Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the evaluation of the new product Amitron 700WG Herbicide

APVMA Product Number 85031

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

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PREFACE

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the Australian Government regulator with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing and State Departments of Primary Industries.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of Public Release Summaries for products containing new active constituents.

The information and technical data required by the APVMA to assess the safety of new chemical products, and the methods of assessment, must be consistent with accepted scientific principles and processes. Details are outlined on the APVMA website.

This Public Release Summary is intended as a brief overview of the assessment that has been conducted by the APVMA and of the specialist advice received from its advisory agencies. It has been deliberately presented in a manner that is likely to be informative to the widest possible audience thereby encouraging public comment.

About this document

This is a Public Release Summary.

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

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

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

Making a submission

In accordance with section 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of Amitron 700WG Herbicide, containing 700 g/kg amicarbazone 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 5 June 2017 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

Relevant comments will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

When making a submission please include:

- contact name
- company or group name (if relevant)
- email or postal address (if available)
- the date you made the submission.

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

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

Case Management and Administration Unit
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[1] A full definition of 'confidential commercial information' is contained in the Agvet Code.

Further information

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

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

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

1 INTRODUCTION

1.1 Purpose of application

Arysta Lifescience North America LLC has applied to the APVMA to register Amitron 700WG Herbicide, containing 700 g/kg amicarbazone water dispersible granule product for control of weeds in plant and ratoon sugarcane. Amicarbazone was approved as an active constituent in 2007. Amitron 700WG Herbicide is the first product containing amicarbazone proposed to be registered through the APVMA.

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product Amitron 700WG Herbicide.

1.2 Product claims and use pattern

Amitron 700WG Herbicide is intended for the control of a large variety of weeds in sugar cane crops. The product may be applied to both plant and ratoon cane, once per season. The product application rate ranges from 500 to 1000 g/ha, in a minimum water volume of 200 L/ha.

1.3 Mode of action

The active constituent, amicarbazone, is a member of the triazolinone group of herbicides. The mode of action is the inhibition of photosynthesis at photosystem II (PS II Inhibitors).

For weed resistance management, the product is a Group C herbicide.

1.4 Overseas registrations

Amicarbazone is registered in South Africa and Brazil on sugarcane and in the United States for turf.

2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

Amicarbazone is a colourless crystalline solid at room temperature. It is very soluble in polar organic solvents and sparingly soluble in water and non-polar organic solvents. Amicarbazone partitions in favour of n-octanol in H_2O-octanol partitioning tests, but is not considered to present a bio-accumulation hazard. Amicarbazone is not explosive and is involatile under typical conditions. It is thermally stable at room temperature in air, and only decomposes when heating at temperatures above 180 °C. Amicarbazone is not a strong Brønsted acid or base.

The APVMA has evaluated the chemistry (manufacturing process, quality control procedures, batch analysis, analytical methods, physio-chemical properties and spectroscopic data) and toxicological aspects of the active constituent amicarbazone and found them to be acceptable. The active constituent was approved on 4 January 2007 under the approval number 60115.

Details of the chemical name, structure, and physiochemical properties of amicarbazone are tabulated below.

Table 1: Nomenclature of amicarbazone

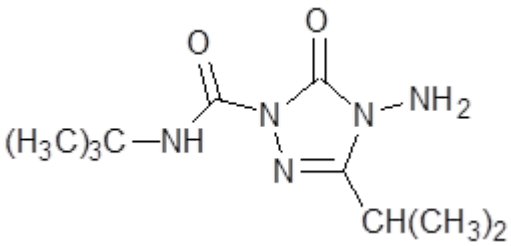
COMMON NAME (ISO):	Amicarbazone
IUPAC NAME:	4-amino-*N*-*tert*-butyl-4,5-dihydro-3-isopropyl-5-oxo-1*H*-1,2,4-triazole-1-carboxamide
CAS REGISTRY NUMBER:	129909-90-6
EMPIRICAL FORMULA:	$C_{10}H_{19}N_5O_2$
MOLECULAR WEIGHT:	241.3 g/mol
STRUCTURAL FORMULA:	

Table 2: Physicochemical properties of amicarbazone

APPEARANCE:	Colourless crystalline solid (pure substance, 99.6%)
ODOUR:	Uncharacteristic faint odour
MELTING POINT:	137.5 °C
BOILING POINT:	Not measurable - decomposition above 180 °C
THERMAL STABILITY:	Thermally stable at ambient temerature under air, with decomposition above 180 °C
DENSITY:	1.12 g/mL at 20 °C
VAPOUR PRESSURE:	1.3 x 10^{-6} Pa at 20 °C 3.0 x 10^{-6} Pa at 25 °C
HENRY'S LAW CONSTANT:	6.8 x 10^{-8} Pa m^3 mol^{-1} at 20 °C
SOLUBILITY IN WATER:	4.6 g/L at 20 °C (pH 4-9)
OCTANOL / WATER PARTITION COEFFICIENT:	1.14 (unbuffered) 1.18 (pH 4) 1.23 (pH 7 and pH 9) All reported as log Pow, at 25°C.
SOLUBILITY IN ORGANIC SOLVENTS:	n-Heptane: 0.07 g/L Xylene: 9.2 g/L 1-Octanol: 43 g/L 2-Propanol: 110 g/L Ethyl acetate: 140 g/L Polyethylene glycol: 79 g/L Acetonitrile: > 250 g/L Acetone: > 250 g/L Dimethyl sulfoxide: > 250 g/L Dichloromethane: > 250 g/L
UV / VISIBLE ABSORPTION:	Peak maxima 221 nm; Molar absorptivity 7772 (1000 cm^2/mol)
PHOTOSTABILITY:	Amicarbazone does not undergo significant degredation when exposed to sunlight
DISSOCIATION CONSTANT:	Amicarbazone technical has no acidic or basic properties in aqueous solutions and as the material has no conductivity in water, it does not dissociate.
PH:	7.06 (2.5% aqueous slurry)
FLASH POINT:	Not applicable—solid at room temperature

APPEARANCE:	Colourless crystalline solid (pure substance, 99.6%)
EXPLODABILITY:	Not applicable—solid at room temperature
OXIDATION STABILITY:	Amicarbazone is oxidised by weak and string oxidisers but is stable in a reducing agent
CORROSION CHARACTERISTICS:	Test materials: stainless steel #316, aluminium, brass, and HDPE are suitable for packaging and general use with amicarbazone. Plain steel and copper are not recommended as the test sample stained these materials although there was no significant loss of active ingredient for any of the materials tested.
DANGEROUS GOODS CLASSIFICATION:	Not classified as a dangerous good

The following APVMA Active Constituent Standard has been established for amicarbazone active constituent.

CONSTITUENT	SPECIFICATION	LEVEL
Amicarbazone	Amicarbazone	Not less than 940 g/kg

2.2 Formulated product

The product Amitron 700WG Herbicide will be formulated overseas and packaged in a polypropylene bag inside a cardboard carton or High Density Polyethylene container or Polypropylene container, ranging from 1–20 kg. Suitable details of the product formulation, specifications for the ingredients, formulation process and quality control, product specifications, stability data for the product when stored in the proposed packaging, analytical methods for the active constituents in the product, and details of the packaging, were provided and evaluated.

