Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the Evaluation of the New Active IPCONAZOLE in the Product

RANCONA C SEED TREATMENT

APVMA Product Number 63309

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator 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 and Environmental Health (OCSEH), Department of Environment, Water, Heritage and the Arts (DEWHA), and State Departments of Primary Industries.

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 products containing new active constituents.

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 MORAG: Manual of Requirements and Guidelines* and *Vet MORAG: Manual of Requirements and Guidelines*.

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from 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.

About this document

This is a Public Release Summary.

It indicates that the Australian Pesticides and Veterinary Medicines Authority (APVMA) is considering an application for registration of an agricultural or veterinary chemical. It provides a summary of the APVMA's assessment, which may include details of:

- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard
- efficacy and target crop or animal safety.

Comment is sought from interested persons on the information contained within this document.

Making a submission

In accordance with sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of **RANCONA C SEED TREATMENT** should be granted. Submissions should relate only to matters that the APVMA is required by legislation to take into account in deciding whether to grant the application. These grounds are **public health aspects, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade** and **efficacy**. Submissions should state the grounds on which they are based. Comments received outside these grounds cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on **26/04/2010** and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments 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.

When making a submission please include:

- Contact name
- Company or Group name (if relevant)
- Postal Address
- Email Address (if available)
- The date you made the submission.

All personal and ***confidential commercial information (CCI)***[1] material contained in submissions will be treated confidentially.

[1] A full definition of "confidential commercial information" is contained in the Agvet Code.

Written submissions on the APVMA's proposal to grant the application for registration that relate to the **grounds for registration** should be addressed in writing to:

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Further information

Further information can be obtained via the contact details provided above.

Copies of full technical evaluation reports covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request.

Further information on public release summaries can be found on the APVMA website:
http://www.apvma.gov.au

1 INTRODUCTION

Applicant

Chemtura Australia Pty Ltd.

Details of Product

It is proposed to register Rancona C Seed Treatment, containing ipconazole (20 g/L) and cypermethrin (4g/L) as an aqueous micro emulsion formulation. The product is intended for use as a seed treatment for wheat, barley and oat seeds to control various smuts, bunt, and stored grain insect control. Rancona C Seed Treatment is intended to be used at 1 L/tonne of seed for on-farm application, in seed sheds and in mobile seed graders and treaters.

Ipconazole is a new active constituent to the Australian market. It is a fungicide which belongs to the triazole-containing class of chemicals and is structurally similar to many other triazole compounds used as pesticides. Ipconazole exerts its effect by inhibiting sterol synthesis in fungi.

Ipconazole is currently registered for use in Japan, Argentina, Uruguay, USA and Canada and recently in Europe. Various formulations of ipconazole are registered around the world in various crops. Currently it is registered in Japan as a seed treatment. Registrations also exist in Argentina on wheat, barley, corn and peanuts. In Uruguay and Europe, ipconazole is registered on cereals.

Rancona C Seed Treatment also contains another active constituent cypermethrin, which has been approved for many years for application as a seed treatment to cereals at the same or greater rate to that proposed. The risk associated with the proposed use of cypermethrin in Rancona C Seed Treatment is not greater than that previously assessed, as the overall application rate is the same or less.

The ipconazole based seed treatment as proposed is new to the Australian market**.** The actives ipconazole and cypermethrin as well as the finished product will be manufactured overseas and imported to Australia. Ipconazole is in the new group 3 for fungicides resistance management and cypermethrin is in group 3a for insecticides resistance management

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Rancona C Seed Treatment and approval of the new active constituent, IPCONAZOLE.

2 CHEMISTRY AND MANUFACTURE

2.1 Active Constituent

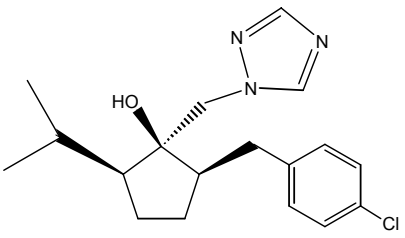
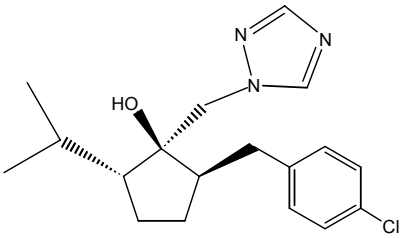
Ipconazole is a new active constituent, used as a seed treatment chemical on rice, wheat, barley, and oats for the control of a wide range of seed diseases in rice and other crops.

Manufacturing Site

The active constituent ipconazole is manufactured by WAKASA AGC Fine Chemicals Co., Ltd., 24-26-1, Hansei, Obama-City, Fukui-Pref, 917-0044, Japan

Chemical Characteristics of the Active Constituent

The chemical active constituent ipconazole has the following properties:

COMMON NAME:	Ipconazole (BSI, PA E-ISO approved)
IUPAC NAME:	(1RS,2SR,5RS;1RS,2SR,5SR)-2-(4-chlorobenzyl)-5-isopropyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS NAME:	2-[(4-chlorophenyl)methyl]-5-(1-methylethyl)-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS REGISTRY NUMBER:	125225-28-7
MANUFACTURER'S CODE:	KNF-317
MOLECULAR FORMULA:	C18H24ClN3O
MOLECULAR WEIGHT:	333.9
STRUCTURE:	 Ipconazole *cc* (*cis-cis* isomer) (*1RS,2SR,5RS*)-2-(4-chlorobenzyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol  Ipconazole *ct* (*cis-trans* isomer) (*1RS,2SR,5SR*)-2-(4-chlorobenzyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol

APVMA Active Constituent Standard for Ipconazole Active Constituent

Constituent	Specification	Level
Ipconazole	Ipconazole	Not less than 944 g/kg

Physical and Chemical Properties of Pure Active Constituent and Technical Material

COLOUR	White powder
PHYSICAL STATE	Solid
ODOUR	Cyanide like (almonds) odour
MELTING POINT	85.5-88°C
VAPOUR PRESSURE AT 20°C	$<5.05\times10^{-5}$ Pa
WATER SOLUBILITY AT 20°C	9.34 mg/L for ipconazole *cc* 4.97 mg/L for ipconazole *ct*
SOLUBILITY IN ORGANIC SOLVENTS	Heptane:1.9 g/L Xylene: 151.0 g/L Toluene: 156.0 g/L *n*-Octanol: 229.6 g/L Acetone: 570.4 g/L Dichloromethane: 583.1 g/L Methanol: 678.7 g/L
PARTITION COEFFICIENTS (N-OCTANOL/WATER)	4.65 for ipconazole *cc* 4.44 for ipconazole *ct*

2.2 Product

DISTINGUISHING NAME	Rancona C Seed Treatment
FORMULATION TYPE	Micro emulsion
ACTIVE CONSTITUENTS CONCENTRATIONS	Ipconazole 20 g/L Cypermethrin 4 g/L

Physical and Chemical properties of the Product

APPEARANCE	Mobile liquid with red to dark red colour
ODOUR	Characteristic fruity odour
ACIDITY/ALKALINITY	pH 4-7 (1% dilution)
DENSITY	1.065
EMULSION CHARACTERISTICS	Max. 0.1 mL oil/cream separation after 30 minutes standing
PERSISTENT FOAM (1:4 DILUTION)	Max. 60 mL foam after 1 minute
VISCOSITY	40-60 mPa.s
FLASH POINT	Not applicable
FLAMMABILITY	Not flammable
EXPLOSIVE PROPERTIES	Not explosive
OXIDISING PROPERTIES	No oxidising properties
CORROSIVE HAZARD	Not applicable
DIELECTRIC BREAKDOWN VOLTAGE	Not applicable, formulation is not intended for use around electrical equipment.
DANGEROUS GOODS CLASSIFICATION	Not dangerous good according to the Australian Code of Transport of Dangerous Goods by Road and Rail.

Recommendation

Based on a review of the chemistry and manufacturing details provided by the applicant, registration of Rancona C Seed Treatment is supported.

3 TOXICOLOGICAL ASSESSMENT

3.1 Summary

Ipconazole is a new fungicide active ingredient to the Australian market. It belongs to the triazole-containing class of chemicals and is structurally similar to many other triazole compounds used as pesticides. Ipconazole exerts its effect by inhibiting sterol synthesis in fungi. The product Rancona C Seed Treatment, containing ipconazole 20 g/L and cypermethrin at 4 g/L, is a micro emulsion liquid formulation, and is intended to be as a seed treatment of wheat, barley and oats for the control of smuts and bunt, and also for stored grain insect control.

In rats, 70 to >90% of aradiolabelled dose was absorbed after oral administration of ipconazole. Maximum plasma concentrations were achieved in about 6 hours, and plasma half-life was 10-36 hours after a single dose and 40-50 hours after repeated doses. The highest level was detected in the liver. The majority (>90% dose) was eliminated in urine and faeces within 72 hours. Overall, tissue accumulation was low.

Both Ipconazole and Rancona C Seed Treatment showed low acute oral, dermal and inhalational toxicity in rats. They were not a skin irritant, but were a moderate (ipconazole) or slight (the product) eye irritant in rabbits. Both showed no potential for skin sensitisation.

Repeat dose studies were conducted in mice, rats and dogs. Dietary administration to mice and rats caused epithelial hyperplasia / hyperkeratosis and subepithelial inflammation in the non-glandular region of the stomach. Oesophageal, pharyngeal, and laryngeal hyperkeratosis were also observed after repeat dermal exposure in rats. Irritation (hyperplasia, hyperkeratosis and/or metaplasia) were also present on the epithelial surface of the oesophagus, hard palate, stomach, larynx and skin of rats following repeat inhalation exposure in rats. Repeat oral dosing induced reddening of the skin (typically the gums, ears, eyes, muzzle and neck), cataracts, lenticular degeneration and anomalies of lenticular fibres in dogs. Histopathological changes were observed in the liver, kidneys and/or adrenal glands in all species tested, in particular, hepatocytic hypertrophy, fatty vacuolation and necrosis, some with bile duct proliferation and/or pigment laden Kupffer cells in the liver.

Ipconazole did not show a potential for genotoxicity, or carcinogenicity. The chemical was neither a reproductive nor a developmental toxicant.

Workers may be exposed to the product when opening containers, mixing/loading and application of the product, cleaning up spills and maintaining equipment, or handling treated seeds. The main route of exposure to the products will be dermal contact.

Based on a health risk assessment, First Aid Instructions, Warning Statements and General Safety Precautions, Safety Directions and Re-handling statement have been recommended and shown on the product label.

Based on an assessment of the toxicology, it was considered that there should be no adverse effects on human health from the use of Rancona C Seed Treatment when used in accordance with the label directions.

3.2 Summary Of The Evaluation Of Toxicological Studies

The toxicological database for ipconazole, which consists primarily of toxicity tests conducted in laboratory 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 that 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

In rats, radio-labelled ipconazole was absorbed rapidly and extensively following administration of two single oral doses (2 and 100 mg/kg bw). The extent of the absorption was >90% at the low dose level and 71% for females at the high dose level. Maximum plasma concentrations were achieved in about 6 hours, and plasma half-lives of 10-36 hours in single dose studies and 40-50 hours in the repeat dose study. The highest level of radioactivity was detected in the liver.

Rats eliminated the majority (>90%) of a single oral dose in urine and faeces within 72 hours. Overall tissue accumulation after single oral doses was low, with less than 1 percent in the liver at 120 hours.

The unchanged ipconazole represented only a small portion (2.2% of the administered dose) in the faeces, and metabolites (from hydroxylation of the parent compound) were detected mainly in the faeces and bile (as glucuronide conjugates). Free triazole was identified as the main component in urine of male rats.

No dermal absorption studies were provided.

Acute Toxicity

Ipconazole displayed low acute oral (LD50 of 1338 mg/kg bw), dermal (LD50 >2000 mg/kg bw) and inhalational toxicity (LC50 >1880 mg/m3, 4-h nose only expousre) in rats. It was a non-irritant to the skin of rabbits, but was a moderate irritant to the eyes of rabbits. It was not a skin sensitiser in guinea pigs.

The formulated product Rancona C Seed Treatment, which contains ipconazole 20 g/L and cypermethrin 4 g/L, showed low acute oral (LD50 of >2500 mg/kg bw), dermal (LD50 >2000 mg/kg bw) and inhalational toxicity (LC50 >4990 mg/m3; 4-h nose only exposure) in rats. It was not a skin irritant in rabbits, but was a slight eye irritant in rabbits. It was not a skin sensitiser in guinea pigs.

Short-term Toxicity

Ipconazole was dosed via the diet to CD-1 mice at 0, 250, 500, 1000 or 2000 ppm in the diet for 4 weeks. The 2000 ppm group was poorly tolerated and terminated on Day 10 after showing weight loss/markedly low weight gain, reduced food consumption and high food scatter indicative of unpalatability of the test diet. Several findings, including epithelial hyperplasia and subepithelial inflammation in the non-glandular region of the stomach, indicated that ipconazole was an irritant after repeat contact. Changes in the liver included hepatocytic hypertrophy, fatty vacuolation at all dietary concentrations and necrosis in individual females at 500 ppm or more and males at 1000 ppm. Plasma cholesterol levels were decreased at all dietary concentrations and this was attributed to the effect of treatment upon hepatocytic fat metabolism. As a consequence of the hypertrophy and increased hepatocytic fat, liver weights were high in animals dosed at 500 or 1000 ppm. In view of the presence of fatty vacuolation in the liver at all dietary concentrations of ipconazole in this study, a NOEL was not established.

