Australian Pesticides & Veterinary Medicines Authority

EVALUATION OF THE NEW ACTIVE

PINOXADEN

IN THE PRODUCT

AXIAL 100EC SELECTIVE HERBICIDE

Public Release Summary

Australian Pesticides & Veterinary Medicines Authority
Canberra, Australia

May 2006

ISSN1443–1335

Published by the Australian Pesticides and Veterinary Medicines Authority

PO Box E240
KINGSTON ACT 2604
AUSTRALIA

FOREWORD

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is an independent statutory authority 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), the Department of the Environment and Heritage (Chemical Assessment Section) and state departments of agriculture and environment.

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 all products containing new active ingredients and for all proposed extensions of use for existing products.

The information and technical data required by the APVMA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the APVMA's publication the *Manual of Requirements and Guidelines for agricultural applications* (Ag MORAG).

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

More detailed technical assessment reports on all aspects of this chemical's evaluation can be obtained by mail order. Simply complete the order form in the back of this publication and send it with payment to the APVMA. Alternatively, the reports can be viewed at the APVMA Library First Floor, 22 Brisbane Avenue, Barton, ACT.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to:

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	acceptable daily intake (for humans)
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft
bw	bodyweight
d	day
DAT	days after treatment
DT50	time taken for 50 per cent of the concentration to dissipate
EbC50	concentration at which the biomass of 50 per cent of the test population is impacted
EC50	concentration at which 50 per cent of the test population are immobilised
EEC	estimated environmental concentration
ErC50	concentration at which the rate of growth of 50 per cent of the test population is impacted
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
kg	kilogram
Koc	organic carbon partitioning coefficient
L	litre
LC50	concentration that kills 50 per cent of the test population of organisms
LD50	dosage of chemical that kills 50 per cent 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
mg	milligram
mL	millilitre
MRL	maximum residue limit
MSDS	material safety data sheet
NDPSC	National Drugs and Poisons Schedule Committee
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	suspensionc
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
g	microgram
vmd	volume median diameter
WG	water dispersible granule
WHP	withholding period

INTRODUCTION

This publication provides a summary of data reviewed and an outline of the regulatory considerations for the proposed registration of Axial100EC Selective Herbicide as a foliar spray to wheat and barley for the control of annual ryegrass, Paradoxa, wild oats and canary grasses. The active constituents of the product are pinoxaden and cloquintocet-mexyl, which have been approved by the APVMA. The APVMA also seeks public comment prior to the chemical product being registered for use in Australia.

Responses to public consultation will be considered prior to registration of the product detailed in this document. They 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.

Copies of the full technical reports on public health, occupational health and safety, environmental impact and residues in food are available upon request.

Written comments should be received by the APVMA by **30 April 2006** and should be addressed to:

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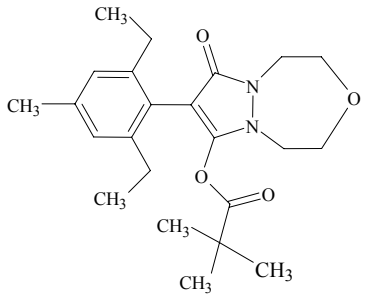
CHEMISTRY AND MANUFACTURE

Chemistry of the active constituent

Chemical name IUPAC	8-(2,6-diethyl-p-tolyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropionate
ISO common name	pinoxaden
CAS registry numbers	243973-20-8 (pinoxaden) 99607-70-2 (cloquintocet-mexyl)
Empirical formula	C23H32N2O4
Molecular weight	400.5
Manufacturer's code	NOA 407855
Structural formula	



Axial 100EC Selective Herbicide contains two active constituents: **pinoxaden**, which will be manufactured by:

- Syngenta Crop Protection Munchwilen AG, Breitenloch 180, CH-4333 Munchwilen, Switzerland (AC approval No. 59021);

and **cloquintocet-mexyl**, which will be manufactured by either:

- Syngenta Crop Protection AG, Schwarzwaldallee 215, CH-4002 Basel, Switzerland (AC approval No. 48478); or

- Syngenta Crop Protection Monthey AG, Usine de Monthey, CH-1870 Monthey, Switzerland (AC approval No. 46336).

Chemistry of the product

Name	Axial 100 EC Selective Herbicide
Formulation type	emulsifiable concentrate
Concentration of active constituents	100 g/L pinoxaden and 25 g/L cloquintocet-mexyl

Use pattern of the product

Manufacture and packaging

The finished product will be manufactured and packaged overseas. The product will be packaged in one litre (neck size of 45 mm) and five litre (neck size of 63 mm) fluorinated high-density polyethylene (HDPE) bottles.

End use pattern

Axial 100 EC Selective Herbicide is a Group A emulsifiable concentrate herbicide containing 100 g/L technical pinoxaden, 25 g/L cloquintocet-mexyl and 559 g/L liquid hydrocarbons, and is proposed for the post-emergence control of grass weeds in wheat and barley. The product may be applied by air or ground equipment at an application rate of 0.15–0.3 L/ha. The spray volume is 50–110 L/ha and 20–30 L/ha for ground and aerial application, respectively. According to the draft label, a 10-week withholding period is required before harvest.

Formulated product

The following specifications for registration were provided for Axial 100 EC Selective Herbicide:

Parameter	Required range
appearance	yellow to orange liquid
pinoxaden content	90–110 g/L (90–110 % label claim)
cloquintocet-mexyl content	21–29 g/L (84–116 % label claim)*
pH (1% in deionised water)	3–7
density (g/mL, at 20 °C)	1.01–1.05 g/mL
emulsion stability 1.2% in CIPAC Water A; 30°C; 2 h 1.2% in CIPAC Water D; 30°C; 2 h	 max. 2 mL cream and/or oil and/or sediment max. 2 mL cream and/or oil and/or sediment
persistent foaming 1.2 % in CIPAC water; 1 min	max. 60 mL

* The APVMA's maximum allowable tolerance is ± 15 per cent (i.e. 21.25–28.75 g/L), this specification is just outside this range by virtue of rounding, this is acceptable.

Recommendation

The Chemistry and Residues program (CRP) has evaluated the chemistry and manufacturing aspects of Axial100 EC Selective Herbicide and is satisfied that the data provided support the application of registration. CRP is satisfied that the chemistry requirements of Section 14 (5) of the Agricultural and Veterinary Codes have been met.

TOXICOLOGICAL ASSESSMENT

Evaluation of toxicology

The toxicological database for pinoxaden, which consists primarily of toxicity tests conducted using animals, is quite extensive. 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. Such dose levels as the No Observable Effect Level (NOEL) 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.

Kinetic/metabolism studies

Following oral gavage administration in rats and rabbits, pinoxaden was almost completely absorbed from the gastrointestinal tract and quickly appeared in the blood. Kidney and liver contained the highest amounts of residual activity and there was no evidence of radioactivity accumulation in tissues after multiple doses. Similar to rats, pinoxaden was excreted mainly via the urine (approximately 90 per cent), and to a lesser extent faeces (less than 10 per cent), within 48 hours in rabbits. In mice, rats and rabbits, the primary route of metabolism consisted of cleavage of the dimethyl propionate group from pinoxaden at the ester linkage, with the residual pinoxaden moiety constituting approximately 90 per cent of radiolabel excreted in urine. The next most significant metabolite was derived from the residual pinoxaden moiety by hydroxylation at the 4-methyl group of the phenyl moiety.

Five days following a six-hour exposure period in rats with pinoxaden at 400 $\mu g/cm^2$ or at 6 $\mu g/cm^2$, in vivo dermal absorption was 20 per cent and eight per cent of the dose for the two preparations, respectively. Absorption was essentially complete by 24 hours after application. In vitro, total absorption after 24-hours exposure was significantly lower in human than in rat skin membranes with total dermal absorption in human skin of 8.58 per cent for 400 $\mu g/cm^2$, and 4.8 per cent for six $\mu g/cm^2$; and for rats 47 and 46 per cent of the administered dose for the two preparations respectively.

For human risk assessment, the rat in vivo dermal absorption factors were adjusted by the ratio of the absorption rates in human and rat skin in vitro. As the proportion of pinoxaden absorbed across the skin did not appear to be dependent on the concentration applied (within the range of six to 400 $\mu g/cm^2$), using the maximum absorption across human skin rounded up to nine per cent and the rat skin absorption factor of 46 per cent

gives an adjustment factor of 0.2. Applying the correction factor of 0.2 gives a human risk assessment factor of four per cent for high concentration exposures and two per cent for low concentration exposures.

Acute studies

Pinoxaden had low acute oral toxicity in rats, with a LD50 of greater than 5000 mg/kg (one death). In rats it also had low dermal toxicity of LD50 greater than 2000 mg/kg (no deaths) and a low inhalation toxicity of LC50 greater than 5220 mg/m^3 (no deaths). It was a severe eye irritant but did not cause skin irritation in rabbits and was not a skin sensitiser in guinea pigs.

Axial 100 EC Selective Herbicide had low acute oral toxicity in rats, with a LD50 of 3129 mg/kg (four deaths). It had low dermal toxicity LD50 greater than 2000 mg/kg (no deaths) and inhalation toxicity in rats LC50 greater than 5000 mg/m^3. It was a moderate eye and skin irritant in rabbits and was not a skin sensitiser in guinea pigs.

Short term studies

Rats received daily dermal applications of 0, 10, 100 or 1000 mg/kg of bw pinoxaden for six hours daily for 28 days. There were no treatment-related effects observed.