Based on the assessment, the APVMA is satisfied that the product will remain stable when for at least 2 years under normal conditions in the proposed packaging.

Table 3: Identification of the proposed product

DISTINGUISHING NAME:	Amitron 700WG Herbicide
FORMULATION TYPE:	Water Dispersible Granule (WG)
ACTIVE CONSTITUENT CONCENTRATIONS:	Amicarbazone (700 g/kg)

Table 4: Physicochemical properties of Amitron 700WG Herbicide

APPEARANCE	Tan solid granular material, approximately 2 mm diameter
ODOUR	Slight odour
BULK DENSITY	480 g/L
WETTABILITY	45 seconds with swirling
DUSTINESS	Nearly dust free
SOLUBILITY IN WATER	Disperses in water
VAPOUR PRESSURE	3.0×10^{-6} @ 25 °C (amicarbazone)
FLAMMABILITY	Does not contain a combustible liquid
EXPLOSIVITY	No impact explosive characteristics are expected on the basis of the chemical nature of the formulation ingredients
OXIDISING PROPERTIES	Does not contain any ingredient which is considered to be an oxidising or reducing agent
CORROSIVENESS	Not corrosive to the test materials: plain steel, stainless steel, aluminium, brass, copper, HDPE, VER fibreglass, Monosol 7030 PVA
DANGEROUS GOODS CLASSIFICATION	Not classified as a dangerous good
PACK SIZES:	1–20 kg
PACKAGING MATERIAL:	Polypropylene bag inside cardboard carton or High Density Polyethylene container or Polypropylene container
PRODUCT STABILITY:	The product should remain within specifications for at least 2 years under normal conditions in a polypropylene bag inside a cardboard carton or High Density Polyethylene container or Polypropylene container

2.3 Recommendations

The APVMA has evaluated the chemistry aspects of Amitron 700WG Herbicide (manufacturing process, quality control procedures, stability, batch analysis results and analytical methods) and found them to be acceptable. The available storage stability data indicate that the formulated product is expected to remain stable for at least two years when stored under normal conditions.

Based on a review of the chemistry and manufacturing details the registration of Amitron 700WG Herbicide is supported from a chemistry perspective.

3 TOXICOLOGICAL ASSESSMENT

3.1 Evaluation of toxicology

The toxicological database for amicarbazone consists primarily of toxicity tests conducted using animals. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposures. The use of high doses increases the likelihood that potentially significant toxic effects will be identified. Findings of adverse effects in any one species do not necessarily indicate such effects might be generated in humans. From a conservative risk assessment perspective however, adverse findings in animal species are assumed to represent potential effects in humans, unless convincing evidence of species specificity is available. Where possible, considerations of the species specific mechanisms of adverse reactions weigh heavily in the extrapolation of animal data to likely human hazard. Equally, consideration of the risks to human health must take into account the likely human exposure levels compared with those, usually many times higher, which produce effects in animal studies. Toxicity tests should also indicate dose levels at which the specific toxic effects are unlikely to occur. Dose levels such as the No Observed-Adverse Effect Level (NOAEL) are used to develop acceptable limits for dietary or other intakes (ADI and ARfD) at which no adverse health effects in humans would be expected.

Chemical class

Amicarbazone is a herbicide that kills weeds by inhibiting plant photosynthesis. Other herbicides which operate by the same mode of action are flucarbazone, procarbazone, azafenidin and carfentrazone ethyl.

Pharmacokinetics

After a single (radioactive labelled) oral administration to rats, amicarbazone was found to be readily absorbed, extensively metabolised and rapidly eliminated. The majority (≈ 91%) of the administered dose was excreted within 24 hours, with urine being the predominant route of elimination. Around 27% of the administered dose was excreted in faeces. Radioactivity levels in organs and tissues were generally very low, representing less than 1% of the total administered dose. Total radioactive residue levels were highest in liver followed by kidney, blood, gastrointestinal tract, spleen and adipose tissue. There appeared to be two main routes of detoxification and excretion for amicarbazone. The first route involved conjugation with glucuronic acid to form an N-glucuronide, which was excreted mainly in the faeces. The second route involved deamination and subsequent oxidation to form a variety of hydroxylated metabolites which were then excreted in the urine.

Acute toxicity

Based on the findings of the acute toxicity studies evaluated, amicarbazone has low oral, dermal and inhalational toxicity, with slight, transient eye irritation, but no skin irritation. Amicarbazone was not a skin sensitiser in the Buehler test.

Repeat-dose toxicity

In a 21-day dermal study in rats, no adverse effects were observed at the highest tested dose of 1000 mg/kg bw/d. In a 13-week dietary study in dogs, cholestasis in the liver was observed at approximately 30 mg/kg bw/d and higher. Increased circulating bile acid and cholesterol levels were also seen in a one-year dog study at a similar dose. Supplementary studies in rats were undertaken using diets containing amicarbazone to determine its effect on thyroid hormone levels and thyroid gland function. Serum levels of thyroxine (T4) and triiodothyronine (T3) were increased in both sexes at approximately 70 mg/kg bw/d; and serum thyroid-stimulating hormone (TSH) was reduced in males, but were unchanged in females. An increased incidence of thyroid follicular cell hyperplasia was seen in both sexes in a dose-dependent manner at the next higher doses of 200 and 400 mg/kg bw/d. In the liver, the activity of uridine glucuronosyl transferase (UDP-GT), a major pathway of thyroid hormone biotransformation (in rats and mice), detoxification and excretion for amicarbazone in rats, was markedly increased in a dose-dependent manner.

Thyroidal function (as measured by the discharge of iodide ion in response to perchlorate) and pituitary function (as measured by deiodinase activity) were also unaffected. Collectively these data suggest that the functional status of the thyroid and pituitary glands was not directly affected by treatment with amicarbazone and that alterations in circulating levels of thyroid hormones were most likely to be mediated through an increased hepatic metabolism and biliary excretion of T4 and T3-glucuronide, causing a stimulation of the thyroid gland. The increased excretion of thyroid hormones induces thyroid follicular cells to produce thyroid hormones leading to hyperplasia.

Increased total protein and severely reduced bodyweight gains without changes to food consumption were observed in a 13-week rat study (the latter was consistently observed in two rat reproduction studies as well as in a 2-year rat study). These observations are consistent with thyrotoxicosis. These effects, however, were not evident in dogs, possibly due to the absence of thyrotoxicosis. Because thyroid follicular cell hyperplasia is a rodent-specific entity and there is no direct correlation between rat and human thyroid disease, increased risks of thyroid disruption by amicarbazone may not be relevant for human health risk assessment.

Chronic toxicity and carcinogenicity

The chronic toxicity of amicarbazone was investigated in the mouse and rat. While a NOAEL could not be established in the mouse study due to an increased incidence of hepatocellular hypertrophy at the lowest dose tested (16/18 mg/kg bw/d in males and females, respectively); a lower NOAEL of 50 ppm equal to 2.3/2.7 mg/kg bw/d for males and females, respectively, was established in rats based on reduced bodyweight gain, increased serum cholesterol levels and liver weights at higher doses. Amicarbazone is not carcinogenic in mice or rats.

