Public Release Summary
on

Evaluation of the new active

PICOLINAFEN

in the products

SNIPER HERBICIDE &
PARAGON HERBICIDE

National Registration Authority
for Agricultural and Veterinary Chemicals

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Malcolm Arney
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E 240
KINGSTON ACT 2604

Ph: (02) [6272 3152]
Fax: (02) [6272 3218]

FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) 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 NRA works in close cooperation with advisory agencies, including the Department of Health and Aged Care (Chemicals and Non-prescription Medicines Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (NOHSC) and State departments of agriculture and environment.

The NRA 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 NRA 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 NRA's publications *AgManual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series.*

This Public Release Summary is intended as a brief overview of the assessment that has been completed by the NRA and 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.

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the NRA. Alternatively, the reports can be viewed at the NRA Library Ground Floor, 22 Brisbane Avenue, Barton, ACT.

The NRA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Executive Manager—Registration, National Registration Authority for Agricultural and Veterinary Chemicals, PO Box E240, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
F_o	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
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
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	Suspension Concentrate
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

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of *SNIPER HERBICIDE (Sniper) and PARAGON HERBICIDE (Paragon),* which contain the new active ingredient, picolinafen.

Responses to this Public Release Summary will be considered prior to registration of the products. They will be taken into account by the NRA in deciding whether the products should be registered and in determining appropriate conditions of registration and product labelling.

Copies of full technical evaluation reports on picolinafen, covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the NRA on request (see order form on last page). They can also be viewed at the NRA library located at the NRA offices, Ground Floor, 22 Brisbane Avenue, Barton ACT 2604.

Written comments should be submitted by **20 December 2000** and addressed to:

Malcolm Arney
AgVet Chemicals Evaluation Section
National Registration Authority
PO Box E240 Phone (02) 62723152
Kingston ACT 2604 Fax (02) 62723218

Applicant
Cyanamid Agriculture Pty Ltd.

Products Details
It is proposed to register *Sniper* containing picolinafen at 750g/kg as a water dispersible granule and *Paragon* containing picolinafen at 50g/L plus MCPA at 500g/L as an emulsifiable concentrate. Both products will be imported fully formulated and packaged in 500g, 2kg, 4kg and 5, 10, 20 litre containers respectively.

Picolinafen inhibits the activity of phytoene desaturase, leading to a reduction in carotenoid pigments and ultimately, destruction of leaf chlorophyll in the foliage of sensitive plants. Symptoms in the field occur as bleaching or whitening (often with mauve discolouration) of leaf tissue, followed by necrosis and death. Picolinafen is an aryloxypicolinamide and as such is classified for weed resistance management purposes as a GROUP F herbicide.

MCPA is a phenoxyalkanoic acid that acts on weeds by disrupting growth. The activity of MCPA combines with the activity of picolinafen to enhance weed control and improve the spectrum of activity. MCPA is a GROUP I herbicide.

Sniper has demonstrated a performance similar to that of diflufenican in terms of weed spectrum and crop selectivity. This application is for the early post emergence use of *Sniper* in narrowleaf lupins *(Lupinus angustifolius)* for the control of wild radish *(Raphanus raphanistrum)* and the suppression of capeweed *(Arctotheca calendula).*

Paragon has demonstrated a performance similar to that of diflufenican plus MCPA iso-octyl ester, also at a ratio of 1:10 in terms of weed control spectrum and crop selectivity. This application is for the post-emergence use of *Paragon* in winter cereals (wheat, barley, oats, triticale and cereal rye) for the control or suppression of various broadleaf weeds.

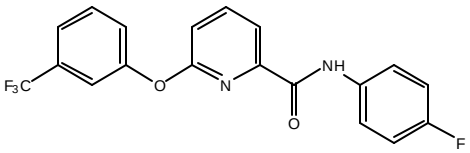
Picolinafen is not as yet registered anywhere in the world. A registration package has been submitted in Europe, where various co-formulations have been developed for the control of *Galium* species and other dicot weeds in winter cereals

CHEMISTRY AND MANUFACTURE

Active Constituent

The active constituent picolinafen is manufactured by American Cyanamid Company at Agricultural Research Centre, Quakerbridge and Clarkesville Road, Princeton, New Jersey, 08543-04000.

Chemical Characteristics of the Active Constituent

Common name:	picolinafen (ISO and Standards Australia proposed)
Synonyms and code number:	AC 900,001; CL 900001
Chemical name:	*N*-(*p*-fluorophenyl)-6-[3-(trifluoromethyl)phenoxy]-2-pyridinecarboxamide (IUPAC)
	N-(4-fluorophenyl)-6-[3-(trifluoromethyl)phenoxy]-2-pyridinecarboxamide (CAS)
CAS Number:	[137641-05-5]
Molecular formula:	$C_{19}H_{12}F_4N_2O_2$
Molecular weight:	376.3
Chemical structure:	

Physical and Chemical Properties of Pure Active Constituent and TGAC

Physical state:	solid
Colour:	white to chalky white
Odour:	musty, similar to phenol
Melting point:	107.2-107.6°C
Solubility in water (mg/mL):	3.8×10^{-5} (pH 5 buffer, 20°C)
	4.7×10^{-5} (pH 7 buffer, 20°C)
	3.8×10^{-5} (pH 9 buffer, 20°C)
	3.0×10^{-5} (deionised water, 10°C)
	3.9×10^{-5} (deionised water, 20°C)
	3.9×10^{-5} (deionised water, 30°C)
Solubility in organic solvents (mg/L at 20°C)	410 (acetone)
	3.87 (n-hexane)
	222 (toluene)
	227 (ethyl acetate)
	28.4 (methanol)
	561 (dichloromethane)

Flash point:	>180°C
Vapour pressure:	1.66 x 10^{-7} Pa at 20°C 3.84 x 10^{-7} Pa at 25°C
Octanol/water partition coefficient:	log K_{ow} = 5.37, 5.36, 5.43 and 5.36 in distilled water, buffer pH 5, 7 and 9 respectively.
Storage stability:	stable for at least 12 months at 37°C
Chemical type:	herbicide
Chemical family:	aryloxypicolinamide

Summary of the NRA's Evaluation of Picolinafen TGAC

The Chemistry and Residues Evaluation Section of the NRA has evaluated the chemistry aspects of the picolinafen TGAC (manufacturing process, quality control procedures, batch analysis results and analytical methods) and found them to be acceptable. On the basis of the data provided it is proposed that the following minimum compositional standards be established for picolinafen TGAC:

Active constituent	
picolinafen	Not less than 950 g/kg
Impurity	
4-fluoroaniline	Not more than 4 g/kg

Formulated Products - Physical and Chemical Properties

Sniper Herbicide

Formulation type:	water dispersible granule
Active constituent concentration:	750 g/L picolinafen
Physical state:	solid
Appearance:	brown free-flowing granules
Odour:	slightly musty
Density:	628 kg/m3 (pour), 693 kg/m3 (tap)
pH:	9.5-9.6 (1% w/v aqueous dispersion)
Corrosive hazard:	not corrosive
Storage stability:	The applicant provided storage stability data demonstrating that the product will be stable for at least 2 years when stored under ambient conditions in coextruded polyethylene/aluminium liner paper bags and in HDPE bottles

Paragon Herbicide

Formulation type:	emulsifiable concentrate
Active constituents concentration:	50 g/L picolinafen, 500 g/L MCPA 2-ethyl hexyl ester
Physical state:	liquid
Colour:	clear brown to amber
Odour:	slightly aromatic
Density:	1.02-1.08 g/mL at 20°C
pH:	4.1-4.4 (1% m/v dilution in demineralised water)
Kinematic viscosity:	39.7 mm2/s at 20°C
Flash point:	>105°C
Flammability/autoignition:	260°C (time lag to autoignition: 12 seconds)
Explodability:	Not classified as explosive, not sensitive to shock or heating under confined conditions.
Oxidising properties:	Not classified as an oxidising liquid
Storage stability:	The applicant provided storage stability data demonstrating that the product will be stable for at least 2 years when stored under ambient conditions in polyethylene/polyamide bottles, fluorinated PE bottles and Epivar lined tinplate cans.

Recommendation

Based on a review of the details provided by the applicant, registration of *Sniper* and *Paragon*, in relation to their Chemistry and Manufacture, is supported.

TOXICOLOGICAL ASSESSMENT

The toxicological database for picolinafen, 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 at which no adverse health effects in humans would be expected.

Toxicokinetics and Metabolism

After a single oral dose in rats, approximately half to two thirds of the administered picolinafen was absorbed. Absorption was lower after a larger dose. Less than 0.5% of the radioactivity in any orally administered dose of picolinafen was found in tissues at sacrifice. Fat, liver and kidneys contained the highest amounts of picolinafen metabolites labelled on the pyridine ring, whereas the blood, liver, spleen and lungs contained the highest amounts of picolinafen metabolites labelled on the aniline ring. Seven days after seven consecutive daily doses of radioactive picolinafen, the radioactivity found in most tissues was approximately seven times higher than that found seven days after a single dose. This, in addition to the relatively high octanol water partition coefficient (log $K_{ow} \approx 5.4$) of picolinafen, suggests that it may have the potential to accumulate in tissues. Picolinafen was metabolised by cleavage of the amide bond followed by a variety of biotranformations including N-acetylation, hydroxylation, methylation, dehalogenation and the formation of glucuronic, mercapturic and sulfate conjugates. Unabsorbed and unmetabolised parent compound accounted for $\geq$ 95% of the radioactivity found in faeces and insignificant amounts (<0.1% of administered dose) of radiolabelled picolinafen metabolites were found in exhaled air. Biliary excretion was the major route of excretion of metabolites of pyridine-ring labelled picolinafen, whereas urinary excretion was the major route of excretion of metabolites of aniline-ring labelled picolinafen.

