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Australian Pesticides and Veterinary Medicines Authority

Public Release Summary

on the evaluation of the new active constituent dimpropyridaz in the product Efficon Insecticide

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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 registration of [Product Name(s)] 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 15 November 2022 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 organisation name (if relevant)
- email or postal address (if available)
- the date you made the submission.

Please note: submissions will be published on the APVMA's website, unless you have asked for the submission to remain confidential, or if the APVMA chooses at its discretion not to publish any submissions received (refer to the public consultation coversheet).

Please lodge your submission using the public consultation coversheet, which provides options for how your submission will be published.

Note that all APVMA documents are subject to the access provisions of the *Freedom of Information Act 1982* and may be required to be released under that Act should a request for access be made.

Unless you request for your submission to remain confidential, the APVMA may release your submission to the applicant for comment.

Written submissions should be addressed to:

Case Management and Administration Unit

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Phone: +61 2 6770 2300

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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.

Introduction

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of Efficon Insecticide, and approval of the new active constituent, dimpropyridaz.

Applicant

BASF Australia Ltd.

Purpose of application

BASF Australia Ltd has applied to the APVMA for registration of the new product Efficon Insecticide, containing 120 g/L, as a soluble liquid (SL) formulation, of the new active constituent dimpropyridaz.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Efficon Insecticide, and approval of the new active constituent dimpropyridaz.

Proposed claims and use pattern

Efficon Insecticide is intended for the control of aphids, Silverleaf Whitefly and Greenhouse Whitefly in cucurbits, brassica vegetables, fruiting vegetables, leafy vegetables, brassica leafy vegetables, and cotton. Proposed target rates are 1 L/ha (120 g a.c./ha) for whitefly and 0.5 L/ha (60 g a.c./ha) for aphids.

Efficon Insecticide will be for professional use only. Up to 4 applications of 120 g a.c./ha are proposed using ground boom sprayer equipment with a medium droplet size and minimum retreatment interval of 7 days between applications.

Mode of action

Efficon Insecticide is a new insecticide containing the new active ingredient dimpropyridaz. Dimpropyridaz is a pyrazole carboxamide insecticide which acts on chordotonal organs, which are important mechanosensors in insects. Chordotonal organs transduce joint position and motion due to muscle contractions or external influences such as wind, gravity, or sound, and are therefore essential for hearing, balance, spatial orientation, and kinaesthesia senses. Dimpropyridaz inhibits firing of chordotonal organ neurons by blocking signalling upstream of the TRPV channel. As a result, signal transduction by the Chordotonal organ is disrupted, the insects are uncoordinated, unable to feed and eventually die.

Although the target site has not yet been defined, extensive investigation conducted demonstrates that the target site is located upstream of the TRPV channel, the target site of active substances belonging to IRAC group 9 and also upstream of the molecular target of IRAC (Insecticide Resistance Action Committee) group 29, which has not been identified yet. Despite having overlapping symptoms, the target site of Dimpropyridaz differs from the site of IRAC groups 9 and 29. Therefore the mode of action is regarded as new, and no

cross-resistance is expected. The application for assigning a new IRAC group to the IRAC committee is foreseen.

Overseas registrations

The active constituent dimpropyridaz is not currently registered overseas.

Chemistry and manufacture

Active constituent

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

Table 1: Nomenclature and structural formula of the active constituent dimpropyridaz

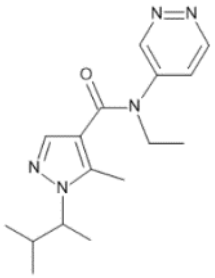
Common name (ISO):	Dimpropyridaz
IUPAC name:	N-ethyl-5-methyl-1-[(2RS)-3-methylbutan-2-yl]-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide
CAS registry number:	1403615-77-9
Molecular formula:	C16H23N5O
Molecular weight:	301.39 g/mol
Structural formula:	

Table 2: Key physicochemical properties of the active constituent dimpropyridaz

Physical form:	Powder (technical active – 95.3% purity)
Colour:	Light brown (technical active – 95.3% purity)
Odour:	Odourless
Melting point:	81.9°C (technical active – 95.3% purity), 88°C (PAI – 99.7% purity)
Boiling point:	Decomposes at 208.0°C (technical active – 95.3% purity) Decomposes at 278.0°C (PAI – 99.7% purity)
Surface tension	52.9 mN/m (20°C, 90% of the saturation solubility) (PAI – 99.7% purity)
Safety properties (technical active):	
Flammability:	Not considered flammable.
Auto-ignition	No auto ignition to a temperature of 400°C.
Explosive properties:	Not considered explosive.
Oxidising properties:	Not oxidizing
Solubility in water:	Results were determined at 20°C applying the shake flask method

Solvent	Solubility [g/L]	pH value (measured)
Deionized water	34.6	6.1
Buffer pH 4	33.2	4.2
Buffer pH 7	28.7	7.0
Buffer pH 9	31.5	8.9

(PAI – 99.5% purity)

Organic solvent solubility:	Results were determined at 25°C applying the shake flask method n-Heptane* <10 g/L Xylene 67-80 g/L 1,2-Dichloroethane >250 g/L Acetone >250 g/L Methanol >250 g/L Ethyl acetate 67 to 80 g/L *With an additional preliminary test with a tenth of the weigh-in of test item the solubility in n-heptane is expected to be in the range of approx. 1 to 2 g/L
Dissociation constant (PKa):	No dissociation was observed in the range between pH 3.5 and pH 10.9. (PAI – 99.7% purity)

Octanol/water partition coefficient (Log Kow/KOW):	log P_{ow}= 1.1 at 20°C (pH 5.8). (PAI – 99.7% purity).
Vapour pressure:	p= 8.7×10^{-6} Pa (20°C) p= 1.7×10^{-5} Pa (25°C) (PAI – 99.5% purity)
PH at 23°C:	Pure water (1.0%) = 4.5 [Pure water, no test item= 5.9] CIPAC water D (1.0%) = 4.5 [CIPAC water D, no test item= 6.4] (Technical active – 95.3% purity)
Corrosion (metals) The corrosion rates for the specimens exposed to the test item for 7 days:	Carbon steel= 0.040 mm/yr Stainless steel= 0.006 mm/yr Aluminium= 0.142 mm/yr Brass= 0.031 mm/yr (Technical active – 95.3% purity)
Stability at 54 °C for 2 weeks and 2-year stability test :	After accelerated storage at 54°C for 2 weeks and 2 years storage at 20°C and 30°C, the technical active ingredient showed good stability.

The purified active constituent is a light beige and odourless powder. Dimpropyridaz is not flammable, explosive, or oxidising. The vapour pressure is low, at 8.7×10^{-6} Pa at 20°C. The water solubility is moderate at 34.6 g/L, with the solubility not appearing to be pH dependent. Dimpropyridaz is very soluble in methanol, acetone, and 1,2-dichloroethane (all >250 g/L). It is also soluble in p-xylene and ethyl acetate (67 to 80 g/L) and sparingly soluble in n-heptane (<10 g/L). The n-octanol/ water partition coefficient (log P_{ow}) is 1.1 at pH 5.8 indicating that dimpropyridaz is neither lipophilic nor hydrophilic. A dissociation constant (pKa) was not reported. Dimpropyridaz (purified active constituent) has a melting point of 88°C. The FTIR, NMR, and MS spectra are consistent with the molecular structure.

Formulated product

The product Efficon Insecticide 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 formulation of the product Efficon Insecticide

Distinguishing name:	Efficon Insecticide
Formulation type:	Soluble Concentrate (SL)
Active constituent concentration:	120 g/L of dimpropyridaz

Table 4: Physicochemical properties of the product Efficon Insecticide

Physical form:	Dark brown liquid with a floral odour
PH (1.0% v/v dilution):	4.93 (pure water), 4.96 (CIPAC water D)
Surface tension:	38.17 mN/m (0.20% in pure water, 21°C).
Relative density and bulk density:	Density= 1.1118 cm^3 and Relative density= 1.1138
Safety properties:	Not explosive, no oxidizing properties and not classified as Dangerous Goods. Has a flash point of 94.5°C and an auto-ignition temperature of 400°C.
Storage stability:	The active content and all of the physico-chemical properties of the formulation remained within product specification after storage at both elevated and low temperatures storage after testing. The product is expected to remain within the specifications for at least 2 years when stored under normal conditions.

Efficon Insecticide is a dark brown liquid with a floral odour. Efficon Insecticide is not explosive, oxidizing, or flammable. The flash point is 94.5°C, and it is a surface-active product. The physico-chemical properties are acceptable.

Recommendations

The APVMA Chemistry section has evaluated the chemistry of the active constituent dimpropyridaz and associated product Efficon Insecticide – including the spectroscopy, physicochemical properties, manufacturing process, quality control procedures, stability, packaging, 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 2 years when stored under normal conditions.

Based on a review of the chemistry and manufacturing details, the registration of Efficon Insecticide, and approval of the active constituent dimpropyridaz, are supported from a chemistry perspective.

Toxicological assessment

The applicant submitted a complete data package, which was sufficient to assess the toxicity of dimpropyridaz.

Evaluation of toxicology

Chemical class

Dimpropyridaz, a racemate, is a member of the 1H-pyrazole-5-carboxamide class of insecticidal, fungicidal and potential anthelmintic compounds. This class also contains fluxapyroxad, tebufenpyrad, and tolfenpyrad. Unlike other members of the pyrazole carboxamide class, dimpropyridaz disrupts the function of chodotonal organ (stretch receptor organ) neurons by blocking signalling upstream of vanilloid transient receptor potential channels. Dimpropyridaz acts upstream of Insecticide Resistance Action Committee (IRAC) group 9 agents (chordotonal organ TRPV channel modulators) and acts at a different site to IRAC group 29 agents (chordotonal organ modulators - undefined target site). Thus, dimpropyridaz is claimed to act by a new insecticidal mode of action.

Pharmacokinetics

In rats, dimpropyridaz is moderately bioavailable following oral dosing, with up to 77% of administered dose absorbed. Dimpropyridaz-derived radioactivity was widely distributed through the tissues and was rapidly and extensively metabolised via mono- or dihydroxylation followed by oxidation or conjugation (to sulphate or glucuronic acid), dealkylation, cleavage of the carboxamide bridge between the pyrazole and the pyridazine moieties, and cleavage of the isopentyl moiety. There may be sex differences in how dimpropyridaz is metabolised and excreted. No significant enantiomeric shifting was observed in liver and plasma; however, an increased R:S ratio was noted in the kidney. Excretion of dimpropyridaz-derived radioactivity was rapid and almost complete (most eliminated within 1 to 2 days after oral dosing). There was no evidence of bioaccumulation. In males, urinary excretion was higher than faecal excretion and the route of excretion was independent of dose. In females, the pattern of excretion was dose-dependent (high dose= higher in urine cf. faeces; low dose= urine and faecal excretion were comparable).

