Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new active Bixafen in the product Aviator Xpro Foliar Fungicide

APVMA Product Number P69361

MARCH 2016

ISSN: 1443-1335 (electronic)
ISBN: 978-1-925390-27-8 (electronic)

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This publication is available from the APVMA website: www.apvma.gov.au.

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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 (OCS), Department of Environment, 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 consistent with accepted scientific principles and processes. Details are outlined on the APVMA's website at: www.apvma.gov.au.

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 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 stakeholders 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 Aviator Xpro Foliar Fungicide 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 matters include aspects of public

health, occupational health and safety, chemistry and manufacture, residues in food, environmental safety, trade, and efficacy and target crop or animal safety. Submissions should state the grounds on which they are based. Comments received that address issues outside the relevant matters cannot be considered by the APVMA.

Submissions must be received by the APVMA by close of business on 18 April 2016 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)
- email or postal address (if available)
- the date you made the submission.

All personal information, and confidential information judged by the APVMA to be *confidential commercial information (CCI)*[1] contained in submissions will be treated confidentially.

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:

Case Management and Administration Unit
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Phone: +61 2 6210 4701
Fax: +61 2 6210 4721
Email: enquiries@apvma.gov.au

Further information

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

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

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

1 INTRODUCTION

1.1 Applicant

Bayer CropScience Pty Ltd.

1.2 Details of the product

The APVMA is considering the proposal to register Aviator Xpro Foliar Fungicide (Aviator Xpro), containing 75 g/L bixafen and 150 g/L prothioconazole, as an emulsifiable concentrate formulation. It is intended for control of blackleg (*Leptosphaeria maculans*) in canola. Aviator Xpro will be applied at a rate of between 550 and 650 mL/ha. A maximum of two applications are allowed however application may not occur after the green bud stage of the crop.

The active constituent bixafen, will be manufactured overseas while the product Aviator Xpro will be manufactured both overseas and in Australia. Aviator Xpro will be available in the following HDPE or COEX pack sizes: 10, 15, 20, 100, 110 or 1000 L.

1.3 Resistance management

Prothioconazole is a triazole fungicide, belonging to the sub-class triazolinthione. Prothioconazole is designated as a Group 3 fungicide and acts as a De-Methylation Inhibitor (DMI).

Bixafen, a new active to the Australian market, is a carboxamide fungicide belonging to the sub-class of the pyrazole-4-carboxamides. Bixafen is a succinate dehydrogenase (SDHI) inhibitor (cellular respiration) of fungal pathogens. The Fungicide Resistance Action Committee (FRAC), a specialist technical group of CropLife International, has designated bixafen as a Group 7 fungicide.

For resistance management purposes, Aviator Xpro Foliar Fungicide is a Group 3 and Group 7 fungicide.

1.4 Overseas registrations

The EC formulation of Aviator Xpro Foliar Fungicide is currently registered for use in the United Kingdom, Norway, Chile, Switzerland, the Ukraine Austria, the Netherlands, New Zealand and The Republic of Moldova. Registrations in these countries cover use in wheat, barley, triticale, oats, rye, rape (canola) and spelt. Luxembourg, Poland, Belgium, Germany, France and Ireland have conditional registrations in place across these same crops, with the exception of canola.

This publication provides a summary of the data reviewed and an outline of regulatory considerations for the proposed registration of Aviator Xpro Foliar Fungicide.

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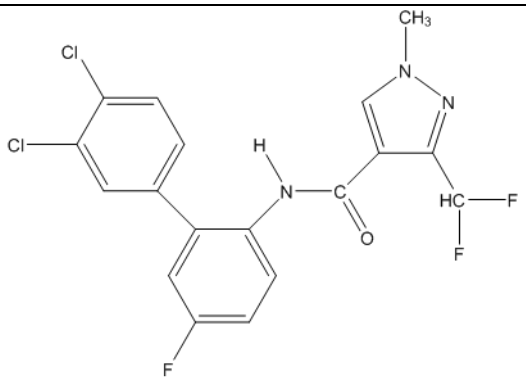
2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

Manufacturing site

The active constituent bixafen is manufactured by Bayer CropScience AG Germany and is proposed to be approved by the APVMA (Approval number: 69362).

Chemical characteristics of active constituent

COMMON NAME (ISO):	Bixafen
IUPAC NAME:	N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide (ISO)
CAS NAME:	N-(3',4'-dichloro-5-fluoro[1,1'-biphenyl]-2-yl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide
CAS REGISTRY NUMBER:	581809-46-3
MINIMUM PURITY:	950 g/kg
MOLECULAR FORMULA:	$C_{18}H_{12}Cl_2F_3N_3O$
MOLECULAR WEIGHT:	414.21 g/mol
STRUCTURE:	
CHEMICAL FAMILY:	pyrazole-4-carboxamide

Physico-chemical properties of active constituent

PHYSICAL FORM:	White powder (98.9% purity) Light brown powder (95.8% purity)
ODOUR:	No noticeable odour
MELTING POINT (98.9% AND 95.8 % PUIRTY):	146.6°C (98.9% purity) 142.9°C (95.8% purity)
BOILING POINT:	No boiling point at atmospheric pressure. Decomposed first at approximately 280°C and 210°C, 98.9 and 95.8% purity, respectively.
RELATIVE DENSITY AT 20°C:	1.43 (98.9% purity) 1.51 (95.9% purity)
PH (1% SOLUTION):	6.45 at 24°C (98.8% purity) 6.5 at 23°C (95.8% purity)
SURFACE TENSION (95.8% PURITY):	70.7 mN/m at 20 °C. Non-surface active according to EC Guideline A.5
SOLUBILITY AT 20°C (99.2%, 98.9%, 98. 9%):	Acetone 250 g/L Ethyl acetate 82 g/L Methanol 32 g/L Dichloromethane 102 g/L Dimethyl sulfoxide >250 g/L Toluene 16 g/L n-heptane 0.056 g/L Water 0.49 mg/L
VAPOUR PRESSURE AT 25°C (98.8% PURITY):	1.1×10^{-7} Pa (extrapolated)
HYDROLYIS RATE (99.4% PURITY):	Hydrolytically stable. No hydrolysis at any pH (4, 7 and 9) over 5 days (120 hours) at 50°C.
UV (98.8% PURITY):	Peak maxima molar absorptivity [1000 cm²/mol] 210 nm 42825.31 233 nm 24115.24
DISSOCIATION CONSTANT (pK_a):	No dissociation constant of bixafen was found in the pH range pH 1–pH 12
STABILITY:	Not degraded over 90 days at 54°C After 12 months at 30°C in polypropylene and polyethylene containers, no degradation of bixafen was observed; the impurity profile did not change.

PARTITION CO-EFFICIENT (98.8% PURITY)	2046 (log Pow = 3.3)
HENRY'S LAW CONSTANT AT 20^{OC}:	3.89 × 10–5 Pa.m3/mol in distilled water (calculated)
DIRECT PHOTO-TRANSFORMATION:	In sterile 0.01 M phosphate buffer solution at pH 7 and 25ºC, [dichlorophenyl-UL-^{14}C] BYF 00587 under artificial sunlight exposure (A >290 nm) for 8 days: DT50 is 82 days of intensive continuous irradiation (791 W/m2 in the wavelength range of 300-800 nm. No major transformation products were formed. Multiple unknown minor products (total 4.6% at the end of test) were observed. Largest individual fraction of these (max. 1.5%) was polar radioactivity. Direct photo-transformation in aqueous solution will only be a minor contributor to the overall fate of BYF 00587 (bixafen) in the environment. It is unlikely that photo-degradation will lead to any relevant degradation products
QUANTUM YIELD:	0.0000218
PHOTO-CHEMICAL OXIDATIVE DEGREDATION:	The half-life (t1/2) of bixafen in air was calculated to be 0.87 days and the chemical lifetime (τ) of bixafen in air to be 1.26 days (by computer program AOPWINTM (version 1.91.) Concluded from the short half-life of bixafen in air, it is expected that bixafen in gaseous phase cannot be transported over large distances and cannot accumulate in the atmosphere. Furthermore, only limited quantities of bixafen will enter the atmosphere, due to the low vapour pressure of the substance.
FLAMMABILITY (95.8% PUIRTY):	Not a highly flammable solid in the sense of EC guideline A.10
AUTO-FLAMMABILITY (95.8% PURITY):	Not to be classified as a self-heating substance. No self-ignition temperature was observed up to the melting and also up to the maximum test temperature of 403°C.
OXIDISING PROPERTIES 95.8% PURITY):	No oxidizing properties in the sense of EC guideline A.17
EXPLOSIVE PROPERTIES (95.8% PURITY)	No danger of explosion according to the explosive properties in the sense of EC guideline A.14
CORROSION CHARACTERISTICS (95% PURITY):	Not corrosive to the polypropylene and polyethylene packaging. The storage vessels showed slightly discolouring after 24 months.
THERMALSTABILITY:	Stable (room temperature to melting point)
DISSOCIATION CONSTANT (pK_a):	No pKa evident in the pH range of 2–12 (20 +/- 1^{0}C in 40% (v/v) ethanol/water)

2.2 Product

The active constituent bixafen will be manufactured overseas while the associated product Aviator Xpro Foliar Fungicide will be manufactured both overseas and in Australia. Aviator Xpro Foliar Fungicide will be available in the following HDPE or COEX pack sizes: 10, 15, 20, 100, 110 or 1000 L.

