Australian Government

Australian Pesticides and Veterinary Medicines Authority

PUBLIC RELEASE SUMMARY

on the Evaluation of the new active Indaziflam in the Product Specticle Herbicide

APVMA Product Number 64673

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Director Public Affairs and Communication
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604 Australia

Telephone: +61 2 6210 4701

Email: communications@apvma.gov.au

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

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PREFACE

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

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing, Office of Chemical Safety (OCS), Department of Environment, and State Departments of Primary Industries.

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

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

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

About this document

This is a Public Release Summary.

It indicates that the 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 sections 12 and 13 of the Agvet Code, the APVMA invites any person to submit a relevant written submission as to whether the application for registration of specticle herbicde 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 Tuesday 15 December 2015 and be directed to the contact listed below. All submissions to the APVMA will be acknowledged in writing via email or by post.

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

When making a submission please include:

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

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

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

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

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

[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.

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

1 INTRODUCTION

1.1 Applicant

Bayer CropScience Pty Ltd.

1.2 Details of the product

It is proposed to register Specticle Herbicide, containing 200 g/L indaziflam, as a suspension concentrate intended for use in the control of Summer grass (*Digitaria* spp), Crowsfoot grass(*Eleusine indica*) and Winter grass (*Poa annua*) in turf on golf course fairways.

The product is to be applied to established turf prior to weed germination at a rate of 250 mL/ha which equates to 50 g ac/ha. The product will be applied in 200–500 L of water/ha by either ground-boom or hand-held (backpack and hand-wand) application methods and requires activation by rainfall or irrigation within weeks of application. A maximum of two applications per annum may be applied with a minimum re-treatment interval of 3 months.

Indaziflam is a new active constituent to the Australian market. Indaziflam is a herbicide that belongs to the alkylazines chemical family and will be the first herbicide registered in this family in Australia. The Herbicide Resistance Management Action Committee (a specialist technical group of CropLife International) has classified indaziflam as having the target site of cellulose synthesis in cell wall biosynthesis (i.e. it acts by inhibiting seed growth prior to germination and during root development). Advice from CropLife Australia's Herbicide Resistance Management Review Group (HRMRG) confirms that indaziflam will be classified as a Group O herbicide (inhibition of cell wall (cellulose) synthesis).

1.3 Overseas registrations

Indaziflam as a 200 g/L suspension concentrate is currently registered for use in Canada (pre-emergent control of annual grass and broadleaf weeds in in pome and stone fruit, grapes and tree nuts), the United States of America (pre-emergent weed control in citrus, stone and pome fruit, grapes, tree nuts and olives), Indonesia, (forestry situations) and Japan. As a 500 g/L suspension concentrate indaziflam is currently registered for use in the United States of America (pre-emergent weed control in citrus, stone and pome fruit, grapes, tree nuts and olives), Argentina (crop and forestry situations), Mexico (forestry situations, sugarcane, citrus and grapes) Indonesia (forestry situations), Malaysia (forestry situations), the Philippines (bananas) and Vietnam (tea, coffee, citrus and rubber trees).

This publication provides a summary of the data reviewed and an outline of regulatory considerations for the proposed registration of Specticle Herbicide.

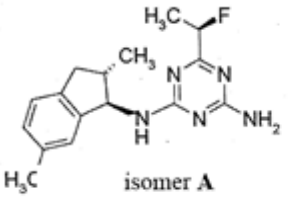
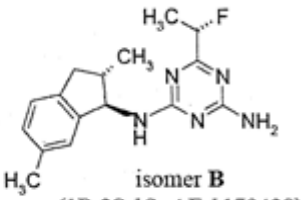
2 CHEMISTRY AND MANUFACTURE

2.1 Active constituent

Indaziflam is a new active constituent to be used as a herbicide in turf. Indaziflam inhibits cellulose biosynthesis and belongs to the alkylazine group of compounds. Indaziflam is a selective herbicide for weed control in warm season turf.

Indaziflam has three asymmetric or chiral carbons and two of eight isomers (isomers A and B below) are defined as the active constituents of indaziflam.

CHEMICAL CHARACTERISTICS OF ACTIVE CONSTITUENT

COMMON NAME (ISO):	Indaziflam (ISO, AS approved)
IUPAC NAME:	*N*-[(1*R*,2*S*)-2,3-dihydro -2,6-dimethyl -1*H*-inden-1-yl]-6-[(1*RS*)-1-fluoroethyl]-1,3,5-triazine-2,4-diamine
CAS NAME:	*N*-[(1*R*,2*S*)-2,3-dihydro-2,6-dimethyl-1*H*-inden-1-yl]-6-(1-fluoroethyl)- 1,3,5-triazine-2,4-diamine
CAS REGISTRY NUMBER:	950782-86-2
MINIMUM PURITY:	890 g/kg
MOLECULAR FORMULA:	$C_{16}H_{20}FN_5$
MOLECULAR WEIGHT:	301.36
STRUCTURE:	 isomer **A** (1R,2S,1R; AE 1170437)  isomer **B** (1R,2S,1S; AE 1170438)
CHEMICAL FAMILY:	Alkylazine

PHYSICO-CHEMICAL PROPERTIES OF ACTIVE CONSTITUENT

COLOUR:	Light beige colour (technical) White powder (pure)
ODOUR:	No characteristic colour
PHYSICAL STATE:	Solid
MELTING POINT:	NA, but isomer A : 183^{0}C and Isomer B 178^{0}C
RELATIVE DENSITY AT 20^{O}C:	1.23 g/cm^3
FLAMMABILITY:	Not highly flammable
EXPLOSIVE PROPERTIES:	Not explosive
OXIDISING PROPERTIES:	Not an oxidizing agent
CORROSIVE CHARACTERISTICS:	Not corrosive
DANGEROUS GOODS CLASSIFICATION:	Not a dangerous Good according to ADG Code; but an environmentally hazardous substance, UN3077, Label 9, packaging group III.

The Chemistry Section has evaluated the chemistry aspects of indaziflam active constituent (manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable.

On the basis of the chemistry and manufacture data provided and the toxicological assessment, it is proposed that the following APVMA Active Constituent Standard be established for indaziflam:

APVMA ACTIVE CONSTITUENT STANDARD FOR INDAZIFLAM

CONSTITUENT	SPECIFICATION	LEVEL
Indaziflam	Indaziflam	Not less than 890 g/kg with the following specified isomers: 1R, 2S, 1R isomer [A] 890 g/kg minimum; 1R, 2S, 1S isomer [B] 50 g/kg maximum.

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2.2 Formulated product

The Chemistry and Manufacture Section of the APVMA has evaluated the chemistry aspects of the product, Specticle herbicide (physico-chemical properties, formulation process, quality control procedures, batch analysis results, stability, analytical methods and packaging).

The product Specticle Herbicide will be manufactured and formulated overseas, and imported to Australia in 1 to 20 L high-density polyethylene (HDPE) containers. The manufacturing and quality control procedures, including compliance with the release specifications, are acceptable.

The Applicant provided the results of real time and accelerated stability testing conducted using samples stored in high-density polyethylene containers (HDPE), the proposed commercial container type. Testing of all important parameters for suspension concentrate formulations were conducted. The results indicate that the formulated product is expected to remain stable for at least two years when stored under normal conditions in the proposed commercial packaging.

