Public Release Summary
on

Evaluation of the new active

CARFENTRAZONE-ETHYL

in the product

AFFINITY 400 DF 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) 62723152
Fax: (02) 62723218

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.

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be in accordance with accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: 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 it 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
bw	body weight
d	Day
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	estimated environmental concentration
Fo	original parent generation
h	Hour
Hct	Haematocrit
Hg	Haemoglobin
HPLC	high pressure liquid chromatography *or* high performance liquid chromatography
id	Intradermal
ip	Intraperitoneal
im	Intramuscular
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
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	Level at which residues can be detected
LOQ	Level at which residues can be quantified
MCH	Mean Corpuscular Haemoglobin
MCV	Mean Corpuscular Volume
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
OECD	Organisation for Economic Cooperation and Development
OM	Organic matter
po	Oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
RBC	Red Blood Cell count
s	Second
sc	Subcutaneous
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
T-Value	a value used to determine the First Aid Instructions for chemical products that contain two or more poisons
TGAC	technical grade active constituent
µg	microgram
US EPA	United States Environmental Protection Agency
WHP	withholding period

SUMMARY

This publication outlines the regulatory considerations and provides a summary of the data evaluated for the proposed registration of ***Affinity 400 DF Herbicide*** (*Affinity*). *Affinity* is a dry flowable formulation containing 400 g/kg carfentrazone-ethyl. It is proposed that the product will be used for post-emergence control of broadleaf weeds in winter cereals such as wheat, barley, oats and triticale.

The NRA has assessed the data submitted by the applicant in support of the proposed use of carfentrazone-ethyl. The following information is provided for public comment before the NRA determines whether to register the product in Australia. Comments should be submitted by **26 May 2000** to the NRA at the address indicated on page 1.

Public Health Aspects

Toxicology

Carfentrazone-ethyl is of very low oral and inhalation toxicity and low dermal toxicity in rats. It is not a skin irritant in rabbits, or a skin-sensitiser in guinea pigs, but is a slight eye irritant to rabbits.

Affinity, a product containing 400 g/kg carfentrazone-ethyl, has very low oral and inhalation toxicity and low dermal toxicity in rats. It is a moderate eye irritant and a slight skin irritant in rabbits and is not a skin sensitiser in guinea pigs.

Repeat-dose studies indicate that the primary targets for carfentrazone-ethyl toxicity are the liver, kidney, and the red blood cell forming system. Liver toxicity in all tested species was characterised by increased liver weight, microscopic changes in liver cells and increases in plasma levels of liver enzymes. Increased kidney weight and the presence of pigment in kidney cells typified kidney toxicity in rats and dogs. Effects on the red blood cell forming system were seen in most studies. These effects included a reduction in the number of red cells in blood and an associated increase in the products of red blood cell degradation appearing in the urine and liver.

Specific studies indicated that carfentrazone-ethyl does not damage genetic material. Additionally, long-term exposure studies in mice and rats indicated that carfentrazone-ethyl does not cause cancer. There were no effects on reproductive behaviour or performance in rats. At doses that were not toxic to the mother, there were no developmental effects on the rat or rabbit foetus.

Conclusion

Based on an assessment of the toxicology, it was considered that there should be no adverse effects on human health from the use of these products when used in accordance with the label directions.

Residues In Food

Australian residue data for carfentrazone-ethyl in cereal crops (wheat, oats, barley and triticale) were presented. Overseas trial data were submitted for wheat. The data from Australian and overseas trials showed that residues of carfentrazone ethyl above the limit of quantitation were not found in any of the harvested cereals grains. Processing data for flour, germ and bran were provided for wheat. However, as the raw commodities contained no detectable residues, the processing data were of limited value, other than to show that no detectable residues are anticipated in processed fractions.

Data for cereal forage and fodder were provided to allow an estimation of residues in animal feed commodities. No detectable residues were found in treated animal feed commodities. Animal commodity MRLs have been set at the Limit Of Quantitation (LOQ) for carfentrazone-ethyl, these MRLs being supported by animal transfer studies in cows and hens. These data from the transfer studies support MRLs for meat (mammalian), *0.05 mg/kg; edible offal (mammalian), *0.05 mg/kg; milks, *0.025 mg/kg; poultry meat, *0.05 mg/kg; poultry offal, *0.05 mg/kg and eggs, *0.05 mg/kg.

