Australian Government

Australian Pesticides and Veterinary Medicines Authority

Molinate Review Technical Report

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Contents

List of tables

Preface

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority with responsibility for the regulation of agricultural and veterinary chemicals in Australia. Its statutory powers are provided in the Agvet Codes scheduled to the *Agricultural and Veterinary Chemicals Code Act 1994*.

The APVMA has legislated powers to reconsider the approval of an active constituent, registration of a chemical product or approval of a label at any time after it has been registered. The reconsideration process is outlined in sections 29 to 34 of Part 2, Division 4 of the Agvet Codes.

A reconsideration may be initiated when new research or evidence has raised concerns about the use or safety of a particular chemical, a product containing that chemical, or its label. The scope of each reconsideration can cover a range of areas including human health (toxicology, public health, work health and safety), the environment (environmental fate and ecotoxicology), residues and trade, chemistry, efficacy or target crop or animal safety. However, the scope of each reconsideration is determined on a case-by-case basis reflecting the specific issues raised by the new research or evidence.

The reconsideration process includes a call for data from a variety of sources, a scientific evaluation of that data and, following public consultation, a regulatory decision about the ongoing use of the chemical or product. The data required by the APVMA must be generated according to scientific principles. The APVMA conducts scientific and evidence-based risk analysis with respect to the matters of concern by analysing all the relevant information and data available.

About this document

This Technical Report is intended to provide an overview of the assessments that have been conducted by the APVMA. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience, thereby encouraging public comment.

This document contains a summary of the assessment reports generated in the course of the chemical review of an active ingredient, including the registered product and approved labels. The document provides a summary of the APVMA's assessment, which includes details of:

- the chemistry of the active constituent
- the toxicology of both the active constituent and product
- the residues and trade assessment
- occupational exposure aspects
- environmental fate, toxicity, potential exposure and hazard.

Summary

Introduction

Molinate is a thiocarbamate herbicide. It is absorbed by plant roots with acropetal (base to apex) translocation to the leaves. The pesticidal mode of action is via the conjugation of acetyl coenzyme A and other sulfhydryl-containing biomolecules which result in inhibition of fatty acid and lipid biosynthesis resulting in reduced cuticular wax deposition, inhibition of the biosynthesis of proteins, isoprenoids (including gibberellins), and flavonoids (including anthocyanins), inhibition of gibberellin synthesis and inhibition of photosynthesis. It has been used to control barnyard grass (*Echinochloa spp.*) and silver top or brown beetle grass (*Diplachne fusca*) in wet rice cultivation in Australia.

The APVMA began its reconsideration (hereafter referred to as review) of the active constituent molinate, all products containing molinate and their associated labels in 2003 due to:

- concerns regarding the potential for impaired fertility and neuropathy in humans which might pose an undue hazard to human health;
- possible risks to workers health associated with short and intermediate term occupational exposure;
- the potential for hazards to worker safety;
- the potential for contamination of waterways indicated by varying levels of molinate recorded in drainage water from rice fields; and
- the adequacy of instructions and warnings on product labels.

The review scope included consideration of public health, work health and safety and environmental aspects of the active constituent molinate, product registrations containing molinate and associated label approvals.

The APVMA published the *Molinate preliminary review findings report* in 2014.

Submissions received in response to the molinate preliminary review findings report

The APVMA published the preliminary review findings report in January 2014. Following the publication of the findings, several submissions were received from holders of active constituent approvals and product registrations as well as the industry grower group Ricegrowers' Association of Australia. These submissions are listed in order of receipt in Table 1.

Table 1: Submissions received from holders or members of the public

Submitted by	Contents	Review comments
Ricegrowers' Association of Australia October 2014	*Mixer and Loader Exposure Study with Molinate*. Preliminary trial with 3 operators (3 replicates) to assess the extent of dermal exposure when wearing specified personal protective equipment (PPE) during mixing and loading (Agrisearch 2014).	Preliminary indication that aerial application of molinate could be supported with appropriate restrictions. Further replicates required to confirm preliminary outcomes.
Ricegrowers' Association of Australia April 2016	Submission of collated water monitoring data for 2010–11 to 2014–15 growing seasons (RGA 2016).	Detections of molinate declined with one detection in the 2013–14 season and zero detections above the environmental guideline in the 2014–15 season.
Crop Care Australasia Pty Ltd/Nufarm Australia February 2017	*Mixer/Loader and Applicator Exposure Study with molinate – Final Study*. Worker exposure study for mixing/loading and application by aircraft (Bickley Boom*; Agrisearch 2016).	Continued use of molinate is supported with restrictions to the amount of molinate that can be mixed and applied per day.

* The Bickley Boom, developed in 2001, uses the Soluble Chemical Water Injection in Rice Technique (SCWIIRT) application method. This method of application involves only one nozzle (jet) per boom per aircraft wing. The delivery through the jet is angled to minimise wind shear effects and thereby reduce spray drift and potential exposure to bystanders.

The additional information received has been considered and based on the evaluation of this information, the APVMA is currently satisfied that the instructions for use for agricultural molinate products can be varied to satisfy the requirements for continued registration.

This document summarises the review and the regulatory decisions that are to be implemented as a result of the review.

Chemistry

Active constituent

Table 2: Nomenclature and structural formula of the active constituent molinate

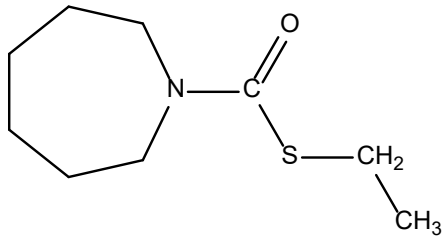
Common name (ISO):	Molinate
IUPAC name:	S-ethyl azepane-1-carbothioate
CAS registry number:	2212-67-1
Molecular formula:	$C_9H_{17}NOS$
Molecular weight:	187.3 g/mol
Structural formula:	

Table 3: Key physicochemical properties of the active constituent molinate[1]

Physical form:	Clear amber liquid with an aromatic odour (technical active)
Melting point:	<–25°C
Boiling point:	277.5 to 278.5°C (atmospheric pressure)
Specific gravity	1.0643 (20 to 25°C)
Solubility in water:	1100 mg/L (20 to 25°C)
Organic solvent solubility (20 to 25°C):	Soluble in acetone, chlorobenzene, dichloromethane, ethanol, ethyl acetate, hexane, kerosene, methanol, n-octanol, toluene and xylene
Octanol/water partition coefficient (Log K_{ow}):	pH 7.85 to 7.94: 2.86
Vapour pressure:	500 mPa at 25°C
Henry's law constant:	0.687 Pa m3/mol-1

Molinate technical active is a moderately volatile amber liquid, with an aromatic odour. It is soluble in a range of polar, aromatic, and aliphatic organic solvents, and only slightly soluble (1.1 g/L) in water.