SPECTICLE HERBICIDE

DISTINGUISHING NAME:	Specticle Herbicide
FORMULATION TYPE:	Suspension Concentrate (SC)
ACTIVE CONSITUENT CONCENTRATION:	Indaziflam (200 g/L)

PHYSICAL AND CHEMICAL PROPERTIES OF THE FORMULATED PRODUCT

FORMULATION TYPE:	Suspension concentrate
APPEARANCE	Off-white liquid suspension
ACTIVE CONSITUENT CONCENTRATION:	Indaziflam, 200 g/L
RELATIVE DENSITY:	1.05 g/cm^3
PH (1% DILUTION):	5.1
SAFETY PROPERTIES:	Not corrosive, flammable or explosive
PACK SIZES:	1–20 L
PACKAGING MATERIAL:	High density polyethylene (HDPE)
STORAGE STABILITY:	The product is expected to remain within specification for at least 2 years when stored under normal conditions in HDPE containers

2.3 Recommendations

Based on a review of the data provide by the Applicant, the APVMA is satisfied that the chemistry and manufacture data details of Specticle Herbicide are acceptable.

3 TOXICOLOGICAL ASSESSMENT

The toxicological database for indaziflam, which consists primarily of toxicity studies conducted in rats, mice, rabbits and dogs, is considered sufficient to determine the toxicology profile of indaziflam and characterise the risk to humans. In interpreting the data, it should be noted that toxicity tests generally use doses that are high compared with likely human exposure. 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 likely to occur. Such dose levels as the No-Observable-Effect-Level (NOEL) are used to develop acceptable limits for dietary or other intakes (ADI (Acceptable Daily Intake) and ARfD (Acute Reference Dose)) at which no adverse health effects in humans would be expected.

3.1 Chemical class

Indaziflam is a member of the alkylazine class of pesticides. Its mode of action is reported to be inhibition of cellulose biosynthesis, thus, it acts by inhibiting seed growth prior to germination and during root development.

3.2 Toxicokinetics and metabolism

Following oral administration in low-dose studies (5–15 mg/kg bw) in rats, indaziflam is rapidly and almost completely absorbed and distributed into systemic circulation (T_{max} = 40–60 min). Metabolism also occurred rapidly in rats and the major metabolic pathway was oxidation and the major metabolite appearing in urine, faeces and bile was an oxidised carboxylic acid form of indaziflam. Elimination was rapid in rats with approximately 85–90% excreted by 24 hours, mainly in the faeces and in urine. In males, more radioactivity was excreted in the faeces (~3:2 ratio) but in females almost equal proportions were excreted in the faeces and urine. Elimination of the administered dose was essentially complete by 48 hours post-dose. Bile cannulation studies in rats showed bioavailability was very high (90%) following oral administration at the low dose. Single high dose oral studies (> 550mg/kg/bw) in rats indicate that a large portion (40%) of the parent chemical is excreted un-absorbed.or un-metabolised after absorption. There was minimal recovered radioactivity from high dose rats sacrificed after 48 hours indicating that the potential for bioaccumulation is low. The highest levels of radioactivity were found in the liver, gastrointestinal tract and the skin.

The *in vivo* human dermal absorption was estimated based in *in vivo* and *in vitro* rat, and *in vitro* human data. For a concentrate product (500 g/L SC formulation), dermal absorption is estimated to be low at 0.49%. Dermal absorption is estimated at 3.42 and 11.3% for diluted concentrations of 0.2 and 0.05 g/L respectively.

Acute toxicity

Indaziflam has low acute oral (LD_{50} >2000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalational (4– hr LC_{50} >2300 mg/$m^{3)}$ toxicity in rats, was not a skin irritant in rabbits but was a slight eye irritant in the same species, and was not a skin sensitiser in an LLNA (Local Lymph Node Assay) in mice.

The formulated product, Specticle Herbicide has low acute oral (LD_{50} >2000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalational (4–hr LC_{50} >3625 mg/m^3), toxicity in rats, was not a skin irritant in rabbits but was a slight eye irritant in the same species, and was not a skin sensitiser guinea pigs.

Systemic effects

A short-term 28–day dermal study was conducted in rats at doses up to 1000 mg/kg/bw/day and no toxicity was observed.

Sub-chronic studies were conducted for 90 days in rats, mice and dogs. Rats and mice were fed indaziflam in the diet at doses up to 689/806 and 218/256 mg/kg bw/day (M/F) respectively. The liver and kidney were the target organs of toxicity in rats and effects in the liver included enlarged liver and increased liver weights. Effects in the kidney in rats include enlarged kidneys, increased relative kidney weights, basophilic tubule and interstitial mono-cellular cell infiltrate. A separate group of rats was allowed a recovery of 28 days following the 90 days dietary administration and recovery from treatment related effects was observed. In mice, there were decreased body weights at statistically significant levels at 218/256 mg/kg bw/day (M/F) and there were also significant changes in clinical chemistry parameters (albumin, total protein and aspartate aminotransferase) though no toxicologically significant changes were seen in the liver or kidneys in the mouse study. Overt clinical signs of toxicity were observed in the 90 day dog study at 30 mg/kg bw/day (seizures) along with effects on the nervous system at 7.5 mg/kg bw/day and above, i.e. micro-pathological indicators of toxicity. There were no toxicologically significant findings in the liver or kidneys in the 90 day dog study.

From the 90 day studies there are a number of species differences following administration of indaziflam. In particular, axonal degeneration was seen in dogs at 15 mg/kg/bw/day and greater, which was not observed in sub-chronic mouse or rat studies at doses of 689/806 and 218/256 mg/kg bw/day (M/F) for rats and mice, respectively. Axonal degeneration of the spinal cord was also seen in the one year chronic dog study at dose levels of 6/7 mg/kg bw/day and greater (M/F), and was also observed at a low incidence in the brain and sciatic nerve of males and females at 12/11 mg/kg bw/day, while possible treatment related seizures and convulsions were noted in one 12 mg/kg bw/day male dog.

Genotoxicity and carcinogenicity

In chronic/carcinogenicity studies, the main toxic effect in rats and mice was decreased body weights and effects in the liver and in the kidneys. In mice kidney and weights were decreased, while in rats no treatment related effects were seen in kidney weight though an increased liver weight was seen. In both species there were microscopic changes in the liver and kidneys. In mice there was centri-lobular vacuolation in the liver, along with hyperplasia, papillary necrosis and observance of intra-tubular yellow/brown material. A decrease of vascuolation was also seen in the kidneys though the significance of this finding is unclear. In rats centri-lobular and pan-lobular hypertrophy was also seen in the liver, along with intracellular brown pigment in the cortical tubules of the kidneys. There were clinical signs of neurotoxicity in rats at the high dose, and it was

apparent that females were more susceptible than males. Additionally, in male and female rats at high dose, median eminence vascuolation was observed in the brain. As for the sub-chronic studies, the long-term studies also illustrate a number of species differences between rats, mice and dogs, with the dog being the most sensitive species to indaziflam toxicity.

There was no evidence of carcinogenicity in long-term rat or mouse studies.

Indaziflam was not mutagenic and/or genotoxic in a battery of *in vitro* (with and without metabolic activation) in i*n vivo* assays. Two indaziflam metabolites (6–(1-Fluorophenyl)-1,3,5-triazin-2,4-diamine and indaziflam-carboxylic acid) were not mutagenic or genotoxic when tested *in vitro* with and without metabolic activation.