Acute toxicity (active constituent)

Dimpropyridaz has moderate acute oral toxicity; low acute toxicity by dermal and inhalational routes; is slight irritant to eyes and skin; but has no potential to be a skin sensitiser.

Acute toxicity (product)

Efficon Insecticide has a low acute oral, dermal, and inhalational toxicity; is a slight irritant to eyes and skin; but has no potential to be a skin sensitiser.

Repeat-dose toxicity

Repeated dietary exposure of rats to dimpropyridaz was associated with decreased body weight and food consumption, with decreased efficiency of food use. Mild vacuolation of the ovarian interstitial glands, and atypical uterine gland hyperplasia were observed in females and mild multifocal testicular tubule degeneration in males. Some effects on serum triglycerides and cholesterol, as well as adaptive changes in the liver were observed. In a 90-day dietary study in rats, the NOAEL was 4000/1000 ppm (382/80 mg/kg bw/d M/F) based on an increased incidence of mild ovarian interstitial gland vacuolation and increased serum triglycerides (+52%).

While there was weak evidence of dimpropyridaz-associated sex hormone effects at high doses in Wistar rats, these effects are not human-relevant at practical levels of exposure as they were seen only in a single hypersensitive strain of rats and were not associated with any other effects on reproduction, development or survival.

In mice repeated dietary exposure was associated with reductions in body weight parameters and minimal evidence of hepatotoxicity. In a 90-day dietary study in mice, the NOAEL was 1000/5000 ppm (250/1641 mg/kg bw/d M/F) based on relatively lower rates of body weight gain (-37%), and 10% lower terminal body weight in males relative to controls. No adverse effects were noted in females at the highest dose tested.

Repeated oral exposure of dogs to dimpropyridaz for 90 days was associated with increased serum urea and creatinine, decreased serum total protein, and urine leucocytosis (lacking anatomic pathology correlates). The NOAEL was 30/90 mg/kg bw/d (M/F) based on increased serum urea (+13%) and creatinine (+17%) and decreased total protein (-6%), and urine leucocytosis (albeit all lacked anatomic pathology correlates). No adverse effects were detected in females.

Chronic toxicity and carcinogenicity

Dimpropyridaz was not a human-relevant carcinogen in rats, and it was not carcinogenic in mice.

In an 18-month dietary study in mice, the NOAEL was 750 ppm (121 mg/kg bw/d), based on reductions in terminal body weights in both sexes relative to controls that may at least be partially due to unpalatability of the admixed diet.

In a 24-month dietary study in rats, the NOAEL was 350 (21/62 mg/kg bw/d) based on relative reductions in bodyweight gain (-16%) and 10% lower terminal body weight attributed to decreased food use efficiency, and liver cell changes (hepatocellular lipofuscinosis) were considered adverse at 1400 ppm in females.

Reproductive and developmental toxicity

Dimpropyridaz produced toxic effects on dams, however, it was not a developmental toxicant in either rats or rabbits. Dimpropyridaz exposure in the diet resulted in reductions in food consumption and body weight parameters, but had no effects on reproduction, development, and survival in a rat multigenerational study.

In a 2-generation reproduction toxicity study in rats, the reproductive NOAEL was established at the top dose of 200 mg/kg bw/day as there were no test substance-related findings on reproductive indices. The parental NOAEL was 60 mg/kg bw/d based on reductions in body weight gain and body weights.

In developmental toxicity study (oral gavage) in rats, both the maternal and developmental NOAEL was 200 mg/kg bw/d based on no effects at the highest tested dose.

In developmental toxicity study (oral gavage) in rabbits, the maternal NOAEL was 50 mg/kg bw/d based on decrease (-23%) in food consumption and in body weight gain (-47%). The NOAEL for developmental toxicity in the rabbit study was 150 mg/kg bw/d base on no effects at the highest tested dose.

Genotoxicity

Dimpropyridaz was negative in *in vitro* and *in vivo* mutagenicity and genotoxicity studies indicating dimpropyridaz is not genotoxic.

Neurotoxicity/immunotoxicity

Dimpropyridaz was not acutely neurotoxic in rats (initial transient changes in motor activity associated with non-specific clinical signs of acute toxicity were observed). The NOAEL for neurotoxicity was 1200 mg/kg bw/d based on no effects at the highest dose. The NOAEL for general toxicity was 400/120 mg/kg bw/d (M/F) based on clinical signs and FOB parameter changes on study day 1 including closed or semi-closed eyelids, piloerection, reduced exploration, apathy, & incoordination.

Toxicity of metabolites and/or impurities

Based on chemical residue studies in food and feeds, the following metabolites, in addition to the parent molecule (dimpropyridaz, BAS 550 I), were present at ≥10% of the total radioactive residue (TRR): M550I002, M550I004, M550I005, M550I006, M550I014, M550I015, M550I028 and M550I049.

Exposure to metabolites M550I002, M550I004, M550I006 and M550I015 in the diet is covered by the health-based guidance values for dimpropyridaz, as they are either major rat metabolites, or, based on data provided, were not considered to be more toxic than the parent compound.

Exposure to metabolites M550I014 and M550I028 should be limited to the Cramer Class III TTC of 1.5 µg/kg bw/day.

Health-based guidance values and poisons scheduling

Poisons Standard

Dimpropyridaz is in Schedule 6 of the Standard for the Uniform Scheduling of Medicines and Poison (SUSMP) except when included in Schedule 5. Preparations containing 13% or less of dimpropyridaz are included in Schedule 5.

Efficon Insecticide, containing 120 g/L or dimpropyridaz, will require a signal header CAUTION on the product label.

Health-based guidance values

Acceptable daily intake

The Acceptable Daily Intake (ADI) for dimpropyridaz is 0.2 mg/kg bw/d, based on a NOAEL of 21 mg/kg bw/d, based on a 10% reduction in body weight, reduced body weight gain, and hepatic lipofuscinosis in females at the next highest dose (101 mg/kg bw/d) in a near life-time dietary study in rats (APVMA 2021).

Acute reference dose

An ARfD be considered unnecessary due to its level acute oral toxicity, lack of acute neurotoxicity, lack of effects on reproduction and development, and lack of any effect that would likely occur following a single exposure event.

Recommendations

There are no objections on human health grounds to the registration of the product Efficon Insecticide, containing 120 g/L of dimpropyridaz, when used in accordance with the directions for use (DFU).

Residues assessment

The applicant has submitted metabolism, residue trial data, analytical methodology, fate in storage, processing data, and residues in trade information, which are considered here.

Metabolism

The metabolism of dimpropyridaz (BAS 550 I) was investigated in 3 plant groups: leafy vegetables (lettuce), pulses and oilseeds (soybean), and fruiting vegetables (tomatoes) as well as in rotational crops (spinach, radish and wheat). Metabolism in livestock was investigated in lactating goats and laying hens. The studies used dimpropyridaz labelled with ^{14}C in either the pyrazolyl or pyridazinyl moieties.

Plant metabolism

In the primary plant metabolism studies, parent dimpropyridaz was the most abundant component in lettuce leaves at 2.3 to 2.6 mg/kg (45 to 47% TRR). Parent compound was also the only component in tomato fruit at 0.068 to 0.074 mg/kg (77 to 85% TRR). Parent compound was not the major component in soybeans but was still significant at 3.0 to 4.6 mg/kg (7.6 to 8.2% TRR) in straw, 0.51 mg/kg (8.0 to 8.1% TRR) in hulls and up to 0.028 mg/kg (0 to 8.1% TRR) in seed. Parent compound was not detected in confined rotational crops.

In lettuce leaves of the pyrazolyl label, M550I006 was the second most abundant component (15% TRR), followed by M550I002 (8.4% TRR). The other metabolites and detected components accounted for up to 5.1% TRR (max 0.26 mg eq/kg). In lettuce leaves of the pyridazinyl label, M550I002 was the second most abundant component (9.2% TRR), followed by M550I042 (6.1% TRR) and M550I004 (1.9% TRR).

For tomatoes, no metabolites were detected in tomato fruit, with only unchanged parent compound identified. M550I004 was the second most abundant component after parent in tomato leaves at 0.55 to 0.84 mg eq/kg (16 to 22% TRR).

For soybeans, M550I002 was the most abundant component in straw and hulls at 6.4 to 10.6 mg eq/kg (17 to 18% TRR) and 0.86 to 0.97 mg eq/kg (14% TRR), but not detected in seed. The only other metabolite found at more than 10% TRR was M550I042 at 3.9 mg eq/kg (10% TRR) in straw. M550I006 was found in seed at 0.03 mg eq/kg (9.7% TRR).

Livestock metabolism

In the goat metabolism study, parent dimpropyridaz was the main component in liver for both labels (Pyridazine Label: 0.76 mg/kg or 33% TRR, Pyrazole Label: 0.61 mg/kg or 30% TRR). Parent was also significant in fat (19 to 26% TRR) but at low concentrations (0.005 to 0.006 mg/kg). In the hen metabolism study, unchanged parent dimpropyridaz was not detected in relevant amounts in any of the matrices for both labels.