[1] *The Pesticide Manual*, British Crop Protection Council, 2016

There are 3 current approvals for molinate, 2 for technical active(s) and one for a manufacturing concentrate.

Table 4: Current active approvals for molinate

Approval number	Approval holder
44008 (molinate manufacturing concentrate)	Nufarm Australia Ltd
44458	Nufarm Australia Ltd
52439	Sipcam Pacific Australia Pty Ltd

A Food and Agriculture Organization (FAO) specification has not been established for molinate or its formulated products. The APVMA proposes to establish a standard for the active constituent molinate. The minimum purity of the standard will be established so that it applies to active constituents and manufacturing concentrates on a dry weight/solvent free basis.

Formulated products

There are 2 registered products containing molinate. How these products are formulated and the composition and form of constituents in the products has previously been assessed as acceptable.

Table 5: Currently registered products containing molinate

Registration number	Holder	Product name
Emulsifiable concentrate (EC) formulation containing 960 g/L molinate		
49597	Nufarm Australia Ltd	Ordram Herbicide
56744	Sipcam Pacific Australia Pty Ltd	Sirion Herbicide

Toxicology

The original assessment of molinate (TUIS, 1986) considered metabolism and toxicokinetics studies, chronic toxicology studies, reproduction and developmental studies, and carcinogenicity studies. The preliminary review findings (APVMA, 2014) considered the toxicology of molinate based on consideration of submitted studies and the *United States Environmental Protection Agency (US EPA) Revised Human Health Risk Assessment for Molinate* (2001). These assessments and other publically available information have been considered here.

Metabolism and toxicokinetics

Available data indicates that following oral dosing ^{14}C-molinate is rapidly metabolized by rats. Under low dose conditions the likely major pathway of metabolism is cytochrome P450-mediated ring hydroxylation to form 4-hydroxy molinate which then undergoes conjugation. Under high dose conditions the predominant pathway is likely via cytochrome P450-mediated sulfoxidation of the thiocarbamate side chain followed by either conjugation with glutathione or further cytochrome P450-mediated oxidation to molinate sulfone (Jewell, W.T. and Miller, M.G (1999)). Glutathione conjugates are then eventually further metabolised to molinate mercapturate. Molinate sulfone is further metabolised by cleavage of the sulfone sidechain and the formation of hexahydroazepine.

Based on studies with thiocabamate-labelled ^{14}C-molinate, about 50% of administered radioactivity is eventually metabolised to carbon dioxide and excreted via exhalation with the remaining balance of the administered radioactivity being excreted in urine and faeces. *In vitro* data suggest that humans are more capable than the rats to detoxify the sulfoxide via glutathione conjugation (Jewell, W.T and Miller, M.G. (1999)).

Following oral dosing of rats with ring labeled ^{14}C-molinate, about 88% of the administered radioactivity was excreted in urine and about 11% was excreted in feces. Excretion was 95% to 96% complete by 48 hours following dosing. Tissue levels were approximately 13.8% of the administered dose after one day and 3.7% after 7 days. There was no evidence of bioaccumulation.

Residues of concern in plants include molinate, 4-hydroxymolinate and molinate acid. However, because of the timing of application of molinate to rice paddies in Australia, plant residues of concern are considered unlikely to occur in treated rice (see Residues and Trade).

No dermal absorption data were submitted for evaluation. The US EPA (2001) has recommended a dermal absorption factor (DAF) of 0.4 (40% dermal absorption), which has been used in this assessment. An inhalation absorption factor (IAF) of 100% has been used for occupational exposure assessment.

Acute toxicology

Based on the study available in the *US EPA Revised Human Health Risk Assessment for Molinate* (2001) and the data submitted to the APVMA by SIPCAM Pacific Australia (SIPCAM), sufficient relevant data were available for evaluation. The acute toxicology findings relevant to human hazard assessment are shown in Table 6 (APVMA, 2004; US EPA, 2001). Critically, the US EPA has determined that acute exposure to molinate is a potential cause of delayed neuropathy in the relevant animal model.

Table 6: Acute toxicology of molinate

Species	Results
Acute oral toxicity	
Rat	LD50 730 mg/kg bw male LD50 700 mg/kg bw female LD50 549 mg/kg bw
Acute dermal toxicity	
Rat	LD50 4350 mg/kg bw
Rabbit	LD50 > 2000 mg/kg bw
Acute inhalation toxicity	
Rat	LC50 2.9 mg/L males LC50 2.4 mg/L females
Skin irritancy	
Rabbit	Slight
Eye irritancy	
Rabbit	Slight
Skin sensitizer	
Guinea pig (maximisation test)	Positive

Repeat dose toxicology

In the original consideration of the toxicology of molinate (TUIS, 1986), chronic studies were submitted and reviewed. A 2-year dietary study in rats supported the establishment of a no-effect level at 0.63 mg/kg bw/day, based on increased testicular weight at 2 mg/kg bw/day. In addition, a combined chronic toxicity and reproductive toxicity 2-year dietary study in mice was reviewed which supported the establishment of a no-effect level of 7.2 mg/kg bw/day. Only short-term repeat oral dose toxicology studies were submitted to the APVMA for assessment under this review.

The key findings of a rat combined chronic/carcinogenicity toxicology study were evaluated in the US EPA (2001) assessment. No repeat dermal dose toxicology studies were available. The dose levels relevant to human health risk assessment are shown in Table 7 (APVMA 2004, US EPA, 2001). The studies were considered to meet the standards of the time and are sufficient for consideration of overall effects.