Reproductive and developmental toxicity

Indaziflam induced minor reproductive effects (decreased number of implants, corpora lutea and smaller litter size in F1 females) in rats. Systemic toxicity was also observed at the same dose level and the observed reproductive effects are considered a likely consequence of the observed maternal toxicity. Therefore, this study provides no robust evidence that indaziflam is a reproductive toxicant.

Indaziflam was not a developmental toxicant in SD rats or NZW rabbits. In the developmental study in rats the maternal and developmental NOEL was 25 mg/kg bw/day for effects on body weights (maternal and developmental) and reduced food consumption (maternal only) at 200 mg/kg bw/day. The observed foetal findings were considered a secondary non-specific consequence of maternal toxicity. In a developmental study in rabbits the maternal NOEL was also 25 mg/kg bw/day for decreased body weight gain and decreased food consumption while no treatment related and toxicologically significant foetal effects were seen up to and including the top dose level of 60 mg.kg bw/day.

Neurotoxicity

From the available data, neurotoxicity appears to be the main toxicological effect in mammalian test systems and the dog was the most sensitive species based on axonal degeneration, most notably in the dorsal sensory tracts (fasciculus cuneatus) which was observed in both sub-chronic and chronic dog studies. These neuropathological lesions were observed in the absence of clear signs of systemic toxicity, although there were clinical signs of neurotoxicity with animals killed *in extremis* in both studies. The lesions in the spinal cord were treatment related and dose dependent at 15 mg/kg bw/day in the sub-chronic study and at 67 mg/kg bw/day (M/F) in the chronic dog study.

There were seizures in 3/8 dogs at 30 mg/kg bw/day in the sub-chronic study with the onset period for observance being between 15–35 days. The animals with seizures were killed *in extremis* on the day of the onset and all remaining dogs were sacrificed early on day 36. Axonal degeneration of the spinal cord was observed in all 30 mg/kg bw/day dosed animals, including dogs killed *in extremis* on day 15. This indicates an early onset of microscopic lesions at this dose level. In addition to seizures, clinical signs possibly attributable to neurotoxicity in the sub-chronic dog study at 30 mg/kg bw/day include tremors, ataxia, salivation and aggressive behaviour. The clinical signs appear to be associated with the overt toxicity observed at 30 mg/kg bw/day and thus, the results of this study do not provide a definitive link between clinical or behavioural signs of neurotoxicity and the observed neuropathological lesions (though an FOB was not conducted in the 90 day dog study).

Axonal degeneration of the spinal cord was also observed in the chronic dog study at 6/7 mg/kg bw/day and greater (M/F), and while seen in the brain and sciatic nerve in males/females at 12/11 mg/kg bw/day, was at a lower incidence and less severe. The only behavioural sign of neurotoxicity observed was a seizure and convulsion in 1/4 males at 12 mg/kg bw/day. This male was sacrificed *in extremis* on day 190. There were no other observations or findings from FOB testing in the chronic dog study, and there were no clear signs of systemic toxicity.

Similar neuropathological lesions were observed in neurotoxicity studies in rats but at notably higher doses than in the dog studies. An acute neurotoxicity study in rats revealed treatment related nerve fibre degeneration in the gasserian ganglion, sciatic nerve, tibial nerve and sural nerve at 2020 mg/kg bw males and sural nerve fibre degeneration only in males at 501 mg/kg bw (noting that 2000 mg/kg bw females were not examined microscopically). Decreased motor and locomotor activity were observed in 501 mg/kg bw females and in 2020 mg/kg bw males and females on day 0 but not on day 7 or 14. The acute neurotoxicity study indicates that nerve fibre degeneration can occur after a single dose of 501 mg/kg bw and greater doses in rats.

A sub-chronic neurotoxicity study in rats was conducted at doses markedly higher than the sub-chronic dog study, and neurotoxicity (tremors, decreased motor and locomotor activity and nerve fibre degeneration in the sural nerve and spinal nerve root) was observed in the presence of systemic toxicity (decreased body weight gain and food consumption) at 585.7/580.9 mg/kg bw/day in males/females. There were no clear signs of neurotoxicity in pups in a development neurotoxicity study in rats up to and including the highest dose of 432 mg/kg bw/day, which produced systemic toxicity in both pups and dams.

The data for neurotoxicity shows considerable species differences in rats and dogs. A battery of neurotoxicity studies in rats (acute, sub-chronic and developmental) confirmed the neurotoxic potential of indaziflam at higher doses (approximately 500 mg/kg bw and greater) based on decreases in motor and locomotor activity and axonal degeneration, but did not demonstrate delayed or developmental neurotoxicity. The chronic and sub-chronic dog studies show clear histopathological changes (at 6/7 [males/females] and 15 mg/kg bw/day and greater respectively), most notably in the form of axonal degeneration in the spinal cord and brain, but also in the sciatic nerve. However, there is no clear indication from the submitted studies of the functional or behavioural relevance of these histopathological changes except for severe seizures observed in dogs in the sub-chronic study at 30 mg/kg bw/day, as the significance of the observed seizures and convulsions in a single animal at 12 mg/kg bw/day in the chronic dog study is questionable. Furthermore, while motor and locomotor activity was seen to be depressed initially, recovery from this initial depression was seen with continued dosing.

3.3 Public health standards

Poisons scheduling

The delegate to the Secretary of the Department of Health and Aging sought advice from the Advisory Committee on Chemical Scheduling (ACCS) on the scheduling of indaziflam. Indaziflam was discussed at the October 2011 meeting of the ACCS. The delegate noted and agreed with the ACCS recommendation that indaziflam be included in Schedule 6 of the Standard for the Uniform Scheduling Of Medicines and Poisons (SUSMP) with no cut-off. The delegate's final decision made on 1 February 2012 confirmed that

indaziflam be included in Schedule 6 of the SUSMP with no cut-off, along with an implementation date of 1 May 2012.

NOEL/ADI/ARfD

The Acceptable Daily Intake (ADI) is the quantity of an agricultural or veterinary chemical which can be safely consumed on a daily basis for a lifetime and is based on the lowest NOAEL (No-Observable- Adverse-Effects-Limit) obtained in the most sensitive species. This NOAEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

Since the current application for registration is not associated with food producing use, no ADI for indaziflam is required at this stage.

The Acute Reference Dose (ARfD) is the maximum quantity of an agricultural or veterinary chemical that can be safely consumed as a single, isolated event. The ARfD is derived from the lowest NOEL (No-Observable-Effect-Limit) as a single or short-term dose which causes no effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

Since the current application for registration is not associated with food producing use, no ARfD for indaziflam is required at this stage.

4 RESIDUES ASSESSMENT

The proposed use for Specticle Herbicide is for the pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*) in turf on golf course fairways. As Specticle Herbicide will not be used on food producing crops, a residues assessment has not been undertaken at this time.

5 ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

The proposed use for Specticle Herbicide is for the pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*) in turf on golf course fairways only. As Specticle Herbicide will not be used on food producing crops, a residues assessment has not been undertaken at this time.

The proposed label prohibits the gazing of treated turf or the feeding of turf clippings from any treated area to poultry or livestock. Therefore the proposed use of Specticle Herbicide will not pose a risk to Australia's international trading status.

6 OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

6.1 Health hazards

Indaziflam (CAS: 950782-86-2) is not listed on Safe Work Australia's (SWA) Hazardous Materials Information System (HSIS) Database (SWA, 2011).