Residues And Trade

Risks to trade on the basis of carfentrazone-ethyl residues in cereal crops are not anticipated. Residues in these crops have been shown to be consistently non-detectable and the Australian MRL in cereal grains of *0.05 mg/kg is supported by appropriate data. Carfentrazone-ethyl residues in grains from treated cereal crops were below the LOQ at crop maturity.

Animal transfer data were presented with the application. These data establish that carfentrazone-ethyl residues in animal commodities resulting from feeding of grain, forage and fodder are below the LOQ in animal tissues, milk and eggs for feeding at 100% in the diet. Carfentrazone-ethyl residues should not present a risk to meat exports as use of the product in crops is likely to result in non-detectable residues in commodities from animals feeding on treated crops.

Occupational Health and Safety Aspects

Carfentrazone-ethyl is not on the NOHSC *List of Designated Hazardous Substances.* Based on the NOHSC *Approved Criteria for Classifying Hazardous Substances,* carfentrazone-ethyl and *Affinity* are classified as non-hazardous.

Affinity will be imported fully formulated and packaged. It will be packed in 2 kg containers.

Affinity possesses low acute oral and dermal toxicity. The product is a slight skin irritant and a moderate eye irritant but not a skin sensitiser.

Affinity is proposed for the post emergence control of broadleaf weeds in winter cereals such as wheat, barley, oats and triticale. It will be applied by boomspray. The proposed application rate is 40 to 60 g of product/ha (16-24 g active ingredient/ha) in 50-100 L of water.

Worker exposure data was not available for carfentrazone-ethyl or *Affinity*.

First Aid Instructions and Safety Directions are provided on the product labels to minimise exposure to the product. Based on the risk assessment, elbow length PVC gloves and face shield or goggles are recommended for users of *Affinity*. A re-entry statement is not recommended for this product.

Environmental Aspects

Carfentrazone-ethyl is likely to degrade rapidly under both aerobic and anaerobic conditions to the ester hydrolysis metabolite F8426-chloropropionic acid. From there, degradation is expected to continue to produce various metabolites retaining both the phenyl and triazolinone rings. Mineralisation of carfentrazone-ethyl and these metabolites is expected to occur reasonably readily in water in the presence of sunlight. However, mineralisation is expected to occur very slowly in soil or in water not exposed to sunlight. Carfentrazone-ethyl is not volatile and is expected to degrade too rapidly to move significantly in soil. However, its major metabolites are mobile to very highly mobile in soil and have potential to leach, though significant downward leaching was not detected in field trials. Carfentrazone-ethyl or its metabolites are not expected to bioaccumulate.

With the proposed use on winter cereals, hazard assessments indicate only a low hazard to birds and mammals, fish, aquatic invertebrates and terrestrial invertebrates (bees and other arthropods, earthworms and soil micro-organisms). However, a hazard was indicated to algae and aquatic plants in shallow waterbodies from direct overspray and potentially from spray drift. Concentrations of certain metabolites potentially hazardous to algae and aquatic plants may also form following direct overspray of carfentrazone-ethyl, but these are expected to degrade to less toxic metabolites and mineralise with exposure to sunlight. Direct overspray or spray drift may also be toxic to susceptible terrestrial plants by foliar exposure, but a low hazard is anticipated from residues reaching soil, due to rapid dissipation and reduced activity compared to foliar exposure. Suitable label advice has been provided to minimise these hazards, including spray drift warnings for non-target vegetation and aquatic areas and advice that the product should not be applied by air to winter cereals.

Efficacy and Crop Safety Aspects

Carfentrazone-ethyl has been evaluated under a wide range of Australian winter cereal growing conditions and in all major winter cereal growing areas.

The optimum use rate range of *Affinity* without compromising crop safety was found to be 40 to 60 g/ha, with or without a surfactant at 50 mL/100L.

Surfactants, when added to *Affinity*, were found to be a key determinant in crop selectivity, particularly when combined with extremes of environmental conditions.

Affinity activity is rapid and any crop injury is first noticed within four to seven days of application. Recovery from injury is rapid and generally occurs within 14 to 21 days after application. Crop injury from *Affinity* does not have a negative impact on crop yields.