Reproduction and developmental toxicity

In a reproduction study, amicarbazone caused reduced bodyweight gains in parental animals but effects in offspring were limited to a reduced bodyweight gain in pups. No teratogenic effects were observed in rat and rabbit developmental studies.

Genotoxicity

Amicarbazone was not genotoxic in a range of standardised in vitro and in vivo tests.

Neurotoxicity

Neurotoxicity studies in rats given a single dose of amicarbazone by oral gavage showed toxic signs such as sedation, salivation and ptosis (drooping of eyelids) within 20 minutes after dosing at 20 mg/kg bw or higher. The duration of the toxic signs was dose-dependent but disappeared between 1.5 and 2 hours after dosing. Similar observations were also seen in mice at 100 mg/kg bw.

A NOAEL for neurotoxicity in rats was established at 10 mg/kg bw based on neurotoxicity signs of sedation, salivation and ptosis at doses of 20 mg/kg bw and higher, within 20 minutes of oral administration of amicarbazone.

3.2 Health-based guidance values and poisons scheduling

Poisons scheduling

Amicarbazone is in Schedule 6 of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP). It has no cutoff or exemptions.

Acceptable Daily Intake (ADI)

The Acceptable Daily Intake is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOAEL obtained in the most sensitive species. This NOAEL is then divided by an uncertainty factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals. The ADI for amicarbazone was established at 0.02 mg/kg bw/day based on a NOAEL of 2 mg/kg bw/d in a 2-year rat feeding study and using a 100-fold uncertainty factor.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event. The ARfD is derived from the lowest single dose which causes no effect in the most sensitive species of experimental animal tested, together with an uncertainty factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals. An ARfD was established at 0.1 mg/kg bw on the basis of a NOAEL (10 mg/kg bw) observed in the single dose neurotoxicity study and using a 100-fold uncertainty factor.

4 RESIDUES ASSESSMENT

4.1 Introduction

As part of the residues assessment of amicarbazone, plant and animal metabolism studies, supervised residue trials, animal transfer studies, analytical methodology, fate in storage and processing data and residues in trade information were considered.

4.2 Metabolism

Metabolism studies on corn, confined rotational crops, laying hens and lactating goats have been provided. Although there is no specific study for sugarcane, the corn and the rotational crop study (for the short plant back interval of 47 days) show qualitatively and quantitatively similar metabolism.

In the corn metabolism study, amicarbazone was the major component of the TRR identified, present at 44% in the forage, 18% in the fodder and 13% in the kernels. The major metabolite was isopropyl-2-hydroxy desamino amicarbazone (iPr-2-OH DA MKH 3586) which was found at 14% in forage, 15% in fodder and 38% in kernels. Desamino amicarbazone (DA MKH 3586) was identified as the next most prominent component at 6% in forage, 9% in fodder and 14% in kernels. Several other minor metabolites were identified, in most cases <5% of TRR.

In goats, amicarbazone was observed at 11% of the TRR in liver, 8% in kidney, 29% in muscle, 45% in fat, 23–24% in milk. DA MKH 3586 was observed at 60% of the TRR in liver, 28% in kidney, 40% in muscle, 42% in fat, 18% in milk. iPR-2-OH DA MKH 3586 was observed at 5% of the TRR in liver, 26% in kidney, 5% in muscle, 4% in fat, 8% in milk.

In hens, amicarbazone was observed at 32% of the TRR in liver, 1% in muscle, 3% in fat, 4-7% in eggs, DA MKH 3586 was observed at 4% of the TRR in liver, 6% in muscle, 9% in fat, 19-26% in eggs, iPr-2-OH DA MKH 3586 was observed at 9% of the TRR in liver, 24% in muscle, 10% in fat, 20-35% in eggs.

4.3 Analytical methods

In plant commodities, residues of amicarbazone, DA MKH 3586 and iPr-2-OH DA MKH 3586 were extracted with water, phosphoric acid or acetonitrile prior to purification by SPE and analysis by LC-MS/MS. In the sugarcane residue trials, the LOQ was 0.02 mg/kg for billets and juice and 0.05 mg/kg for tops for each analyte.

In animal commodities, residues of amicarbazone, DA MKH 3586 and iPr-2-OH DA MKH 3586 were extracted with acetonitrile for tissues and acetic acid in acetonitrile for milk. Magnesium sulphate and sodium chloride were added to liver, muscle, kidney and milk extracts. The samples were mixed, centrifuged and an aliquot of the supernatant diluted prior to analysis by LC-MS/MS. The LOQ was 0.01 mg/kg for each matrix.

4.4 Stability of the pesticide in stored analytical samples

Sugarcane samples were held in frozen storage for up to 30 months prior to analysis. Samples from the processing study were held in frozen storage for up to 23 months prior to analysis. In a storage stability study DA MKH 3586 iPr-2-OH DA MKH 3586 were stable in corn forage, grain and stover when stored frozen for 27 months. Parent amicarbazone was stable in grain for 27 months and in stover for 12 months. Parent amicarbazone was not stable in forage or stover. However, its direct degradation products (DA MKH 3586 and iPr-2-OH DA MKH 3586) are stable so the total measured residues should remain the same for the duration of the storage periods in the residue trials.

In animal commodities, amicarbazone and desamino amicarbazone was stable in milk, fat and muscle for 1, 3 and 6 months and for one month in liver but showed some decomposition in cattle liver after 3 and 6 months frozen storage. The majority of liver samples were extracted within 28 days of collection. All other tissue and milk samples were extracted within the demonstrated stable durations.

4.5 Residue definition

Based on the results of the available metabolism and residue studies and as amicarbazone, DA MKH 3586 and iPr-2-OH DA MKH 3586 can be determined by the same analytical method, the recommended residue definition for amicarbazone is:

Sum of amicarbazone, N-(1,1-dimethylethyl)-4,5-dihydro-3-(1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide (DA MKH 3586) and N-(1,1-dimethylethyl)-4,5-dihydro-3-(1-hydroxy-1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide (iPr-2-OH DA MKH 3586), expressed as amicarbazone.

4.6 Residue trials

Eight Australian trials on sugarcane were conducted across the main sugarcane growing regions of Queensland and NSW.

Residues of total amicarbazone in sugarcane billets at 147 days after a soil directed spray at final hill-up/out of hand stage (1–1.5 m high) at 980 g ac/ha (1.4× proposed rate) were <0.03 (3), 0.055 (119 DAT at 8–10 leaf) and <0.06 mg/kg. Residues in sugar cane billets at 147 days after an over the top spray to young cane (20–40 cm high) at 980 g ac/ha (1.4× proposed maximum label rate) were <0.03 and <0.06 (2) mg/kg.