With the available toxicological information The Office of Chemical Safety (OCS) recommends classification of indaziflam as a hazardous substance according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 20004), with the following risk phrases:

Xn: R48/22	Harmful: Danger of serious damage to health by prolonged oral exposure.

The following cut-off concentration applies for indaziflam:

Conc. ≥ 10% Xn: R48/22

6.2 Formulation, packaging, transport, storage and retailing

The active constituent indaziflam will be manufactured overseas. The product Specticle Herbicide will be manufactured and formulated overseas, and imported to Australia in 1 to 20 L high-density polyethylene (HDPE) containers.

6.3 Use pattern

The product is to be applied prior to weed germination at a rate of 250 mL/ha which equates to 50 g ac/ha. The product will be applied in 200–500 L of water/ha by either ground-boom or hand-held (backpack and hand-wand) application methods and requires activation by rainfall or irrigation within weeks of application.

6.4 Exposure during use

Golf course owners and their employees will be the main users of the product. Workers will be exposed to the product when opening containers, mixing and loading, application and cleaning up spills and equipment. The main route of exposure to the product/spray will be dermal and inhalation, although ocular exposure is also possible.

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

The MOE takes into account both inter-species and intra-species variability and the seriousness of the critical health effect of concern.

The MOE's for mixing and loading and ground-boom, low and high pressure hand-wand are all at an acceptable level (i.e. >100) when the operator us wearing single layer of clothing (cotton overalls or equivalent clothing), with or without gloves.

The MOE for backpack application is acceptable (i.e. >100) only when the operator is wearing gloves and a 2nd layer of clothing (cotton overalls over normal clothing) during application. For mixing and loading prior to back-pack application, the MOE is considered acceptable when a single layer of clothing (cotton overalls or equivalent clothing) is worn, with or without gloves.

6.5 Exposure during re-entry

No re-entry statement is required.

6.6 Recommendations for safe use

Users should follow the First Aid Instruction and Safety Directions on the product label.

6.7 Conclusion

The registration of Specticle Herbicide containing indaziflam at 200 g/L, for the pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*) in turf is supported.

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

7 ENVIRONMENTAL ASSESSMENT

7.1 Introduction

BayerCrop Science Pty Ltd has applied for the registration of the new product Specticle Herbicide containing 200 g/L of the new active constituent, indaziflam. Specticle Herbicide is a suspension concentrate for use on golf course fairway turf for the pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*).

The product is to be applied prior to weed germination at a rate of 250 mL/ha which equates to 50 g ac/ha. The product will be applied in 200–500 mL of water/ha by either ground-boom or hand-held (backpack and hand-wand) application methods and requires activation by rainfall or irrigation within weeks of application. A maximum of two applications per annum may be applied with a minimum re-treatment interval of 3 months.

7.2 Environmental fate and behaviour

Fate and behaviour in soil

Photolysis is not a major route of degradation in soil (DT_{50} 11 days). Indaziflam is slightly to moderately persistent in soil under laboratory conditions (DT_{50} 22–176 days) and under field conditions in the United States (DT_{50} 9.3–71 days). The two stereoisomers showed comparable degradation behaviour in soil. Indaziflam was found to have medium to low mobility in soil (Koc 396–742 L/kg).

Three major metabolites were identified in soil: triazine indanone, carboxylic acid and diaminotriazine (Table 1). Triazine indanone and carboxylic acid were not persistent; however, diaminotriazine is more persistent than its parent indaziflam (DT_{50} 15–320 days). The major metabolites were more mobile than the parent indaziflam (diaminotriazine Koc 10–47 L/kg; triazine-indanone Koc 183–304 L/kg; carboxylic acid Koc 29–132 L/kg).

Fate and behaviour in water

Indaziflam is a weak acid, has low solubility in water (isomer A: 2.8 mg ac/L, isomer B 1.2 mg ac/L), and is stable to hydrolysis. Indaziflam is expected to degrade rapidly by photolysis in clear shallow waters (DT_{50} 1.4 days). Two major metabolites were detected in the photolysis study: hydroxyethyl and olefin. In aquatic systems (water/sediment), indaziflam partitions rapidly from water to sediment where it is persistent (water DT_{50} 2.7–4.8 days; whole system DT_{50} 127–651 days). Two major metabolites were formed in the tested aquatic systems: triazine-indanone and carboxylic acid.

Fate and behaviour in air

On the basis of the vapour pressure (2.5×10^{-8} Pa) and short chemical half-life of indaziflam in air (5.8–17 hours), it is expected that indaziflam will not be transported in the gaseous phase over large distances and will not accumulate in the atmosphere.

7.3 Environmental risk

Risk to terrestrial vertebrates

Indaziflam is considered to be practically non-toxic to terrestrial vertebrates (avian LD_{50} values > 2000 mg ac/kg bw and LC_{50} values > 5000 mg ac/kg diet; rat LD_{50} >5000 mg ac/kg bw). There were no reproductive effects observed in the avian studies at the highest test concentration (NOEC 1000 mg ac/kg feed). A two-generation study on reproduction and fertility in the rat showed indaziflam to cause chronic toxicity effects in the parents and F1 and F2 generations that would impact reproductive capabilities at 317 mg ac/kg bw/day (NOAEL 69 mg ac/kg bw/day). Risks of adverse effects on terrestrial vertebrates following dietary exposure of food items directly treated with two applications of 250 mL product/ha (50 g ac/ha), with a 3–month interval between applications, were determined to be acceptable.

Risk to aquatic species

Indaziflam was not toxic to freshwater & sediment-dwelling invertebrates at the limit of water solubility (isomer A: 2.8 mg ac/L, isomer B 1.2 mg ac/L). However, indaziflam was moderately toxic to saltwater invertebrates (96h EC_{50} and LC_{50} values 1.0–1.5 mg ac/L), highly toxic to fish (96h LC_{50} 0.32–0.77 mg ac/L), and very highly toxic to algae (96h ErC_{50} 0.082–3.9 mg ac/L) and aquatic plants (ErC_{50} 0.073 µg ac/L). As a result, protection statements are required indicating high toxicity to aquatic life.

Early life stage exposure of fish to indaziflam was found to cause a reduction in fry survival at 1.0 mg ac/L (35d NOEC 0.465 mg ac/L). Chronic exposure of *Daphnia magna* to indaziflam caused a reduction in growth at 0.80 mg ac/L (21d NOEC 0.34 mg ac/L).

A bio-concentration study was conducted in fish which indicates that the major residue in all fish tissues was indaziflam. The steady-state BCF for indaziflam based on whole fish is 16 and when normalised to 6% lipid content is 11. These results indicate that indaziflam is unlikely to bio-accumulate in aquatic organisms.

Higher tier microcosm studies were conducted to further assess the toxicity of indaziflam to macrophyte species. The communities present in the microcosms were typical for lentic, shallow macrophyte-dominated freshwater ecosystems. A six-week chronic study with floating and submerged macrophytes exposed to indaziflam in outdoor ponds showed signs of chlorotic leaves and decreased biomass at concentrations of 1 µg ac/L (NOEC 0.32 µg ac/L). A second ten-week outdoor microcosm study conducted with a number of macrophyte species including *Potamogetan* species (in addition to zooplankton, and phytoplankton), showed effects to a number of species at different concentrations. A NOEC of 0.32 µg ac/L was established at which concentration no effects or slight transient effects were reliably observed in the ten-week study.