M550I015 was the most abundant component in goat milk of both labels accounting for 0.12 mg eq/kg or 54% TRR (pyridazine label) and for 0.13 mg eq/kg or 63% TRR (pyrazole label). M550I015 was also the main metabolite in goat kidney of both labels amounting to 0.28 mg eq/kg or 31% TRR (pyridazine label) and

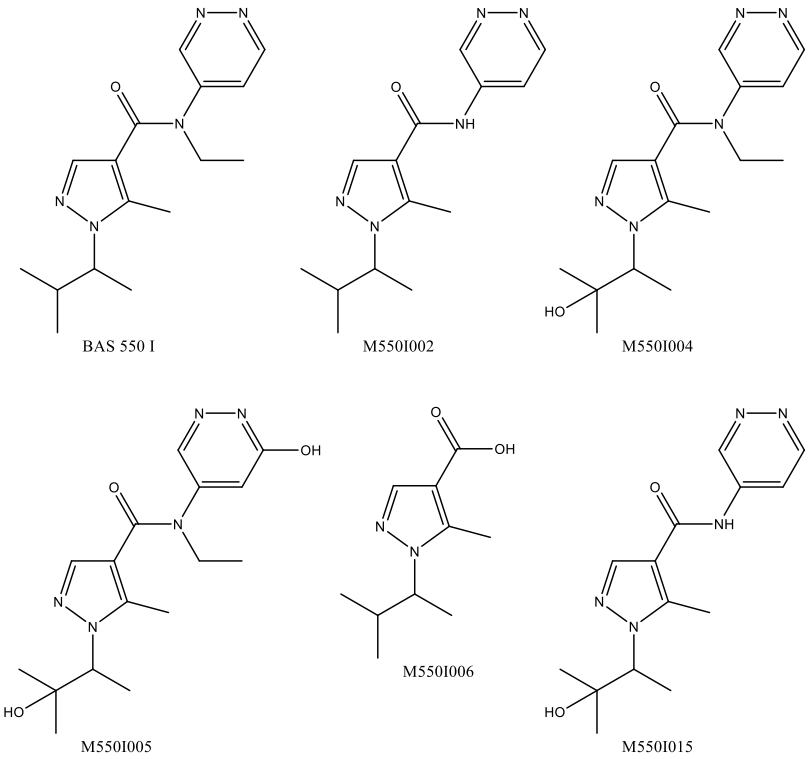
to 0.26 mg eq/kg or 30% TRR (pyrazole label). M550I015 was found in goat muscle at 0.02 mg eq/kg (15 to 19% TRR). M550I015 was significant in the hen metabolism study: (egg white: 46% and 49% TRR; muscle: 61% and 67% TRR; liver: 52% and 57% TRR; fat: 27% and 38% TRR; egg yolk (second most abundant component): 26% and 25% TRR)).

M550I004 was the most prominent metabolite in goat muscle, accounting for 0.05 mg eq/kg or 41% TRR (pyridazine label) and for 0.05 mg eq/kg or 44% TRR (pyrazole label). M550I004 was the second most prominent metabolite in goat kidney of the pyridazine label (25% TRR, 0.22 mg eq/kg) and accounted for 14% TRR, 0.12 mg eq/kg in the kidney sample of the pyrazole label.

M550I002 was the second most prominent component in the goat liver extracts of both labels amounting to 20% TRR, 0.47 mg eq/kg (pyridazine label) and 20% TRR, 0.40 mg eq/kg (pyrazole label). M550I002 was also found in goat muscle at 0.02 mg eq/kg (14% TRR). M550I002 was the main component in the egg yolk extracts (39% and 47% TRR for the pyridazine label and the pyrazole label, respectively) and the second most abundant component in extracts from egg white, hen muscle and liver (17% to 30% TRR).

M550I005 was significant in goat kidney and liver at 16 to 19% TRR (0.14 to 0.16 mg eq/kg) and 10 to 14% (0.24 to 0.29 mg eq/kg) respectively. M550I014 and M550I028 were significant only in goat milk at 12 to 13% TRR (0.03 mg eq/kg) and 10 to 11% TRR (0.02 mg eq/kg) respectively.

Figure 1: Structures of dimpropyridaz (BAS 550 I) and its main metabolites



Analytical methods and storage stability

Plant commodities (based on L0376/01 and L0376/02)

In Australian vegetable trials provided by the applicant, dimpropyridaz and its metabolite residues (M550I002, M550I004, M550I005, M550I006, Reg. No. 6065040 and Reg. No. 6123135) were extracted twice from each sample with methanol, and then further diluted with water. Residues were determined by LC-MS/MS using external matrix matched standards. The LOQ was 0.01 mg/kg for each analyte, the LOD was 0.003 mg/kg. Recoveries from fortified control samples were within acceptable limits.

For high oil samples from the Australian cotton trials, extraction was completed with a mixture of methanol and water. An aliquot of the extract was diluted with methanol after clean-up by SPE. Residues were determined by LC-MS/MS using external matrix matched standards. The LOQ was 0.01 mg/kg for each analyte, the LOD was 0.003 mg/kg. Recoveries from fortified control samples were within acceptable limits.

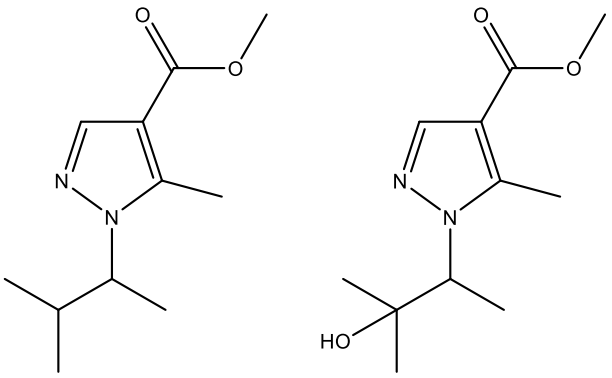
Alternative analysis for plant commodities

Samples from the Australian trials were also sent to Europe for analysis by an alternative method. BASF Method L0376/03 was adapted for dimpropyridaz, M550I002, M550I004, M550I005, M550I006, Reg. No. 6065040 and Reg. No. 6123135 using LC-MS/MS using microwave extraction with methanol (for high water commodities), or with methanol/water (for high starch and high oil commodities). Extracts from high water commodities were cleaned up using a QuEChERS dSPE kit. A QuE Z-Sep/C18 dSPE kit was used to clean

up the extracts from high starch and high oil commodities. The method has a limit of quantitation (LOQ) of 0.010 mg/kg for all analytes (0.011 mg/kg for M550I002, 0.0095 mg/kg for M550I004, 0.0090 mg/kg for M550I005, 0.015 mg/kg for M550I006, 0.014 mg/kg for Reg. No. 6065040 and 0.013 mg/kg for Reg. No. 6123135; if expressed as parent equivalent).

Under the microwave extraction conditions of method L0376/03, a cleavage and/or conversion of dimpropyridaz and its metabolites M550I002, M550I004, and M550I006 to the respective methyl-esters can occur. The 2 possible methyl-esters are represented by the additional analytes Reg. No. 6065040 and Reg. No. 6123135.

Figure 2: Structures of additional analytes formed under microwave extraction



Reg. no. 6065040 Reg. no. 6123135

Animal commodities

A method has been provided for the determination of dimpropyridaz and its metabolite M550I015 in animal matrices. Milk and egg were extracted with methanol by shaking. Following centrifugation, an aliquot was taken and diluted with water. Liver, kidney, muscle, and fat were extracted with methanol using a Geno grinder. An aliquot was taken and diluted with water. The final determination of dimpropyridaz and M550I015 was conducted with LC-MS/MS monitoring 2 mass transitions. The LOQ was 0.01 mg/kg for each analyte. The LOD was 0.002 mg/kg. Recoveries were within acceptable limits.

Storage stability

Decline of dimpropyridaz and some of its metabolites was observed in some commodities following frozen storage. Parent dimpropyridaz was stable for <2 months in lettuce (incurred residue, 45% recovered after 2 months) using analytical methods equivalent to the primary method. However, parent dimpropyridaz was stable for at least 10 to 24 months in the other commodities tested (melon, cucumber, zucchini, broccoli, Brussels sprouts, cauliflower, cabbage, tomato, pepper, spinach and rape seed). M550I002 was stable for <2 months in lettuce (42% recovery), Brussels sprouts (32% recovery) and cauliflower (65% recovery). M550I004 was stable for <2 months in incurred samples of lettuce (quantifiable residues not recovered, noting a low initial residue of 0.02 mg/kg), but stable in standard lettuce samples and in all other commodities tested.

In the residue trials submitted, all samples were maintained under freezer conditions (i.e. –18°C) prior to analysis and tested within 96 days of collection (Australian cucurbit trials). For most of the Australian

vegetable trials, analysis was generally within 1 to 2 months of sampling. This is still longer than the demonstrated period of stability for some metabolites, in some commodities. Stability has been shown for the total residue in all commodities when analysed by method L0376/03. However, it is not practicable to consider an enforcement residue definition that requires a microwave extraction for a sum of total residues. For MRL setting purposes, consideration must be given to correcting residue results for storage stability recoveries in instance where parent or metabolite is not stable for the storage period in a particular commodity (e.g., lettuce, cauliflower and Brussels sprouts). Correction of residues for storage stability is discussed for each commodity below, when required.

Residue definition

Plant commodities

A simple analytical method is available for parent compound in plant commodities, and it is generally equally or more stable in stored samples for methods L0376/01 and L0376/02 when compared to its metabolites. For this reason, and because the parent is the most suitable marker for misuse based on the results of the plant metabolism studies, an enforcement definition of parent compound only is recommended for commodities of plant origin.

The most significant components in plants apart from parent were M550I002, M550I004 and M550I006. All 3 of these metabolites were observed at varying degrees above the LOQ in the crop field trials. The toxicological evaluation of these metabolites indicated that they would be covered by the health-based guidance values recommended for dimpropyridaz. A risk assessment definition of the sum of parent, M550I002, M550I004, and M550I006, expressed as parent, will be recommended for commodities of plant origin.

Animal commodities

The proposed uses on vegetables and cotton do not include any significant feeds for livestock. As M550I015 was significant in most commodities from goats and hens, an enforcement definition of the sum of parent and M550I015, expressed as parent, will be recommended for commodities of animal origin. A suitable analytical method is available for the determination of parent and M550I015 in commodities of animal origin. The risk assessment definition will also include M550I002, M550I004 and M550I005, as these were significant in several goat or hen matrices.

Residues in food and animal feeds

Cucurbits

The proposed use of dimpropyridaz on cucurbits is for up to 4 applications, each at 120 g a.c./ha, in conjunction with a 1-day harvest withholding period.

Highest residues of parent dimpropyridaz at 1 day after the last of 4 applications (or following 2 applications if the results were higher in the same trial) at 120 g a.c./ha were 0.01, 0.02, 0.02, 0.03, 0.05 and 0.06 mg/kg

in rockmelons; 0.03, 0.09, 0.14 and 0.15 mg/kg in cucumber; 0.02, 0.05, 0.06 and 0.06 mg/kg in zucchini (results for crops grown in protected situations in italics).

The combined dataset suitable for MRL determination is 0.01, 0.02, 0.02, 0.02, 0.03, 0.03, 0.05, 0.05, 0.06, 0.06, 0.06, 0.09, 0.14 and 0.15 mg/kg. The OECD MRL Calculator recommends an MRL of 0.3 mg/kg (n= 14, STMR= 0.05 mg/kg). An MRL of 0.3 mg/kg is recommended for dimpropyridaz on VC 0045 Fruiting vegetables, cucurbits in conjunction with the proposed 1-day harvest withholding period.

Based on the risk assessment definition residues were 0.05, 0.08, 0.08, 0.09, 0.09 and 0.09 mg/kg in rockmelons, 0.07, 0.13, 0.24 and 0.36 mg/kg in cucumbers and 0.04, 0.10, 0.14 and 0.16 mg/kg in zucchini. The combined dataset for cucurbits based on the risk assessment definition is 0.04, 0.05, 0.07, 0.08, 0.08, 0.09, 0.09, 0.09, 0.10, 0.13, 0.14, 0.16, 0.24 and 0.36 mg/kg. The STMR is 0.09 mg/kg (n= 14).