Table 7: Repeat dose toxicology dose levels relevant to the human health risk assessment of molinate

Species	Study type	Route of exposure	Critical effect	Lowest relevant NOEL or NOAEL	Lowest relevant LOEL or LOAEL
Short-term studies					
Rat	90 day repeat dose study	Oral (dietary)	Reduced body weight gain. Irreversible testicular degeneration occurred at and above 100 ppm (equivalent to 10 mg/kg bw/d). Bodyweight gain was significantly reduced at every dose.	Not determined	20 ppm (equivalent to 2 mg/kg bw/d)
Long-term studies					
Rat	Chronic toxicity Carcinogenicity study	Oral	Degeneration/demyelination in sciatic nerve and atrophy/reserve cell hyperplasia of muscle	Not determined	0.3 mg/kg bw/d
Rat	Chronic toxicity	Oral	Increased testicular weight	0.63 mg/kg bw/d	2 mg/kg bw/d

† LOED = lowest observed effect; LOAEL = lowest observed adverse effect level; NOEL = no observed effect level; NOAEL = no observed adverse effect level

Genotoxicity studies

In the *Molinate preliminary review findings* (APVMA, 2014), molinate was determined not to be mutagenic based on the findings; in a forward mutation assay in mouse lymphoma L5178Y cells, it did not induce sister chromatid exchanges in Chinese hamster ovary cells or unscheduled DNA synthesis in HeLa cells either in the presence or absence of exogenous metabolic activation. Molinate did not induce micronuclei in mouse bone marrow erythrocytes.

Carcinogenicity studies

Carcinogenicity studies were relied on for the initial approval of molinate (TUIS, 1986). The US EPA (2001) considered the available studies insufficient for human health risk assessment. The US EPA HED Cancer Assessment Review Committee (CARC) has therefore determined that the available evaluations of molinate provide 'suggestive evidence for carcinogenicity but not sufficient to assess human carcinogenic potential' based on the limited evidence of kidney tumours in rats. Based on the current Australian use pattern (one to 2 applications per season to rice) with no detectable food residues, long-term repeat daily exposure is not considered likely.

Reproductive and developmental toxicology studies

The APVMA was satisfied on the reproductive and developmental aspects of Molinate (TUIS, 1986). No additional reproductive or developmental toxicology studies were submitted for consideration as part of the review. Additional

summary data that are available from the US EPA assessment (US EPA, 2001) is shown in Table 8, the APVMA is satisfied with these findings.

Table 8: Reproductive and developmental toxicology dose levels relevant to the human health risk assessment of molinate

Species	Study type	Route of exposure	Critical effects	Lowest relevant NOEL or NOAEL	Lowest relevant LOEL or LOAEL
Developmental neurotoxicology studies					
Rat	Developmental neurotoxicology study	Oral (gavage)	Reduction in startle amplitude	Not determined	1.8 mg/kg bw
Reproductive and developmental toxicology studies					
Rat	3 generation reproduction study	Oral	Reproductive effects including decrease in following: % viable sperm, % motile sperm, % normal sperm, sperm counts, number of implants, number of viable fetuses; increase in implantation loss	0.2 mg/kg bw/d	Not reported
Rat	Reproduction and developmental toxicity study	Inhalation	Reproductive effects including decreased number of implants and increased % of abnormal sperm	0.0003 mg/mL	Not reported

Neurotoxicology studies

The APVMA has considered and accepted the findings on information assessed by the US EPA (2001) as the basis for consideration of these aspects of the toxicology of molinate. The acute delayed neurotoxicity study in hens supported a NOAEL of 0.2 g/kg, based on axonal degeneration in brain and cervical spinal cord and an acute inhalation study in rats supported an acute inhalation NOAEL of 0.12 mg/L due to the presence of hind leg muscle weakness at higher doses.

In an acute oral neurotoxicity study in rats, the US EPA noted effects on motor activity, however the study was not considered acceptable for regulatory purposes because the measurement of effects on neurotarget esterase, cholineasterase and glial fibrillary acidic protein were not performed appropriately.

Table 9: Acute neurotoxicity toxicology of molinate

Species	Results
Hen (acute delayed neurotoxicity)	NOAEL = 0.2 g/kg, based on axonal degeneration in brain and cervical spinal cord; delayed neurotoxicant.
Rat (acute inhalation study)	NOAEL of 0.12 mg/L due to the presence of hind leg muscle weakness at higher doses.

Although the chronic dietary exposure in rats resulted in sciatic nerve neuropathy and microscopic anatomic findings consistent with denervation myopathy, the use pattern (one to 2 applications per season to rice) with no detectable food residues does not indicate any potential long-term repeat daily exposure.

Health-based guidance values and points of departure for human health risk assessment

Acceptable daily intake

Based on the additional information considered under this review, a new acceptable daily intake (ADI) will be established for molinate. The lowest appropriate point of departure is the oral dietary LOAEL of 0.3 mg/kg bw/d from the rat chronic toxicity/carcinogenicity study. A total safety factor of 1,000 should be applied (10 for extrapolation from the LOAEL to the NOAEL, 10 for interspecies extrapolation and 10 for intraspecies extrapolation). Thus the new ADI is 0.3/1000 ≈ 0.0003 mg/kg bw/d.

An ADI of 0.0003 mg/kg bw/d is considered to be sufficiently protective against the testicular effects seen in the rat 3 generation reproduction study (NOAEL of 0.2 mg/kg bw/d; the point of departure used for the current molinate ADI established in 1986), the fertility effects seen in the rat reproduction and developmental study (NOAEL 0.2 mg/kg bw/d) and the effects on body weight and the male reproductive system seen in the 90 day repeat dose oral toxicity study in rats (LOAEL 2 mg/kg bw/d). It is also considered sufficiently protective for the delayed neurotoxicity observed in hens (NOAEL 0.2 mg/kg bw/day).