The key regulatory endpoint for assessing risk to aquatic species was based on the NOEC of 0.32 µg ac/L from the macrophyte microcosms. Risks of spray drift and runoff following two applications of 250 mL product/ha (50 g ac/ha), with a 3–month interval between applications, were determined to be acceptable provided a mandatory no-spray zone of 5 metres is observed. Standard restraints are also required to minimise risk of runoff.

Risk to bees and other non-target arthropods.

Indaziflam is considered to be practically non-toxic to bees (oral and contact LD_{50} values >100 µg ac/bee) and other beneficial (predatory and parasitic) arthropods (glass plate LR_{50} values >1000 g ac/ha, SC formulation). Therefore, risks to bees and other non-target arthropods are considered to be acceptable.

Risk to earthworms and other soil organisms

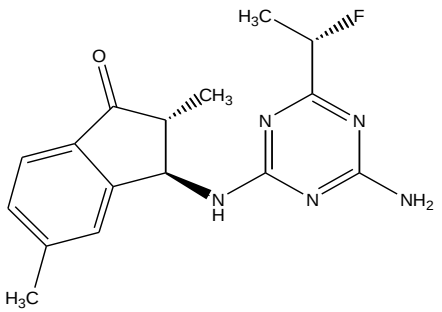
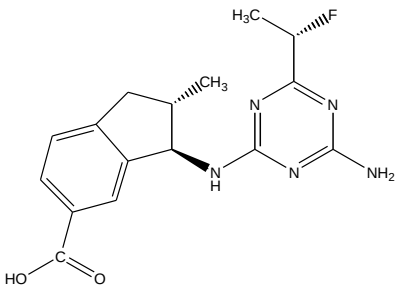
Indaziflam was not acutely toxic to earthworms (14d LC_{50} >1000 mg ac/kg soil). Following chronic exposure to indaziflam, there was a 13% reduction in earthworm offspring at 8900 g ac/ha, equivalent to 12 mg ac/kg soil (56d NOEC 5000 g ac/ha, equivalent to 6.7 mg ac/kg soil). Risks of adverse effects on earthworms following direct exposure to soil treated with two applications of 250 mL product/ha (50 g ac/ha), with a 3–month interval between applications, were determined to be acceptable.

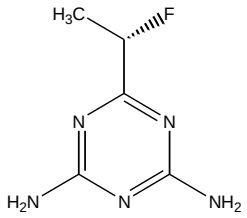
Soil micro-organisms, as measured by carbon mineralisation or nitrogen transformation activities, were not affected by indaziflam at concentrations up to 1.1 mg ac/kg soil (equivalent to 750 g ac/ha). Therefore, risks to soil micro-organisms were also determined to be acceptable.

Risk to non-target terrestrial plants

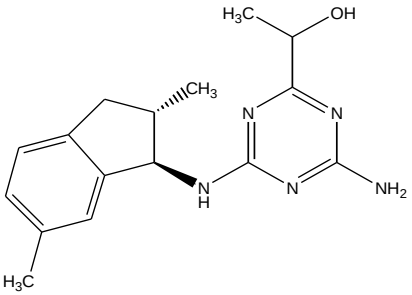
Indaziflam is a herbicide that inhibits seedling emergence and root development by inhibiting cellulose biosynthesis (CB inhibitor as per other herbicides in the triazine family). Therefore, pre-emergent and growing plants are most at risk. Monocots and dicots exhibited similar sensitivity to indaziflam (SC formulation) in vegetative vigour and seedling emergence testing of 12 plant species. Following post-emergent exposure (vegetative vigour tests), the most sensitive endpoint was ER_{50} 3.8 g ac/ha (ryegrass survival) with an HD5 of 5.2 g ac/ha based on a species sensitivity distribution of the ER_{50} values. Following pre-emergent exposure (seedling emergence tests), the most sensitive endpoints were ER_{50} 0.28 g ac/ha (onion growth) and LR_{50} is 0.33 g ac/ha (oilseed rape emergence) with an HD5 of 0.17 g ac/ha. Risks of spray drift following two applications of 250 mL product/ha (50 g ac/ha), with a 3–month interval between applications, were determined to be acceptable provided a mandatory no-spray zone of 25 metres is observed.

TABLE 1 STRUCTURES OF ENVIRONMENTAL METABOLITES

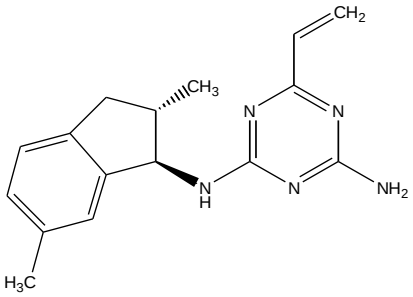
 Triazine-indanone	 Carboxylic acid



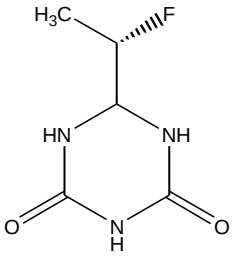
Diaminotriazine



Hydroxyethyl



Olefin



Dihydrotriazine

7.4 Conclusion

The APVMA has considered the available environmental fate and effects data in support of the proposed use and has concluded that the risks to the environment are acceptable.

Indaziflam is slightly to moderately persistent in soil with biodegradation as the major route of dissipation. Photolysis and volatilization are not important routes of dissipation from soil. Indaziflam is moderately mobile in soil and is not expected to leach. Indiziflam can reach aquatic systems by runoff or spray drift. It is stable to hydrolysis but is expected to rapidly photodegrade in clear shallow water. Indaziflam rapidly partitions to sediment where it is persistent.

Indaziflam is not toxic to birds and wild mammals, bees and other beneficial arthropods, or to earthworms and other soil organisms, including micro-organisms. Its toxicity to aquatic invertebrates is limited by its solubility in water; however, Indaziflam is highly toxic to fish and very highly toxic to algae and aquatic plants. A mandatory no-spray zone of 5 metres must be observed for the protection of aquatic systems. Indaziflam is also toxic to non-target terrestrial plants and a mandatory no-spray zone of 25 metres must be observed for the protection of non-target vegetation.

Based on an assessment of the environmental data, it was considered that there should be no unacceptable adverse effects on non-target organisms from the use of Specticle Herbicide.

8 EFFICACY AND SAFETY ASSESSMENT

8.1 Proposed product use pattern

The proposed use of Specticle Herbicide, containing indaziflam at 200 g/L, is for the pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*) in turf on golf course fairways.

The product is to be applied prior to weed germination at a rate of 250 mL/ha which equates to 50 g ac/ha. The product will be applied in 200–500 mL of water/ha by either ground-boom or hand-held (backpack and hand-wand) application methods and requires activation by rainfall or irrigation within weeks of application. A maximum of two applications per annum may be applied with a minimum re-treatment interval of 3 months.

8.2 Assessment of evaluation of efficacy and crop safety

A total of nine efficacy and safety field trials and three turf species/cultivar safety-specific trials conducted over five seasons, in three states, were relied on in support of this application. Submitted trials covered the following areas of efficacy and crop safety:

1. Control of summer grass (*Digitaria sanquinalis*/*ciliaris*) by Specticle Herbicide (6 trials)
2. Control of crowsfoot grass (*Elusine indica*) by Specticle Herbicide (2 trials)
3. Control of winter grass (*Poa annua*) by Specticle Herbicide (3 trials)
4. Tolerance of warm season turf grasses to Specticle Herbicide (3 trials)

Two trials were conducted in Western Australia, eight in New South Wales and two in Queensland in the period 2005 to 2009 inclusive.