As the residue data provided included crop grown in protected situations, the use on cucurbits is also supported in protected cropping situations.

Brassica vegetables

The proposed use of dimpropyridaz on brassica vegetables is for up to 4 applications, each at 120 g a.c./ha, in conjunction with a 1-day harvest withholding period.

Highest residues of parent dimpropyridaz at 1 day after the last of 4 applications (or following 2 applications if the results were higher in the same trial) at 120 g a.c./ha were 0.15 and 0.35 mg/kg in broccoli; <0.01 and 0.16 mg/kg in cauliflower; <0.01 (4), 0.05 and 0.10 mg/kg in cabbage; 0.03, 0.05, 0.05 and 0.07 mg/kg in Brussels sprouts.

The combined dataset suitable for MRL determination is <0.01 (5), 0.03, 0.05, 0.05, 0.05, 0.07, 0.10, 0.15, 0.16 and 0.35 mg/kg. The OECD MRL calculator recommends an MRL of 0.5 mg/kg (STMR= 0.05 mg/kg, n = 14). It is noted that parent dimpropyridaz residues tended to be higher in broccoli and cauliflower (Subgroup 10A, Flowerhead brassicas), with residues of <0.01, 0.15, 0.16 and 0.35 mg/kg, and that the OECD MRL calculator recommends a MRL of 0.8 mg/kg (0.73 mg/kg unrounded) for this subgroup. An MRL of 0.7 mg/kg will be recommended for dimpropyridaz on VB 0040 Brassica (cole or cabbage) vegetables, head cabbages, flowerhead brassicas, in conjunction with the proposed 1-day harvest withholding period.

For calculation of the total residue for dietary risk assessment, M550I002 residues in cauliflower and Brussels sprouts were corrected for the storage stability recoveries for 2 months of storage of 65% and 32% respectively. Total residues for risk assessment were 0.20 and 0.38 mg/kg in broccoli; <0.03 and 0.20 mg/kg in cauliflower; <0.02 (4), 0.010 and 0.18 mg/kg in cabbage; 0.08, 0.11, 0.12 and 0.13 mg/kg in Brussels sprouts.

The combined dataset for brassica vegetables based on the risk assessment definition is <0.02 (4), <0.03, 0.08, 0.10, 0.11, 0.12, 0.13, 0.18, 0.20, 0.20 and 0.38 mg/kg. The STMR is 0.10 mg/kg (n= 14).

Fruiting vegetables, other than cucurbits

The proposed use of dimpropyridaz on fruiting vegetables, other than cucurbits, is for up to 4 applications, each at 120 g a.c./ha, in conjunction with a 1-day harvest withholding period.

The highest residues of parent dimpropyridaz at 1 day after the last of 4 applications (or following 2 applications if the results were higher in the same trial) at 120 g a.c./ha were 0.07, 0.09, 0.10, 0.11, 0.14 and 0.80 mg/kg in tomatoes; 0.02, 0.03, 0.05, 0.06, 0.11 and 0.18 mg/kg in capsicums (results for crops grown in protected situations in italics).

The combined dataset for MRL recommendation is 0.02, 0.03, 0.05, 0.06, 0.07, 0.09, 0.10, 0.11, 0.11, 0.14, 0.18 and 0.80 mg/kg. The OECD MRL calculator recommends an MRL of 1 mg/kg (STMR= 0.095 mg/kg, n= 12). An MRL of 1 mg/kg is recommended for dimpropyridaz on VO 0050 Fruiting vegetables, other than cucurbits, in conjunction with the proposed 1-day harvest withholding period.

Total residues for risk assessment were 0.10, 0.13, 0.14, 0.14, 0.21 and 1.33 mg/kg in tomatoes: 0.05, 0.06, 0.12, 0.18, 0.28 and 0.32 mg/kg in capsicums. The combined dataset for fruiting vegetables, other than cucurbits, based on the risk assessment residue definition is 0.05, 0.06, 0.10, 0.12, 0.13, 0.14, 0.14, 0.18, 0.21, 0.28, 0.32 and 1.33 mg/kg. The STMR is 0.14 mg/kg (n= 12).

As the residue data provided included crops grown in protected situations, the use on fruiting vegetables is also supported in protected cropping situations.

Leafy vegetables

The proposed use of dimpropyridaz on leafy vegetables is for up to 4 applications, each at 120 g a.c./ha, in conjunction with a 1-day harvest withholding period.

Highest residues of parent dimpropyridaz at 1 day after the last of 4 applications (or following 2 applications if the results were higher in the same trial) at 120 g a.c./ha were 0.12, 0.37, 0.37, 0.43, 1.7, 2.7 and 3.7 mg/kg in lettuce. Corrected for a storage stability recovery for parent for 2 months of storage of 45% in lettuce residues were 0.27, 0.82, 0.82, 0.96, 3.8, 6.0 and 8.2 mg/kg. Parent residues in spinach were 0.84, 3.0, 3.1 and 4.2 mg/kg. Parent residues in Chinese cabbage were 0.01, 0.19, 0.34 and 0.63 mg/kg. While there was no direct stability study for Chinese cabbage, residues were stable in spinach and cabbage so residues in Chinese cabbage (and spinach) will not be corrected for storage stability reasons.

The combined dataset for MRL determination is 0.01, 0.19, 0.27, 0.34, 0.63, 0.82, 0.82, 0.84, 0.96, 3.0, 3.1, 3.8, 4.2, 6.0 and 8.2 mg/kg. The OECD MRL Calculator recommends an MRL of 15 mg/kg (STMR= 0.84 mg/kg, n= 15). An MRL of 15 mg/kg is recommended for dimpropyridaz on VL 0053 Leafy vegetables in conjunction with the proposed 1-day harvest withholding period.

For calculation of the total residue for dietary risk assessment, Parent and M550I002 residues in lettuces were corrected for the storage stability recoveries of 45% and 42% respectively. Total residues for risk assessment were 0.57, 1.1, 1.3, 1.3, 4.3, 7.1 and 8.8 mg/kg in lettuce; 1.7, 3.8, 5.7 and 7.6 mg/kg in spinach; 0.02, 0.32, 0.41 and 0.97 mg/kg in Chinese cabbage.

The combined dataset for leafy vegetables based on the risk assessment residue definition is 0.02, 0.32, 0.41, 0.57, 0.97, 1.1, 1.3, 1.3, 1.7, 3.8, 4.3, 5.7, 7.1, 7.6 and 8.8 mg/kg. The STMR is 1.3 mg/kg (n= 15).

Cotton

The proposed use of dimpropyridaz on cotton is for up to 4 applications, each at 120 g a.c./ha, in conjunction with a 4-week (28 day) harvest withholding period.

Four Australian trials were sampled at a 1- or 3-day PHI. Residues of parent in cotton seed at 30 days after the last of 3 applications at 120 g a.c./ha (1× proposed) in 5 Brazilian trials were <0.002 (4) and 0.011 mg/kg. The OECD MRL calculator recommends an MRL of 0.02 mg/kg (n= 5, STMR= 0.002 mg/kg), noting a high uncertainty due to the small dataset, and the high level of censoring. In the Australian decline trials, the typical half-lives of parent in cotton seed were in the range of 1 to 2 days (in the trials with sufficient initial residue to show a clear decline). Based on a half-life of 2 days, the parent HR of 0.058 mg/kg in cotton seed at a 1-day PHI in the Australian trials is estimated to have declined to <LOD (0.002) mg/kg at a 28-day PHI.

An MRL of 0.02 mg/kg is recommended for dimpropyridaz on SO 0691 Cotton seed in conjunction with a 4-week harvest withholding period.

The total residues in seed based on the risk assessment definition and a 4-week PHI (from the Brazilian trials) were <0.009 (2), <0.017, 0.035 and 0.038 mg/kg. The STMR was 0.017 mg/kg (n= 5).

The Brazilian trials did not sample cotton trash, forage or stubble and that residues in cotton trash from the Australian trials were significantly above the threshold for requirement of a feeding study. The following grazing restraint has been proposed “DO NOT feed cotton fodder, stubble or trash to livestock” which is accepted.

Processing – tomatoes

Tomato pomace is a feed for livestock in Australia. Processing factors for parent dimpropyridaz in wet tomato pomace were 0.92×, 1.25× and 2.32×. Based on a parent HR of 0.80 mg/kg in tomatoes, the estimated HR in wet pomace is 1.86 mg/kg (0.80× 2.32). The OECD Feed Calculator indicates that wet tomato pomace contains 20% dry matter. The HR in tomato pomace on a dry weight basis is 9.3 mg/kg. An MRL of 10 mg/kg is recommended for dimpropyridaz on Tomato pomace, dry.

The parent STMR in tomatoes was 0.11 mg/kg. The STMR-P for wet tomato pomace is 0.14 mg/kg (0.11× 1.25) or 0.69 mg/kg on a dry weight basis.

Processing – cotton

Cotton is processed to oil and meal. A cotton processing study has not been provided. However, residues in cotton seed were below the 0.1 ppm threshold for the requirement of a processing study. In addition, the partition coefficient (log P_{ow}) of dimpropyridaz is 1.1, suggesting it is unlikely to concentrate in cotton seed oil.

Crop rotation

Full details of a GLP field crop rotation study conducted in Europe involving application to bare soil at 300 g a.c./ha have been provided. Treated plots were planted with wheat, carrots/radish, cauliflower, spinach/lettuce and tomato at 3 plant back intervals (30, 120 and 365 days).

Low levels of M550I005 residues, up to 0.03 mg/kg, were observed only in commodities grown after the shortest 30-day plant back interval. Finite residues of parent dimpropyridaz, or the metabolites to be included in the risk assessment residue definition (were M550I002, M550I004 and M550I006), were at, or below the LOQ (0.01 mg/kg) at the 30-day plant back interval. Residues of dimpropyridaz and its metabolites were all below the LOQ (0.01 mg/kg) after longer planting intervals (120 and 365 days).

Parent compound, which is the recommended residue definition for enforcement in plant commodities, was at or below the LOQ, even after the shortest plant back interval. In commodities for human consumption, parent compound was <LOD (0.003 mg/kg) in all samples (apart from one radish root sample) after a 30-day PBI, where residues were at the LOD (0.003 mg/kg).

