{CO}_2$  with the phenyl-labelled fenbuconazole by 363 DAT while the triazole labelled material only showed  $\leq 1.5\%$ . No degradation was observed when these soils were anaerobically incubated for 30 d (following 30 d aerobic ageing) and the company confirmed the long persistence potential under anaerobic conditions. In other soils incubated aerobically for 96 d with parent  $^{14}\text{C}$ -labelled in the triazole ring, biodegradation was relatively rapid in two (DT50 of 38-74 d) but slow in a third (DT50 of 532 d); no apparent reason was found for the difference and only one unidentified metabolite (reaching 15%) was found at  $>10\%$ .  $^{14}\text{CO}_2$  was low at  $\leq 2.3\%$  by 96 DAT.

Parent fenbuconazole rapidly dissipated from the water to sediment (DT50 of 1.2-4.3 d) but was persistent in the anaerobic sediments with 79-92% still present at 105 DAT. No metabolites were found at  $>10\%$  of the originally applied radioactivity.

- Mobility

In batch equilibrium studies, parent fenbuconazole was slightly mobile to immobile in four soils and slightly mobile in a fifth soil although the result is questionable. After 30 d ageing in an aerobic soil followed by leaching with 1 L of water,  $\geq 99.0\%$  of the radioactivity (the only metabolite identified was the lactone diastereomer RH-9130 at 13%) remained in the top 6 cm of soil with only 0.2% found in the leachate.

In a soil column leaching study, fenbuconazole was not detected at  $0.75 \mu\text{g a.i./L}$  (the limit of detection) in the total filtrate from three German soils when treated at  $75 \text{ g a.i./ha}$  and leached with 200 mm of water.

- Field dissipation

Dissipation from US soils (three bare and one with a wheat cover crop) was relatively rapid soon after multiple applications but slowed after this initial phase (possibly due to a presampling error) to give DT50 values of 229-464 d and DT90 values of 761-1,541 d (calculated by the Department of the Environment and Heritage). No parent fenbuconazole was found deeper than 15.2 cm with the highest concentration of  $0.28 \text{ mg a.i./kg soil}$  at 14 d after the fifth treatment. The lactone diastereomer metabolite RH-9130 was found at a maximum depth of 46-61 cm at  $0.013 \text{ mg/kg soil}$ . Traces of other metabolites including triazole residues were found intermittently but were generally  $\leq \text{LOQ}$ . When the same total amounts were applied in single treatments at one site, the DT50 and DT90 values were 192-217 d and 640 d, respectively. As before, the rapid initial dissipation (half-life of 56 d) was followed by a slow lag phase of half-life 257 d. The lactone diastereomer metabolites RH-9129 and RH-9130, and the ketone RH-6467, were found. Another study treating a bare Californian soil at high rates twice per year for five years showed annual carryover of about  $0.08 \text{ mg a.i./kg soil}$  but no accumulation from year to year of parent or metabolites. Only a few trace detections of fenbuconazole and the metabolite RH-9130 were found deeper than 15 cm.

The half-life and DT90 after a single application of  $74.6 \text{ g a.i./ha}$  to one bare soil in Germany were 117 and 388 d. Two other soils showed relatively rapid initial dissipation with half-lives of about 22 and 76 d, but slowed considerably with about 20% and 50% of the initial amount still present at 504 DAT. The fourth soil also had 11-22% remaining at this time.

- Bioconcentration and Bioaccumulation

When bluegill sunfish were exposed to a low concentration of fenbuconazole for 28 d, the bioconcentration factors for fillet, viscera and whole fish were relatively low at 44, 330 and 160, respectively. Depuration was rapid with a half-life of 1.4 d and 95-98% clearance after 14 d in clean water, indicating bioconcentration in fish and other aquatic organisms is not likely.

### Environmental toxicology

- Birds

Fenbuconazole was practically nontoxic to bobwhite quail with a single oral dose LD<sub>50</sub> > 2,150 mg a.i./kg body weight despite its adverse effect on food consumption and body weight. A 5-d dietary exposure followed by 3 d observation found an LC<sub>50</sub> of 4,953 (3,317, 24,131) mg a.i./kg food to quail chicks; the extremely wide 95% confidence limits and the deviations from acceptable protocols indicate this result should be treated with caution. When mallard ducklings were exposed similarly, the 8-d LC<sub>50</sub> was 2,013 (1,486, 2,738) mg a.i./kg food which is considered slightly toxic. In a chronic 26-week reproductive study, the shell thickness of quail eggs was potentially adversely affected giving NOEC and LOEC values of 142 and 618 mg a.i./kg food, respectively. When this study was repeated using mallards for 19 weeks, the most sensitive parameters of food consumption and body weight gain gave the NOEC and LOEC of 138 and 618 mg a.i./kg food, respectively.