Aviator Xpro Foliar Fungicide

DISTIGUISHING NAME:	Aviator Xpro Foliar Fungicide
FORMULATION TYPE:	Emulsifiable Concentrate (EC)
ACTIVE CONSITUENT CONCENTRATION:	75 g/L bixafen and 150 g/L prothioconazole

Physical and chemical properties of the product

PHYSICAL FORM:	Clear brown liquid
ODOUR:	Amine-like odour
PH VALUE:	4.8 (1% in de-ionised water at room temperature)
SPECIFIC GRAVITY:	1.01
RELATIVE DENSITY:	1.006 at 20ºC
SURFACE TENSION:	32 mN/m at 25ºC (surface active according to EC Guideline A
VISCOSITY:	v= 80.3 mm²/s (calculated for 20 °C + 20 s^{-1}) v = 77.7 mm²/s (calculated for 20 °C + 100 s^{-1}) v = 33.7 mm²/s (calculated for 40 °C + 20 s^{-1}) v = 31.0 mm²/s (calculated for 40 °C + 100 s^{-1})
FLASH POINT:	Higher than 100ºC
OXIDISING PROPERTIES:	No oxidising properties
EXPLOSIVE PROPERTIES:	Not explosive
AUTO-IGNITION TEMPERATURE:	375°C
PACK SIZES:	10, 15, 20, 100, 110 or 1000 L
PACKAGING MATERIAL:	High density polyethylene (HDPE) or COEX(PA), COEX (E-VAL)
PRODUCT STABILITY:	The product should remain within specifications for at least 2 years when stored under normal conditions in COEX) PA, (COEX) E-VAL and fluorinated HDPE

Recommendations

Based on a review of the chemistry and manufacturing details provided by the applicant, registration of Aviator Xpro Foliar Fungicide is supported.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological database provided for bixafen is extensive and comprises a full contemporary suite of acute and repeat dose toxicity studies in mice, rats and dogs as well as *in vitro* and *in vivo* genotoxicity studies, reproductive, developmental and neurotoxicity studies. The majority of studies have been conducted according to OECD Test Guideline specifications under GLP and QA conditions. The studies were considered reliable to establish the toxicity profile of bixafen.

In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur.

Chemical class

Bixafen is a carboxamide fungicide belonging to the sub-class of the pyrazole-carboxamides, a succinate dehydrogenase inhibitor of fungal pathogens.

Toxicokinetics and metabolism

Overall, bixafen was rapidly absorbed and distributed throughout the body, highly metabolised and rapidly excreted primarily *via* the faecal pathway. There was a slight sex difference in the ADME of bixafen with slower absorption and elimination of the compound in females compared to males at higher doses and after repeated dosing. Excretion was rapid and extensive, with the majority of the administered dose excreted within 24 hours, indicating a low probability of bioaccumulation of the parent compound or metabolites.
The main metabolic pathways for bixafen, regardless of the different positions of radio-label, consist primarily of demethylation in the pyrazole ring followed by either hydroxylation of the parent compound or the demethylated metabolite, leading to multiple hydroxylated compounds.

Percutaneous absorption

An *in vitro* dermal absorption study on a 125 g/L bixafen aqueous formulation in humans and rat skin was submitted with this application; however, an *in vivo* dermal absorption study in rats was not submitted. Therefore, consistent with the OECD Guidance Notes on Dermal Absorption (OECD, 2011), in the absence of *in vivo* dermal absorption data, the human *in vitro* dermal absorption values of 1 per cent and 4 per cent for mixing/loading and application respectively, were used in the current risk assessment.

Acute toxicity

In acute toxicity studies in rats, bixafen was of low acute oral toxicity (LD_{50} >2000 mg/kg bw), low acute dermal toxicity (LD_{50} >2000 mg/kg bw) and low acute inhalational toxicity (LC_{50} >5383 mg/m³, 4–hour exposure). It was not a skin or eye irritant in rabbits. A non-validated and non-test guideline compliant local lymph node assay in mice (LLNA/IMDS) was submitted and so the sensitising potential of the test material was not able to be adequately determined.

Clinical signs observed in acute toxicity studies included bradypnea, laboured breathing, reduced motility, piloerection ungroomed hair-coat, limp, high-legged gait flaccid paralysis of hind legs, giddiness and mydriassis.

Aviator Xpro Foliar Fungicide was of low acute oral (LD_{50} >2000 mg/kg bw) and low acute dermal (LD_{50}>2000mg/kg bw) toxicity in rats, was a slight skin and a severe eye irritant in rabbits, and was not a skin sensitiser in mice (LLNA). Based on estimation of the product ingredients the product is expected to have low acute inhalational toxicity.

Systemic toxicity

The systemic toxicity of bixafen in dietary studies consisted primarily of decreases in body weight and body weight gain, liver toxicity such as increased liver weight and centrilobular hepatocellular hypertrophy with associated clinical chemistry changes, and thyroid effects (eg follicular cell hypertrophy) generally seen at higher dose levels. This systemic toxicity profile was observed in short-term, sub-chronic and chronic toxicity studies in rats, mice and dogs, with the available data indicating that rats and mice were equally sensitive. A mechanistic study indicated that hepatotoxicity may be due to induction of both phase I and II hepatic enzymes.

Genotoxicity and carcinogenicity

There was no evidence of increased cancer incidence rates in bixafen treated-animals when compared to concurrent study controls in lifetime oral exposure studies of rats and mice.

There was no evidence of a mutagenic/genotoxic potential *in vitro* with and without metabolic activation, or a genotoxic potential *in vivo*.

Reproductive and developmental toxicity

In a dietary two generation study in rats, parental systemic toxicity was seen at the top (2500 ppm) and mid dose (400 ppm) levels. At the top dose, decreased body weight (5–6 per cent decrease seen in dams of both generations throughout gestation), decreased body weight gain (15–18 per cent decrease in body weight gain in dams of both generations throughout gestation and lactation), and increased liver, spleen, thyroid, thymus (females only) and kidney (males only) weights were noted in both genders. At the mid dose level, male liver weights were increased (P_0 only) while female liver weights were increased in all doses in the P_1 generation. Liver hypertrophy was also sharply increased in high dose rats of both generations and sexes. Reproductive findings were not affected by treatment. In offspring, decreased pup body weight (8–12 per cent decrease seen in pups of both generations on day 21) and pup body-weight gain, and decreased

spleen, thymus (F1 only) and brain weights were also seen at the top dose level. However, OCS considers that the observed effects in offspring were a secondary non-specific consequence of maternal toxicity. Bixafen is not considered to be a reproductive toxicant.

No evidence of a developmental toxicity potential was seen in an oral (gavage) developmental toxicity study in rats at the mid and high dose levels that produced marked maternal toxicity (e.g. body weight gain was 42 per cent lower during the dosing period compared to controls at the high dose), with foetal weights also decreased at mid and high dose levels. Maternal body weight gains were decreased at the high dose during the treatment period and liver weights were increased in both the mid and high dose dams.

In an oral (gavage) developmental toxicity study in rabbits maternal body weight gains were decreased at the high dose during the treatment period and liver weights were increased in both the mid and high dose dams, along with an increased incidence of visceral and skeletal findings at the high dose. While these findings were outside of the historical control range they were seen in the presence of marked maternal toxicity (eg body weight gain was reduced (↓74 per cent) at several time intervals between GD 6 and 26 and overall (GD 6 to 29; ↓59 per cent) as well as reduced foetal weights (↓6 per cent combined). Thus, bixafen was not considered to be a developmental toxicant in rabbits as the observed skeletal findings in foetuses were considered a secondary non-specific consequence of marked maternal toxicity.

Neurotoxicity

No evidence of neurotoxicity was seen in acute and repeat dose studies; however, this was not investigated independently in standard neurotoxicity studies.

3.2 Public health standards

Poison scheduling

On 27 November 2015, the Delegate to the Secretary of the Department of Health published a final scheduling decision to create a new Schedule 5 entry for bixafen in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP), with no exemption cut-off, and an implementation date of 1 February 2016.

Prothioconazole is considered not to require control by scheduling and is listed in Appendix B of the SUSMP.

ADI

The acceptable daily intake (ADI) for humans is the level of intake of an agricultural or veterinary chemical which can be ingested daily over an entire lifetime without appreciable risk to health. It is calculated by dividing the overall NOEL (No Observable Effect Limit) for the most sensitive toxicological endpoint from a suitable study (typically an animal study) by an appropriate safety factor. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans, intra-species variation, and the completeness of the toxicological database and the nature of the potential toxicologically significant effects.

The ADI for bixafen is established at 0.02 mg/kg bw/d using the NOEL of 2 mg/kg bw/d from a 104 week dietary chronic/carcinogenicity study in male Wistar rats, based on increased liver weights and accompanying changes in histopathology at 12.1 mg/kg bw/d.

The ADI for prothioconazole is 0.01 mg/kg bw/d in a 2–year rat study on prothioconazole-desthio (major metabolite) and was established in 2006, based on a NOEL of 1.1 mg/kg bw/d with increase liver weight, hepatocellular hypertrophy and liver vacuolation with fatty change at the next highest dose 8 mg/kg bw/d in rats.

ARfD

The acute reference dose (ARfD) is the estimate of the amount of a substance in food or drinking water, expressed on a milligram per kilogram body weight basis, that can be ingested over a short period of time, usually in one meal or during one day, without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation.

The ARfD for bixafen is established at 0.2 mg/kg bw using the NOEL of 20 mg/kg bw/d in females from a developmental study in rats, based on decreased body weight gain in dams and foetuses (at 75 mg/kg bw/d).

The ARfD for prothioconazole is 0.03 mg/kg bw and was established in 2008, based on a NOEL of 3 mg/kg bw/d in a rat developmental toxicity study on prothioconazole-desthio based on increased incidence of 14th rib, increased resorption, decreased litter size, cleft palate, and decreased foetal weight gain at the next highest dose of 10 mg/kg bw/d.

4 RESIDUES ASSESSMENT

4.1 Introduction

Aviator Xpro Foliar Fungicide contains the new active constituent bixafen (figure 1) and the approved active constituent prothioconazole for use on canola. It is proposed that two applications of Aviator Xpro Foliar Fungicide (75 g/L bixafen and 150 g/L prothioconazole) be made to canola at a maximum rate of 650 ml product/ha (48.75 g bixafen/ha and 97.5 g prothioconazole/ha). Application may not occur after the green bud growth stage of the crop and a harvest withholding period is 'NOT REQUIRED when used as directed' is proposed. The grazing withholding period for livestock not producing milk for human consumption is 4 weeks while livestock producing milk for human consumption may not be grazed on treated areas.

As part of the residue assessment for bixafen, plant and animal metabolism studies, supervised residue trials and trade aspects were considered. Supervised residue trials and trade aspects were also considered for prothioconazole.