The application rate used in the study to bare soil was at 300 g a.c./ha, which is 2.5× the proposed single application rate, or 0.63× the proposed total seasonal rate per crop for Australia (480 g a.c./ha), noting that the confined rotational crop study was conducted at the same rate (300 g a.c./ha). While the available rotational crop studies did not address the maximum seasonal application rate, applications were made to bare soil in the study, when in practice they will be intercepted by the crop, as the proposed uses will involve application when the plant is actively growing and approaching maturity. In addition, parent residues (the proposed residue definition for MRL enforcement) in the rotated crops were ≤LOD (0.003 mg/kg) in all samples for human consumption from the 30-, 120-, and 365-day PBI and were <LOD in all samples including animal feeds from a 120- or 365-day PBI.

Based on the available information, it is considered unlikely that quantifiable residues of dimpropyridaz will occur in following crops from the proposed uses. Plant back intervals to manage rotational residue issues or the establishment of an “All other foods” MRL are not required for the proposed use patterns.

Residues in animal commodities

Cotton seed and meal and tomato pomace are feeds for mammalian livestock in Australia. The estimated livestock dietary burdens for beef and dairy cattle are summarised below (assuming the STMR for cotton seed will also apply to cotton seed meal):

Table 4: Estimated total dietary burden to dimpropyridaz for beef cattle

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	AU diet content (%)	AU residue contribution (ppm)
Tomato pomace, wet	AB	0.14	STMR	20	0.7	10	0.070

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	AU diet content (%)	AU residue contribution (ppm)
Cotton meal	SM	0.002	STMR	89	0.0	30	0.001
Cotton undelinted seed	SO	0.002	STMR	88	0.0	30	0.001
Total						70	0.071

Table 5: Estimated total dietary burden to dimpropyridaz for dairy cattle

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	AU diet content (%)	AU residue contribution (ppm)
Tomato pomace, wet	AB	0.14	STMR	20	0.7	10	0.070
Cotton meal	SM	0.002	STMR	89	0.0	15	0.000
Cotton undelinted seed	SO	0.002	STMR	88	0.0	20	0.000
Total						45	0.071

An animal transfer study for dimpropyridaz has not been provided, noting the dietary burden (with the exclusion of cotton trash as a grazing restraint has been recommended) is just below the 0.1 ppm threshold when a feeding study would be required. Residues in tissues and milk will be estimated based on the results of the lactating goat metabolism study.

Table 6: Summary of dimpropyridaz residues expected in edible tissues and milk of cattle, and the recommended MRLs for mammalian animal commodities

Feeding level (ppm)	Milk	Muscle	Liver	Kidney	Fat
	Parent+ M550I015 residue (mg/kg)				
12	0.138	0.033	1.021	0.325	0.01
0.071 – beef, estimated burden	–	0.0002	0.0060	0.0019	0.00006
0.071 – dairy, estimated burden	0.0008	–	–	–	–
Established MRLs	–	–		–	–
Recommended MRLs	*0.02	*0.02		*0.02 (offal)	–

Cotton seed meal is a feed for poultry. The estimated dietary burden for poultry is summarised below:

Table 7: Estimated total dietary burden to dimpropyridaz for poultry

Commodity	CC	Residue (mg/kg)	Basis	DM (%)	Residue dw (mg/kg)	AU diet content (%)	AU residue contribution (ppm)
Cotton meal	SM	0.002	STMR	89	0.002	10	0.0002
Total						10	0.0002

Residues in tissues and eggs will be estimated based on the results of the laying hen metabolism study.

Table 8: Summary of dimpropyridaz residues expected in edible tissues and eggs of poultry, and the recommended MRLs for poultry commodities

Feeding level (ppm)	Eggs	Muscle	Liver	Kidney	Fat
					Parent+ M550I015 residue (mg/kg)
12	0.014	0.024	0.158	-	0.010
0.0002 – broilers, estimated burden	-	<<0.02	<<0.02	-	<<0.02
0.0002 – layers, estimated burden	<<0.02	-	-	-	-
Established MRLs	-	-		-	-
Recommended MRLs	*0.02	*0.02		*0.02 (offal)	-

Spray drift

In a lactating goat metabolism study, feeding at 12 ppm gave a maximum residue of parent of 0.764 mg/kg in liver, while residues of the metabolites were lower. The feeding level for parent residues (and therefore the metabolites also) to be at the LOQ of the analytical method is 0.157 ppm, noting there are no Codex or overseas MRLs established for dimpropyridaz in animal commodities. A Regulatory Acceptable Level (RAL) of 0.157 ppm was therefore used for estimation of mandatory no-spray zones for protection of international trade (see Labelling requirements).

Dietary risk assessment

The chronic dietary exposure to dimpropyridaz 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 dimpropyridaz is equivalent to <1% of the ADI. It is concluded that the chronic dietary exposure to dimpropyridaz is acceptable.

The acute dietary exposure is estimated by the National Estimated Short-Term Intake (NESTI) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR with 97.5th percentile food consumption data derived primarily from the 2011-12 National Nutritional and Physical Activity Survey. NESTI calculations are conservative estimates of short-term exposure (24-hour period) to chemical residues in food. As noted in the previous section, an acute reference dose for dimpropyridaz was considered to be unnecessary. A NESTI calculation is not required.

Recommendations

The following amendments are required to be made to the APVMA MRL Standard (Table 5).

Table 9: Amendments to the APVMA MRL Standard

Amendments to Table 1		
Compound	**Food**	**MRL (mg/kg)**
Add:		
Dimpropyridaz		
VB 0040	Brassica (cole or cabbage) vegetables, head cabbages, flowerhead brassicas	0.7
SO 0691	Cotton seed	0.02
MO 0105	Edible offal (mammalian)	*0.02
PE 0112	Eggs	*0.02
VC 0045	Fruiting vegetables, cucurbits	0.3
VO 0050	Fruiting vegetables, other than cucurbits	1
VL 0053	Leafy vegetables	15
MM 0095	Meat (mammalian)	*0.02
ML 0106	Milks	*0.02
PM 0110	Poultry meat	*0.02
PO 0111	Poultry, edible offal of	*0.02
Amendments to Table 3		
Compound	**Residue**	
Add:		

Amendments to Table 1		
Compound	**Food**	**MRL (mg/kg)**
Dimpropyridaz	Commodities of plant origin for enforcement: Dimpropyridaz	
	Commodities of plant origin for dietary risk assessment: sum of dimpropyridaz, 5-methyl-1-(3-methylbutan-2-yl)-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I002), N-ethyl-1-(3-hydroxy-3-methylbutan-2-yl)-5-methyl-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I004) and 5-methyl-1-(3-methylbutan-2-yl)-1H-pyrazole-4-carboxylic acid (M550I006), expressed as dimpropyridaz	
	Commodities of animal origin for enforcement: sum of dimpropyridaz and 1-(3-hydroxy-3-methylbutan-2-yl)-5-methyl-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I015), expressed as dimpropyridaz	
	Commodities of animal origin for dietary exposure assessment: sum of dimpropyridaz, 1-(3-hydroxy-3-methylbutan-2-yl)-5-methyl-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I015), 5-methyl-1-(3-methylbutan-2-yl)-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I002), N-ethyl-1-(3-hydroxy-3-methylbutan-2-yl)-5-methyl-N-(pyridazin-4-yl)-1H-pyrazole-4-carboxamide (M550I004) and N-ethyl-1-(3-hydroxy-3-methylbutan-2-yl)-N-(6-hydroxypyridazin-4-yl)-5-methyl-1H-pyrazole-4-carboxamide (M550I005), expressed as dimpropyridaz	

Amendments to Table 4		
Compound	**Animal feed commodity**	**MRL (mg/kg)**
Add:		
Dimpropyridaz		
	Tomato pomace, dry	10

Assessment of overseas trade aspects of residues in food

Commodities exported and main destinations

The proposed vegetable crops on the label are not major export commodities. However, cotton seed and its derived oils and meals are considered to be major export commodities, as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed feeds produced from treated cotton seed and meal, and tomato pomace. Residues in these commodities resulting from the use of Efficon Insecticide may have the potential to unduly prejudice trade.

In the 2020 fiscal year, Australia exported 35.21 kt of cotton seed and 14.98 kt of cottonseed oil. Exports of cotton seed meal were 0.01 kt in 2020 (ABARES).[1]

Major markets for cotton seed were Japan and Korea. Markets for cottonseed oil in 2020 were not listed by ABARES. The major markets for cotton seed meal in earlier years were New Zealand, and Korea.

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

Overseas registrations and approved label instructions

The applicant indicated that dimpropyridaz products are not yet registered elsewhere globally. The applicant indicated that submissions are planned for the EU, the UK and China.

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. Codex 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. Dimpropyridaz has not been considered by Codex and no international MRLs are established. The applicant has indicated that a submission to the 2023 JMPR is planned based on the proposed Australian label.

Potential risk to trade

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

[1] Australian Bureau of Agricultural and Resource Economics and Sciences (ABARES), 2021. *Agricultural commodity statistics*, Department of Agriculture, Fisheries and Forestry website, accessed March 2022.

As detectable residues are not expected to occur in animal commodities as a result of the proposed uses, the risk to trade in animal commodities is considered to be low. The risk to trade for the proposed vegetable crops is also considered to be low, as vegetable crops are not considered to be major export commodities.

An MRL of 0.02 mg/kg is proposed for cotton, which represents a possible risk to trade as Codex or international MRLs are not established for dimpropyridaz. However, the STMR in cotton seed in the available trials was <0.002 mg/kg.

The following trade advice is on the draft label:

> Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for labelled crops treated with Efficon Insecticide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing crops for export, please check with BASF Australia Ltd for the latest information on MRLs and import tolerances BEFORE using this product.

Comment is sought from relevant industry groups on the potential for the proposed use on cotton to prejudice Australian trade of cotton seed (including oil and meal).

Work health and safety assessment

Health hazards

Efficon Insecticide has low acute oral, dermal, and inhalational toxicity; is slightly irritant to eyes and skin; but has not potential to be a skin sensitiser.

Occupational exposure

Efficon Insecticide containing 120 g/L dimpropyridaz, formulated as a soluble concentrate (SL), is proposed to be used for control of aphid, silver leaf white fly, and thrips in leafy vegetables, brassica vegetables, fruiting vegetables, cucurbits, and cotton. It is intended for professional use and will be applied mechanically by ground boom application methods. The draft product label includes statements to not apply by aerial spray equipment.

The product is intended for professional use and will be applied mechanically by boom sprayer. The product will be available in 1 to 1000 L pack sizes.

Occupational risk assessment is based on both acute exposure to the product and repeat exposure to the active constituent. Workers may be exposed to the product from dermal and/or inhalation routes during mixing, loading, and application (M/L/A) and dermal exposure during post-application activities. Minor or accidental ocular exposure may also occur.