Acute reference dose

An acute reference dose (ARfD) has been established for molinate. The lowest relevant point of departure is the LOAEL of 1.8 mg/kg bw for the rat developmental neurotoxicity study. A total safety factor of 1,000 should be applied (10 for extrapolation from the LOAEL to the NOAEL, 10 for interspecies extrapolation and 10 for intraspecies extrapolation). Thus the ARfD is 1.8/1000 ≈ 0.002 mg/kg bw. An additional supporting study is the acute delayed neurotoxicity study in hens, where a NOAEL of 0.2 mg/kg bw/day was observed. The application of a total safety factor of 100 to this value (10 for interspecies extrapolation and 10 for intraspecies extrapolation) yields a similar ARfD of 0.002 mg/kg bw.

Short-term exposure points of departure for work health and safety risk assessment

The lowest relevant point of departure is the oral LOAEL of 1.8 mg/kg bw for the rat developmental neurotoxicity study. A DAF of 0.4 and a MOE of greater than or equal to 1,000 are appropriate for dermal exposure assessment.

Intermediate-term exposure points of departure for work health and safety risk assessment

The lowest relevant point of departure is the oral LOAEL of 1.8 mg/kg bw for the rat developmental neurotoxicity study. A DAF of 0.4 and a MOE of greater than or equal to 1,000 are appropriate for dermal exposure assessment. This is considered suitably protective for the effects of delayed neurotoxicity in hens, where a NOAEL of 0.2 mg/kg bw/day was observed.

Long-term exposure points of departure for work health and safety risk assessment

The use pattern (one to 2 applications per season to rice) indicates that long-term occupational exposure points of departure for occupation exposure risk assessment associated with the pesticidal use of molinate in Australia are not required.

Poisons scheduling

The scheduling of molinate was considered by the National Drugs and Poisons Scheduling Committee on 4 June 2004. The committee recommended that molinate be included in Schedule 7 of the Standard for the Uniform Scheduling of Medicines and Poisons, and also be included in Appendix J. On this basis, molinate is not available except to authorised or licensed persons. No additional authorisation considerations are recommended for molinate.

No changes are proposed to the scheduling of molinate.

Recommendations

Very limited new toxicology information was submitted for consideration during the review, and certain recommendations have been built on the APVMA's consideration of information drawn from the US EPA 2001 review of molinate. The review concludes the following:

- The approval of molinate active constituents and registration of products containing molinate would not be an undue health hazard to the safety of people exposed to it during its handling or people using anything containing its residues, provided label restrictions are followed.
- The ADI should be revised to 0.0003 milligrams of molinate per kilogram body weight per day, based on degeneration or demyelination in the sciatic nerve in rats at 0.3 mg/kg bw/day following dosing for 2 years. The ADI incorporates a 1,000-fold uncertainty factor to account for inter- and intra-species variation in sensitivity, as well as for the use of a low observed adverse effect level rather than a no observed adverse effect level.
- An ARfD should be established at 0.002 mg/kg bw, based on a low observed adverse effect level of 1.8 mg/kg bw in a rat development neurotoxicity study, and the application of a 1,000-fold safety factor to account for inter- and intra-species variation in sensitivity, as well as for the use of a low observed adverse effect level rather than a no observed adverse effect level.
- Molinate should remain in Schedule 7 and Appendix J of the Standard for the Uniform Scheduling of Medicines and Poisons.

Work health and safety

Advice received from the Ricegrowers' Association of Australia and CropCare Australasia indicated that the area treated by aerial application of molinate is likely to be in the range of 150 to 300 ha/d over a 4 to 8 week period during the rice growing season. Accordingly the short-term exposure points of departure for work health and safety risk assessment are considered to be appropriate.

In 2006, an interim work health and safety (WHS) assessment was completed by the Office of Chemical Safety. From this interim assessment, it was concluded that the ground application of molinate via herbigation/SCWIIRT methods could no longer be supported given that they posed an unacceptable dermal and inhalation risk to workers. In 2011, as an interim collaborative effort with the APVMA, registrants voluntarily amended product labels for use in closed supply and delivery systems by tractor or helicopter only to reduce worker exposure to molinate. The interim measure was implemented while additional WHS information was sought from registrants and interested parties.

In 2012, the additional WHS assessment work concluded that the worker exposure concerns raised in the 2006 interim risk could still not be adequately addressed. No specific occupational exposure studies using the SCWIIRT method and Bickley Boom (single nozzle delivery per wing) were available at that time and the risk assessment was based on available exposure data in the PHED database (US EPA 1998) that did not closely address the exposure scenario. The WHS assessment concluded that there was an unacceptable risk to operators involved in closed system mixing and loading and for pilots during fixed wing and helicopter application (APVMA, 2012). For a copy of the full 2012 WHS assessment refer to the *Occupational Health and Safety risk assessment of the ground and aerial application of molinate*.

In 2014, a preliminary study with 3 operators (3 replicates) was conducted to assess the extent of dermal exposure when wearing specified PPE during mixing and loading of a registered molinate herbicide (Agrisearch, 2014). The purpose of this study was to assess whether the proposed PPE provided adequate health and safety protection following application of a molinate formulation containing 960 g ac/L at a rate of 3.75 L/ha when utilising appropriate personal protective equipment. The personal protective equipment used for mixing and loading was: cotton overalls buttoned to the neck and wrist, water resistant footwear (gumboots), a washable hat, elbow length chemical resistant PVC gloves and a PVC or rubber apron extending down over the water resistant footwear.

Based on the results of this pilot study, using the short and intermediate exposure point of departure of 1.8 mg/kg bw, a DAF of 0.4 and an acceptable MOE of greater than or equal to 1,000, the dermal occupational exposures associated with mixing and loading were considered to be acceptable provided the quantity of product handled did not exceed 900 L per day (i.e. sufficient to treat around 250 ha of rice fields). An inhalation exposure assessment was not conducted and was not considered to be necessary since the product was not sprayed during mixing and loading. It was concluded that a full study, with additional replicates, would be required to confirm the outcome of the preliminary trial.

Following this preliminary trial, a worker exposure study for mixing/loading and application by aircraft was submitted in 2017 (Agrisearch, 2016), which measured occupational exposure arising from the aerial application of

molinate to rice fields at the recommended label rate. The study involved closed mixing/loading systems[2] in fixed wing aircraft that were fitted with Bickley Booms. The study was conducted in accordance with OECD Guidelines (OECD 1997) and commercial best practice for application methods. The PPE used for the study were cotton overalls buttoned to the neck and wrist, a washable hat, elbow-length PVC gloves, PVC or rubber apron and water resistant footwear (gumboots) for mixing/loading, and cotton overalls buttoned to the neck and wrist, water-resistant footwear (gumboots) and a pilot helmet for applicators.