Acute Studies

Picolinafen has low acute oral (LD_{50} >5000 mg/kg bw), dermal (LD_{50} >5000 mg/kg bw) and inhalation toxicity (LC_{50} >5900 mg/m^3) in rats. It was not a skin irritant in rabbits or a skin sensitiser in guinea pigs but it was a slight eye irritant in rabbits.

The product *Sniper* containing 750 g/kg picolinafen has low acute oral (LD_{50} >5000 mg/kg bw), dermal (LD_{50} >4000 mg/kg bw) and inhalation (LC_{50} >3830 mg/m^3) toxicity in rats. It was not a skin irritant in rabbits or a skin sensitiser in guinea pigs but it was a slight eye irritant in rabbits.

The product *Paragon* containing 50g/L picolinafen and 500 g/L MCPA has low acute oral (LD_{50} = 1768 mg/kg bw), dermal (LD_{50} >4000 mg/kg bw) and inhalation toxicity (LC_{50} >5180 mg/m^3) in rats. It was a moderate skin and eye irritant in rabbits but was not a skin sensitiser in guinea pigs.

Short-Term Studies

All mice fed picolinafen at dietary concentrations of 0, 100, 1000, 2000, 3500 or 7000 ppm for 28 days survived, but body weight gain was reduced in males at 7000 ppm. Discolouration of the extremities, discoloured organs (kidney, liver, lungs, testes and heart) and haematological changes (increased MCH, MCHC, reticulocyte and Heinz bodies numbers) were observed at 3500 and 7000 ppm. Spleen and liver weights were increased at ≥ 2000 ppm and the breakdown products of blood cells accumulated in the liver and spleen and the production of blood cells in the spleen were increased in males at ≥ 1000 ppm and females at ≥ 2000 ppm. The severity of these histopathological changes increased in a dose-related manner.

In a study in which groups of two dogs per sex were fed picolinafen at dietary concentrations of 0, 100, 1000, 2000, or 10000 ppm for 28 days, food consumption and body weight gain were reduced at 10000 ppm. Haemoglobin, Hct and RBC were reduced at 10000 ppm and reticulocyte counts were increased in females at ≥ 2000 ppm. Livers were enlarged, liver weights and liver glycogen increased and serum cholesterol was increased in males at ≥ 1000 ppm and females at ≥ 2000 ppm. Thyroid weight was increased in a dose-related manner in dogs at all doses and thyroid enlargement accompanied by histopathological changes was observed at ≥ 1000 ppm.

In mice fed picolinafen at dietary concentrations of 0, 50, 500, 1000 or 2000 ppm for 13 weeks, food consumption was decreased in males at 1000 and 2000 ppm. Haemoglobin, Hct and RBC were slightly reduced and MCH, MCHC, reticulocyte counts and Heinz body numbers were increased at ≥1000 ppm. Liver weight and pigment deposition were increased at 2000 ppm with other histopathological changes observed in the liver of males at ≥ 500 ppm and females at ≥1000 ppm. The spleens of some mice were enlarged and spleen weights were increased in females at ≥1000 ppm. Pigment deposition was increased in the spleen at ≥ 500 ppm and extramedullary haematopoiesis was increased in females at ≥ 500 ppm males at ≥1000 ppm. The NOEL in this study was 50 ppm, equal to 10 mg/kg bw/day in males and 13 mg/kg bw/day in females.

In rats fed picolinafen at dietary concentrations of 0, 80, 400 or 800 ppm for 13 weeks body weight gain was slightly reduced in females at 800 ppm. Haemoglobin, Hct and RBC were reduced at 400 and 800 ppm and MCV was increased at 800 ppm. Spleen weights were

increased at 400 and 800 ppm in males and 800 ppm in females. Liver to body weight ratios were increased in males at 800 ppm and females at 400 and 800 ppm. Pigment deposition was increased in the liver and spleen at 400 and 800 ppm. The NOEL in this study was 80 ppm, equal to 6.4 mg/kg bw/day in males and 6.8 mg/kg bw/day in females.

In groups of four dogs per sex fed picolinafen at dietary concentrations of 0, 50, 500 or 2500 ppm for 90 days haemoglobin, Hct and RBC were reduced in females at 500 and 2500 ppm and males at 2500 ppm. Serum cholesterol was slightly increased in females at 500 and 2500 ppm and in males at 2500 ppm. Thyroids were enlarged at 2500 ppm and thyroid weights were increased in males at ≥500 ppm and in females at 2500 ppm. Liver weights were increased in males at 2500 ppm. Follicular hypertrophy was observed in the thyroid at 500 and 2500 ppm with hyperplasia at 2500 ppm. The NOEL in this study was 50 ppm equal to 1.7 mg/kg bw/day in males and 1.8 mg/kg bw/day in females.

Long-Term Studies

In mice fed picolinafen at dietary concentrations of 0, 40, 400 or 800 ppm for 18 months, there was no increase in the incidence of neoplasms. Body weight gain was slightly reduced in males at 800 ppm. Reticulocyte counts were increased at 3 months in males at 400 and 800 ppm. Increased liver weights and histopathological changes were observed in females at 800 ppm with histopathological changes observed in the livers of males at 400 and 800 ppm. Splenic enlargement was slightly increased in incidence in females at 400 and 800 ppm. Extramedullary haematopoiesis was observed in the spleens of mice at 800 ppm with increased pigment deposition observed in males at 800 ppm and females at 400 and 800 ppm. The NOEL in this study was 40 ppm, equal to 6.9 mg/kg bw/day for males and 8.2 mg/kg bw/day for females.

In rats fed picolinafen at dietary concentrations of 0, 50, 250, or 500 ppm for 24 months there was no increase in the incidence of neoplasms. Haemoglobin, Hct and RBC were reduced at 3 and 6 months only at 250 and 500 ppm. Spleen weights were increased at 500 ppm and the amount of brown pigment observed in the spleen was increased at 250 and 500 ppm at both 12 and 24 months. The NOEL in this study was 50 ppm, equal to 2.4 mg/kg bw/day for males and 3.0 mg/kg bw/day for females.

In dogs fed picolinafen at dietary concentrations of 0, 50, 150 or 1500 ppm for 12 months body weight gains were decreased in all groups of treated males. Haemoglobin, Hct and RBC were transiently reduced and platelet counts increased throughout treatment in females at 1500 and platelets transiently increased in females at 150 ppm. MCV was increased throughout treatment in males at 1500 ppm. Enlarged thyroids and increased thyroid weights were observed at 1500 ppm. Increased follicular hypertrophy in the thyroid was observed in both sexes at 1500 ppm and hyperplasia in the thyroid was observed in females at 1500 ppm. A NOEL could not be established in this study since body weight gain was reduced at all tested doses. The LOEL in this study was 50 ppm, equal to 1.4 mg/kg bw/day in males and 1.6 mg/kg bw/day in females.

Reproduction and Developmental Studies

Rats were fed picolinafen at dietary concentration of 0, 50, 250 or 500 ppm in a two-generation reproduction study. Food consumption was slightly increased in F_0 rats at 250 and 500 ppm and F_1 parental rats at 500 ppm prior to mating. Consistent haematological alterations across the generations included reduced Hb, Hct and RBC and increased MCHC, MCV and reticulocyte and leukocyte counts. These changes were generally observed at 500 ppm with some parameters affected at 250 ppm. In adult rats, liver weight was increased in males at 500 ppm and spleen weight was increased in females at 250 ppm and both sexes at 500 ppm. The spleen also showed congestion, increased amounts of brown pigment and extramedullary haematopoiesis at 250 and 500 ppm. In neonates, the only finding was haematological changes at 250 and 500 ppm. Fertility and reproduction were unaffected at any dose. The NOEL in this study is 50 ppm, equal to 3.7 mg/kg bw/day for males and 4.2 mg/kg bw/day for females.
Picolinafen was given to pregnant rats by oral gavage at 0, 100, 500 or 1000 mg/kg bw/day on days 6 to 19 of gestation. One dam at 1000 mg/kg bw/day appeared emaciated and body weight losses associated with reduced food consumption were observed on days 6-12 of gestation at ≥ 500 mg/kg bw/day. Spleen weights were increased in dams at ≥100 mg/kg bw/day and liver to body weight ratios were slightly increased at ≥ 500 mg/kg bw/day. Haemoglobin, Hct and RBC were reduced and MCV, MCH, MCHC and nucleated red blood cell and reticulocyte counts were increased in all treated groups. The incidence and severity of extramedullary haematopoiesis and haemosiderosis in the spleen was increased in a dose dependent manner in all treated groups. The incidence of bipartite ossification in the thoracic vertebrae in foetuses at 1000 mg/kg bw/day was increased, but no other alterations were observed. Since a NOEL for maternal toxicity was not established in this study, a follow-up study using 0, 5, 25 or 50 mg/kg bw/day was conducted. No treatment-related effects were observed on dams or on foetal development. The NOEL for maternal toxicity was 50 mg/kg bw/day and the NOEL for foetal toxicity was 500 mg/kg bw/day.