Rats were dosed by oral gavage with pinoxaden at 0, 300, 600 or 1000 mg/kg bw/d for 28 days. At 1000 mg/kg bw/d, body weight gain was reduced in males without changes to food consumption. Higher neutrophil and lymphocyte counts were observed in males at 1000 mg/kg bw/d. At a dosage rate of 600 mg/kg bw/d and above, plasma urea and creatinine levels were increased in males, while increased inorganic phosphate and decreased chloride levels were seen in both sexes. Increased bilirubin levels were observed in males at 1000 mg/kg bw/d. Urinary volume and ketones levels were increased in both sexes at 600 mg/kg bw/d and above. Higher kidney and liver weights were observed in both sexes at 600 mg/kg bw/d and above. Increased incidence and severity of renal tubular atrophy and dilatation at 600 mg/kg bw/d was seen in both sexes. Single cell necrosis was also observed in three quarters of males at 1000 mg/kg bw/d, but not in females. The NOEL was 300 mg/kg bw/d.

In a dose range finding study, two dogs were treated orally with pinoxaden at various concentrations ranging from 125–500 mg/kg bw/d for up to 36 days. Lower food consumption and vomiting were observed at 325, 400 and 500 mg/kg bw/d. At 250 mg/kg bw/d, no clinical signs were seen in either animal.

Dogs were dosed with pinoxaden in gelatine capsules at 0, 250, 500 or 1000 mg/kg bw/d for 28 days. The only notable observation was a high incidence of vomit and food regurgitation at the dosage rate of 500 and 1000 mg/kg bw/d. The NOEL was 1000 mg/kg bw/d, which was the highest dose tested.

Dogs received pinoxaden orally at 0, 25, 100 or 250 mg/kg bw/d for 28 days. There were no treatment-related effects observed other than loose stools in animals at 100 and 250 mg/kg bw/d.

Subchronic studies

In a dose range finding study, mice received pinoxaden orally by gavage at 0, 10, 100, 400, 700 or 1000 mg/kg bw/d for 13 weeks. A slight anaemia was seen in females at

400 mg/kg bw/d and above. Platelet counts were significantly increased at 1000 mg/kg bw/d in females. Increases in liver weights were observed in both sexes at 400 mg/kg bw/d and above, but liver histology was not affected. Microscopic examinations revealed a high incidence and grading of tubular basophilia at 700 mg/kg bw/d and above in males. The NOEL was 100 mg/kg bw/d for both sexes based on mild anaemia in females, increased liver weights in both sexes at 400 mg/kg bw/d and above and on an increased incidence of tubular basophilia in males at 700 mg/kg bw/d and above.

Rats received pinoxaden orally by gavage at 0, 3, 10, 30, 100 or 300 mg/kg bw/d for 13 weeks. Both sexes had elevated serum inorganic phosphate at 30 mg/kg bw/d and above, creatinine and urea at 300 mg/kg bw/d, ketones in urine at 100 and 300 mg/kg bw/d, urine volume at 300 mg/kg bw/d and acidity at 100 and 300 mg/kg bw/d. Serum levels of chloride were decreased at 100 and 300 mg/kg bw/d. Liver weights were increased at 300 mg/kg bw/d in both sexes. The NOEL was 10 mg/kg bw/d for both sexes based on increased levels of inorganic phosphate at 30 mg/kg bw/d and on changes in serum chemistry, urinalysis and liver weights at higher doses.

Rats were dosed with pinoxaden at 0, 150, 1000, 5000 or 10000 ppm in the diet for four weeks for the satellite group and for three months for the main group. At 10000 ppm, decreased RBC counts, haemoglobin concentration and haematocrit were observed in females of the main group. At 5000 and 10000 ppm, serum creatinine levels were increased in males of the satellite group and in females of the main group. Total cholesterol levels were lower at 10000 ppm in both sexes of the satellite group and at 5000 ppm and above in the main group. Females of the main group had lower urinary volume and pH at 10000 ppm. Increased incidences of mild cortical basophilia with tubular dilation and/or atrophy were noted in both sexes at 10000 ppm. The NOEL was 1000 ppm (approximately 100 mg/kg bw/d).

Dogs were dosed with pinoxaden in gelatine capsules at 0, 25, 100, 250 or 500 mg/kg bw/d for 90 days. All females treated with 500 mg/kg bw/d were terminated at week five due to excessive loss of bodyweight. Reduced bodyweight gains with a slight reduction in food consumption were observed in females at 250 mg/kg bw/d. Total serum protein was lower in males at 500 mg/kg bw/d throughout the study and in females at 250 mg/kg bw/d at week 13. The NOEL was 100 mg/kg bw/d.

Chronic studies

Mice

Mice were dosed by oral gavage with pinoxaden at 0, 5, 40, 300 or 750 mg/kg bw/d for 18 months. Bodyweight gains were reduced in both sexes at 750 mg/kg bw/d and in females at 300 mg/kg bw/d without changes to food consumption. Increased platelet counts were seen in males at 300 and 750 mg/kg bw/d. Increased relative liver weights were observed in both sexes at 300 mg/kg bw/d and above, while relative kidney weights were increased in females at 750 mg/kg bw/d. Increased incidences of foamy outflow from the bronchi were observed in both sexes at 300 mg/kg bw/d and above. At 300 and 700 mg/kg bw/d, higher incidences of epithelial thickening in the small intestine and lower incidences of cytoplasmic vacuolation in the epididymides were observed in males at 300 and 700 mg/kg bw/d. The incidences and nature of tumours were comparable across all treated and control groups. The NOEL was 40 mg/kg bw/d.

Rats

In a chronic toxicity and carcinogenic study, rats received pinoxaden orally by gavage at 0, 1, 10, 100, 250 or 500 mg/kg bw/d for 105 weeks. Mortality rates were high in males at 500 mg/kg bw/d during the first year and this group was terminated in week 61. Bodyweight gains were significantly reduced at 500 mg/kg bw/d, and to a lesser extent at 250 mg/kg bw/d in both sexes during the first 52 weeks of the study. At weeks 27 and 53, both sexes had a slight anaemia at 250 and 500 mg/kg bw/d, elevated serum urea and creatinine and decreased serum sodium and chloride at 500 mg/kg bw/d. Increased serum inorganic phosphate was observed at 100 mg/kg bw/d and above in both sexes at weeks 53 and 79. Serum potassium was higher at 250 and 500 mg/kg bw/d in males and at 100 mg/kg bw/d and above in females at week 53, while ketones in urine were higher in males at 250 and 500 mg/kg bw/d at week 27 only and in females throughout the course of the study. At week 105, females had lower haemoglobin and hematocrit at 500 mg/kg bw/d, higher inorganic phosphate at 250 and 500 mg/kg bw/d and higher potassium at 500 mg/kg bw/d compared to control. Serum sodium and chloride were lower in males at 250 mg/kg bw/d and in females at 100 mg/kg bw/d and above. Liver weights were increased in both sexes at 250 and 500 mg/kg bw/d at weeks 53 and 105 for females and at week 53 for males, but was not associated with any histological changes. Higher incidences of kidneys with granulated surface and chronic nephropathy were observed, particularly in males, at 250 and 500 mg/kg bw/d at weeks 53 and 105. In females, the incidence and grading of tubular vacuolation were increased at 100, 250 and 500 mg/kg bw/d at 105 weeks. The incidence and nature of tumours was comparable across all treated and control groups. The NOEL was 10 mg/kg bw/d based on increased inorganic phosphate levels at 100 mg/kg bw/d and on changes in haematology, serum chemistry, urinalysis, liver weights and histopathological evidence of renal toxicity at higher doses.

Dogs

Dogs were dosed with pinoxaden in gelatine capsules at 0, 5, 25 or 125 mg/kg bw/d for one year. Increased incidences of vomiting and mucous in faeces were observed at the highest dose. No other abnormal findings were seen. The NOEL was 125 mg/kg bw/d, the highest dose tested.

Reproduction study

Rats received pinoxaden orally by gavage at 0, 10, 50, 250 or 500 mg/kg bw/d throughout two generations. There were no effects of treatment on parent mortality, clinical signs, reproductive performance and food consumption. Liver weights were higher in first generation male parents at 250 and 500 mg/kg bw/d and in female parents at 50 mg/kg bw/d and above. Kidney weights were higher in first generation parental males at 250 and 500 mg/kg bw/d and in second generation males at 50 mg/kg bw/d and above. Microscopic findings revealed higher incidences of chronic nephropathy and tubular atrophy in both sexes at 500 mg/kg bw/d compared to the control groups. At 500 mg/kg bw/d, bodyweight gains of pups from birth to day seven were reduced (10 to 15 per cent) during the first half of the lactation period but were similar thereafter. There were no other treatment-related effects on number of pups delivered, sex ratio, clinical signs and microscopic findings. The NOEL was 10 mg/kg bw/d for parents based on increased liver and kidney weights at higher doses and 250 mg/kg bw/d for offspring based on reduced bodyweight gains at 500 mg/kg bw/d.