- Fish

Technical fenbuconazole was very toxic to bluegill sunfish, rainbow trout and sheepshead minnow with the most sensitive 96-h EC<sub>50</sub> that of the sunfish of 0.42-0.92 mg a.i./L. Rainbow trout were slightly less sensitive in a chronic 21-d study with NOEC and LOEC values of 0.70 and 1.5 mg a.i./L, respectively, based on growth and mortality, but these results should be treated with caution. Fathead minnow were the most sensitive showing an adverse effect on mean wet weight with 35-d NOEC and LOEC of 0.082 and 0.16 mg a.i./L, respectively.

- Aquatic invertebrates

Technical fenbuconazole was very toxic to water fleas and mysid shrimp with a 48-h EC<sub>50</sub> of 0.78-1.4 mg a.i./L and 96-h LC<sub>50</sub> of 0.33-0.94 mg a.i./L, respectively. Eastern oysters were slightly less sensitive with a 96-h EC<sub>50</sub> of 1.2 (0.65, 1.9) mg a.i./L based on shell deposition. In a chronic 21-d exposure, daphnid reproductive parameters were moderately sensitive showing NOEC and LOEC values of 0.078 and 0.15 mg a.i./L, respectively, based on time to first brood, number of young and survival. Chronic 31-d exposure to chironomids showed NOEC and LOEC values of 4.4 and 8.5 mg a.i./kg sediment at initiation based on emergence.

- Aquatic plants

Fenbuconazole (technical grade) was very toxic to freshwater green algae with 120-h EC<sub>50</sub> of 0.47 (0.39, 0.57) mg a.i./L (*Pseudokirchneriella subcapitata*) and a 96-h E<sub>b</sub>C<sub>50</sub> of 0.29 mg a.i./L (95% confidence limits not reported, *Scenedesmus subspicatus*). A freshwater diatom (*Navicula pelliculosa*) showed similar sensitivity to a water soluble powder formulation with a 96-h EC<sub>50</sub> of 1.0 (0.94, 1.1) mg a.i./L. The macrophyte duckweed was slightly less sensitive to the formulated material as its 7-d IC<sub>50</sub> was 2.4 (1.6, 3.5) mg a.i./L.

- Terrestrial invertebrates

Fenbuconazole was only slightly toxic to earthworms with 14-d NOEC and LOEC values of 98 and >98 mg a.i./kg soil, respectively. When exposed for 28 d, the NOEC and LOEC based on fecundity were 39 and 100 mg a.i./kg manure dw, respectively, and the author estimated 204 d were required to bioconcentrate 50% of the exposure concentration. In a test carried out under an older protocol, honeybees were not adversely affected by contact doses of 292 µg a.i./bee which is considered relatively nontoxic. When bees were exposed in the laboratory by inhalation of vapours, contact with dry residues, direct spraying and oral ingestion, the vapours caused the most severe effect of complete mortality in two of four replicates. Additional information indicated inhalation toxicity was probably caused by volatile solvents present in the 5 EC formulation, which are not present in the proposed SC formulation in Australia. Foraging bees directly sprayed at 164 g a.i./ha in tents over flowering plants in the field apparently showed no effects different from controls, but considerable uncertainty exists with this result. A summary reported that five foliar insect pests and two soil insect pests were not affected by 560 g a.i./ha and 8 mg a.i./kg soil treatments, respectively, but these results must be treated with caution due to limited details.

- Soil nitrification and respiration

Technical fenbuconazole at a soil concentration of 11 times higher than the proposed application rate in bananas caused 15-17% deviation from controls for respiration and nitrogen mineralisation at 28-29 DAT. A 5.4% formulation of fenbuconazole at up to 7.4 times the rate in bananas caused no adverse effect on microbial dehydrogenase activity over 28 d, and ammonium, nitrate and nitrite concentrations all deviated from controls by <15% by the end of the incubation. Three species of bacteria were not adversely affected at 250 mg a.i./L and two species of fungi had minimum inhibitory concentrations of 2 and 0.12 mg a.i./L.