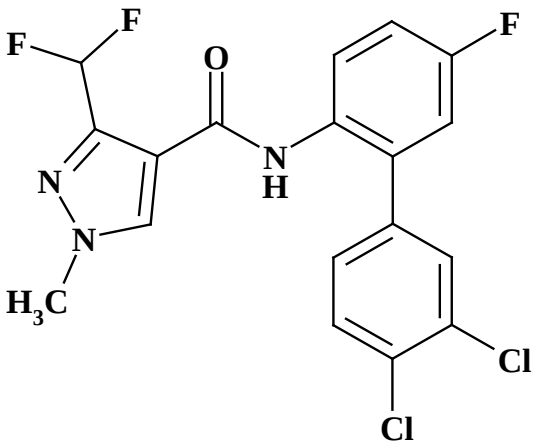


Figure 1: Bixafen

4.2 Metabolism

Plants

For soya beans, three foliar applications of ^{14}C-bixafen were made at 60 g ai/ha each when first flowers opened (BBCH 60), at the end of flowering (BBCH 69) and finally when approximately 80 per cent of the pods were ripe (BBCH 88). Samples were collected for forage (5 days after 2nd application), hay (29 days after 2nd application), straw and seed (26 days after the 3rd application). Total radioactive residues (TRR) were 4.0–5.3 mg eq/kg for forage, 2.8–4.0 mg eq/kg for hay, 9.5–13 mg eq/kg for straw and 0.005–0.024 mg eq/kg for seeds. In all plant parts directly affected by the spray solution, unchanged bixafen was the major residue representing 96–98 per cent of the TRR in forage, 92 per cent in hay, 90–92 per cent in straw and 30 per cent in the seed. The only other metabolite identified was M21 bixafen-desmethyl (M21), present at 0.5–2.6 per cent of the TRR in forage, hay and straw.

For wheat, one foliar application of ^{14}C-bixafen was made at 125 g ai/ha at the end of tillering / beginning of stem elongation (BBCH 29–31) followed by a second application of 150 g ai/ha at the end of flowering (BBCH 69). Forage was harvested 9 days after the 1st application, hay 9 days after the 2nd application and straw and grain at maturity (50 days after the 2nd application). Total radioactive residues were 1.6–1.7 mg eq/kg for forage, 6.6–7.6 mg eq/kg for hay, 23–24 mg eq/kg for straw and 0.16–0.23 mg eq/kg for seeds.
In all samples unchanged bixafen was the major residue, representing >90 per cent of the TRR. The only other metabolite identified was (bixafen-desmethyl) at 0.8–2.4 per cent of the TRR.

For rotational crops, one application of ^{14}C-bixafen was made to bare soil at 790 or 850 g ai/ha. Following a 30, 138 or 285 day Plant Back Interval, Swiss chard, turnips and wheat were planted. In plant commodities, bixafen (11–78 per cent TRR) and bixafen-desmethyl, 3–73 per cent TRR (M21) were the major residue components found.

The proposed metabolic pathway for bixafen in plants is presented below.

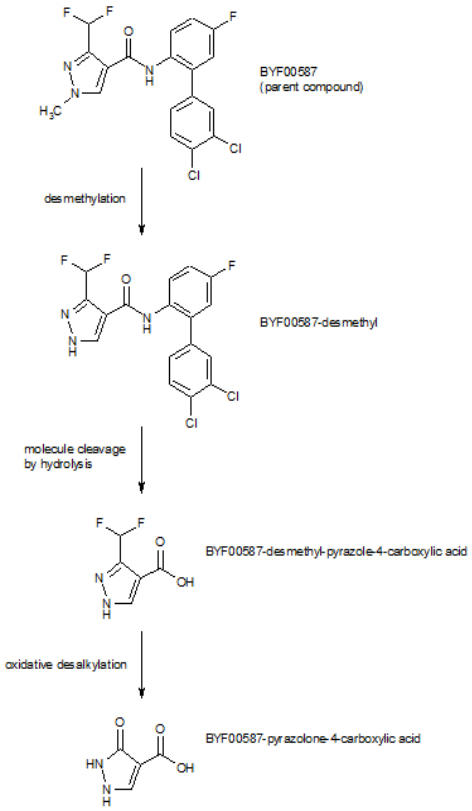


Figure 2: The proposed metabolic pathway for bixafen in plants

Animals

For lactating goats, ^{14}C-bixafen was orally administered daily for 5 consecutive days at an actual dose of 35 or 46 ppm in the feed. In milk (TRR: 0.064–0.17 mg eq/kg), muscle (TRR: 0.047–0.057 mg eq/kg) and fat (TRR: 0.47–0.61 mg eq/kg) unchanged bixafen was the major residue, representing 74–77 per cent, 56– 66 per cent and 89 per cent of the total radioactivity, respectively. M21, bixafen-desmethyl was the only major metabolite being present at 16–18 per cent of the TRR in milk, 34–43 per cent in muscle and 10–11 per cent in fat. For kidney (TRR: 0.14–0.2 mg eq/kg) and liver (TRR: 0.74–1.2 mg eq/kg) parent bixafen (44–46 per cent of the total radioactivity in kidney and 18–23 per cent in liver) and bixafen-desmethyl (37–38 per cent of the TRR in kidney and 19–21 per cent TRR in liver) were the major residues.

The proposed metabolic pathway for bixafen in lactating goat is presented below.

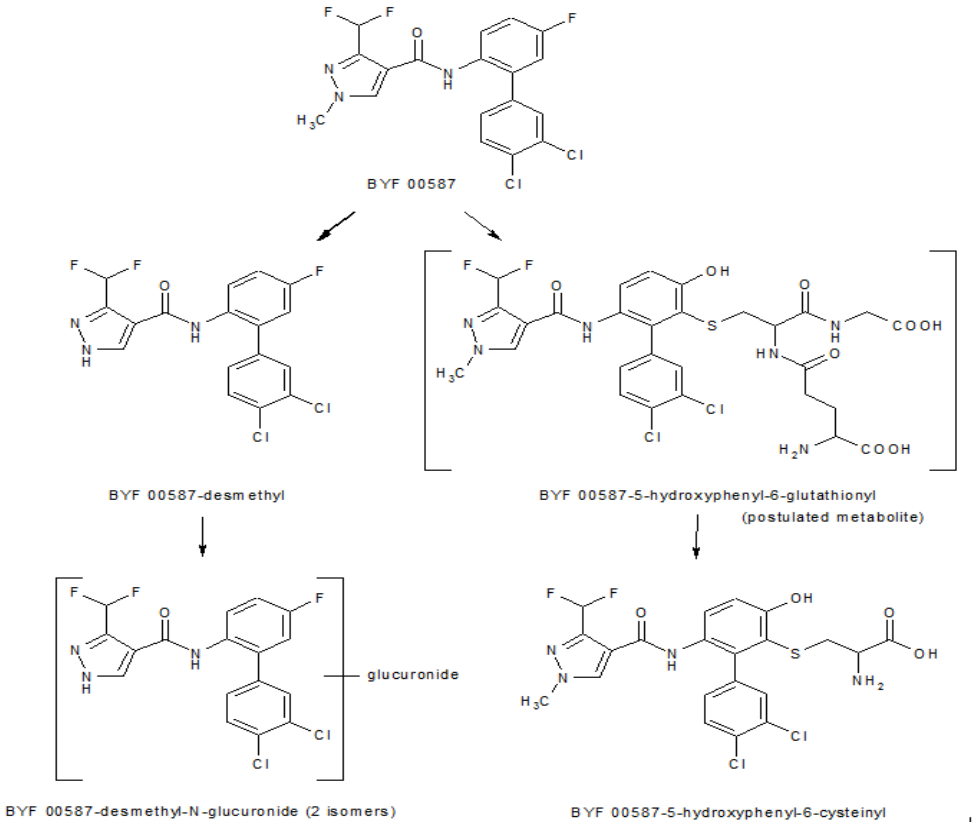


Figure 3: The Proposed metabolic pathway for bixafen in lactating goats

For laying hens, ^{14}C-bixafen was orally administered daily for 14 consecutive days at an actual dose of 26 or 32 ppm in the feed. Total radioactive residues were 0.53–0.9 mg eq/kg in eggs, 0.032–0.037 mg eq/kg in muscle, 0.23–0.38 mg eq/kg in fat and 0.64–0.81 mg eq/kg in liver. Parent bixafen was a major residue in eggs and all tissues except liver, representing 51–69 per cent of the TRR in eggs, 23–41 per cent in muscle and 80 per cent in fat. In hen liver, only minor amounts of bixafen were detected (4.5–6.7 per cent TRR). M21 (bixafen-desmethyl) was the only major metabolite found in poultry tissues and eggs, contributing 26–39 per cent of the TRR in eggs, 35–51 per cent in muscle, 19–20 per cent in fat and 24–26 per cent in liver.