Developmental studies

Pregnant rats were administered pinoxaden orally by gavage at 0, 3, 30, 300 or 800 mg/kg bw/d from days six to 20 of gestation. One animal at 800 mg/kg was sacrificed in a moribund condition on day 17 of gestation. From days six to 21, mean maternal body weight gain and daily food consumption were significantly reduced at 800 mg/kg bw/d, and to a lesser extent at 300 mg/kg bw/d. Implantation sites, post-implantation losses, foetal viability and foetal sex ratios were similar in control and treated groups. At 800 mg/kg bw/d, mean foetal bodyweight was eight per cent lower and incidences of foetal shortening of innominate artery, accessory lobulets of the liver and renal pelvic dilatation were slightly higher. No foetal malformations were observed, but incidences of incomplete ossification of cranial bones as well as unossified and incomplete ossification of digits were higher at 300 and 800 mg/kg bw/d. Lower foetal bodyweight and increased incidences of foetal visceral and skeletal anomalies were likely to be secondary to decreased maternal nutritional status and not due to teratogenic effects by pinoxaden. The NOEL for both maternal and foetal toxicity was 30 mg/kg bw/d, based on reduced body weight gain and food consumption (maternal) and on delayed ossification of cranial bones and digits (foetal) at higher doses. The NOEL for developmental toxicity was 800 mg/kg bw/d, the highest dose tested.

Female rabbits were artificially inseminated with semen from only one male donor. Pregnant rabbits were dosed by oral gavage with pinoxaden at 0, 30, 150, 300, 700 or 1000 mg/kg bw/d from days 7–28 of gestation. Because of severe toxic effects at 300, 700 and 1000 mg/kg bw/d, these groups were terminated. At 150 mg/kg bw/d, one animal was sacrificed due to moribund condition. Bodyweight gains were reduced but food consumption was only slightly reduced. At 150 mg/kg bw/d, increased incidences of early resorption, implantation loss, lower number of live foetuses and reduced foetal weight were observed. The NOEL was 30 mg/kg bw/d for both maternal and foetal toxicity.

Female rabbits were artificially inseminated with semen from only one male donor. Pregnant rabbits were dosed by oral gavage with pinoxaden at 0, 3, 10, 30 or 100 mg/kg bw/d from days 7–28 of gestation. Maternal bodyweight gains and food consumption were reduced at 100 mg/kg bw/d. At this dose, foetal body weight was reduced and higher incidences of malformed diaphragm were seen.

To determine if the higher incidences of malformed diaphragm were reproducible, pregnant female rabbits (artificially inseminated with semen from only one male donor) were dosed by oral gavage with pinoxaden at 0 or 100 mg/kg bw/d from days 7–28 of gestation. Maternal bodyweight gains and food consumption were reduced at 100 mg/kg bw/d. There were no other abnormal findings. Therefore, the NOEL was 30 mg/kg bw/d for maternal toxicity and 100 mg/kg bw/d for developmental toxicity.

Pregnant rabbits (artificially inseminated with semen from multiple male donors) were dosed by oral gavage with pinoxaden at 0 or 100 mg/kg bw/d from days 7–28 of gestation. At 100 mg/kg bw/d, three out of 12 animals died and another two were sacrificed due to moribund condition. Maternal bodyweight gains were reduced without changes to food consumption at 100 mg/kg bw/d. Also at this dose, increased incidences of early resorption, post-implantation loss and lower number of live foetuses were seen. There were no foetal abnormal findings.

Pregnant rabbits (artificially inseminated with semen from only one male donor) were dosed by oral gavage with pinoxaden at 0, 3, 10, 30 or 100 mg/kg bw/d from days 7–28 of gestation. At 100 mg/kg bw/d, four out of 24 animals died and another two were sacrificed due to moribund condition. Maternal bodyweight gains were reduced at 30 mg/kg bw/d and above. At 100 mg/kg bw/d, increased incidences of early resorption, post-implantation loss and lower number of live foetuses were seen. There were no abnormal foetal findings. The NOEL was 10 mg/kg bw/d for maternal toxicity and 100 mg/kg bw/d for developmental toxicity.

Genotoxicity studies

Pinoxaden did not induce mutations in *S. typhimurium* or *E. coli*, nor did it induce micronuclei in the bone marrow of mice administered single oral doses of 500, 1000 or 2000 mg/kg. Pinoxaden was not mutagenic to mouse lymphoma cells. It was positive for chromosomal aberrations in Chinese hamster lung cells, but was negative for unscheduled DNA synthesis both in vitro and in vivo. It was concluded that pinoxaden was unlikely to be genotoxic in vivo.

Neurotoxicity studies

Rats were dosed with a single dose of pinoxaden by oral gavage at 0, 100, 500 or 2000 mg/kg bw and were observed for the following 14 days. There were no changes in the battery of functional observations or in motor activity that could be attributed to treatment.

Rats were administered pinoxaden by oral gavage at 0, 10, 100 or 500 mg/kg bw/d for 13 weeks. There were no changes in the battery of functional observations or in motor activity that could be attributed to treatment.

Public health standards

Poisons scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under the states' poisons regulations to prevent the occurrence of poisoning. On the basis of its toxicity, the NDPSC has included pinoxaden in Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate safety directions on the product label.

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 NOEL obtained in the most sensitive species. This NOEL 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. The ADI for pinoxaden was established at 0.1 mg/kg bw/day based on a NOEL of 10 mg/kg bw/day in a 24-month study in rats and using a 100-fold safety factor in recognition of the extensive toxicological database available for pinoxaden.

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 and isolated event. The ARfD is derived from the lowest single or short term dose which causes no effect in the most sensitive species of experimental animal tested, together with a safety factor that reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals. In a rat developmental study, a NOEL of 30 mg/kg bw/d was identified, based on reduced maternal bodyweight gains and increased foetal incidences of reduced ossification of cranial bones and digits. In a rabbit developmental study, a NOEL of 30 mg/kg bw/d was also identified, based on reduced maternal bodyweight gains, increased incidences of early resorption, implantation loss and lower number of live foetuses observed at 100 mg/kg bw/d. Using a 100-fold safety factor and the no effect level of 30 mg/kg bw/d, an ARfD of 0.3 mg/kg bw can be derived.

Conclusions of the toxicological assessment

Axial 100 EC Selective Herbicide can be used safely if handled in accordance with the instructions and safety directions on the product label.

There are no objections on toxicological ground to the registration of Axial 100 EC Selective Herbicide containing 100 g/L pinoxaden and 25 g/L cloquintocet-mexyl.

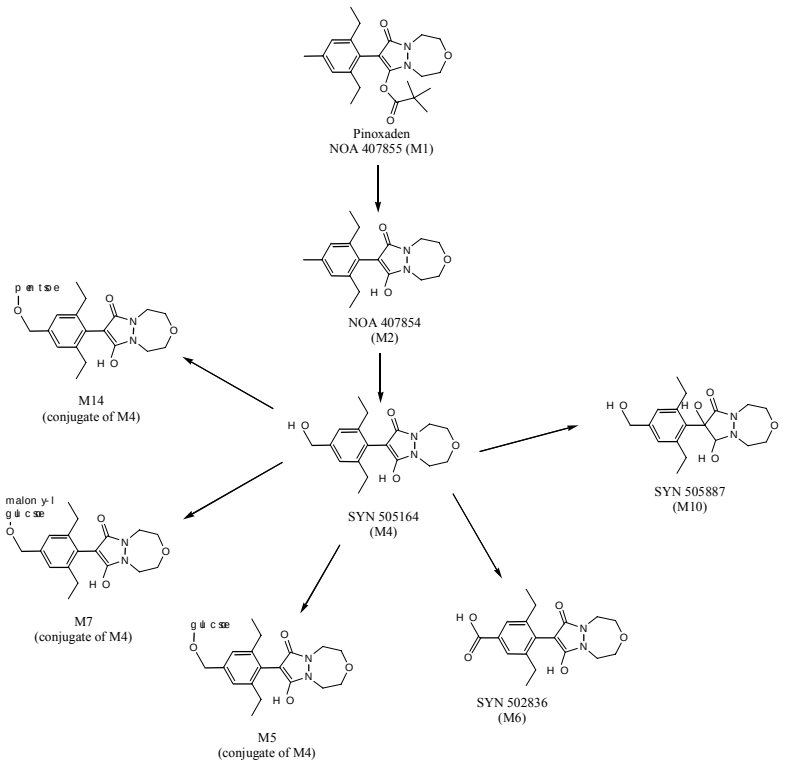
RESIDUES ASSESSMENT

As part of the residues assessment for pinoxaden, plant and animal metabolism studies, supervised residue trials, processing studies, trade aspects, environmental fate and chemistry were considered, and details are provided below. Residues and trade aspects were also assessed for cloquintocet-mexyl, which is co-formulated in the product. However, details of the cloquintocet-mexyl assessment are not included as this active constituent was the subject of a separate Public Release Summary previously published.

Metabolism of pinoxaden

The results from the metabolism studies in wheat show that parent pinoxaden (M1) is only a minor component of total residues at all sampling times after the day of treatment. Immediately following application, the parent ester (pinoxaden, M1) is rapidly hydrolysed to metabolite M2 (NOA 407854), which is the major metabolite in wheat tops (foliage) at zero days post-treatment. M2, in turn, undergoes hydroxylation to form M4 (SYN 505164), and by 21 days post-treatment, the levels of M2 are non-detectable in forage. M4, which is the main metabolite in wheat tops (forage) at 7–14 days post-treatment, is also a significant residue component in wheat grain, husks and straw. Metabolism of M4 follows three main pathways: (i) conjugation of M4 with glucose, giving rise to M5 which is found in wheat samples at all sampling times after the day of treatment; (ii) oxidation of M4 to form the acid metabolite M6 (SYN 502836), which is a relatively minor residue component (less than 10 per cent) at most sampling times; and (iii) hydroxylation of M4 to give M10 (SYN 505887), which is a minor metabolite in all wheat samples, except straw. The metabolism of pinoxaden in plants is summarised in the following figure.