In a developmental study, picolinafen was given to rabbits by oral gavage at 0, 5, 20 or 50 mg/kg bw/day on days 6-28 of gestation. Soft or liquid faeces were observed at 50 mg/kg bw/day and body weight gain and food consumption were reduced at 20 and 50 mg/kg bw/day. Haemoglobin, Hct and RBC were slightly reduced and MCV and reticulocyte counts slightly increased at 20 and 50 mg/kg bw/day. Congestion and haemosiderosis in the spleen were increased in incidence and severity at 20 and 50 mg/kg bw/day and increased extramedullary haematopoiesis was observed at 50 mg/kg bw/day. The number of resorptions was slightly increased at 50 mg/kg bw/day and an increased incidence of fused sternal centra was observed in foetuses at 50 mg/kg bw/day. The NOEL for maternal toxicity in this study was 5 mg/kg bw/day and the NOEL for embryotoxicity and foetotoxicity was 20 mg/kg bw/day.

Genotoxicity

Picolinafen did not increase the incidence of gene mutation in bacterial or mammalian mutation assays *in vitro*. It did not induce formation of micronuclei in mouse bone marrow cells *in vivo* nor did it increase the frequency of chromosomal aberrations in mammalian cells *in vitro*.

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 States' poisons regulations to prevent the occurrence of poisoning. On the basis of its toxicity, the NDPSC has recommended that picolinafen need not be included in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP).

NOEL/ADI

Amongst the species tested, dogs were the most sensitive to the effects of picolinafen. Since reduced body weight gain was observed in males at all tested concentrations, a NOEL could not be established in a 1-year dog study. The LOEL in this study was 1.4 mg/kg bw/day. To reflect the use of a LOEL to establish the ADI and considering the nature of the endpoint, an additional 2-fold safety factor was applied. Thus an ADI of 0.007 mg/kg bw/day for picolinafen was established by using the dog study LOEL of 1.4 mg/kg bw/day and a 200-fold safety factor.

RESIDUES ASSESSMENT

The Chemistry and Residues Evaluation Section of the NRA has undertaken a residues assessment of two formulated products based on the new active constituent picolinafen. *Sniper* is a water dispersible granular formulation (WDG) containing 750 g/kg picolinafen. *Paragon* is an emulsifiable concentrate (EC) formulation containing 50 g/L picolinafen and 500 g/L MCPA as the active ingredients. Data concerning picolinafen residues in lupins and cereals, metabolism in crops and animals, environmental fate and chemistry were considered as part of the residue evaluation of the application. Since MCPA is currently registered for use on cereals at rates higher than proposed on the *Paragon* label, no data were provided relating to MCPA residues in crops.

Metabolism

Plant metabolism studies using ^{14}C-labelled picolinafen were provided for wheat and lupin. Most of the radioactive residues (50-95% TRR) in wheat and lupins were present as the parent compound, in straw and foliage at the various sampling times. Parent residues declined over time, and at harvest parent accounted for 50% of the TRR. The metabolite CL153815 {6-[3-trifluoromethyl)phenoxy]-2-pyridine carboxylic acid}, which is produced from cleavage of the amide bond in picolinafen, accounted for <9% of TRR in wheat foliage 86 days after treatment with *Sniper*. None of this metabolite was detected in the lupin metabolism study. Translocation of residues into the seeds and untreated parts of the plant was minimal.

Animal metabolism studies using ^{14}C-labelled picolinafen were provided for rats and lactating goats. The animals were orally administered labelled picolinafen at nominal dose rates of 5 and 50 ppm in the feed. In goats, >90% of the radioactive dose was eliminated in the faeces and urine within 48 hours of administration. The major residue in urine was picolinafen (ca. 85%) and in faeces was the metabolite CL153815 (ca. 85%). Radioactivity in tissues, blood and milk accounted for <1% of the administered dose. Highest radioactive residues in tissues were present in liver and kidney, with the major residue component being the metabolite CL153815. Residues in milk and fat were only detected in animals administered the exaggerated dose. In these cases, picolinafen was the highest residue in fat while milk contained several metabolites including CL153815, at comparably low levels. No picolinafen parent residues were found in any tissue or milk when dosed at the nominal low level of 5 ppm in the feed.

The first step in the metabolism of picolinafen in animals involves cleavage of the amide bond between the pyridine and aniline ring systems, to give CL153815 and 4-fluoroaniline. The metabolite CL153815 undergoes no further significant transformation, while fluoroaniline is rapidly transformed into a number of structurally related compounds and conjugates.

Residue Definition

The plant metabolism studies support a residue definition of parent compound. In animals, however, the major residue component in tissues is the metabolite CL153815.
On this basis the definition of the picolinafen residue should be:
in commodities of plant origin: Picolinafen (parent compound), and
in commodities of animal origin: Sum of picolinafen and {6-[3-trifluoromethyl)phenoxy]-2-pyridine carboxylic acid} (metabolite CL153815).
The residue analytical method provided is capable of determining both picolinafen (parent) and the metabolite CL153815 in animal commodities.

Analytical methods

Determination of picolinafen in lupin and cereals
Validated analytical methods were used to determine picolinafen residues in cereals and lupin commodities. The methods involve extraction of the residues from the plant samples with acetone, which are then partitioned between ethyl acetate and brine and concentrated before purification using gel permeation chromatography. For lupin commodities the residues are quantified by HPLC with UV detection, and confirmed using GC with NPD detection. For cereal commodities, picolinafen is quantified using GC with NPD detection, and confirmed using GC with MSD detection. The methodology is considered adequate for determination of picolinafen residues in cereal and lupin commodities. The LOQ of the methods was determined to be 0.05 mg/kg for foliage and 0.02 mg/kg for grain and straw samples.

Determination of picolinafen (and metabolite) in animal tissues, fat and milk
A validated analytical method was used to determine picolinafen and metabolite CL153815 {6-[3-trifluoromethyl)phenoxy]-2-pyridine carboxylic acid} residues in muscle, eggs, milk and fat. The method involves extraction of the residues from the samples with acetonitrile and partitioning into heptane or ethyl acetate. The crude extracts are cleaned up by gel permeation chromatography and analysed by reverse phase HPLC/MS/MS. The methodology is considered adequate for determination of picolinafen and {6-[3-trifluoromethyl)phenoxy]-2-pyridine carboxylic acid} residues in tissues and milk. The LOQ of the method was determined to be 0.01 mg/kg for milk and 0.02 mg/kg for tissues, egg and fat for both picolinafen parent and the major metabolite, CL153815. The LOD for these commodities was 0.001 and 0.002 mg/kg, respectively.

Storage stability

A storage stability study of picolinafen was presented in the application. Picolinafen residues were stable on storage at -18°C for up to 12 months in cereal grain, straw and foliage samples.

Residue Trials

Lupins
Five Australian residue trials were presented. Picolinafen (as *Sniper*) was applied to the lupin crops at the 2-6 leaf stage according to the maximum label rate of 37.5 g ai/ha, and at 48, 75 and 96 g ai/ha. In lupin grain, all samples contained residues at or below the LOQ of 0.02 mg/kg when harvested 94-138 days after treatment at either 1× or 1.3× the label rate. The residue data support an MRL of *0.02 mg/kg for picolinafen in lupins. No harvest WHP is considered necessary when the product is used as directed.

Processing studies
No processing studies were provided. As lupins are only a minor human food commodity in Australia, and are not processed prior to use as an animal feed, processing studies are not considered necessary in this instance.

Cereals
Five Australian residue trials were presented. Picolinafen was applied to the cereals at the late tillering growth stage, at rates of 18 and 36 g ai/ha using the 750 g/kg WDG formulation (*Sniper*) and at 25 and 50 g ai/ha using the 50 g/L EC formulation *(Paragon)*. Residues in cereal grains harvested 95-126 days after treatment were present at <0.02 mg/kg at all application rates from 18-36 g ai/ha (0.7-1.4× label rates). An MRL of *0.02 mg/kg is recommended The residue data support the applicant's proposed MRL of *0.02 mg/kg for picolinafen in cereal grains. No harvest WHP is considered necessary when the product is used as directed.

Processing studies
Since no detectable residues of picolinafen were observed in cereal grains, no processing studies were provided. Grain commodities may be processed to give flour and other milled products. In the absence of detailed studies no MRLs are recommended for processed commodities. The MRL of the whole commodity (RAC) also applies to any processed commodities.

Animal Feed Commodity MRLs

Lupin straw and forage
When treated with picolinafen at 1× and 1.3× the maximum label rate, straw harvested 83-138 days after treatment contained picolinafen residues below the limit of analytical quantitation of 0.02 mg/kg. To simulate a failed crop situation, crops were also treated with picolinafen at 1× and 1.3× the maximum label rate and harvested prior to plant maturity between 10-45 days after application with picolinafen. Residues in forage harvested 36-43 days after application ranged from <0.33 to 0.93 mg/kg on a dry weight basis. An MRL of *0.02 mg/kg is recommended for Lupin straw (dry) and 2 mg/kg for AL 0545 Lupin, forage (dry). The following WHP statement is required for lupin treated with picolinafen:
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION.