Ipconazole was administered to rats at 0, 300, 1000 or 3000 ppm in the diet for 4 weeks. The 3000 ppm group was terminated before the end of week 3 after animals showed weight loss or markedly low weight gain, reduced food consumption and high food scatter indicative of unpalatability of the test diet. Histopathological changes that were attributed to treatment with ipconazole occurred in the stomach (non-glandular region), oesophagus and the adrenals. In the stomach there was epithelial hyperplasia and hyperkeratosis in animals dosed at 1000 ppm. In females dosed at 1000 ppm and animals dosed at 3000 ppm there was an increase in γ-glutamyl transpeptidase activities which is indicative of membrane damage and a degree of hepatotoxicity, though there was no histopathological change in the liver that would account for these findings. The NOEL in this study was 30.5 mg/kg bw/day (300 ppm) for males. The NOEL for females was not established, and the LOEL was 31.3 mg/kg bw/day (300 ppm) based on reduced body weight gain and food consumption, hyperkeratosis and epithelial hyperplasia in the non-glandular region of the stomach and reduced urinary volume. Therefore, due to the effects seen in females, a NOEL could not be established for this study.

Ipconazole was administered to beagle dogs by oral capsules for 4 weeks at 0, 24, 60 or 150 mg/kg bw/day. Loose/liquid faeces, inappetence and reddening of skin (typically inside the ears, gums, lips, and abdomen and around the eyes) were apparent in animals receiving 60 or 150 mg/kg bw/day. The condition of one male and both females receiving 150 mg/kg bw/day was such that they were sacrificed due to reddening of the skin and, in the females, ocular discharge. No NOEL was established based on the finding of bile duct proliferation and reddening in the ears in males at all doses. In females bile duct proliferation and reduction in food intake was observed in the 60 mg/kg bw/d dose group, resulting in a NOEL of 24 mg/kg bw/d. Therefore, due to the effects seen in males, no NOEL was established for this study.

Ipconazole was administered to the shaved skin of rats for 5 days/week for 4 weeks at 0, 10, 150 or 1000 mg/kg bw/day. At the application site, erythema was observed at 1000 mg/kg bw/d during the last 2 weeks of the study. Minimal hypertrophy/hyperplasia of the adrenal cortical was in some females at all doses. Minimal to mild hypertrophy/hyperplasia of the skin was seen in some males and females at all dose levels. Minimal to moderate oesophageal, pharyngeal, and laryngeal hyperkeratosis were also observed within the non-glandular portions of the stomach at all dose levels. The effects seen in the non-glandular portions of the stomach are considered to be due to inadvertent oral ingestion of the test material. Therefore, no NOEL was established in this study.

Ipconazole was administered to Sprague-Dawley rats by dynamic nose-only exposure at concentrations of 0, 30, 100, 300 or 1000 mg/m3 for 6 hours per day, 5 days/week for 4 weeks. Exposures resulted in decreased body weight gain/lower absolute body weight in the ≥100 mg/m3 males and 1000 mg/m3 females, increased incidence of ano-genital stains in males at 1000 mg/m3 and in females at ≥300 mg/m3, decreased feed consumption in males at ≥300 mg/m3. Increased adrenal weight and decreased thymus weight in the 300 mg/m3 females were associated with corresponding histopathological observations. Absolute liver weights were increased in females at ≥300 mg/m3. Spleen weights in males at 300 were decreased. Brain, epididymides and testes weights relative to body weight were significantly increased in males at ≥300 mg/m3. Relative liver weights were increased in females at ≥300 mg/m3, but not males. By light microscopy, changes suggestive of irritation (hyperplasia, hyperkeratosis and/or metaplasia) were present on the epithelial surface of the oesophagus (100-1000 mg/m3), hard palate (100-1000 mg/m3), stomach (1000 mg/m3), larynx (30-1000mg/m3) and skin (300-1000 mg/m3). No NOEC was established due to upper respiratory tract and upper digestive tract toxicity at all doses.

Subchronic Toxicity

In CD-1 mice, ipconazole at doses of 0, 30, 150 or 500 ppm was administered in the diet for 13 weeks. Body weight gain was low in males at 500 ppm. Liver weights were higher in males and females given 500 ppm. Macroscopic examination after 13 weeks of treatment revealed pale livers for one male and one female given 500 ppm. Histopathological findings related to treatment comprised hepatocyte vacuolation in the livers of males given 150 ppm and males and females given 500 ppm, a generalised increase of Oil-Red-O (ORO)-positive staining in males and females given 500 ppm, increased centrilobular ORO-positive staining in females given 500 ppm, an increase in severity of centrilobular hepatocyte hypertrophy in males given 500 ppm and focal hyperplasia of the non-glandular region of the stomach in two males given 500 ppm. The NOEL was 30 ppm (4.4 mg/kg bw/day in males and 5.1 mg/kg bw/day in females), based on liver hypertrophy and fatty vacuolation, along with some changes in haematological parameters in females and some changes in clinical chemistry parameters in males.

Ipconazole was administered to rats for 13 weeks at 0, 30, 70, 150 or 300 ppm in the diet, with an additional group of 600 ppm for males. The neurobehavioral investigations did not reveal any treatment-related findings. Histopathological changes attributed to treatment occurred in the stomach, kidneys and uterus. In the stomach epithelial hyperplasia of the non-glandular region was present in one male given 150 ppm, two males and five females given 300 ppm and in four males given 600 ppm. Hyperkeratosis and subepithelial oedema and inflammation were also seen in one male given 150 ppm and in one female given 300 ppm, with ulceration also being present in the female. In the kidneys there was a dose-related increase in the incidence and severity of cortico-medullary mineralisation in treated females, though only at 150 or 300 ppm was statistical significance attained. When compared with the controls, a reduced incidence of luminal dilatation of the uterus was seen in females given 300 ppm. The NOEL was 70 ppm (5.8 mg/kg bw/day) based on the effects seen in males at 150 ppm.

Ipconazole was administered to Beagle dogs by oral capsule for 13 weeks at dosages of 0, 2, 10 or 40 mg/kg bw/day. At 40 mg/kg bw/d, reddening of the skin (typically the gums, ears, eyes, muzzle and neck) was apparent from week 2 in animals, and occasional ocular discharge was seen in two females from week 2 and a single male from week 4. In addition, hair loss/thinning around eye/muzzle were apparent in three females and three males. At 10 mg/kg bw/day, reddening of the skin occurred in one male and, transiently, in one female. The biological significance of this minimal finding at 10 mg/kg bw/day in a single animal of each

sex is unknown. Three males and all females receiving 40 mg/kg bw/day had cataracts to varying degrees. Lenticular degeneration was seen in the eyes in two females given 40 mg/kg bw/day. In one animal this was associated with keratitis, iritis and oedema of the iris. An anomaly of lenticular fibres was seen in all males given 40 mg/kg bw/day and in two males given 10 mg/kg bw/day. Total plasma cholesterol concentration was reduced for both sexes receiving 40 mg/kg bw/day. In addition, calcium concentrations were also reduced in these animals. Urinalysis at week 13 indicated an increase in specific gravity and protein in males receiving 40 mg/kg bw/day. The urine of animals receiving 40 mg/kg bw/day tended to be darker than that of the controls at week 13. High liver weights and low thymus weights were apparent in males and females receiving 40 mg/kg bw/day. In the liver there was central lobular hypertrophy and bile duct proliferation in males and females given 40 mg/kg bw/day and pigment laden Kupffer cells were seen in three out of four males and females given 40 mg/kg bw/day. Reduced cellularity of the thymic cortex was seen in three males and two females given 40 mg/kg bw/day. The NOEL was 2 mg/kg bw/day based on anomalies of lenticular fibres at 10 mg/kg bw/day.

Chronic Toxicity and Carcinogenicity

Ipconazole was given to mice at 0, 15, 175 or 350 ppm in the diet for 78 weeks. In the stomach there was an increase in the incidence of epithelial hyperplasia in the non- glandular region in females given 175 or 350 ppm. There were treatment-related findings, hepatocyte hypertrophy (centrilobular) in the liver of males at all treatment concentrations, along with a tendency towards an increase in the degree and/or incidence of hepatocyte vacuolation (generalised). Though there was no evidence of treatment-related neoplastic change. No NOEL was established due to effects in the livers of male mice at all dose levels.

Ipconazole was administered to rats at 0, 30, 80, 200 or 300 ppm in the diet for 52 (toxicity phase) and 104 weeks (carcinogenicity phase). The two highest dietary concentrations for females were reduced from week 2 to 120 and 200 ppm. Mortality was not affected by treatment. The appearance and behaviour of the animals in a standard arena and sensory reactivity and grip strength were unaffected by treatment. In the motor activity investigations there was an increase of total low-beam activity scores in males receiving 300 ppm. There was no effect of treatment upon the incidence, multiplicity and mean time of onset of palpable masses. There were no treatment-related ocular changes. The haematology investigations did not indicate any changes in the peripheral blood or in the composition of the bone marrow that were attributable to treatment. There were a number of inter-group differences that attained statistical significance but these were inconsistent between investigations, lacked dose-relationship or were confined to one sex and were therefore attributed to normal biological variation. Similarly, biochemical changes in urea concentrations, phosphorous concentrations and creatine levels were either seen in one sex, not seen at later time points and/or observed in the absence of a dose response and, thus, are not considered to be of toxicological significance. Necropsy did not indicate any treatment-related differences in organ weights or any macroscopic change due to treatment. There were no treatment-related histopathological findings after 52 weeks of treatment in the toxicity phase of this study, and no neoplastic or non-neoplastic findings after 104 weeks in the carcinogenicity phase of this study. Thus, the NOEL was 300 ppm (13.3 mg/kg bw/day) in males and 200 ppm (12.6 mg/kg bw/day) in females for the carcinogenicity phase, and 300 ppm (15.9 mg/kg bw/day) for the toxicity phase.

Ipconazole was administered orally, by capsule, to Beagle dogs at dose levels of 1.5, 5 or 20 mg/kg bw/d for 52 weeks. There was reddening of various regions of the skin which was apparent in two males and two females receiving 5 mg/kg bw/day and in all animals receiving 20 mg/kg bw/day. The reddening was initially

seen in particular regions of the body but in some animals, particularly in one male and one female receiving 5 mg/kg bw/day and in all dogs receiving 20 mg/kg bw/day, it eventually became present over the whole body. Lenticular opacities were seen after 52 weeks in two males and one female animal receiving 20 mg/kg bw/day. One male had a very faint opacity of the posterior lens capsule, one male had opacities on the anterior and posterior lens capsule, whilst the female had posterior suture line opacity in one eye. Bilateral lenticular degeneration was seen in the eyes of one male given 20 mg/kg bw/day. Plasma alkaline phosphatase activities were increased consistently in males and females receiving 20 mg/kg bw/day and one female at this dose had a consistently high plasma alanine amino-transferase activity. Total plasma cholesterol concentrations were reduced in males and females receiving 20 mg/kg bw/day, with females receiving 5 mg/kg bw/day being similarly affected in week 13. After 52 weeks of treatment the liver weights of males and females given 20 mg/kg bw/day were high in comparison with that of the controls. In addition, kidney weights were high in two males given 5 mg/kg bw/day and in males and females given 20 mg/kg bw/day. In the liver, there was an increase in the incidence and severity of bile duct proliferation in males and females at 5 mg/kg bw/day and above, along with an increased incidence in centrilobular hepatocyte hypertrophy in males. In the adrenals there was an increased incidence and degree of severity of cortical fatty vacuolation in all males and females given 20 mg/kg bw/day. Thus, the NOEL in this study was concluded to be 1.5 mg/kg bw/day based on reddening of the skin and liver toxicity.

Reproduction Toxicity

In a 2-generation reproduction study, rats were fed a diet containing 0, 30, 100, 300 ppm of ipconazole for 10 weeks before pairing, throughout pairing, gestation and lactation. Among F0 females, mean food consumption at 100 or 300 ppm was significantly reduced during the first week of treatment, and also during Days 0-12 of gestation and during lactation. Selected F1 animals in the 300 ppm group were smaller and their bodyweight gains were lower than controls, with the difference more marked in males than in females. Mean bodyweights of F1 animals at 300 ppm at termination were lower. During gestation, overall bodyweight gain of females at 300 ppm was significantly lower. Reproductive performance of adult animals in both generations was considered to be unaffected at all doses. Sexual maturation of F1 females at 300 ppm, assessed by the age at attainment of vaginal opening, was significantly delayed as compared to the controls. The pattern of oestrous cycles, mating performance, pre-coital interval, gestation length, litter size and subsequent offspring survival were not affected. At 300 ppm the F1 live litter size from day 14 to day 25 of age was significantly lower. There were no toxicologically significant effects on F0 or F1 sperm parameters or F1 reproductive organ weights. No treatment-related microscopic changes were detected in reproductive organs in F0 animals. The survival and general condition of the F1 and F2 offspring were not affected up to 300 ppm. Mean bodyweights of F1 and F2 offspring on day 1 of age were similar in all groups. There were no toxicologically significant effects on offspring weight gain at 30 or 100 ppm. At 300 ppm, bodyweight gain was lower in the F2 generation. Among F1 males and females at 300 ppm, there was an increase in the number of animals with pale areas on the lungs, correlated with the microscopic finding of minimal or slight foci of foamy alveolar macrophages. Necropsy findings for the F2 offspring were unremarkable. At 300 ppm the live litter size from day 14 to day 25 of age was significantly lower. The NOEL for reproductive performance in the F0 and F1 adults was 300 ppm (22 mg/kg bw/day). Significant reductions in bodyweight gain during gestation and food consumption during gestation and lactation in F0 and F1 females receiving 300 ppm, along with decreased terminal body weights and minimal/slight foci of foamy alveolar macrophages in the lungs of both sexes resulted in a NOEL for general toxicity of 100 ppm (8-9.3 mg/kg bw/day). Reduced bodyweight and significant differences in organs weights relative to bodyweight in the F1

and F2 offspring at 300 ppm resulted in a NOEL of 100 ppm (8-9.3 mg/kg bw/d) for offspring. This study provides no robust evidence of ipconazole being a reproductive toxicant.