The worker exposure data for mixing/loading comprised a combined dataset of 10 replicates (mixing/loading) undertaken by 5 different operators, and the exposure to applicators (pilots) data comprised a total dataset of 5 replicates (application events) undertaken by 2 pilots. Dermal exposure was measured using whole body dosimeters, worn under protective clothing.

Results from the mixer/loader studies indicated that handling 292 L (280 kg active constituent) of registered molinate herbicide results in a maximum systemic dose of 0.000371 mg molinate/kg bw/d based on a body weight of 70 kg. Results from the applicator study indicated that applying 247 L of registered molinate herbicide results in a maximum systemic dose of 0.000417 mg molinate/kg bw/d.

Using the short and intermediate exposure point of departure of 1.8 mg/kg bw and a DAF of 0.4 acceptable MOEs (greater than 1,000) were obtained for mixing and loading molinate up to 1,415 L product per day (or 5,185 L of diluted spray mix). This is sufficient to treat up to 377 ha/d when operators wear the PPE used in the exposure study. However, acceptable MOEs (>1,000) were only obtained for applicators (pilots) applying up to 1,066 L product per day (or 3,866 L of diluted spray mix), sufficient to treat up to 281 ha/d.

It is noted that the exposure data was limited to consideration of dermal exposure, without assessment of inhalation exposure. The spraying method used results in droplet sizes with a low respirable component, and it is not considered that exposure by inhalation for pilots is likely to be of concern.

The results from the submitted mixer/loader and applicator exposure studies indicate that a registered molinate herbicide, containing 960 g/L molinate, when used according to the label instructions will not present an unacceptable risk to:

- applicators (pilots), provided the quantity of product handled does not exceed 1066 L per day. At the label mixing rate of 3.75 L product in 10 L water, this is equivalent to 3866 L of diluted spray mix, sufficient to treat 281 ha
- mixers/loaders, provided the quantity of product handled does not exceed 1415 L per day. At the label mixing rate of 3.75 L product in 10 L water, this is equivalent to 5185 L of diluted spray mix, sufficient to treat 377 ha

Provided that separate mixer/loaders and applicators are used (i.e. pilots/applicators must not mix and load; and mixer/loaders must not pilot or apply).

Occupational post application exposures are expected to be minimal because of the nature of the activities associated with rice cultivation (e.g., scouting and water management) and the PPE that is commonly worn during

[2] Australian Pesticides and Veterinary Medicines Authority, *Occupational health and safety (Part 6)*, paragraph 2.4.1.1., APVMA website, 20 July 2020.

these activities (e.g., waterproof boots for walking through flooded rice paddies). Thus, a quantitative exposure and risk assessment for post-application activities was not performed by the APVMA. Due to the acute risks from inhalation and eye/skin irritation, a 24-hour re-entry interval (REI) is considered appropriate.

Recommendations

To ensure that the use of molinate does not present any unacceptable risk to applicators (pilots) and mixers/loaders, labels will need to be varied to include:

- restrictions on the amount of product to be handled/applied per day
- a requirement for separate mixer/loaders and applicators (i.e. pilots/applicators must not mix and load; and mixer/loaders must not pilot or apply).

First aid instructions for products containing molinate should read:

- If swallowed, splashed on skin or in eyes, or inhaled, contact a Poisons Information Centre (Phone Australia 13 11 26; New Zealand 0800 764 766) or a doctor at once. Remove any contaminated clothing and wash skin thoroughly. If swallowed, activated charcoal may be advised. Give atropine if instructed.

Safety directions should be included on the label as follows:

- Harmful if inhaled or swallowed. May irritate the eyes and skin. Repeated exposure may cause allergic disorders. Repeated minor exposure may have a cumulative poisoning effect. Avoid contact with eyes and skin. Do not inhale vapour or spray mist. When mixing and loading for aerial spraying equipment, wear cotton overalls buttoned to the neck and wrist and a washable hat, PVC or rubber apron, elbow length PVC gloves and water resistant footwear. If applying by aerial spraying equipment wear cotton overalls, buttoned to the neck and wrist (or equivalent clothing) and water resistant footwear. After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water. After each days use wash gloves and contaminated clothing.

Precautions to appear on the label are:

- DO NOT use if pregnant.

Restrictions/restraints to appear on the label are:

- DO NOT use open mixing and loading systems (use closed mixing and loading only).
- DO NOT apply by ground based methods.
- DO NOT apply by aerial application (fixed-wing or helicopter) unless using SCWIIRT (soluble chemical water injection in rice technique) application.
- A single operator MUST NOT be involved in BOTH mixing/loading AND application in the same day.
- A single operator involved in mixing/loading of the product MUST NOT handle more than 1,400 L neat product per day.
- A single operator (pilot) MUST NOT apply the product spray to an area exceeding 280 hectares per day.

A re-entry period is applicable and should appear on the label as follows:

- DO NOT enter treated areas for 24 hours.

Environment

Monitoring data for the period 1996 to 2001 provided by the NSW Environment Protection Agency (NSW EPA) established an extensive and detailed picture of molinate levels in surface waters from the Coleambally, Murray and Murrumbidgee irrigation areas during the rice growing season. While many of the analyses show molinate levels are below the limits of quantification, the level of molinate was quantifiable in a number of the samples examined. The initial scope for the molinate review raised the potential for contamination of waterways indicated by varying levels of molinate recorded in drainage water from rice fields and also the potential hazard of those molinate levels to non-target fauna and flora.

In 2004, the APVMA considered water monitoring data provided by the NSW EPA. Following additional comments from the Ricegrowers' Association of Australia and the former Industry and Investment NSW, the revised environmental assessment was completed in November 2005. The risks of molinate to the environment could not be adequately assessed based on the information provided to the review, and further information was identified as being required to complete the reconsideration of molinate (APVMA, 2014).