An MRL of 0.1 mg/kg is considered appropriate for amicarbazone on sugar cane. A sugarcane processing study at exaggerated rates indicated quantifiable residues (<0.01 mg/kg) of amicarbazone did not occur in refined sugar when residues in cane were 0.11 mg/kg.

Residues of total amicarbazone in sugarcane tops at 147 days after a soil directed spray at final hill-up/out of hand stage (1–1.5 m high) at 980 g ac/ha (1.4× proposed maximum label rate) were <0.22, 0.45, <0.50, 1 (91 DAT) and 2 mg/kg on a dry weight basis. Residues in sugar cane tops at 147 days after an over the top spray to young cane (20–40 cm high) at 980 g ac/ha (1.4× proposed maximum label rate) were 0.16, 1.4 and 1.7 mg/kg on a dry weight basis.

An MRL of 5 mg/kg is appropriate for amicarbazone on sugar cane fodder in conjunction with a 21 week grazing withholding period.

Rotational crops

A field study indicates that residues of amicarbazone should not be present in the soil by 12 months after application. The applicant's proposed 24 month plant back restraint for crops other than sugarcane should ensure that residues of amicarbazone will not occur in following crops. It is not necessary to establish MRL for amicarbazone in following crops / animal feeds.

4.7 Animal commodity MRLs

Ruminants

Animal transfer studies were considered for lactating cattle where the animals were dosed with amicarbazone at levels approximating that present in animal feeds for 30 days.

For beef and dairy cattle the estimated maximum livestock burden for amicarbazone is 2 mg/kg, based on a diet of 100% sugarcane tops (HR = 2 mg/kg dry weight). (The STMR-Ps for molasses and bagasse which can also be fed to livestock are 0.301 and 0.172 mg/kg respectively).

The expected residues and proposed MRLs for ruminants are summarised as:

Cattle, 500 kg bw (20 kg DM/day)

FEEDING LEVEL (ppm)	MILK	MUSCLE	LIVER	KIDNEY	FAT
	TOTAL AMICARBAZONE RESIDUE (mg/kg)				
4.5	<0.01	0.021	1.193	0.127	0.012
2 – estimated burden	<0.01	0.0093	0.53	0.056	0.0053
Recommended MRLs	*0.01	0.01	0.7 (offal)		na

The following animal commodity MRLs are appropriate for amicarbazone:

MO 0105 Edible offal (Mammalian) 0.7 mg/kg

MM 0095 Meat [mammalian] 0.01 mg/kg

ML 0106 Milks *0.01 mg/kg

A dairy cattle transfer study which involved dosing for 28 days at 39.7 ppm in the feed followed by a depuration period showed that after 3 days on clean feed, residues of amicarbazone and its metabolites in tissues were all <LOQ (0.01 m/kg).

Poultry

Commodities from sugarcane are not fed to poultry. It is not necessary to establish poultry commodity MRLs at this time.

4.8 Estimated dietary intake

The chronic dietary exposure to amicarbazone 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. 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 amicarbazone is equivalent to <1% of the ADI. It is concluded that the chronic dietary exposure to amicarbazone 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. NESTI calculations are conservative estimates of short-term exposure (24 hour period) to chemical residues in food. The highest acute dietary intake was estimated at <1% of the ARfD. It is concluded that the acute dietary exposure is acceptable.

4.9 Bioaccumulation potential

The Kow logP of amicarbazone is 1.18 at pH 4 and 1.23 at pH 7 and 9. The fat solubility and potential for bioaccumulation are predicted to be low.

4.10 Spray drift

The draft label indicates that amicarbazone should not be applied by aerial application. The proposed droplet size is medium. For larger cane up to the ‘out of hand’ stage the spray should be applied as a directed spray. For application at earlier growth stages a broadcast spray or a band spray may be used.

Based on the animal transfer information and the APVMA standard scenario for ground application (high boom, medium droplets), it is not necessary to recommend mandatory no-spray zones for protection of international trade for livestock commodities.

4.11 Recommendations

The following amendments are proposed to be made to the APVMA MRL Standard:

Table 1

COMPOUND		FOOD	MRL (mg/kg)
ADD:			
	Amicarbazone		
MO	0105	Edible offal (Mammalian)	0.7
MM	0095	Meat [mammalian]	0.01
ML	0106	Milks	*0.01
GS	0659	Sugarcane	0.1

Table 3

COMPOUND	RESIDUE
ADD:	
Amicarbazone	Sum of amicarbazone, N-(1,1-dimethylethyl)-4,5-dihydro-3-(1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide (DA MKH 3586) and N-(1,1-dimethylethyl)-4,5-dihydro-3-(1-hydroxy-1-methylethyl)-5-oxo-1H-1,2,4-triazole-1-carboxamide (iPr-2-OH DA MKH 3586), expressed as amicarbazone

Table 4

COMPOUND		ANIMAL FEED COMMODITY	MRL (mg/kg)
ADD:			
	Amicarbazone		
AM	0659	Sugarcane fodder	5

MRL amendments recommended for Tables 1 and 3 above will be considered for inclusion in Schedule 20 of the Australia New Zealand Food Standards Code.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

5.1 Commodities exported

Sugar is considered to be a major export commodity[2], as are commodities of animal origin, such as meat, offal and dairy products, which may be derived from livestock fed feeds produced from treated sugarcane.

5.2 Destination of exports

Sugar

In 2016–17 Australia exported 4009 kt of sugar valued at $2.2 billion (ABARES 2017). Major export markets included Korea, Indonesia, Japan, China, Malaysia, United States, Taiwan and New Zealand.

Beef, sheep and pig meat and offals

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

5.3 Overseas registrations and approved label instructions

The applicant indicated that amicarbazone products are registered for use on corn in the USA and a number of other countries, and sugarcane in Brazil, Cameroon, Columbia, Ivory Coast, Kenya, Morocco, South Africa and Thailand.

[2] APVMA Regulatory Guidelines – Data Guidelines: Agricultural - Overseas trade (Part 5B)

5.4 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. Amicarbazone has not been considered by Codex. The following relevant overseas MRLs have been established for amicarbazone:

COMMODITY	MRL/TOLERANCE (mg/kg)	
	AUSTRALIA (PROPOSED)	USA
Edible offal (Mammalian)	0.7	1 (cattle, liver) 0.1 (cattle, meat byproducts, except liver)
Meat [mammalian]	0.01	0.01 (cattle, meat) 0.01 (cattle, fat)
Milks	*0.01	0.01
Sugarcane	0.1	-

The residue definition in the USA is the same as proposed for Australia: sum of amicarbazone, DA amicarbazone and iPr-2-OH DA amicarbazone calculated as parent equivalents. MRLs for amicarbazone have not been established by the EU, Japan, Korea or Taiwan.

5.5 Potential risk to trade

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

A processing study indicates that detectable residues of amicarbazone should not occur in refined sugar from the proposed use. The risk to Australian trade in sugar from the proposed use is low.