Developmental Toxicity

Ipconazole was administered orally via a stomach tube to mated female rats (from days 6 through 15 of gestation) at 0, 3, 10, or 30 mg/kg bw/day. With regard to the maternal rats, body weight gains and food consumption were significantly reduced at 30 mg/kg bw/day group. At caesarean section on day 20 of gestation, no significant differences were noted for the numbers of corpora lutea, implants, and live foetuses, placental weights, and foetal sex ratio in any of the treated groups. Teratological examination revealed various types of malformations and variations for several foetuses in all groups including the control group. The incidences of foetuses with total visceral or skeletal variations in the 30 mg/kg bw/day group were significantly increased. However, the incidence of dilation of the renal pelvis and/or ureters and lumbar ribs in the 30 mg/kg bw/day group were within the historical control values, while the incidence of thymic remnants is not statistically significant and does not have a dose relationship. The incidence of left umbilical artery was above the historical control values. However, all these findings were additionally seen in the presence of marked maternal toxicity (i.e. a 25% decrease in body weight gain in dams) and, consequently, considered a non-specific secondary consequence of such. Thus, this study provides no evidence of ipconazole being a developmental toxicant. A NOEL of 10 mg/kg bw/day was identified in this study for both maternal and developmental toxicity.

Ipconazole was administered orally via a stomach tube to artificially inseminated Japanese White female rabbits at dose levels of 0, 2, 10, or 50 mg/kg bw/day from day 6 through 18 of gestation. With regard to the maternal rabbits, no treatment related adverse effects were noted in the 2 and 10 mg/kg bw/day groups. In the 50 mg/kg bw/day group, body weight gains and food consumption showed a tendency to be reduced during the dosing period. At caesarean section on Day 27 of gestation, no significant differences were noted for the numbers of corpora lutea, implants, and live foetuses, the percent incidence of resorptions and foetal deaths, foetal and placental weights, and foetal sex ratio. However, foetal and placental weights in the 50 mg/kg bw/day group showed a tendency to be decreased. Teratological examination of live foetuses revealed no treatment-related external, visceral, and skeletal malformations and variations in the 2 and 10 mg/kg bw/day groups. In the 50 mg/kg bw/day group, the incidence of splitting of the parietal bones was significantly higher than that in the control group. However, historical control data indicates that the incidence of splitting and/or fissure of the parietal bones ranges from 0 to 14.3% and, thus, the value of 13.0 % at the top dose of 50 mg/kg bw/day is within the historical control range. Based on the results of the study, it is considered that the dose level of 10 mg/kg bw/day is the NOEL for both maternal rabbits and foetuses, as the dose level of 50 mg/kg bw/day is a minimally toxic level for both maternal rabbits and foetuses. This study provides no robust evidence of ipconazole being a developmental toxicant.

Genotoxicity

The battery of in vitro mutagenicity and genotoxicity tests with and without S9 (i.e. point mutation, chromosomal damage, and DNA damage and repair), and an in vivo genotoxicity test (mouse micronucleus assay), yielded negative results with ipconazole. Thus, this data did not indicate any predisposition for neoplastic lesion(s) or tumour development in vivo.

Ipconazole is not likely to be a human carcinogen and there is no concern for mutagenicity.

3.3 Public Health Standards

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) agreed to include ipconazole as a new entry in Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) with a cut-off to Schedule 5 for preparations containing 2 per cent or less of ipconazole.

NOEL/ADI /ARfD

The Acceptable Daily Intake (ADI) is the quantity of an agricultural compound which can safely be ingested on a daily basis for a lifetime and is based on the NOEL for the most sensitive toxicological endpoint 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.

Ipconazole is not intended for direct application to food producing crops, but to be used as a seed treatment. An ADI for ipconazole was established at 0.015 mg/kg bw/day based on a NOEL of 1.5 mg/kg bw/day in a 1-year chronic toxicity study in the most sensitive species, the dog, and using a default 100-fold safety factor.

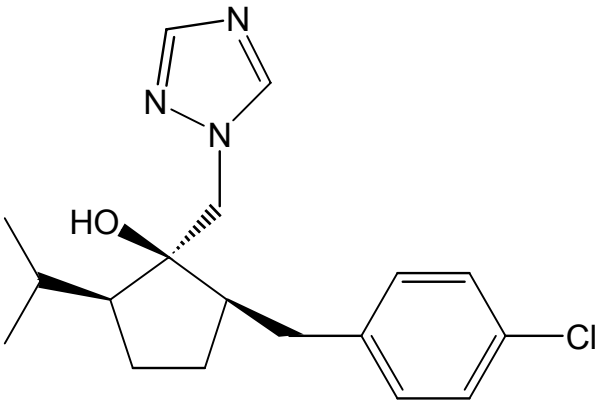
The acute reference dose (ARfD) is the maximum quantity of an agricultural or veterinary chemical that can safely be ingested as a single isolated event or over 1 day. The ARfD is derived from the NOEL as a single or short term dose which causes no effect in the most sensitive species of experimental 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.

No ARfD is required to be established, as ipconazole is not considered likely to present an acute hazard (including developmental toxicity) to humans.

4 RESIDUES ASSESSMENT

4.1 Introduction

As part of the residues assessment for ipconazole, plant and animal metabolism studies, supervised residue trials, trade aspects and chemistry were considered. Details are provided below.



Ipconazole

Cypermethrin has been approved for many years for application as a seed treatment to cereals at the same or greater rate to that proposed for Rancona C Seed Treatment. The risk associated with the proposed use of cypermethrin in Rancona C Seed Treatment is not greater than that previously assessed, as the overall application rate is the same or less. Therefore the use of cypermethrin is not discussed here.

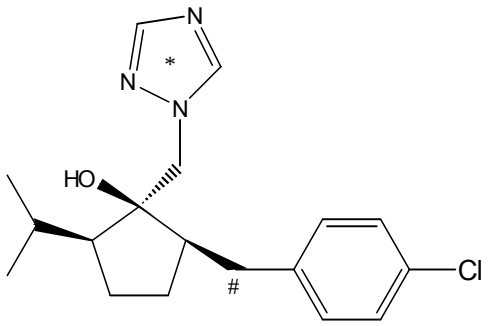
4.2 Metabolism

Metabolism studies in plants, rats and goats have been submitted for ipconazole.

Plant Metabolism

Studies were conducted on wheat and soybean to determine the TRRs in these commodities after treatment with either [triazole 3, 5-^{14}C]-ipconazole or [benzylmethylene-^{14}C]-ipconazole at nominal rates of 1.5, 2.5 and 10.0 g a.i./100 kg seed (*i.e.* 0.75, 1.25 and 5x the proposed application rate of 2 g ipconazole/100 kg seed).

Ipconazole Radiolabels



# Denotes position of [^{14}C-benzyl methylene] radiolabel
* Denotes position of [^{14}C-triazole] radiolabel

Wheat forage was harvested 136 days after planting (DAP). Wheat hay was harvested 157 DAP and mature wheat grain and straw were harvested 207 DAP. TRRs in wheat samples grown from seeds which had been treated with [triazole-3, 5-^{14}C]-ipconazole at rates of 1.65g a.i./100 kg seed (0.83x), 2.42 g a.i./100 kg seed (1.21x) or 10.54 g a.i./100 kg seed (5.27x) were greater than the LOQ of 5 ppb for all samples except the forage sample from seeds treated at 1.65 g a.i./100 kg seed (TRR = 4.43 ppb). TRRs in wheat samples grown from seeds which had been treated with [benzylmethylene-^{14}C]-ipconazole at rates of 1.76 g a.i./100 kg seed (0.88x), 2.70 g a.i./100 kg seed (1.35x) or 10.69 g a.i./100 kg seed (5.35x) were less than the MQL of 5 ppb for all RAC samples except the straw sample from seed treated at 10.69 g a.i./100 kg (TRR = 5.10 ppb).

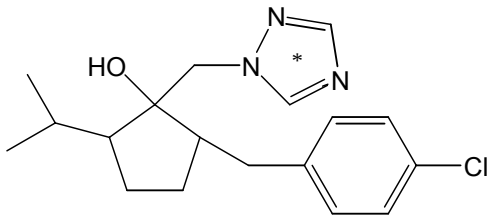
Soybean forage was harvested 63 DAP. Soybean hay was harvested 90 DAP and mature seed was harvested at 168 DAP. TRRs in forage samples grown from soybean seeds which had been treated with [triazole-3, 5-^{14}C]-ipconazole at rates of 1.73g a.i./100 kg seed (0.87x), 2.23 g a.i./100 kg seed (1.12x) or 10.70 g a.i./100 kg seed (5.35x) were less than 5 ppb for the two lower rates, while the TRR for soybean forage grown from seeds treated at 10.70 g a.i./100 kg was 7.7 ppb. TRRs in soybean hay and seed samples were all higher than the LOQ at all treatment rates (maximum 22.4 ppb in hay and 58.9 ppb in seed). TRRs in immature soybean forage and hay samples and mature soybean seed samples grown from seeds which had been treated with [benzylmethylene-^{14}C]-ipconazole at rates of 1.33 g a.i/100 kg seed (0.67x), 2.30 g a.i./100 kg seed (1.15x) or 10.01 g a.i./100 kg seed (5.01x) were less than 5 ppb in all samples.

Further studies were conducted to identify and characterise the radioactivity found in wheat grain and soybean hay and grain samples grown from seeds treated with [triazole-3, 5-^{14}C]-ipconazole at an application rate of 10g a.i./100 kg seed. The TRR in soybean grain, soybean hay and wheat grain was 59.6 ppb, 22.4 ppb and 38.1 ppb (ipconazole equivalents) respectively (determined by combustion analysis/ LSC).

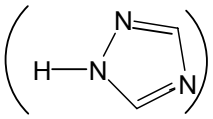
Triazolylpyruvate was the only metabolite identified in soybean grain (41.6 ppb, 69.8% TRR), soybean hay (11.9 ppb, 53.1% TRR) and wheat grain (25.1 ppb, 65.9% TRR). Triazole, triazolylacetic acid and triazolylalanine were not observed in this study. The largest unidentified peaks in extracts of soybean grain,

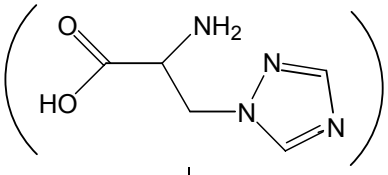
soybean hay and wheat grain were found at levels of 5.3 ppb, 3.0 ppb and 4.9 ppb respectively. In addition ipconazole was not observed at its limit of detection.

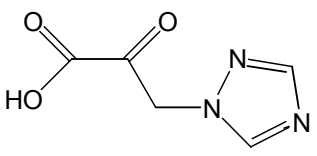
The proposed biotransformation pathway is based on the metabolites identified in soybean grain, soybean hay and wheat grain. Triazolylpyruvate was formed from ipconazole in several steps: the first step is the formation of triazole which reacts with serine or cysteine to form triazolylalanine. (The absence of triazole favours a concerted mechanism in the formation of triazolylalanine). The metabolite triazoylpyruvate is formed from triazolylalanine by oxidation or transamination.



Ipconazole







Triazolylpyruvate

Proposed biotransformation pathway based on the metabolites identified in soybean grain, soybean hay and wheat grain.

The distribution and metabolism of ipconazole in spring wheat and winter wheat were also studied.

Spring wheat seeds were treated with either [^{14}C-triazolyl]-ipconazole or [benzylmethylene-^{14}C]-ipconazole at nominal rates of 2.5 or 25 g a.i./100 kg seed (*i.e.* 1.25x – 12.5x the proposed application rate: actual application rates 2.8 (1.4x) and 26.2 (13.1x) g a.i./100 kg seed respectively). Wheat forage and hay were harvested at 49 days and 69 days after planting (DAP) respectively. Mature grain and straw were harvested at 103 DAP. Total radioactive residues (TRR) in forage, hay, straw and grain were determined by combustion analysis/ LSC. The higher residue levels found in spring wheat RACs grown from [^{14}C-triazolyl]-ipconazole treated seed compared with RACs grown from [^{14}C-benzyl methylene]-ipconazole treated seed at the same rates, suggests that there may be selective uptake of metabolites containing the triazole moiety relative to the benzylmethylene moiety. When ipconazole is applied as a seed treatment, it is extensively metabolised to a large number of polar metabolites. In general residues levels were higher in straw than in grain, hay or forage.