Wheat straw and forage
Five Australian trials on wheat using a post-emergent application of picolinafen were conducted at 0.7, 1.0, 1.4 and 2.0× (18, 25, 36 and 50 g ai/ha) the maximum label rate. Forage was sampled up to 43 days after application with picolinafen, and straw was sampled at harvest of mature

plants. Residues in wheat forage harvested 35-43 days after treatment at 0.7 – 1.4× label rates were <0.05 mg/kg (fresh weight), and <0.3 mg/kg on a dry weight basis allowing for moisture content in the samples. Residues in straw at harvest were <0.02 mg/kg when treated at 0.7-1.4× label rates.

Barley straw and forage
Five Australian trials on barley using a post-emergent application of picolinafen were conducted at 0.7, 1.0, 1.4 and 2.0× (18, 25, 36 and 50 g ai/ha) the maximum label rate. Forage was sampled up to 43 days after application with picolinafen, and straw was sampled at harvest of mature plants. Forage harvested 35-43 days after application of picolinafen contained residues below the 0.05 mg/kg on a fresh weight basis, and <0.4 mg/kg on a dry weight basis, when treated at 0.7 and 1.0× label rates. Finite residues were detected at higher rates in some forage samples. Overall, residues in forage were <0.5 mg/kg (dry weight) when treated at 0.7, 1.0 and 1.4× the maximum label rate of 25 g ai/ha. Residues in straw were present at <0.02 mg/kg in all samples treated at 0.7, 1.0 and 1.4× label rates.

Oat straw and forage
Five Australian trials on oats using a post-emergent application of picolinafen were conducted at 0.7, 1.0, 1.4 and 2.0× (18, 25, 36 and 50 g ai/ha) the maximum label rate. Forage was sampled up to 43 days after application with picolinafen, and straw was sampled at harvest of mature plants. Residues were present in oat forage at <0.3 mg/kg in all samples treated at 0.7, 1.0 and 1.4× the maximum label rate except for one samples treated at 25 g ai/ha (1×), which contained picolinafen residues at 0.40 mg/kg. Overall, residues in forage were <0.5 mg/kg (dry weight) when treated at 0.7, 1.0 and 1.4× the maximum label rate of 25 g ai/ha. Straw contained residues at <0.02 mg/kg in all samples treated at 0.7, 1.0 and 1.4× the maximum label rate.

In summary, cereal forage harvested 35-43 days after application of picolinafen at the maximum label rate of 25 g ai/ha contained picolinafen residues at <0.5 mg/kg on a dry weight basis. Cereal straw contained residues at <0.02 mg/kg when treated at the label rate. The residue data support an MRL of 0.5 mg/kg for cereal forage and *0.02 mg/kg for cereal straw. The following WHP statement is required for cereals treated with picolinafen:
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION.

Animal Commodity MRLs

No animal transfer studies were provided by the applicant. Residues in animal feed commodities from treated crops were below the analytical limit of quantitation in the fresh commodities when treated at label rates. Metabolism studies show that only a small proportion of the administered dose is transferred to tissues. Picolinafen is rapidly metabolised by initial cleavage of the amide bond to give CL153815 as the predominant metabolite, which is present mainly in liver and kidney. 4-Fluoroaniline, which is the other portion of the cleaved picolinafen molecule, is metabolised further to structurally related fluoroaniline derivatives and conjugates.

When *Sniper* and *Paragon* are used according to the maximum label rates, residues are expected to be <0.02 mg/kg in lupin and cereal (grain and straw) and <0.5 ppm in cereal forage (dry weight). The maximum residue in lupin forage treated at the label rate and harvested 36-38 days post application was 0.64 mg/kg (dry weight). Since it is unlikely that animals will be fed a diet

containing any single treated commodity, it is estimated that a typical diet containing a mixture of treated lupin and cereal commodities may contain picolinafen residues up to 0.5 ppm. This level of picolinafen residues in a typical animal feed is considered to be conservative, given the very low picolinafen residues expected in straw and grains, which may comprise a significant proportion of an animal feed mixture.

At this level of consumption, residues of picolinafen (unchanged parent) in fat are estimated, from the goat metabolism study, at 0.002 mg/kg. Residues of the major metabolite in liver and kidney are estimated at 0.006 and 0.02 mg/kg, respectively, and 0.0002 mg/kg in milk. Based on these calculations the following MRLs are recommended: mammalian offal (0.05 mg/kg), mammalian meat [in the fat] (*0.02 mg/kg) and milk (*0.01 mg/kg). In the absence of poultry metabolism or feeding studies, no MRLs were set for poultry commodities. Detection of picolinafen residues in these commodities would constitute a violation.

Estimated Dietary Intakes

The national estimate of dietary intake of picolinafen from the proposed use pattern is approximately 4% of the ADI of 0.003 mg/kg bw/day, using ANZFA's mean consumption figures of 1995 for consumers aged 2 years and above.

Bioaccumulation Potential

Although the log octanol/water partition coefficient of 5.4 indicates that picolinafen has the potential to bioaccumulate, animal metabolism studies show that picolinafen is not stored or readily accumulated in tissues or milk. The majority of the administered dose is excreted in urine and faeces, and the remainder is metabolised to give the metabolite CL153915 as the predominant residue in tissues.

Recommendation for Registration

Based on a review of the relevant residue data provided by the applicant, registration of *Sniper*, for use on narrow-leaf lupins, and *Paragon*, for use on cereal crops, is supported.

Recommended amendments to the MRL Standard:

Table 1

Compound	Food		MRL (mg/kg)
ADD:			
Picolinafen			
	VD 0545	Lupin seed (dry)	*0.02
	GC 0080	Cereal grains	*0.02
	MM 0095	Meat (mammalian) [in the fat]	*0.02
	MO 0105	Mammalian offal	0.05
	ML 0106	Milks	*0.01

* Denotes MRL set at or about the limit of analytical quantitation

The MRL recommendations indicated above will be conveyed to the Australia and New Zealand Food Authority (ANZFA) for consideration for incorporation into Standard A14 of the Food Standards Code and consequent adoption into the State/Territory food legislation.

Table 3

Compound	Residue Definition
ADD:	
Picolinafen	Commodities of plant origin: *Picolinafen* Commodities of animal origin: *Sum of picolinafen and 6-[3-trifluoromethyl)phenoxy]-2-pyridine carboxylic acid.*

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
ADD:			
Picolinafen			
	AL 0545	Lupin forage	2
		Lupin straw (dry)	*0.02
		Forage of cereal grains (green)	0.5
	AS 0081	Straw and fodder (dry) of cereal grains	*0.02

The following WHPs are recommended in relation to the above MRLs for *Sniper* and *Paragon*:

Grazing
DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION

Crop Harvest
NOT REQUIRED WHEN USED AS DIRECTED

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Overseas Registration Status

Picolinafen is not registered for use in any other country, and no overseas MRLs have been established.

CODEX Alimentarius Commission MRL

CODEX has not established an MRL for picolinafen.

Potential Risk To Australian Export Trade

In assessing the risk to Australian export trade the destination, volume and value of lupin seed and cereal grains exported was considered. In 1998-9 Australia's total production of lupin (seed) was 1421 kt. Approximately 70% (970 kt) of lupin produced in Australia is exported for use as the protein component for cattle and pig diets, with the primary markets being Germany, Spain, Portugal and Italy, Japan and South Korea. The value of lupin exports in that year was about $170m.

Australia's trade in cereal grains is very large. In 1996/7, Australia's export of wheat was valued at $4346m, the major importers of Australian wheat being China, Indonesia, Iran and Japan. Export of barley was valued at $989m, with major markets being Japan, Saudi Arabia and China. Oats are a much smaller export commodity than wheat and barley. In 1996/7 Australia exported oats valued at $26m, and the major destinations for Australian oats are not known.

Products containing picolinafen as the active ingredient are not registered for use in any overseas country, and no overseas MRLs exist for picolinafen. Any detection of picolinafen residues by importers of treated produce would constitute a violation and therefore present a risk to Australian trade in lupin and cereal commodities.

However, residue trial data show that quantifiable residues in treated grain (lupin and cereal) are not expected, and detection of residues in treated produce by importing countries is therefore unlikely. Metabolism data show that neither picolinafen nor the major metabolite CL153815 accumulates in animal tissues or milk, and therefore animals feeding on treated produce are not expected to contain residues. On this basis, the actual risk to Australian trade is low and the risk is considered acceptable.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

NOHSC has conducted a risk assessment on *Sniper* containing picolinafen at 750 g/kg as a water dispersible granule formulation and *Paragon* containing picolinafen at 50 g/L and MCPA at 500 g/L as an emulsifiable concentrate formulation. It is proposed to use *Sniper* for the post-emergence control and/or suppression of annual broadleaf weeds in narrowleaf lupins and *Paragon* for the control of certain broadleaf weeds in winter cereals. *Sniper* and *Paragon* can be safely used by workers when handled in accordance with the control measures indicated in this assessment.