A dairy cattle transfer study indicates that detectable residues of amicarbazone should not occur in animal commodities for export if a 3 day Export Slaughter Interval (ESI) is observed. The proposed 3 day ESI should ensure residues in the tissues of animals that have been fed sugarcane fodder will be below detectable levels. An ESI cannot readily be applied to by-products such as molasses and bagasse. The estimated HR in liver from feeding on molasses is 0.075 mg/kg, while finite residues are not expected in other tissues. Based on the results of the depuration study, the half-life of the main metabolite in liver is calculated to be approximately 0.4 days and it is estimated that residues in liver as a result of feeding treated molasses at 30% of the diet will decline from 0.075 mg/kg to <0.01 mg/kg in approximately 1.2 days.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Use pattern

Amitron 700WG Herbicide is to be applied using a tractor mounted or tractor drawn spray rig, as a broadcast (pre-emergence or early post-emergence) or directed (post-emergence) spray. The application window for Amitron 700WG Herbicide is approximately 2 months for both pre- and post-emergence treatments.

6.2 Exposure during use

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

The main routes of exposure to the product will be dermal and inhalational.

In the absence of exposure data for the proposed mode of application, the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) was used to estimate exposure. The toxic endpoint of concern and identified NOAEL is derived from a repeat dose study in animals, and in this instance a margin of exposure (MOE) of 100 or above is considered acceptable. The MOE takes into account potential interspecies and intraspecies variation.

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

Amitron 700WG Herbicide is a moderate eye irritant, and the use of PPE (face shield or goggles) during mixing and loading operations is recommended.

6.3 Exposure during re-entry

Acceptable MOEs (ie MOE > 100) are achieved for the product on Day 0 for low exposure activities (such scouting immature plants) and high exposure activities (such as scouting mature plants). Therefore no re-entry statement is required.

6.4 Recommendations for safe use

The following First Aid Instructions, Safety Directions and Precautionary Statements are recommended for the product label.

First aid instructions

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

Safety directions

Harmful if swallowed. Will irritate the eyes. Avoid contact with eyes. When opening the container and preparing product for use, wear face shield or goggles. If product in eyes, wash it out immediately with water. Wash hands after use. After each day's use wash face shield or goggles

6.5 Conclusion

The registration of Amitron 700WG Herbicide, containing 700 g/kg amicarbazone in a water dispersible granule product for control of weeds in plant and ratoon sugarcane, is supported from a human health perspective.

Amitron 700WG Herbicide can be used safely if handled in accordance with the instructions on the product label and any other control measures described above.

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

Amitron 700WG Herbicide is proposed for pre- or early post-emergence application to sugarcane (including over the top of green trash following harvest). The environmental assessment considered one application per year using ground application equipment at a high boom setting, a MEDIUM spray droplet size, and a maximum rate of 1000 g/ha (700 g ac/ha).

7.2 Fate and behaviour in the environment

Fate and behaviour in soil

Laboratory studies indicate that amicarbazone is moderately persistent and very mobile in soil. Biodegradation appears to be the main route for its environmental dissipation in aerobic soils with half-lives ranging from 14-87 days (laboratory conditions) and 18–30 days (field). In Australian field studies (sugarcane plots), amicarbazone degraded with half-lives 4–18 days (with or without a trash blanket). Degradation of amicarbazone is expected to occur faster under alkaline conditions due to possible additional contribution of hydrolysis. Amicarbazone is stable under anaerobic conditions. Photolysis is not expected to be an important route of degradation in soil. Limited data suggest that the major degradates (DA, MDA, DCA) are also highly persistent in soil. DCA is only expected to be formed in alkaline soils. Amicarbazone and its degradates DA, MDA & DCA are very mobile in soils. Amicarbazone does not dissociate, therefore its mobility in soil is unlikely to be affected by pH.

Fate and behaviour in water

Amicarbazone can reach aquatic systems through spray drift or runoff. Amicarbazone is considered to be relatively stable in aquatic systems. The half-life in the water column is ~ 116 days. Up to 34% of amicarbazone that enters the water is expected to partition to sediment where it persists. DA is a major degradate which slowly forms over time with half distributed to the water phase and half to the sediment. Amicarbazone and its degradates DA, MDA, and DCA are expected to reach groundwater.

Fate and behaviour in air

Based on the vapour pressure (3.0×10^{-6} Pa) and Henry's law constant (6.8×10^{-8} Pa m^3 mol^{-1}), amicarbazone is not expected to volatilize from soil, plant, or water surfaces. Therefore, amicarbazone residues in air are expected to be negligible, As a result, long-range transport of amicarbazone in air is not of concern.

7.3 Effects and associated risks to non-target species

Terrestrial vertebrates

Amicarbazone has low toxicity to birds (LD_{50} >2000 mg ac/kg bw) and mammals (LD_{50} ~1200 mg ac/kg bw). In long-term reproductive toxicity tests, no reproductive effects were observed in birds but decreased body weight and body weight gain for pup and parents were observed in rats up to 500 ppm (NOEL 100 ppm or 6.4 mg ac/kg bw/d). A screening level risk assessment assuming birds and mammals obtain 100% of their diet within the treatment area indicated that risks of adverse effects are unlikely. Therefore risks to terrestrial vertebrates to be acceptable.

Aquatic species

Toxicity of amicarbazone was determined for four species of fish, three species of aquatic invertebrates and four species of algae. Amicarbazone was not acutely toxic to fish (all LC_{50} >100 mg ac/L); however, reduced weight of fry was observed following long-term exposure to 13 mg ac/L (NOEC 7.3 mg ac/L). Amicarbazone was moderately toxic to aquatic invertebrates (lowest EC_{50} 41 mg ac/L, *Daphnia magna*). Reduced body length of adult *Daphnia magna* was observed following long-term exposure to 0.76 mg ac/L (NOEC 0.52 mg ac/L). Amicarbazone was very toxic to algae (lowest E_rC_{50} 0.035 mg ac/L, marine diatom), which was the endpoint used in the aquatic risk assessment. Spray drift risks were determined to be acceptable provided a downwind no-spray zone of 30 metres is observed. Runoff risks were determined to be acceptable provided slope and/or seasonal restrictions in certain regions are observed as specified on the label.

Bees and other non-target arthropods

Amicarbazone is not considered to be toxic to bees by contact exposure (LD_{50} >200 µg ac/bee) while some toxicity is observed following oral exposure (LD_{50} 25 µg ac/bee). The assessment considered that there is little plant forage for bees in sugar cane fields, pre- or post-emergent up to leaf stage eight, or in sugar cane trash. As such, residues in pollen and nectar are not likely to be realistic for cane trash. Considering that bee foraging in sugarcane fields would be expected to be minimal, low risks were concluded from oral and contact toxicity to bees.

Tier 1 laboratory toxicity testing with a representative WG formulation of amicarbazone was conducted with the indicator species for parasitic arthropods (LR_{50} >10 g ac/ha; ER_{50} 2.6 g ac/ha) and predatory arthropods (LR_{50} >958 g ac/ha; ER_{50} >958 g ac/ha). In the absence of higher tier testing, unacceptable risks to parasitic arthropods could not be ruled out. As a result, Amitron 700WG Herbicide is not considered to be compatible with integrated pest management programs utilising beneficial arthropods.