Under subsection 33(1) of the *Agricultural and Veterinary Chemicals Code Act 1994*, the APVMA sent a notice requiring the holders of molinate registrations to provide additional information necessary for the purposes of the review of molinate. Environmental water monitoring data from areas where molinate is used were requested, including information from non-drought seasons, i.e., years when rice production and rainfall were more typical. Details were also sought on standard procedures that are in place to protect natural waterways from accidental release of molinate. The Ricegrowers' Association of Australia provided collated water monitoring data (RGA, 2016).

Most of the rice grown in Australia is concentrated in the Murrumbidgee and Murray valleys of southern NSW and most rice growers receive water from one of 3 irrigation companies: Murray Irrigation, Murrumbidgee Irrigation and Coleambally Irrigation. Irrigation companies are required to monitor the water being released back into natural waterways through discharge points for pollutants, including molinate. Action levels are established by the Australian and New Zealand Environment Conservation Council and Agriculture and Resource Management Council of Australia and New Zealand (ANZECC/ARMCANZ) water quality guidelines (3.4 µg/L) to ensure protection of aquatic ecosystems (ANZECC/ARMCANZ, 2000). Acceptable rates are also determined by the NSW EPA to ensure environmental contamination is minimised and each irrigation company has their own documented procedures for required action should molinate be detected at a NSW EPA monitoring site. The NSW EPA water quality limits listed for molinate under NSW EPA Environment Protection Licences for Murray Irrigation, Murrumbidgee Irrigation and Coleambally Irrigation are:

- environmental guideline: 2.5 µg/L
- notification level: 3.4 µg/L
- action level: 14 µg/L

During the 2010–11 to 2014–15 growing seasons, 1,110 samples were analysed for molinate across the 3 irrigation areas, out of which only 10 samples recorded detections of molinate above the notification (3.4 µg/L) or action (14 µg/L) levels (RGA, 2016).

Five of the total detections occurred in the seasons 2010–11 and 2011–12, which saw higher-than-average rainfall and flooding events that caused rice bays treated with molinate to overflow into holding areas. The high volume of water leaving the discharge points resulted in molinate levels decreasing below environmental guideline levels (2.5 µg/L) quickly after detection. The highest detection event of 68 µg/L occurred at a discharge point during the 2010–11 season. Also from October to November 2011, an additional 3 detections of molinate above the action level of 14 µg/L were recorded at the same location. An investigation was conducted to determine the source and cause of molinate detections. It was concluded that these recordings were possibly a result of over spray by an aerial operator, or from leakage in a rice paddy bank or drainage inlet, which was then rectified by the land owner (RGA, 2016).

Continual improvements to water management plans of irrigation companies such as chemical contingency plans, and improvements to land, irrigation layouts and recirculation systems has led to a decline in molinate detections over the 5 year period. Detections of molinate have been declining with only one detection in the 2013–14 season and zero detections above the environmental guideline (2.5 µg/L) from 2014 to 2019 (RGA 2016; Coleambally Irrigation 2016, 2017, 2018, 2019; Murray Irrigation 2016, 2017, 2018, 2019; Murrumbidgee Irrigation 2016, 2017, 2018, 2019).

The trigger level established by ANZECC/ARMCANZ for molinate to protect 95% of aquatic ecosystems is set at 3.4 µg/L and the monitoring data of molinate in irrigation waters present evidence of a trend toward zero detections of molinate leaving rice-growing areas. After assessing the submitted water monitoring data, and noting the decline in molinate detections, the APVMA did not conduct a full environmental assessment as recent monitoring data do not indicate a potential hazard to non-target Australian fauna and flora.

Recommendations

The water quality monitoring data considered during the review demonstrate adequate management of discharge to the environment from the current use pattern. Therefore, continued approval of the active constituent molinate and registration of agricultural chemical products containing molinate, is not, or would not be, likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

Residues and trade

Molinate is approved for use on rice only and a maximum residue limit (MRL) at *0.05 mg/kg is established for rice[3]. The available information supports the retention of the current rice MRL.

Considering the revised ADI and ARfD for molinate discussed in Section 3, in accordance with the APVMA *Residues and Trade Risk Assessment Manual* (APVMA, 2019b), the dietary exposure associated with the use of molinate on rice is acceptable.

The chronic dietary exposure to molinate 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 molinate is equivalent to <10% of the ADI. The chronic dietary exposure of molinate remains 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. The acute dietary intake for molinate in rice was estimated at <30% of the ARfD. The acute dietary exposure is acceptable.

Based on this information, the continued approval of the active constituent molinate and registration of agricultural chemical products containing the active molinate, is not, or would not be, likely to have an unintended effect that is harmful to human beings through residues in food.

The APVMA is not aware of any trade incidents associated with the use of molinate in rice. The MRL is set at *0.05 mg/kg (the limit of quantification) and the risk to international trade is considered to be low.

[3] Agricultural and Veterinary Chemicals Code (MRL Standard) Instrument 2019

Efficacy and target crop safety

No new efficacy or target crop (rice) safety information was submitted for consideration during the review, and this assessment has considered the history of use of the product with no adverse experience reports received.

Currently registered molinate products target different weeds or different weed growth stages with each of 3 registered label rates. The 5.2 L/ha rate is targeted at barnyard grass at the 5-leaf to early tillering growth stages, whereas the 2.5 L/ha rate is targeted at barnyard grass at the 0-2 leaf stage, and the 3.75 L/ha rate is targeted at barnyard grass at the 1 to 4 leaf stage and silvertop grass at the 2 leaf stage. The required label elements set out in section 9 of this report include a reduction in the maximum application rate from 5.2 L/ha in 20 L water volume, to 3.75 L/ha in 10 L water volume.

Efficacy

Based on a demonstrated history of effective use at rates of 2.5 L and 3.75 L/ha in 10 L of water when applied to weeds at the stated growth stages as an aerial application using the SCWIIRT method, the APVMA is satisfied that molinate products will meet the criteria laid out in the Agricultural and Veterinary Chemicals Code (Efficacy Criteria) Determination 2014 when used according to the modified label elements set out in section 9 of this report.