Picolinafen is not on the NOHSC *List of Designated Hazardous Substances*.
Picolinafen cannot be classified as a hazardous substance.

Picolinafen is in the form of a white powder with a faint musty odour. It has low acute oral, dermal and inhalation toxicity in rats. It is not a skin irritant but is a slight eye irritant in rabbits. It is not a skin sensitising agent in guinea pigs.

Sniper possesses low acute oral, inhalation and dermal toxicity in rats. The product is a slight eye irritant in rabbits. *Sniper* cannot be classified as hazardous.

Paragon has low acute oral, dermal and inhalation toxicity in rats. Data show the product to be a moderate skin irritant and eye irritant in rabbits, but not a skin sensitiser in guinea pigs. *Paragon* is classified as hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1999b) based on its skin and eye irritation properties. This classification is based on the MCPA component, which is the same as that for numerous other MCPA products that are registered for comparable use patterns.

Formulation, repackaging, transport, storage and retailing

Sniper will be formulated overseas and imported into Australia in 500g, 2kg and 4kg high density polyethylene (HDPE) bottles with neck diameters of 38 and 63 mm respectively. *Paragon* also will be formulated overseas and imported into Australia in 5 L epon-lined tinplate can and 10 and 20 L epon-lined mild steel drums with neck diameters of 44 and 56 mm respectively. Transport workers, store persons and retailers will handle the packaged products and could only become contaminated if the packaging were breached.

Advice on safe handling of the products during routine use is provided in the Material Safety Data Sheets (MSDSs) for *Sniper* and *Paragon*.

Use and Exposure

Sniper is proposed for the post-emergence control and/or suppression of annual broadleaf weeds in lupins. The proposed rate is 33-50 g/ha in a minimum of 50L water/ha for ground application. *Paragon* is indicated for the post-emergence control and/or suppression of annual broadleaf

weeds such as wild radish (*Raphanus raphanistrum*), mustard (*Sisymbrium* spp) and capeweed (*Arctotheca calendula*) in winter cereals. The proposed rate is 250-500 mL/ha in a minimum of 50L water/ha for ground application, or a minimum of 30 L water/ha for aerial application. Either product is expected to be used no more than once per crop.

The primary route of occupational exposure is dermal, inhalational and ocular. Workers can be exposed to the products while mixing, loading, spraying, cleaning up spills and equipment or when re-entering treated areas.

In the absence of worker exposure data on picolinafen and the product, NOHSC used the UK Predictive Exposure Model (POEM) and margin of exposure (MOE) to determine worker exposure.

Results from POEM estimates show that workers require personal protective equipment (PPE) when mixing/loading and during application of *Sniper* and *Paragon*. To protect workers from repeated exposure the use of PPE is recommended.

During aerial application, pilots will be protected from direct contact with the spray. However, the use of human flaggers is possible in aerial operations. Exposure of these workers cannot be quantified and POEM estimates showed a high risk from spray. The use of human flagging is not acceptable unless flaggers are protected by engineering controls such as vehicles with cabs.

Entry into Treated Areas or Handling Treated Crops

The main route of exposure upon re-entering sprayed areas is via dermal contact.

Crops are only treated once with a single application of either product, therefore exposure to residues when re-entering treated fields is expected to be limited in time. In addition, re-entry is not expected immediately after spraying. Re-entry statements are recommended for *Sniper* and *Paragon*.

Recommendations for Safe Use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of cotton overalls, a washable hat, face shield or goggles and elbow-length PVC gloves. The PPE recommended should meet the relevant *Standards-Australia* standards specified below:

AS 3765-1990	Clothing for protection against hazardous chemicals
AS 2161-1978	Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)

Re-entry Statements

Sniper

"Do not allow entry into treated areas until spray has dried. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist and a washable hat and chemical resistant gloves. Clothing must be laundered after each day's use".

Paragon

"Do not allow entry into treated areas for 24 hours. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist a face shield or goggles and chemical resistant gloves. Clothing must be laundered after each day's use".

Precautionary Statement

"Precaution: Do not use human flaggers unless they are protected by engineering controls such as vehicles with cabs."

ENVIRONMENTAL ASSESSMENT

Introduction

Cyanamid Aust Pty Ltd has applied for the registration of two products, *Sniper* and *Paragon*, which contain the new active, picolinafen. This active is of the aryloxypicolinamide type and its proposed use is for the post-emergent control of a range of broadleaf weeds in lupins and cereal crops.

Environmental Fate

Hydrolysis

A preliminary study at 50°C in sterile buffered solutions at pH 4, 7 and 9 showed that there was no significant degradation of picolinafen at any pH level.

Photolysis

In two studies conducted according to SETAC and OECD Guidelines, aquatic photolytic half-lives were ~23-31 days for buffered solutions of pH 5, 7 and 9 and ~12 days at pH 7, respectively. A similar study investigated the photolysis of the major metabolite CL 153,815 (picolinic acid moiety) at pH 5, 7 and 9, but photolysis was very slow at pH 5 and did not occur at higher pHs. In soil the degradation was similar and after 15 days only 30% degradation occurred. The half-life was calculated as 30 days. The lamps/filters used for these studies provided exposures similar to natural sunlight in Schwabenheim, Germany, during late summer.

Photolysis on soil under Australian autumn conditions might be expected to be a route of degradation, given the use pattern, but photolysis in water and on soil appear to be relatively slow.

Metabolism

In three aerobic soil degradation studies, conducted to meet EC/BBA requirements, the half-lives in sandy/loamy soils were 1-2, and 10-14 days (at 20 ^{o}C) or 7 days (at 8 ^{o}C). There were two principal metabolites identified, CL 153,815, which peaked between 25-45% of applied label in all studies and 4-fluoroaniline, and both rapidly bound to soil, with soil bound label reaching >60% of applied material after 4 months. Significant amounts of $^{14}CO_2$ (28-50% AR) were produced in one test and 12-30% in the others, indicating further soil degradation of these products.

A soil anaerobic study was conducted according to SETAC guidelines and degradation of picolinafen occurred similarly to the aerobic tests, but complete mineralisation to CO_2 appears much slower. The half-life in this test was 6-7 days, but much of this degradation may have occurred while conditions were largely aerobic.

Two ready biodegradation tests were performed using synthetic and natural sewage according to OECD Guidelines. There was little biodegradation of picolinafen during the tests, but it was non-toxic to the inoculum. Picolinafen is rated as not readily biodegradable.

In an aerobic/anaerobic aquatic degradation study, conducted to satisfy EC requirements two water-sediment systems (river and pond) were used and dosed with picolinafen or the metabolite CL 153815. Picolinafen and the metabolite partition rapidly to sediment where they have half-lives of ~13 days and ~140 days, respectively. Picolinafen degrades readily in aquatic conditions, however, it is likely to go to sediment, due to the low water solubility and high K_{oc}, but where degradation products may persist longer.

Mobility

Two batch adsorption/desorption studies were performed according to OECD Guidelines using 4 different soils from Germany. In the first, K_{oc} values were relatively low (100-2000), caused by the low solubility for picolinafen and data points being limited. An identical repeat study with greater detail was conducted in the US using the same soils and this achieved much higher K_{oc} values (15-32 000). Desorption occurred at a relatively low rate.

A further study using the same four soils, but equilibrated with the major metabolite CL153815, gave K_{oc} values (400-800), which are lower than the parent, and it was desorbed at similar rates. This is typical of an ionisable entity more dependent on other soil characteristics (pH, CEC). No specific study was conducted for adsorption of the other major metabolite (CL7693), however, this moiety became strongly bound to soil during degradation studies.

Three column leaching studies used fresh and aged material on a range of eight different soils, generally sandy loams and silt loams. The vast majority of the applied picolinafen or metabolites were detected in the surface layer (0-5 or 0-10 cm) with very little appearing in leachate (mostly <0.1%).

Picolinafen and its major metabolites can be rated as immobile in soils.

Surface Volatility

Losses were assessed in a volatility chamber after picolinafen was sprayed onto mature bean plants and soils. Recoveries from soils averaged 97% and 91% from plants and these were basically constant during the 24 hours test. The residue was entirely parent compound indicating volatile losses and degradation were negligible.

Field Studies

There were 8 field dissipation studies performed in Europe and the first order half-lives were calculated as between 9-64 days for picolinafen applied to bare soils at ~200 g ai/ha. Picolinafen was not detected in any soil below 10 cm, nor was the principal metabolite, CL 153,815, which had half-lives in the range of 40-131 days. Picolinafen may range from readily degradable to

fairly degradable in soils with the main metabolites (picolinic acid moiety and 4-fluoroaniline) somewhat slower to degrade. However, both these appear to bind strongly to soil.

Environmental Toxicity

Avian
In acute oral and dietary toxicity tests on mallards and bobwhite quail, conducted to US EPA and SETAC guidelines, there were few treatment related effects noted at the maximum doses used, approximately 2000 mg/kg bw and 5000 mg/kg (in feed), respectively. Dose related histological effects were noted in one dietary study at >1968 mg/kg in feed. There were no reproductive effects in the long-term reproductive studies with picolinafen up to 864 mg/kg in the feed. Picolinafen is rated as practically non-toxic to birds in respect of mortality, but as moderately to slightly toxic based on the chronic 8-day quail trial.

