Australian Government

Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of the new active bixlozone in the product Overwatch Herbicide

APVMA product number 86427

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This publication is available from the APVMA website.

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator responsible for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia. Before approving an active constituent and/or registering a product, the APVMA must be satisfied that the statutory criteria, including the safety, efficacy, trade and labelling criteria, have been met. The information and technical data required by the APVMA to assess the statutory criteria of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website.

The APVMA has a policy of encouraging transparency in its activities and seeking community involvement in decision making. Part of that process is the publication of public release summaries for products containing new active constituents. 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 advisory agencies, including other Australian Government agencies and State departments of primary industries. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience to encourage public comment.

About this document

This Public Release Summary 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 approval of the active constituent bixlozone and registration of the product Overwatch Herbicide 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 14 January 2020 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. Unless requested by the submitter, the APVMA may release a submission, with any CCI redacted, to the applicant for comment.

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

GPO Box 3262

Sydney NSW 2001

Phone: +61 2 6770 2300

Email: enquiries@apvma.gov.au

Further information

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

Copies of technical evaluation reports covering chemistry, efficacy and safety, 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.

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

1 INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Overwatch Herbicide, and approval of the new active constituent, bixlozone.

1.1 Applicant

FMC AUSTRALASIA PTY LTD

1.2 Purpose of application

FMC AUSTRALASIA PTY LTD has applied to the APVMA for approval of the new active constituent bixlozone and registration of the new product Overwatch Herbicide, containing 400 g/L bixlozone, formulated as a suspension concentrate.

1.3 Proposed claims and use pattern

The proposed product Overwatch Herbicide is intended for selective control of certain grasses and broad leaf weeds in wheat, barley and canola.

1.4 Mode of action

Overwatch Herbicide acts by blocking carotenoid biosynthesis in susceptible plants. The loss of the protective function of carotenoids leads to bleached leaves on the plants. Bleaching of crop leaves may also occur, so crop safety is an important consideration when applying Overwatch Herbicide.

Overwatch Herbicide controls the germinating weed seedling through uptake predominantly via roots and young shoots. Studies have shown that movement occurs in xylem tissue (transpiration pathway), and Overwatch Herbicide does not appear to demonstrate downward movement, or translocation from leaf to leaf.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

The active constituent bixlozone is manufactured overseas. Details of the chemical name, structure, and physicochemical properties of bixlozone are listed below (Tables 1 and 2).

Table 1: Nomenclature and structural formula of the active constituent bixlozone.

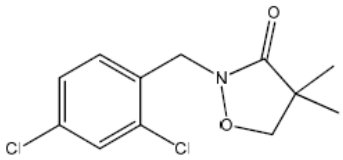
Common name (ISO):	Bixlozone
IUPAC name:	2-[(2,4-dichlorophenyl)methyl]-4,4-dimethyl-1,2-oxazolidin-3-one
CAS registry number:	81777-95-9
Molecular formula:	$C_{12}H_{13}Cl_2NO_2$
Molecular weight:	274.14 g/mol
Structural formula:	

Table 2: Key physicochemical properties of the active constituent bixlozone

Physical form:	Crystalline Solid at 20°C with various sized, easily friable, agglomerates.
Colour:	White (purified active), pale yellow/brown (Technical material)
Odour:	No discernible odour
Melting point:	81.5°C to 83.5°C (purified active)
Boiling point:	The test substance thermally decomposed before reaching the intrinsic boiling point under both atmospheric and reduced pressure
Relative density	1.37 g/cm^3 (20^{o}C)
Surface tension (purified active):	Surface tension at 90% of the saturation solubility (in pure water at 20°C) was found to be 66.5 mN/m.
Stability (TGAC):	The test item (F9600 TC) was found to be stable with respect to active ingredient content when stored for a period of 14 days at 54 ± 2°C. Additionally, the test substance showed no sign of physical changes after storage for a period of 14 days at 54 ± 2°C.

Corrosion characteristics:	The test item (F9600 TC) was stored in HDPE bottles for a period of 14 days at 54 ± 2°C. There were no visible signs of cracking, swelling, or deformation in the sample container after competition of the test.
Complex Formation with Metals:	No evidence was found for the formation of complexes between F9600 technical and the metal ions of copper, cadmium, lead, cobalt, chromium or zinc in water.
Safety properties (TGAC): **Flammability:**	Not considered highly flammable.
Explosive properties:	Not considered explosive.
Auto flammability:	Technical active constituent was found to have an auto-ignition temperature of 382°C
Oxidising properties:	None oxidizing
Solubility in water (TGAC):	Purified water: 42.0 ± 0.3 mg/L pH 4 buffer solution: 42.3 ± 2.2 mg/L pH 7 buffer solution: 39.6 ± 1.6 mg/L pH 9 buffer solution: 41.9 ± 1.8 mg/L
Organic solvent solubility (TGAC at 20°C):	Acetone: >250 g/L, Methanol: 120 g/L Dichloromethane: >250 g/L, *n*-Octanol: 52 g/L Ethyl acetate: >250 g/L, *n*-Heptane: 14 g/L Toluene: >250 g/L
PH (technical active):	Reported pH 5.86 ± 0.02 at a 1% dilution in ultrapure water.
Octanol/water partition coefficient (Log K_{ow}/K_{OW}):	@ pH 4: $\log_{10}P_{ow}$ = 3.3; P_{ow} = 2100 @ pH 7: $\log_{10}P_{ow}$ = 3.3; P_{ow} = 2160 @ pH 9: $\log_{10}P_{ow}$ = 3.3; P_{ow} = 2060
Vapour pressure:	2.3×10^{-3} Pa at 25°C
Henry's law constant:	7.2×10^{-3} Pa m^3/mol^{-1}
Photochemical properties (TGAI):	Photo-degradation of F9600 was moderate in buffer, yielding DT50 and DT90 values of 466 and >1000 hours, respectively. When calculated as equivalent days of summer sunlight at 30–50° N the DT50 and DT90 for the irradiated buffer were 17.4 days and 41.7 days, respectively. The results of this experiment indicate that F9600 degrades slowly by photolysis in buffer when exposed to artificial sunlight under laboratory conditions.

2.2 Summary

The purified active ingredient is a white, solid, odourless, crystalline solid, while the technical material is a pale yellow/brown solid with no characteristic odour. Bixlozone is neither flammable, explosive, nor oxidising.

The vapour pressure is 2.3 × 10–3 Pa at 25°C. The water solubility amounts to 42.0 ± 0.3 mg/L at 20°C. The n-octanol/ water partition coefficient (log Pow) is 3.3 indicating that bixlozone is moderately lipophilic. Surface tension at 90 per cent of the saturation solubility (pure water at 20°C) was found to be 66.5 mN/m. The active ingredient has good solubility in dichloromethane, acetone, toluene and ethyl acetate (> 250 g/L), while the solubility in methanol is (120 g/L). It has a lower solubility in n-heptane (14 g/L) and n-octanol (52 g/L). The relative density of the pure active is 1.37 g/cm3 at 20°C.

2.3 Formulated product

The product Overwatch Herbicide will be manufactured overseas. Tables 3 and 4 outline some key aspects of the formulation and physicochemical properties of the product.

Table 3: Key aspects of the product Overwatch Herbicide

Distinguishing name:	Overwatch Herbicide
Formulation type:	Suspension Concentrate (SC)
Active constituent concentration:	400 g/L

Table 4: Physicochemical properties of the product Overwatch Herbicide

Physical form:	A uniform, mobile liquid, with opaque colour and a characteristic smell.
PH:	7.34 (neat, @ 20°C) 7.18 (1% dilution @ 20°C)
Relative density:	1.1
Kinematic viscosity:	103 mPa.s (20°C, 100 s^{-1}) 75.5 mPa.s (40°C, 100 s^{-1})
Surface tension at 20°C	37.20 mN/m (neat) 46.71 mN/m (1 g/L dilution), 34.65 mN/m (minimum dilution at 10 mL product/L water) and 47.73 mN/M (minimum dilution at 0.63 mL product/L water)
Pourability:	Maximum 5% residue; maximum 0.25% rinsed residue
Spontaneity of dispersion:	60–105%
Suspensibility:	60–105%
Wet sieve analysis:	Maximum 2% retained on a 75 µm sieve
Persistent foam:	Maximum 60 mL foam after 1 minute
Safety properties: **Explosive properties,** **Oxidising properties.**	This is an aqueous-based preparation, and does not exhibit either oxidising or explosive properties.
Auto-ignition temperature (Auto flammability):	423°C
Corrosive hazard:	Not corrosive
Storage stability:	The active content and all of the physico-chemical properties of formulation remained within product specification after storage at both elevated and low temperatures and cold storage after testig. The product is expected to remain within the specifications for at least two (2) years when stored under normal conditions.
Packaging	HDPE bottle with screw top lid. No product bottle interaction

2.4 Summary

The formulated product is a uniform, mobile liquid, with opaque colour and a characteristic smell in form of a suspension concentrate formulation. It has a pH of 7.34 when neat, at 20°C and 7.18 at one per cent dilution at 20°C. Viscosity of the product is 103 mPa.s at 20°C, 100 s-1 and 75.5 mPa.s at 40°C, 100 s-1. Overwatch Herbicide is an aqueous-based preparation and not explosive, oxidising or corrosive. The active content and all of the physico-chemical properties of formulation remained within the product specifications at both elevated temperature and under cold storage. It is expected that the product should remain within specifications for at least two years when stored under normal conditions.

2.5 Recommendations

The APVMA has evaluated the chemistry of the active constituent bixlozone and associated product Overwatch Herbicide, including the manufacturing process, quality control procedures, identification, stability, batch analysis results and analytical methods, and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least two years when stored under normal conditions.

The registration of Overwatch Herbicide, and approval of the active constituent bixlozone, are supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

The toxicological database for bixlozone, which consists primarily of toxicity studies conducted in vitro and in vivo, in rats, mice, rabbits and dogs, is considered sufficient to determine the toxicology profile of bixlozone and characterise the risk to humans. 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 does 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 robust 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 takes into account the likely human exposure levels compared with those 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-Adverse-Effect-Level (NOAEL) are used to develop acceptable limits for dietary or other intakes at which no adverse health effects in humans would be expected.

3.1 Evaluation of toxicology

Chemical class

Bixlozone is a member of the chlorophenyl isoxazolidinones class of herbicides. Bixlozone inhibits the terpenoid synthesis pathway between isopentenyl pyrophosphate and geranylgeranyl pyrophosphate. This pathway provides the precursors for the major plant pigments, chlorophyll and carotenoids.

Pharmacokinetics

Radiolabelled bixlozone was rapidly and extensively absorbed following single or 14 day repeat doses of 5 mg/kg bw, excreted primarily in the urine with the balance excreted primarily in the faeces following biliary excretion into the gut. Excretion as exhaled CO_2 is minimal. Comparison of intravenous and single or 14 day repeat oral doses of radiolabelled bixlozone indicate bioavailability of the radiolabel is high but that for the parent compound is very low due to a high first pass metabolism by the liver. Parent bixlozone accounts for only 0.5 to six per cent of the circulating radiolabel. Consequently, oral toxicology studies have primarily investigated the toxicity of the metabolites, except for the liver which experiences the highest exposure to the parent compound (other than the gut). Radiolabelled bixlozone has a moderate half-life of approximately 10–16 hours but does not accumulate in the tissues and most of an administered dose/radiolabel is excreted over 48 hours. Parent bixlozone has a shorter half-life of approximately two hours.