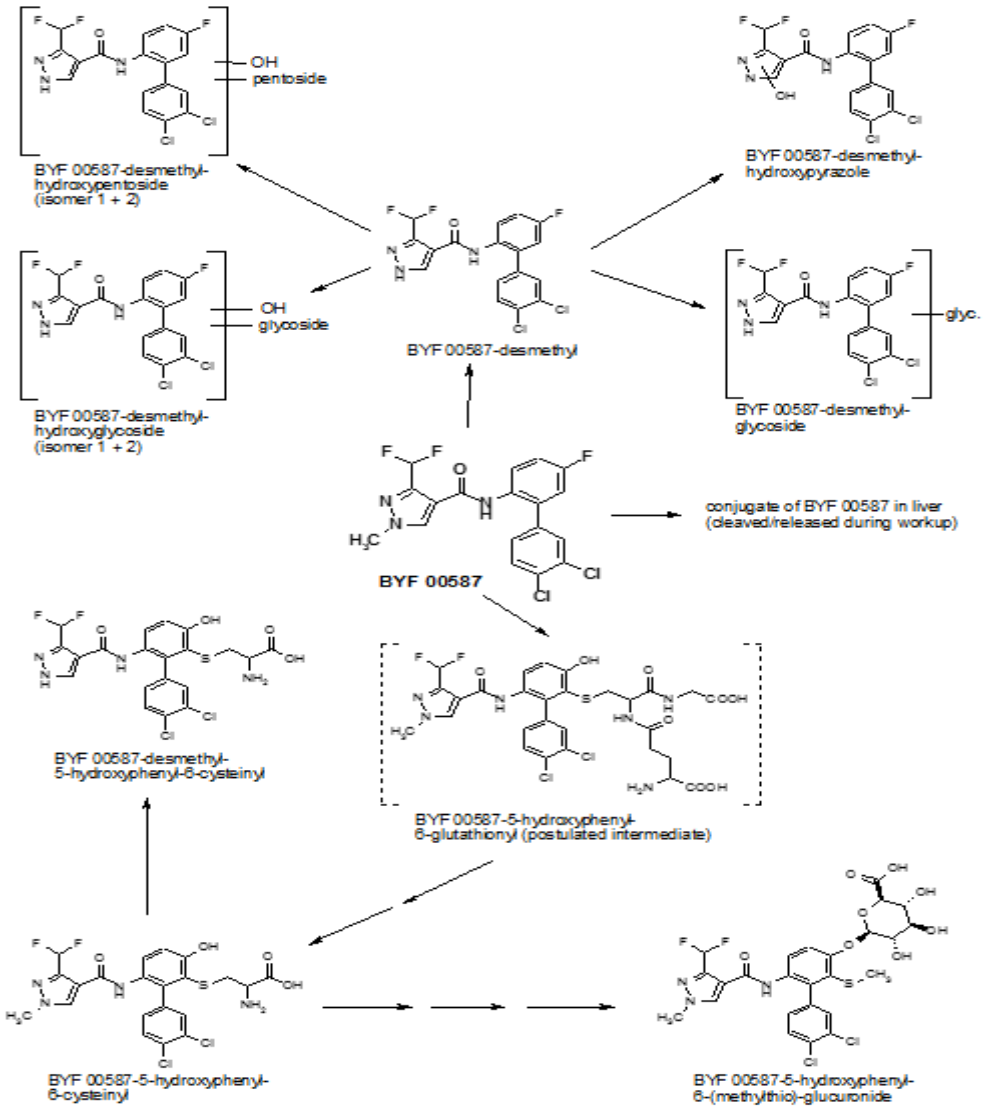


Figure 4: The proposed metabolic pathway for bixafen in laying hens

4.3 Analytical methods

For bixafen and bixafen-desmethyl, analytical methods were provided following a comparable procedure. Plant and animal samples were extracted using acetonitrile/water and after filtration and clean-up, residues were measured by HPLC—MS/MS. The LOQ was 0.01 mg/kg for each analyte and the recoveries in plant and animal matrices were found to be acceptable (70–120 per cent, <20 per cent RSD).

4.4 Stability of the pesticide in stored analytical samples

The storage stability of bixafen and its primary metabolite M21 (bixafen-desmethyl) in wheat grain, wheat straw, wheat green material, lettuce head, potato tuber and rape seed following storage (≤ – 18°C) for up to 24 months were within acceptable limits.

4.5 Residue definition

Based on the results of the metabolism and residue studies, it is recommended that the residue definition for bixafen in plant commodities be parent only for enforcement. As bixafen-desmethyl was a significant residue in rotational crops, it is recommended that the dietary exposure definition for plants be the sum of bixafen and bixafen-desmethyl, expressed as bixafen.

It is recommended that the residue definition for commodities of animal origin be the sum of bixafen and bixafen-desmethyl, expressed as bixafen.

4.6 Residue trials

For bixafen in canola grain, five Australian residue trials were undertaken with two applications of bixafen at the proposed application timing of 4–6 leaf and green bud at approximate application rates of 49, 60 and 97.5 g ai/ha (1, 1.25 and 2X the proposed rate respectively). This resulted in parent bixafen residues <LOQ (ie <0.01 mg/kg) at commercial maturity (88–107 days after final application). This dataset supports the establishment of a bixafen MRL at *0.01 mg/kg for SO 0495 Rape seed.

For bixafen in canola forage, the proposed Australian use pattern resulted in parent bixafen residues of 0.11, 0.29, 0.30, 0.35 and 1.0 mg/kg on a dry weight basis at the proposed grazing withholding period of 4 weeks (26–29 days). For canola stubble, the proposed Australian use pattern resulted in parent bixafen residues of <LOQ (n=4) and 0.04 mg/kg on a dry weight basis at harvest. This dataset supports of the establishment of bixafen MRLs at 2 mg/kg for ‘Canola forage’ and 0.1 mg/kg for ‘Canola straw and fodder (dry)’.

Processing factors for parent bixafen were <0.5, 0.72, 0.82 and 2X for canola meal, 0.5, <1, 2.4 and 2.5X for crude canola oil and <0.5, 1, 2.1 and 2.1X for refined canola oil, based on exaggerated application rates. MRLs for canola oil and meal are not required at this time.

For prothioconazole in canola grain, five Australian residue trials were undertaken with two applications of prothioconazole at the proposed application timing of 4–6 leaf and green bud at approximate application rates of 97.5, 120 and 190 g ai/ha (1, 1.25 and 2X the proposed rate respectively). This resulted in total residues (expressed as prothioconazole) of <LOQ (i.e. <0.01 mg/kg) at commercial maturity (88–107 days after final application). This dataset confirms that the established prothioconazole MRL of *0.02 mg/kg for SO 0495 rape seed remains appropriate.

For prothioconazole in canola forage, the proposed Australian use pattern resulted in total residues (expressed as prothioconazole) of 0.16, 0.41, 0.50, 0.53 and 2.6 mg/kg on a dry weight basis at the proposed grazing withholding period of 4 weeks (26–29 days). For canola stubble, the proposed Australian use pattern resulted in total residues (expressed as prothioconazole) of <LOQ (n=4) and 0.04 mg/kg on a dry

weight basis at harvest. This dataset supports a prothioconazole MRL for Rape seed [canola] forage, fodder and straw of 5 mg/kg.

4.7 Animal commodity MRLs

For bixafen, the lactating cattle feeding study involved feeding levels of 4, 12 and 40 ppm in the feed for 28 consecutive days (three animals per group). The proposed residue definition for animal commodities is the sum of bixafen and bixafen-desmethyl, expressed as bixafen. Residue levels according to the proposed residue definition in muscle for the 4, 12 and 40 ppm groups ranged 0.039–0.065 mg/kg, 0.081–0.26 mg/kg and 0.63–1.0 mg/kg, respectively. In liver, residues were 0.42–0.69 mg/kg, 1.2–1.7 mg/kg and 4.8–5.4 mg/kg for the 4, 12 and 40 ppm groups. In kidney, residues were 0.1–0.15 mg/kg, 0.28–0.37 mg/kg and 1.0–1.3 mg/kg for the 4, 12 and 40 ppm groups. In perirenal fat, residues were 0.14–0.21 mg/kg, 0.33–0.48 mg/kg and 0.8–1.9 mg/kg for the 4, 12 and 40 ppm groups.

The estimated dietary burden for mammalian livestock associated with the proposed use of bixafen on canola is 1 ppm in the feed. Bixafen MRLs for MM 0095 Meat [mammalian] [in the fat] at 0.1 mg/kg and MO 0105 Edible offal (Mammalian) at 0.3 mg/kg is required for the proposed use on canola with a 4 week grazing withholding period.

The lactating cattle feeding study included a depuration phase in which cattle were placed on clean feed for 7, 14 and 21 days following 28 days of dietary exposure to bixafen at 40 ppm in the feed. Following 7 days of depuration, total bixafen residues were <0.02 mg/kg in muscle and kidney, 0.107 mg/kg in subcutaneous fat and 0.127 mg/kg in liver. Following a 7 day depuration period, the highest residue level expected in cattle tissues as a result of the proposed use on canola was 0.0032 mg/kg in liver. It is therefore concluded that a 7 day depuration period should result in residue levels below the LOQ of 0.02 mg/kg in mammalian animal commodities.

A restraint prohibiting dairy cattle from grazing treated crops has been proposed so canola meal is the only feed item relevant to dairy cattle. In the lactating cow feeding study, the highest mean residue levels in milk were 0.039 mg/kg, 0.077 mg/kg and 0.218 mg/kg for the 4, 12 and 40 ppm group. Residue levels expected in milk as a result of the feeding of treated canola meal were 0.00003 mg/kg. Bixafen residues were found to concentrate into cream (9.9X) and milk fat (15X), however as expected residues were so low in milk, quantifiable residues in cream and milk fat are not expected. A bixafen MRL for Milks at *0.02 mg/kg is required for the proposed use on canola.

The laying hen feeding study for bixafen involved feeding levels of 1.5, 4.5 and 15 ppm in the feed for 28 consecutive days. In eggs, total residues at the plateau phase ranged < 0.02–0.02 mg/kg for the 1.5 ppm group and ranged between 0.06 to 0.07 mg/kg for the 4.5 ppm and between 0.13 to 0.22 mg/kg for the 15 ppm group. In tissues no residues above the LOQ were found in muscle. Residue levels in fat for the 1.5, 4.5 and 15 ppm groups were <0.02–0.02 mg/kg, 0.05–0.06 mg/kg and 0.06–0.09 mg/kg, respectively. In liver residues were <0.02–0.02 mg/kg, 0.02–0.04 mg/kg and 0.03–0.05 mg/kg for the 1.5, 4.5 and 15 ppm groups.

The estimated dietary burden for poultry associated with the proposed use of bixafen on canola is 0.007 ppm in the feed. Bixafen MRLs at *0.02 mg/kg for PE 0112 Eggs, PO 0111 poultry, edible offal of and PM 0110 poultry, meat [in the fat] are required for the proposed use on canola.

The proposed use of prothioconazole on canola in similar to that currently approved and requires a MRL for rape seed [canola] forage and fodder at 5 mg/kg. No further consideration is necessary at this time.

4.8 Estimated dietary intake

The chronic dietary exposure 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 primarily from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with WHO Guidelines and is a conservative estimate of dietary exposure to chemical residues in food. The NEDI for bixafen is equivalent to <1 per cent of the ADI. It is concluded that the chronic dietary exposure to bixafen is acceptable. The NEDI for prothioconazole is equivalent to <10 per cent of the ADI. It is concluded that the chronic dietary exposure to bixafen and prothioconazole is acceptable.

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 primarily from the 1995 National Nutrition Survey of Australia. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. The highest acute dietary intake for bixafen was estimated at <2 per cent of the ARfD.
The highest acute dietary intake for prothioconazole was estimated at <5 per cent of the ARfD. It is concluded that the acute dietary exposure of bixafen and prothioconazole is acceptable.

4.9 Bioaccumulation potential

The octanol-water partition coefficient ($log_{10}K_{OW}$) for bixafen is 3.3 (20 C), indicating a degree of fat solubility. The lactating cow feeding study suggests that bixafen is fat soluble as residues were higher in fat than muscle and higher in cream than milk. Processing studies for rape seed found that parent bixafen residues may potentially concentrate into refined canola oil (processing factor were <0.5, 1, 2.1 and 2.1X).