- Terrestrial plants

An application rate of 750 g a.i./ha to soil did not affect the emergence of seedlings of 11 grain and horticultural crops, although the results must be treated with caution due to limited details.

## **Environmental hazard**

- Estimated Environmental Concentrations

The maximum single application rate of Indar Fungicide is 101 g a.i./ha on bananas. Given a direct application to bare soil at the maximum rate of 101 g a.i./ha, incorporation into the top 6 cm (based on mobility and soil adsorption studies) and a soil bulk density of 1,300 kg/m<sup>3</sup>, the estimated environmental concentration (EEC) of fenbuconazole in soil from a single application would be 0.13 mg a.i./kg soil.

As the aerobic soil metabolism half-life is quite variable (38-532 d), confirmed by the field dissipation DT50 values of 192-464 d, significant accumulation in soil may be expected. The company indicated that no more than three sprays on bananas would be likely in a 12 month period. Assuming three applications per year applied as a single spray of 303 g a.i./ha (101 g a.i./ha X 3 sprays), the resulting soil EEC would be 0.39 mg a.i./kg soil. Using the best and worst case field dissipation DT50 values of 192 and 464 d respectively, the Department of the Environment and Heritage modelled soil accumulation peaking at about 0.53 mg a.i./kg soil after three years and 0.93 mg a.i./kg soil after ten years, in the best and worst cases respectively, from direct application to

soil. However, a field dissipation study treating bare soil twice per year for five years at high application rates of 548-590 g a.i./ha measured a maximum soil concentration of only 0.45 mg a.i./kg soil with an annual carryover of 0.08 mg a.i./kg soil.

In the worst case application to bananas, a fine spray would be used which could be amenable to drift. As bananas are grown in tropical and semi-tropical climates, their canopy is assumed to be fully developed year round, which is approximately equivalent to that of late season fruit crops for the purposes of estimating spray drift. Three sprays under these conditions would result in 11.0% drift at 3 m, equating to 33.3 g a.i./ha (101 X 3 X 11.0%) presuming no dissipation between applications. This would lead to a soil concentration of 0.043 mg a.i./kg soil in the top 6 cm. If the sprays were applied as one application per year (assuming minimal dissipation between treatments as fenbuconazole is relatively persistent), the best and worst case accumulation in soil, using the field dissipation DT50 values of 192-464 d, from spray drifting 3 m from the sprayer would peak at 0.06 mg a.i./kg soil after two years and 0.10 mg a.i./kg soil after about four years.

In a worst-case scenario of a direct overspray of a 15 cm deep body of water with the maximum single application rate of 101 g a.i./ha, the EEC of fenbuconazole would be 0.067 mg a.i./L. Three direct oversprays would give an EEC of 0.20 mg a.i./L assuming no dissipation between treatments in the worst case. Accounting for the best and worst-case DT50 of 1.2-4.3 d in water (Volkl 1992) and applications every three weeks to bananas, there would be no accumulation of fenbuconazole in water and the maximum EEC would be 0.067 mg a.i./L. For stone fruit, three direct fortnightly oversprays at 90 g a.i./ha with dissipation would give 0.06 and 0.07 mg a.i./L in the best and worst cases, respectively.

Although the dissipation from water is expected to be rapid, fenbuconazole is expected to persist in sediments as 79-92% was still present at 105 DAT in Volkl (1992). A total application rate of 270 g a.i./ha (comprising three sprays of 90 g a.i./ha each), would equate to 0.35 mg a.i./kg in the top 6 cm of sediment over 1 ha. After about 105 d, 79-92% or 0.28-0.32 mg a.i./kg would be expected to remain.

- Hazard to Terrestrial and Aquatic Organisms

The proposed use pattern of Indar Fungicide for the control of certain diseases in stone fruit and bananas will result in exposure of nontarget organisms. Due to the relatively low toxicity and limited number of applications (a maximum of three per year expected in stone fruit and bananas), the acute and chronic hazards from fenbuconazole to birds, earthworms, honeybees terrestrial plants, and soil microorganism respiration and nitrogen mineralisation processes are expected to be low. No conclusive data were presented for other terrestrial arthropods therefore this risk cannot be assessed and a label warning statement for IPM is recommended for inclusion on the label.