Soil organisms

Amicarbazone is considered to have moderate toxicity to earthworms (LC_{50} 931mg ac/kg dry soil). No effects were observed in earthworms following chronic exposure to 400mg ac/kg dry soil (highest dose tested). .

Less than 25% effect of amicarbazone on soil processes (nitrogen transformation and carbon mineralisation) was observed at soil concentrations up to 0.84 mg ac/kg (1.26 kg ac/ha).

Risks to soil organisms were determined to be acceptable within the treatment area at the maximum rate of application (700 g ac/ha).

Non-target terrestrial plants

Non-target plants adjacent to the treatment area may be exposed to the product via spray drift. Tier 2 toxicity testing with a representative WG formulation of amicarbazone was conducted on 10 crop species by pre-emergent exposure (lowest ER_{50} 69 g ac/ha, buckwheat) and post-emergent exposure (lowest ER_{50} 8.8 g ac/ha, sugar beet). Spray drift risks were determined to be acceptable provided a downwind no-spray zone of 10 metres is observed.

7.4 Conclusion

The registration of Amitron 700WG Herbicide, containing 700 g/kg amicarbazone in a water dispersible granule product for control of weeds in plant and ratoon sugarcane, is supported from an environmental safety perspective provided regional restraints and specified downwind no-spray zones on the product label are observed for the protection of aquatic environments and non-target vegetation.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed use pattern

Amitron 700WG Herbicide (700 g/kg amicarbazone) is proposed as a pre-emergent and early post emergent herbicide for residual control of a variety of grass, broadleaf, vine and sedge weeds in sugarcane. Amitron 700WG Herbicide can be applied to plant or ratoon sugar cane crops either pre-emergent or early post emergent at 0.5–1.0 kg/ha of the product (350–700 g ac/ha).

8.2 Summary of efficacy and crop safety

Amitron 700WG Herbicide is a mainly soil active herbicide which is mobilized in soil water and actively taken up by plant roots. Data from 41 efficacy and 24 safety trials were provided from trials undertaken in representative sugar cane growing regions of Queensland and northern NSW. The trials were conducted between 1996 and 2008 and included a mix of small plot trials and large scale commercial trials.

Application rates in the trials ranged from 350 to 980 g ai/ha and were applied pre-emergent to either plant cane (newly established sugar cane), or ratoon cane (cane growing from crown left after the previous seasons harvest) or early post-emergent. Commercial standard treatments were included in the trials to establish a benchmark of weed control and crop safety. Two application methods were investigated; ‘Over the top’ where the entire surface area of the paddock was treated with herbicide, and “Directed treatments” which are aimed at the row space and applied by directed nozzles and/or shielded sprayers.

Assessments were made of weed control at 2–4 weeks after treatment (WAT), 6–8 WAT and 10–14 WAT. These assessments were made using either visual scores (0–100) of biomass or else weed plant numbers (/m2). Crop safety of sugar cane was assessed through visually scoring plant damage and cane yield from the treated crop.

Grass weeds

Efficacy against 5 different grass weeds was assessed.

Crowsfoot Grass (*Eleusine indica*), Summer Grass (*Digitaria ciliaris*) and Green Summer Grass (*Brachiaria subquadriparia*)—Amitron 700WG Herbicide applied at rates of 700 g ai/ha pre-emergent was effective (up to 100% control) against and gave residual control up to 3 months after treatment. Lower rates (350–560 g ai/ha) were effective giving control of up to ≥90% on the same weeds, however the length of residual control was limited to about a month. Post-emergent applications at the same rates were also effective provided the weeds had not passed the 4 leaf stage of growth.

Awnless Barley Grass (*Echinochloa colona*)—Effective control of up to 92% was achieved in 10 trials, with reapplication rates of at 560 g ai/ha. Higher rates (700 g ai/ha) displayed up to 100% control when applied pre-emergent. Residual control (70–90% over 2 months) was observed at relatively low rates of 350–560 g ai/ha and at the higher rates residual control of up to 100% was observed at 2–3 months.

Guinea Grass (*Panicum maximum* var. maximum)—While all trialled rates were able to achieve effective early control of the weed, the residual control was very short with the control at 6–8 weeks after treatment rarely more than 80%. Post-emergent control of 2–4 leaf stage was also quite good with a range of rates (350–700 g ai/ha) of Amitron 700WG Herbicide mixed with 0.2% Agral to enhance coverage, achieving levels of control up to 100%.

Broadleaf weeds

Efficacy was assessed against a range of broadleaf weeds.

When applied pre-emergent Amitron 700WG Herbicide gave up to 100% control 8 to 12 weeks after treatment of Bluetop/Billygoat Weed (*Ageratum* spp.), vine spp. including Bellvine (*Ipomea plebeia*), Morning Glory (*I. purpurea*), Pink Convolvulus (*I. trilobia*), and Red Convolvulus (*I.hederfolia*), pasture vine legumes including Calapo (*Calopogonium muconoides*) and Centra (*Centrosema pubescens*), and tropical legumes including Sesbania Pea (*Sesbania cannabini*), Common Sensitive plant (*Mimosa pudica*), Pink Burr (*Urena lobata*), Rattle Pod (*Crotolaria* spp.), Sickle pod (*Cassia obtusifolia*), Wild Rose (*Cleome aculeate*) and Joint Vetch (*Aeschynomene* spp.). In addition, when applied at rates of 700 g ai/ha, Amitron 700WG Herbicide gave excellent post-emergent control (90–100%) of these weeds (provided they were not more than the 6 leaf stage of growth at the time of application).

When applied at 350–560 g ai/ha, Amitron 700WG Herbicide effectively controlled; Fat Hen (*Chenopodium album*), Amaranth (*Amaranth* spp.), Sowthistle (*Sonchus oleracus*), Milkthistle (E*uphorbia heterophylla*), Phyllanthus (*Phyllanthus* spp.), Bittercress (*Coronopus didymus*), Cudweed (*Gamocheara pensylvanica*), Annual Sedge (*Cyperus* sp.), Bunchy Sedge (*Cyperus ploystachus*), Nutgrass (*Cyperus rotundus*), Wild Hops (*Nicandra physallodes*) , Paddy's Lucerne (*Sida rhombifolia*) and Common Pigweed (*Portulaca oleracea*). The level of control achieved was typically ≥90 and a similar response was seen in the post-emergent treatments so long as the stage of growth of the weed were relatively young (6 leaf and less).

Application rates of 700 g ai/ha of Amitron 700WG Herbicide were required to effectively control Blackberry Nightshade (*Solanum nigrum*), Potato Weed (*Galinsoga parviflora*), Thickhead (*Crassocephalum crepidioides*), White Eclipta (*Eclipta prostrate*), Square Weed (*Spermacoce latifolia*) and Yellow Nutsedge (*Cyperus esculentus*). Residual control in these species was generally limited to the first month after treatment.