Carfentrazone-ethyl is a non residual herbicide. As such, the use of *Affinity* will not restrict rotation to following crops.

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 label.

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of ***Affinity 400 DF Herbicide*** *(Affinity),* which contains the new active ingredient, carfentrazone-ethyl.

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

Copies of full technical evaluation reports on carfentrazone-ethyl, 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 **26 May 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
FMC International A.G.

Product Details
It is proposed to register *Affinity* containing carfentrazone-ethyl at 400g/kg as a dry flowable formulation. *Affinity* will be imported fully formulated and packaged in 2 kg containers.

Carfentrazone-ethyl is a member of the Group G (aryl triazolinone) type of post-emergence herbicides. It controls weeds by the inhibition of the enzyme, protoporphyrinogen oxidase (PPO). Its action results in membrane disruption, which ultimately kills sensitive weeds by interfering with the chlorophyll biosynthetic pathway.

The proposed use of *Affinity* will be for the early post-emergence control of a wide range of broadleaf weeds in winter cereals such as wheat, barley, oats and triticale applied from after the three-leaf stage of the crop up to tillering.

Carfentrazone-ethyl is registered under a number of trade names in the following countries:

- China
- Czech Republic
- Pakistan
- Philippines
- Poland
- Switzerland
- United Kingdom
- USA (approved as "reduced risk pesticide")

CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent carfentrazone-ethyl is manufactured in the USA by FMC Corporation at Quality Chemicals Inc., Tyrone Industrial Park, Tyrone Pennsylvania 16686-0216. The TGAC has been approved by the NRA (Approval Number: 44431).

Chemical Characteristics of the Active Constituent

Common name: carfentrazone-ethyl

Synonyms and code number: F8426, F116426

Chemical name:

(IUPAC): ethyl 2-chloro-3-[2-chloro-4-fluoro-5-(4-difluoromethyl-4,5-dihydro-3-methyl-5-oxo-1*H*-1,2,4-triazol-1-yl)phenyl]propionate

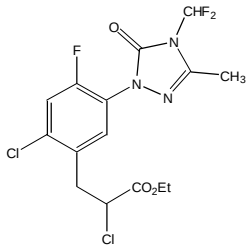
(CA):ethyl-a,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoate

CAS Registry Number: [128621-72-7] (for the acid); [128639-02-1] (for the ethyl ester)

Molecular formula: $C_{15}H_{14}C_{l2}F_3N_3O_3$

Molecular weight: 412.2

Chemical structure:



Physical and Chemical Properties of Pure Active Constituent

Physical state: viscous liquid at room temperature

Colour: yellow

Boiling point: 350-355°C / 760 mm Hg, 182°C / 2 mm Hg

Density/specific gravity: 1.457 (20°C)

pH: 5.8 (1% solution)

Solubility in organic solvents: miscible with acetone, ethanol, ethyl acetate, methanol and methylene chloride (all at 23°C)

Solubility in water: 12 µg/mL (20°C), 22 µg/mL (25°C), 23 µg/mL (30°C)

Vapour pressure: 1.6×10^{-2} mPa (20°C)

Flashpoint: 229°C

Octanol/water Partition Coefficient: log K_{OW} = 3.36

Storage stability: stable for at least 3 years when stored at 23°C (study conducted with TGAC material)

Chemical type: herbicide

PRODUCT

Distinguishing name: Affinity 400 DF Herbicide
Formulation type: dry flowable
Active constituent concentration: 400 g/kg
Mode of Action: inhibition of protoporphyrinogen oxidase

Physical and Chemical Properties of the Product

Physical state: solid granules
Colour: light to dark brown
Odour: slightly musty
Density: 0.4895 g/cm^3
pH value: 7.5, as an aqueous dispersion at 22°C
Storage stability: Stability data provided by applicant demonstrated that the product will be stable for 2 years when stored at ambient temperature.