4.10 Spray drift

MRLs for bixafen have not been established by Codex, Korea, Taiwan and the US and therefore bixafen residues in animal commodities must be below the LOQ of 0.02 mg/kg for the protection of international trade.

Spray drift modelling, using the average deposition (over 300m) from APVMA spray drift standard application scenarios, shows that with respect to no-spray zones (using an application rate of 48.75 g ai/ha), for a ‘broadacre high ground boom—medium’ application, a downwind buffer of 3 m is required. Due to the insignificant size of the calculated buffer it is considered that a no-spray zone is not required for ground application.

For prothioconazole, the proposed use of on canola is closely similar to that approved and the spray drift potential remains unchanged. No buffer zones for the protection of international trade are associated with the approved use.

4.11 Residues in rotational crops

For bixafen, the proposed use on canola involves a maximum of two foliar applications at a maximum rate of 48.75 g bixafen/ha (97.5 g ai/ha annually). The first application is to be made at the 4 to 6 leaf growth stage and the second application is to be made at the green bud stage if required. Canola is grown in rotation with other broadacre crops (such as cereals and pulses) in Australia and it is unlikely that bixafen will be applied to the same paddock ever year as the proposed use of bixafen on canola will be the only approved use of bixafen.

The four field rotational crop studies undertaken in Europe in 2006–2007 found that two applications of bixafen to a primary crop (barley) at 160 g ai/ha at mid heading and 125 g ai/ha at the end of flowering (285 g ai/ha annually; 2.9X the proposed maximum annual rate) did not result in bixafen or bixafen-desmethyl residues above LOQ (0.01 mg/kg) in rotational crops (turnip/carrots, lettuce and wheat) following a plant back interval (PBI) of 60–180 and 270–365 days. The four rotational crop studies included a treatment that involved an application to bare soil at 281 g ai/ha and a plant back interval of 30 days, to simulate a failed crop situation. Parent bixafen and bixafen-desmethyl residue levels were below the LOQ of 0.01 mg/kg with the exception of two detections. One sample of wheat straw (282 DAA) contained 0.02 mg/kg bixafen desmethyl and one immature lettuce (60 DAA) sample contained 0.05 mg/kg parent bixafen with the residue being <0.01 mg/kg in mature lettuce (74 DAA) in that trial.

It is concluded that quantifiable bixafen residues are unlikely to occur in rotational crops as a result of the proposed use of bixafen on canola.

For prothioconazole, the proposed use of on canola is closely similar to that approved and the rotational crop potential remains unchanged.

4.12 Recommendations

The following amendments to the APVMA MRL Standard are required for the current application:

Table 1

COMPOUND		FOOD	MRL (mg/kg)
ADD:			
	Bixafen		
PE	0112	Eggs	*0.02
MO	0105	Edible offal (Mammalian)	0.3
MM	0095	Meat [mammalian] [in the fat]	0.1
ML	0106	Milks	*0.02
PO	0111	Poultry, Edible offal of	*0.02
PM	0110	Poultry meat [in the fat]	*0.02
SO	0495	Rape seed	*0.01

Table 3

COMPOUND	RESIDUE
ADD:	
Bixafen	Commodities of plant origin for enforcement: Bixafen
	Commodities of plant origin for dietary exposure assessment: Sum of bixafen and N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1H-pyrazole-4-carboxamide (bixafen-desmethyl), expressed as bixafen
	Commodities of animal origin: Sum of bixafen and N-(3',4'-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1H-pyrazole-4-carboxamide (bixafen-desmethyl), expressed as bixafen

Table 4

COMPOUND	ANIMAL FEED COMMODITY	MRL (mg/kg)
ADD:		
Bixafen		
	Canola forage	2
	Canola straw and fodder (dry)	0.1
Prothioconazole		
ADD:		
	Rape seed [canola] forage, fodder and straw	5

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported

Canola (including derived oils and meals) are considered to be major export commodities, as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed feeds produced from treated canola. Residues in these commodities resulting from the use of Aviator Xpro Foliar Fungicide may have the potential to unduly prejudice trade.

5.2 Destination of exports

Australian exports of canola grain, oil and meal totalled 3,194 kt (value $1,929 million), 152 kt and 42 kt respectively in 2013–14 (Australian Commodity Statistics 2014). The major export markets for canola grain in 2013–14 included China, Belgium, Japan, Pakistan and the Netherlands. Destinations for canola oil included Malaysia, the Republic of Korea, China and New Zealand. The major markets for Canola meal included New Zealand and the Republic of Korea.

The significant export markets for Australian beef, sheep, pig meat and offals are listed in the APVMA Regulatory Guidelines—Data Guidelines: Agricultural—Overseas trade (Part 5B).

5.3 Proposed use pattern

Aviator Xpro Foliar Fungicide (75 g/L bixafen and 150 g/L prothioconazole)

DIRECTIONS FOR USE			
Crop	Pest	Rate	Critical Comments
Canola	Blackleg (*Leptosphaeria maculans*)	550–650 mL/ha (≡ 41.25–48.75 g bixafen/ha and 82.5–97.5 g prothioconazole/ha)	Apply at the 4 to 6 leaf stage of blackleg susceptible varieties (blackleg ratings of MS or lower) or in situations of high blackleg risk (refer to General Instructions—Disease control in Canola). Will reduce lodging and stem canker from blackleg. A follow up application may be required at green bud in high disease risk situations or where an effective blackleg seed treatment has not been used. Use the higher rate in higher yielding crops where disease risk is high. DO NOT apply after the green bud growth stage.

RESTRAINTS
A maximum of two applications may be made per canola crop.

WITHHOLDING PERIODS
Harvest: Not required when used as directed
Grazing: Livestock Not Producing Milk For Human Consumption
Do not graze or cut for stock food for 4 weeks after application.
Livestock Producing Milk For Human Consumption
Do not graze livestock producing milk for human consumption on treated crops.

EXPORT SLAUGHTER INTERVAL (ESI)—7 DAYS

Livestock not producing milk for human consumption that have been grazing on treated crops should be placed on clean feed for 7 days prior to export slaughter.

GENERAL INSTRUCTIONS
Disease control in canola
Higher blackleg risk can be expected in higher rainfall districts (above 500 mm annual rainfall), where crops are grown within 500 m of a previous years stubble and in later sown crops (May to August). Other factors will also increase the risk of blackleg infection, including the intensity of canola cropping in a district, rainfall before sowing and the frequency of growing the same canola cultivar. Consult industry guidelines for more detailed assessment of blackleg risk in specific situations. Up to two sprays of Aviator Xpro may be applied per season to the crop.

Export of treated produce
Growers should note that MRLs or import tolerances do not exist in all markets for produce treated with Aviator Xpro. If you are growing produce for export, please check with Bayer CropScience for the latest information on MRLs and import tolerances before using Aviator Xpro.

Application
Ground:
Apply product using a spray volume of 60–100 L/ha and a MEDIUM spray quality as defined by the ASABE S572 Standard.

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a MEDIUM spray droplet category as defined by the ASABE S572 Standard. Users MUST ONLY USE nozzles classified as suitable for delivering a MEDIUM spray droplet category according to the nozzle manufacturer's specifications.
DO NOT apply when wind speed is less than 3 or more than 20 km/h as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.
Users of this product MUST make an accurate written record of the details of each spray application within 24 hours following application and KEEP this record for a minimum of 2 years. The spray application details that must be recorded are: 1.date and start and finish times of application; 2.location address and paddock/s sprayed; 3.full name of this product; 4.amount used per hectare and number of hectares applied to; 5.crop/situation and weed/pest; 6.wind speed and direction during application; 7.air temperature; 8.nozzle brand, model and type and spray system pressure measured during application; 9.name and address of person applying this product. (Additional record details may be required by the State or Territory where this product is used.)

5.4 Overseas registration and approved label instructions

Other than EU (cereal and canola uses are approved), Japan and New Zealand (cereal uses are approved), international MRLs have not been established for bixafen.

5.5 Comparison of Australian MRLs with Codex and International MRLs

Codex has established a residue definition for bixafen but have not established MRLs at this time. JMPR considered bixafen in 2013, however further crop rotation studies at rates specific to European use patterns for bixafen were required to satisfy the JMPR requirements for establishment of Codex MRLs for bixafen.

The following relevant international MRLs have been established for bixafen:

CURRENT AND PROPOSED AUSTRALIAN AND OVERSEAS MRLS/TOLERANCES FOR BIXAFEN

COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF BIXAFEN (mg/kg)					
	AUSTRALIA	EU2	NEW ZEALAND3	JAPAN4	CODEX5	USA6, TAIWAN7 AND KOREA8
Residue Definition	Plants: Bixafen (enforcement) Animals: Sum of bixafen and bixafen-desmethyl, expressed as bixafen (PROPOSED)	Plants: Bixafen (enforcement) Animals: Sum of bixafen and bixafen-desmethyl, expressed as bixafen	Plants: Bixafen Animals: Sum of bixafen and bixafen-desmethyl	Plants: Bixafen Animals: Sum of bixafen and bixafen-desmethyl	Plants: Bixafen (enforcement) Animals: Sum of bixafen and bixafen-desmethyl, expressed as bixafen	Not established
Rape seed (canola)	*0.01 (proposed)	0.07	-	-	-	-

[2] ec.europa.eu

[3] www.foodsafety.govt.nz

[4] www.m5.ws001.squarestart.ne.jp

[5] www.codexalimentarius.net

[6] www.ecfr.gov

[7] www.fda.gov.tw/EN/law.aspx

[8] eng.kfda.go.kr/file/PesiticideMRLs.pdf

COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF BIXAFEN (mg/kg)					
	AUSTRALIA	EU2	NEW ZEALAND3	JAPAN4	CODEX5	USA6, TAIWAN7 AND KOREA8
Meat (mammalian)	T0.3 (ESTABLISHED)	0.15 a	0.15	0.2	-	-
Fat (mammalian)	0.1 (in the fat) (REQUIRED)	0.4 a	0.4	0.4	-	-
Kidney (mammalian)	T1 (offal (ESTABLISHED)	0.3 a	0.3	0.3	-	-
Liver (mammalian)	0.3 (offal) (REQUIRED)	1.5 a	1.5	2	-	-
Milk	T*0.02 (ESTABLISHED) *0.02 (proposed)	0.04 a	0.04	0.04	-	-

Note a: presented mammalian MRLs were for cattle (bovine), sheep and goats only and not for swine or horses that had LOQ (0.02 mg/kg) set.