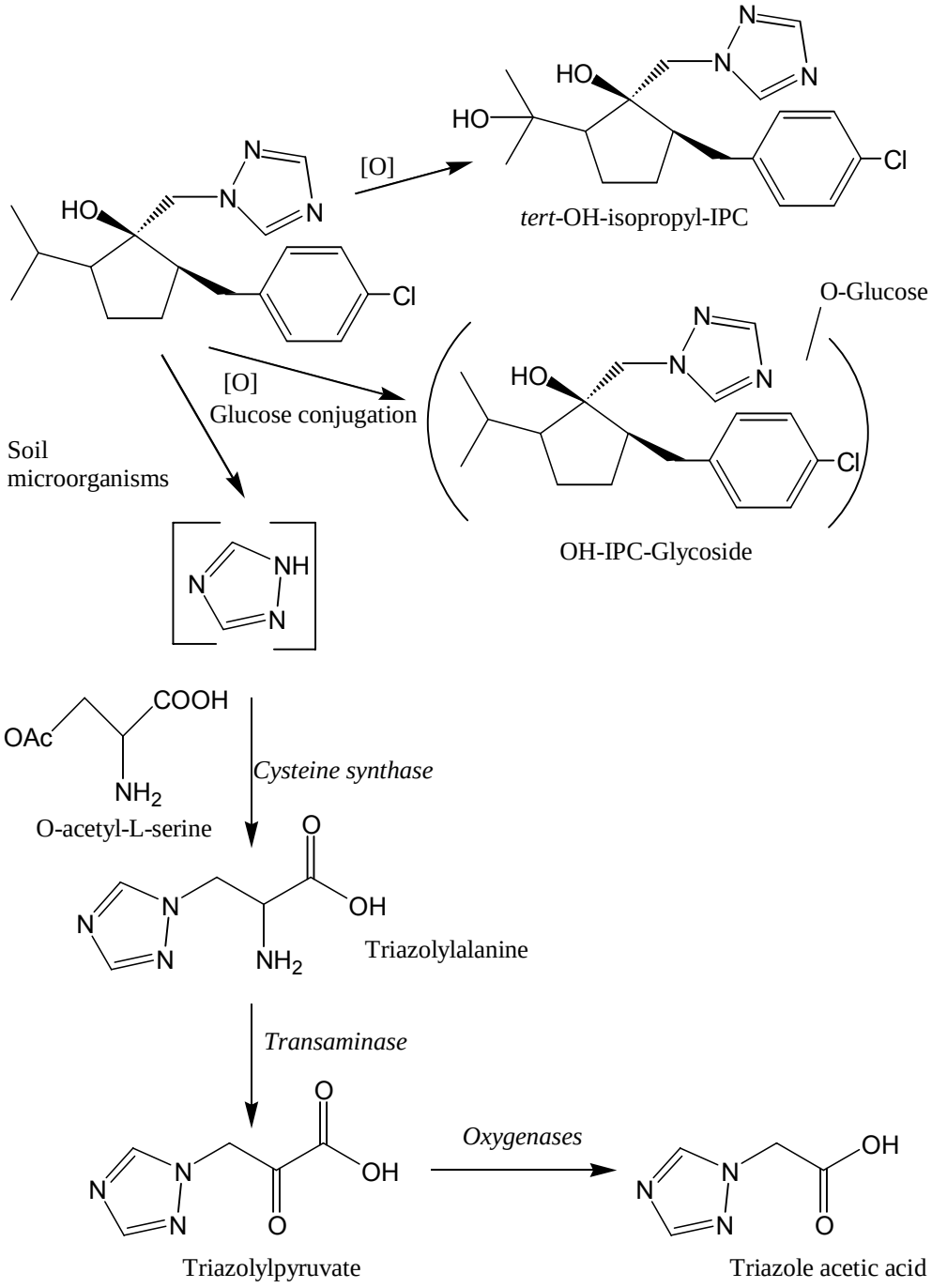
Radioactivity was sequentially extracted from homogenised wheat RACs using acetonitrile, acetonitrile: water (4:1, 1:1 and 1:4 v/v were used most often) and water when necessary and resulted in 80 - 100% TRR recovered in the extracts while very little radioactivity was found in the post-extraction solids. Due to very low levels of residues (less than 0.01 mg equiv./kg) in 1.25x-forage, 1.25x-hay and 1.25x and 12.5x-grain samples grown from seeds treated with [^{14}C-benzyl methylene]-ipconazole, solvent extraction of radioactivity in these RACs was not done.

The radioactivity in the extracts of forage, hay and straw obtained from [^{14}C-triazolyl]-ipconazole treated seeds was pre-purified by solid phase extraction (SPE) and separated into SPE aqueous and SPE acetonitrile fractions. The SPE acetonitrile fractions were analysed by reverse phase HPLC and the SPE aqueous fractions and the grain extracts were analysed by normal-phase HPLC.

HPLC radiochromatograms of the extracts of RACs grown from seeds treated at 1.25x and 12.5x nominal rates showed similar profiles, indicating that the application rate did not effect the nature of the metabolites. The distribution of radioactivity in the extracts was determined by HPLC fraction collection and LSC. Nearly quantitative HPLC column recovery was obtained in each case. The HPLC radiochromatogram of the grain extract and the radiochromatograms of the SPE aqueous fractions of forage, hay and straw obtained from [^{14}C-triazolyl]-ipconazole treated seeds showed similar profiles and three peaks (identified as triazolylpyruvate, triazole acetic acid and triazolylalanine by LC/MS and LC/MS/MS) were present in each radiochromatogram. The highest ppb value for any metabolite was triazolyl acetic acid (138 ppb, 42.6% TRR) in straw and the highest % TRR was for triazolylalanine (88.3 ppb, 56.6% TRR) in grain, both from wheat seeds treated with [^{14}C-triazolyl]-ipconazole at 26.2 g a.i./100 kg seed (13.1x). Ipconazole was only identified in the straw, hay and forage samples [maximum 8.49% of TRR, 3.91 ppb in forage from wheat seeds treated with [^{14}C-triazolyl]-ipconazole at 26.2 g a.i./100 kg seed (13.1x)].

The HPLC radiochromatograms of the SPE acetontrile fractions of forage, hay and straw grown from seeds treated with [^{14}C-triazolyl]-ipconazole were qualitatively identical to the extracts of forage, hay and straw derived from [benzylmethylene-^{14}C]-ipconazole treated seeds. Four peaks were present in each radiochromatogram which were identified as hydroxy-ipconazole-glycosides (2 overlapping peaks), *tert*-hydroxyisopropyl-ipconazole and unchanged ipconazole.

This study showed that when ipconazole is applied as a seed treatment it is extensively metabolised to a large number of more polar metabolites. The proposed metabolic pathway for the metabolism of ipconazole in wheat is shown below:



Proposed metabolic pathway for the metabolism of ipconazole in wheat

Winter wheat seeds were treated with [^{14}C-triazolyl]-ipconazole at nominal rates of 2.5 or 20g a.i./100 kg seed (*i.e.* 1.25x - 10x the proposed application rate). This study was carried out in order to confirm some results observed in a previous study in which the level of the ^{14}C in the grain was consistently twice that observed in the straw whereas typically in metabolism studies of cereal crops, levels of ^{14}C are much higher in straw than in grain. In addition triazolylpyruvate was identified as the major if not only ^{14}C metabolite in the wheat grain, contrary to the literature of 'azoles' in which triazolylalanine is the main plant metabolite.

Wheat forage was harvested at 188 days after planting (DAP) and wheat hay at 220 DAP. Immature grain was harvested at 241 and 254 DAP and mature grain and straw were harvested at 266 DAP. Total radioactive residues (TRR) in the forage, hay, straw and grain which were determined by combustion/ LSC are summarised below. The TRRs in winter wheat grain, straw, hay and forage grown from seed treated with [triazole-3, 5-^{14}C]-ipconazole were grain 3.9 ppb (1.25x), 23.7 ppb (10x); straw 2.9 ppb (1.25x), 31.5 ppb (10x); hay 2.4 ppb (1.25x), 22.0 ppb (10x) and forage 1.8 ppb (1.25x) and 15.4 ppb (10x).

Ground wheat grain from the 10x treatment level was extracted sequentially with water/MeOH (8:2) four times and about 99% TRR was recovered in the extracts. About 2% of the TRR was found in the post extraction solid (PES). The major metabolite in the extract of 10x wheat grain was isolated using solid phase extraction and reverse phase HPLC. The purified metabolite was identified as triazolylpyruvate. The level of triazolylpyruvate was about 17 ppb (about 70% TRR) in 10x wheat grain. Neither triazolylalanine nor triazole was seen in the mass spectra. Ipconazole was not observed at the limit of detection (0.5 ppb).

The biotransformation pathway, which was proposed for the formation of triazolylpyruvate is the same as that proposed for soybean grain, soybean hay and wheat grain (see above).

Metabolism studies in canola, sorghum and cotton were carried out in order to determine the levels and translocation of ipconazole when applied as a seed treatment at target rates of 1.5, 2.50 and 10.0 g a.i./100 kg seed (canola and sorghum) and 2.5, 5.0, 10.0 and 25.0 g a.i./100 kg seed (cotton). The results showed that no significant translocation of ipconazole occurred in canola, sorghum or cotton seed as well as cotton gin byproducts, when seed was treated with ipconazole. All treated canola, sorghum samples and cotton gin byproduct samples were below the LOQ set at 5 ppb (0.005 ppm). TRRs in mature harvest cotton seed samples were greater than the LOQ only when seeds were treated at 5.30, 10.76 and 26.45 g a.i./100 kg seed (*i.e.* at 2.65 - 13.23x the proposed application rate) [TTRs 7.96, 17.00 and 37.15 ppb respectively]. No further work was carried out to identify or further characterise the radioactivity in these commodities.

A metabolism study in corn was carried out to determine the magnitude of ipconazole residues after seed treatment. Total radioactive residues (TRRs) were below the LOQ (5 ppb) in forage, kernel plus cob with husk removed, and stover grown from seed treated with [triazole-3, 5-^{14}C]-ipconazole at treatment levels of 1.47 g a.i./100 kg and 2.31 g a.i./100 kg while at a treatment level of 10.61 g a.i./100 kg seed, TRRs were highest in seed (24.4 ppb). No further work was performed to identify or further characterise the radioactivity in any of the corn commodities.

A study was carried out to determine the residues in hay and nuts from peanut plants grown from seeds treated with [^{14}C-triazolyl]-ipconazole. The TRRs in hay and nuts ranged from 7.2 - 45.1 ppb and in nuts from 9.0 - 27.0 ppb at three levels of 1.41 g a.i./100 kg (0.71x), 2.67 g a.i./ 100 kg (1.34x) and 4.44 g a.i./100 kg (2.22x) respectively. No metabolic pathway was proposed and no further studies have been performed on the metabolism of ipconazole in peanuts.

Studies were also performed to determine the level of residues in carrots, cucumbers and lettuce. For all three crops no significant translocation of radioactivity occurred in carrots, cucumbers or leaf lettuce grown from seed treated with [triazole-3, 5-^{14}C]-ipconazole at nominal levels of 2.5 and 10.0 g a.i./100 kg. No further work was carried out to identify or further characterise the radioactivity in these commodities.

In general, the plant metabolism studies, which have been submitted show that when ipconazole is applied as a seed treatment it is extensively metabolised to a large number of polar metabolites. It is anticipated that levels of ipconazole and metabolites will be very low.

Animal Metabolism

Metabolism in rats has been studied after a single oral dose of [^{14}C-benzylmethylene]-ipconazole at 2 mg/kg bodyweight (bw) and 100 mg/kg bw and after 14 consecutive daily doses at 2 mg/kg bw. Metabolism in rats has also been studied after single oral doses of [^{14}C-triazole]-ipconazole at 2 mg/kg bw.

Following a single oral dose of [^{14}C-benzyl methylene]-ipconazole at 2 mg/kg bw and 100 mg/kg bw or [^{14}C triazole]-ipconazole at 2 mg/kg bw, >90% of the dose was excreted within 72 hours mainly *via* the faeces. Urinary excretion was slightly higher in females accounting for 18 - 25% dose at both dose levels compared with 13 - 15% dose for the males.

Excretion (collected for 24 hour periods after the first and seventh doses) and retention of radioactivity during 0 - 120 hours after the final dose following administration of 14 consecutive daily oral doses of [^{14}C-benzylmethylene]-ipconazole was investigated. Excretion was rapid with >90% of the dose excreted within 48 hours after the final dose (expressed as % dose administered on Day 14). There were no substantial differences in excretion patterns between single and repeat low level oral doses of [^{14}C-benzylmethylene]-ipconazole. In general urinary excretion was much lower than faecal excretion and lower in males than in females. Following sacrifice at 120 hours after the administration of the final dose, radioactivity remaining in the carcass accounted for 0.8 - 1.4% of the daily dose. Concentrations of radioactivity in tissues at sacrifice were relatively low with the highest concentrations in liver (0.404 mg equiv./kg in males and 0.872 mg equiv./kg in females). Accumulation of radioactivity in tissues following repeat doses was generally in the range 4-9x that found after single doses.