All trials were conducted under field conditions in turf amenity situations or research station turf field environments under mostly commercial cultural and management practices. In this respect, the soil types, seasonal conditions and treatment application conditions reflected anticipated commercial conditions.

Trials were all small plot replicated trials, mostly as randomized complete blocks and compared Specticle Herbicide with appropriate industry standard herbicides and un-treated controls. All treatments were applied pre-emergent to the weeds and watered in by irrigation. In the combined efficacy and safety trials Specticle Herbicide was applied at rates between 187.5 (1.5 x label rate to 1000 mL/ha (4 x label rate), with rates of 250 (1 x label rate), 500 (2 x label rate) and 750 (3 x label rate) mL/ha common across most trials. In two of the dedicated turf tolerance (safety) trials, Specticle Herbicide was applied at a single rate of 1000 mL/ha (4 x label rate) and at 375 mL/ha (1.5 x label rate) and 750 mL/ha (3 x label rate) in the third.

Seven of the efficacy trials were conducted on couch (*Cynodon dactylon*) turf, one on a couch/kikuyu mix and one on pure kikuyu (*Pennisetum clandestinum*). Between fifteen to twenty-eight turf grass cultivars were evaluated for safety including Cynodon, Axonopus, Bothriochloa, Digitaria, Paspalum, Pennisetum Sporobolus, Stenotaphrum, Eremochloa, and Zoysia species.

Trials assessing weed control efficacy used a rating scale of 0 to 10, with assessments based on either an estimate of weed cover on a whole plot basis or the percentage control of a weed relative to the untreated control, based on weed counts or visual assessment of the plots. Assessments were conducted at varying intervals between trials and the various weeds and ranged from 27 days after treatment (DAT) to 163 DAT.

In the turf safety assessment trials, phytotoxicity to turf species was assessed at intervals from 2 to 60 DA and a combination of visual assessment and a turf colour meter were used to indicate discolouration and damage.

Summer Grass trials

Six trials evaluated the efficacy of indaziflam for the control of summer grass (*Digitaria* spp) in couch/kikuyu turf over a five year period in NSW and Western Australia. Trials results demonstrated the reliable control of summer grass by Specticle Herbicide at rates of 200–500 L/ha. The level of control achieved by Specticle Herbicide was equivalent to, or superior than, the commercial industry standards tested. One of the trials indicated temporary discolouration and growth retardation to the couch/kikuyu turf. This was believed to be due to the turf being in poor condition at the commencement of the trial due to heavy winter wear and tear.

Crowsfoot Grass trials

Two trials evaluated the efficacy of Specticle Herbicide for the control of crowsfoot grass (*Eleusine indica*) in turf. In both trials, 100% control was achieved at rates down to either 200 mL/ha or 250 mL/ha (equivalent to the industry standard). No phytotoxicity effects were observed in either trial.

Winter Grass trails

Winter grass (*Poa annua*) control was evaluated in three trials, one of which evaluated a single rate of Specticle Herbicide (375 mL/ha) at monthly intervals between February and August inclusive. In this trial all application timings proved effective. In the other two trials, at rates down to 200 mL/ha, Specticle Herbicide achieved good weed control (up to 100%) equivalent to the industry standard. No phytotoxicity effects were observed in any of the trials.

Crop Safety/Turf variety tolerance trials

Of the three large scale dedicated turf tolerance trials conducted in NSW (1) and Queensland (2), no phytotoxic effects of Specticle Herbicide at the rates of 350 mL (1.5 x label rate) and 750 m L/ha (3 x label rate) were reported in the NSW trial. One of the trials conducted in S.E. Queensland reported increasing damage, up to the final assessment at 60 DAT at the application rate of 1000mL/ha (4 x label rate). Explanation for the damage was attributed to the cool growing conditions during the assessment period. In a similar trial conducted at the same site in 2009, and undertaken earlier in the year, did not record any significant phytotoxicity at 30 days after treatment application. While some discolouration of several grass species was observed the level of damage was minimal.

8.3 Crop safety

In all trials where Specticle Herbicide was applied at the recommended label rate and at rates up to 750 mL (i.e. 3 x label rate), no adverse symptoms were reported in any of the turf varieties tested.

The information and data presented indicate that Specticle Herbicide is safe to use on warm season turf grass when used as directed.

8.4 Resistance management

Indaziflam is a member of the alkylazine class of pesticides. The Herbicide Resistance Management Action Committee (a specialist technical group of CropLife International) has classified indaziflam as having the target site of cellulose synthesis in cell wall biosynthesis (i.e. it acts by inhibiting seed growth prior to germination and during root development). CropLife Australia's Herbicide Resistance Management Review Group (HRMRG) has advised that indaziflam will be classified as a Group O Herbicide (inhibition of cell wall (cellulose) synthesis).

8.5 Conclusion

The claims on the proposed label that Specticle Herbicide provides acceptable pre-emergent control of Summer grass (*Digitaria* spp), Crowsfoot grass (*Eleusine indica*) and Winter grass (*Poa annua*) in turf on golf course fairways when used as directed is supported by the results from the Australian trials.

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

The application by BayerCrop Science Pty Ltd for the registration of Specticle Herbicide is supported on efficacy and crop safety grounds when used in accordance with label instructions.

9 LABELLING REQUIREMENTS

POISON

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

Specticle®

HERBICIDE

ACTIVE CONSTITUENT:
200 g/L INDAZIFLAM

GROUP O HERBICIDE

For pre-emergent control of summer grass, crowsfoot grass and winter grass in turf on golf course fairways

1 to 20 L

DIRECTIONS FOR USE

RESTRAINTS

DO NOT apply to turf under stress
DO NOT apply with aircraft.
DO NOT apply with a nozzle height greater than 50cm above the ground.
DO NOT apply through any type of irrigation equipment.
DO NOT apply if heavy rain has been forecast within 48 hours.
DO NOT apply to waterlogged soil.
DO NOT irrigate turf to the point of run-off within 48 hours of application.

SPRAY DRIFT RESTRAINTS
DO NOT apply with spray droplets smaller than a **COARSE** spray droplet size category according to *"APVMA Compliance Instructions for Mandatory COARSE or Larger Droplet Size Categories"* located under this title in the GENERAL INSTRUCTIONS section of this label.

DO NOT apply when wind speed is less than 3 or more than 20 km 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 paddocks/areas sprayed;
3. full name of this product;
4. amount of product used per hectare and number of hectares treated;
5. crop/situation and weed;
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 **25 metres** downwind from the application area.

DO NOT apply if there are aquatic or wetland areas including aquacultural ponds, surface streams and rivers within **5 metres** downwind from the application area.

DIRECTIONS FOR USE

SITUATION	WEEDS CONTROLLED	RATE	CRITICAL COMMENTS
TURF -golf course fairways only Warm season turf grasses only, including: Bahia grass (*Paspalum notatum*); Buffalo grass (*Stenotaphrum secundatum*); Common couch (*Cynodon dactylon*) and Hybrid couches; Queensland Blue Couch (*Digitaria didactyla*); Kikuyu (*Pennisetum clandestinum*); Zoysia (*Zoysia* spp.)	Summer grass or Crab grass (*Digitaria* spp.) Crowsfoot grass (*Eleusine indica*) Winter grass *(Poa annua)*	250 mL/ha in 200 to 500 L water per ha	Turf should be in robust and healthy condition at the time of treatment. Apply prior to germination of the weeds. Ensure adequate coverage for optimum weed control. A repeat application may be required after not less than three months. Do not apply more than two applications per annum. Refer to the Application section in the General Instructions for detailed information.