Aquatic
The acute studies on fish and daphnia using both ai and product, conducted to meet US EPA and EEC requirements, showed no effects at the maximum concentrations used, 280-680 µg/L, noting the solubility limitations of this compound. Similarly, the chronic toxicity studies for fish showed no effects at the maximum test levels (~100 µg/L), but in the early life-stage test over 90 days picolinafen did affect the growth of fry at concentrations >12 µg/L. Chronic tests showed daphnia were highly sensitive with maximum acceptable toxicant concentrations (MATCs) of 4-10 µg/L, however, in a benthic test midge larvae were at least an order of magnitude less sensitive (290 µg/L). Picolinafen rates as potentially highly toxic in the acute tests where no effects are noted, but exposure levels were low due to its low solubility. In chronic tests it does cause adverse effects at very low concentrations within its solubility range, and is ranked as very highly toxic to fish and daphnia based on these studies, noting there is a high ratio for the acute:chronic test results.

Acute tests with the main metabolite (CL 153,815), which is much more soluble than the parent is, indicate that this metabolite is practically non-toxic to fish and daphnia.

In US EPA Tier 2 studies there were adverse effects on freshwater algae at extremely low concentrations (0.12-0.18 µg ai/L nominal), which correspond to ~200 X less than the EEC (25 µg/L) from direct overspray of a 15 cm pond using the maximum Australian use rate, but less so to blue-green algae (LC_{50} 340 µg ai/L). In a test conducted to US EPA requirements, picolinafen was toxic to duckweed, with an LC_{50} (biomass) of 57 µg ai/L. The metabolite (CL 153,815) appears much less active and the single test result ranks the metabolite as slightly toxic to green algae.

Non-target invertebrates
In studies conducted to EC and OECD requirements, picolinafen was non-toxic to bees and earthworms. Likewise, the major metabolite (CL 153,815) does not affect earthworms. Picolinafen and the metabolite did not affect the respiration or nitrification of soil microbes at 100 g ai/ha and is therefore considered non-toxic to these microbes at the proposed lower rates for use in Australia (12-38 g ai/ha). "Beneficial" invertebrate species (parasitic wasp, predatory mite, beetle and spider) were studied and the effects of were generally harmless to this range of non-target organisms at these test exposures, approximating maximum European field rates.

Phytotoxicity

Little specific plant test information was provided, but as a herbicide effective at low dose rates picolinafen is likely to adversely effect non-target plants if they are directly contacted by spray drift. Some data on crop and weed tolerances indicate adverse effects on both plant groups (grasses and broad leafs) that were directly sprayed. However, the short aerobic soil half-lives indicate other exposure routes, eg with run-off erosion, are likely to be limited, noting the very high toxicity to algae and aquatic plants. The combination product *Paragon* (with MCPA) can be expected to exacerbate this hazard to algae and aquatic plants since MCPA is a selective herbicide with a different mode of action, and toxic effects are expected to be additive in susceptible plants.

Prediction Of Environmental Hazard

Picolinafen will be used for the post-emergent control of a limited spectrum of broadleaf weeds in lupins and cereal crops in NSW, Victoria, SA and WA. The products will be applied at a rate of 25-38 g ai/ha for lupins and 12-25 g ai/ha for cereals, largely using boom sprayers and flat fan nozzles in dryland farming areas. Application is during the early growth stages of the crops. While off-target damage is possible through spray drift, herbicide applied to the target area should be associated mostly with the soil compartment and movement from the crop site limited to run-off during heavy rain events.

Exposure of non-target organisms may occur through direct contact with spray drift, run-off or from ingestion of residues on vegetation, soil or sprayed insects. Volatilisation from plant or soil surfaces is unlikely to occur.

Terrestrial organisms
Birds could be exposed to picolinafen from residues on sprayed plants or insects. Picolinafen will be applied post-emergent to crops early in their growth and therefore the plants will be small. Using EPA methodology the residues are expected to be ~8 ppm on short grass and ~5 ppm on small insects at the proposed higher application rate (~ 38 g ai/ ha).

These levels are well below the eight-day dietary NOEC values for both bobwhite quail and mallard duck (>2,000 ppm). Therefore under normal conditions of use this herbicide should present a negligible hazard to herbivorous or insectivorous birds. Similar calculations performed for herbivorous mammals also indicate negligible hazard. Given that the NOEC for bees is >100 µg/bee, picolinafen is unlikely to present a hazard to bees.

Picolinafen is not expected to have any adverse effects on earthworms, with the NOEC >100 mg ai/kg. Likewise, soil microbes are unlikely to be affected, given that in tests at 5 times the proposed use rate picolinafen did not effect these organisms and was rated harmless to four non-target beneficial invertebrates.

Aquatic organisms

Fish and aquatic invertebrates: Assuming an absolute "worst-case" scenario, ie direct application at 38 g ai/ha to pond water 15 cm deep, the water EEC is 25 µg/L. This concentration is around 10 times less than the acute NOEC for fish and *Daphnia magna* and this is considered an adequate safety margin. However, chronic and ELS tests for daphnia and fish provided NOECs of the same order as this EEC ($0.25 < Q < 4$) indicating the hazard assessment needs to be refined. While picolinafen shows some tendency to bioaccumulate this should be limited by the single low annual rate of application together with the rapid movement to sediment, and picolinafen should not provide an acute hazard to fish or aquatic invertebrates in surface waters adjacent to application areas.

Algae and aquatic plants: The "worst case" EEC for a pond (25 µg/L) gives excessive Q-values (>200) for algae and a presumption of unacceptable risk exists. As a next step, if we assume 10% drift as the worst case for spray drift, the corresponding EEC becomes 2.5 µg/L in pond water, but Q is still ~10 for algae and picolinafen would present a hazard, but is acceptable to aquatic plants. The hazard from spray drift needs to be refined further using more realistic considerations.

Spray Drift

A further refinement uses recent methodology for estimating spray drift from the German BBA trials and is based on spray drift studies using tractor mounted equipment and referred to as the Ganzelmeier Tables. Using these figures, the concentration in a waterbody 15 cm deep is 0.17 and 0.09 µg/L, respectively, at 5 and 10 m from the boom sprayer for the lupin use. The 10 m Q-value for green algae is then reduced to ~0.2, still marginally high.

Aerial application causes greater spray drift over longer distances than ground application, and using the US EPA's AgDRIFT model EA estimates that similar algal Q-values (lupins 0.28-0.42, cereals 0.17-0.25) are only achieved when a 250 m buffer zone is used between the plane and a downwind 20 m wide, shallow pond.

Factors likely to ameliorate these adverse effects are the relatively low use rates (12-38 g ai/ha) and the single application per season, both limiting off target effects and allowing recovery of the most sensitive indicators, algae. Additionally, these products are for use in what are predominantly dryland cropping areas where wetlands and standing water are relatively rare. Most importantly, picolinafen is speedily removed from the water column through rapid dissipation to sediment with a DT_{50} of ~1 day, and algal populations are known to recover quickly suggesting any adverse effects would be transient only.

The company has agreed the label should include directions instructing users not to allow spray drift onto any natural wetland or standing water body. The label will instruct users to use downwind buffer zones of 20 m for ground application and 250 m for aerial application, which should reduce the hazard to aquatic plants/algae.

Run-off
Run-off from treated fields could represent a significant hazard to aquatic plants. Calculations with worst case assumptions for run-off showed that there was unlikely to be a hazard to aquatic organisms except for algae. The "worst case" Q-values (7-11) indicate there may be a hazard to algae arising from single applications of picolinafen at the label rates, unless users avoid any accessions to water. As above, the single, low rate use and the rapid binding to soil will mean that picolinafen in run-off will be bound to soil particles/organic matter and largely ameliorate this problem. In particular, preventing run-off for several days after application should allow significant degradation and binding to soil to occur. The company has agreed to a label restraint instructing users to avoid spraying when field and weather conditions are likely to cause run-off.

Leaching
The field dissipation studies showed that under field conditions leaching was not observed, despite rates higher than that proposed for Australia. The laboratory column leaching studies and the physical properties of the chemical indicate a low potential for leaching. Leaching under Australian conditions would not be anticipated based on these studies.

Desirable vegetation
When used according to label directions, the hazard to native and non-target vegetation should be negligible. The phytotoxicity data showed that there were visible effects on a variety of crop and weed seedlings at levels similar to label rates, and significant plant mortality occurred in 80% of broadleaf weeds sprayed. Using the Ganzelmeier figures for ground sprayers in field crops, then expected spray drift at 5m is ~0.7% of ai, and in the large field scenario in Australia significant phytotoxic effects on non-target plants are not expected. The labels contain a warning to prevent spray drifting to nearby plants/crops, etc, and this should specifically recommend limiting spray drift onto non-target native plants.

Conclusion

The application contains adequate environmental fate and toxicity data. These demonstrate that the use of picolinafen according to the label and good agricultural practice is unlikely to result in acute poisoning of wildlife, fish, and most non-target organisms, except for algae, which may be adversely affected by very low accessions to natural bodies of standing water.