Recommendation

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

TOXICOLOGICAL ASSESSMENT

The toxicological database for carfentrazone-ethyl, 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 to 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 oral dosing, carfentrazone-ethyl appeared rapidly in both plasma and red blood cells of rats and mice. Peak concentrations and total amount absorbed were dose related. Carfentrazone-ethyl was eliminated rapidly from plasma and red blood cells. There were no significant sex or dosing regime differences in excretion or metabolism in rats. Most of an orally administered dose was excreted in the urine rather than the faeces. Two major metabolites were identified (carfentrazone-ethyl-chloropropionic acid and 3-hydroxymethyl-carfentrazone-ethyl-chloropropionic acid) in the plasma of mice and rats. Six metabolites were identified in excreta; carfentrazone-ethyl-chloropropionic acid, 3-hydroxymethyl-carfentrazone-ethyl-chloropropionic acid, 3-hydroxymethyl-carfentrazone-ethyl-propionic acid, carfentrazone-ethyl-cinnamic acid, 3-hydroxymethyl-carfentrazone-ethyl-cinnamic acid, and carfentrazone-ethyl-propionic acid in descending order. A maximum of 2.8% of an oral dose was excreted unchanged.

Acute Studies

Carfentrazone-ethyl has a very low acute oral toxicity (LD_{50} >5000 mg/kg in male rats and =5143 mg/kg in female rats), low acute dermal toxicity (>4000 mg/kg, no deaths), and very low inhalation toxicity to rats (LC_{50} >5090 mg/m^3). The oral LD_{50} in mice was >500 mg/kg (no deaths) and the dermal LD_{50} >200 mg/kg (no deaths) in the same species. Carfentrazone-ethyl was not a skin irritant to rabbits, was non-sensitising to guinea pigs, and was a slight eye irritant to rabbits.

Affinity has very low oral (LD_{50} >5000 mg/kg bw) and inhalation toxicity (LC_{50} >5270 mg/m^3) and low dermal (LD_{50} >5000 mg/kg bw) toxicity in rats. It is a moderate eye irritant and a slight skin irritant in rabbits and is not a skin sensitiser in guinea pigs (Buehler test).

Short-Term Studies

In mice fed carfentrazone-ethyl at concentrations up to 20000 ppm for 28 days, decreased defecation was observed at 14000 and 20000 ppm. Blood haemoglobin concentration was reduced in females at concentrations ≥ 4000 ppm and mean corpuscular volume and mean corpuscular haemoglobin were reduced at the highest concentration. Liver weight was increased in both males and females at concentrations ≥ 8000 ppm and spleen weights were reduced in males at the highest concentration.

Carfentrazone-ethyl applied to rat skin for six hours at doses up to 1000 mg/kg bw/day for 21 days, caused a slight decrease in plasma aspartate aminotransferase in all treated groups and a slight increase in plasma chloride concentration in treated males. However, these effects were only statistically significant at 1000 mg/kg bw/day.

To ascertain the maximum tolerated dose, two dogs (1/sex) were fed 10000, 20000 and 40000 ppm carfentrazone-ethyl (570, 1140 and 2280 mg/kg bw/day) for one week each over three consecutive weeks followed by capsule administration of 2400 mg/kg bw/day during the following week. Body weight and food consumption were reduced during dietary administration, but recovered during administration of capsules. On day thirty, erythrocyte related parameters, ie. Hb, RBC, Hct, MCH, MCV were reduced.

The body weight of dogs (1/sex) given 1000 mg/kg bw/day carfentrazone-ethyl in capsules for 14 days was reduced; food consumption of the female also reduced. Mean corpuscular haemoglobin and mean corpuscular volume were reduced. In the female, haematocrit was also reduced with white blood cell counts and neutrophils increased. The female had a pale kidney and the male had reduced relative spleen and testes weights.

In dogs (1/sex/group) given capsules containing carfentrazone-ethyl at doses up to 1000 mg/kg bw/day for 28 days, food consumption and body weight gain were decreased, plasma urea was slightly increased and plasma glucose was slightly decreased. Total urinary porphyrins were elevated in the male at 1000 mg/kg bw/day and in females at ≥ 500 mg/kg bw/day. Decreased thymus weight and cortical atrophy were observed in animals at 1000 mg/kg bw/day and decreased uterus weights were observed in females at this dose.