Metabolism of pinoxaden in plants



The metabolism of pinoxaden in animals is somewhat similar to that observed in plants. Pinoxaden undergoes rapid metabolism via initial hydrolysis of the ester group, to give the metabolite M2 (NOA 407854). In laying hens, M2 then undergoes further metabolism to give the metabolites M4 (SYN 505164) and M6 (SYN 502836). Thus, the metabolic routes in laying hens are similar to those observed in plants. However, in lactating goats, metabolite M2 appears to undergo conjugation with glucuronide to form metabolite M12, and these metabolites (M2 and M12) are the main components of urinary TRRs. Metabolite M4 is not a significant component of pinoxaden residues in tissues from lactating goats.

Analytical methods

Details were provided for the validated analytical methods used to determine the concentrations of the pinoxaden metabolites, free and conjugated SYN 505164 (M4) and NOA 407854 (M2) in plant commodities. Briefly, the methodology involves acid digestion of the homogenised samples (1M HCl, reflux for two hours), followed by extraction of the residue analytes using dichloromethane/diethyl ether/acetone (40:7:3). The extracts are cleaned up on SPE cartridges, and the levels of free and conjugated SYN 505164 (metabolite M4) are determined using a two-column HPLC system with UV detection at 223 nm. The levels of NOA 407854 (metabolite M2) are determined using a second two-column HPLC system with UV detection at 243 nm.

Details were also provided for a validated analytical method to quantify residues of SYN 505164 (M4) and SYN 502836 (M6) in animal commodities. Briefly, the methodology involves acid digestion of homogenised samples (1M HCl, reflux for two hours), followed by filtration and clean-up on SPE cartridges. The levels of residue analytes are determined using an HPLC system with two column-switching techniques and tandem MS detection (LC-MS/MS). Detection conditions for SYN 505164 (M4): multiple reaction monitoring – m/z 333 → 303, positive mode. Detection conditions for SYN 502836 (M6): multiple reaction monitoring – m/z 345 → 175, negative mode.

It is noted that the analytical method for pinoxaden residues in animal commodities does not measure metabolite M2. Therefore, assessment of the grazing WHP must take into consideration the time when M2 is absent from forage (so that animals are not exposed to M2 in the diet).

Residue definition

The available data and analytical methodology support pinoxaden residue definitions of:

(i) the sum of metabolite M2, plus the free and conjugated forms of metabolite M4, expressed as pinoxaden for commodities of **plant origin**; and

(ii) the sum of free and conjugated forms of metabolite M4, plus metabolite M6, expressed as pinoxaden for commodities of **animal origin**.

Metabolites M2, M4 and M6 do not have a common names. Therefore, the full chemical names must be used. The following residue definitions are recommended for pinoxaden:

Commodities of plant origin

Sum of 8-(2,6-diethyl-4-methylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxadiazepine-7,9-dione, and the free and conjugated forms of 8-(2,6-diethyl-4-

hydroxymethylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxa-diazepine-7,9-dione, expressed as pinoxaden.

Commodities of animal origin

Sum of the free and conjugated forms of 8-(2,6-diethyl-4-hydroxymethylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxa-diazepine-7,9-dione, and 4-(7,9-dioxohexahydropyrazolo[1,2-d][1,4,5]oxadiazepin-8-yl)-3,5-diethyl-benzoic acid, expressed as pinoxaden.

The residue definitions for pinoxaden are under consideration for revision, where only the relevant metabolites are included in the definition, subject to the suitability of the regulatory analytical methods, and whether they can be adapted to meet the requirements of compliance monitoring.

Residue trials

The maximum proposed Australian use rate for Axial 100 EC Selective Herbicide involves the application of 30 g/ha pinoxaden and 7.5 g/ha cloquintocet-mexyl to wheat and barley crops between two leaf and flag leaf development stages of crop development i.e. GS 12–39 (single application per crop). No harvest WHP is required when the product is used as directed. Treated crops are not to be grazed or cut for stock food for 21 days after application.

Cereals

Details of 22 Australian residues trials conducted at the maximum 100 per cent of the proposed rate on wheat (n=12) and barley (n=10) were provided with the submission. A further 129 overseas (European) residues trials were conducted at 200 per cent of the proposed Australian rate on wheat (n=50) and barley (n=79). A summary of the results from these trials (corrected to reflect the 100 per cent use rate, where applicable) is tabulated below.

Commodity	Cereal	Trial location	PHI range (DALT)	n	Pinoxaden residues (mg/kg)	
					Range	STMR
Grain*	Wheat	Australia	62–146	12	<0.05–0.07	<0.05
		Europe	64–105	44	<0.01–0.21[ζ]	0.01
	Barley	Australia	73–147	10	<0.05–0.07	<0.05
		Europe	49–99	64	<0.01–0.09	0.03
Straw	Wheat	Australia	64–146	11	<0.02–0.49	<0.06
		Europe	64–105	44	<0.01–0.54	0.04
	Barley	Australia	73–147	8	<0.02–0.12	<0.03
		Europe	48–99	66	<0.01–0.29	0.05
Forage[†]	Wheat	Australia	20–22	12	0.08–2.11	1.10
			41–42	11	<0.05–0.78	0.12
			68–70	6	<0.06–<0.12	<0.07
	Barley	Australia	17–21	10	0.06–1.1	0.33
			41–42	10	<0.07–0.20	<0.13
			65–70	8	<0.05–0.12	<0.08

[*] Four of the 44 results for **wheat grain** were above the proposed pinoxaden MRL of 0.1 mg/kg. It is noted that two of these results came from trials where pinoxaden residues were detected in foliage samples prior to the second application of herbicide. It is further noted that the proposed Australian use pattern is for a single application of Axial 100 EC Selective Herbicide per cereal crop.

[†] Pinoxaden residues are expressed on a dry weight basis.

The results of the Australian and overseas (European) supervised residues trials in cereal crops support the establishment of pinoxaden MRLs of: 0.1 mg/kg for wheat and barley grains, three mg/kg for wheat and barley forage (green), and one mg/kg for wheat and barley straw and fodder (dry).

Processing studies

In a processing study with barley, it was determined that the transfer of pinoxaden residues into processed commodities did not result in significant accumulation of residues in any commodity. Thus, separate MRLs for pinoxaden residues in processed barley grain fractions are not required. In contrast, in a processing study with wheat, it was noted that most of the residues in wheat grain are associated with the bran fraction (transfer factor of 3.6–4.7). Therefore, a pinoxaden MRL of 0.5 mg/kg (i.e. 500 percent of the grain MRL) is recommended for wheat bran, unprocessed.

Animal commodity MRLs

In an animal transfer study conducted with lactating dairy cows, animals were orally dosed for 28 consecutive days with dosage of 10 ppm SYN 505164 (M4) in the feed. Pinoxaden residues in milk and edible tissues were all below the limit of quantitation for the analytical method. The maximum dietary exposure of cattle to pinoxaden residues in feed is estimated to be 2–3 ppm in the diet (i.e. cereal forage (green) comprising 100 per cent of the diet), which is three to five-fold lower than the dose level used in the animal transfer study. Therefore, it is recommended that pinoxaden MRLs be set at or about the LOQ of the analytical method for milks (0.01 mg/kg), mammalian meat (0.02 mg/kg) and edible mammalian offal (0.02 mg/kg).

In a second animal transfer study with laying hens, birds were fed rations containing 5 ppm SYN 505164 (M4) in the feed ad libitum for 28 consecutive days. Pinoxaden residues in eggs and edible tissues from treated hens were all below the limits of quantitation for the analytical method. The maximum dietary exposure of poultry to pinoxaden residues in feed is estimated to be 0.1 ppm in the diet (i.e. cereal grain comprising 100 per cent of the diet), which is 50-fold lower than the dose level used in the animal transfer study. Therefore, it is recommended that pinoxaden MRLs be set at or about the LOQ of the analytical method for eggs (0.04 mg/kg), poultry meat (0.04 mg/kg) and poultry offal (0.04 mg/kg).

Spraydrift

Axial 100 EC Selective Herbicide is to be applied either by ground application or by aerial application. The Applicant did not provide any residues data to address the issue of spraydrift. However, an estimate of likely drift was considered: if pasture is exposed to drift at 10 per cent of the recommended application rate for cereal, and yields 1500 kg of dry matter per hectare, gives an estimated exposure level of two ppm in the feed. This exposure level is lower than the 10 ppm feeding level used in the animal transfer study with dairy cattle, where pinoxaden residues in milk and edible tissues were non-detectable. Thus, it is concluded that consumption of spraydrift contaminated feed by livestock is unlikely to result in detectable pinoxaden residues in animal commodities.

Conclusions: risk assessment of residues

Dietary risk assessments

The chronic and acute dietary intake estimates of pinoxaden have been assessed. The national estimated daily intake (NEDI) of pinoxaden is equivalent to less than one per cent of the ADI of 0.1 mg/kg bw/d. With respect to acute dietary intake, the highest acute dietary intake was estimated at less than two per cent of the ARfD of 0.3 mg/kg bw/d. It is concluded that the chronic and acute dietary exposure to pinoxaden is low, and residues in food will not pose an undue hazard to the safety of people.