In rat, mouse, dog and human liver cells in vitro, bixlozone was extensively or substantially metabolised with no unique human metabolites observed. No gender or radiolabel differences in metabolite profile were seen in human hepatocytes. The common metabolic reactions in all species tested included oxidation (hydroxylation) and conjugation (glucuronidation, sulphation).

A dermal absorption study in rats using a product formulation to model exposure to the product concentrate and spray dilutions, found absorption of the concentrate was < 0.3 per cent and for the dilute preparations was < five per cent (3.33 g/L active) and < 16 per cent (0.25 g/L active).

Acute toxicity (active constituent)

Bixlozone has low acute oral, dermal and inhalational toxicity. It is not an eye or skin irritant and is not a skin sensitiser.

Acute toxicity (product)

The product Overwatch Herbicide has low acute oral, dermal and inhalational toxicity. It is not an eye irritant or skin sensitiser and is at most a slight skin irritant following prolonged contact under a semi occlusive dressing.

Repeat-dose toxicity

In repeat dose studies the primary target organ for toxicity was the liver, manifest at lower doses by an adaptive increase in liver weight with hepatocellular hypertrophy. This is indicative of enzyme induction due to a high chemical load. Little evidence of frank liver toxicity after high and prolonged dosing was observed with effects limited to increases in relative liver weights > 20 per cent above control with no liver necrosis or unequivocal liver dysfunction observed. The other effects tending to set NOAELs in repeat dose studies were lower body weights and body weight gains. These effects are largely a non-specific indicator of toxicity or general malaise.

Due to low dermal penetration, toxicity via the dermal route is low. In a 21-day dermal toxicity study in rats, bixlozone was applied daily at doses of 0, 100, 300 and 1000 mg/kg bw/d. There were no treatment related effects on any parameter examined and the NOAEL was 1000 mg/kg bw/day, the highest dose tested.

Chronic toxicity and carcinogenicity

Bixlozone was not carcinogenic in long term studies in rats administered bixlozone in the diet at 0, 250, 1000 or 5000/4000 ppm (male/female) for two years or in mice administered bixlozone in the diet at levels of 0, 250, 1000, and 5000 ppm. The NOAEL for both chronic toxicity and carcinogenicity in mice was 5000 ppm equal to 647 mg/kg bw/day, which was the highest dose tested. The NOAEL for carcinogenicity in the rat study was 3000 ppm, equal to 167 mg/kg bw/day, which was the highest dose tested. In the chronic toxicity arm of the rat study, decreased terminal weight was seen in females at 3000 ppm, with bodyweights more than 10 per cent below controls. This effect was associated with a loss of skin tone, as well as thin body condition. The NOAEL for chronic effects was thus set at 1000 ppm equal to 53 mg/kg bw/day.

Neither the rat nor the mouse study indicates bixlozone presents a carcinogenic risk to humans

Reproductive and developmental toxicity

In a two generation reproduction study bixlozone was administered to rats at doses of 0, 150, 750 or 3000 ppm from at least 70 days prior to mating. There were no effects on reproductive performance at any dose.

The NOAEL for reproductive performance was therefore 3000 ppm equal to 238 mg/kg bw/day. The NOAEL for parental toxicity was 750 ppm (equal to 34 mg/kg bw/day) based on persistent perturbations of weight gains in F0 & F1 females and F1 males at 3000 ppm. The NOAEL for neonatal toxicity was 750 ppm (34 mg/kg bw/day) based on lower F2 pup body weights and body weight gains in both sexes at 3000 ppm during the pre-weaning period only.

In a dose ranging study pregnant rats were administered bixlozone by oral gavage at 0, 25, 75, 225, and 675 mg/kg bw/day from gestation days six through 19. One rat at 675 mg/kg bw/day was sacrificed in extremis and lower maternal body weight and gravid uterine weights, as well as lower foetal body weights, were seen at this dose. Elevated absolute and relative liver weights were seen at 225 and 675 mg/kg/day. There were no malformations or developmental abnormalities observed at any dose. This is a range finding study and the design is not intended to yield a robust NOAEL.

In the definitive rat developmental study, pregnant rats were administered bixlozone by oral gavage at 0, 75, 225, and 550 mg/kg bw/day on gestation days six to 19. There were no effects on foetal toxicity or development and the NOAEL for foetal effects was therefore 550 mg/kg bw/day, the highest dose tested. The NOAEL for maternal toxicity was 225 mg/kg bw/day based on reduced body weight gains and elevated liver weights with associated mild to moderate hepatocellular hypertrophy at 550 mg/kg bw/day.

In a dose range finding study bixlozone was administered orally by gavage to time-mated female rabbits from gestation days (GD) seven through 28 at doses of 0, 100, 350, 750, and 1000 mg/kg/day. Mortality was seen at 750 and 1000 mg/kg bw/day. Animals at 100 and 350 mg/kg bw/day lost weight during gestation associated with reduced mean food consumption and had lower liver weights, likely secondary to reduced food consumption. This was a non-guideline range finding study with small group sizes and is not suitable for the establishment of a NOAEL. No foetal or developmental effects were observed at < 350 mg/kg bw/day.

In the definitive rabbit developmental study pregnant rabbits were administered bixlozone by oral gavage at 0, 25, 75, 200, and 400 mg/kg/day from gestation day seven through 28. There were no effects on maternal animals or foetuses. The NOAEL for maternal toxicity was 400 mg/kg bw/day the highest dose tested. The NOAEL for foetal toxicity and teratogenicity was 400 mg/kg bw/day the highest dose tested.

Bixlozone is not a teratogen in rabbits or rats.

Genotoxicity

Bixlozone was tested for genotoxicity in an adequate range of in vitro and in vivo assays. Bixlozone was negative in a mouse bone marrow micronucleus test in vivo and in all in vitro genotoxicity tests (Bacterial Point Mutations Assay × 2, Mouse lymphoma L5178Y Tk locus gene mutation assay, V79 Chinese hamster cells, HPRT test).

Neurotoxicity/immunotoxicity

Bixlozone is not an acute neurotoxin at doses tested at up to 2000 mg/kg bw/day and was not neurotoxic in a 90-day study at 351 mg/kg bw/day.

3.2 Health-based guidance values and poisons scheduling

Poisons standard

A Delegate of the Secretary of the Department of Health published a final decision to include bixlozone in Appendix B of the Poisons Standard. The reasons for the decision was based on the low toxicity profile.

Health-based guidance values

Acceptable Daily Intake (ADI)

The ADI for humans is considered to be a level of intake of a chemical that can be ingested daily over an entire lifetime without any appreciable risk to health. An ADI of 0.3 mg/kg bw/d has been established for bixlozone, utilising a NOAEL of 34 mg/kg bw/d in a two generation reproduction based on reduced parental body weight gains and reduced neonatal weight gains during pre-weaning at the next higher dose.

Acute Reference Dose (ARfD)

The ARfD is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed in a single meal or over a single day as an isolated event. Based on its acute toxicity profile it was concluded that the establishment of an ARfD was not necessary for bixlozone on the basis of its low acute toxicity, the lack of evidence for any acute neurotoxicity and the absence of any other toxicologically relevant effect that might be attributable to a single dose, or single day exposure, at realistically achievable dietary intakes.

3.3 Recommendations

There are no objections on human health grounds to the approval of the active bixlozone and registration of the product Overwatch Herbicide, containing 400 g/L of bixlozone.

4 RESIDUES ASSESSMENT

4.1 Metabolism

The APVMA reviewed details of bixlozone metabolism studies on wheat, canola, sugar beet, rice and confined rotational crops (lettuce, radish, wheat). Studies on the metabolism of bixlozone in lactating goats and laying hens was also assessed.

Plant metabolism

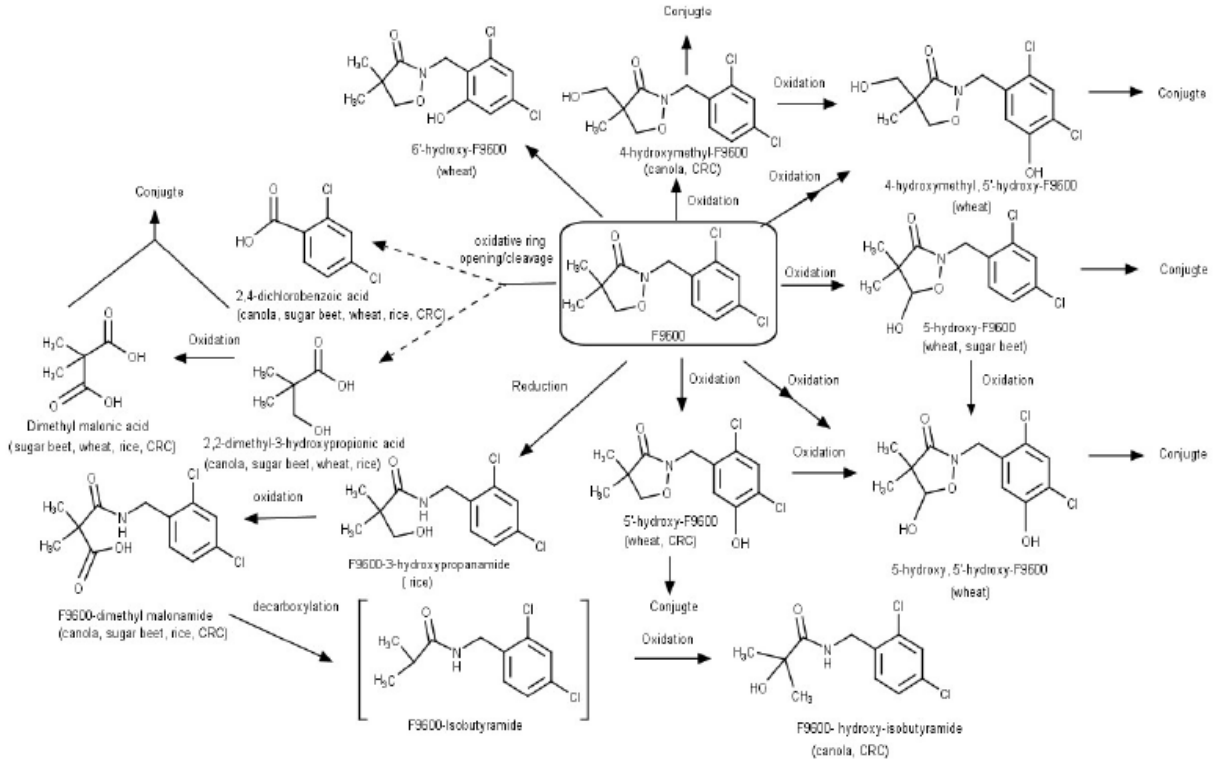
Early post emergent applications of ^{14}C phenyl or carbonyl labelled bixlozone (F9600) were made to wheat, canola, sugar beet and rice at 300–375 g ai/ha. For the confined rotational crop study, application was made to bare soil and the following crops of lettuce, wheat and radish sown after periods of 30, 120 and 310 days. Crops were harvested at appropriate intervals.

No parent was detected in any of the crop commodities after pre- and early post emergence application of ^{14}C-bixlozone on wheat, canola, sugar beet or rice. In confined rotational crops, parent was also not detected in lettuce and wheat crops; however, detectable levels of parent were present in radish tops and root, particularly in earlier plant back intervals of 30 and 120 days (up to 76 per cent TRR, 0.037 mg/kg in radish roots).