A worst case direct overspray of a shallow body of water is not expected to be an acute hazard to algae or duckweed but may be an acute risk to other aquatic organisms. Three sprays with no dissipation would be an acute and chronic risk to fish and aquatic invertebrates but only an acute risk in the best case dissipation. However, the more realistic exposure caused by spray drift of 10% reduces the risk to an acceptable level for all organisms living in the water column even accounting for the worst case dissipation half-life. This is mainly due to fenbuconazole's rapid dissipation from the water column into sediment where it is persistent, but not expected to be a risk to benthic organisms. A worst case runoff of fresh residues from a treated area is also not considered to be a risk to aquatic organisms.

## **Conclusions and Recommendations**

Provided the IPM and other label recommendations to prohibit application to stone fruit by aircraft and reduce the risk of spray drift are adopted, the proposed use of Indar Fungicide would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

## EFFICACY AND SAFETY ASSESSMENT

### Justification and proposed use pattern

Fenbuconazole is a new fungicide of the triazole group. With respect to fungicide resistance, fenbuconazole is classed as a Group C fungicide. Indar Fungicide will provide growers with an additional Group C fungicide for use in disease control programs.

The applicant proposes that Indar Fungicide be used as a foliar spray for the control of brown rot (*Monilinia spp.*) in nectarines, and leaf spot or yellow sigatoka (*Mycosphaerella musicola*) and black sigatoka (*Mycosphaerella fijiensis*) in bananas. The proposed rate of use is 15 mL/100L in nectarines and 420 mL/ha in combination with a water miscible oil (at the rate of 5 L/ha) in bananas.

Indar Fungicide will be available in 5L and 20L high density polythene (HDPE) containers.

### Evaluation of efficacy

#### *Nectarines*

The data presented support the claim for control of brown rot (*Monilinia spp.*) in nectarines. Detailed efficacy data was presented including results from a range of Australian field trials.

Data from 5 trials conducted in nectarines in 4 Australian states were presented to support the application. The trial layout, design and statistical assessment of the data were appropriate. The trial locations and dates were suitable for the disease being assessed. Whilst poor disease pressure was an issue in most of the trials, in general, the data demonstrate the efficacy of Indar Fungicide for brown rot control when applied in accordance with the proposed label direction. No useful data were generated for blossom blight and as such this phase of the disease is not supported for inclusion on the label.

#### *Bananas*

The data presented support the claim for control of leaf spot or yellow sigatoka (*Mycosphaerella musicola*) and black sigatoka (*Mycosphaerella fijiensis*) in bananas. Detailed efficacy data was presented including results from a range of Australian and overseas field trials.

Data from 6 Australian trials and 3 overseas were presented in support of the application. The trials were conducted at a range of locations, were appropriately designed, adequately replicated and assessed systematically for disease levels. The application methods used in the trials were in line with the proposed label direction and current industry practice. Overall the disease pressure was sufficient to enable realistic assessment of the treatments and the statistical analysis was appropriate. Whilst the data for black sigatoka was collected from overseas trials, this is acceptable given the limited presence of the disease in Australia (and as it is subject to quarantine protocols) and as the trials are considered to emulate Australian conditions. The data demonstrate the efficacy of Indar Fungicide when applied in accordance with the proposed label direction.

## **Crop safety**

In nectarines, applications of Indar Fungicide did not cause leaf or fruit burning, or leaf russetting, even at rates up to twice the proposed label rate.

In bananas phytotoxicity was only observed in one trial when a fenbuconazole formulation was mixed with a spray oil. However the applicant has clarified that this did not occur in the treatments involving the product to be registered, but in treatments where other experimental formulations of fenbuconazole were used. On this basis Indar Fungicide is considered to be acceptable from a crop safety perspective.

## **Conclusion**

The data as presented were adequate to demonstrate the efficacy and crop safety aspects of the product when used for the control of brown rot in nectarines, and leaf spot (yellow sigatoka) and black sigatoka in bananas when used according to the proposed label instructions. Registration of this product is therefore recommended.