Standards

The following changes to Tables 1, 3,and 4 of the *MRL Standard* are recommended:

Table 1

Compound	Food		MRL (mg/kg)
Cloquintocet-mexyl			
DELETE	GC 0640	Barley	T*0.1
ADD	GC 0640	Barley	*0.1
Pinoxaden			
DELETE	GC 0640	Barley	T*0.02
	MO 0105	Edible offal (mammalian)	T*0.05
	PE 0112	Eggs	T*0.05
	MM 0095	Meat (mammalian)	T*0.05
	ML 0106	Milks	T*0.02
	PO 0111	Poultry, edible offal of	T*0.05
	PM 0111	Poultry meat	T*0.05
	GC 0654	Wheat	T*0.02
ADD	GC 0640	Barley	0.1
	MO 0105	Edible offal (mammalian)	*0.02
	PE 0112	Eggs	*0.04
	MM 0095	Meat (mammalian)	*0.02
	ML 0106	Milks	*0.01
	PO 0111	Poultry, edible offal of	*0.04
	PM 0111	Poultry meat	*0.04
	GC 0654	Wheat	0.1
	CM 0654	Wheat bran, unprocessed	0.5

Table 3

Compound	Residue
Pinoxaden	
DELETE	Sum of 8-(2,6-diethyl-4-methylphenyl)-tetrahydro-pyrazolo[1,2-d][1,4,5]oxadiazepine-7,9-dione and 8-(2,6-diethyl-4-hydroxymethylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxadiazepine-7,9-dione, expressed as pinoxaden.
Pinoxaden	
ADD	Commodities of plant origin: Sum of 8-(2,6-diethyl-4-methylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxadiazepine-7,9-dione, and the free and conjugated forms of 8-(2,6-diethyl-4-hydroxymethylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxa-diazepine-7,9-dione, expressed as pinoxaden. Commodities of animal origin: Sum of the free and conjugated forms of 8-(2,6-diethyl-4-hydroxymethylphenyl)-tetrahydro-pyrazolo [1,2-d][1,4,5]oxa-diazepine-7,9-dione, and 4-(7,9-dioxohexahydropyrazolo[1,2-d][1,4,5]oxadiazepin-8-yl)-3,5-diethyl-benzoic acid, expressed as pinoxaden.

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
Cloquintocet-mexyl			
DELETE	AS 0640	Barley straw and fodder, dry	T*0.1
ADD	AS 0640	Barley straw and fodder, dry	*0.1
Pinoxaden			
DELETE	AS 0640	Barley straw and fodder, dry	T*0.05
		Cereal forage	T3
	AS 0654	Wheat straw and fodder, dry	T*0.05
ADD		Barley forage (green)	3
	AS 0640	Barley straw and fodder, dry	1
		Wheat forage (green)	3
	AS 0654	Wheat straw and fodder, dry	1

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Overseas registration and approved label instructions

The applicant indicated that Axial 100 EC Selective Herbicide holds conditional registration in the USA and Canada. Provisional registration has been granted in Germany and Great Britain. An application for registration in New Zealand should be finalised in June 2006 under the tradename *Twinax*. A summary of the registered/provisional overseas use patterns is provided in the following table.

Country	Crop	Rate and timing of application	WHPs/Restraints
USA	Wheat and barley	60 g pinoxaden/ha Single application per crop season, applied from the 2-leaf stage to pre-boot stage (GS 12-39).	Do not harvest grain for 60 days following application. Do not graze livestock or harvest forage for hay for 50 days following application.
Canada	Wheat and barley	60 g pinoxaden/ha Single application per crop season. Do not apply past flag leaf stage (GS 39).	Do not harvest grain and straw for 60 days following application. Do not harvest hay for 30 days following treatment. Do not graze livestock on treated crops for 7 days following application.
UK	Wheat and barley	60 g pinoxaden/ha Single application per crop season. Apply before flag leaf sheath extending stage (GS 12–41).	Harvest WHP: None specified on product label Grazing restraint: None specified on product label.
Europe	Wheat and barley	Up to two applications per crop: 45 g pinoxaden/ha during Autumn application, followed by 60 g pinoxaden/ha during the Spring application. Latest time of application at GS 39.	Harvest WHP: unknown Grazing restraint: unknown

Commodities exported and main destinations

The following commodities are considered by the APVMA to be major export food commodities: cereal grains, meat, dairy products, poultry and eggs (Appendix 1 of Part 5B: Overseas trade aspects of residues in food commodities).

Cereal grains

Australian wheat and flour production in 2003–04 was 26,132 ktonne, of which 15,073 ktonne was exported at a value of approximately A$3.5 billion. The six largest export markets for Australian wheat by volume for 2004–05 are shown below (ABARE).

Destination	Volume, ktonne
Indonesia	2700
China	1900
Iraq	1570
Korea	1200
Japan	1170
Egypt	740

Exports are of wheat (including spelt, groats, meal and pellets) and meslin (mixed grain, especially rye mixed with wheat), plus plain white flour, wholemeal flour and self-raising white flour in wheat equivalent (conversion 1:1.29).

Australian barley and malt production in 2003–04 was 10,382 ktonne, of which 5,306 ktonne was exported (value unknown). The six largest export markets for Australian barley by volume for 2004–05 are shown below (ABARE).

Destination	Volume, ktonne
Saudi Arabia	2180
China	1290
Japan	1260
Iran	500
United Arab Emirates	235
Kuwait	235

Exports are of barley (including the grain equivalent to malt).

Proposed Australian use pattern

The maximum proposed Australian use rate for Axial 100 EC Selective Herbicide involves the application of 30 g pinoxaden/ha and 7.5 g cloquintocet-mexyl/ha to wheat and barley crops between two leaf and flag leaf development stages of crop development i.e. GS 12–39 (single application per crop). No harvest WHP is required when the product is used as directed. Treated crops are not to be grazed or cut for stock food for three weeks after application.

Comparison of Australian MRLs with Codex and overseas 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. Pinoxaden has not been considered by Codex, and the applicant has indicated that there are no plans to establish Codex MRLs for pinoxaden at this stage.

Comparison of Australian and Overseas MRLs and residue definitions

Commodity	Overseas MRLs/tolerances (mg/kg)				Australian MRLs (proposed)
	USA	Canada	UK/Europe‡	Japan*	
Residue definition†	Parent and metabolites M2 + M4 + M6	Parent and metabolites M2 + M4 + M6	Metabolite M2 only	Parent only	Plants: M2 + M4 Animals: M4 + M6
Cereal Commodities					
Barley grain	0.9	0.9	0.05	0.5	0.1
Barley bran	1.6	1.6	--	--	--
Wheat grain	1.3	1.3	0.05	0.7	0.1
Wheat bran	3	3	--	--	0.5
Animal Commodities					
Cattle (fat)	0.04	0.04	--	--	--
Cattle (meat)	0.04	0.04	--	--	--
Cattle (meat by-product)	0.04	0.04	--	--	--
Eggs	0.06	0.06	--	--	*0.04
Milk	0.02	0.02	--	--	*0.01
Edible offal (mammalian)	--	--	--	--	*0.02
Meat (mammalian)	--	--	--	--	*0.02
Poultry, edible offal of	--	--	--	--	*0.04
Poultry meat	--	--	--	--	*0.04
Animal Feed Commodities					
Barley hay	1.5	1.5	--	--	--
Barley straw	1	1	--	--	--
Wheat forage	3.5	3.5	--	--	--
Wheat hay	2	2	--	--	--
Wheat straw	1.5	1.5	--	--	--
Barley forage (green)	--	--	--	--	2
Barley straw and fodder, dry	--	--	--	--	1
Wheat forage (green)	--	--	--	--	2
Wheat straw and fodder, dry	--	--	--	--	1

† Parent = pinoxaden; M2 = NOA 407854; M4 = SYN 505164; and M6 = SYN 502836.

‡ The UK, as rapporteur member state has reviewed pinoxaden/axial on behalf of the EU. The result of this evaluation needs to be adopted by all member states following a joint review process.

* For commercial reasons axial 100 EC Selective Herbicide will not be registered in Japan. However, Japan has established pinoxaden MRLs to avoid any trade barriers for import.

Potential risk to Australian trade

Japan

The Japanese MRLs for pinoxaden in barley grain (0.5 mg/kg) and wheat grain (0.7 mg/kg) are significantly higher than the corresponding Australian MRLs of 0.1 mg/kg. It is also noted that the Japanese residue definition for pinoxaden consists of the parent compound only. In fact, the available metabolism studies show that pinoxaden is rapidly hydrolysed to metabolite M2; less than five per cent of total residues in wheat foliage at 14 days post-treatment were identified as parent pinoxaden. Additionally, the parent compound was not detected in ears, grain, husks or straw at mature harvest. Therefore, it is concluded that cereal commodities from crops treated in accordance with the proposed Australian product label will comply with the Japanese MRLs for pinoxaden.

UK/Europe

The UK/European MRLs for pinoxaden in cereal grains (0.05 mg/kg) are lower than the corresponding Australian MRLs of 0.1 mg/kg, despite the UK/European use-rate being 200 per cent of that proposed for use in Australia. However, the UK/European residue definition for pinoxaden is metabolite M2 only. The available residue trial data demonstrate that metabolite M2 residues are non-detectable in mature grain, when cereal crops are treated between GS 12 and GS 39. In fact, metabolite M2 is essentially non-detectable in cereal forage within 21 days of application. Therefore, it is concluded that cereal commodities from crops treated in accordance with the proposed Australian product label will comply with the UK/European MRLs for pinoxaden.