The majority of the metabolites of bixlozone were common to all crops, however, unlike in other crops, 5'-hydroxy-F9600 constitutes the major residue in wheat (up to 49 per cent TRR, 0.48 mg eq/kg in forage). There is evidence of formation of double-hydroxylated metabolites: 4-hydroxymethyl, 5'-hydroxy-F9600 and 5-hydroxy, 5'-hydroxy-F9600 metabolites in wheat forage and straw. 2,2-Dimethyl-3-hydroxypropionic acid was significant in wheat grain (44 per cent TRR, 0.038 mg eq/kg), but this metabolite was found in untreated control samples in the residue trials and is considered to be a natural plant product. 2,4-Dichlorobenzoic acid was also found in wheat grain for the phenyl label (26 per cent TRR, 0.037 mg eq/kg). Metabolism of bixlozone is qualitatively similar in primary and rotated crops, although significantly higher residue levels of F9600-hydroxy-isobutyramide were present in rotated crops.

A metabolic pathway for bixlozone in crops is summarised below. Metabolism in plants primarily occurs via hydroxylation of the aromatic or isoxazolidinone moieties followed by conjugation. The hydroxylated metabolites include 5-hydroxy-F9600, 4-hydroxymethyl-F9600 formed on isoxazolidinone ring; and 5'-hydroxy-F9600 and 6'-hydroxy-F9600 on aromatic moiety. Additional pathways include oxidative ring opening of F9600 leading to the formation of F9600-3-hydroxy-propanamide, which oxidizes to F9600-dimethyl-malonamide followed by decarboxylation to yield F9600-hydroxy-isobutyramide. Other reactions include oxidative ring opening/cleavage to form 2,4-DCBA, 2,2-dimethyl-3-hydroxypropionic acid and dimethyl-malonic acid.

Figure 1: Proposed metabolic pathway for bixlozone in primary and rotational crops



Metabolism in target animals

Lactating goats were orally dosed with ^{14}C phenyl or carbonyl labelled bixlozone for seven consecutive days at approximately 21 ppm in the feed. The goats were milked by hand twice daily (morning and afternoon). Milk was collected prior to dosing each morning. The goats were sacrificed approximately six to eight hours after administration of the final dose and tissues collected for analysis.

The ^{14}C residue in milk reached a steady state after the second dose. Highest TRRs (up to 0.369 mg equiv./kg) were in kidney and liver, with lower values in other tissues and milk. Parent compound was not detected in tissues or milk. 5-OH-F9600 (up to 46 per cent, 0.158 mg equiv./kg), F9600-3-OH-propanamide (up to 30 per cent, 0.102 mg equiv./kg), F9600-dimethyl malonamide (up to 16 per cent, 0.058 mg equiv./kg) and the natural product 2,2-dimethyl-3-OH-propionic acid represented the major metabolites in goats. Metabolic pathways of bixlozone in lactating goats constituted hydroxylation, oxidative ring opening and deamination followed by conjugation as summarised below:

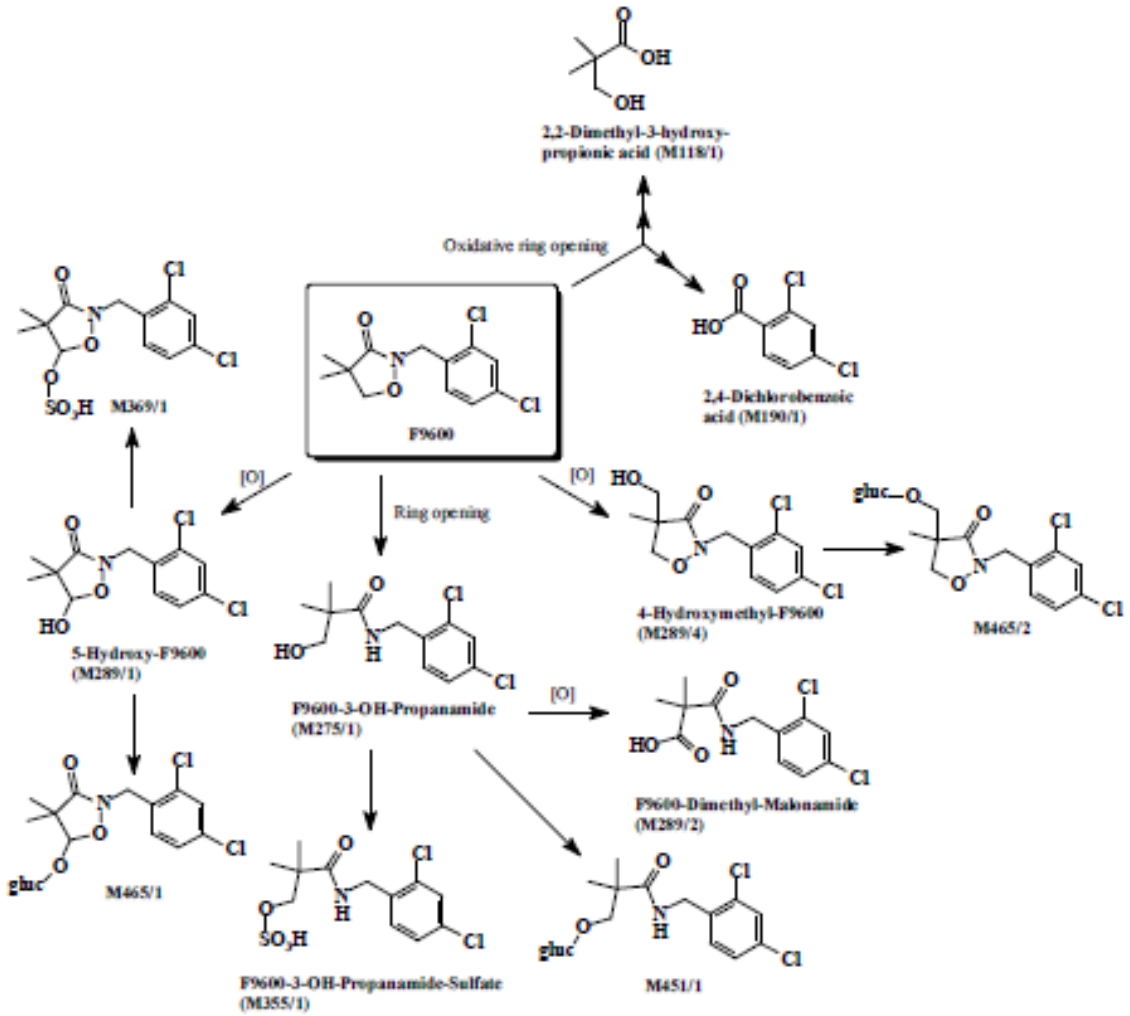


Figure 2: Proposed metabolic pathway for bixlozone in lactating goats

Laying hens were orally dosed with phenyl or carbonyl labelled ^{14}C-bixlozone for 13 consecutive days at approximately 20 ppm in the feed. Eggs were collected daily (morning and afternoon) throughout the study. The morning egg collection was performed prior to dosing. The hens were sacrificed approximately six to eight hours after administration of the final dose and tissues collected for analysis.

The ^{14}C residue in eggs reached a steady state around nine days. Highest TRRs were in liver (up to 0.609 mg equiv./kg). Low levels of parent compound were detected in fat from the phenyl label (9.3 per cent, 0.025 mg/kg). 5-OH-F9600, 4-hydroxy-methyl-F9600 , dimethyl-malonamide-F9600 (up to 0.104 mg equiv./kg in liver, 21 per cent TRR), 2,4-dichlorobenzoic acid (M190/1), dimethylmalonic acid, 2,2 dimethyl-3-OH – propionic acid (up to 0.196 mg equiv./kg in liver, 40 per cent TRR), 2,4-Dichlorobenzaldoxime were observed in hens.

Metabolic pathways of bixlozone in laying hens constituted hydroxylation, oxidative ring opening and deamination followed by conjugation as summarised below:

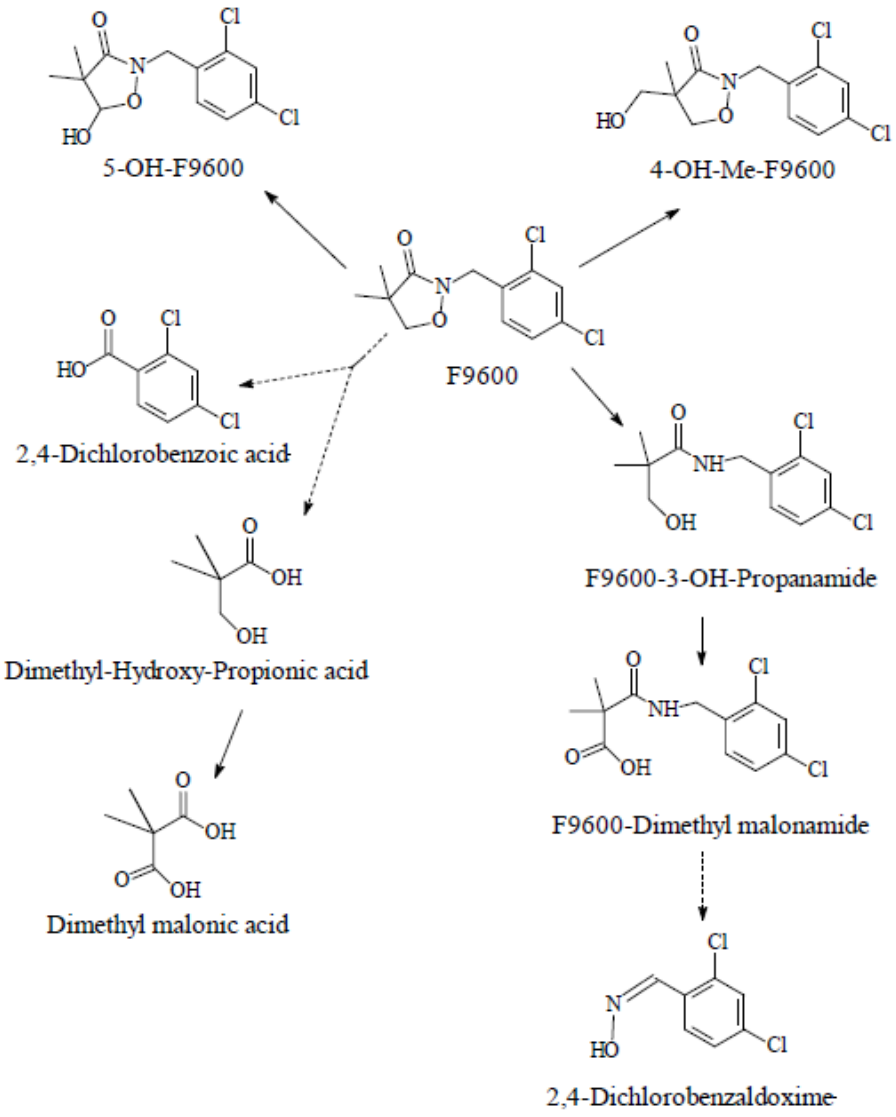


Figure 3: Proposed metabolic pathway for bixlozone in the laying hen

4.2 Analytical methods and storage stability

Method for plant commodities

Details of a method for the determination of bixlozone and its metabolites 2,4-dichlorobenzoic acid, 5-hydroxy-F9600, 5'-hydroxy-F9600 and 2,2-dimethyl-3-hydroxy propionic acid in crop matrices were provided.

Crop matrices were extracted by refluxing in 1N hydrochloric acid (HCl) then using a QuEChERS salt mixture with addition of acetonitrile. The final extract was analysed by LC-MS/MS.