## LABELLING REQUIREMENTS

# CAUTION

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



# INDAR\*

## Fungicide

ACTIVE CONSTITUENT: 240g/L FENBUCONAZOLE



For the control of certain disease in bananas and nectarines as specified in the Directions For Use

CONTENTS: 5, 20 LITRES

**Dow AgroSciences Australia Limited**

ABN 24 003 771 659

Level 5, 20 Rodborough Road

Frenchs Forest NSW 2086

[www.dowagrosciences.com.au](http://www.dowagrosciences.com.au)

**CUSTOMER SERVICE TOLL FREE**

**1-800 700 096**

\*Trademark of Dow AgroSciences

GMID:

## DIRECTIONS FOR USE:

<b>THE USE OF THIS PRODUCT IS SUBJECT TO AN AVCARE RESISTANCE MANAGEMENT STRATEGY</b>			
<b>Crop</b>	<b>Disease</b>	<b>Rate</b>	<b>Critical Comments</b>
Nectarines	<b>Brown Rot</b> ( <i>Monilinia spp.</i> )	<b>15 mL/100L</b>  <b>For Concentrate Spraying</b> Refer to the <b>Mixing/ Application</b> section	For protection against brown rot of fruit apply 2 sprays at 3 weeks and 1 week before harvest. In the case of susceptible varieties or conditions which are favourable for disease development, additional sprays before or during harvest may be required (note resistance management strategy). Apply by dilute or concentrate spraying equipment. Apply the same total amount of product to the target crop whether applying this product by dilute or concentrate spraying methods. Do not use at concentrations greater than 40mL/100L of water.
<b>Resistance Management Strategy (Nectarines)</b> Apply Indar Fungicide in a protective spray program. Do not wait until disease levels have built up to make applications as this reduces the effectiveness of control and increases the risk of resistance development. DO NOT apply more than 2 consecutive sprays of Indar Fungicide or other Group C fungicide before changing to another group.			
<b>Bananas (NSW, NT, QLD &amp; WA only)</b>	<b>Leaf Spot</b> (Yellow Sigatoka) <sup>(a)</sup>  <b>Black Sigatoka</b> <sup>(b)</sup>	<b>420 mL/ha</b> + <b>5L of water miscible oil</b>	<b>Tropical Areas (Nth Qld., NT and Northern WA)</b> Apply on a schedule of 14 - 21 day intervals using the shorter interval during periods of high disease pressure ( <i>e.g.</i> during the wet season). When changing to protectant products ( <i>e.g.</i> Dithane*) in the program after using Indar Fungicide, ensure the protectant is applied within 14 days of the last Indar application. <b>Sub-tropical Areas (Sth Qld., and Northern NSW)</b> Apply on a schedule of 21 - 28 day intervals using the shorter interval during periods of high disease pressure.
<i>(a) Mycosphaerella musicola and (b) Mycosphaerella fijiensis</i>			
<b>Resistance Management Strategy (Bananas)</b> <b>Tropical Areas</b> Apply a regular schedule of protectant fungicides. When disease potential is high apply 2-3 consecutive Indar Fungicide sprays before changing to a fungicide from a different activity group (not Group C). No more than 6 Group C sprays should be used in any 12 month period (Indar is a Group C fungicide). Do not use Group C fungicides during July, August or September. <b>Sub-tropical Areas</b> When using Indar Fungicide, always apply at least 2 consecutive sprays. Do not use more than 5 Group C fungicides in any 12 month period (Indar is a Group C fungicide).			

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

### WITHHOLDING PERIODS

NECTARINES, BANANAS: DO NOT HARVEST FOR 1 DAY AFTER APPLICATION.

Grazing Withholding Period:

DO NOT ALLOW LIVESTOCK TO GRAZE ORCHARDS OR PLANTATIONS OR CUT FODDER FROM TREATED AREAS FOR STOCKFEED FOR 4 WEEKS AFTER APPLICATION

### GENERAL INSTRUCTIONS

#### Fungicide Resistance Warning

GROUP	<b>C</b>	FUNGICIDE
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For fungicide resistance management the product is a Group C fungicide. Some naturally occurring individual fungi resistant to Indar Fungicide and other Group C fungicides may exist through normal genetic variability in any fungal population. The resistant individuals can eventually dominate the fungal population if these fungicides are used repeatedly. These resistant fungi will not be controlled by Indar Fungicide or other Group C fungicides, thus resulting in a reduction in efficacy and possible yield loss. Since the occurrence of resistant fungi is difficult to detect prior to use, Dow AgroSciences accepts no liability for any losses that may result from the failure of Indar Fungicide to control resistant fungi.