USA/Canada

The US/Canadian MRLs for pinoxaden in **cereal commodities** are significantly higher than the corresponding Australian MRLs. However, it is noted that the US/Canadian residue definition for pinoxaden is more comprehensive that the proposed Australian residue definition, and includes parent pinoxaden and metabolites M2, M4 and M6.

Review of the available metabolism and residues trial data reveals the following facts:

- after application, parent pinoxaden is rapidly metabolised such that it is not detectable in any plant fraction at 21 days post-application;
- metabolite M2 is non-detectable in cereal forage within 21 days of application, and was not detected in any plant fraction at mature harvest; and
- metabolite M6 is not detected in grain/straw at mature harvest, but may be present at levels of up to one mg/kg DW in cereal forage at 21 days post-application.

The main residue component in cereal **grains** and **bran** is metabolite M4 (free and conjugated forms). Therefore, it is concluded that grain and bran from crops treated in accordance with the proposed Australian product label will comply with the US/Canadian MRLs for pinoxaden. Similarly, for cereal **straw**, metabolite M4 is the main residue component, and the Australian MRLs for straw and fodder (one mg/kg DW) are consistent with the US/Canadian MRLs of 1–1.5 mg/kg. The Australian cereal **forage** (green) MRL of three mg/kg is lower than the US/Canadian

MRL of 3.5 mg/kg. However, this difference is attributed to the inclusion of metabolite M6 in the US/Canadian residue definition.

The US/Canadian MRLs for pinoxaden residues in **animal commodities** are also slightly higher than the corresponding Australian MRLs. However, review of the available animal transfer data shows that residues of metabolites M4 and M6 are non-detectable in all edible commodities from animals dosed at the highest rate. Thus, detectable residues are not expected in tissues, milk or eggs from animals that consume feedstuff contaminated with pinoxaden residues.

Overall, it is concluded that both cereal and animal commodities will comply with the relevant US/Canadian MRLs for pinoxaden.

Other major importing countries

Export of treated cereal grains (wheat and barley) containing measurable residues of pinoxaden may pose a risk to Australian trade in situations where:

(i) importing countries have not set tolerances for residues of this chemical in food commodities; or

(ii) (ii) tolerances in the importing countries are lower than the corresponding Australian MRLs. To date, there are no pinoxaden MRLs established for any edible commodities by the other major importers of Australian cereals (Indonesia, China, Iraq, Iran, Korea, Saudi Arabia, United Arab Emirates and Kuwait).

Conclusions of the assessment of overseas trade aspects

Cereal grains

The available residues trial data show that grain (wheat and barley) from crops treated with pinoxaden may have low levels of residues when harvested (range of residues from supervised Australian residue trials (n=22) was less than 0.05 to 0.07 mg/kg (STMR=<0.05 mg/kg).

The proposed Australian MRLs of 0.1 mg/kg for wheat and barley may potentially impact upon the export of Australian cereal grain to the major importing countries. The APVMA welcomes comment in relation to whether pinoxaden residues will unduly prejudice Australian trade in wheat and barley grains.

Livestock

The APVMA has considered a trade statement for livestock that have been exposed to pinoxaden through grazing or feeding of treated cereal crops, forage or straw. When Axial 100 EC Selective Herbicide is used in accordance with the instructions on the draft product label, consumption of cereal grain, forage, fodder and hay by animals is not expected to produce detectable residues in any animal commodities (meat, offal, eggs, milk). Accordingly, use of Axial 100 EC Selective Herbicide on cereals does not require the establishment of export slaughter intervals (ESIs). The following trade advice statement has been included on the product label:

> **Livestock export intervals:** Not required when Axial is used as directed.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Axial 100 EC Selective Herbicide is intended for the post-emergence control of selected grass weeds in wheat and barley. Axial 100 EC Selective Herbicide can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Pinoxaden is a new active ingredient, which is not tolerated alone in cereal crops and therefore, needs to be used with a safener. Cloquintocet-mexyl is a herbicide safener and is mixed with pinoxaden in the product formulation to achieve good crop tolerance. The OCS or NOHSC has not previously assessed any products containing pinoxaden, but has previously assessed a product containing cloquintocet-mexyl (OHS file number: 1993/1845–02).

Pinoxaden has low acute oral, dermal and inhalation toxicity in rats. It is a severe eye irritant, but not a skin irritant in rabbits or a skin sensitiser in guinea pigs. Pinoxaden is not on the NOHSC Hazardous Substance Information System.

The draft label recommends an application rate of 150–300 mL/ha product. The product will be applied by ground boom spray equipment with 50–110 L/ha spray volume (maximum concentration: 0.06 per cent pinoxaden and 0.6 per cent product in spray) and by aircraft with 20–30 L/ha spray volume (maximum concentration: 0.15 per cent pinoxaden and 1.5 per cent product in spray).

There were no worker exposure studies on pinoxaden or Axial 100 EC Selective Herbicide. The occupational health and safety risk assessment was based on the acute hazards of the product and on exposure estimates obtained from exposure models/databases (UK Predictive Operator Exposure Model and the Pesticide Handlers Exposure Database Surrogate Exposure Guide). Based on the risk assessment, cotton overalls buttoned to the neck and wrist, a washable hat, elbow-length PVC gloves, goggles, and a disposable fume mask covering mouth and nose, should be worn when opening the container and preparing spray.

The product label requires the following re-entry statement:

> Do not allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

Based on the information provided in the toxicology report, the OCS classified pinoxaden as a hazardous substance according to *NOHSC Approved Criteria for Classing Hazardous Substances* (NOHSC, 2004), with the following risk phrase:

> R36 Irritating to eyes

The product will be formulated overseas and imported into Australia in ready-for-sale packages of one litre high-density polyethylene (HDPE) or fluorinated HDPE bottles with 45 mm opening and five litre HDPE or fluorinated HDPE bottles with 63 mm opening. Transport workers and store persons will handle the packaged product and could only become contaminated if packaging were breached.

Axial 100 EC Selective Herbicide has low acute oral, dermal and inhalation toxicity in rats. It is a moderate eye and skin irritant in rabbits, but is not a skin sensitiser in guinea pigs. The product is likely to cause irritation to the mucosa of the upper respiratory tract.

There were no worker exposure studies on pinoxaden or Axial 100 EC Selective Herbicide. The occupational health and safety risk assessment was based on the acute hazards of the product and on exposure estimates obtained from exposure models/databases (UK Predictive Operator Exposure Model and the Pesticide Handlers Exposure Database Surrogate Exposure Guide). Based on the risk assessment, cotton overalls buttoned to the neck and wrist, a washable hat, elbow-length PVC gloves, goggles, and disposable fume mask covering mouth and nose, should be worn when opening the container and preparing spray.

The product label requires the following re-entry statement:

> Do not allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

The product label requires the following precautionary statement:

> Do not use human flaggers/markers unless they are protected by engineering controls such as enclosed cabs.

Axial 100 EC Selective Herbicide is classified as a hazardous substance in accordance *with NOHSC Approved Criteria for Classing Hazardous Substances (NOHSC, 2004),* with the following risk phrases:

R36/37/38	Irritating to eyes, respiratory system and skin
R65	Harmful: may cause lung damage if swallowed

Conclusions of the occupational health and safety assessment

Axial 100 EC Selective Herbicide can be safely used by workers when handled in accordance with the control measures indicated in this assessment. There are no objections on toxicological grounds and occupational health and safety grounds to the registration of Axial 100EC Selective Herbicide.

ENVIRONMENTAL ASSESSMENT

Environmental exposure

The properties of pinoxaden (moderate hydrophilicity and low volatility) indicate that the portion not retained by the crop can be expected to become associated with the soil and interstitial water after application of Axial 100 EC Selective Herbicide. There may be some indirect aquatic exposure through spray drift or runoff. Atmospheric exposure is expected to be insignificant.

Pinoxaden is rapidly hydrolysed under environmental conditions, particularly in alkaline media. Hydrolysis may be abiotic or mediated by microbial activity. Pinoxaden and its metabolites are mobile in soils, but low application rates and rapid degradation limit the extent of leaching.

Cloquintocet-mexyl is similar to pinoxaden in being a hydrophilic and readily hydrolysed ester, and is expected to share its environmental fate.

Testing has confirmed the foregoing expectations, as outlined below.

Standard hydrolysis studies under sterile conditions in the dark indicated that pinoxaden hydrolysed to pivalic acid and the diketone, which resisted further hydrolysis under these conditions. The half-life of pinoxaden was 17 days at pH 5 and 0.2 days at pH 9.

Pinoxaden was photolysed in aqueous solution and on the surface of soil under laboratory conditions. Photodegradation of pinoxaden is expected to be a minor pathway for its degradation as abiotic hydrolysis in solution and soil catalysed/microbial hydrolysis in soils proceeds more rapidly, with typical half-lives of less than a day.

Pinoxaden is metabolised rapidly through ester hydrolysis in soils under laboratory conditions. The herbicidally active diketone so formed is hydroxylated through microbial activity under aerobic conditions, but stable under anaerobic conditions. Further aerobic metabolism leads to unextractable residues and carbon dioxide. The same metabolic pathways prevail in aquatic systems, but the hydroxylation step proceeds more slowly and only in sediment, while the hydroxylation product degrades more rapidly. The primary metabolite arising from ester hydrolysis of pinoxaden is stable in anaerobic aquatic systems.