In mice fed up to 20 000 ppm dietary carfentrazone-ethyl for 90 days, a pink/brown staining of the litter tray was observed at concentrations ≥ 14000 ppm. Although red blood cell counts were increased in males at concentrations ≥ 14000 ppm, mean corpuscular volume and mean corpuscular haemoglobin were reduced in males at concentrations ≥ 8000 ppm and in females at concentrations ≥14000 ppm. In addition, mean corpuscular haemoglobin concentration was reduced in females at the highest concentration. Aspartate aminotransferase and alanine aminotransferase activities were increased at 20000 ppm and albumin was increased in females at concentrations ≥ 1400 ppm. Liver weights were increased at concentrations ≥ 8000 ppm and spleen weights were decreased in all treated females. Treatment related histopathological changes in livers were observed in males at concentrations ≥ 8000 ppm and in females at doses ≥ 4000 ppm. A NOEL was not established for this study, because a reduction in spleen weights was observed in females at the lowest concentration tested (1000 ppm, equivalent to 150 mg/kg bw/day).

In rats fed up to 20 000 ppm carfentrazone-ethyl in the diet for 90 days, abdominogenital staining and pink-brown discolouration of the cage-pan liner was observed at concentrations ≥

4000 ppm. Body weight and food consumption were reduced in males at concentrations ≥ 8000 ppm and in females at concentrations ≥ 8000 and 4000 ppm respectively. Erythrocyte parameters (Hb, Hct, MCV, MCH) were reduced at concentrations ≥ 8000 ppm and platelets were increased in males at the same concentrations. Plasma ALT, AST, potassium, phosphorus and bilirubin were increased at concentrations ≥ 8000 ppm whereas glucose was reduced. Total urinary porphyrins were increased in males at concentrations ≥ 8000 ppm and in females at concentrations ≥ 4000 ppm. Dark livers and kidneys with treatment related histopathological changes were observed at concentrations ≥ 8000 ppm. Liver weights were increased in females at concentrations ≥ 8000 ppm and in males at the highest concentration. The NOEL for this study was 1000 ppm (equivalent to 72 mg/kg bw/day) based on the presence of porphyrin in the urine, pink-brown discolouration of pan liners and reduced food consumption at ≥ 4000 ppm.

Dogs given capsules containing carfentrazone-ethyl at doses up to 1000 mg/kg bw/day for 90 days exhibited subdued behaviour, salivation and vomiting at the highest dose. Mean corpuscular haemoglobin was reduced at doses ≥ 500 mg/kg bw/day and mean corpuscular volume was reduced in males at this dose. Red blood cell count was increased in males receiving the highest dose. Total urinary porphyrins were increased at doses ≥ 500 mg/kg bw/day and liver weight was increased in females at this dose. Liver and kidney weights were increased in males at the highest dose. The NOEL for this study was 150 mg/kg bw/day based on decreases in mean corpuscular haemoglobin and mean corpuscular volume, increases in urinary porphyrins and increased liver weight and liver to body weight ratios at 500 mg/kg bw/day.

Long-Term Studies

Mice fed carfentrazone-ethyl at concentrations of 0, 70, 700 or 7000 ppm for 80 weeks had increased mortality at concentrations ≥ 700 ppm. Body weights and body weight gains were reduced at 7000 ppm in females and in all treated males. Red blood cell count and haematocrit were reduced and mean corpuscular volume was increased in females at concentrations ≥ 70 ppm. Haemoglobin was reduced at concentrations ≥ 700 ppm and mean corpuscular volume and mean corpuscular haemoglobin concentration were increased in males at concentrations ≥ 70 ppm. Haemosiderosis, porphyrin deposits and treatment related histopathological changes were observed in males at concentrations ≥ 700 ppm and in females at the highest concentration. A NOEL was not established for this study, because reduced body weight gain was observed in males at the lowest concentration tested (70 ppm, equal to 10 mg/kg bw/day).

In rats fed 0, 50, 200, 800 or 4000 ppm carfentrazone-ethyl for 52 or 104 weeks slight decreases in red blood cell counts in males and increases in mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration were observed at ≥ 200 ppm. Dark urine with brown/orange masses was observed intermittently throughout the study at concentrations ≥ 800 ppm. There was a slight increase in urinary porphyrins, increased liver weight, pigment deposits and histopathological changes in the liver of females at the highest concentration. Pigment deposits and red fluorescence in the liver was observed in males at concentrations ≥ 800 ppm and red fluorescence was observed in the liver of females at ≥ 200 ppm. The NOEL was concluded to be 50 ppm (3 mg/kg bw/day), based on red fluorescence in the liver at 200 ppm.