Crop safety

Crop damage was observed in a number of trials from treatment of plant cane or ratoon cane both over the top and directed application. In general, the observed level of damage was considered to be at commercially acceptable levels. Although symptoms of phytotoxicity such as leaf scorching, necrosis and stalk stunting were often seen in the first 2–3 weeks after treatment, these symptoms diminished and assessments of the crops showed there was no significant losses incurred by the early damage. Yield losses were also observed in trials where sugar cane was planted in sandy soils and subject to application rates of 1.4–2 times (980–1400 g ai/ha) the maximum label rate (700 g ai/ha). In view of these findings the APVMA recommends the following additional critical use comments:

- *This product may cause transient leaf chlorosis and necrosis and stunting on some sugar cane varieties.*
- *In plant cane, pre-emergent application should be carried out within 5 days of planting to avoid risk of crop injury.*
- *Do not use these rates on very sandy soils (>90% sand).*

8.3 Conclusions

Amitron 700WG Herbicide when used as directed is expected to provide control the listed range of weeds and acceptable levels of crop safety in sugarcane when used as directed.

9 LABELLING REQUIREMENTS

POISON

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

AMITRON®
700WG
Herbicide

ACTIVE CONSTITUENT: 700 g/kg AMICARBAZONE

GROUP **C** HERBICIDE

For pre- and post-emergent control of various weeds in plant and ratoon sugarcane as per the directions for use.

NET CONTENTS: 1–20 kg

DIRECTIONS FOR USE

RESTRAINTS

DO NOT apply with aircraft.
Follow or Rotational Crops: DO NOT use Amitron 700WG 24 months prior to planting any crop other than sugarcane.

SPRAY DRIFT RESTRAINTS

DO NOT apply with spray droplets smaller than a MEDIUM spray droplet size category according to the nozzle manufacturer specifications that refer to the ASAE S572 Standard or the British Crop Production Council guideline.

DO NOT apply when wind speed is less than 3 or more than 20 kilometres per hour, as measured at the application site.
DO NOT apply during surface temperature inversion conditions at the application site.

Users of this product **MUST make an accurate written record** of the details of each spray application within 24 hours following application, and **KEEP** this record for a minimum of 2 years. The spray application details that must be recorded are:

1 Date with start and finish times of application, **2** Location address and paddock(s) sprayed, **3** Full name of this product, **4** Amount of product used per hectare and number of hectares applied to, **5** Crop or situation and weed or pest, **6** Wind speed and direction during application, **7** Air temperature and relative humidity during application, **8** Nozzle brand, type, spray angle, nozzle capacity and spray system pressure measured during application, **9** Name and address of person applying this product. (Additional record details may be required by the state or territory where this product is used.)

MANDATORY NO-SPRAY ZONES

DO NOT apply if there are sensitive crops, gardens, landscaping vegetation, protected native vegetation or protected animal habitat within 10 metres downwind from the application area.

DO NOT apply if there are aquatic and wetland areas including aquacultural ponds, surface streams and rivers within 30 metres downwind from the application area.

For prevention of Run-off to adjacent waterways.

Slop restrictions:
Mackay/Whitsunday region: DO NOT apply on slopes steeper than 3%
No-spray time intervals:
Wet tropics: no restriction
Burdekin: no restriction
Mackay/Whitsunday region: DO NOT apply during October, November or December.
Mary/Burnett region: DO NOT apply during October, November or December.
Northern NSW: No restriction.

CROP	WEEDS CONTROLLED	WEED STAGE	STATE	RATE g/ha	CRITICAL COMMENTS
Sugarcane	Awnless barnyard grass *(Echinochloa colonum)* Bellvine *(Ipomea plebeia)* Calopo *(Calopogonium mucunoides)* Centro *(Centrosema pubescens)* Crowsfoot grass (*Eleusine indica)* Guinea grass *(Panicum maximum)*	Early post-emergence control (up to 4 leaf stage)	Qld and NSW only	500 + non-ionic surfactant (600 g/L) at 200 mL/100 L (0.2% v/v)	**CROP STAGE**: **Plant and Ratoon Cane - Pre-emergence to early post-emergent (up to 8 leaf)** This product may cause transient leaf chlorosis and necrosis and stunting on some sugarcane varieties. **In Plant Cane, pre-emergent applications should be carried out within 5 days of planting to avoid risk of crop injury.** **Application:** Where shading of cane leaves prevents contact with the soil surface or small weeds, droppers with wide angle nozzle tips and/or leaf lifters should be used to provide complete soil coverage. Use a minimum spray volume of 200 L/ha.
	Bluetop/Billygoat weed (*Ageratum* spp.) Calopo *(Calopogonium mucunoides)* Common pigweed *(Portulaca oleracea)* Common sowthistle *(Sonchus oleraceus)* Cudweed (*Gamochaeta pensylvanica)* Green amaranth *(Amaranthus viridis)* Paddy's lucerne *(Sida rhombifolia)* Pink burr (*Urena lobata)* Wild hops *(Nicandra physalodes)*	Pre-emergence: Short term residual control (up to 4 weeks)		500	
	Annual sedges *(Cyperus* spp.*)* Rattle pod (*Crotalaria* spp.*)*	Early post-emergence control (up to 6 leaf stage)		800	

CROP	WEEDS CONTROLLED	WEED STAGE	STATE	RATE g/ha	CRITICAL COMMENTS
Sugarcane *cont.*	Annual Sedges *(Cyperus* spp.*)* Awnless barnyard grass Bellvine Bittercress *(Coronopus didymus)* Bluetop/Billygoat weed Calopo Centro Common sensitive plant *(Mimosa pudica)* Crowsfoot grass Fat hen *(Chenopodium album)* Green amaranth Green summer grass *(Brachiaria subquadripara)* Guinea grass Joint vetch *(Aeschynomene indica)* Morning glory *(Ipomea purpurea)* Paddy's lucerne Pink convolvulus *(I. triloba)* Potato weed *(Galinsoga parviflora)* Rattle pod Sesbania pea *(Sesbania cannabina)* Summer grass *(Digitaria ciliaris)* Thickhead *(Crassocephalum crepidioides)*	Pre-emergence: Short to medium term residual control (up to 8 weeks)	Qld and NSW only	800	**CROP STAGE**: **Plant and Ratoon Cane—Pre-emergence to early post-emergent (up to 8 leaf)** This product may cause transient leaf chlorosis and necrosis and stunting on some sugarcane varieties. **In Plant Cane, pre-emergent applications should be carried out within 5 days of planting to avoid risk of crop injury.** **Application:** Where shading of cane leaves prevents contact with the soil surface or small weeds, droppers with wide angle nozzle tips and/or leaf lifters should be used to provide complete soil coverage. Use a minimum spray volume of 200 L/ha.
	Common pigweed Cudweed Phyllanthus *(Phyllanthus* sp.*)*	Pre-emergence: Long term residual control (10-14 weeks)			