After administration of single low and high level oral doses of [^{14}C-benzylmethylene] ipconazole to bile duct-cannulated rats the extent of absorption was assessed as the sum of the mean values for bile, urine, liver and carcass. Absorption was higher at the low dose level than the high dose level and higher in male rats than female rats (2 mg/kg bw: Male 102 %, Female 91 %; 100 mg/kg bw: Male 91 %, Female 71 %). Bile was an important route of excretion. An increase in retention was observed for female rats as the high dose level, which was consistent with the patterns of excretion observed for intact animals.

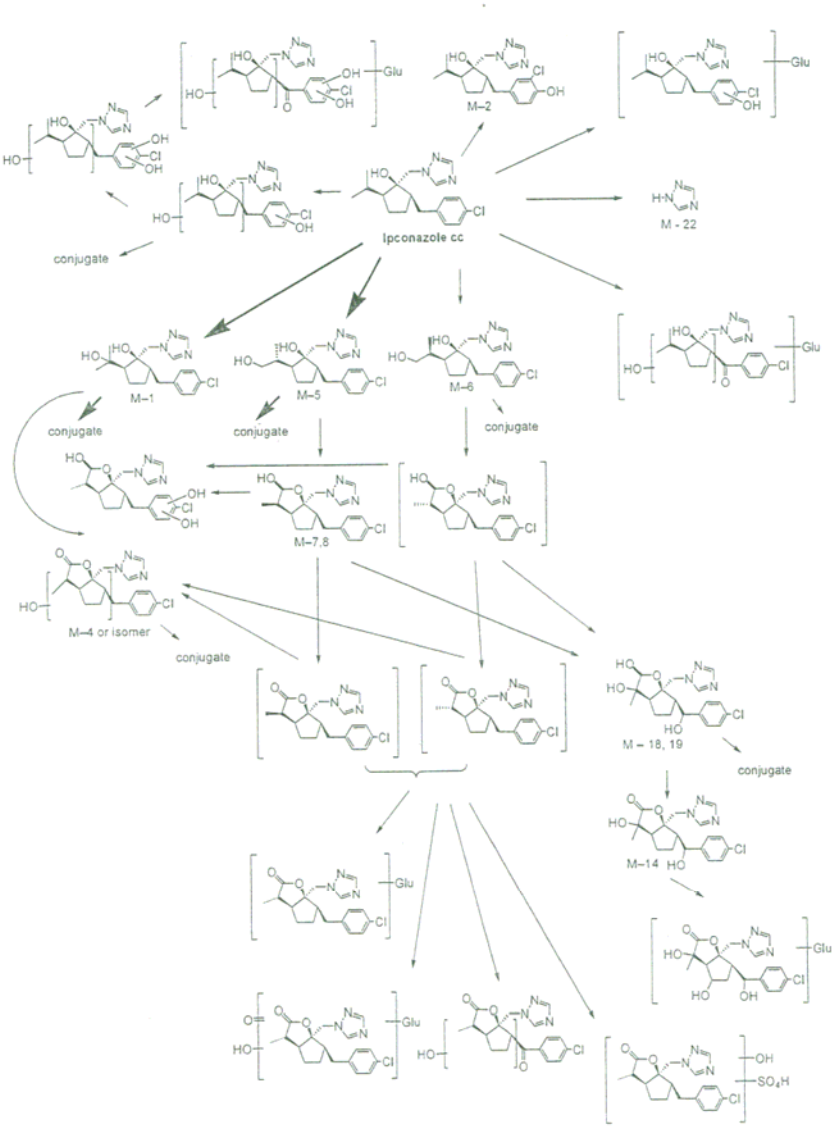
Radioactivity in tissues was observed to be primarily concentrated in the liver for both sexes and for both dose levels. Overall tissue concentration after single oral doses was low with only a small proportion of the dose retained in tissues at 120 hours (≤ 0.7% dose). Concentrations of radioactivity in tissues after repeated dosing were generally in the range of 4-9x higher than after single oral doses.

The proportions of radioactive components in urine and faeces after single oral doses of [^{14}C]-ipconazole at 2 mg/kg bw and 100 mg/kg bw to rats (Groups 2, 3 and 4) were determined. Metabolites were identified by

co-chromatography with authentic reference standards (reverse phase HPLC and/or normal phase TLC) or mass spectrometry either directly or following isolation by HPLC. Unchanged ipconazole represented a maximum of 2.2% of the dose (faeces). One major fraction was observed in faecal extracts accounting for a maximum of 16.4% of the dose, which was identified as M-1 and M-5, which were formed by hydroxylation of the isopropyl group.

All other components accounted for less than 10% of the dose. The major fraction in bile, B16 accounted for a maximum of 22.0% of the dose and was identified as a mixture of glucuronide conjugates of M-1 and M-5. A number of other major bile metabolites accounted for 5.0 - 11.0% of the dose and were all identified as glucuronide conjugates. Free triazole was identified as the main component in the urine of male rats administered with [^{14}C-triazole] ipconazole and accounted for 6.9% of the dose. All other urinary metabolites accounted for less than 5.0% of the dose.

The proposed biotransformation pathway for ipconazole in rats is shown below.



The proposed biotransformation pathway for ipconazole in rats

The metabolism of ipconazole has also been studied in goats. Two goats were administered five consecutive daily oral (capsule) doses of either [^{14}C-benzyl methylene]- or [^{14}C-triazole]-ipconazole at a nominal rate equivalent to 10 ppm in the diet (20 mg/goat/day). [^{14}C-benzylmethylene]-ipconazole was administered at an actual rate of 10.6 mg/kg in the diet and [^{14}C-triazole]-ipconazole was administered at an actual rate of 12.6 mg/kg in the diet.

Milk, urine, faeces, cage washes and plasma were all sampled throughout. At sacrifice (approximately 23 hours after the last dose) the liver, fat, muscle, kidney, bile and gastrointestinal tract and contents were sampled.

After five consecutive daily doses of [^{14}C-benzylmethylene]-ipconazole or [^{14}C-triazole]-ipconazole to a lactating goat, overall recoveries at 23 hours after the final dose were 93.0 and 93.4% of the cumulative dose, respectively. Of these amounts 30.9 - 41.1% (highest for [^{14}C-triazole]-ipconazole label administration) and 40.1 - 61.1% (highest for [^{14}C-benzylmethylene]-ipconazole application) were excreted in the urine and faeces, respectively.

Radioactivity in tissues and milk accounted for 0.5 - 1.0% of the dose (highest for [^{14}C-triazole]-ipconazole administration). TRRs in milk reached a plateau at 0.008 mg/kg ([^{14}C-benzyl methylene] radiolabel) and 0.017 - 0.018 mg/kg ([^{14}C-triazole] radiolabel) after approximately 3 days. Total radioactive residues (TRRs) in tissues taken at sacrifice at 23 hours after the final dose were determined. TRRs in edible tissues were highest in liver (0.367 - 0.658 mg/kg) and kidney (0.096 - 0.157 mg/kg). Residues in muscle and fat were 0.004 - 0.014 mg/kg. Residues observed for both radiolabels were slightly higher in muscle (foreleg and rump) than in fat (omental, peritoneal and subcutaneous), although in both cases quite low, suggesting there may not be the potential for bioaccumulation in the fat.

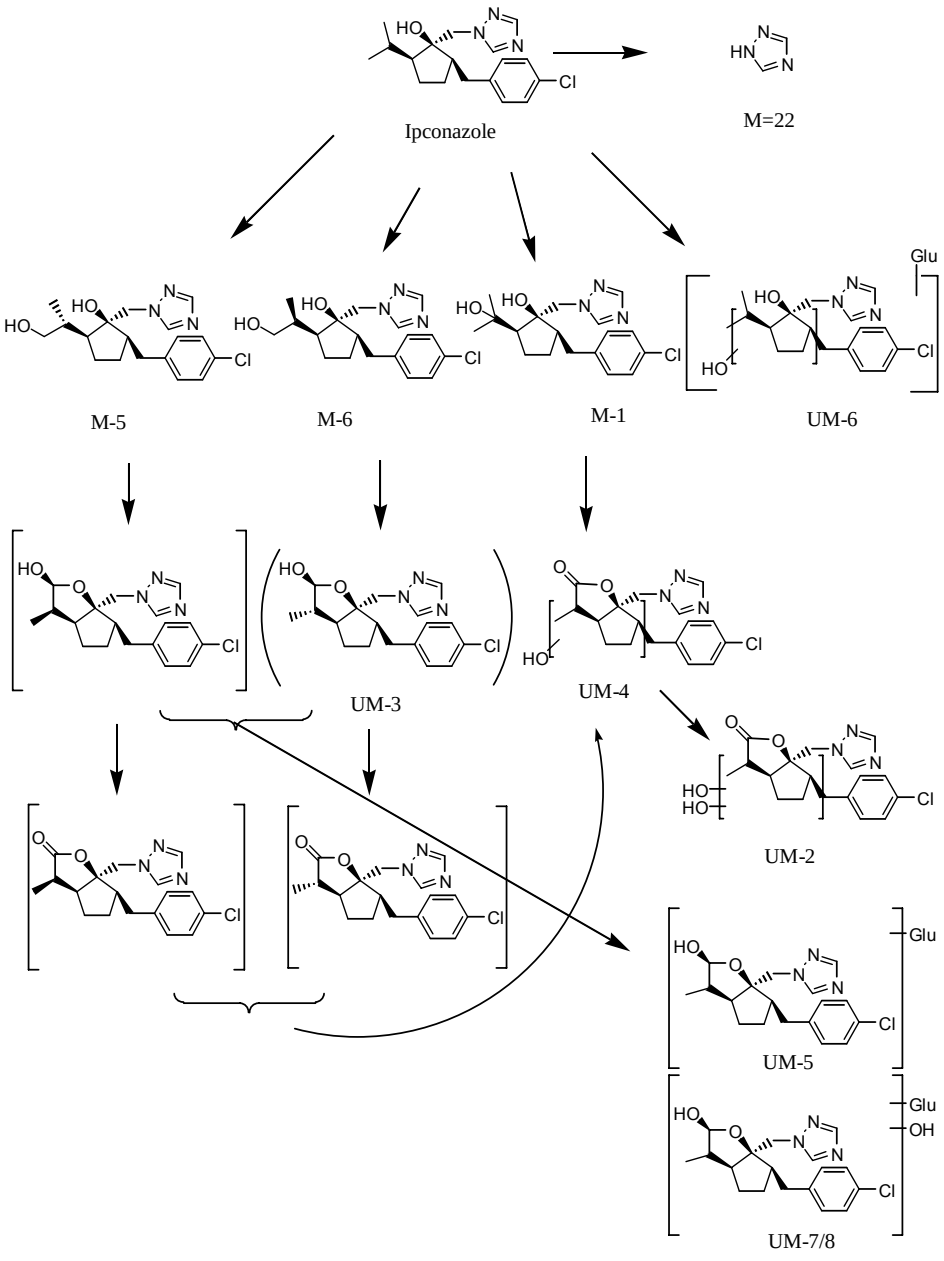
Based on the above results edible tissues containing significant residues (> 0.01 ppm) were investigated further to characterise the nature of the radioactive residue. Characterisation was undertaken on liver (both radiolabels), kidney (both radiolabels), milk (triazole radiolabel) and muscle (triazole radiolabel).

The majority of the radioactivity was extracted using various solvents (acetonitrile, methanol, ethyl acetate) / water mixtures. In the liver, further treatment with protease (both radiolabels) and acid/base ([^{14}C-benzylmethylene]) was conducted to extract the residue. The neutral solvents were analysed by reverse phase HPLC and normal phase TLC and components were identified by co-chromatography with reference substances or by mass spectroscopy. Unmetabolised ipconazole was detected in liver (0.040 - 0.056 mg/kg, 8.5 - 10.9% TRR) and kidney extracts (0.005 - 0.006 mg/kg, 3.4 - 6.7% TRR). Identified metabolites found were UM-4 in liver (0.130 mg/kg, 19.7% TRR; triazole radiolabel only) and hydroxylated metabolites KNF-317-M-5 and KNF-317-M-6 in liver and kidney (0.001 - 0.025 mg/kg, 1.1 - 6.8% TRR). These three metabolites were also observed in the rat metabolism study. All other components in liver and kidney accounted for <0.05 mg/kg.

Metabolites in muscle and milk extracts were identified using two different TLC phases, silica and cellulose. The total radioactive residues and identified metabolites in extracts of muscle (foreleg and rump) and pooled milk after administration of [^{14}C-triazole]-ipconazole were determined. In extracts of muscle and pooled milk from the triazole radiolabel, the major metabolite detected was KNF-317-M-22 (free triazole) accounting for 0.004 - 0.007 mg/kg (28.6 - 42.7% TRR). In urine and faecal extracts, metabolites were UM-2 (0.2 - 2.7%

dose), UM-3 (0.1-0.3% dose), UM-5 (2.8% dose), UM-6 (3.2% dose), UM-7/UM-8 (3.4% dose), KNF-317-M-5 (1.6 - 7.4% dose) and KF-317-M-6 (2.5 - 13.7% dose). Parent ipconazole was present at 0.3 - 2.5% dose.