Although no worker exposure data were submitted, APVMA concluded that adequate data were available to undertake an occupational risk assessment for the proposed uses of Efficon Insecticide.

Risk during use

Given the low toxicity of dimpropyridaz following short-term exposures and taking into consideration the predominant route of exposure, a repeat dose dermal exposure study is considered appropriate for risk assessment. A suitable 28 day repeat semi-occlusive dermal exposure study is available. In this study about 10% of the total body surface area was semi-occlusively exposed at up to 1000 mg/kg bw/d of dimpropyridaz for 6 hours per day for 28 days. No adverse effects were detected at 1000 mg/kg bw/d.

A quantitative risk assessment was considered not necessary as no toxicological adverse effects were identified in a 28-day dermal toxicity study at the limit dose. A qualitative modelling of worker exposure during application by groundboom, mechanically pressurised hand wand and backpack spraying was carried out based on the APVMA Compendium of Farming Practices. The margin of exposure (MOE was acceptable (>100)) for all activities without additional personal protective equipment (PPE).

Further, considering inhalation exposure accounts for ≤0.6% of total body exposure during the activities where the highest chemical exposure occurs, formal exposure assessments was not required for occupational inhalation exposure, occupational re-entry exposure, bystander exposure and spray drift exposure.

Risk during re-entry or rehandling

Formal assessment of re-entry risk was considered unnecessary. Therefore, due to very low dermal exposure risk and limited acute hazard associated with the product, no re-entry statement will be required.

Public exposure

Efficon Insecticide is intended for professional use only. Therefore, risks from use are not relevant for the general public.

Application of Efficon Insecticide by groundboom may lead to unintended bystander exposure via chemical spray drift. Dermal exposure risk was considered to be low and therefore no buffer zones are required.

Exposure to dimpropyridaz residues is possible from ingestion of residues in cucurbits, brassica vegetables, fruiting vegetables, and leafy vegetables treated with BAS 550 01I. APVMA Residues establishes maximum residue limits (MRLs) in these crops to ensure the Acceptable daily intake (ADI) is not exceeded.

Recommendations

The following first aid instructions, safety directions and precautionary (warning) statements are recommended for the product label.

First aid instructions

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

Safety directions

May irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), and elbow length chemical resistant gloves. Wash hands after use.

Precautionary (warning) statements

Not required.

Restraints/restrictions

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

Re-entry statement

A re-entry statement is not required.

Environmental assessment

Fate and behaviour in the environment

Soil

Irradiation in the soil photolysis experiments with dimpropyridaz did not show an influence of light on the degradation behaviour and metabolite formation in soil. The estimated DT^{50} values of the photolysis experiment and the dark control were both 12 days.

The degradation rate of dimpropyridaz was evaluated in the laboratory on 4 soils when applied as the active constituent under both aerobic and anaerobic conditions at 20°C in the dark. In aerobic soils, degradation followed either first order or bi-phasic kinetics and soil half-lives ranged 16 to 98 days (geomean 30 days). Mineralisation was <3.5% in all soils. Non-extractable residues ranged 20 to 29% AR at the end of the studies. The degradation of dimpropyridaz first resulted in the formation of the 2 metabolites M550I001 (hydroxylated at the pyridazine moiety) and M550I004 (hydroxylated at the pentyl moiety (maximum 10%)) of which M550I001 was found at higher concentrations (maximum 51% in aerobic soil). Both metabolites degraded further to mainly M550I005 (maximum 29%) where both moieties are hydroxylated. Alternatively, M550I001 may to some extent degrade to M550I007 (which carries a carboxylic acid function at the pentyl moiety, maximum 8.4%). M550I005 is either degraded to M550I009 (which lacks the pentyl moiety, maximum 14%) or to non-extractable residues and CO^2. M550I007 may also be degraded to M550I009 or directly to non-extractable residues and CO^2. Chiral analysis showed that there was preferential metabolism of the S- versus the R-enantiomer in soil (geometric mean DT_{50} values of 15 and 30 days, respectively). The results described above are for the enantiomeric mixture.

Laboratory soil metabolism studies were provided for the soil metabolites of dimpropyridaz. Geomean DT_{50} values for M550I001, M550I004, M550I005, M550I006, M550I007 and M550I009 were 117, 22, 430, 4.6, 172 and 223 days, respectively.

A total of 12 field dissipation studies were provided (6 from Europe and 6 from the USA). All applied dimpropyridaz to bare soil. Dimpropyridaz tended to be retained in the top 30 cm soil layer. The range of half-lives was 9.1 to 81 days (geomean 22 days). Dissipation in this layer was mainly described by first order kinetics in the European studies and biphasic kinetics in the American studies. Significant metabolites reflected those observed in laboratory studies with M550I001, M550I005, and M550I009 being the main metabolites measured. M550I001 DT_{50} values were determined within the field studies and ranged 21 to 577 days (geomean 135 days). Separate field dissipation studies for M550I005, M550I007, and M550I009 were provided for 4 to 5 sites in Europe. M550I005 degraded following first order kinetics with DT_{50} values ranging 27 to 199 days (geomean 64 days). M550I007 generally degraded following first order kinetics with DT_{50} values ranging 16 to 75 days (geomean 28 days). M550I009 degraded following biphasic kinetics with modelling DT_{50} values ranging 88 to 990 days (geomean 285 days). These are slow phase half-lives and significant removal of the parent compound (>50%) was observed during the first phase of degradation.

The mobility of dimpropyridaz and its major soil metabolites was tested in standard batch equilibrium studies. Freundlich KF values for dimpropyridaz (8 soils, 1 sediment) ranged 0.17 to 5.0 L/kg (KFOC 19 to 248 L/kg) indicating dimpropyridaz could be mobile in the soil environment. A positive relationship between KF and soil

organic carbon was apparent and regression derived KF values for 1% and 5% soil organic carbon are 0.66 and 3.3 mL/g, respectively. The average 1/n was 0.93. Metabolites were tested on 5 or 6 soils. 2 metabolites (M550I001 and M550I009) showed a positive relationship between sorption and soil organic carbon and calculated KF values for a 1% OC soil were 0.23 and 0.16 L/kg, respectively. Geometric mean KF values for M550I004, M550I005, M550I006 and M550I007 were 0.32, 0.26, 0.066 and 0.057 L/kg, respectively. All metabolites are expected to be mobile in soil.

Water

Dimpropyridaz was stable in aqueous solution at pH 4, 5, and 7 (25°C). The kinetic evaluation of hydrolysis at pH 9 determined reliable degradation endpoints for dimpropyridaz, with a DT_{50} of 185 days and a DT90 of 615 days. In an aqueous photolysis study, the DT50 was calculated to be 47 days and the DT90 was calculated to be 155 days with continuous irradiation. The quantum yield calculation for dimpropyridaz resulted in a value of 1.5 × 10-5.

When applied to aerobic water-sediment systems that were incubated in the dark, dimpropyridaz was not persistent with water DT50 values ranging 38-56 days, sediment DT50 values ranging 82-158 days and whole system half-lives ranging 86-117 days. M550I001 was the main component in most of the samples. Its concentration continuously increased in both water/sediment systems (maximum occurrence of 25% AR in water phases and 19% AR in sediment extracts. The two-fold hydroxylated (at ring and side chain) derivative M550I005 occurred later in the incubation period increasing to 11% AR and 4.4% AR in the water phases and the sediment extracts in one of the tested systems, respectively.

Chiral analysis showed that there was preferential metabolism of the S-enantiomer over the study period in one system, but no clear tendency for enantiomer specific transformation in the second system. Dimpropyridaz is not readily biodegradable.

Air

Standard modelling was undertaken to predict the atmospheric half-life of dimpropyridaz through reaction with hydroxyl radicals. Based on a global, annual average concentration of 1.5 × 106 OH/cm3 and a 12-hour day, an atmospheric DT50 was calculated to be 0.36 days. Dimpropyridaz is not volatile (vapour pressure 8.7 × 10-6 Pa), so is not expected to partition to the atmospheric compartment.

Effects and associated risks to non-target species

Terrestrial vertebrates

Dimpropyridaz has moderate toxicity to mammals (LD_{50} 465 mg a.c./kg bw, *Rattus norvegicus*) and birds (LD50 1778 mg a.c./kg bw, *Colinus virginianus*). Following long-term dietary exposure in reproductive or developmental toxicity studies, maternal toxicity of was observed in mammals at doses as low as 150 mg a.c./kg bw/d (NOAEL 50 mg a.c./kg bw/d, *Oryctolagus cuniculus*), while no adverse effects were observed in birds at the highest tested concentration (NOEL 97 mg a.c./kg bw/d, *Colinus virginianus*). The toxicity of metabolites of dimpropyridaz in potential food items of terrestrial vertebrates are expected to be covered by the parent substance.

Risks to terrestrial vertebrates were determined to be acceptable for a realistic worst-case scenario (direct dietary exposure within the treatment area following foliar treatments at 4× 120 g a.c./ha in 7-day intervals). No protection statements are required for terrestrial vertebrates.

Aquatic species

At the limit of solubility, dimpropyridaz has low toxicity to fish (lowest LC50 >30 mg ac/L, 2 species tested), aquatic invertebrates (EC_{50} >30 mg ac/L, *Daphnia magna*), sediment dwellers (EC_{50}>105 mg ac/L, *Chironomus riparius*), and algae (ErC_{50}>95 mg ac/L, *Pseudokirchneriella subcapitata*). Dimpropyridaz is not expected to be toxic to aquatic plants. However, a representative SL formulation was moderately toxic to fish (lowest LC_{50} 2.4 mg ac/L, *Oncorhynchus mykiss*), and a protection statement is required on the label to identify the hazard.

M550I001, M550I004, M550I005, M550I006, M550I007, M550I009, and M550I041 were investigated for toxicity to fish, aquatic invertebrates, sediment dwellers and algae. All had low toxicity (LC/EC_{50}>100 mg/L), with the exception of the minor soil metabolite M550I006 (ErC_{50} 50 mg/L, *Pseudokirchneriella subcapitata*), and the aqueous photoproduct M550I041 (LC_{50} 41 mg/L, *Oncorhynchus mykiss*; EC_{50} 23 mg/L, *Daphnia magna*; ErC_{50} 11 mg/L, *Pseudokirchneriella subcapitata*).

Following long-term exposure to dimpropyridaz, no adverse effects on fish in the early life stages were observed at the highest test concentration (NOEC 11 mg ac/L, *Pimephales promelas*). Reduced reproduction of aquatic invertebrates was observed at concentrations as low as 2.0 mg ac/L (NOEC 1.0 mg ac/L, *Daphnia magna*). Reduced growth, reproduction and development rate of sediment dwellers were observed at concentrations as low as 34 mg a.c./kg dry sediment (NOEC 11 mg a.c./kg dry sediment, *Chironomus riparius*).