CROP	WEEDS CONTROLLED	WEED STAGE	STATE	RATE g/ha	CRITICAL COMMENTS
Sugarcane *cont.*	Bittercress Blackberry nightshade *(Solanum nigrum)* Common pigweed Milkweed *(Euphorbia heterophylla)* Paddy's lucerne Common sowthistle	Early post-emergence control (up to 6 leaf stage)	Qld and NSW only	1000	**CROP STAGE:** **1. Plant and Ratoon Cane—Post-emergence (30 cm to 1.2 m high)** This product may cause transient leaf chlorosis and necrosis and stunting on some sugarcane varieties. **Do not use these rates on very sandy soils (>90% sand).** **Application:** Apply as a directed spray with equipment to minimize contact with cane foliage and maximize contact with the soil surface and small weeds. Droppers with wide angle nozzle tips and/or leaf lifters or Irvine Boom configurations should be used to minimize cane leaf contact and provide complete soil coverage. **2. Ratoon Cane—Pre-emergence to 5 leaf stage including post harvest on to trash blankets** This product may cause transient leaf chlorosis and necrosis and stunting on some sugarcane varieties. **Do not use these rates on very sandy soils (>90% sand).** **Application:** Where shading of cane leaves prevents contact with the soil surface or small weeds, droppers with wide angle nozzle tips and/or leaf lifters should be used to provide complete soil coverage.
	Bellvine Bluetop/Billygoat weed Cudweed Morning glory Thickhead	Post-emergent control (up to flowering)			
	Annual sedges Bellvine Blackberry nightshade Calopo Centro Common sensitive plant Morning glory Pink burr Potato weed Red convolvulus *(Ipomea hederifolia)* Sesbania pea Thickhead White eclipta (*Eclipta prostrata)* Wild rose (*Cleome aculeata)*	Pre-emergence: Medium to long term residual control (up to 10–14 weeks)			

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

WITHHOLDING PERIODS
Grazing: DO NOT GRAZE OR CUT FOR STOOK FOOD FOR 21 WEEKS AFTER APPLICATION.
Harvest: NOT REQUIRED WHEN USED AS DIRECTED
EXPORT SLAUGHTER INTERVAL (ESI) – 3 DAYS

LIVESTOCK DESTINED FOR EXPORT MARKETS: The grazing withholding period only applies to stock slaughtered for the domestic market. Some export markets apply different standards. To meet these standards, an Export Slaughter Interval needs to be observed before stock are sold or slaughtered.
LIVESTOCK THAT HAS GRAZED ON OR BEEN FED TREATED CROPS SHOULD BE PLACED ON CLEAN FEED FOR 3 DAYS PRIOR TO EXPORT SLAUGHTER.

GENERAL INSTRUCTIONS
Amitron 700WG Herbicide is a soil residual broad spectrum herbicide for control of important grass and broadleaf weeds and sedges in sugarcane. Amitron 700WG can be applied pre- or early post-emergence to either plant or ratoon sugarcane including over the top of green trash blankets. Best results occur if Amitron 700WG is applied shortly before weeds germinate (growth occurs). Established and germinating weeds should be controlled by chemical or mechanical means. Results vary with soil type (lower rates are effective on lighter soils, higher rates will be necessary for effective control on heavier soils) and environmental conditions. Temporary chlorosis of lower leaves may occur. To minimise this injury use low directed spray application. Tolerance of cane variety should be determined before treating large areas. Contact an Arysta representative for further information.

Mixing
This product mixes readily with water. Add the required amount of AMITRON 700WG directly to the spray tank which should be 50% full with clean water. After the product is fully dispersed complete filling the tank. The agitation system should be running during mixing and spraying. If agitation ceases and settling occurs, resuspend contents thoroughly before spraying. Ensure that all in-line strainer and nozzle screens in the sprayer are 100 mesh or coarser.

Soil Moisture
Best results will be achieved by applying to moist soil. Since the product acts mainly through root absorption, full efficacy may be delayed in dry conditions.

Ground Application
A minimum water volume of 200 L/ha should be used. The spray can be applied as an overall broadcast spray or as a band spray 30–35 cm wide over the drill row of sugarcane up to the 8 leaf stage. For larger cane up to the “out-of-hand” stage, the spray should be applied as a directed spray to minimise spray contact with sugarcane foliage as injury may occur at the higher rates.

Tank Mixtures
If knockdown control of emerged weeds is required, include paraquat as a tank mix with Amitron 700WG.

A non-ionic surfactant (600 g/L) added to the low rate of Amitron 700WG (500 g/ha) will provide knockdown of grass seedlings up to the 4 leaf stage as per the Directions for Use table.

Compatibility
Amitron 700WG is compatible with the following products: 2,4-D amine, ametryn, metribuzin, diuron, diuron + hexazinone, paraquat, pendimethalin and imazapic.

Do not tank mix AMITRON 700WG with more than one of the above products without doing a jar test beforehand. However, physical compatibility does not guarantee biological compatibility. Do not tank mix with other products without reference to a Arysta representative.

Resistant Weeds Warning

GROUP C HERBICIDE
AMITRON 700WG Herbicide is a member of the triazolinone group of herbicides. The product has the inhibitors of photosynthesis at photosystem II (PS II Inhibitors) mode of action. For weed resistance management, the product is a Group C herbicide.
Some naturally occurring weed biotypes resistant to the product and other Group C herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by this product or other Group C herbicides.
Since the occurrence of resistant weeds is difficult to detect prior to use, Arysta LifeScience North America LLC accepts no liability for any losses that may result from the failure of this product to control resistant weeds.

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

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
Very toxic to aquatic life. DO NOT contaminate wetlands or watercourses with this product or used containers.

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

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight.
Single-rinse or shake remainder into spray tank. Do not dispose of undiluted chemicals on site. 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
Harmful if swallowed. Will irritate the eyes. Avoid contact with eyes. When opening the container and preparing product for use, wear face shield or goggles. If product in eyes, wash it out immediately with water. Wash hands after use. After each day's use wash face shield or goggles.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131 126.

SAFETY DATA SHEET
Additional information is listed in the Safety Data Sheet available from your supplier**.**

Conditions of Sale
To be added

In a Transport Emergency Dial **000** Police or Fire Brigade	24 HOUR EMERGENCY RESPONSE SERVICE AUSTRALIA **1800 033 111** INTERNATIONAL **+61 3 9663 2130**

AMITRON* is a registered trademark of Arysta LifeScience.

APVMA Approval No: 64379/xxxxxx

Batch No.:
Date of Manufacture:

ABBREVIATIONS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DA	Des-amino amicarbazone (degradate)
DAT	Days After Treatment
DCA	Decarboxamide amicarbazone (degradate)
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
ER_{50}	Rate at which 50% of the test population is impacted
EI	Export Interval
EGI	Export Grazing Interval
ESI	Export Slaughter Interval
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice

GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
Kd	soil adsorption coefficient
Kf	soil Freundlich sorption coefficient
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
MDA	N-methyl des-amino amicarbazone (degradate)
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit

MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NER	non-extractable residues
NESTI	National Estimated Short Term Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
TTR	Total Radioactive Residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
vmd	volume median diameter

WG	Water Dispersible Granule
WHP	Withholding Period

GLOSSARY

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

REFERENCES

APVMA, 2008. APVMA Operating Principals in Relation to Spray Drift. Australian Pesticides and Veterinary Medicines Authority (APVMA), 15 July 2008.