The LOQ for bixlozone, 2,4-dichlorobenzoic acid, 5-hydroxy-F9600 and 5'-hydroxy-F9600 in all crop matrices is 0.01 mg/kg. The LOQ for 2,2-dimethyl-3-hydroxy propionic acid in wet and acidic matrices is 0.01 mg/kg

and for dry and oily matrices is 0.05 mg/kg. Recoveries from fortified control samples were generally within acceptable limits in the field trials.

Method for animal commodities

A method was presented for the determination of bixlozone, and its metabolites 5-OH-F9600, F9600-3-OH propanamide and F9600-dimethyl malonamide in foodstuff of animal origin (milk, muscle, kidney, liver, fat and eggs) with an intended limit of quantification (LOQ) of 0.01 mg/kg.

Samples of milk, muscle, kidney, liver, fat and egg were extracted with acetonitrile and if necessary, after addition of water. A salt mixture containing magnesium sulphate, sodium chloride and sodium citrate was added and the extract was shaken. After centrifugation an aliquot of the acetonitrile phase was diluted with water containing 0.05 per cent acetic acid. Only for fat samples an aliquot of the acetonitrile extract was kept at ≤ -18°C for at least one hour and then an aliquot was diluted with water containing acetic acid. Quantification was by LC-MS/MS. Recoveries from fortified control samples were within acceptable limits.

Storage stability

The stability of bixlozone and its metabolites (2,4- dichlorobenzoic acid, 5-hydroxy-F9600 and 2,2-dimethyl-3-hydroxy propionic acid) was investigated in four representative crop matrices [wheat straw (dry plant commodity), oilseed rape seed (high oil content commodity), potato (high water and high starch content commodity) and grapes (high acid and high water content commodity)] following frozen storage for up to 24 months. Individual specimens of each crop matrix were fortified with bixlozone (F9600) and its metabolites at a concentration level of 0.1 mg/kg and stored at ≤-18°C.

There was no significant decrease (<30 per cent compared to the zero-time value) in the observed residue levels of bixlozone (F9600), 2,4-dichlorobenzoic acid or 2,2-dimethyl-3-hydroxy propionic acid in any of the tested crop matrices when stored frozen at <-18°C for a period up to 24 months or in 5-hydroxy-F9600 in any of the tested crop matrices when stored frozen at <-18°C for a period of up to 18 months (the 24 month time point was not tested).

In the residue trials submitted, all samples were maintained under freezer conditions, (ie -18°C) prior to analysis and tested within three years of collection for one canola study and ≤ two years for the remaining studies. This is acceptable for the purposes of the current application.

4.3 Residue definition

Plant commodities

Parent compound was not detected in the available plant metabolism studies with the exception of some samples of radish in the confined rotational crop study. In the available canola and cereal residue trials parent was detected in forage at earlier sampling times and at low levels in some samples of straw/stubble at harvest.

The main plant metabolites were 5-hydroxy-F9600, 5'-hydroxy-F9600, 2,4-dichlorobenzoic acid, F9600-dimethyl-malonamide and 2,2-dimethyl-3-hydroxypropionic acid. However, 2,2-dimethyl-3-hydroxypropionic acid was found in some untreated samples at comparable levels to the treated samples in the residues trials and is considered to be a natural plant product so is not suitable for inclusion in the residue definition for bixlozone. 2,4-Dichlorobenzoic acid is the target for some common moiety analytical methods for propiconazole (2007 JMPR) and is also not considered suitable for inclusion in the residues definition. F9600-dimethyl-malonamide was significant in rice straw, but not observed in wheat as a primary crop and was <0.01 mg/kg in the canola metabolism study. It was not analysed for in the residue trials.

Given the low residues of parent and metabolites expected in grain/seed and straw/stubble and the fact that parent residues in forage were generally the main component in the residue trials that analysed for parent, 5-OH-F9600, 5'OH-F9600, 2,4-DCBA and HPA, a residue definition of parent only is suitable for enforcement for commodities of plant origin for the use patterns considered here. This is also suitable for risk assessment given quantifiable residues are not expected to occur in animal commodities consuming treated forage (see below).

Animal commodities

5-Hydroxy-F9600, F9600-3-hydroxy-propanamide, F9600-dimethyl malonamide and the natural product 2,2-dimethyl-3-OH-propionic acid represented the major metabolites in goats. 5-Hydroxy-F9600, 4-hydroxy-methyl-F9600, dimethyl-malonamide-F9600, 2,4-dichlorobenzoic acid, dimethylmalonic acid, 2,2 dimethyl-3-OH –propionic acid and 2,4-Dichlorobenzaldoxime (M189/1) were observed in hen.

The main plant metabolites 2,2-dimethyl-3-hydroxypropionic acid, 2,4-dichlorobenzoic acid and 5-hydroxy-9600 were observed in goats and hens. The exception was 5'-hydroxy-9600 which was not observed in the goat and hen metabolism studies. However, 5'-hydroxy-9600 was <LOD in the available canola residue trials, <LOD in cereal grain (where analysed) and <0.1 mg/kg in cereal forage and straw after the proposed withholding period and when scaled for application rate. 2,4-Dichlorobenzoic acid was also <0.1 mg/kg dry weight in forage and straw after the proposed grazing WHP and scaling for application rate.

The highest combined residue of parent + 5-hydroxy-9600 in forage at the proposed grazing WHP was 0.47 mg/kg in parent equivalents scaled for application rate. In the lactating goat metabolism study dosing at 20.9 ppm gave a maximum total radioactive residue in kidney of 0.369 mg eq/kg. Dosing at 0.47 ppm would give a predicted total residue of 0.008 mg eq/kg. Given this is a total residue, the proposed use should not result in quantifiable residues of bixlozone or its metabolites in animal commodities. A residue definition of parent compound only is recommended for bixlozone in animal commodities for both enforcement and risk assessment. This residue definition may be revised in the future should a use pattern be applied for that would result in higher residues of bixlozone or its metabolites in animal feeds.

4.4 Residues in food and animal feeds

Canola

Six Australian GLP trials investigated residues in canola seed after application at higher rates than proposed. Residues of bixlozone in canola seed at harvest after a post planting/pre-emergent application at a nominal

rate of 1000 g ai/ha (2×) were <0.005 (6) mg/kg. An MRL of *0.01 mg/kg is recommended for bixlozone on SO 0495 Rape seed [canola].

Residues of parent bixlozone in canola forage at 84 days after a post planting/pre-emergent application at a nominal rate of 1000 g ai/ha (2×) were 0.15, 0.17, 0.32, 0.33 and 0.44 mg/kg dry weight. Scaled for the proposed application rate residues were 0.08, 0.09, 0.16, 0.17 and 0.22 mg/kg dry weight. The OECD MRL calculator recommends and MRL of 0.5 mg/kg, the STMR is 0.16 mg/kg, n = 5. An MRL of 0.5 mg/kg is recommended for bixlozone on Canola forage in conjunction with a 12 week grazing WHP.

Residues of bixlozone in canola stubble at harvest after a post planting/pre-emergent application at a nominal rate of 1000 g ai/ha (2×) were <0.005 (3), <0.01 (2) and 0.023 mg/kg. Scaled for application rate residues were <0.01 (5) and 0.01 mg/kg. The OECD MRL calculator recommends an MRL of 0.015 mg/kg. An MRL of 0.02 mg/kg is recommended for bixlozone on Canola fodder, dry.

Wheat and barley

Fourteen Australian GLP trials on cereals (wheat, barley and oats) investigated residues in grain after application at higher rates than proposed. Residues of bixlozone in cereal grain at harvest after a pre-emergent application at a nominal rate of 1000 g ai/ha (2×) were <0.003 (5), 0.004 and <0.005 (8) mg/kg. MRLs of *0.01 mg/kg are recommended for bixlozone on GC 0640 Barley and GC 0654 Wheat.

Residues of bixlozone in cereal forage at 77–84 days after a post pre-emergent application at a nominal rate of 1000 g ai/ha (2×) were <0.003 (3), <0.005, 0.028, 0.035, 0.042, 0.045, 0.049, 0.050, 0.053, 0.070, 0.092, 0.11 and 0.16 mg/kg dry weight. Scaled for the proposed application rate residues were <0.01 (4), 0.014, 0.018, 0.021, 0.023, 0.025 (2), 0.027, 0.035, 0.046, 0.055 and 0.08 mg/kg dry weight. The OECD calculator recommends an MRL of 0.15 mg/kg, the STMR is 0.023 mg/kg (n = 15).

Residues of bixlozone in cereal straw at harvest after a pre-emergent application at a nominal rate of 1000 g ai/ha (2×) were <0.003, <0.005 (2), 0.006, 0.01, 0.012 (2), 0.017, 0.020, 0.025, 0.030, 0.048, 0.055, 0.12 and 0.36 mg/kg dry weight. Scaled for the proposed application rate residues were <0.01 (8), 0.01, 0.013, 0.015, 0.024, 0.028, 0.06 and 0.18 mg/kg dry weight. The OECD MRL calculator recommends an MRL of 0.2 mg/kg, the STMR is 0.01 mg/kg.

MRLs of 0.2 mg/kg are recommended for bixlozone on barley forage, fodder and straw and wheat forage, fodder and straw, in conjunction with a 12 week grazing withholding period.

4.5 Crop rotation

Two field rotational crop trials were conducted on radish, leaf lettuce and wheat during 2016 and 2017 in Germany and Spain. A single application of an SC formulation of bixlozone was made to maize at growth stage BBCH 11–13 at a target rate of 300 g ai/ha (0.6× proposed) in a spray volume of 150 to 400 L/ha. Three nominal plant back intervals (PBI's) were investigated: 30, 60 and 220 days. Maize plants were incorporated into the soil before planting / drilling of rotational crops with a PBI of 30 days. For crops with a 60 and 220 day PBI, the maize plants were cut above the soil, removed from the plot and discarded. The remaining maize stems and roots were incorporated into the soil.

The rotational crop field trials involved a lower application rate (300 g ai/ha) than proposed (0.6×). Residues were generally not detected in the Spanish trial, with only two detections of parent bixlozone approximately at the LOQ (0.01 mg/kg) in the German trial in radish leaves and lettuce from crops grown after a 220 day plant back interval. It is noted that detectable residues were not observed in canola or cereal grains at harvest in the primary crop residue trials involving application at 2× the proposed rate. It is not necessary to set separate MRLs for other cereal, oilseed or pulse crops to cover the potential for residues in these commodities in rotational situations. For other commodities, including leafy crops, the scaled high parent bixlozone residue from the German rotational field trial would be 0.018 mg/kg (in lettuce leaves after a 220 day PBI), although residues were not observed in the Spanish trial, which would be expected to be closer to Australian conditions than the trial conducted in Northern Europe. It is therefore considered that an “all other foods” MRL is not required in the APVMA MRL standard for the use patterns considered here.

4.6 Residues in animal commodities

APVMA guidelines indicate that oilseed or cereal forage and fodder can form 100 per cent of the diet for mammalian livestock. Highest residues of parent in these feeds in the available trials were 0.18 mg/kg in cereal straw and 0.22 mg/kg in canola forage. The maximum mammalian livestock dietary burden will be 0.22 ppm resulting from consumption of canola forage as 100 per cent of the diet.