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

GENERAL INSTRUCTIONS

SPECTICLE is a selective, pre-emergent herbicide that provides residual control of certain grass weeds on established warm-season turf on golf course fairways. Specticle controls weeds by reducing the emergence of seedlings through inhibition of cellulose biosynthesis (CB inhibitor). Specticle needs to be activated prior to weed germination for most effective control. For maximum activity against germinating weeds, Specticle requires rainfall or irrigation prior to weed germination.

MIXING

Ensure that the spray tank is completely clean prior to mixing. Half fill the spray tank with water, then with agitators in motion, add the correct amount of Specticle directly into the spray tank. Complete filling the tank with agitators in motion. Agitation must continue before and during spraying.

APPLICATION

Ensure spraying equipment is properly calibrated before use. Uniform application is essential for satisfactory weed control. Ensure that complete and even spray coverage is achieved. DO NOT overlap sprayed areas.

APVMA Compliance Instructions for Mandatory COARSE or Larger Droplet Size Categories

Important Information: These instructions inform users of this chemical product how to lawfully comply with the requirement of a COARSE or larger spray droplet size category for spray application. Spray droplet size categories are defined in the ASAE S572 Standard (newer name may also be shown as ASABE) or the BCPC guideline. Nozzle manufacturers may refer to one or both to identify droplet size categories, but for a nozzle to comply with this requirement, the manufacturer must refer to at least one.

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

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

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

SPRAYER CLEAN UP

The sprayer must be thoroughly decontaminated before being used again to spray susceptible plants or turf. Ensure that the following operation is carried out in an area that is clear of waterways, desirable vegetation and tree roots, and preferably in an area where drainings can be contained.

1. Drain sprayer completely and wash out tank, boom and hoses with clean water.
2. Drain again.
3. Fill the tank with clean water and add 300 mL of chlorine bleach (containing 4% chlorine) per 100 L of water with agitation running.
4. Flush some bleach solution through booms and hoses and allow remainder to agitate in tank for 10 minutes.
5. Remove nozzles and filters and leave to soak in a bleach solution of 500 mL per 10 L of water while tank cleaning is in progress.
6. Briefly run the pump at periodic intervals to refresh chlorine solution in spray lines.
7. Drain tank and repeat the procedure of flushing with bleach solution.
8. Flush the tank, boom and hoses with clean water.

USE OF SPECTICLE ON TURF IN COARSE AND SANDY SOILS: Soil conditions can affect the tolerance of turf to Specticle. Coarse or sandy soils may allow for downward movement of Specticle into the root zone and cause significant damage and phytotoxicity. Prior to application of Specticle in coarse or sandy soils, confirm texture with a soil test. Turf grown in soil exceeding 80% sand or 20% gravel may be at risk. If Specticle is to be applied on these soils, evaluate treated soils for tolerance prior to large scale application.

IRRIGATION AND WATERING AFTER APPLICATION: Specticle will provide residual weed control when adequate moisture is present and the application is followed by rain or irrigation (3 to 6 mm) within 21 days and prior to weed seed germination. DO NOT create conditions that cause visible run-off of irrigation water. Adequate rainfall following an application will negate the need for irrigation.

APPLICATION NEAR SENSITIVE GRASSES: Specticle can cause turf injury and stand reduction to sensitive grasses. Specticle may affect sensitive grasses downslope from treated areas after excessive rainfall. To minimize off-target effects of Specticle on sensitive grasses, irrigate after application as directed in the IRRIGATION AND WATERING AFTER APPLICATION section of this label and observe the MANDATORY No-Spray zones. Allow turf to dry before allowing foot traffic or equipment through treated areas near sensitive grasses. DO NOT apply Specticle on uphill slopes and adjacent to greens overseeded with cool season grasses. DO NOT apply Specticle to annual and perennial ryegrass or to couchgrass overseeded with ryegrass. Specticle may be applied in situations where warm season grasses such as couchgrass are adjacent to sensitive cool season grasses. The applicator, however, must take care not to apply Specticle directly to sensitive grasses or injury may occur. Application of Specticle may be made adjacent to sensitive cool season grasses if the grass is established for at least 16 months.

DEACTIVATING SPECTICLE: Activated charcoal has been shown to deactivate Specticle if applied within several days of application. Application of activated charcoal within 2 weeks of an application of Specticle will not reverse phytotoxic symptoms immediately but it will aid in recovery over time. If it should be necessary to re-sod areas treated with Specticle, remove damaged turf to a depth of at least 5 cm, cultivate the soil and apply activated charcoal to bare ground prior to laying sod. Follow directions for the amount of charcoal to apply on the label of the activated charcoal.

SEEDING, RE-SEEDING AND OVERSEEDING: Timing of seeding, re-seeding, overseeding, sprigging and sodding turf relative to an application of Specticle needs to be monitored carefully. Specticle can inhibit root development as well as the emergence of seed. Roots of newly emerged seedlings may be damaged and establishment of sod may be affected if Specticle is applied to turf that is not well established.

APPLICATION OF SPECTICLE PRIOR TO OVERSEEDING COUCHGRASS WITH PERENNIAL RYEGRASS OR RESEEDING INTO WARM-SEASON TURF: Specticle may be used to control weeds in couchgrass prior to overseeding with a cool season grass or re-seeding seeded cultivars of couchgrass, provided that the interval between application and seeding is appropriate. The minimum interval between application of Specticle and seeding or overseeding is 12 months. Applications made sooner than the minimum interval may decrease the establishment of the new seedlings and reduce turf coverage.

WARM-SEASON GRASSES ESTABLISHED WITH SPRIGS: Specticle may be applied to sprigs of warm season grasses. The sprigs need to be well rooted prior to application. Apply Specticle no sooner than 16 months after sprigging to allow for good stand establishment. Prior to application, check rooting to make sure new roots are developing. If roots are not growing, delay application of Specticle.

SODDING WARM SEASON GRASSES: Delay sodding into bare ground or turf treated with Specticle until 6 months after application. Sodding before 6 months may inhibit stand establishment and reduce turf quality. For maximum establishment of sod, follow the directions for use for deactivation of Specticle using activated charcoal. Sod needs to be actively growing / established at least 3 months prior to an application of Specticle. Prior to application, check the turfgrass sod to make sure new roots are developing. If roots are not growing, delay application of Specticle.

HERBICIDE RESISTANCE WARNING

GROUP	O	HERBICIDE

SPECTICLE Herbicide is a member of the O group of herbicides (alkylazines) and has the inhibitor of cell wall [cellulose] synthesis mode of action. For weed resistance management SPECTICLE is a Group O herbicide. Some naturally-occurring weed biotypes resistant to SPECTICLE, and other Group O herbicides, may exist through normal genetic variability in any weed population. These resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by SPECTICLE or other Group O herbicides. DO NOT rely exclusively on SPECTICLE for weed control. Use as part of an integrated weed management program involving herbicides with other modes of action and non-chemical methods of control. Since occurrence of resistant weeds is difficult to detect prior to use Bayer CropScience Pty Ltd accepts no liability for any losses that may result from the failure of SPECTICLE to control resistant weeds.