Dimpropyridaz did not demonstrate effects that would indicate interference with the endocrine system in *Xenopus laevis* tested up to 9.8 mg ac/L.

Risks of dimpropyridaz and its metabolites to aquatic species were determined to be acceptable for a worst-case scenario (direct overspray of shallow water at 4× 120 g a.c./ha in 7-day intervals). Spray drift risks of the product formulation to fish were sufficiently low that a buffer zone is not required for the protection of natural aquatic areas.

Bees

Dimpropyridaz had low toxicity to adult bees by contact exposure (lowest LD_{50}>50 µg a.c./bee, 2 species tested) and oral exposure (lowest LD_{50}>42 µg a.c./bee, 2 species tested), and low toxicity to bee larvae (LD_{50}>45 µg a.c./bee, *Apis mellifera*). The SL formulation did not enhance toxicity to bees. M550I001, M550I004, M550I005, M550I006, M550I016, and M550I040 similarly had low toxicity to bees.

Following continuous dietary exposure for 10 days, significant mortality of adult bees was observed at doses as low as 13 µg a.c./bee/d (NOEDD 7.4 µg a.c./bee/d, *Apis mellifera*). There were no effects observed in a multi-dose test following repeated dietary exposure during the larval development period (NOED 46 µg a.c./bee, *Apis mellifera*).

Behavioural effects of adult bees were observed in the acute and chronic studies with effects decreasing over time, suggesting a transient, reversible effect. This was further investigated and confirmed with an additional laboratory trial conducted at 2 test doses (realistic exposure and 10× higher). The results showed reversible short-term effects on behavioural parameters that were strong at all doses after 4h but absent already at the next observation point (24 h) in the low/ realistic exposure dose.

Two semi-field and 2 field studies on bees were also conducted with the representative SL formulation according to the European GAP (2× 120 g a.c./ha pre-bloom). All studies showed no biologically relevant effects on mortality, foraging activity, and colony development. Although these studies do not match the GAP proposed in Australia where an application during flowering is possible, they were submitted with the Australian dossier as supportive information.

Risks to bees were determined to be acceptable for realistic worst-case scenarios (direct contact or dietary exposure following overspray of blooming plants at 120 g a.c./ha). No protection statements are required for bees.

Other non-target arthropods

In Tier 1 laboratory tests, fresh-dried residues of the representative SL formulation on an inert substrate resulted in LR_{50} 546 g a.c./ha for indicator species of predatory arthropods (*Typhlodromus pyri*) and LR_{50} 34 g a.c./ha for indicator species of parasitic arthropods (*Aphidius rhopalosiphi*). In Tier 2 laboratory tests, fresh-dried residues on natural substrates resulted in LR_{50} and ER_{50} values >450 g a.c./ha for both indicator species. One additional extended laboratory test with the green lacewing also resulted in LR_{50} and ER_{50} values >450 g a.c./ha (*Chrysoperla carnea*).

Risks to non-target arthropods were determined to be acceptable for a realistic worst-case scenario (direct contact exposure to foliar residues following foliar treatments at 4× 120 g a.c./ha in 7-day intervals). No protection statements are required for other non-target arthropods, and the product can be considered to be compatible with integrated pest management (IPM) programs utilising beneficial arthropods.

Soil organisms

Dimpropyridaz has low toxicity to soil macro-organisms such as earthworms (LC_{50} >1000 mg a.c./kg dry soil, *Eisenia fetida*). Following long-term exposure, reduced reproduction was observed at concentrations as low as 427 mg a.c./kg dry soil (NOEC 285 mg a.c./kg dry soil, *Eisenia andrei*). Dimpropyridaz did not adversely affect soil processes such as nitrogen transformation at exaggerated soil concentrations (NOEC 2.0 mg a.c./kg dry soil).

The representative SL formulation had higher chronic toxicity to soil macro-organisms (EC_{10} 141 mg a.c./kg dry soil, *Folsomia candida*), but it did not influence microbial soil processes.

M550I001, M550I004, M550I005, M550I006, M550I007, and M550I009 were less toxic than dimpropyridaz to soil macro- and micro-organisms, with the exception of the minor soil metabolite M550I006 for which reproductive effects were observed on earthworms (EC_{10} 47 mg/kg dry soil, *Eisenia andrei*).

Risks were determined to be acceptable for a realistic worst-case scenario (direct overspray of soil at 4× 120 g a.c./ha in 7-day intervals). No protection statements are required for soil organisms.

Non-target terrestrial plants

The representative SL formulation of dimpropyridaz had low toxicity to a standard suite of 10 terrestrial plant species tested at a single application rate of 2.5 L product/ha (300 g a.c./ha) when applied as either pre-emergent (seedling emergence study) or early post-emergent (vegetative vigour study). The ER_{25} and ER_{50} values were all >300 g a.c./ha. Risks were determined to be acceptable for a direct overspray. Therefore, no protection statements are required for non-target terrestrial plants.

Recommendations

In considering the environmental safety of the proposed use of Efficon Insecticide, the APVMA had regard to the toxicity of the active constituent in relation to relevant organisms and ecosystems. Based on the available information, the APVMA can be satisfied that the proposed use of the product is unlikely to have an unintended effect that is harmful to animals, plants or things or to the environment.

Efficacy and safety assessment

Proposed product use pattern

Proposed uses are for the control of aphids, Silverleaf Whitefly and Greenhouse Whitefly in cucurbits, brassica vegetables, fruiting vegetables, leafy vegetables, brassica leafy vegetables and cotton. Proposed target rates are 1 L/ha (120 g a.c./ha) for whitefly and 0.5 L/ha (60 g a.c./ha) for aphids. Up to 4 applications of 120 g a.c./ha are proposed using ground boom sprayer equipment with a medium droplet size and minimum retreatment interval of 7 days between applications.

Efficacy and target crop/animal safety

Data from 26 efficacy/crop safety Australian field trials and one overseas efficacy glasshouse trial were provided, along with argument, to support the proposed uses. Australian trials were conducted between 2016 and 2021, across major growing regions in New South Wales, Queensland, Victoria, South Australia and Tasmania. All trials used appropriate experimental designs, locations, timing, methods of spray application and pest assessment methodology, with 3 or 4 replicates. The trial data were analysed using appropriate statistical tests.

Efficacy assessments were made by comparing numbers of insects on Efficon Insecticide-treated plants alongside plants treated with several registered industry standards (applied at label rates) and an untreated control. Assessments were made before treatment and at varying intervals after treatment. In most trials, 2 consecutive spray applications were made, approximately 1 or 2 weeks apart. Efficacy of a range of Efficon Insecticide rates were tested, with or without a spray adjuvant and using various droplet sizes.

Phytotoxicity was assessed by scoring the percentage of the total area of fruit or foliage affected by chlorosis and/or necrosis, on a scale ranging from 0 (nil effect) to 100 (complete loss of crop).

Efficacy

Aphids

Efficon Insecticide effectively controlled high infestations of 4 aphid species in 5 major crop groupings (n = 16 trials). Efficon Insecticide was generally equivalent to, or more effective than registered aphicides containing the active ingredients: pymetrozine (4 trials), imidacloprid (2 trials), dimethoate (1 trial), spirotetramat (12 trials), pirimicarb (1 trial), flupyradifurone (6 trials), sulfoxaflor (12 trials) and afidopyropen (4 trials).

Control of green peach aphid (GPA), *Myzus persicae*, was demonstrated in 6 trials conducted in brassica vegetables and brassica leafy vegetables. Control of cotton/melon aphid, *Aphis gossypii*, a major pest of cotton and cucurbits, was demonstrated in 5 trials. Control of cabbage aphid, *Brevicoryne brassicae*, a major pest in brassicas and leafy vegetables, was demonstrated in 3 trials. Considering the product was clearly efficacious against this and GPA in brassicas and equivalent to other registered aphicides, the low number of trials conducted is considered acceptable from an efficacy perspective. Control of lettuce aphid, *Nasonovia*

ribisnigri, a pest of lettuce only, was also demonstrated in 2 trials but further data is required to support a label claim for this species.

Whiteflies

Efficacy of Efficon Insecticide to control Silverleaf Whitefly, *Bemesia tabaci*, and Glasshouse Whitefly, *Trialeurodes spp*., was demonstrated in 12 field trials and 1 glasshouse trial conducted in cotton, cucurbits and fruiting vegetables. Levels of control achieved were generally equivalent to, or greater than, industry standards containing the active ingredients: cyantraniliprole (3 trials), pymetrozine (1 trial), imidacloprid (1 trial), flonicamid (2 trials), spirotetramat (10 trials), flupyradifurone (8 trials), sulfoxaflor (1 trial) and afidopyropen (2 trials).

Crop safety

Crop safety was assessed in all 26 efficacy field trials, covering 13 crop types belonging to 6 crop groupings. No phytotoxicity was observed in any trial. The safety of applying Efficon Insecticide at rates higher than the maximum proposed for registration (120 g a.c./ha) was assessed in 7 of the efficacy trials and in 5 crops: cotton (150 and 180 g a.c./ha), eggplant (150 g a.c./ha), cucumber (150 g a.c./ha), pumpkin (150 g a.c./ha) and tomato (150 g a.c./ha). Further evidence of crop safety, at rates higher than the maximum proposed for registration, was also provided in additional trials conducted as part of the residues studies.

Resistance management

The mode of action of dimpropyridaz is new. It disrupts the function of chordotonal organ (stretch receptor organ) neurons by blocking signalling upstream of vanilloid transient receptor potential channels. Dimpropyridaz acts upstream of the Insecticide Resistance Action Committee (IRAC 2022) group 9 agents (chordontal organ TRPV channel modulators) and at a different site to IRAC group 29 agents (chorodontal organ modulators – undefined target site). Therefore, the mode of action is regarded as new, and no cross-resistance is expected. The application for assigning a new IRAC group to the IRAC committee is foreseen.

Where the resistance mechanism(s) is unknown, the intelligent use of alternations, sequences, or rotations of insecticidal agents from different MoA classes remains an entirely viable resistance management technique, since such a practice will always minimise selection pressures (IRAC 2022).

Recommendations

The results of the field trials confirmed efficacy and crop safety for the proposed product, when used according to label directions.

The APVMA has no objections on efficacy and target-crop safety grounds to the registration of Efficon Insecticide.

Spray drift assessment

Regulatory Acceptable Levels (RALs) were established by each risk area in order to calculate the appropriate spray drift buffer zones for Efficon Insecticide (Table 6).