An animal transfer study for bixlozone is not available. In the lactating goat metabolism study dosing at 20.9 ppm gave a maximum total radioactive residue in kidney of 0.369 mg eq/kg. The total estimated residue in kidney from feeding parent at 0.22 ppm is 0.004 mg/kg. Given that this is a total residue it is appropriate to establish mammalian animal commodity MRLs at the LOQ for the analytical method. The following MRLs are recommended:

MO 0105 Edible offal (mammalian)	*0.01 mg/kg
MM 0095 Meat (mammalian)	*0.01 mg/kg
ML 0106 Milks	*0.01 mg/kg

Poultry

Detectable residues of bixlozone are not expected to occur in cereal grain or canola seed/meal from the proposed uses. Poultry should not be exposed to residues of bixlozone. Poultry commodity MRLs will be established at the LOQ for the analytical method. The following MRLs are recommended:

PE 0112 Eggs	*0.01 mg/kg
PO 0111 Poultry, edible offal of	*0.01 mg/kg
PM 0110 Poultry meat	*0.01 mg/kg

4.7 Spray drift

The product will be applied by ground application only using a coarse spray droplet size.

An animal transfer study for bixlozone is not currently available to allow for a refined determination of the Regulatory Acceptable Level (RAL) for livestock areas, which is the level residue in animal feed that should

not result in residues in animal commodities that may present an undue risk to international trade. As bixlozone MRLs have not yet been established overseas, the LOQ for animal commodities of 0.01 mg/kg is considered as the endpoint. A lactating goat metabolism study is available for consideration and the highest individual component residue will be considered noting that residue definitions have not been established overseas at this time.

The highest individual component (5-Hydroxy-F9600) in the goat metabolism study was found at 0.158 mg equiv/kg in kidney after dosing at 20.5 ppm (phenyl label). The feeding level for this component of the total residue to be at the LOQ (0.01 mg/kg) is 1.30 ppm. If a RAL of 1.30 ppm is used in the APVMA spray drift risk assessment tool a buffer is not required for application by boom spray and is 28 metres (unrounded) if the release height is >0.5 metres. The following label instructions are appropriate:

DO NOT apply by a boom sprayer unless the following requirements are met:

- spray droplets not smaller than a COARSE spray droplet size category
- minimum distances between the application site and downwind sensitive areas (see 'Mandatory buffer zones' section of the following table titled 'Buffer zones for boom sprayers') are observed.

Table 5: Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Livestock areas
Up to maximum label rate	0.5 m or lower	Not required
	Over 0.5 m	30 metres

4.8 Dietary risk assessment

The chronic dietary exposure to bixlozone 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 2011–12 National Nutritional and Physical Activity Survey. 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 bixlozone is equivalent to <one per cent of the ADI. It is concluded that the chronic dietary exposure to bixlozone is acceptable.

An acute reference dose was considered unnecessary for bixlozone. A National Estimated Short Term Intake (NESTI) calculation for acute exposure was not required.

4.9 Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 6).

Table 6: Amendments to the APVMA MRL Standard

Amendments to Table 1			
Compound		**Food**	**MRL (mg/kg)**
ADD:			
Bixlozone			
GC	0640	Barley	*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
SO	0495	Rape seed [canola]	*0.01
GC	0654	Wheat	*0.01

Amendments to Table 3	
Compound	**Residue**
ADD:	
Bixlozone	Bixlozone

Amendments to Table 4			
Compound		**Animal feed commodity**	**MRL (mg/kg)**
ADD:			
Bixlozone			
		Barley forage, fodder and straw	0.2
		Canola fodder, dry	0.02
		Canola forage	0.5
		Wheat forage, fodder and straw	0.2

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported and main destinations

Canola seed, oil and meal and wheat and barley 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, wheat and barley. Residues in these commodities resulting from the use of Overwatch Herbicide may have the potential to unduly prejudice trade.

Total exports of canola seed and oil in 2017–18 were 2,252 kt, and 159 kt respectively (ABARES). No canola meal was exported in 2017–18, while 6.1 kt was exported in 2016–17. The main export markets for canola seed were the EU (Germany, France, Belgium, the Netherlands), Japan, Bangladesh and China.

Total exports of barley were 7 997 kilotonnes in 2017–18, valued at $2.30 billion. Total exports of wheat (including flour) were 15 492 kilotonnes in 2017–18, valued at $4.67 billion (ABARES). Major export destinations are summarised below:

Table 7: Major export destinations of wheat and barley

COMMODITY	MAJOR DESTINATIONS
Barley	China, Japan, Korea, Vietnam, the Philippines, Taiwan, Saudi Arabia, Kuwait, United Arab Emirates
Wheat	Indonesia, India, Korea, China, Japan, Thailand, Malaysia, Philippines, Vietnam, Egypt, Nigeria, Yemen, Kuwait, New Zealand

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).

5.2 Overseas registrations and approved label instructions

Bixlozone is not currently approved overseas, however the applicant indicated that a similar registration is proceeding in the EU.

5.3 Comparison of Australian MRLs with Codex and international MRLs

The Codex Alimentarius Commission (Codex) is responsible for establishing Codex Maximum Residue Limits (CXLs) for pesticides. CXLs are primarily intended to facilitate international trade, and accommodate differences in Good Agricultural Practice (GAP) employed by various countries. Some countries may accept Codex CXLs when importing foods. Bixlozone has not been considered by Codex. No relevant international MRLs have been established for bixlozone.

5.4 Potential risk to trade

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

As detectable residues of bixlozone are not expected to occur in canola seed or wheat and barley grain, or in animal commodities from the proposed use, the risk to trade is considered to be low.

6 WORK HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

The product Overwatch Herbicide has low acute oral, dermal and inhalational toxicity is not an eye irritant or skin sensitiser and is at most a very slight skin irritant. No treatment related effects were observed in a 21-day dermal toxicity study in rats at doses up to 1000 mg/kg bw/d.

6.2 Occupational exposure

Exposure during use

Farmers and contract workers will be the main end-users of the product. Such users may be exposed to Overwatch Herbicide when opening containers, mixing, loading, and cleaning up spills and equipment. Workers are unlikely to be exposed significantly during application due to the incorporation by sowing (IBS) application technique.

The main route of exposure to the product will be dermal.

In the absence of exposure data for the proposed mode of application, the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure. As an IBS (Incorporated by Sowing) application model is not included in the current PHED, Scenario 3 (All liquids, open mixing and loading) plus Scenario 13 (Ground boom application, Open cab) have been used for the modelling to estimate the worker exposure. Given the IBS application method, the resulting exposure calculations for applicators are likely to be substantial overestimates, and the MOEs under-estimates, as a consequence.

The toxic endpoint of concern, and identified NOAEL**,** 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 potential interspecies and intraspecies variation.

The MOE's for workers associated with short-term use of the product, conducting mixing and loading and application by ground boom or aerial spray are acceptable (ie MOE >>100) without the use of specific personal protective equipment.

Exposure during re-entry or rehandling

Acceptable MOEs (ie MOE >> 100) are achieved for the product on Day 0 and therefore no re-entry statement is required.

6.3 Public exposure

Overwatch Herbicide is not intended for use by the general public or in areas accessible by the general public. As the product is applied using IBS methods, directly to the soil during sowing, the potential for spray

drift is low, further reducing the potential for bystander or public exposure. Public and bystander exposure is therefore considered likely to be negligible and mandatory no-spray buffer zones are not required.

6.4 Recommendations

The following first aid instructions, and safety directions are recommended for the product label. Overwatch Herbicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described below.

First aid instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131 126 New Zealand 0800 764 766.

Safety directions

Wash hands after use.

7 ENVIRONMENTAL ASSESSMENT

7.1 Fate and behaviour in the environment

Soil

Under laboratory conditions in the dark, bixlozone was persistent under aerobic conditions (DT_{50} 64-330 days, geomean DT_{50} 153 days in seven soils) and very persistent under anaerobic conditions (DT_{50} 206-741 days, geomean DT_{50} 433 days in four soils). Up to 54 per cent mineralisation and 18 per cent bound residues were observed after 120 days under aerobic conditions, while lower rates were observed under anaerobic conditions (21 per cent and 9.2 per cent, respectively).

The persistence of bixlozone in soil was investigated under field conditions at seven sites in Europe. Both SC (suspension concentrate) and CS (capsule suspension) formulation types were tested as well as incorporated and non-incorporated application methods. There was no apparent difference between formulation types; however, bixlozone was shown to be more persistent following soil incorporation, with DT_{50} values ranging 46 to 267 days (geomean DT_{50} 93 days) when not incorporated and DT_{50} values ranging from 31 to 446 days (geomean DT_{50} 179 days) when incorporated.

Photolysis is not considered to be an important route of transformation in the soil environment. Based on a soil photolysis study following continuous irradiation in the laboratory, the degradation rates in terms of summer equivalents (30–50°N) ranged from 75 to 142 days, depending on the radiolabel.

Based on batch equilibrium studies, bixlozone is considered to be moderately mobile in soil (K_f 1.6–8.3 L/kg, K_{foc} 334–465 L/kg, eight soils). The average Freundlich exponent (1/n) across all soils was 0.84, which indicates sorption is non-linear. Based on a strong linear relationship between soil sorption and organic carbon, predicted K_f values were 3.8 L/kg (one per cent OC), 7.6 L/kg (two per cent OC) and 19 L/kg (five per cent OC). It is noted that vertical movement of bixlozone was not significant in the field dissipation studies.

F9600-3-OH-propanamide[2] was the only major metabolite formed in soil (up to 15 per cent under anaerobic conditions). It is non-persistent under aerobic conditions (DT_{50} 9.3–12 hours in three soils) but persistent under anaerobic conditions (DT_{50} 106 days, one soil). F9600-3-OH-propanamide was also observed under field conditions, but levels were generally low. Based on batch equilibrium studies, it is expected to be mobile in soil (K_f 0.73–2.5 L/kg, K_{foc} 4.9–15 L/kg, four soils).

The metabolite 2,4-dichlorobenzoic acid (2,4-DBA) reached 5.8 per cent after 120 days and was still increasing under anaerobic conditions. It is non-persistent under aerobic conditions (DT_{50} 3.5–8.9 days in three soils) but persistent under anaerobic conditions (DT_{50} 209 days, one soil). 2,4-DBA was also observed under field conditions, but levels were generally low. Based on batch equilibrium studies, it is expected to be very mobile in soil (K_f 0.10–0.13 L/kg, K_{foc} 4.9–15 L/kg, four soils).

[2] N-[(2,4-dichlorophenyl)methlyl]-3-hydroxy-2,2- dimethylpropanamide

Water

Bixlozone is not readily biodegradable and is stable to hydrolysis. Photolysis is also not expected to be an important route of transformation in the aqueous environment (DT_{50} 49 days under natural summer sunlight at 30–50°N).

Mineralization in surface water was investigated in one study under aerobic conditions in a 'pelagic' test system (natural fresh water). DT_{50} values were 1040 and 818 days for the 10 µg/L and 100 µg/L test systems respectively. As such, bixlozone is not expected to degrade in the water phase.

In two aerobic and two anaerobic water/sediment systems, bixlozone dissipated relatively slowly from the water phase (geomean DT_{50} 15 days), but is considered to be non-persistent in the system as a whole (geomean DT_{50} 29 days). Mineralisation was extensive (up to 52 per cent) and bound residues were relatively low (up to 14 per cent).

The major metabolites in the aerobic water/sediment systems were 2,4-DBA (41 per cent) and 4-COOH-F9600[3] (24 per cent). In the anaerobic water/sediment systems, the major metabolite was F9600-3-OH-propanamide (69 per cent). F9600-dimethyl malonamide (F9600-DMM) was a major metabolite under both aerobic (17 per cent) and anaerobic conditions (10 per cent). The metabolites were mostly associated with the water phase.