Based on the analysis in tissues, urine and faeces, ipconazole was extensively metabolised in the goat through a number of pathways including glucuronidation (urine and faeces) and hydroxylation (liver, kidney, urine and faeces). In milk and muscle, free triazole was the major residue although never exceeding 10 ppb even at an exaggerated dose. The feeding level of approximately 10 ppm is significantly higher than the expected residues intake from the feeding of harvested crops. The proposed biotransformation pathway of ipconazole in goats is depicted below.



The proposed biotransformation pathway for ipconazole in goats

4.3 Analytical methods

Commodities of plant origin

In the Australian trials, samples of cereal grain, straw and forage were hydrated with water before ipconazole residues were extracted by homogenising the sample with acetonitrile/water (50:50). After centrifuging the extract the supernatant was filtered. The extraction was repeated and the extracts were combined.

Ipconazole and triazolylalanine: An aliquot of the extract was acidified with HCl and cleaned-up on a SCX disposable SPE cartridge. The eluate from the SPE column that contains the ipconazole and triazloylalanine was evaporated to dryness. The extract was reconstituted in a methanol/water mixture. An aliquot of the extract was reacted with borax and 9-fluoromethyl chloroformate (FMOC) and residues of ipconazole and the FMOC derivative of triazolylalanine were then determined by LC/MS/MS analysis.

Triazolylacetic acid: An aliquot of the extract was basified with ammonia/water and cleaned-up on a SCX disposable SPE cartridge. The eluate from the SPE column that contains the triazloylacetic acid was evaporated to dryness. The extract was reconstituted in 0.1% formic acid in water (1:2). Residues of triazolylacetic acid were then determined by LC/MS/MS analysis.

The LOQ for ipconazole, triazolylalanine and triazolylacetic acid in forage and grain was 0.01 mg/kg. The LOQ for straw for ipconazole, triazolylalanine and triazolylacetic acid was 0.05 mg/kg.

Commodities of animal origin

Tissue, milk and chicken egg samples were analysed for residues of ipconazole using high performance liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). The method of analysis comprised 5 stages: extraction into acetonitrile: water followed by acetonitrile, clean-up by solid phase extraction (SPE) cartridge, evaporation of elution solution, re-suspension of residue in appropriate final solvent and analysis by LC-MS/MS in the SRM (selected reaction monitoring mode). The LOQ was determined to be 0.01 mg/kg for ipconazole in bovine liver, kidney, muscle, fat and chicken eggs and milk.

Stability of pesticide residues in stored matrices and stored analytical solutions

No stability data for pesticides in stored matrices or analytical solutions were provided as samples were stored for less than 6 months.

4.4 Residue Definition

Metabolism studies which were conducted on wheat grain and soybean grain and hay showed that the major pathways for the breakdown of ipconazole were formation of triazolylpyruvate in several steps. In another study conducted on spring wheat, the major metabolites identified were triazolylpyruvate, triazole acetic acid and triazolylalanine, the formation of which is thought to be mediated by soil microorganisms.

Residues of the three metabolites observed in grain from spring wheat treated with [^{14}C-triazolyl]-ipconazole, were highest for triazolylalanine (0.007 mg/kg after conversion to residues expected at 1x the proposed application rate). Residues observed in straw from spring wheat treated with [^{14}C-triazolyl]-ipconazole were

highest for triazolyl acetic acid (0.010 mg/kg after conversion to residues expected at 1x the proposed application rate). Triazolyl acetic acid and triazolylalanine are common metabolites of triazoles in plants.

In another study winter wheat seeds were treated with [^{14}C-triazolyl]-ipconazole at 1.25 and 10x the proposed application rate. The major metabolite in the extract of 10x wheat grain was identified as triazolylpyruvate (about 17 ppb or approximately 0.0017 mg/kg when calculated as expected residues from application at the proposed rate). Neither triazolyl acetic acid nor triazole was observed in the mass spectra. Ipconazole was not observed at the limit of detection.

The metabolism of ipconazole has been studied in rats which showed that following a single oral dose of [^{14}C-benzyl methylene]-ipconazole at 2 mg/kg and 100 mg/kg or [^{14}C triazole]-ipconazole at 2mg/kg, >90% of the dose was excreted within 72 hours mainly *via* the faeces. Urinary excretion was slightly higher in females accounting for 18 – 25% dose at both dose levels compared with 13-15% dose for the males.

A goat metabolism study showed that 23 hours after the last of five daily doses of [^{14}C-benzyl methylene]-ipconazole (10.6 ppm) or [^{14}C- triazole]-ipconazole (12.6 ppm), 30.9 - 41.1% and 40.1 - 61.1% had been excreted in the urine and faeces respectively. Parent ipconazole was present at 0.8 - 2.5% of dose in urine and faecal extracts. TRRs in edible tissues were highest in liver and kidney. Unmetabolised ipconazole was detected in both liver (0.040 - 0.056 ppm, 8.5 - 10.9% TRR) and kidney extracts (0.005 - 0.006 ppm, 3.4 - 6.7% TRR). Identified metabolites found were UM-4 in liver (0.130 ppm, 19.7% TRR; triazole radiolabel only) and hydroxylated metabolites KNF-317-M-5 and KNF-317-M-6 in liver and kidney (0.001 - 0.025 ppm, 1.1 - 6.8% TRR). In extracts of muscle and pooled milk from the triazole radiolabel, the major metabolite detected was free triazole.

The K_{ow} log P value (4.21) is greater than the general threshold designating a chemical as fat soluble (log P = 3). The goat metabolism study however indicated that when lactating goats were administered either ^{14}C-benzyl methylene- or ^{14}C-triazole-ipconazole at 10 ppm per day for 5 consecutive days, TRRs observed in muscle (foreleg and rump) and fat (omental, peritoneal and subcutaneous) were comparable, suggesting there may not be potential for bioaccumulation in the fat.

Relevant analytical methods are available which have been validated for the parent ipconazole and the metabolites triazolylalanine and triazolyl acetic acid in cereal forage, grain and straw and for ipconazole in bovine liver, kidney, muscle, fat, milk and chicken eggs.

The Office of Chemical Safety of the Department of Health and Ageing has undertaken an assessment of the active constituent ipconazole. There were no metabolites identified in the animal metabolism studies as being toxicologically significant. An ADI has been established for ipconazole (0.015 mg/kg bw/day). No ARfD was established as ipconazole was considered unlikely to present an acute hazard to humans.

The residue definition for ipconazole in the U.S.A. and the European Union is “ipconazole”.

Field trials submitted with this application in which ipconazole was applied to wheat, barley and oats at 1x and 2x the proposed application rate, suggest that no quantifiable residues of ipconazole and the metabolites triazolylalanine and triazolyl acetic acid will be present in cereal grain and straw at harvest and in forage after a grazing WHP of 6 weeks. Furthermore triazolylalanine and triazolylacetic acid are common metabolites observed in plant metabolism studies of other triazole fungicides.

It is proposed that the residue definition be:

Ipconazole “Ipconazole”

4.5 Residue Trials

Australian GLP-compliant residue trials were conducted in the field in 2006 at two test sites: Redbanks in South Australia (Site 1) and Narrabri in New South Wales (Site 2).

Seed was sown at a rate of 100 kg/ha (Site 1) and 55 kg/ha (Site 2) following treatment with the product at 100 mL/ 100 kg seed (2 g ipconazole; (1x)) or 200 mL/ 100 kg seed (4 g ipconazole; (2x)).

Test samples of forage (wheat, barley and oats) were collected at 28/29, 42/43, 56, 84 and 112 days after treatment and samples of grain and straw (wheat, barley and oats) were collected at normal harvest. For each sample primary and reserve samples of forage, grain and straw were taken. Samples were stored frozen. Primary samples were dispatched under frozen conditions to the analytical laboratory for the residue analysis.

Grain Data

No residues of ipconazole were observed at harvest in any grain sample following treatment at 2 or 4 g ipconazole / 100 kg seed (1x or 2x).

Metabolism studies conducted on wheat, as discussed previously, showed that no ipconazole was observed in grain from spring wheat treated with [^{14}C-triazolyl]-ipconazole, even at 12.5x. In another study winter wheat seeds were treated with [^{14}C-triazolyl]-ipconazole at 1.25 and 10x the proposed application rate. Ipconazole was not observed at the limit of detection (0.5 ppb).

On the basis of these data an MRL of *0.01 mg/kg is recommended for ipconazole in cereal grain.

Fodder/ Straw Data

No residues of ipconazole were observed at harvest in any sample following treatment at 2 or 4 g ipconazole / 100 kg seed (1x or 2x).

Residues of ipconazole in straw and hay from spring wheat treated with [^{14}C-triazolyl]-ipconazole or [^{14}C-benzylmethylene]-ipconazole were <0.001 mg/kg when corrected for application rate. Ipconazole was not observed at the limit of detection (0.5 ppb) in straw and hay samples from winter wheat seeds which had been treated with [^{14}C-triazolyl]-ipconazole at 1.25 and 10x the proposed application rate.

On the basis of these data an MRL of *0.05 mg/kg is recommended for ipconazole in cereal fodder/straw.

Forage Data

No residues of ipconazole were detected after a withholding period of 6 weeks in any sample following treatment at 2 or 4 g ipconazole / 100 kg seed (1x or 2x).

Ipconazole was not observed at the limit of detection (0.5 ppb) in forage samples from winter wheat seeds which had been treated with [^{14}C-triazolyl]-ipconazole at 1.25 and 10x the proposed application rate.

On the basis of these data, an MRL of *0.01 mg/kg is recommended for ipconazole in cereal forage.

Processing

The applicant did not provide any processing data relevant to potential residues of ipconazole in processed wheat portions, *eg*: wheat bran. As residues were below the limit of quantitation of ipconazole in cereal grain, processing studies were not required.

4.6 Animal Commodity MRLs

Potential animal feed commodities derived from crops treated with ipconazole include cereal grain and forage and fodder, which are all significant animal feeds. Cattle and other grazing livestock could consume forage from failed crops or straw and grain from harvested crop, which could contain residues of ipconazole. In addition poultry could be exposed to ipconazole in the diet from the consumption of grain from treated crops or through the consumption of processed grain fractions at up to 20% of the dietary intake.

There are not likely to be quantifiable residues in grain and straw at harvest and forage after a 6 week withholding period and consumption of these commodities is unlikely to result in detectable residues in animal tissues, milk and eggs. The establishment of animal commodity MRLs at the analytical limits of quantification is appropriate.

A validated analytical method with an LOQ of 0.01 mg/kg has been provided for the detection and quantitation of residues in animal commodities. The following animal commodity MRLs for ipconazole are proposed:

MO	0105	Edible offal (mammalian)	*0.01
PE	0112	Eggs	*0.01
MM	0095	Meat [mammalian]	*0.01
ML	0106	Milks	*0.01
PO	0111	Poultry, edible offal of	*0.01
PM	0110	Poultry meat	*0.01

4.7 Estimated Dietary Intake

The chronic dietary exposure to ipconazole is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and the mean daily dietary consumption data derived from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with WHO Guidelines[2] and is a conservative estimate of dietary exposure to chemical residues in food. Chronic dietary exposure is also estimated using the DIAMOND model of Food Standards Australia New Zealand for new chemicals.

The NEDI for ipconazole is equivalent to 1 % of the ADI. It is concluded that the chronic dietary exposure of ipconazole is acceptable and residues in food will not pose an undue risk to the safety of people. The DIAMOND model also estimated the chronic dietary exposure of ipconazole as 1% of the ADI for the general population.

The acute dietary exposure is estimated by the National Estimated Short Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR with 97.5th percentile food consumption data derived from the 1995 National Nutrition Survey of Australia. NESTI calculations are conservative estimates of acute exposure (24 hour period) to chemical residues in food.

An ARfD has not been established for ipconazole as it is not likely to present an acute hazard to humans. Hence the NESTI is not required.

4.8 Bioaccumulation Potential

Ipconazole has a K_{ow} log P = 4.21 (25°C). The K_{ow} log P value is greater than the general threshold designating a chemical as fat soluble (log P = 3). The goat metabolism study indicated that when lactating goats were administered either ^{14}C-benzyl methylene- or ^{14}C-triazole-ipconazole at 10 ppm per day for 5 consecutive days, TRRs observed in muscle (foreleg and rump) were slightly higher than in fat (omental, peritoneal and subcutaneous) although in both cases quite low, suggesting there may not be potential for bioaccumulation in the fat. It is not possible to be definitive about the potential for bioaccumulation in the fat.

In the absence of a livestock feeding study and/or a longer metabolism study.

4.9 Spray Drift

Spray drift is not considered for application as a seed treatment.

[2] Guidelines for predicting dietary intake of pesticide residues, WHO, 1997.

4.10 Recommendations

The following MRLs will be established:

MRL Standard - Table 1 Amendments

COMPOUND		FOOD	MRL (mg/kg)
IPCONAZOLE			
ADD:			
GC	0080	Cereal grains	*0.01
MO	0105	Edible offal (Mammalian)	*0.01
PE	0112	Eggs	*0.01
MM	0095	Meat [mammalian]	*0.01
ML	0106	Milks	*0.01
PO	0111	Poultry, edible offal of	*0.01
PM	0110	Poultry meat	*0.01

MRL Standard - Table 3 Amendments

COMPOUND	RESIDUE
ADD:	
Ipconazole	Ipconazole

MRL Standard - Table 4 Amendments

COMPOUND	ANIMAL FEED COMMODITY	MRL (mg/kg)
IPCONAZOLE		
ADD:		
AS 0081	Straw and fodder (dry) of cereal grains	*0.05
AF 0080	Forage of cereal grains	*0.01

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

Harvest: No withholding period required when used as directed.