Table 11: Summary of RALs for Efficon Insecticide

Sensitive area	Regulatory Acceptable Level	
	Level of active	Units
Bystander	NR[1]	g/ha
Livestock	0.157	ppm
Aquatic	240	µg/L
Pollinator	8333	g/ha
Vegetation	150	g/ha

[1]NR= calculation of a RAL for bystander exposure was not required due to the conservativeness of the exposure assessment and risk characterisation for Efficon Insecticide (see above Worker health and safety assessment).

Buffer zones calculated by the APVMA Spray Drift Risk Assessment Tool (SDRAT) using the above RALs, were incorporated into the Efficon Insecticide label spray drift instructions (see Labelling Requirements below).

Labelling requirements

BASF
We create chemistry

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Efficon® Insecticide

ACTIVE CONSTITUENT: 120 g/L DIMPROPYRIDAZ

GROUP	UN	INSECTICIDE

For the control of Whiteflies and aphids in certain vegetable crops and cotton as per directions for use table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USING THIS PRODUCT

CONTENTS: 1 – 1000L

BASF Australia Ltd ABN 62 008 437 867
Level 12, 28 Freshwater Place Southbank VICTORIA 3006
Website: crop-solutions.basf.com.au

® Registered trademark of BASF

DIRECTIONS FOR USE

RESTRAINTS

DO NOT apply by aircraft.

DO NOT feed cotton fodder, stubble or trash to livestock

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. 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 2 hours before sunset and persist until one to 2 hours after sunrise.

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

Spray droplets not smaller than a MEDIUM spray droplet size category

Minimum distances between the application site and downwind sensitive areas are observed (see ‘Mandatory buffer zones’ section of the following table titled ‘Buffer zones for boom sprayers’).

MANDATORY NO-SPRAY ZONES

Buffer zones for boom sprayers

Application rate	Boom height above the target canopy	Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas	Livestock areas
Up to maximum label rate	0.5 m or lower	0 metres	0 metres	0 metres	0 metres	30 metres
	1.0 m or lower	0 metres	0 metres	0 metres	0 metres	120 metres

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
Cucurbits	Silver Leaf White Fly (*Bemisia tabaci*), Greenhouse Whitefly (*Trialeurodes spp*)	1 L/Ha	1 day	Efficon Insecticide disrupts insect behaviour, coordination and feeding and will provide slow knockdown. Monitor crops and commence applications as local threshold levels are reached. Apply a maximum of 2 sprays before rotating to an alternative insecticide. Do Not apply more than 4 applications per crop. Apply in sufficient water to ensure thorough coverage of the target crop up to the point of runoff. Efficon Insecticide will provide residual control of whiteflies and aphids out to 21 days. Continue to monitor crops and make subsequent applications after 14 days where necessary.
	Cotton/melon aphid (*Aphis gossypii*)	0.5 L/Ha		
Fruiting vegetables, (capsicum, chilli, eggplant, okra, tomato)	Silver Leaf White Fly (*Bemisia tabaci*), Greenhouse Whitefly (*Trialeurodes* spp.)	1 L/Ha		
Brassica vegetables (including broccoli, broccolini, Brussels sprouts, cabbage, cauliflower, kohlrabi) Leafy vegetables and Brassica Leafy Vegetables including chard (silver beet), cress spinach, lettuce (head and leafy), bok choy, Chinese cabbage, choy sum, gai lan, kale, leafy mustard, pak choy, rocquette	Green peach aphid (*Myzus persicae*) Cabbage aphid (*Brevicoryne brassicae*)	0.5 L/Ha		
Cotton	Silver Leaf White Fly (*Bemisia tabaci*), Greenhouse Whitefly (*Trialeurodes* spp.)	1 L/Ha	4 weeks	

CROP	PEST	RATE	WHP	CRITICAL COMMENTS
	Cotton/melon aphid (*Aphis gossypii*)	0.5 L/Ha		

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

WITHHOLDING PERIOD

Brassica vegetables, cucurbits, fruiting vegetables (other than cucurbits), leafy vegetables (including brassica leafy vegetables):

Harvest: DO NOT HARVEST FOR 1 DAY AFTER APPLICATION

Cotton:

Harvest: DO NOT HARVEST FOR 28 DAYS AFTER APPLICATION

TRADE ADVICE

Export of treated commodities

Growers should note that Maximum Residue Limits (MRLs) or import tolerances do not exist in all markets for labelled crops treated with Efficon Insecticide. Additionally, some export markets have established MRLs different to those in Australia. If you are growing crops for export, please check with BASF Australia Ltd for the latest information on MRLs and import tolerances BEFORE using this product.

GENERAL INSTRUCTIONS

APPLICATION

To be effective, thorough crop coverage is required. Apply in a minimum of 200L water/ha. Adjust water volumes according to the crop growth stage to ensure thorough coverage up to the point of runoff.

Instructions for Ground Application

These instructions inform those using this chemical product how to lawfully comply with the requirement of a MEDIUM or larger spray droplet size category for spray application.

Spray droplet size categories are defined in the ASAE S572 Standard (newer name may also be shown as ASABE) or the BCPC guideline. Nozzle manufacturers may refer to one or both of these documents, to identify droplet size categories; however, for a nozzle to comply with this requirement, the manufacturer must refer to at least one.

Complying with the label requirement to use a specific droplet size category means using the correct nozzle that will deliver that droplet size category under the spray operation conditions being used. The APVMA has approved only the following specific methods for choosing the correct nozzle. Use one of the methods specified in these instructions to select a correct nozzle to deliver a MEDIUM or larger droplet size category.

USE ONLY nozzles that the nozzles' manufacturer has rated to deliver MEDIUM, COARSE, a VERY COARSE or an EXTREMELY COARSE droplet size category, as referenced in ASAE S572 or BCPC. Choose a nozzle that is specified to provide the droplet size category required in the label Spray Drift Restraints.

DO NOT use a higher spray system pressure than the maximum the manufacturer specifies for the selected nozzle to deliver the droplet size category required in the label Spray Drift Statement.

COMPATBILITY

Efficon Insecticide is a soluble concentrate (SL) formulation. When using in a tank mix with other products, the following mix order should be observed:

1. Half fill the spray tank with water. Maintain constant agitation
2. Add solid formulation types such as water dispersable granule (WDG/WG), wettable powder (WP), water soluble granule (SG) formulated products first and allow dispersion
3. Add simple liquid formulations such as Efficon (soluble concentrate (SL)) or liquid suspension formulations such as suspension concentrate (SC) formulations
4. Add any liquid formulations for dispersion such as emulsifiable concentrate (EC) and liquid formulation emulsions such as micro-emulsions (ME) formulations
5. Add any water-soluble salts
6. Add any adjuvants as required
7. Add any foliar fertilizer as required
8. Add remaining water

For further information on compatibility please contact your local reseller or BASF representative.

INSECTICIDE RESISTANCE WARNING

GROUP	UN	INSECTICIDE

For insecticide resistance management dimpropyridaz is a Group UN insecticide. Some naturally-occurring insect biotypes resistant to dimpropyridaz and other Group UN insecticides may exist through normal genetic variability in any insect population. The resistant individuals can eventually dominate the insect population if

dimpropyridaz or other dimpropyridaz insecticides are used repeatedly. The effectiveness dimpropyridaz on resistant individuals could be significantly reduced. Since occurrence of resistant insects is difficult to detect prior to use, BASF Australia Ltd accepts no liability for any losses that may result from the failure of dimpropyridaz to control resistant insects. Dimpropyridaz may be subject to specific resistance management strategies. For further information contact your local supplier, BASF Australia Ltd representative or local agricultural department agronomist.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

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 dry, cool, well-ventilated area out of direct sunlight. 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.

SAFETY DIRECTIONS

May irritate the eyes and skin. Avoid contact with eyes and skin. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), and elbow length chemical resistant gloves. Wash hands after use.

FIRST AID

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

SAFETY DATA SHEET

Additional information is listed in the Safety Data Sheet.

CONDITIONS OF SALE

All conditions and warranties rights and remedies implied by law or arising in contract or tort whether due to the negligence of BASF Australia Ltd or otherwise are hereby expressly excluded so far as the same may legally be done provided however that any rights of the Buyer pursuant to non- excludable conditions or warranties of the Competition and Consumer Act 2010 or any relevant legislation of any State are expressly preserved but the liability of BASF Australia Ltd or any intermediate Seller pursuant thereto shall be limited if so permitted by the said legislation to the replacement of the goods sold or the supply of equivalent goods and all liability for indirect or consequential loss or damage of whatsoever nature is expressly excluded. This product must be used or applied strictly in accordance with the instructions appearing hereon. This product is

solely sold for use in Australia and must not be exported without the prior written consent of BASF Australia Ltd.

Batch No:
Date of Manufacture:
Website: crop-solutions.basf.com.au
® = Registered trademark of BASF

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FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY PHONE 1800 803 440 TOLL FREE-ALL HOURS-AUSTRALIA WIDE.

Acronyms and abbreviations

Shortened term	Full term
ABARES	Australian Bureau of Agricultural and Resource Economics
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
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
FOB	Functional observational battery
FTIR	Fourier-transform infrared spectroscopy
g	Gram
GAP	Good agricultural practice
GLP	Good laboratory practice
GVP	Good veterinary practice
h	Hour
ha	Hectare
HPLC	High pressure liquid chromatography *or* high-performance liquid chromatography
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
JMPR	Joint FAO/WHO meeting on pesticide residues
kg	Kilogram

Shortened term	Full term
K_{OC}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	Concentration that kills 50% of the test population of organisms
LD_{50}	Dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of detection – level at which residues can be detected
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
RAL	Regulatory acceptable level
s	Second
SC	Suspension concentrate
SL	Soluble liquid
STMR	Supervised trial mean residue
STMR-P	Supervised trial mean residue-processed
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TRPV	Transient receptor potential vanilloid

Shortened term	Full term
TRR	Total radioactive residue
µg	Microgram
WG	Water dispersible granule
WHO	World Health Organisation
WHP	Withholding period

Glossary

Term	Description
Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration
CAS number	Unique numerical identifier assigned by the Chemical Abstracts Service (CAS) to every chemical substance
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
Henry's law constant	A gas law that states that the amount of dissolved gas in a liquid is proportional to its partial pressure above the liquid
Hydrophobic	Repels water
Immunotoxicity	Adverse effect on the structure or function of the immune system, or on other systems as a result of immune system dysfunction
Leaching	Removal of a compound by use of a solvent
Metabolism	The chemical processes that maintain living organisms
Pharmacokinetics	The study of the movement of substances within the body
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

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