Air

Available data indicate volatilisation and atmospheric transport following application are not likely to be significant for bixlozone. Bixlozone has low vapour pressure (2.3×10^{-3} Pa at 25°C) and is considered to be non-volatile under environmental conditions (Henry's Law Constant 7.2×10^{-3} Pa·m^3/mol). The half-life for the degradation of bixlozone by hydroxyl radicals was calculated to be 0.25 days assuming 12 h sunlight/day. In a wind tunnel study, the highest deposition of bixlozone was measured at the 48 h and 72 h sampling at the 1 m distance and corresponded to 0.42 per cent of applied. As such, bixlozone is not considered to be a relevant residue in air.

7.2 Effects and associated risks to non-target species

Terrestrial vertebrates

Bixlozone is considered to have low toxicity to mammals (LD_{50} >2000 mg ac/kg bw, *Rattus norvegicus*) and birds (LD_{50} >2000 mg ac/kg bw, *Colinus virginianus*). Following short-term dietary exposure, some mortality was observed in passerine birds at high doses (LD_{50} 887 mg ac/kg bw/d, *Taeniopygia guttata*). Following long-term dietary exposure to bixlozone in a two-generation rat reproduction study, lower F2 pup body weight and body weight gain was observed in mammals at doses at low as 238 mg ac/kg bw/d (NOAEL 34 mg ac/kg bw/d, *Rattus norvegicus*). Following long-term dietary exposure to bixlozone in avian one-generation reproduction studies, reduced 14 day survivor/hatchling weight was observed at doses as low as 103 mg ac/kg bw/d (NOEL 70 mg ac/kg bw/d, two species tested). There was no evidence of enhanced

[3] 2-(2,4-dichlorobenzyl)-4-methyl-3-oxoisoxazolidine-4- carboxylic acid

toxicity due to formulation. The toxicity of any metabolites are considered to be covered by the toxicity studies on bixlozone.

The major potential routes of exposure to terrestrial vertebrates are considered to be feeding on food items (eg vegetation and invertebrates) directly contaminated from spray application of the product. The screening level assessment assumed that terrestrial vertebrates feed exclusively on oversprayed food items within the treatment area. Risks were determined to be acceptable at the screening level. Therefore, risks to terrestrial vertebrates were considered to be acceptable and no specific protection statements are required.

Although the log K_{ow} of 3.3 indicates potential for bioaccumulation of bixlozone, a food chain assessment indicated that any accumulated residues in earthworms or fish are not expected to reach levels harmful to predators under the proposed conditions of use. In addition, based on toxicokinetic studies, biomagnification is not expected along the food chain.

Aquatic species

Bixlozone is moderately toxic to fish (lowest LC_{50} 9.8 mg ac/L, *Oncorhynchus mykiss*), very toxic to aquatic invertebrates (lowest EC_{50} 0.11 mg ac/L, *Thamnocephalus platyurus*; HC_5 0.056 mg ac/L based on eight species), non-toxic to sediment dwellers (EC_{50} >84 mg ac/kg dry sediment, two species tested), very toxic to algae (lowest E_rC_{10} 0.24 mg ac/L, E_rC_{50} 0.76 mg ac/L, *Skeletonema costatum*), and very toxic to aquatic plants (lowest E_rC_{10} 0.0080 mg ac/L, E_rC_{50} 1.8 mg ac/L, *Myriophyllum spicatum*). Following long-term exposure to bixlozone, reduced larval length was observed in fish at concentrations as low as 0.81 mg ac/L (NOEC 0.38 mg ac/L, *Pimephales promelas*), and reduced number of offspring was observed in aquatic invertebrates at concentrations as low as 0.17 mg ac/L (NOEC 0.12 mg ac/L, *Americamysis bahia*). No adverse effects were observed in sediment dwellers following long-term exposure to spiked sediment at high concentrations (NOEC 59 mg ac/kg dry sediment, *Chironomus dilutus*). There was no evidence of enhanced toxicity due to formulation. All relevant metabolites were less toxic than the parent substance bixlozone.

The major potential routes of exposure of aquatic species are considered to be spray drift or runoff from the treatment area. Although the product is not applied to water, a screening level risk assessment assumed the worst-case scenario of a direct overspray of shallow aquatic habitat in order to determine which aquatic species are not at risk. Acceptable risks could be concluded at the screening level for fish and sediment dwellers.

The aquatic plant endpoint was the basis of the regulatory acceptable concentration in aquatic systems. The spray drift assessment determined that a buffer zone is not required if the boom height is 0.5 metres or lower above the target canopy; however, higher boom heights require a buffer zone of 30 metres for the protection of natural aquatic areas. Runoff risks were determined to be acceptable in a refined assessment that considered state-specific soils and site characteristics, provided standard precautions are followed to minimise risks.

Bees and other non-target arthropods

Bixlozone has low toxicity to adult bees by contact exposure (LD_{50} >100 µg ac/bee, three species tested) and oral exposure LD_{50} >100 µg ac/bee, three species tested), and low toxicity to bee larvae (LD_{50} 58 µg ac/bee, *Apis mellifera*). Following long-term dietary exposure to bixlozone, no adverse effects were observed in adult

bees at the highest dose tested (NOEL 9.5 µg ac/bee/d, *Apis mellifera*), and reduced survival of bee larvae was observed at 13 µg ac/larvae/day (NOEL 6.3 µg ac/bee/d, *Apis mellifera*). There was no evidence of enhanced toxicity due to formulation.

A screening level risk assessment assumed the worst-case scenario of a direct overspray of blooming plants that are frequented by bees. Risks to bee were determined to be acceptable at the screening level for contact exposure (adults), oral exposure (adults) and larvae through acute and chronic exposure. However, adverse effects could not be ruled out for chronic exposure to flowering weeds. Considering no adverse effects were observed at the highest dose, and chronic exposure is unlikely for a single application of a herbicide to flowering weeds, the risks are considered to be acceptable. Therefore no specific protection statements (including downwind buffer zones for Pollinator areas) are required on the label.

For other non-target arthropods, a representative SC formulation of bixlozone caused mortality in the standard indicator species *Typhlodromus pyri* and *Aphidius rhopalopiphi* in Tier 1 laboratory (glass plate) toxicity tests (LR_{50} values of 100 and 667 g ac/ha, respectively). *Typhlodromus pyri* was further tested in an extended laboratory study on natural substrates (leaf discs) and the LR_{50} was determined to be 473 g ac/ha. In another extended laboratory test (leaf discs) on green lacewing (*Chrysoperla carnea*) showed LR_{50} greater than 489 g ac/ha.

Beneficial (predatory and parasitic) arthropods could be directly exposed to the active constituent within the crop during treatment or as a result of spray drift. A screening level risk assessment utilises Tier 1 toxicity data and assumes the non-target arthropods are exposed to fresh-dried residues within the treatment area immediately after application. Risks were determined to be acceptable for parasitic arthropods at tier 1 (considering glass plate tests); however, acceptable risks could not be concluded for predatory arthropods at tier 2 (considering natural substrates). While unacceptable risk was only marginal, no soil-dwelling species have been tested which are relevant to a bare soil application. As such, insufficient information is available to confirm compatibility with integrated pest management programs (IPM) utilising beneficial arthropods. Therefore, an IPM protection statement is required on the label.

Soil organisms

Bixlozone is moderately toxic to soil macro-organisms such as earthworms (LC_{50} 607 mg ac/kg dry soil for technical active; LC_{50} 238 mg ac/kg dry soil for representative SC formulation, *Eisenia fetida*). Following long-term exposure, reduced reproduction of soil macro-organisms was observed at concentrations as low as 58 mg ac/kg dry soil (NOEC 29 mg ac/kg dry soil, *Eisenia fetida*). No adverse effects were observed on soil processes such as nitrogen mineralisation at exaggerated soil concentrations (NOEC 1000 mg ac/kg dry soil). All relevant metabolites were no more toxic than the parent substance bixlozone.

A screening level risk assessment assumes the worst-case scenario of a direct overspray of soil without interception. Risks to soil organisms were determined to be acceptable at the screening level, and therefore no specific protection statements are required.

Non-target terrestrial plants

Standard tier 2 studies were undertaken on ten plant species for both pre-emergent and post-emergent exposures to a representative SC formulation up to 380 g ac/ha. In the seedling emergence study (pre-

emergent exposure), eight species had ER_{50} values exceeding the highest rate (ER_{50} >380 g ac/ha); while nine species had both ER_{25} and ER_{50} values exceeding this rate in the vegetative vigour study (post-emergent exposure). The most sensitive species following pre-emergent exposure was tomato based on shoot dry weight (ER_{25} 11 g ac/ha, ER_{50} 19 g ac/ha, *Lycopersicon esculentum*), while onion was the most sensitive species following post-emergent exposure (ER_{25} 41 g ac/ha, ER_{50} of 100 g ac/ha, *Allium cepa*). Considering the majority of species were not sensitive to the herbicide at rates relevant to spray drift, the standard assessment factor of 10 was reduced to three to establish the regulatory acceptable rate for non-target terrestrial plants. A spray drift assessment determined buffer zones of 15 metres (boom heights up to 0.5 metres) and 45 metres (boom heights up to 1.0 metre) are required for the protection of vegetation areas.

7.3 Recommendations

The following restraints and protection statements are advised from the viewpoint of environmental safety.

General restraints

- DO NOT apply by aircraft
- DO NOT apply by vertical sprayer
- DO NOT apply if heavy rains or storms are forecast within three days
- DO NOT irrigate to the point of runoff for at least 3 days after application.

Spray drift restraints

DO NOT apply by a boom sprayer unless the following requirements are met:

- spray droplets not smaller than a COARSE spray droplet size category
- minimum distances between the application site and downwind sensitive areas (see ‘Mandatory buffer zones’ section of the following table titled ‘Buffer zones for boom sprayers’) are observed.

Table 8: Application rate with spray drift restraints

Application rate	Boom height above the target canopy	Mandatory buffer zones		
		Natural aquatic areas	Vegetation areas	Pollinators
Up to maximum label rate	0.5 m or lower	Not required	15 metres	Not required
	1.0 m or lower	30 metres	45 metres	Not required

Protection statements

Toxic to beneficial arthropods. Not compatible with integrated pest management (IPM) programs utilising beneficial arthropods. Minimise spray drift to reduce harmful effects on beneficial arthropods in non-crop areas.

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

Overwatch Herbicide is for selective control of certain grasses and broad leaf weeds in winter barley, winter wheat and canola.

8.2 Efficacy and target crop/animal safety

Overwach Herbicide was compared in three pot and 95 field trials in Victoria, NSW, South Australia and Western Australia, to several industry standards containing, 850 g/kg pyroxasulfone, 480 g/L trifluralin, 800 g/L prosulfocarb and 120 g/L s-metolachlor, 480 g/L sulfentrazone, 500 g/kg propyzamide, 500 g/L triallate and 750 g/kg chlosulfuron for the control of grass and broadleaf weeds in wheat, barley and canola.

The trials used appropriate trial design, scientific methodology and assessment parameters, with multiple replicates, industry standards and untreated controls. Results were analysed using standard statistical procedures (ANOVA and LSD).