The following relevant Codex and international MRLs have been established for prothioconazole:

CURRENT AND PROPOSED AUSTRALIAN AND OVERSEAS MRLS/TOLERANCES FOR PROTHIOCONAZOLE

COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF PROTHIOCONAZOLE (mg/kg)				
	AUSTRALIA	CODEX	EU	JAPAN	USA
Residue Definition	Plants: Prothioconazole and the desthio metabolite Animals: Prothioconazole and the desthio, 3-hydroxy-desthio and 4-hydroxy-desthio metabolites (established)	Plants: Prothioconazole-desthio Animals: prothioconazole-desthio.	Plants: Prothioconazole-desthio Animals: the sum of prothioconazole-desthio and its glucuronide conjugate, expressed as prothioconazole-desthio.	Plants: Prothioconazole and the desthio metabolite Animals: metabolites M17 [2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1H-1,2,4-triazole-1-il)-2 propanol] calculated as prothioconazole and glucronic acid conjugates of prothioconazole and metabolite M17	Plants: Prothioconazole and the desthio metabolite Animals: prothioconazole and its metabolites prothioconazole-desthio, or α-(1-chlorocyclopropyl)-α-[(2-chlorophenyl)methyl]-1H-1,2,4-triazole-1-ethanol, and conjugates that can be converted to these two compounds by acid hydrolysis.
Rape seed (canola)	*0.02 (established)	0.1	0.15	0.2	0.15

COMMODITY	TOLERANCE FOR RESIDUES ARISING FROM THE USE OF PROTHIOCONAZOLE (mg/kg)				
	AUSTRALIA	CODEX	EU	JAPAN	USA
Offal	0.2 (established)	0.5	0.5	0.5 (liver and kidney)	0.2 (MEAT BY-PRODUCTS)
Meat	0.02 (establsihed)	0.01	0.05	0.01 (meat), 0.05 (fat)	0.02 (MEAT), 0.01 (FAT)
Milk	*0.004 (established)	*0.004	*0.01	0.004	0.02

5.6 Potential risk to trade

Export of treated produce containing finite (measurable) residues of bixafen and prothioconazole 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.

The following label advice relating to export is supported:

> **EXPORT SLAUGHTER INTERVAL (ESI)—7 DAYS**
>
> *Livestock not producing milk for human consumption that have been grazing on treated crops should be placed on clean feed for 7 days prior to export slaughter.*
>
> **Export of treated produce**
>
> *Growers should note that MRLs or import tolerances do not exist in all markets for produce treated with Aviator Xpro. If you are growing produce for export, please check with Bayer CropScience for the latest information on MRLs and import tolerances before using Aviator Xpro.*

No changes to established prothioconazole MRLs for rape seed and animal commodities are proposed and therefore the proposed use of prothioconazole is unlikely to increase the risk to international trade.

The proposed residue definition for bixafen is the same as that established by Codex, the EU and New Zealand. International MRLs have not been established for bixafen by Codex, the USA, Korea and Taiwan.

An MRL for canola is proposed at the LOQ (*0.01 mg/kg) and therefore the export of treated canola is unlikely to result in an undue risk to international trade.

Bixafen MRLs for meat [mammalian] [in the fat] and edible offal (Mammalian) at 0.1 and 0.3 mg/kg respectively are required for the proposed use on canola. The proposed Export Slaughter Interval of 7 days should adequately prevent residues above the LOQ of 0.02 mg/kg in animal commodities destined for export.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Bixafen (CAS: 581809-46-3) is not currently listed on the Safe Work Australia (SWA) Hazardous Substances Information System (HSIS) Database (SWA, 2015). Based on the toxicological information presented in this submission and NOHSC's *Approved Criteria for Classifying Hazardous Substances* (2004), no HSIS listing or risk phrases have been proposed for bixafen.

Prothioconazole (CAS: 178928-70-6) is listed on the Safe Work Australia Hazardous Substances Information System (HSIS) Database (SWA, 2015) with the following risk phrases:

R48/22	Danger of serious damage to health by prolonged exposure if swallowed.

Based on the product toxicology studies and information on product ingredients on SWA's HSIS Database (2015), Aviator Xpro Foliar Fungicide (containing 15 per cent prothioconazole and 7.5 per cent bixafen) is classified as a hazardous substance in accordance with NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 2004) with the following risk phrases:

R48/22	Danger of serious damage to health by prolonged exposure if swallowed
R36	Irritating to eyes

6.2 Formulation, packaging, transport, storage and retailing

The active constituent bixafen will be manufactured overseas while Aviator Xpro Foliar Fungicide will be manufactured both overseas and in Australia. Aviator Xpro Foliar Fungicide will be available in the following HDPE or COEX pack sizes: 10, 15, 20, 100, 110 or 1000 L.

6.3 Use pattern

Aviator Xpro Foliar Fungicide, an emulsifiable concentrate (EC) product, containing 75 g/L bixafen and 150 g/L prothioconazole is proposed for the control of blackleg in canola. Aviator Xpro Foliar Fungicide is intended only for professional use, and will be applied by various ground boom up to a maximum of two times per canola crop. The maximum use rate proposed is 650 mL product/ha equivalent to 48.75 g bixafen and 97.5 g prothioconazole.

6.4 Exposure during use

Farmers and their employees will be the main users of the product. Workers may be exposed to the product when opening containers, mixing/loading, application, cleaning up spills, maintaining equipment and entering treated areas.

The main route of exposure to the product spray will be dermal and inhalation with possible ocular exposure.

In the absence of exposure data for bixafen and for proposed aerial mode of application for prothioconazole, the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure. The database was also used to verify the calculated exposure of workers to prothioconazole via ground boom application from submitted exposure studies.

The toxicity endpoint of concern and identified NOEL for risk assessment is derived from a repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account both potential inter-species extrapolation and intra-species variability. Based on the risk assessment, the proposed use of the product is acceptable (MOE >100) when a single layer of PPE and chemical-resistant gloves are worn by workers during application of the product. In addition to the aforementioned PPE, goggles will also be required for workers during mixing and preparation of the product for use.

6.5 Exposure during re-entry

Re-entry into treated crops may be required to scope the disease load on the crop and to harvest the crop.

The OCS notes that the re-entry risks associated with conducting activities where the product has been applied are expected to be by the dermal route, and that exposure to bixafen is expected to occur at specific periods of time after application to a crop. The potential re-entry activities for crops treated with Aviator Xpro Foliar Fungicide are considered to have low exposure risk, and the estimated MOEs for bixafen were acceptable (MOE >100) on day zero after application. The OCS considers that the risks associated with re-entry activities is low after the spray has dried, and the following standard re-entry statement is recommended:

Do not enter treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

6.6 Recommendations for safe use

Based on the risk assessment, the product is appropriate for professional use; users should follow the First Aid Instructions, Safety Directions and Re-entry statements on the product label.

6.7 Conclusion

The registration of Aviator Xpro Foliar Fungicide, containing 75 g/L bixafen and 150 g/L prothioconazole, for professional use is supported.

Aviator Xpro Foliar Fungicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above. Additional information is available on the product l Safety Data Sheet.

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

Bayer CropScience Pty Ltd has applied for registration of a 225 g/L emulsifiable concentrate end-use product, Aviator Xpro™ Foliar Fungicide. The product contains the currently registered fungicide prothioconazole at a concentration of 150 g/L, and the new active constituent bixafen at 75 g/L. The product is for the control of blackleg (*Leptosphaeria maculans*) in canola.

The environmental fate and ecotoxicity information following in the PRS relate to the new active constituent, bixafen, or for test results relating to the end-use product.

7.2 Environmental fate

Hydrolysis

Bixafen is expected to be hydrolytically stable under normal environmental conditions.

Photolysis/photodegradation

Bixafen is not susceptible to photolysis in either soil or water with half-lives from 82 days (water) to 90 days (soil).

Biodegradation

Soil metabolism

The bio-degradation of bixafen was studied in four European soils for 120 days under aerobic conditions in the dark at 20°C. The main compound was unchanged bixafen accounting for 86.5–90.7 per cent at the end of the study. Thus, the half-life of bixafen in aerobic soils under the test conditions was >1 year indicating that in aerobic soils bixafen is not readily degraded.

In field studies, bixafen dissipated from soil of all test sites with an apparent biphasic behaviour. The non-normalised concentration values could kinetically be described with a Hockey-Stick model with DT_{50} values ranging from 45 days to >1000 days.

In field dissipation studies, bixafen did dissipate faster than laboratory data indicated. Half-lives ranged from around 35 days to >1000 days. Degradation was bi-phasic and DT_{90} values extended beyond 20 years in cases. Soil accumulation testing confirmed this with annual applications for 8 years at one site and 6 years at a second showing plateau concentrations were not reached. At one site, annual carryover was around 82 per cent of applied chemical and the field half-life at this site was around 1200 days. Modelling indicates that continual application may not result in peak soil concentrations until after 25 years, and the risk assessment to soil exposed organisms took this into account. No major soil metabolites were identified and movement through the soil profile was limited with very little bixafen found below the top 10 cm soil horizon.

Aquatic metabolism

In two water/sediment systems bixafen dissipated steadily from the water phase to the sediment phase over the course of 118 days. The radioactivity in terms of percentage of total applied declined from approx. 93–98 per cent in the water phase at time zero to approx. 7–8 per cent at day 118 for one, and from 93–95 per cent to 10–17 per cent for the second system. Conversely, the radioactivity detected in the sediment increased from zero at time zero to 74–88 per cent at the end of the study. In all cases the radioactivity consisted largely of the parent compound. One minor component was observed at a maximum level of 1.5 per cent in the water in the second system at day 14, pyrazole label and to ca 1.2 per cent in the corresponding sediment extracts at day 59. No other degradate was observed. The amounts of radioactivity converted to non-extractable sediment residues were generally below 5 per cent of the applied radioactivity. The amount of radioactivity detected as volatiles was also low (up to 1 per cent of the applied dose) by day 118 in both systems and for both labels.

The disappearance time (DT_{50}) of bixafen from the water phase was 22.5 days and 25.5 days (best fit kinetics) of both test systems. Due to the limited decline of bixafen observed during the course of the study, it was not possible to determine a reliable DT_{50} or DT_{90} for the total system. It can be concluded that bixafen was stable under the conditions of the test.