Grazing: DO NOT graze or cut for stock food for 6 weeks after sowing.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Commodities Exported

Export commodities affected by the use of Rancona C Seed Treatment are wheat, barley and oat grain and all livestock commodities derived from animals fed on wheat, barley and oat grain, forage and straw. In addition, oaten hay is exported to a number of countries with the majority going to Japan's dairy industry. Wheat, barley and oats and all livestock species are considered to be major export commodities. Residues in these commodities have the potential to unduly prejudice trade.

Destination and Value of Exports

In 2007/2008 Australia exported 7,421 kt of wheat and flour valued at $2,997 million.[3] The major export markets are summarised below.

Export Markets for Australian Wheat and Flour in 2007/2008

EXPORT MARKET	QUANTITY (KT)
Indonesia	1621
Japan	878
Korea, Rep. of	694
Malaysia	623
Yemen	408
Egypt	284
New Zealand	275
Thailand	255
Kuwait	233
Iraq	198
Papua New Guinea	153

[3] Australian Commodity Statistics 2008, ABARE

In 2007/2008 Australia exported 4,050 kt of barley (including grains and the grain equivalent of malt exported), valued at $1,496 million. In 2007/2008 Australia exported 115 kt of oats, valued at $37 million.[3]

Oat forage is harvested as an animal feed. No detailed information on the export of oaten hay is available. However, in broad terms, the export market for Australian hay has grown from 423,000 tonnes in 2001 to approximately 700,000 tonnes in 2005/2006 (worth about $100 million), with the majority going to Japan's dairy industry[4, 5, 6].

Animal commodities derived from livestock fed on wheat, barley and oats grain, forage and straw are considered to be major export commodities. No animal commodity MRLs/ tolerances for ipconazole have been established by major trading partners, however residues are not expected in those commodities.

Comparison of Australian MRLs with Codex and Overseas MRLs

The following relevant residue tolerances for plant and animal commodities have been established.

COMMODITY[A]	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF IPCONAZOLE (MG/KG)		
	AUSTRALIA	EU	USA
PLANT COMMODITIES			
Residue Definition	Ipconazole	Ipconazole	Ipconazole
Barley		*0.01	
Oats		*0.01	
Wheat		*0.01 (Spelt triticale)	
Cereal straw and fodder, dry	*0.05		
Cereal forage (green)	*0.01		
Other cereal grains	*0.01 (Cereal grains)	*0.01 (Buckwheat)	0.01 (Grain, cereal group 15, except rice)

[4] GRDC - Media Release - Hay making a viable alternative as the sun keeps on shining - Elmore GRDC Update. http://www.grdc.com.au/director/events/mediareleases.cfm?item_id=4828B9A5C81CD6B3E6B2620345E2AF16&pageNumber=12

[5] http://www.agric.wa.gov.au/objtwr/imported_assets/content/fcp/cer/export_hay_quality_fn.pdf

[6] http://www.agric.wa.gov.au/PC_92043.html?s=1001#o

			0.01 (Grain, cereal, forage, fodder and straw, Group 16 except rice)
ANIMAL COMMODITIES			
Residue Definition	Ipconazole		
Edible offal (mammalian)	*0.01		
Other poultry edible offal	*0.01 (Poultry, edible offal of)		
Meat [mammalian]	*0.01		
Other poultry muscle	*0.01(Poultry meat)		
Milks	*0.01		
Eggs	*0.01		

MRLs have not been established for ipconazole by Codex, or in Japan (MAFF or MHLW), Taiwan or Korea and are not known to be established in other markets for cereal grain.

Potential Risk to Trade

Export of treated produce containing finite (measurable) residues of ipconazole 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.

Residues of ipconazole in cereal grains through the use of ipconazole in Rancona C Seed Treatment will be <LOQ. The export of cereal grains should not unduly prejudice trade between Australia and places outside Australia.

Forage and fodder of treated crops, as well as grain, may be used as livestock feed and oaten hay may be exported. Residues of ipconazole in all of these commodities are expected to be below the LOQ, thus it is considered unlikely that the proposed use of ipconazole on oats would unduly prejudice trade.

Ipconazole residues in animal commodities following consumption of feeds produced from treated grain are expected to be below the LOQ. Hence the use of ipconazole in Rancona C Seed Treatment should not unduly prejudice trade in animal commodities between Australia and places outside Australia.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Health hazards

Ipconazole has low acute oral, dermal and inhalation toxicity. It is moderately irritant to the eyes, but neither a skin irritant, nor a skin sensitiser.

Ipconazole is not listed in Safe Work Australia's (SWA) Hazardous Substances Information System (HSIS) Database (2009). With the available toxicology information, ipconazole is classified as a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004), with the following risk phrases:

Xn R20 Harmful by inhalation

R22 Harmful if swallowed

The following cut-off concentrations apply for ipconazole:

Conc. ³ 25% Xn: R20/22

Cypermethrin (CAS: 52315-07-8), cis/trans 40/60, is listed on Safe Work Australia's (SWA) Hazardous Substances Information System (HSIS) Database (2009) with the following risk phrases:

Xn R20/22 Harmful by inhalation and if swallowed

R37 Irritating to respiratory system

The following cut-off concentrations apply for cypermethrin:

Conc. ³ 25% Xn: R20/22; R37

20% ≤ Conc. < 25% Xi: R37

Rancona C Seed Treatment has low acute oral, dermal and inhalation toxicity. It is slight irritant to the eyes, but neither a skin irritant nor a skin sensitiser. It is not listed in the HSIS Database (2009). With the available toxicology information it is not classified as a hazardous substance according to NOHSC Approved Criteria for Classifying Hazardous Substances (2004).

Formulation, packaging, transport, storage and retailing

Ipconazole and Rancona C Seed Treatment will be manufactured and formulated overseas and imported into Australia. The product will be packaged in 10L Rheem DG 737 Jerrycans, high molecule weight high density polyethylene, 20L Rheem DG Compact Cubes high molecule weight high density polyethylene, 100L Nylex Rotomould E1422 Microbulk, crosslinked polyethylene construction, 200L Rheem DG Mauser Drums, Ultra high molecular weight high density polyethylene. Transport workers and store persons will handle the packaged products and could only become contaminated if the packaging was breached.

Use pattern

Rancona C Seed Treatment is a seed treatment to be used on wheat, barley and oats for the control of smuts and bunt. It also contains cypermethrin for stored grain insect control.

Rancona C Seed Treatment is intended to be used at 1 L/tonne of seed for on-farm application, in seed sheds and in mobile seed graders and treaters.

Commercial seed treating facilities use batch treaters that are fully enclosed systems. The treatment equipment draws a calibrated amount of the product through peristaltic pump attached to the containers, dilutes it with water and applies it to the seed in the batch treater. During on-farm seed treatment, the farmer mixes the product with water to prepare the required amount of slurry and adds it to the seed being rotated in the mixer.

Exposure during use

Professional seed treaters (seed treating sheds or mobile seed treaters) and farmers will be the main users of the product. Workers may be exposed to the product when opening containers, preparing and loading slurry and cleaning up spills and equipment. The main route of exposure to the product will be by dermal contact.

There are no worker exposure studies on ipconazole or the product Rancona C Seed Treatment available for assessment. In the absence of worker exposure data, the OCSEH used the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate the worker exposure during mixing/loading and application based on the maximum product use rate according to the Australian use pattern. The estimation in conjunction with toxicology data demonstrated that workers should wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow-length chemical resistant gloves, when using the product, or handling treated seed.

Exposure during re-handling

Exposure to product residues is expected when workers re-handling the treated seeds. Based on the exposure assessment for workers; the following re-handling statement is proposed: “When using the product or handling treated seed, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. Clothing must be laundered after each day's use.”

Recommendations for safe use

Users should follow the First Aid Instructions, Warning Statements, Safety Directions and Re-handing statement on the product label.

Conclusion

The registration of the product Rancona C Seed Treatment, containing ipconazole 20 g/L and cypermethrin at 4 g/L, for the treatment of wheat, barley and oats to control smuts and bunt, and also for insect control of stored grain, is supported.

Rancona C Seed Treatment 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 on the product MSDS.

7 ENVIRONMENTAL ASSESSMENT

Chemtura Australia Pty Ltd is seeking registration from the Australian Pesticides and Veterinary Medicines Authority (APVMA) of a new product, Rancona C Seed Treatment, an aqueous micro emulsion formulation containing a new active constituent, ipconazole (20 g/L) and cypermethrin (4 g/L). The product is intended for use as a seed treatment for wheat, barley and oat seeds to control various smuts, bunt, and stored grain insect control.

7.1 Environmental fate summary

Ipconazole is hydrolytically stable in aqueous solution, with the half-life being considered to be greater than one year. Ipconazole is also not considered to be readily biodegradable in water. However, ipconazole degraded upon irradiation in water, with the half-life calculated to be 32.1 days at pH 5 and 25 ± 1˚C. Given the slow metabolism, photolysis may be a significant degradation pathway for ipconazole.

Ipconazole is stable in soil under all conditions in the laboratory. It does not readily undergo photolysis on soil. The overall DT50 for the photodegradation on soil was determined to be 241 days at latitude 40˚N in summer sunlight. Very little degradation of ipconazole took place in either anaerobic or aerobic soils. The DT50 for ipconazole in five aerobic soils was calculated to be 170-593 days under normal conditions depending on the type of soil. The DT50 for ipconazole in the anaerobic soil was calculated to be 779 days.

Ipconazole has a low solubility in water and a moderately high POW. Studies show that ipconazole readily adsorbs to soil, with a Koc range of 3500 to 5696 mL/g for adsorption. The aged soil column leaching study indicates that the chemical is not mobile in soil. However, ipconazole dissipates relatively rapidly in the field under normalised moisture and temperature conditions. Normalized field soil kinetics parameters were assessed for the German and Italian trial sites by considering SFO kinetic, and the DT50s were determined to be 35 days to 67 days. Another field study conducted in Spain showed a tested DT50 of 757 days (normalized data to reference conditions not available), which may be more representative to the drier climate conditions in Australia.

A few metabolites of ipconazole were identified, with KNF-317-M-1 and KNF-317-M-11 being the main two. There was no appreciable change in the ratio between the cc and ct isomers of ipconazole in all the tests conducted.

The measured BCF value range of 95-321 in fish indicates a moderate potential for bioaccumulation of the chemical in aquatic organisms. However, rapid depuration occurred (DT50 < 1 day) once exposure ceased.

7.2 Environmental toxicity summary

Ipconazole is slightly toxic to northern bobwhite quail with an acute LD50 of 962 mg/kg. However, it is practically non-toxic to birds on dietary basis with an LC50 of > 5620 ppm to both bobwhite quail and mallard duck. Studies on reproduction yielded NOEC values of 50 ppm for the bobwhite quail and 200 ppm (the highest test concentration) for the mallard duck. The LD50 value of 468 mg/kg bw for a female mouse indicates that ipconazole may be moderately toxic to mammals on an acute oral basis.

Ipconazole is considered moderately toxic to fish and daphnids with tested 96-hour LC50s of 1.5 and 1.3 mg/L for rainbow trout and bluegill sunfish, respectively, a 48-hour EC50 of 1.7 mg/L for daphnia. It is considered to be moderately toxic to algae based on the 96-hour ErC50 of > 2.2 mg/L. The study on the early-life stage exposure of ipconazole to newly fertilised fathead minnow showed an LC50 of > 2.9 mg/L for length and an LC50 of 1.63 mg/L for weight. The NOEC based on mortality was determined to be 0.18 mg/L, indicating ipconazole is slightly toxic to fish on a chronic basis. The study on reproductive/chronic exposure of Daphnia magna gave a 21 d NOEC of 0.0109 mg/L based on the parental growth, suggesting that ipconazole is moderately toxic to daphnids on a chronic basis. The 28 d NOEC of 3.5 mg/L to Chironomus riparius indicates that ipconazole is very slightly toxic to sediment-dwelling organisms. The 3 h EC50 of > 100 mg/L to active sludge micro-organisms indicates that ipconazole is practically non-toxic to sludge micro-organisms.

Ipconazole is very slightly toxic to worker bees based on the estimated 48-hour LD50 value of > 100 µg/bee on both a contact and an acute oral basis. It is slightly toxic to earthworms with an acute 14 day LC50 value of 597 ppm. However, ipconazole was not chronically toxic to earthworms at a rate of 586 g ac/ha. Based on the test results of nitrogen and carbon transformation in soil, ipconazole is not considered to have a long-term effect on soil micro-organisms.

7.3 Risk Assessment

Rancona C Seed Treatment is a micro emulsion formulation containing the active constituents ipconazole (20 g/L) and cypermethrin (4 g/L). The proposed application is for seed treatment of wheat, barley and oat seeds for smuts, bunt, and stored grain insect control. The proposed application rate of the product is 100 mL/100 kg seed as indicated in the draft label.