Efficacy

A preliminary pot trial evaluated rates from 200 to 600 g ai/ha (0.406 to 1.489 L/ha) applied post sowing pre-emergence (PSPE) to annual ryegrass, sowthistle, wild oats, brome grass, wild radish and volunteer canola. Herbicide susceptible and ALS and glyphosate resistant varieties were used. Total control of susceptible and resistant types of annual ryegrass and sowthistle was achieved at the lowest application rate. Brome grass, wild oats, wild radish and canola (seeds sown on surface) were controlled at higher rates indicating suppression only. Sand, loam and heavy clay soils were used but had no influence on weed control. The rate of 200 g ai/ha applied PSPE in pot trials was effective, but this application timing in early field trials, did not provide the same level of control. Results indicated that the 500 g ai/ha with IBS timing provided the best residual control of the target weeds whilst maintaining acceptable crop safety.

Efficacy was assessed as weed counts and visual weed control in field trials for selected weeds including, annual ryegrass, *Lolium rigidum, (*susceptible and resistant, Roundup resistant), wild oats, *Avena sterilis*, *Avena fatua,* brome grass, *Bromus diandrus*, wild radish, *Raphanus raphanistrum* (susceptible and ALS resistant), volunteer canola (Clearfield ALS resistant), sowthistle, *Sonchus oleraceus* (susceptible and ALS resistant), silvergrass, *Vulpia bromoides,* wireweed*, Polygonum aviculare*, lesser loosestrife*, Lythrum hyssopifolia,* wild oats*,* phalaris, *Phalaris paradoxa,* capeweed, *Arctotheca calendula,* bifora, *Bifora testiculata,* bedstraw, *Gallium tricornutum*, prickly lettuce, *Lactuca spp.* and barley grass*, Hordeum murinum.*

Trial data indicated that Overwatch Herbicide applied IBS at the proposed label rate of 1.25 L/ha, provided control of all the weeds assessed. Applied to barley, wheat and canola at 1.25 L/ha, commercial control (greater than 80 per cent) was achieved in most trials. Out of 28 trials on wheat, annual ryegrass control ranged from 83 per cent to 94 per cent in 18 trials. Applied to barley and canola at 1.25 L/ha, annual ryegrass control ranged from 80 per cent to 94 per cent (11 trials) and 83 per cent to 95 per cent (five trials) respectively. Overwatch Herbicide was equivalent or superior to industry standards in these trials. Applied to

Barley cv Uranbie at 1.25 L/ha, Overwatch Herbicide resulted in 80 per cent control of wild radish at 45 days after planting, which was superior to the industry standards.

Trial data demonstrated consistent commercial control of annual ryegrass, silvergrass, bifora, sowthistle, wireweed and lesser loosestrife and suppression of barleygrass, wild oats, brome grass, phalaris, bedstraw, capeweed, prickly lettuce and wild radish. Trial data also demonstrated efficacy on herbicide resistant plant varieties.

Crop safety

Crop safety was assessed on multiple cultivars of wheat, barley and canola by seed germination and emergence, visual biomass reduction, crop vigour, phytotoxicity, including bleaching, chlorosis, necrosis, stunting, thinning and delay in growth stages and yield from 11 to 209 days after treatment. Plantback safety and re-cropping times were assessed on a range of soil types from acid to alkaline and growing regions in 20 trials over two years on wheat, barley, canola, faba bean, chickpea and field pea.

Applied at the label rate of 1.25 L/ha to Wheat cvs. Baxter, Calingiri, Cobra, Corak, Cosmic, Elmore, Eradu, Gregory, Lancer, Mace, Meckering, Naparoo, Rudd, Sceptor and Spitfire, resulted in minor transient bleaching, however, this was resolved before the end of the trial and did not adversely affect crop yields. Seedling emergence was not adversely affected and there was no adverse effect on yield. There was minor biomass reduction at 30 days after planting, however, this was equivalent to the industry standards.

Although bleaching was recorded in some trials on barley and canola after application of Overwatch Herbicide at 1.25 L/ha, yield was not reduced and in some cases was significantly improved. Thus crop safety was demonstrated for barley cvs. Bass, Baudin, Scope, Commander, Hindmarsh, La Trobe and Spartacus and canola cvs. ATR Mako, ART Gem, Bonito TT, Clearfield 44Y87CL, Crusher TT, Hyola 555TT, Hyola 474CL, Hyola 559TT, Hyola 404RR and Stringray TT Turbine.

8.3 Recommendations

Overwatch Herbicide provided effective control of the weeds evaluated in field and pot trials and confirmed the proposed label rate and IBS application timing.

Trial data confirmed efficacy against common grass weeds and crop safety for wheat, barley and canola. The data also confirmed plantback safety at the proposed label intervals on a range of crops. The proposed label indicates that there may be some transient phytotoxicity however no effect is expected on crop yield. The registration of Overwatch Herbicide is supported.

9 LABELLING REQUIREMENTS

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Overwatch™
HERBICIDE

ACTIVE CONSTITUENT: 400 g/L BIXLOZONE

GROUP Q HERBICIDE

For selective control of certain grasses and broad leaf weeds in Wheat, Barley, and Canola, as per the Directions for Use Table

CONTAINS: 5 L – 1000 L

DIRECTIONS FOR USE
RESTRAINTS
DO NOT apply Overwatch™ Herbicide by aircraft.
DO NOT apply by vertical sprayer.
DO NOT apply if heavy rains or storms are forecast within 3 days.
DO NOT irrigate to the point of runoff for at least 3 days after application.

Incorporate by sowing no later than 3 days after application.
DO NOT apply more than one application of Overwatch™ Herbicide per cropping season.

SPRAY DRIFT RESTRAINTS

Specific definitions for terms used in this section of the label can be found at apvma.gov.au/spraydrift.

DO NOT allow bystanders to come into contact with the spray cloud.

DO NOT apply in a manner that may cause an unacceptable impact to native vegetation, agricultural crops, landscaped gardens and aquaculture production, or cause contamination of plant or livestock commodities, outside the application site from spray drift. The buffer zones in the buffer zone table below provide guidance but may not be sufficient in all situations. Wherever possible, correctly use application equipment designed to reduce spray drift and apply when the wind direction is away from these sensitive areas.

DO NOT apply unless the wind speed is between 3 and 20 kilometres per hour at the application site during the time of application.

DO NOT apply if there are hazardous surface temperature inversion conditions present at the application site during the time of application. Surface temperature inversion conditions exist most evenings one to two hours before sunset and persist until one to two hours after sunrise.

DO NOT apply by a boom sprayer unless the following requirements are met:
- Spray droplets are not smaller than a COARSE spray droplet size category
- Minimum distances between the application site and downwind sensitive areas are observed (see the table titled ‘Buffer zones for boom sprayers in the ‘Mandatory buffer zones’ section below).

Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Mandatory downwind buffer zones				
		Livestock areas	Natural aquatic areas	Vegetation areas	Bystander areas	Pollinator areas
Up to maximum label rate	0.5 m or lower	Not required	Not required	15 metres	Not required	Not required
	1.0 m or lower	30 metres	30 metres	45 metres	Not required	Not required

CROPS	WEED	RATE	CRITICAL COMMENTS
Wheat, Barley & Canola	Annual ryegrass (*Lolium rigidum*), Bifora *(Bifora testiculata)*, Hog weed/wireweed (*Polygonum aviculare),* Lesser loosestrife (*Lythrum hyssopifolia*), Silvergrass (*Vulpia bromoides*) Sowthistle *(Sonchus oleraceus),* **Supression of:** Barley grass *(Hordeum murinum)* Bedstraw (*Galium tricornutum)*, Brome grass (*Bromus* spp*)*, Capeweed (*Arctotheca calendula*), Phalaris (*Phalaris paradoxa).* Prickly lettuce *(Lactuca* spp*.)* Wild oats *(Avena fatua*), Wild radish *(Raphanus raphanistrum)*	1.25 L/ha	Apply prior to sowing and incorporate by sowing (IBS) with knife point tines and press wheels. Best results are achieved when applied to a moist soil profile and sowing occurs soon after application. Refer to GENERAL INSTRUCTIONS for recommendations of best use. Efficacy of Overwatch™ Herbicide can be reduced by the following factors (alone or in combination): • Excessively cloddy soil which create shadow areas that do not allow for uniform spray coverage of soil • Depth and distribution of weed seed. Weed seeds germinating from moist soil deeper in the profile may not be controlled. Also seeds that germinate from the base of an overturned clod of soil which has no treated soil to pass through. • Late germinating weeds. • Poor performance of the knockdown herbicide application on established weeds. Overwatch Herbicide does not control established weeds. • Heavy rainfall causing runoff removes the active from the desired soil area. Erosion of treated soil will also cause gaps in soil coverage allowing weeds to germinate unhindered. • Heavy stubble load (>50% ground coverage) may restrict the amount of active reaching the soil. This is especially true in cases where the stubble is lying on the ground. • Paddocks covered in ash following stubble burning • Insufficient soil moisture to move the active within the soil for ready uptake. This greatly depends on soil type, however, in dry conditions this factor will be amplified in soils with clay content over 35%. • IBS application timing displaces treated soil away from the seed furrow therefore reducing the amount of active present in the seed furrow or on the 'shoulder' of the furrow. Avoid overlapping spray swaths. Especially in corners and headlands as this may increase crop phytotoxicity. Refer to 'General Instructions' in this label for more crop safety recommendations.

WITHHOLDING PERIOD

HARVEST:

BARLEY, CANOLA, WHEAT: NOT REQUIRED WHEN USED AS DIRECTED

GRAZING / STOCKFOOD:

BARLEY, CANOLA, WHEAT: DO NOT HARVEST, GRAZE OR CUT FOR STOCK FOOD OR FOR SEED FOR 12 WEEKS AFTER APPLICATION.

GENERAL INSTRUCTIONS

Overwatch™ Herbicide is a soil applied, pre-emergence herbicide that is absorbed by the roots and shoots of germinating plants. It is upwardly transported via the plants xylem / transpiration system. Overwatch™ Herbicide mode of action is through blocking carotenoid biosynthesis. After absorption of Overwatch™ Herbicide, susceptible germinating plants are deprived of protective carotenoids which disrupts their ability to photosynthesise. Weed seedlings that have absorbed Overwatch™ Herbicide commonly emerge with a bleached and/or purple appearance. The seedlings then rapidly desiccate over a few weeks when their seed energy store is depleted.

Apply prior to sowing and incorporate by sowing (IBS) with knife point tines and press wheels. Activity of Overwatch™ Herbicide requires placement near germinating seeds and in broadacre cropping this is most consistently achieved by mechanical incorporation. Best results are achieved when applied to a moist soil profile and sowing occurs soon after application. Weed control may be significantly reduced where there is insufficient soil moisture to mobilise the active for uptake of the germinating weed seedling. This can be exaggerated when the weeds germinate from depth and if there is sufficient moisture for sustained growth.

APPLICATION

Ensure complete and uniform spray coverage on soil. Reduced effectiveness may occur where there is either reduced contact of the herbicide with the soil surface. Spray coverage may be compromised where application is made to a ridged or excessively cloddy soil surface or where cover of crop or weed residues restrict contact with the soil surface. Efficacy may be unsatisfactory if ground cover is shielded by heavy stubble. For example, stubble can be observed in header rows where stubble and trash has not been distributed evenly. Stubble lying horizontally on the ground will have higher active ingredient interception than standing stubble. It is best to delay application to recently burnt paddocks or windrows until rainfall occurs to disturb the layer of ash as Overwatch™ Herbicide may be strongly adsorbed to ash therefore inhibiting passage through to the soil.