Target crop safety

The APVMA has not received adverse experience reports in relation to crop damage from molinate products, and no issues with target crop safety have been reported to the APVMA in other fora. The required label elements set out in this report (see ‘Required label elements’) would result in a reduction in the maximum application rate of molinate products Therefore they would result in a reduction in the amount of active constituent applied by area, reducing risk of target crop damage attributable to the spray product itself. Accordingly, the APVMA is satisfied that the product will meet the safety criteria as they relate to target crop safety when molinate products are used according to the modified label elements set out in the ‘Required label elements’ section of this report.

Spray drift assessment

A spray drift assessment was conducted according to APVMA's approach to spray drift management which specifies regulatory acceptable levels resulting from spray drift in bystander areas, livestock areas, natural aquatic areas, pollinator areas and vegetation areas. The only currently approved application method is aerial SCWIIRT (also called Bickley Boom) application into permanent water with closed mixing and loading.

Regulatory acceptable levels considered

In assessing spray drift the following regulatory acceptable levels (RALs) were considered.

Bystander areas

Given the use pattern of molinate (one to 2 applications per year), it is considered appropriate to utilise an intermediate exposure duration point of departure, as has been used for occupational exposure. An oral LOAEL of 1.8 mg/kg bw for the rat developmental neurotoxicity study, with the application of a 1,000-fold safety factor is considered appropriate. A dermal absorption factor of 40% was used. Using the methodology established in the APVMA's published spray drift guidance (APVMA, 2019d), the RAL for bystander exposure is calculated at 15 g ac/ha.

Livestock areas

A RAL for livestock areas is not considered to be necessary as application methods limit off target movement and molinate has been used on rice for many years without a known residue related trade incident.

Natural aquatic areas

Based on aquatic toxicity endpoints reported by EC (2003) and US EPA (2006), aquatic invertebrates are the most sensitive taxonomic group to molinate. Following long-term exposure, larval survival was reduced at concentrations as low as 45 µg ac/L (NOEC 26 µg ac/L, *Neomysis mercedis*). An assessment factor of 1 is applied to NOEC values and therefore the RAL for aquatic species is also 26 µg ac/L.

Pollinator areas

Molinate is not considered to be toxic to bees (oral LD50 >11 µg ae/bee, EC 2003). Based on available data, risks of contact toxicity are expected to be low. Therefore, a spray drift assessment is not required for pollinators.

Vegetation areas

Information on the toxicity of molinate to non-target terrestrial plants is limited to one vegetative vigour study reported by the US EPA (2001). ER25 values were reported to range 246 g ac/ha to >4,480 g ac/ha. Applying an assessment factor of 2 to the lowest ER25, the RAL is 123 g ac/ha for the protection of vegetation areas.

Spray drift buffer zones

Required spray drift buffer zones were calculated separately for application by fixed wing and rotary wing aircraft due to the effects of different flying speed on droplet size. The standard deposition curves in the Spray Drift Risk Assessment Tool (SDRAT) with a very coarse droplet size were considered appropriate for modelling molinate application by SCWIIRT on fixed wing aircraft (APVMA, 2019d). To model the application of molinate by SCWIIRT for helicopters the APVMA standard scenario input file to AGDISP (APVMA, 2019d) was used with the following changes:

1. Nozzle placement: A total of 4 nozzles, equally spaced to 66% of rotor diameter, mounted on droppers 1 m below the standard boom.
2. Droplet size distribution (DSD): Specific DSD information for spraying molinate through SCWIIRT or Bickley Boom was not available. The AGDISP droplet size library includes data measured by the Spray Drift Task Force for nozzles of the same general type to the SCWIIRT system, i.e. solid stream nozzles with large orifices. The closest entry available for this application was that for a D10 nozzle so this was selected for the 2.07 bar pressure, 22.35 m/s aircraft speed option. This spray has a Dv0.5 of 1021 µm with a relative span of 1.14. It is considered to be conservative because in reality the nozzle type used in the field is larger than 10/64 inch or 4 mm diameter (the nomenclature used by spraying systems is that the orifice diameter is X/64 inch where X is the D orifice value). Droplet size from this type of nozzle is very dependent on air speed so a maximum flying speed of 50 knots is applied.

Based on the assessment parameters set out above the restraint statements indicated in the required label elements are required.

Required label elements

Signal heading:	DANGEROUS POISON KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Product name:	[INSERT HERE]

Constituent statement:	ACTIVE CONSTITUENT: 960 g/L MOLINATE

Mode of action:	GROUP	J	HERBICIDE

Statement of claims:	Post emergence control of grass weeds in rice in permanent water

Net contents:	[INSERT HERE]

Directions for use:	See directions for use section below. This can be uploaded as a separate section when submitting a label application

Withholding period:	NOT REQUIRED WHEN USED AS DIRECTED

General instructions:	For aerial application by SCWIIRT (Soluble Chemical Water Injection In Rice Technique) only

Resistance warning:	[INSERT PRODUCT NAME] is a member of the thiocarbamates group of herbicides. [INSERT PRODUCT NAME] has the inhibitor of fat synthesis mode of action. For weed resistance management [INSERT PRODUCT NAME] is a Group J herbicide. Some naturally occurring weed biotypes resistant to [INSERT PRODUCT NAME] and other Group J herbicides may exist through normal genetic variability in any week population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by [INSERT PRODUCT NAME] of other Group J herbicides. Since the occurrence of resistant weeds is difficult to detect prior to

Signal heading:	DANGEROUS POISON KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING
	use, [INSERT COMPANY NAME] accepts no liability for any losses that may result from the failure of [INSERT PRODUCT NAME] to control resistant weeds.

Precautions:	DO NOT use if pregnant

Re-entry period:	DO NOT allow entry to treated area for 24 hours.

Protection statements:	PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT DO NOT contaminate streams, rivers or watercourses with the chemical or used containers

Storage and disposal:	STORAGE AND DISPOSAL: For general containers: Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Store in a locked room away from children, animals, food, feedstuffs, seed and fertilisers. 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. For containers carrying the drumMUSTER logo: Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Store in a locked room away from children, animals, food, feedstuffs, seed and fertilisers. This container can be recycled if it is clean, dry, free of visible residues and has the drumMUSTER logo visible. Triple-rinse container for disposal. Dispose of rinsate by adding it to the spray tank. Do not dispose of undiluted chemical on site. Wash outside of the container and the cap. Store cleaned container in a sheltered place with cap removed. It will then be acceptable for recycling at any drumMUSTER collection or similar container management program site. The cap should not be replaced, but may be taken separately.