Given the use pattern of the product for seed treatment, the risk of exposure to both active constituents was assessed for both above ground terrestrial organisms and aquatic life. For the aquatic risk assessment, runoff modelling was used as a very conservative consideration for the worst case scenario. No unacceptable risk to the environment was predicted from the modelling results. Therefore, the proposed application of the product Rancona C Seed Treatment is not considered to pose a potential risk to the aquatic compartment. The assessment for the leaching of the active constituents to groundwater was conducted and it was not considered an issue in Australia.

Risk for the exposure of the product to terrestrial organisms, including mammals, birds, bees, micro-organisms and earthworms, was assessed based on the available endpoints and proposed application rate of the product. The assessment shows that the risk from the proposed use of the product will be acceptable to terrestrial organisms. The potential risk on non-target plants from the application of the product is considered acceptable even though no data was available, based on the low exposure resulting from the proposed use pattern of the product. No data is available for the toxicity of cypermethrin to soil micro-organisms. However, given the low proposed application rate of cypermethrin for the proposed use of the product and the relatively rapid dissipation in soil, the risk to the organisms is considered acceptable.

8 EFFICACY AND SAFETY ASSESSMENT

The applicant, Chemtura Australia Pty Ltd, seeks for registration of the proposed new product, RANCONA C SEED TREATMENT, for the control of various smut diseases in wheat, barley and oats. The product is a micro-emulsion containing 20 g/L ipconazole (fungicide) + 4 g/L cypermethrin (insecticide).

8.1 Proposed use pattern

The intended use of RANCONA C SEED TREATMENT is for the control of various smut diseases in wheat, barley and oats. The inclusion of cypermethrin in the product is to protect the cereal seed from insects during storage. The product will be used as seed dressing prior to sowing. Use is proposed all Australian states and territories.

8.2 Summary of Evaluation of Efficacy and Crop safety

RANCONA C SEED TREATMENT is a micro-emulsion formulation containing 20 g/L ipconazole + 4 g/L cypermethrin (insecticide). The intended use of RANCONA C SEED TREATMENT is for the control of various smut diseases in wheat, barley and oats. The inclusion of cypermethrin in the product is to protect the seed from insects during storage.

An appropriate evaluation program comprising 32 field trials and a glasshouse trial was conducted in four Australian States – NSW (8) including northern NSW (3), Victoria (4), South Australia (3) and Western Australia (17). The objectives of the program were to determine the efficacy of CRUSOE ME SEED TREATMENT on the control of seed-borne bunt and smut diseases of cereals (wheat, barley, oats) and to evaluate the safety of CRUSOE ME SEED TREATMENT on the target crops. The replicated experiments were conducted and reported according to an appropriately high standard of scientific investigation, including the use of statistical designs and analyses that were sufficiently robust to determine meaningful treatment effects.

The information available and the results from each set of trials were adequately and accurately presented and summarised by the applicant. However, there were some unnecessary typographical and presentation errors in the draft label submitted for registration, and these errors need correction.

Overall, the performance of RANCONA C SEED TREATMENT, which was always applied as a seed treatment prior to sowing, was consistent in terms of both efficacy and crop selectivity (safety) across the experimental sites and years. At the rate recommended (100 mL/100 kg seed), the fungicide generally provided excellent to complete control (90-100%) of the cereal bunts/smuts in the heads of infected crops. Likewise, it was demonstrated that RANCONA C SEED TREATMENT consistently produced no signs of crop injury with wheat or barley, either at emergence, during the growth phase or at harvest. Two oat varieties showed slight but acceptable emergence or seedling effects in response to double the recommended rate of RANCONA C SEED TREATMENT – as a consequence, the directions for use section stressed the importance of using the recommended application rate (100 mL/100 kg seed).

Hence, in terms of the evidence for the efficacy of the product and its safety to target and non-target species, the application by Chemtura Australia Pty Ltd for the registration of RANCONA C SEED TREATMENT is supported.

Assessment of study/trial data

The evaluation program submitted by the applicant, Chemtura Australia Pty Ltd, comprised descriptions and summaries from 29 efficacy/crop safety trials and 3 additional crop safety trials conducted by contractors or State departments. The experiments were small-plot field (31) or glasshouse (1) trials, replicated 4-6 times and statistically analysed by Analysis of Variance (ANOVA) techniques. The reported trials were conducted in NSW (8) including northern NSW (3), Victoria (4), South Australia (3) and Western Australia (17).

In each of the experiments, the design of the experiment (always a randomised complete block, replicated 4-6 times), the relevant treatments and rates of the fungicides (including a nil treatment), the parameters measured (seedling emergence counts, visual assessments of crop vigour or injury, incidence of smut infection in cereal heads at or near maturity, crop grain yields) and the statistical analyses, were all well designed, conducted and presented, sufficient to evaluate comprehensively the efficacy and safety of RANCONA C SEED TREATMENT, its analogues and the reference fungicides. Tables of means were shown for observations on the treatments in each experiment, and mean separation was achieved by the use of letters to define similar/dissimilar means using a test at the appropriate probability level (P=0.05).

Several rates of the analogous product formulation were used on a range of cereal types (wheat, barley oats) and cultivars, both to establish an overall optimum rate and to assess crop phytotoxicity, if any. Overall, the performance of RANCONA C SEED TREATMENT was consistent in terms of both efficacy and crop selectivity (safety) across the experimental sites and years. At the rate recommended (100 mL/100 kg seed), this fungicide usually provided excellent (> 90%) or complete control of cereal bunt and smuts in the maturing grain heads of the cereal crops. The experiments covered the range of cereal crop environments in Australia.

Crop safety

The information and data presented indicate that RANCONA C SEED TREATMENT is safe to use on cereal crops. In most experiments, the product either had no effect on seedling emergence or emergence was improved. Two of four varieties of oats showed either slight adverse effects of the product on seedling emergence or phytotoxicity symptoms but these effects were evident only at the double rate. No symptoms were apparent in any crop at the recommended rate.

Resistance management

The new active ipconazole is in Group 3 for Fungicides Resistance Management. The other approved active cypermethrin is in Group 3A for Insecticides Resistance Management.

9 CONCLUSION

The claims on the proposed product label that the product is capable of providing control of a specified list of bunt and smut diseases in cereal crops are supported by the results from the Australian efficacy experiments. The draft Directions for Use are clear. Appropriate advice is given on specific restraints, such as applying the product to seed, resistance warnings, and precautions. The directions and recommendations are in harmony with the experimental results. Advice or critical comments on application techniques, withholding periods, compatibility and a resistant weeds warning all appear appropriate.

Therefore, in terms of the evidence for the efficacy of the product and its safety to target and non-target species, the application by Chemtura Australia Pty Ltd for the registration of RANCONA C SEED TREATMENT is supported when used in accordance with the proposed label instructions and Good Agricultural Practice (GAP).

10 LABELLING REQUIREMENTS

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

Rancona™ C Seed Treatment

ACTIVE CONSTITUENTS: 20 g/L IPCONAZOLE
4 g/L CYPERMETHRIN

GROUP	**3**	**FUNGICIDE**
GROUP	**3A**	**INSECTICIDE**

Seed treatment for the control of various smut diseases in wheat, barley and oats.

Contents: (10, 20, 100, 200L)

Chemtura Australia Pty Ltd
Level 7, 435 King William Street, Adelaide, SA, 5000
Tel: (08) 8112 0900 Fax: (08) 8112 0999

DIRECTIONS FOR USE:

CROP	PEST	RATE	COMMENTS
Wheat	Bunt Loose smut Flag smut (soil & seed borne)	100 mL / 100 kg seed	Rancona can be used neat or diluted with water if required, to achieve optimum coverage of grain. If using diluted, as a guide, use a maximum of 400 mL of mixture (i.e. Rancona plus water) with each 100 kg of seed. Whatever solution is used it is essential that the correct application rate i.e. 100 mL of Rancona is applied to 100 kg seed. If using water, the mixture should be gently stirred regularly.
Barley	Covered smut Loose smut		
Oats	Covered smut Loose smut		
Wheat Barley Oats	Protection against insect pests of stored grains: Granary weevil, indian meal moth, lesser grain borer, rice weevil, rust-red flour beetle, sawtoothed 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:

HARVEST: No withholding period required when used as directed.

GRAZING: Do not graze or cut for stock food for 6 weeks after sowing

GENERAL INSTRUCTIONS

Rancona is a micro emulsion (liquid) seed dressing containing ipconazole for treatment of wheat, barley and oats for control of various fungal smut diseases. Rancona also contains cypermethrin for control of stored grain insects.

MIXING AND APPLICATION

Rancona may be applied to seed undiluted or may be mixed with water if required to achieve optimum coverage of grain. This requirement will depend on the equipment in use and the rates to be applied. Use only through equipment designed to apply suspension concentrate or slurry seed treatments to grain.

Uniform application to seed is necessary to ensure best disease protection and optimum performance.

Diluted product should be agitated before and during application. Do not allow diluted product to stand for long periods, e.g. overnight, without agitating thoroughly before continuing application.

Seed Quality: Seed treatment should not be used on seed with more than 12% moisture content, or on sprung, damaged or severely pinched seed, or seed of poor viability. If in doubt, have a germination test carried out on the seed before treatment to ensure that it is of acceptable standard.

FUNGICIDE RESISTANCE WARNING

GROUP	3	FUNGICIDE

Rancona is a member of the DMI group of fungicides. For fungicide resistance management the product is a Group 3 fungicide.

Some naturally occurring individual fungi resistant to the product and other Group 3 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 this product or other Group 3 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, Chemtura Australia accepts no liability for any losses that may result from the failure of this product to control resistant fungi.

INSECTICIDE RESISTANCE WARNING

GROUP	3A	INSECTICIDE

For insecticide resistance management Rancona is a Group 3A insecticide.

Some naturally occurring insect biotypes resistant to Rancona and other Group 3A insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if Rancona or other Group 3A insecticides are used repeatedly. The effectiveness of Rancona on resistant individuals could be significantly reduced. Since occurrence of resistant individuals is difficult to detect prior to use, Chemtura Australia Pty Ltd accepts no liability for any losses that may result from the failure of Rancona to control resistant insects.

Rancona may be subject to specific resistance management strategies. For further information contact your local supplier, Chemtura Australia Pty Ltd representative or local agricultural department agronomist.

COMPATIBILITY

DO NOT mix with any other products.

PRECAUTIONS

DO NOT use treated seed for animal or human consumption. DO NOT allow treated seed to contaminate grain or other seed intended for animal or human consumption. DO NOT feed treated seed, or otherwise expose, to wild or domestic birds.

PROTECTION OF LIVESTOCK AND OTHERS

Seed treated with this product must not be used for animal consumption or poultry feed or mixed with animal feed. DO NOT allow seed treated with this product to contaminate seed intended for animal consumption.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND THE ENVIRONMENT

DO NOT feed treated seed or otherwise expose to animals including wild or domestic birds. Any spillages of treated seed, however minor, must be cleaned up immediately, preferably by recovery and re-use. If disposal is required, ensure treated seeds are thoroughly buried and not accessible to birds and other wildlife. Very highly toxic to aquatic life. DO NOT contaminate dams, rivers, ponds, waterways or drains with this product, used containers or bags which have contained treated seed.

STORAGE & DISPOSAL

Keep out of reach of children. Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight.

10L, 20L, 200L containers:

Triple or preferably pressure rinse containers before disposal. Add rinsings to application equipment, or dispose of rinsings according to State/Territory legislative requirements. DO NOT dispose of undiluted chemicals on site. If not recycling, break, crush or puncture and deliver empty packaging to an approved waste management facility. DO NOT burn empty containers or product.

If recycling, replace cap and return clean containers to recycler or designated collection point.

100L returnable containers:

Empty contents fully into application equipment. Close all valves and return (to point of supply/designated collection point/other specific collection details) for refill or storage.

SAFETY DIRECTIONS

May irritate the eyes. When using the product, or handling treated seed, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves.

Wash hands after use.

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

Re-handling Statement

When using the product or handling treated seed, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow length chemical resistant gloves. Clothing must be laundered after each day's use.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26; New Zealand 0800 764 766

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet available from the manufacturer.

CONDITIONS OF SALE

Chemtura Australia Pty Ltd will not accept any responsibility whatsoever and howsoever arising and whether for consequential loss or otherwise in connection with the supply or use of these goods other than responsibility for the merchantable quality of the goods and such responsibilities mandatorily imposed by Statutes applicable to the sale or supply of these goods. To the extent allowed by such Statutes the liability of Chemtura Australia Pty Ltd is limited to the replacement of the goods or (at the option of Chemtura Australia Pty Ltd) the refund of the price paid and is conditional upon a claim being made in writing and where possible sufficient part of the goods to enable proper examination being returned to Chemtura Australia Pty Ltd within thirty days of delivery.

UN No. 3082	**ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S.** **(CONTAINS IPCONAZOLE)** **MARINE POLLUTANT**
In an Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 033 111** ALL HOURS – AUSTRALIA WIDE
P.G. III	

(include ‘Environmentally Hazardous’ symbol.)

APVMA Approval No. 63309/XXX/XXXX

(insert: batch number, date of manufacture, barcode)

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography

id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment

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

GLOSSARY

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

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