COMPATIBILITY

As formulations of other manufacturers' products are beyond the control of Bayer and water quality varies with location, any mixture should be tested prior to mixing commercial quantities.

PRECAUTIONS

DO NOT use on golf greens, tees or collars.

DO NOT use on turf:

- exhibiting injury from previous applications of other products;
- stressed under cool or cold growing season conditions.
- which is not well established (turf is defined as established at least 16 months after seeding or sprigging);
- which is newly seeded, sodded or sprigged;
- recovering from wear, scarification, aeration or coring.

INTEGRATED PEST MANAGEMENT

The possible effects of this product on integrated pest management (IPM) strategies in the turf industry have not been studied at the proposed rates.

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 LIVESTOCK

DO NOT graze treated turf or feed turf clippings from any treated area to poultry or livestock.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

DO NOT apply under weather conditions, or from spraying equipment, that may cause spray to drift onto nearby susceptible plants/crops, cropping lands or pastures. DO NOT use clippings from treated areas for mulch around vegetables or fruit trees.

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Triple-rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and deliver empty packaging to an approved waste management facility. If an approved waste management facility is not available, bury the empty packaging 500 mm below the surface in a disposal pit specifically marked and set up for this purpose, clear of waterways, desirable vegetation and tree roots, in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product. DO NOT re-use empty container for any other purpose.

SAFETY DIRECTIONS

May irritate the eyes. Avoid contact with eyes. When opening the container, mixing and loading and using the prepared spray, wear cotton overalls buttoned to the neck (or equivalent clothing). If applying by equipment carried on the back of the user wear cotton overalls, over normal clothing, buttoned to the neck and wrists and elbow-length chemical resistant gloves. Wash hands after use. After each day's use, wash gloves and contaminated clothing.

FIRST AID

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

SAFETY DATA SHEET

Additional information is listed in the Safety Data Sheet which may be found at www.environmentalscience.bayer.com.au.

EXCLUSION OF LIABILITY

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

APVMA Approval No.: 64673 / 48927

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FOR 24 HOUR SPECIALIST
ADVICE
IN EMERGENCY ONLY
PHONE 1800 033 111

Bayer CropScience Pty Ltd
ABN 87 000 226 022
391-393 Tooronga Rd
Hawthorn East, Vic. 3123
Phone: (03) 9248 6888
Technical enquiries: 1800 804 479
Website: www.environmentalscience.bayer.com.au

Batch Number:
Date of Manufacture:

ABBREVIATIONS

ac	active constituent
ACN	Acetonitrile
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ANOVA	Analysis of variance
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
BCF	Bio-concentration Factor
BrdU	Bromodeoxyuridine
bw	bodyweight
oC	Degrees Centigrade
14C	Carbon 14
Cd-1	Cluster of differentiation 1
d	Day(s)
cm	Centimetre
DAT	Days After Treatment
DT50	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
EbC50	concentration at which the biomass of 50% of the test population is impacted
EC50	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
ErC50	concentration at which the rate of growth of 50% of the test population is impacted
EL50	Effective Loading rate lethal to 50% of the test population
EI	Export Interval

EGI	Export Grazing Interval
ERC50	Median effect concentration based on growth rate
ER50	Median effective rate
ESI	Export Slaughter Interval
EUP	End Use Product
Fo	original parent generation
FOB	Functional Observational Battery
F1	First Generation
F2	Second generation
F2b	Second generation backcross
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GPMT	Guinea Pig Maximisation Test
GVP	Good Veterinary Practice
h	Hour(s)
ha	Hectare(s)
HCl	Hydrogen chloride
Hct	Heamatocrit
HD5	Hazardous dose giving 50% effect to 5% of the species
HDPE	High Density Polyethylene
Hg	Haemoglobin
HR	Highest residue
HPLC	High Pressure Liquid Chromatography or High Performance Liquid Chromatography
IARC	International Agency for Research on Cancer
id	intradermal

im	intramuscular
Pa	Pascal(s)
pH	Potential of hydrogen.
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
Koc	Organic carbon partitioning coefficient
L	Litre(s)
LC50	concentration that kills 50% of the test population of organisms
LD50	dosage of chemical that kills 50% of the test population of organisms
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observable Adverse Effect Level
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
LR50	Lethal rate required to kill half (50%) of the test population
MgSO4	Magnesium Sulphate
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
NESTI	National Estimated Short Term Intake
ng	nanogram

NHMRC	National Health and Medical Research Council
NaCl	Sodium Chloride
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
STMR	Supervised Trials Medium Residues
STMR-P	STMR corrected for processing
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product
Acute	Having rapid onset and of short duration.
Ames Test	A biological assay to determine the mutagenic potential of chemical compounds
ANOVA	Analysis of Variance (ANOVA) is a statistical model used to test differences between group means.
Bio-concentration Factor (BCF)	The concentration of a contaminant in an organism compared to the surrounding ambient environment
Back Cross	Crossing a hybrid with one of its parents (or a genetically similar individual) to produce offspring with genetic identities which are closer to that of the parent
Clara Cells	The Clara cells are a group of cells, sometimes called "non-ciliated bronchiolar secretory cells", found in the bronchiolar epithelium of mammals including man, and in the upper airways of some species such as mice. One of their main functions is to protect the bronchiolar epithelium
Carcinogenicity	The ability to cause cancer
CD1 Mice	A laboratory strain of outbred mice used extensively in toxicological and chemical carcinogenicity bioassys
Central Tendency	In statistics, a central tendency is a central or typical value for probability distribution
Chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
Chronic	Of long duration
Desorption	Removal of a material from or through a surface
Efficacy	Production of the desired effect
Eukaryote	Any organism having as its fundamental structural unit a cell type that contains a nucleus and other organelles enclosed within membranes.
Fischer's LSD	Statistical method to calculate the smallest significant difference between two means
Formulation	A combination of both active and inactive constituents to form the end use product
Functional Observational Battery (FOB)	A neuro-behavioural assessment tool designed to detect gross functional deficits in young adult rats resulting from exposure to
Formulation	A combination of both active and inactive constituents to form the end use product
Filial 1 (F1)	The first filial generation of offspring of distinctly different parental types that have a combination of characteristics from both parents.

Genotoxicity	The ability to damage genetic material
Guinea Pig Maximisation Test (GPMT)	Is an in vivo test to screen for substances that cause human skin sensitisation (i.e. allergens)
Hematocyst	A blood-containing cyst that develops abnormally in a body structure
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
Mean	In statistics, mean refers to the mean or average that is used to derive the central tendency of the data in question. It is determined by adding all the data points in a population and then dividing the total number by the number of points.
Metabolism	The chemical processes that maintain living organisms
Micronucleus Test	A test used in toxicological screening to determine a chemicals ability to induce numerical or structural chromosomal damage
Oomycetes Fungi	Fungus-like, eukaryotic micro-organisms. Formerly classified as fungi due to their filamentous bodies, nutrition by absorption and reproduction via spores, they are more closely related to algae and green plants.
pH	A figure expressing the acidity or alkalinity of a solution on a logarithmic scale on which 7 is neutral, lower values are more acid and higher values more alkaline. The pH is equal –log10 [H+] where [H+] is the hydrogen ion concentration in moles per litre
Phenochromocytoma	A rare tumour of adrenal gland tissue. It results in the release of too much epinephrine and norepinephrine, hormones that control heart rate, metabolisms and blood pressure.
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