The metabolism studies indicate that pinoxaden and its main metabolites partition mainly to water rather than sediment and are likely to be mobile in soil, although the non-persistence of pinoxaden will limit its mobility. This has been confirmed using standard laboratory leaching tests under continuous water flow. Lysimeter studies under field conditions with intermittent rainfall/irrigation indicate that low concentrations of pinoxaden's main metabolites can be detected in some leachate samples at depths in the order of a metre.

As pinoxaden is moderately soluble in water and very slightly volatile, volatilisation from soil or vegetation would not be expected to be a significant mode of transport. This has been confirmed by laboratory studies.

Pinoxaden dissipated rapidly (with a half-life of generally less than a day) in field studies conducted in Germany, Italy and Spain. Its primary metabolite, the herbicidally active diketone, also dissipated rapidly with a typical half-life of a few days and a maximum half-life of 12 days. The hydroxylated diketone was more persistent. Half-lives could not easily be determined because of ongoing formation from the diketone. In radiolabelled studies, the DT50 was determined as 12–15 days, but with DT90s of 109 days. This metabolite did not accumulate in soils, even with two applications per season.

Studies on a well drained silt loam in Germany indicated that losses of pinoxaden and its two main metabolites to subsurface drainage at 70–90 cm depth generally remained below one per cent of applied, although losses reached two and a half per cent in one exceptionally wet winter. Concentrations in receiving waters remained below one µg/L.

Pinoxaden would not be expected to bioaccumulate in fish because of its moderate water solubility (200 mg/L). Bioaccumulation would also not be expected to occur in fish because of the rapid hydrolysis of pinoxaden to the weakly acidic and more hydrophilic diketone. Therefore, no bioaccumulation tests were conducted.

In summary, residues of pinoxaden and its metabolites will mainly become associated with the soil and interstitial water following application of Axial 100 EC Selective Herbicide. Pinoxaden and its metabolites are mobile in soils. A minor proportion, typically less than one per cent may be transported to aquatic environments in runoff. Residues in soil and water are not expected to persist, or to accumulate in soils or living organisms. Use of Axial 100 EC Selective Herbicide in cereals as proposed is not expected to lead to any significant contamination of the environment by pinoxaden or cloquintocet-mexyl, or their metabolites.

Environmental effects

Birds

Standard testing indicates that pinoxaden is practically non-toxic to birds exposed by acute oral administration or by subacute or chronic administration through the diet. Reproduction in bobwhite quail was unaffected at concentrations of 300 mg/kg in the diet, and in mallards at concentrations of 1000 mg/kg.

Aquatic life

Standard testing found technical pinoxaden to be slightly toxic to fish and aquatic invertebrates under acute or chronic exposure conditions, but highly toxic when formulated. The most sensitive endpoint for technical pinoxaden was a 96-hour EC50 of 0.40 mg/L for shell deposition in eastern oysters. Testing with the two main metabolites found them to be practically non-toxic to fish and daphnids.

Technical pinoxaden was slightly to moderately toxic to algae and duckweed. Again, formulated pinoxaden was highly toxic to green algae, and to duckweed when adjuvant was added. The two main metabolites were practically non-toxic to green algae, but the primary metabolite was slightly toxic to duckweed, returning similar results to pinoxaden.

Honey bees, earthworms and soil microbial function

Testing according to standard procedures found technical pinoxaden to be practically non-toxic to honey bees, earthworms and soil microbial function. As with the aquatic toxicity, pinoxaden was more toxic as the formulated product, being moderately toxic to honeybees and toxic to earthworms. Testing with the formulated product in beneficial arthropods (parasitic wasps, predatory mites, green lacewings and rove beetles) found no harmful effects from dried spray deposits on vegetation or, for the rove beetles, residues on soil. However, survival and fecundity of wasps and mites were impaired by residues of the formulated product on glass surfaces following application at rates below those proposed for Australian cereals. The latter exposure may be more relevant to the field situation where invertebrates in the crop will initially be directly exposed to the spray mix rather than dried foliar deposits.

Phytotoxicity

Phytotoxicity testing with the formulated product found no effects on dicotyledonous plants at application rates above those proposed for Australia. The monocotyledonous plants field corn, oats and perennial ryegrass (Family *Poaceae*) were sensitive to the formulated product when exposed post-emergence at rates below those proposed for Australia. Perennial ryegrass was sensitive to pre-emergence applications.

Environmental risk assessment

The predicted residues of pinoxaden on vegetation and in soil are well below levels that might cause harmful effects in birds and soil dwelling organisms. Similarly, the predicted exposure of bees to spray will be well below levels that could be harmful.

It appears that the formulation may be harmful to some beneficial invertebrates if they are directly exposed to the spray mix. However, effects on invertebrate species within some early wheat and barley crops would not be expected to harm their populations at the landscape level, while the dried foliar residues will not present an obstacle to repopulation.

The main risk arising from the proposed use of pinoxaden is its potential to cause phytotoxicity in non-target grasses. Grasses growing outside the treatment area may suffer some adverse effects but are unlikely to be killed by Axial 100 EC Selective Herbicide as a 10 per cent spray drift event would deliver a maximum of three g/ha pinoxaden, which is below the NOEC in ryegrass but slightly above the NOEC in oats (although below the ER25). Thus some limited damage to grasses may be expected in small areas close to the crop under worst case conditions if care is not taken to minimise spray drift. The draft label for Axial 100 EC Selective Herbicide contains adequate instructions to limit the exposure of non-target vegetation to spray drift.

The predicted residues of pinoxaden in shallow water contaminated by direct overspray of Axial 100 EC Selective Herbicide are well below concentrations that could be harmful to fish, aquatic invertebrates, algae or aquatic plants, even with the addition of adjuvant to the spray mix. The risk of Axial 100 EC Selective Herbicide to aquatic life is assessed as low.

The risk of groundwater contamination is considered low, notwithstanding the high mobility of pinoxaden, because of the low application rates and limited persistence.

Risk assessment indicates that use of Axial 100 EC Selective Herbicide as proposed is unlikely to adversely affect non-target organisms, with the possible exception of some grasses given their sensitivity. However, this is likely to be restricted to areas within the crop when pinoxaden is used at the low rates proposed for wheat and barley.

Conclusions of the DEH assessment

DEH concludes that the use of Axial 100 EC Selective Herbicide in accordance with label instructions is unlikely to have any unintended effects that are harmful to plants, animals, or things or to the environment.

EFFICACY AND CROP SAFETY ASSESSMENT

Proposed use pattern

Axial 10EC Selective Herbicide is a Group A herbicide designed for post-emergence grass weed control in barley and wheat. Claims include control of wild oats, paradoxa and canary grasses and suppression of annual ryegrass in wheat and barley crops (in the growth stages two leaf to full boot (GS 12–49)).

Evaluation of efficacy

Pinoxaden is a representative of the phenylpyrazolin class of chemistry, an Acetyl CoA carboxylase (ACCase) inhibitor, and has a slight advantage in that it inhibits chloroplastic and cystolic ACCase enzymes in grasses.

Efficacy data have been generated from several trials in the Australian winter cereal production zones, these include 45 trials for wild oats, 15 trials for *Phalaris spp*., 12 trials for annual ryegrass, 15 trials for broadleaf weeds. These trials were appropriate in design and plot size and appropriate statistical analyses were conducted.

Crop safety

The data provided for target crop safety indicated that crop phytotoxicity did not occur in either barley or wheat when Axial was used at the recommended rates.

Conclusions

The data adequately supported the label claims; specific application rates for specific weeds in targeted regions. The claims for control of wild oats, Paradoxa and canary grasses, and the suppression of annual ryegrass were well supported. It is recommended that on the basis of efficacy and crop safety Axial 100 EC Selective Herbicide be considered for registration.

LABELLING REQUIREMENTS

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

AXIAL®

100 EC SELECTIVE HERBICIDE

ACTIVE CONSTITUENTS:	**100 g/L**	**PINOXADEN**
	25 g/L	**CLOQUINTOCET- MEXYL**
SOLVENT:	**559 g/L**	**LIQUID HYDROCARBONS**

GROUP A HERBICIDE

For the control of key grass weeds in Barley and Wheat

1 or 5 LITRES

Syngenta Crop Protection Pty Limited
Level 1, 2-4 Lyon Park Road, North Ryde NSW 2113

In a transport emergency dial 000, Police or Fire Brigade
For specialist advice in an emergency only, call 1800 033 111 (24 hours)

APVMA Approval No: 59024/1 or 5/
Item number
UN-Free

syngenta

DIRECTIONS FOR USE

RESTRAINTS

DO NOT apply if rainfall is expected within 30 minutes
DO NOT apply to weeds under stress from factors including very dry, waterlogged, cold, frosty conditions, nutrient deficiency or the use of pre-emergent herbicides