The principal degradation pathway of picolinafen is soil metabolism via enzymatic or microbial breakdown in aerobic soils. There was little degradation via hydrolysis or aquatic metabolism. Laboratory studies indicate a low potential for leaching, while field dissipation studies indicate that picolinafen binds strongly to soils and is readily degradable.

Picolinafen is essentially non-toxic to birds, bees, earthworms and soil microbes, but exhibits potentially high toxicity to fish and aquatic invertebrates, and is very highly toxic to plants and algae. It could adversely affect non-target plants, both terrestrial and aquatic, although some terrestrial plants are not affected at the proposed use rates. Since picolinafen is very highly toxic to aquatic plants and to reduce the hazard to aquatic systems every care should be taken not to contaminate water with this product. The draft labels contain warning statements to this effect and EA suggests the addition of stronger statements (prohibitions as above) regarding spray drift and run-off. Picolinafen is expected to be toxic to some native vegetation and the draft labels include warning statements to avoid spray drift contacting desirable vegetation or other crops.

EFFICACY AND SAFETY ASSESSMENT

This summarizes the field trials conducted in Australia and overseas with *Sniper* and *Paragon* which contain the active constituent picolinafen and picolinafen plus MCPA respectively. Information is provided in relation to efficacy and crop safety of both products.

Picolinafen inhibits the activity of phytoene desaturase, an enzyme responsible for the conversion of phytoene to phytofluene in the carotenoid biosynthesis pathway of plants. Inhibition of this enzyme leads to a reduction in carotenoid pigments and ultimately, destruction of leaf chlorophyll in the foliage of sensitive plants. Symptoms in the field occur as bleaching or whitening (often with mauve discolouration) of leaf tissue, followed by necrosis and death.

Picolinafen belongs to the chemical family Aryloxypicolinamide and for weed resistance management purposes is classified as a GROUP F herbicide.

In Australia, *Sniper* has demonstrated a performance similar to that of diflufenican in terms of weed spectrum and crop selectivity. *Sniper* will provide producers with an alternative product for the early post emergence control of wild radish *(Raphanus raphanistrum)* and the suppression of capeweed *(Arctotheca calendula)* in narrowleaf lupins *(Lupinus angustifolius).*

Sniper has been shown to provide robust control of wild radish, possibly the most significant dicot weed in southern Australia. Data was provided which demonstrate that *Sniper* effectively controls wild radish up to 6 leaf at only 37.5g ai/ha giving the potential to significantly reduce the amount of chemical applied per hectare.

Sniper is to be marketed as a 750g/kg WDG formulation. This offers an alternative for growers who prefer dry formulations and for those growers whose spray rigs experience problems with the viscosity of SC formulations. Container disposal will be minimised as the product has a high active content

Paragon is a foliar applied, post-emergence herbicide for the control of dicot (broadleaf) weeds in winter cereals. The herbicide has two active constituents, a new compound, picolinafen, and, MCPA 2-ethyl hexyl ester in a ratio of 1:10. MCPA, which for weed resistance management purposes is classified as a GROUP I herbicide, is a phenoxyalkanoic acid that acts on weeds by disrupting growth. The activity of MCPA combines with the activity of picolinafen to enhance weed control and improve the spectrum of activity.

Paragon has demonstrated a performance similar to that of diflufenican plus MCPA iso-octyl ester, also at a ratio of 1 :10 in terms of weed control spectrum and crop selectivity.

The proposed use of *Paragon* is for post-emergence application in winter cereals (wheat, barley, oats, triticale and cereal rye) for the control or suppression of various broadleaf weeds.

The product is to be marketed as a 50/500g/L EC formulation. This offers the marketplace a higher strength compound, which has the potential to reduce the volume of product and the number of containers required for similar spray operations.

Efficacy

- **Trial design in relation to provision of controls, treatment group size, number of replicates, age and type of animal, plant varieties and stage of growth etc:**
  Trials have been well designed with appropriate replicates, treatments and analysis of results.

- **Experimental conditions in relation to relevant variables, such as pest/disease pressure, weather conditions, soil type etc:**
  Experimental conditions have been adequately recorded and all relevant details supplied in the data in a well laid out manner. A range of conditions has been tested by carrying out trials in the states, which grow significant commercial areas of the crops under consideration.

- **Analysis of trial data and its interpretation, including efficacy relative to dose/application rate and application/administration:**
  The proper analysis of data has been carried out and presented. Where necessary, stage of growth of the weeds has been specified to achieve best results with relevant dose rates.

- **Trial validation with respect to the person responsible for the trial, location of the trial, date of trial:**
  All trials have been carried out by qualified personnel and reported in a suitable format.

- **General applicability of the trial data to the use of the candidate preparations under commercial conditions:**
  The research carried out has been appropriate for the requested registration and work done in areas directly applicable to commercial use of the products.

- **Efficacy data supporting the label claims:**
  Data have covered those claims, which appear on the draft labels.

Crop Safety

Crop tolerance was demonstrated to be generally good. In a few trials significant damage and yield reduction did occur however this was related to crops stressed through disease. Label statements have been added to alert users to this.

Conclusion

Sufficient data from suitably designed, scientifically conducted and statistically analysed trials has been presented to substantiate the claims for use as shown on the draft labels. As long as the products are used according to label instructions and Good Agricultural Practice they should be suitable for the proposed purpose.

LABELLING REQUIREMENTS

***Sniper* Draft Label**

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

SNIPER* Herbicide

Active Constituent: 750g/Kg PICOLINAFEN

GROUP	**F**	**HERBICIDE**

For the control of wild radish and the suppression of capeweed in narrowleaf lupins as indicated in the DIRECTIONS FOR USE table.

[CYANAMID LOGO]

Cyanamid Agriculture Pty Limited
5 Gibbon Road, Baulkham Hills, NSW 2153

500g, 2, 4 kg

* Registered trademark

DIRECTIONS FOR USE:

RESTRAINTS:

Do NOT apply to crops that are stressed through disease, insect damage, frost, nutrient deficiencies, other herbicide use, excessively moist or dry conditions, or inappropriate soil type as CROP DAMAGE MAY RESULT.

Do NOT apply to weeds that are moisture stressed.

Do NOT apply if frost is imminent.

Do NOT apply in spray mixes containing crop oils.

Do NOT apply if rain is expected within four hours.

CROP	WEEDS CONTROLLED	STATE	RATE g/ha	CRITICAL COMMENTS
Narrowleaf lupins	Wild radish (*Raphanus raphanistrum*)	NSW, Vic, SA, WA only	33 to 50	Apply to actively growing crops at the 2-6 leaf stage of the crop, when most wild radish plants are at the 2-6 leaf stage. Use the lower rate on 2-4 leaf weeds in WA only. 6-8 leaf stage weeds can also be effectively controlled at the higher rate but good spray coverage of weeds is essential. Younger plants and subsequent germinations of radish will be controlled in most situations. Residual control can be impaired by dry conditions and by inadequate soil surface coverage. Ensure that crop shading does not protect weeds from spray contact. Good soil moisture before and after application will assist performance.
	Capeweed (*Arctotheca calendula*)	WA only	50	**Suppression only** Apply when most capeweed plants are at the 2-4 leaf stage. Capeweed must be actively growing and free from environmental and herbicidal stress. Transplanted plants will not be adequately controlled.

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

WITHHOLDING PERIOD

DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION.

GENERAL INSTRUCTIONS

SNIPER Herbicide is an early post-emergence, foliar-absorbed product with some soil activity. Under favourable conditions, this pre-emergence activity will provide adequate control of subsequently germinating weed seedlings through to crop canopy.

Leaves of affected plants pale and bleach in irregularly shaped white and mauve blotches. These blotches spread in susceptible plants leading to their death.

MIXING

Half fill the spray tank with clean water. Commence agitation and add the required amount of product to the tank. Maintain agitation while filling the tank and throughout the spraying operation. If in-line filters cannot be by-passed during agitation, pre-mix granules before adding to spray tank.

APPLICATION

Ground application: Apply in a minimum of 50 litres of water per hectare. In dense radish and crop situations, increase the water volume to ensure good coverage.

Following application, spraying equipment can be cleaned by flushing with clean water, with or without the addition of a commercial cleaning agent.

COMPATIBILITY

SNIPER Herbicide is physically compatible with simazine, Select® and FASTAC* Duo.
The use of SNIPER in tank mix with pesticides that require adjuvants is not recommended as these adjuvants may increase crop sensitivity. Apply at least ten days apart.

If water quality is suspected as poor or hard, it is recommended that mixtures be bottle tested in the water intended for spraying, prior to mixing commercial quantities.

CROP SAFETY

Following application, some transient bleaching of lupin foliage may occur. This spotting is confined to leaves present at application. The development of the crop and subsequent new growth is unaffected. In certain situations some minor crop height reduction may occur. Symptoms will be most pronounced in crops that are growing under stress or if SNIPER Herbicide is applied with adjuvants.

Avoid swath overlaps when spraying. Overlapped areas may suffer some crop retardation and bleaching will be more severe.