The level of weed control achieved by Overwatch™ Herbicide depends on the positioning of weed seed relative to the layer of treated soil. Weeds that germinate from deeper within the soil profile may escape due to a lack of herbicide treated soil solution in that root zone. This occurs where the soil has undergone recent disturbance (eg tillage) whereby the weed seed was incorporated from the soil surface lower into the soil profile or where application is to a dry surface and the weed seeds are located deeper in the profile in sufficient moisture to provide vigour to break through the treated soil zone above. This is particularly relevant for weeds like Annual ryegrass which take up Overwatch™ Herbicide predominantly via their roots.

As with all pre-emergent herbicides, it is important that treated fields are constantly monitored for weed germinations throughout the season and treated with corrective post-emergent herbicides as required.

Avoid holding Overwatch™ Herbicide spray solutions overnight in equipment. If this occurs ensure that the spray solution is vigorously agitated so that the product is thoroughly resuspended.

In case of equipment breakdown, flush spray lines out and maintain agitation on the spray vessel to prevent settling.

SEED PLACEMENT & EQUIPMENT
Sowing with knife points and press wheels is regarded as the safest sowing configuration when using Overwatch™ Herbicide. Crop safety when using disc seeding systems is variable based on seed placement and influence of stubble, whereby causing insufficient soil cover to the seed. Overwatch™ Herbicide should be applied prior to sowing and incorporated by sowing using knife point and press-wheel equipment. Incorporation with a knife point and press-wheel may result in reduced weed control in the drill row. If using a knife point and press-wheel planter, adjust working speed to avoid excessive soil throw into the adjoining seeding row. Weeds germinating from depth, weeds about to emerge or emerged weeds not controlled by knockdown herbicides may not be controlled by Overwatch™ Herbicide.

ENVIRONMENTAL CONDITIONS
Overwatch™ Herbicide requires adequate soil moisture for effective weed control. Overwatch™ Herbicide is most effective when applied evenly to moist soils just prior to incorporation by sowing. Sufficient rainfall soon after application allows Overwatch™ Herbicide to move with soil moisture into the weed's root zone therefore increasing uptake potential.

CROP SAFETY
For all crops, there may be some risk of interim crop phytotoxicity. In most situations, phytotoxicity is expressed as bleaching of the older leaves. The effect is transient and generally localized as the new leaves emerge unaffected. Crop bleaching disappears and there is no yield penalty.

In serious cases of overdosing or unfavourable conditions, phytotoxicity can also lead to stunting and a reduction in crop plant populations (or thinning). Incidences of elevated crop phytotoxicity may occur in the following situations:

- Overlapping of spray swaths effectively doubling the desired application dose rate
- Heavy rain or strong wind soon after planting causing treated soil erosion or solubilised active moving into the seeding furrow concentrating Overwatch™ Herbicide on top of the germinating crop seedling
- High/heavy rainfall events in light soil types with low organic content leaching the active ingredient into the crop's root zone. This situation may also occur if Overwatch™ Herbicide is applied to dry soil with limited soil/carbon absorption taking place. In light soils, bleaching of crops can still occur >1 month after application if a heavy rainfall event occurs.
- Increased phytotoxicity may be observed when crops are stressed due to various factors such as:
    - excessively wet / waterlogged soils, drought conditions, unseasonal heat, severe frost
    - crop disease, nematode or insect damage
    - seed treatment / weathered seed stock causing poor and/or slow germination
    - depth of seed placement causing delayed and slow germination
    - variation in seeding depth due to damaged, worn or incorrectly set-up tines
    - soil type variation in the paddock that results in shallower seeding eg gravel rise
    - excessive soil alkalinity or acidity and/or poor or unbalanced nutrient status
    - sowing crops outside of the ideal sowing window (recommended by seed company)
- Above optimal operating speed of sowing – throwing treated soil into adjacent seed furrows
- Shallow seeding depth. Any seedlings germinating within 3 cm of soil may be at risk of increased crop phytotoxicity.
- When Overwatch™ Herbicide is applied in conjunction with other herbicides which may cause crop phytotoxicity. It is the responsibility of the end-user to understand all risks associated with using other herbicides in a tank-mix with Overwatch™ Herbicide. Ensure that all precautions on the label of the tank mix partner are closely followed. Refer to 'Compatibility' section of this label for further detail on tank-mix compatibility or contact an FMC representative.

GROUP Q HERBICIDE

RESISTANCE WEED WARNING

Overwatch™ Herbicide is a member of the isoxazolidinone group of herbicides. For weed resistance management this is a Group Q Herbicide. Some naturally occurring weed biotypes resistant to Group Q herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by Overwatch™ Herbicide or Group Q herbicides.

Since the occurrence of resistant weeds is difficult to detect prior to use, FMC accepts no liability for any losses that may result from the failure of Overwatch™ Herbicide to control the resistant weeds.

Advice as to strategies and alternative treatments that can be used should be obtained from your local supplier, consultant, local Departments of Agriculture or Primary Industries, or FMC representative.

To prolong the development of weed resistance it is strongly advised that growers use Overwatch Herbicide as a part of an integrated weed management (IWM) program. Such programs incorporate different methods of weed management involving both chemical and non-chemical solutions. Weedsmart (weedsmart.org.au) and CropLife (croplifeaustralia.org.au) provide comprehensive information on IWM programs. Local agronomists and advisors should also be able to assist in implementing tailor made IWM programs for individual farming systems.

EQUIPMENT

Always ensure the sprayer is clean, using a suitable tank cleaner as directed. Defer to the most rigorous cleanout procedure if tank mixing with a partner. It is recommended that Overwatch™ Herbicide be applied in at least 80 L/ha as a coarse quality spray.

The most preferred application regime for Overwatch™ Herbicide involves use of:

- Standard boom ground sprayers fitted with by-pass or mechanical agitation
- TeeJet TTI nozzles operated at between 3 and 5 bar and angled backwards to direction of travel to reduce horizontal movement
- narrow nozzle spacing of 25 – 50 cm
- A drift mitigating adjuvant in the tank mix at label rates 0.25 per cent v/v to further minimise fine droplet production and enhance soil deposition in standing stubble
- a minimum application volume of 60 L water/ha on bare soil; 80L/ha in light standing stubble and 100 L/ha in heavy stubble situations
- a maximum travel speed of 20 km/h, preferably 16 km/hr
- the minimum boom height that still ensures double overlap

COMPATABILITY

Overwatch™ Herbicide is formulated as a suspension concentrate. It has been shown to be physically compatible with the following herbicide active ingredients:
Atrazine, Glyphosate, Metribuzin, Metazachlor, Pendimethalin, Propyzamide, Prosulfocarb, Triallate, Trifluralin, Terbuthylazine, Pyroxasulfone, S-Metolachlor.

When mixing Overwatch™ Herbicide in a tank with other products suited for pre-em application timing, the following mixing sequence should be followed:

1. Water conditioning agents;
2. Water dispersible granules (WG)/ Dry flowable products (DF);
3. Wettable powders (WP);

4. Flowables or suspension concentrates (eg Overwatch Herbicide)
5. Emulsifiable concentrates (EC);
6. Water-soluble concentrates (eg glyphosate);
7. Surfactants and oils (eg On-Coarse®, Canopy®, Dead Sure®, BS1000^);
8. Soluble fertilisers.

Physical compatibility with Overwatch™ Herbicide should be determined prior to mixing with a product not listed above, or when mixing Overwatch™ Herbicide as a component of a 3-way tank mix. Always read the product label for the manufacturer's tank mix recommendations and to determine individual product compatibility options and correct mixing orders for individual products. If unsure, perform a jar test before proceeding to determine physical compatibility. Physical compatibility does not always guarantee biological compatibility and should be undertaken only with careful consideration.

Crop Rotation Recommendations

Overwatch™ Herbicide is predominantly broken down in the soil through microbial degradation. Microbial activity is typically favoured by moist and warm aerobic soils. Minimum re-cropping intervals for Overwatch™ Herbicide have been recommended to minimise the risk of damage to rotational crops (see table below). However, considerable variations in environmental, edaphic and agronomic factors affecting the soil microbial activity, mean that it is not possible to absolutely eliminate all risks and potential for damage to following crops.

Land previously treated with Overwatch™ Herbicide should not be rotated to other crops other than those listed in the following table.

Overwatch™ Herbicide treated area may be replanted to any of the specified crops after the interval indicated in the following table:

Minimum re-cropping interval (months after application)	**0**	**11**
Crops	Barley	Chickpea
	Wheat	Faba bean
	Canola	Field pea

^Provided there has been sufficient rainfall (estimated >250mm) after application to support microbial activity and degradation. Conditions that are not conducive to adequate soil microbial degradation may result in extended re-cropping intervals.

For advice on crops and situations not mentioned above, contact FMC.

RE-ENTRY PERIOD

No re-entry period applies to Overwatch™ Herbicide

INTEGRATED PEST MANAGEMENT

Toxic to beneficial arthropods. Not compatible with integrated pest management (IPM) programs utilising beneficial arthropods. Minimise spray drift to reduce harmful effects on beneficial arthropods in non-crop areas.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product 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.

5–200 L

Triple-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 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.

1000 L
Empty contents fully into application equipment. Close all valves and return to point of purchase or collection point for refill or storage.

SAFETY DIRECTIONS
Wash hands after use.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26.

SAFETY DATA SHEET
Additional information is listed in the Safety Data Sheet available from www.fmccrop.com.au

NOTICE TO BUYER
To the extent permitted by the Competition and Consumer Act (2010) or any relevant legislation of any State or Territory (the “Legislation”) all conditions and warranties and statutory or other rights of action, whether arising in contract or tort or whether due to the negligence of FMC or Seller, which buyer or any other user may have against FMC or Seller are hereby excluded provided however that any rights of the buyer pursuant to non-excludable conditions or warranties of the Legislation are expressly preserved. FMC hereby gives notice to buyer and other users that to the extent permitted by the Legislation it will not accept responsibility for any indirect or consequential loss of whatsoever nature arising from the storage, handling or use of this Product. Where permitted by the Legislation FMC’s liability shall in all circumstances be limited to the replacement of the product, or a refund of the purchase price paid therefor.
The Product must be used and applied strictly in accordance with the label instructions and other directions for use. It is impossible to eliminate all risks associated with the use of this product. Such risks may arise from factors such as weather conditions, soil factors, off target movement, unconventional technique, presence of other materials, the manner of use or application, or other unknown factors, all of which are beyond the control of FMC or the Seller. Buyer accepts these risks.

APVMA Approval No: 86427/115745

Batch No:

Date of Manufacture:

Drummuster logo – relevant pack sizes

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SPECIALIST ADVICE IN EMERGENCY ONLY 1800 033 111 ALL HOURS – AUSTRALIA WIDE

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
ai	active ingredient
ARfD	Acute Reference Dose
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
EC_{50}	concentration at which 50% of the test population are immobilised
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
g	gram
GAP	Good Agricultural Practice
h	hour
ha	hectare
IPM	Integrated Pest Management
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection—level at which residues can be detected

Log K_{OW}	Log to base 10 of octanol water partitioning co-efficient, synonym P_{OW}
LOQ	Limit of Quantitation—level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram
NOEC/NOEL	No Observable Effect Concentration Level
NOAEL	No Observed Adverse Effect Level
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
REI	Re-Entry Interval
s	second
SC	Suspension Concentrate
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
µg	microgram
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
Metabolism	The chemical processes that maintain living organisms
Photolysis	Breakdown of chemicals due to the action of light
Toxicology	The study of the nature and effects of poisons

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