In dogs given carfentrazone-ethyl in capsules at doses of 0, 50, 150, 500 or 10000 mg/kg bw/day for 52 weeks, increased urinary porphyrins were observed at doses ≥ 150 mg/kg bw/day. A slight reduction in mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration was observed in males at the same doses and an increase in liver to body weight ratio was observed in females at doses ≥ 500 mg/kg bw/day. The NOEL for this study was 50 mg/kg bw/day based on the slight increase in urinary porphyrins at 150 mg/kg bw/day.

In long-term repeat dose studies, no increases in neoplasms were noted in mice or rats.

Reproduction and Developmental Studies

In reproduction studies in rats were fed up to 8000 ppm carfentrazone-ethyl from 8-10 weeks prior to mating until the end of lactation. The effects recorded were similar to those observed in short term studies. Staining of litter trays with orange/brown pigment occurred at all concentrations in a concentration dependent manner. Body weight gains were reduced in $F_{0,}$ F_1, and F_2 generations at concentrations ≥ 4000 ppm, reductions in erythrocyte parameters (Hb, Hct, MCV, MCH), increased liver weights with pigment deposition and pathohistological changes consistent with hepatotoxicity were observed. No effects on reproductive functions or behaviour were observed.

Carfentrazone-ethyl was orally administered to pregnant female rats, at doses of 0, 100, 600, or 1250 mg/kg bw/day from day 6 to day 15 of gestation. Brown, yellow, or pink abdominogenital staining, and pink staining on the cage liner were observed at doses ≥ 600 mg/kg bw/day. Significant increases in the incidence of wavy and thickened ribs were recorded for the 1250 mg/kg bw/day litters. The maternal NOEL was 100 mg/kg bw/day and the NOEL for foetal development was 600 mg/kg bw/day.

Carfentrazone-ethyl was orally administered to pregnant female rabbits, at doses of 0, 10, 40, 150 or 300 mg/kg bw/day from day 7 to day 19 of gestation. Slight increases in abdominogenital, and pink or red pan liner staining were recorded at doses ≥150 mg/kg bw/day. Skeletal variations in rabbits (angulated hyoids, unilateral and floating ribs, and non-ossified 6th sternabrae in rabbit litters), were slight and not dose-related at materno-toxic doses. Maternal and foetal NOELs were 40 and 10 mg/kg bw/day respectively, in rabbits.

Genotoxicity

Carfentrazone-ethyl was genotoxic in an *in vitro* mammalian cytogenetic test in the absence of metabolic activation, and gave an overall equivocal response in a *Salmonella* mutagenicity assay (strain TA1538). Carfentrazone-ethyl was not genotoxic in the following studies;- two Ames tests, a CHO/HGPRT mutation assay, a micronucleus cytogenetic assay in mice, an *in vivo - in vitro* rat hepatocyte unscheduled DNA synthesis assay, and an *in vitro* mammalian cytogenetic test in the presence of metabolic activation. The negative results for *in vivo* and *in vitro* studies with external metabolic activation, suggest that carfentrazone-ethyl is not a genotoxin *in vivo*. 3-Desmethyl-carfentrazone-ethyl-chloropropionic acid (a plant metabolite) and carfentrazone-ethyl-benzoic acid were not genotoxic in *Salmonella/Escherichia coli* mutagenicity assays, and two intermediates (FMC 92090 and FMC 92089) were not genotoxic in micronucleus cytogenetic assays in mice.

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 low toxicity, the NDPSC recommended that carfentrazone-ethyl not be scheduled in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The lowest overall NOEL for carfentrazone-ethyl was 3 mg/kg bw/day. This NOEL was established in the 2-year rat study, based on pigment deposition, red fluorescence and histopathological changes in the liver of rats at the next highest dose. A safety factor of 100 is considered appropriate for the ADI, due to the extensive, high quality toxicology database for carfentrazone-ethyl. This results in an ADI of 0.03 mg/kg bw/day.