RESISTANT WEEDS WARNING GROUP **F** HERBICIDE

SNIPER Herbicide is a member of the aryloxypicolinamide group of herbicides and acts by inhibiting carotenoid biosynthesis. For weed resistance management SNIPER is a Group F herbicide. Some naturally occurring weed biotypes resistant to this product and other inhibitors of carotenoid biosynthesis may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by this product or other inhibitors of carotenoid biosynthesis. Since the occurrence of resistant weeds is difficult to detect prior to use, Cyanamid Agriculture Pty Limited accepts no liability for any losses that may result from the failure of this product to control resistant weeds.

RE-ENTRY PERIOD
Do not allow entry into treated areas until spray has dried. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist 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 and pastures. Canola is regarded as the crop most sensitive to spray drift of this product.

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

DO NOT apply to portions of fields within 20 m upwind of sensitive water bodies.

DO NOT apply under meteorological conditions or from spray equipment that will cause spray drift onto non-target native vegetation or adjacent areas and in particular avoid any natural wetland or standing water body.

DO NOT allow run-off within two days of application - avoid application to waterlogged soil, over-irrigation or use when heavy rains are forecast.

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight. Rinse empty containers before disposal. Do NOT dispose of undiluted chemicals on site. Dispose of at a local authority landfill. If no landfill is available, bury the containers below 500mm 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. Avoid contact with eyes. Wash hands after use. When opening the container, preparing spray and using the prepared spray, wear cotton overalls buttoned to the neck and wrist and a washable hat and elbow-length PVC gloves. After each day's use, wash gloves and contaminated clothing.

MSDS
Additional information is listed in the Material Safety Data Sheet.

WARRANTY
This product is designed only to be used in accordance with the label directions, which reflect the opinion of experts based on field use and tests. If it is so used, Cyanamid Agriculture Pty Limited warrants its effectiveness, but takes no responsibility whatsoever for the consequences of the used failing to follow these directions exactly.

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD AND RAIL.

FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY
PHONE 1 800 033 111
TOLL FREE – ALL HOURS
AUSTRALIA WIDE

Product No.:

Batch No.:

Date of Manufacture:

NRA approval No.:

***Paragon* Draft Label**

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

PARAGON* Herbicide

Active Constituents: 50g/L PICOLINAFEN
500g/L MCPA PRESENT AS THE ETHYL HEXYL ESTER

GROUP	F I	HERBICIDE

For the control of certain broadleaf weeds in winter cereals as indicated in the DIRECTIONS FOR USE table.

CYANAMID

Cyanamid Agriculture Pty. Limited
5 Gibbon Road, Baulkham Hills, NSW 2153

5, 10, 20L

*Registered trademark

DIRECTIONS FOR USE:

RESTRAINTS:

Do NOT apply to crops that are stressed through disease, insect damage, frost, nutrient deficiencies, other herbicide use, excessively moist or dry conditions, or inappropriate soil type.

Do NOT apply to weeds that are stressed due to dry conditions, prior herbicide application, etc.

Do NOT apply if rain is expected within four hours.

Do NOT add spraying oil to PARAGON or PARAGON tank mixes.

Crop	Weeds	State	Weed stage	Rate/ha	Critical Comments
Wheat, barley, oats, triticale, cereal rye	Wild radish (Raphanus raphanistrum)	NSW, Vic, Tas, SA, WA	Up to the 4 leaf stage	250mL	Apply to actively growing weeds, free from stress. See "Restraints". Apply to crops in the 3 to 5 leaf stage prior to late tillering. Do NOT use the 500mL/ha rate on crops younger than 5 leaf. Do NOT apply rates higher than 250 mL/ha to crops in the 3 leaf stage, especially long-season varieties.
			Up to the 6 leaf Stage	375mL	
	Mustard (*Sisymbrium* spp), prickly lettuce (*Lactuca serriola*), shepherd's purse (*Capsella bursa-pastoris*), wild turnip (*Brassica tournefortii)*		Up to the 2 leaf stage	250mL	PARAGON may cause transient yellowing of cereals, with oats being potentially most sensitive. Residual control can be impaired by dry soil conditions and by inadequate soil surface coverage. Good soil moisture before and after application will assist performance.
			Up to the 4 leaf stage	375mL	
	Capeweed (*Arctotheca calendula*)		Up to the 2 leaf stage	250mL	Good spray coverage of weeds is essential. Spray before crop canopy begins to close. Increase spray volume when weed or crop density is high. Transplanted weeds will not be adequately controlled.
			Up to the 4 leaf stage	500mL	
	Common sowthistle** (*Sonchus oleraceus*), doublegee** (*Emex australis*)		Up to the 2 leaf stage	500mL	
	Deadnettle** (*Lamium amplexicaule*), fumitory** (*Fumaria* spp) , volunteer lupins** (*Lupinus angustifolius*)		Up to the 4 leaf stage		** <u>Suppression only</u>. These species are not consistently controlled by PARAGON Herbicide, but are usually significantly affected.

WITHHOLDING PERIOD

DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 6 WEEKS AFTER APPLICATION.

GENERAL INSTRUCTIONS
PARAGON Herbicide is a post-emergence, foliar-absorbed product with short soil residual activity. Under favourable conditions, this pre-emergence activity will provide adequate control of subsequently germinating weed seedlings through to when the crop canopy closes.

MIXING
Half fill the spray tank with clean water. Commence agitation and add the required amount of product to the tank. Maintain agitation whilst filling the tank and throughout the spraying operation.

APPLICATION
Ground application: Apply in a minimum of 50 litres of water per hectare. In dense weed and crop situations, increase the water volume to ensure complete coverage.

Aerial application: Apply in a minimum 30 litres of water per hectare. Good coverage of weeds is essential.

COMPATIBILITY
PARAGON Herbicide is physically compatible with OnDuty* Herbicide. Do NOT add spraying oil to PARAGON or PARAGON tank mixes.
As water quality can influence compatibility, it is recommended that mixtures should be bottle-tested in the water intended for spraying, prior to mixing commercial quantities.

CROP SAFETY
Following application, some transient yellowing of cereal foliage may occur. This spotting is confined to leaves present at application. The development of the crop and subsequent new growth is unaffected in crops growing free of stress. Symptoms will be more pronounced and persistent in crops that are growing under stress (see Restraints).

Avoid swath overlapping.

RESISTANT WEEDS WARNING

GROUP	F I	HERBICIDE

PARAGON Herbicide is a member of the aryloxypicolinamide and phenoxy groups of herbicides and acts by inhibiting disrupting plant cell growth and carotenoid biosynthesis. For weed resistance management PARAGON is a Group FI herbicide. Some naturally occurring weed biotypes resistant to this product and other inhibitors of carotenoid biosynthesis and/or disruptors of plant cell growth may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by this product or other inhibitors of carotenoid biosynthesis and/or disruptors of plant cell growth. Since the occurrence of resistant weeds is difficult to detect prior to use, Cyanamid Agriculture Pty Limited accepts no liability for any losses that may result from the failure of this product to control resistant weeds.

RE-ENTRY PERIOD
Do not allow entry into treated areas for 24 hours after application. When prior entry is necessary, wear cotton overalls buttoned to the neck and wrist, face-shield or goggles 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 and pastures. Canola, cotton, tobacco, grapevines, lupins, fruit trees, ornamentals, tomatoes and other vegetables are especially susceptible to spray drift and vapour movement.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT:

Toxic to algae. DO NOT contaminate streams, rivers or waterways with the chemical or used containers.

DO NOT apply by ground application to portions of fields within 20 m upwind of sensitive water bodies.

DO NOT apply by aerial application to portions of fields within 250 m upwind of sensitive wetlands or water bodies.

DO NOT apply under meteorological conditions or from spray equipment that will cause spray drift onto non-target native vegetation or adjacent areas and in particular avoid any natural wetland or standing water body.

DO NOT allow run-off within two days of application - avoid application to waterlogged soil, over-irrigation or use when heavy rains are forecast.

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 500mm 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
Harmful if swallowed. Will irritate the eyes and skin. Avoid contact with eyes and skin. If product on skin, immediately wash area with soap and water. If product in eyes, wash it out immediately. Wash hands after use. When opening the container, preparing spray and using the prepared spray, wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and face shield or goggles. After each day's use, wash gloves, face-shield or goggles and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Telephone 131126 Australia-wide. If swallowed, and if more than 15 minutes from a hospital, induce vomiting, preferably using Ipecac Syrup APF.

MSDS
Additional information is listed in the Material Safety Data Sheet.

WARRANTY
This product is designed only to be used in accordance with the label directions which reflect the opinion of experts based on field use and test. If it is so used, Cyanamid Agriculture Pty. Limited warrants its effectiveness, but takes no responsibility whatsoever for the consequences of the user failing to follow these directions exactly.

THIS PRODUCT IS NOT CONSIDERED TO BE A DANGEROUS GOOD UNDER THE AUSTRALIAN CODE FOR THE TRANSPORT OF DANGEROUS GOODS BY ROAD AND RAIL.

FOR SPECIALIST ADVICE IN AN EMERGENCY ONLY
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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 partitioning 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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NRA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of picolinafen in the products *Sniper* and *Paragon*, please fill in this form and send it, along with payment of $30 to:

David Hutchison
AgVet Chemicals Evaluation Section
National Registration Authority for Agricultural and Veterinary Chemicals
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
David Hutchison AVCES at (06) 6272 3218.

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