Mobility

Bixafen is not mobile in soil, however, with limited movement only detected below 10 cm in field studies. In standard batch equilibrium studies in five soils with organic carbon levels ranging from 1.1 per cent to 2.62 per cent, Koc values were all between 3000 and 5000. The substance is therefore not expected to migrate to groundwater.

Bioaccumulation

Despite its persistence, bixafen is not expected to bioconcentrate in organisms (lipid normalised BCF = 322 days), and was shown to be readily depurated from fish following exposure (elimination half-life of 1.3 days).

7.3 Environmental effects

Avian

Bixafen is practically nontoxic to birds with acute oral or short term dietary exposure (acute oral LD_{50} >2000 mg ac/kg bw for bobwhite quail; 5 d dietary LC_{50} >5000 ppm for both bobwhite quail and mallard duck). Reproduction studies with bobwhite quail showed a lowest NOEC (No Observable Effects Concentration) of 24.5 mg ac/kg bw/d.

Fish

Based on the results of acute toxicity studies conducted with the active constituent, bixafen is categorised as very highly toxic to fish. The 96 h LC_{50} to rainbow trout was calculated to be 0.095 mg ac/L while for fathead minnow the 96 h LC_{50} was 0.105 mg/L.

Early life stage toxicity studies with bixafen indicated a 33 d NOEC of 0.0046 mg ac/L to fathead minnow. Thus bixafen can be classified as highly toxic to fish with chronic exposure.

No major metabolites of bixafen were identified.

Aquatic invertebrates

Based on the results of acute toxicity studies conducted with the active constituent, bixafen is classified as moderately toxic (EC_{50} = 1.2 mg ac/L).

A 21 day chronic toxicity study of bixafen to *Daphnia magna* indicated a NOEC of 0.125 mg ac/L based upon parental growth effects, and a reduction in the number of offspring produced above this concentration.

Sediment organisms were more sensitive when exposed through spiked water. The NOEC to midge in a 28 day chronic water/sediment test with spiked water was 0.016 mg/L indicating bixafen is moderately toxic to these organisms through chronic exposure.

Algae, diatoms and aquatic plants

Tests were provided for four algal species and one vascular aquatic plant (*Lemna gibba*). The growth rate EC_{50}s for two algal species indicated bixafen was very highly toxic to algae (E_rC_{50} = 0.097 mg/L, *Pseudokirchneriella subcapitata* and 0.03 mg/L, *Navicula pelliculosa*).

Growth rate EC_{50} values for the other two algal species and *Lemna gibba* could not be calculated as 50 per cent inhibition was not achieved at the highest rates tested (0.241 mg/L to 0.737 mg/L).

Terrestrial invertebrates

Bixafen was shown to not be toxic to bees with oral and contact LD_{50}s of >121 µg/bee and >100 µg/bee respectively.

In bixafen only testing on non-target arthropods, the most sensitive species was the parasitoid (*Aphidius rhopalosiphi*) in tier 1 testing with an LR_{50} = 36.4 g ac/ha. However, in extended laboratory testing the LR_{50} was 250 g ac/ha.

The end-use product was tested on the standard beneficial insects, the parasitoid (*Aphidius rhopalosiphi*) and the predatory mite (*Typhlodromus pyri*) in extended laboratory dose/response tests. The LR_{50}s for these species were 3485 mL product/ha and 1296 mL product/ha respectively. Testing on additional non-target arthropods with the end use product showed these to be less sensitive.

Acute toxicity tests for earthworms showed bixafen to not be toxic with an LC_{50} >1000 mg/kg dw soil. For reproductive toxicity testing, bixafen resulted in a NOEC of 100 mg/kg soil dw, the highest rate tested. The end use product, tested as a soil spray had a 56 d NOEC to earthworms of 75 L product/ha.

Bixafen showed a NOEC of 6.25 mg ac/kg soil to the soil predatory mite (*Hypoaspis aculeifer*) and 7.74 mg ac/kg soil to the collembolan (*Folsomia candida*). The end use product was also tested for toxicity to collembola and resulted in a NOEC of 104 mg product/kg dw soil.

Microorganisms

Exposure of bixafen to soil microorganisms showed no significant adverse effects on the soil nitrogen cycle or soil respiration at levels up to 1.67 mg ac/kg dw soil, the highest tested rate. The end use product showed no effects (<25 per cent compared to control soils) up to the maximum tested rate of 16.77 mg product/kg soil.

Terrestrial plants

Only tier 1 tests were available for bixafen or the end use product to terrestrial plants. In all testing, 10 species of standard test species were used. In all cases, <50 per cent effects were observed. The most sensitive species for bixafen in vegetative vigour testing was corn with 32.1 per cent dry weight inhibition at 1 L/ha of the bixafen formulation (125 g ac/ha) while the most sensitive species in seedling emergence testing was buck wheat with 38.9 per cent dry weight inhibition at 2 L/ha of the bixafen formulation (250 g ac/ha).

Testing with the end use product in the vegetative vigour study showed <50 per cent effects up to 1.25 L product/ha. There was 31.9, 30.9, 35.3, 35.9 and 37.2 per cent dry weight inhibition in cucumber, oilseed rape soya bean, tomato and buck wheat respectively. At the same rate in the seedling emergence study there was 38.5, 42.6, 32.7 and 36.7 per cent dry weight inhibition in oilseed rape, sugarbeet, tomato and rye grass respectively.

7.4 Risk assessment

Bixafen has been assessed for a maximum application rate of 60 g ac/ha, with maximum of 2 sprays per season and 14–21 days between applications. The risk assessment, which was performed using standard methodology, showed an acceptable risk to all environmental organisms considered.

The spray drift risk assessment was undertaken as per the APVMA spray drift policy and demonstrated risk to aquatic organisms and terrestrial plants is acceptable, provided the inclusion of appropriate downwind aquatic and terrestrial spray drift buffer zones are applied. The runoff risk assessment to aquatic organisms was undertaken as per the Department of the Environment screening model and demonstrated that risk to aquatic organisms from runoff of both active constituents was acceptable.

The APVMA is satisfied that the proposed use of this product is unlikely to have an unintended effect that is harmful to animals, plants or things or the environment.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Aviator Xpro Foliar Fungicide (Aviator Xpro), containing the new active constituent bixafen(75 g/L) and the approved active constituent, prothioconazole (150 g/L), as an emulsifiable concentrate, is intended for the control of blackleg (*Leptosphaeria maculans*) in canola. It is proposed that two applications of Aviator be made to canola at a maximum rate of 650 ml product/ha (48.75 g bixafen/ha and 97.5 g prothioconazole/ha), with application not to occur after the green bud growth stage of the crop.

8.2 Summary of evaluation of efficacy and crop safety

In a series of small plot replicated trials widely spread across all southern states of Australia; Aviator Xpro was applied as a foliar spray at 400, 550, 650 and 800 mL/ha to canola generally at the 4 to 6 leaf stage. In a number of trials a second application was applied at green bud. All trials contained an untreated control (UTC).

Fifteen canola trials were conducted; all using a similar small plot randomised complete block design; with the majority conducted utilising three or four replicates. One trial was conducted as a single strip design, not replicated. Total spray volumes used were from 80 to 105 L/ha. Trial results were all statistically analysed.

A series of assessments were undertaken to evaluate crop safety, disease severity and disease incidence and crop yields. Crop phytotoxicity assessments were undertaken using a rating scale of 0–100 where: 0 = No discolouration evident and 100 = Total discolouration of crop. A rating of 40 or above is commercially unacceptable.

Crop biomass reduction assessments were undertaken using a rating scale of 0–100 where: 0 = No damage evident. 100 = Complete loss of plant (or) crop yield. A rating of 30 or above is commercially unacceptable.

Disease severity and incidence on leaves was determined by examining and estimating the percentage leaf area infected of each leaf (per cent LAI) for the second leaf on each of 10 plants per plot. Disease severity and incidence in the stem was determined by pulling plants, cutting the stems at ground level, examining the cut stem and estimating the percentage stem area infected (per cent SAI) on each of 20 plants per plot.

Aviator Xpro at 550 to 650 mL/ha provided control, as measured by disease severity and incidence on leaves and stems, of blackleg in canola when applied as a foliar spray at the 4 to 6 leaf crop stage. At these rates control was comparable to that of the registered standard used in the trials. There was a rate response in several trials; generally rates lower than 550 mL/ha of Aviator Xpro were less reliable, but there were few trials where any useful additional control or yield increase was observed above 650 mL/ha of Aviator Xpro. In a number of trials the lower rate of 400 mL/ha was statistically inferior to the higher rate of 550 mL/ha.

At rates of 550 to 650 mL/ha Aviator Xpro was generally comparable and statistically equivalent to the industry standard at 375 and 450 mL/ha respectively.

Generally, a single foliar application of Aviator Xpro (or the industry standard) was sufficient to give adequate protection from blackleg at the 4 to 6 leaf stage of the crop and to reduce leaf lesions and stem canker.

In some situations of high disease pressure an additional spray just before flowering may be useful to further reduce infection.

The trial was harvested with a small plot harvester and grain weights per plot were converted to tonnes per hectare. In a number of trials with moderate to high disease levels a yield response was generally seen with all Aviator rates

The data presented supports the claim for use of Aviator Xpro at 550 to 650 mL/ha for the control of blackleg (*Leptosphaeria maculans*) in canola.

Crop safety

The tolerance of canola to Aviator Xpro was evaluated and trial data demonstrates an acceptable level of crop safety when the product is applied according to the proposed recommendations. In the majority of trials there was little or no crop phytotoxicity or biomass reduction. In a small number of trials there were low levels of crop phytotoxicity and biomass reduction, which the canola quickly grew out of. It can be concluded that Aviator can be safely applied to canola at the proposed label rates.

Resistance management

Prothioconazole is a triazole fungicide, belonging to the sub-class triazolinthione. Prothioconazole is a Group 3 Fungicide and acts is as a De-Methylation Inhibitor (DMI) (Sterol Biosysnthesis in membranes). Prothioconazole is designated as a Group 3 fungicide by CropLife Australia

Bixafen is a carboxamide fungicide belonging to the sub-class of the pyrazole-4- carboxamides .Bixafen is a succinate dehydrogenase (SDHI) inhibitor (cellular respiration) of fungal pathogens. The Fungicide Resistance Action Committee (a specialist technical group of CropLife International) has designated bixafen as a Group 7 fungicide.