Crop	Weeds	State	Rate/ha	Critical Comments
Barley, Wheat 2 leaf to full boot (GS 12–49)	Canary Grass (*Phalaris minor*), Paradoxa Grass (*Phalaris paradoxa*) (Annual phalaris) 2 leaf to end of tillering (GS 12–22)	All States	200 to 250 mL plus 500 mL ADIGOR®/100 L water	**Rate Selection:** Use the lower rate when weeds are actively growing without stress, small in size and of low density. Use the higher rate when growing conditions are not ideal and weeds are under minor stress, larger in size or in high density. Low level or minor stress can be caused by factors including dry conditions, waterlogging, cold or nutrient deficiency, providing they are not severe or of prolonged duration. **Mixtures:** Apply in mixtures for broadleaf weed control only when weeds are actively growing. Mixing with some broadleaf weed herbicides can result in a reduction in grass weed control. Use the higher rate of AXIAL when applying mixtures. **Resistance Management:** For suspected Group A resistant populations refer to the Resistant Weeds Warning.
	Wild Oats (Black Oats) (*Avena* spp) 2 leaf to end of tillering (GS 12–22)	Sth NSW, Vic, Tas, SA, WA only	150 to 200 mL plus 500 mL ADIGOR/100 L water	
		Qld, Nth NSW only	200 mL plus 500 mL ADIGOR/100 L water	
	Suppression of Annual Ryegrass *(Lolium rigidium)* 2 leaf to 1st tiller detectable (GS 12–21)	All States	250 to 300 mL plus 500 mL ADIGOR/100 L water	To get best results apply only to actively growing Annual Ryegrass until the start of tillering. DO NOT apply under poor growing conditions or to weeds under stress. **Rate Selection:** Use the lower rates when weed density is light and weeds are small in size. Use the higher rate when weed density is moderate and weed size is large. Preferably apply in a program with a pre-emergent herbicide and avoid applying Group A herbicides to high densities of Annual Ryegrass. **Mixtures:** Mixing with some broadleaf herbicides may reduce Annual Ryegrass control. Use the higher rate of AXIAL when applying mixtures. **Resistance Management:** For suspected Group A resistant populations refer to the Resistant Weeds Warning.

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

WITHHOLDING PERIODS

Barley, Wheat: **Harvest:** **NOT REQUIRED WHEN USED AS DIRECTED**
Grazing: **DO NOT GRAZE FOR 2 WEEKS AFTER APPLICATION**

GENERAL INSTRUCTIONS

AXIAL should be applied to weeds that are actively growing. Weeds under stress are more difficult to control. Under the influence of low level stresses weeds may still be controlled, but a higher rate of AXIAL is required. As stress becomes more severe weed control may fail. Stress can be caused by a range of factors including, dry conditions, waterlogging, cold or nutrient deficiency.

Mixing

Thoroughly clean the sprayer prior to use. For appropriate cleaning instructions, refer to the label of the product sprayed previously.

Fill the spray tank to half full with clean water. Start agitation. Add AXIAL by pouring it into the stream of incoming water and continue filling. Add the required amount of ADIGOR just before the tank is full and continue agitation.

Mixing order: Some products may react with other products if they are not mixed in the correct order. The general mixing order of products should be:

1. Water conditioners or buffers
2. Water dispersable granules (WG)
3. Wettable powders (WP)
4. Flowable or suspension concentrates (SC)
5. Emulsifiable concentrates (EC)
6. Water based or soluble concentrates
7. ADIGOR

It is important to ensure that each individual component of the tank mix is fully dissolved and in solution before the next product is added to the tank mix, otherwise mixing problems may occur.

Application

***Ground application*:** Ensure good spray coverage is obtained. Apply using a minimum of 50 L of water/ha. Ideal droplet size is 200 to 300 microns VMD, to achieve a fine to medium spray quality.

Aerial application: Apply using a minimum of 20 L water/ha and spray at 2 m to 3 m above the crop. Ideal is a medium spray quality, droplet size is 250 to 350 microns VMD. Avoid applying if wind speeds are greater than 18 km/hr. For aerial application use ADIGOR at 500 mL/ha.

Compatibility

When AXIAL is applied alone or with other products always use ADIGOR.

AXIAL is compatible with most common broadleaf herbicides. As formulations of other manufactures' products are beyond the control of Syngenta, and water quality varies with location, all mixtures should be tested prior to mixing commercial quantities.

Weed control: Some products, including broadleaf herbicides, can result in reduced grass weed control when applied with AXIAL. For the latest information on compatibility of AXIAL with broadleaf herbicides refer to the AXIAL compatibility chart available from your local reseller, Syngenta Territory Manager, Syngenta website www.syngenta.com.au, or technical advice line Freecall 1800 067 108

Crop injury: Some products can result in crop yellowing or crop injury when applied with crop oils including ADIGOR. Refer to the label of mixing partners to determine if they can be used with crop oils. For example, Paragon*, Sniper*, Brodal* and Tigrex* may cause crop injury when used with crop oils including ADIGOR.

If necessary, to avoid reduced grass weed control or crop injury, apply AXIAL first and then allow at least 10 days between its application and application of other product.

Cleaning Spray Equipment

After using AXIAL, empty the tank completely and drain the whole system. Thoroughly wash inside the tank using a pressure hose, drain the tank and clean any filters in the tank, pump, line and nozzles.

***To rinse*:** After cleaning the tank as above, quarter fill the tank with clean water and circulate through the pump, lines, hoses and nozzles. Drain and repeat the rinsing procedure twice.

***To decontaminate*:** Before spraying cereals (except wheat or barley), maize, sorghum or other sensitive crops, wash the tank and rinse the system as above. Drain and repeat the rinsing procedure. Then quarter fill the tank and add a liquid alkali detergent

(eg SURF*, OMO*, DRIVE*) at 0.5 L/100 L water and circulate throughout the system for at least 15 minutes. Drain the whole system. Remove filters and nozzles and clean them separately. Finally flush the system with clean water and allow to drain. Dispose of all water used for cleaning in a disposal pit specifically marked and set up for this purpose clear of waterways, vegetation and roots.

Resistant Weeds Warning

GROUP	A	HERBICIDE

AXIAL 100 EC Selective Herbicide has the inhibition of fat (lipid) synthesis, (or inhibitors of acetyl CoA carboxylase) mode of action. For weed resistance management AXIAL is a Group A herbicide. Some naturally occurring weed biotypes resistant to AXIAL and other Group A 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 AXIAL or other Group A herbicides. Since the occurrence of resistant weeds is difficult to detect prior to use, Syngenta Crop Protection accepts no liability for any losses that may result from the failure of Axial to control resistant weeds.
Large numbers of healthy surviving weeds can be an indication that resistance is developing. Efforts should be made to prevent seed set of the surviving weeds. DO NOT make more than 1 application of a Group A herbicide with the inhibition of fat (lipid) synthesis (or inhibitors of acetyl-CoA carboxylase) mode of action to a crop in the same season. If the user suspects that the target weed population is resistant to herbicides with this mode of action, AXIAL or other Group A herbicides should not be used.
Strategies to minimise the risk of herbicide resistance are available. The above recommendations should be incorporated into an Integrated Weed Management (IWM) Program. Consult your farm chemical supplier, consultant, local Department of Agriculture or Primary Industries, or local Syngenta Crop Protection representative for details.

PRECAUTIONS
DO NOT use human flaggers/markers unless they are protected by engineering controls such as enclosed cabs.
Re-entry Period: DO NOT allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use.

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.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT
DO NOT contaminate streams, rivers or waterways with the chemical or used containers.

STORAGE AND DISPOSAL
Store in the closed, original container in a cool, well ventilated area. DO NOT store for prolonged periods in direct sunlight. Triple or preferably pressure 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 bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS
Will irritate the eyes, nose, throat and skin. Avoid contact with eyes and skin. DO NOT inhale vapour. When opening the container and preparing spray wear:

- **cotton overalls buttoned to the neck and wrist**
- **a washable hat**
- **elbow-length PVC gloves**
- **goggles**
- **disposable fume mask covering mouth and nose**

If product on skin, immediately wash the area with soap and water. If product in eyes, wash it out immediately with water. After each day's use, wash gloves, goggles and contaminated clothing.

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

MATERIAL SAFETY DATA SHEET
If additional hazard information is required, refer to the Material Safety Data Sheet. For a copy phone 1800 067 108 or visit our website at www.syngenta.com.au

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY
Syngenta has no control over storage, handling, and manner of use of this product. Where this material is not stored, handled or used correctly and in accordance with directions, no express or implied representations or warranties concerning this product (other than non-excludable statutory warranties) will apply. Syngenta accepts no liability for any loss or damage arising from incorrect storage, handling or use.

Batch No	
Date of Manufacture	

Barcode

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 an absorbed material from 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	Water repelling
leaching	Removal of a compound by use of a solvent
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient
metabolism	The conversion of food into energy
photodegradation	Breakdown of chemicals due to the action of light
photolysis	Breakdown of chemicals due to the action of light
subcutaneous	Under the skin
toxicokinetics	The study of the movement of toxins through the body
toxicology	The study of the nature and effects of poisons

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Updated versions of these documents are available on the APVMA website at http://www.apvma.gov.au.

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APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of Pinoxaden in the product Axial 100 EC Selective herbicide please fill in this form and send it, along with payment of $30 to:

Mr D. Hutchison
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:

Dr G F Smart
Pesticides Program
Australian Pesticides and Veterinary Medicines Authority

Fax: (02) 6272 3218

Please send me a copy of the full technical report for the evaluation of Pinoxaden in Axial 100 EC Selective herbicide.

Name (Mr, Mrs, Ms, Dr)_____

Position _____

Company/organisation _____

Address _____

Contact phone number (___) _____

☐ I enclose payment by cheque, money order or credit card for $_____

☐ Make cheques payable to 'Australian Pesticides and Veterinary Medicines Authority'.

☐ ___ Bankcard ___ Visa ___ MasterCard

Card number _____/_____/_____/_____ Expiry date /

Signature_____ Date _____