**Precaution:** Indar Fungicide may be harmful to beneficial arthropods and may not be suitable for use in IPM programs.

**APPLICATION: *Nectarines***

**DO NOT** apply to nectarines by aircraft.

Apply in a sufficient volume of water to achieve thorough coverage of all blossoms, fruit and foliage. The volume of water required to achieve this will depend on the size of the trees.

Apply by dilute or concentrate spraying equipment. Apply the same total amount of product to the target crop whether applying this product by dilute or concentrate spraying methods.

Do not use at concentrations greater than 40mL/100L of water.

**Dilute Spraying**

Use a sprayer designed to apply high volumes of water up to the point of run-off and matched to the crop being sprayed.

Set up and operate the sprayer to achieve even coverage throughout the crop canopy. Apply sufficient water to cover the crop to the point of run-off. Avoid excessive run-off.

The required water volume may be determined by applying different test volumes, using different settings on the sprayer, from industry guidelines or expert advice.

Add the amount of product specified in the Directions for Use table for each 100 L of water. Spray to the point of run-off.

The required dilute spray volume will change and the sprayer set up and operation may also need to be changed, as the crop grows.

**Concentrate Spraying**

Use a sprayer designed and set up for concentrate spraying (that is a sprayer which applies water volumes less than those required to reach the point of run-off) and matched to the crop being sprayed.

Set up and operate the sprayer to achieve even coverage throughout the crop canopy using your chosen water volume.

Determine an appropriate dilute spray volume (See Dilute Spraying above) for the crop canopy. This is needed to calculate the concentrate mixing rate.

The mixing rate for concentrate spraying can **then** be calculated in the following way:

**EXAMPLE ONLY**

1. Dilute spray volume as determined above: **For example** 1200 L/ha
2. Your chosen concentrate spray volume: **For example** 600 L/ha
3. The concentration factor **in this example is:** 2 X (i.e.  $1200\text{ L} \div 600\text{ L} = 2$ )
4. If the dilute label rate is 15 mL/100 L, then the concentrate rate becomes  $2 \times 15$ , which is 30mL/ 100 L of concentrate spray.

The chosen spray volume, amount of product per 100 L of water, and the sprayer set up and operation may need to be changed as the crop grows. For further information on concentrate spraying, users are advised to consult relevant industry guidelines, undertake appropriate competency training and follow industry Best Practices.

**APPLICATION: *Bananas:***

**Ground Application**

Apply by misting or air-blast machines to provide thorough coverage of all foliage.

**Aerial Application**

Apply by aircraft in a minimum total volume of 20L/ha.

## RE-ENTRY PERIOD

Do not allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day.

## PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

**DO NOT** apply Indar Fungicide to nectarines by aircraft. Spray drift may occur under adverse meteorological conditions or from certain spray equipment. **DO NOT** apply under weather conditions or from equipment that may cause spray drift onto sensitive areas including, but not limited to, non-target plants/crops, cropping land, pasture, natural streams, rivers, wetlands or waterways and human dwellings.

**DO NOT** contaminate streams, rivers or waterways with the chemical or used containers.

## STORAGE AND DISPOSAL

Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight. Store in a locked room or place away from children, animals, food, feedstuffs, seed and fertilisers.

Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. **DO NOT** dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500mm in a disposal pit specifically marked and set up for this purpose clear of water ways desirable vegetation and tree roots. Empty containers and product should not be burnt.

## SAFETY DIRECTIONS

When opening the container, preparing spray and using the prepared spray (by ground application only), wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and a washable hat and elbow-length PVC gloves.

After each day's use, wash gloves and contaminated clothing.

## FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126.

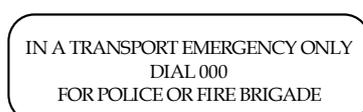
## MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet for Indar Fungicide which is available on request from Dow AgroSciences. Call Customer Service Toll Free on 1-800 700 096

## NOTICE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under off-label permits not endorsed by Dow AgroSciences, or under abnormal conditions.

**APVMA Approval Number: 54526/XX/XXXX**



**UN No 3082 ENVIRONMENTALLY HAZARDOUS SUBSTANCES,  
LIQUID, N.O.S. (CONTAINS FENBUCONAZOLE)  
MARINE POLLUTANT PG111 HAZCHEM 2X**

Batch No:

DOM

Made in USA

Barcode  
for stock  
identification

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## GLOSSARY

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

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### Footnote:

Updated versions of these documents are available on the APVMA website <http://www.APVMA.gov.au>.

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