For resistance management purposes, Aviator Xpro is a Group 3 and Group 7 fungicide. At this time the proposed use pattern is not currently subject to a CropLife ant-resistance management strategy.

8.3 Conclusions

The claims on the proposed label that Aviator Xpro Foliar Fungicide provides acceptable control of blackleg in canola when used as directed is supported by the results from the Australian trials.

Acceptable crop safety is expected when the product is used as directed. The directions for use are appropriate and consistent with fungicide use in commercial agriculture in Australia.

The application by Bayer CropScience Pty Ltd for the registration of Aviator Xpro Foliar Fungicide is supported on efficacy and crop safety grounds when used in accordance with label instructions.

9 LABELLING REQUIREMENTS

CAUTION

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

Aviator® Xpro™

FOLIAR FUNGICIDE

ACTIVE CONSTITUENTS: 150 g/L PROTHIOCONAZOLE
75 g/L BIXAFEN

GROUP 3 7 FUNGICIDE

For the control of blackleg in canola as specified in the DIRECTIONS FOR USE table

*** L**

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

* 10, 15, 20, 100, 110, 1000 L

CAUTION

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

AVIATOR XPRO FOLIAR FUNGICIDE

ACTIVE CONSTITUENTS: 150 g/L PROTHIOCONAZOLE
75 g/L BIXAFEN

For the control of blackleg in canola as specified in the DIRECTIONS FOR USE table.

DIRECTIONS FOR USE

RESTRAINTS
DO NOT apply by aircraft
A maximum of two applications may be made per canola crop.

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a **MEDIUM** spray droplet category as defined by the ASAE S572 Standard. Users **MUST ONLY USE** nozzles classified as suitable for delivering a **MEDIUM** spray droplet category according to the nozzle manufacturer's specifications.
DO NOT apply when wind speed is less than 3 or more than 20 km/h as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.

Users of this product **MUST make an accurate written record** of the details of each spray application within 24 hours following application and **KEEP** this record for a minimum of 2 years. The spray application details that must be recorded are: **1**.date and start and finish times of application; **2**.location address and paddock/s sprayed; **3**.full name of this product; **4**.amount used per hectare and number of hectares applied to; **5**.crop/situation and weed/pest; **6**.wind speed and direction during application; **7**.air temperature; **8**.nozzle brand, model and type and spray system pressure measured during application; **9**.name and address of person applying this product. (Additional record details may be required by the State or Territory where this product is used.)

MANDATORY NO-SPRAY ZONES

DO NOT apply if there are aquatic and wetland areas, including aquacultural ponds, surface streams and rivers downwind from the application area and within the **mandatory no-spray zones** shown in Table A below.

Table A – No-Spray Zones for Protection of the Aquatic Environment	
Wind Speed Range at Time of Application	**Downwind Mandatory No-Spray Zone**
FOR GROUND APPLICATION	
From 3 to 20 kilometres per hour	5 metres

DO NOT apply if there are sensitive crops, gardens, landscaping vegetation, protected native vegetation or protected animal habitat downwind from the application area and within the **mandatory no-spray zones** shown in Table B below.

Table B – No-Spray Zones for Protection of the Terrestrial Environment	
Wind Speed Range at Time of Application	**Downwind Mandatory No-Spray Zone**
FOR GROUND APPLICATION	
From 3 to 20 kilometres per hour	5 metres

CROP	STATE	DISEASE	RATE	CRITICAL COMMENTS
Canola	All States	Blackleg (*Leptosphaeria maculans)*	550 to 650 mL/ha	Apply at the 4 to 6 leaf crop stage of blackleg susceptible varieties (blackleg ratings of MS or lower) or in situations of high blackleg risk (refer to General Instructions – Disease control in Canola). Will reduce lodging and stem canker from blackleg. A follow up application may be required at green bud in high disease risk situations or where an effective blackleg seed treatment has not been used. Use the higher rate in higher yielding crops where disease risk is high. DO NOT apply after the green bud growth stage of canola.

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

WITHHOLDING PERIODS

Harvest - NOT REQUIRED WHEN USED AS DIRECTED

Grazing - <u>Livestock Not Producing Milk For Human Consumption:</u>
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 4 WEEKS AFTER APPLICATION
<u>Livestock Producing Milk For Human Consumption:</u>
DO NOT GRAZE LIVESTOCK PRODUCING MILK FOR HUMAN CONSUMPTION ON TREATED CROPS

EXPORT SLAUGHTER INTERVAL (ESI) – 7 DAYS

Livestock not producing milk for human consumption that have been grazing on treated crops should be placed on clean feed for 7 days prior to export slaughter.

A MANDATORY NO-SPRAY ZONE IS REQUIRED FOR PROTECTION OF THE ENVIRONMENT. REFER TO RESTRAINTS.

GENERAL INSTRUCTIONS

Disease control in canola

A higher blackleg risk can be expected in higher rainfall districts (above 500 mm annual rainfall), where crops are grown within 500 m of a previous year's stubble or in later sown crops (May to August). Other factors will also increase the risk of blackleg infection, including the intensity of canola cropping in a district, rainfall before sowing and the frequency of growing the same canola cultivar. Consult industry guidelines for more detailed assessment of blackleg risk in specific situations. Up to two sprays of Aviator Xpro may be applied per season to the crop.

Fungicide Resistance Management Warning

GROUP	3	7	FUNGICIDE

Aviator Xpro is a member of the SDHI and DMI groups of fungicides. For fungicide resistance management the product is a Group 3 and a Group 7 fungicide. Some naturally occurring individual fungi resistant to the product and other Group 3 and Group 7 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 and other Group 3 and Group 7 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, Bayer Crop Science accepts no liability for any losses that result from failure of this product to control resistant fungi.

Export of treated produce
Growers should note that MRLs or import tolerances do not exist in all markets for produce treated with Aviator Xpro. If you are growing produce for export, please check with Bayer Crop Science for the latest information on MRLs and import tolerances before using Aviator Xpro.

Mixing
Emulsifiable concentrate (EC) formulations such as Aviator Xpro are known to strip chemical residues out of boomsprays and pumping/mixing equipment which can result in damage to sensitive crops. It may be necessary to clean or decontaminate spray and mixing/pumping equipment before applying Aviator Xpro to sensitive crops.

This decontamination should be to the level of removing any ALS inhibitor herbicides (Group B) such as imidazolinones, triazolopyrimidines or sulfonyl urea herbicides e.g. Ally®, Glean®, Logran®, Intervix® etc used in previous crops or by previous equipment owners. If a product has been used which requires a different or more rigorous decontamination then use the more rigorous decontamination process ensuring that all ALS inhibitor herbicides (Group B) will be thoroughly removed.

Application
Ground:
Apply product using a spray volume of 60 – 100 L/ha and a MEDIUM spray quality as defined by the ASABE S572 Standard.

Compatibility
Always consult Bayer Crop Science before mixing Aviator Xpro with other products. When Aviator Xpro is used in canola with herbicides that require an adjuvant (as per their registered label) significant adverse crop effects may result. These mixtures should be avoided. No more than one herbicide may be mixed with Aviator Xpro at any one time. DO NOT mix Aviator Xpro with liquid fertilisers when applying to canola prior to the commencement of flowering.

PRECAUTIONS
Re-entry or re-handling
Do not enter treated areas until the spray has dried, unless wearing cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical-resistant gloves. Clothing must be laundered after each day's use.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
DO NOT apply under weather conditions, or from spraying equipment, that may cause spray to drift onto nearby susceptible plants, crops, cropping lands or pastures.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Very toxic to aquatic life. DO NOT contaminate streams, rivers, drains or waterways with the chemical or used containers.

STORAGE AND DISPOSAL
Store in the closed, original container in a cool, well ventilated area. Do not store for prolonged periods in direct sunlight.

(10 L, 15 L, 20 L, 100 L, 110 L non returnable containers only)
Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and deliver empty packaging for appropriate disposal to an approved waste management facility. If an approved waste management facility is not

available bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots, in compliance with relevant Local, State or Territory government regulations. DO NOT burn empty containers or product. Do not re-use empty container for any other purpose.

(100 L, 110 L returnable containers only)
If tamper evident seals are broken prior to initial use then the integrity of the contents cannot be assured. Empty container by pumping through dry-break connection system. Do not attempt to breach the valve system or the filling point, or contaminate the container with water or other products.
Ensure that the coupler, pump, meter and hoses are disconnected, triple rinsed and drained after each use. When empty, or contents no longer required, return the container to the point of purchase. This container remains the property of Bayer CropScience Pty Ltd.

(1000 L containers)
If tamper evident seals are broken prior to initial use then the integrity of the contents cannot be assured. The container must be vented before discharging contents. To empty connect a camlock fitted hose to the bottom valve. Remove top cap when discharging for venting purposes. When the container is empty, close all caps and valves and return the container to the point of purchase.

SAFETY DIRECTIONS
Will damage eyes. May irritate the skin. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), chemical-resistant gloves and goggles. When using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical-resistant gloves. If product on skin, immediately wash area with soap and water. If product or spray in eyes, wash it out immediately with water. Wash hands after use. After each day's use wash gloves, goggles and contaminated clothing.

FIRST AID
If poisoning occurs contact a doctor or Poisons Information Centre (telephone 13 11 26).

ADDITIONAL USER SAFETY INFORMATION

WARNING: May cause birth defects.

SAFETY DATA SHEET
Additional information is listed in the Safety Data Sheet, which can be obtained from www.bayercropscience.com.au.

EXCLUSION OF LIABILITY
This product must be used strictly as directed, and in accordance with all instructions appearing on the label and in other reference material. So far as it is lawfully able to do so, Bayer CropScience Pty Ltd accepts no liability or responsibility for loss or damage arising from failure to follow such directions and instructions.

APVMA Approval No.: 69361/60590

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Batch Number: DOM: Barcode

Bayer

ABBREVIATIONS

ac	Active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	Active ingredient
ARfD	Acute Reference Dose
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
EI	Export Interval
EGI	Export Grazing Interval
ESI	Export Slaughter Interval
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
LLNA	Local lymph node assay
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
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
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 a material from or through 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	Repels water
Leaching	Removal of a compound by use of a solvent
Log Pow	Log to base 10 of octanol water partitioning co-efficient, synonym KOW
Metabolism	The chemical processes that maintain living organisms
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