SAFETY DIRECTIONS:	Harmful if inhaled or swallowed. May irritate the eyes and skin. Repeated exposure may cause allergic disorders. Repeated minor exposure may have a cumulative poisoning effect. Avoid contact with eyes and skin. DO NOT inhale vapour or spray mist. When mixing and loading for

Signal heading:	DANGEROUS POISON KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING
	aerial spraying equipment, wear cotton overalls buttoned to the neck and wrist and a washable hat, PVC or rubber apron, elbow-length PVC gloves and water resistant footwear. If applying by aerial spraying equipment, wear cotton overalls, buttoned to the neck and wrist (or equivalent clothing), and water resistant footwear. After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water. After each day's use wash gloves and contaminated clothing.

FIRST AID:	If swallowed, splashed on skin or in eyes, or inhaled, contact a Poisons Information Centre (phone Australia 13 11 26; New Zealand 0800 764 766) or doctor at once. Remove any contaminated clothing and wash skin thoroughly. If swallowed, activated charcoal may be advised. Give atropine if instructed.

Batch Number:	[INSERT HERE]
APVMA approval No:	[INSERT HERE]

MATERIAL SAFETY DATA SHEET:	Additional information can be obtained from the material safety data sheet which can be obtained from the supplier.

DIRECTIONS FOR USE

RESTRAINTS

Under very cold conditions DO NOT apply to permanent water too early as crop may be drowned. A proportion of the first leaf must show above the water.

DO NOT apply by ground-based methods.

DO NOT use open mixing and loading systems (use closed mixing and loading only).

A single operator MUST NOT be involved in BOTH mixing/loading AND application in the same day.

A single operator involved in mixing/loading of the product MUST NOT handle more than 1,400 L neat product per day.

A single operator (pilot) MUST NOT apply the product spray to an area exceeding 280 hectares per day.

SPRAY DRIFT RESTRAINTS

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

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

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

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

DO NOT apply if there are hazardous surface temperature inversion conditions present at the application site during the time of application. Surface temperature inversion conditions exist most evenings one to two hours before sunset and persist until one to 2 hours after sunrise.

DO NOT apply by helicopter unless the following additional requirements are met:

- apply only by SCWIIRT (Soluble Chemical Water Injection In Rice Technique)
- the release height is not greater than 2 metres above the ground
- the flying speed is not greater than 50 knots (92 km/hr)
- minimum distances between the application site and downwind sensitive areas that appear in the 'Mandatory downwind buffer zones' section of the following table titled ‘Buffer zones for helicopter using SCWIIRT’) are observed.

Buffer zones for helicopter using SCWIIRT				
Application Rate	Mandatory downwind buffer zones			
	Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas
2.5L in minimum 10L/ha water	10 metres	10 metres	0 metres	0 metres
3.75L in minimum 10L/ha water	15 metres	10 metres	0 metres	5 metres

DO NOT apply by fixed wing aircraft unless the following additional requirements are met:

- apply only by SCWIIRT (Soluble Chemical Water Injection In Rice Technique)
- the release height is not greater than 3 m or 25% of wingspan above the ground whichever is the greatest
- minimum distances between the application site and downwind sensitive areas (see 'Mandatory buffer zones' section of the following table titled 'Buffer zones for fixed-wing aircraft using SCWIIRT) are observed.

Buffer zones for fixed-wing aircraft using SCWIIRT				
Application Rate	Mandatory downwind buffer zones			
	Bystander areas	Natural aquatic areas	Pollinator areas	Vegetation areas
2.5L in minimum 10L/ha water	150 metres	85 metres	0 metres	30 metres
3.75L in minimum 10L/ha water	200 metres	110 metres	0 metres	45 metres

Directions for use				
CROP/SITUATION	WEEDS CONTROLLED	STATE	RATE	CRITICAL COMMENTS
Rice – Permanent water Combine sown, sod sown and aerial sown rice	Barnyard Grasses (*Echinochloa* spp.) Silver top grass (*Diplachne fusca*)	NSW only	3.75L in minimum 10L/ha water	Apply when Barnyard grass in in the 1-4 leaf stage and Silver top is up to the two leaf stage. Weeds are usually 5-10cm high. NO MORE than one-third plant bulk should be above water at spraying, nor should more than one-third of the bay be covered by these plants. DO NOT allow movement of water through bays for 2 hours before spraying. ALLOW ONLY MINIMUM water movement through bays for 3 days after application.

Directions for use				
CROP/SITUATION	WEEDS CONTROLLED	STATE	RATE	CRITICAL COMMENTS
				After this time normal water coverage should be maintained. DO NOT use if excess rice and weed vegetation will impede re-distribution of [the product] in water resulting in inadequate control.
	Barnyard Grasses (*Echinochloa* spp.) 0-2 leaf stage	NSW only	2.5L in minimum 10L/ha water	Coverage of the rice field with permanent water must be maintained after spraying. Water movement to and through bays should cease 2 hours before application. Minimum water movement should be maintained for 3 days after application. After this time normal water coverage should be maintained.

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

Appendix

Acronyms and abbreviations

Shortened term	Full term
ADI	Acceptable daily intake (for humans)
ARfD	Acute reference dose
bw	Bodyweight
d	Day
DAF	Dermal Absorption Factor
FAO	Food and Agriculture Organization of the United Nations
g	Gram
ha	Hectare
in vitro	outside the living body and in an artificial environment
kg	Kilogram
L	Litre
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOAEL	Lowest Observed Adverse Effect Level
mg	Milligram
mL	Millilitre
MRL	Maximum Residue Limit
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
NOEC/NOEL	No Observable Effect Concentration Level
NOAEL	No Observed Adverse Effect Level
OECD	Organisation for Economic Co-operation and Development
PHED	Pesticide Handler Exposure Database
PPE	Personal Protective Equipment
ppm	parts per million
µg	Microgram

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