RESIDUES ASSESSMENT

Residues In Food Commodities

Australian residue data for carfentrazone-ethyl in cereal crops (wheat, oats, barley and triticale) were presented. Overseas trial data were also provided for wheat. Processing data for flour, germ and bran were provided for wheat. However, as the raw commodity contained no detectable residues so the processing data were of limited value, other than to show that no detectable residues are anticipated in processed fractions. Data for cereal forage and fodder were provided to allow an estimation of residues in animal diets. Animal commodity MRLs have been set at the Limit Of Quantitation (LOQ) for analysis of carfentrazone-ethyl in these commodities, these MRLs being supported by animal transfer studies in cows and hens.

Cereal crops

Australian trials in cereal crops were based on a single, post-emergence treatment at ≥24 g ai/ha (the proposed maximum label rate is 24 g ai/ha). Cereal crops treated at this rate resulted in no detectable residues (<0.05 mg/kg) in grain samples harvested at maturity (a minimum interval of 74 days). A harvest withholding period is not considered necessary for use of the product according to the draft label instructions. A MRL of *0.05 mg/kg is recommended for cereals, in accordance with the proposed use-pattern in Australia.

Overseas trial data for carfentrazone-ethyl in wheat and rice crops were provided. In the majority of the trials, crops were treated at ~2x the maximum proposed label rate in Australia which resulted in no detectable residues in mature grain.

The Australian trials in cereal grains addressed residues in potential animal feed commodities. The MRL proposed for cereal forage and fodder of *0.05 mg/kg is considered appropriate on the basis of the trial data. No detectable residues were observed in forage samples collected at 13-14 DAT, or in straw samples taken at harvest. The proposed grazing withholding period of 14 days is considered appropriate, as forage samples collected at intervals earlier than 13 days contained residues above the LOQ.

Animal commodities

No detectable residues are expected to be found in treated animal feed commodities. Animal transfer data was presented for feeding of carfentrazone-ethyl at levels up to 10 ppm to cows and metabolism data for feeding at up to 10 ppm ^{14}C-labelled carfentrazone-ethyl was available for hens. In the cow study, the compound was fed to the animals for 28 consecutive days; no detectable residues of the parent compound were present in milk (<0.005 mg/kg) or tissues (<0.01 mg/kg). The study in hens, which involved feeding of the labelled parent at 10 ppm for 7 consecutive days, led to no detectable residues (<0.01 mg/kg) in tissues or eggs, with the exception of liver which contained total radioactive residues at a maximum level of 0.055 mg/kg. As the expected residues in grain will not be above 0.05 mg/kg, MRLs for eggs and poultry commodities are set at the limits of quantitation of 0.05 mg/kg for tissues and eggs.

These data support MRLs for meat (mammalian), *0.05 mg/kg; edible offal (mammalian), *0.05 mg/kg; milks, *0.025 mg/kg; poultry meat, *0.05 mg/kg; poultry offal, *0.05 mg/kg and eggs, *0.05 mg/kg.

Metabolism Studies

Plant Metabolism:
In a wheat study, grain and straw were collected at maturity, 63 days after treatment (DAT) in addition to the collection of forage at 19 DAT. The radioactive residue found in grain was 0.001 mg/kg parent equivalents and therefore metabolites in grain were not further characterised. Characterisation of metabolites in forage and straw resulted in extractable and non-extractable residues. Non-extractable residues were identified as being incorporated in cellulose and starch. The major metabolites identified in the organic soluble fraction were carfentrazone, 3-hydroxy carfentrazone, a cinnamic acid derived from dehydrochlorination of carfentrazone, 3-desmethyl carfentrazone and a derivative of carfentrazone which has the α-chlorine substituent replaced by SO_3H. The major routes of metabolism were hydrolysis of the ethyl ester linkage of the parent and subsequent hydroxylation of the methyl group of the triazolinone functionality. The largest component of the total radioactivity was 3-hydroxy carfentrazone.

Metabolism in corn showed the formation of carfentrazone (hydrolysis of the ester) as was observed in wheat. 3-desmethyl carfentrazone was also identified in corn and this metabolite is thought to be formed from hydroxylation of the methyl group of the triazolinone functional group followed by oxidation of the methylene hydroxy group to a carboxy functionality which may then decarboxylate to form desmethyl carfentrazone. The intermediate hydroxy and carboxy substituted compounds are considered not to accumulate to any degree in corn.

The studies indicate consistency of metabolism in grain crops and little translocation of the active or metabolites from leaves of plants into grain.

Animal Metabolism:
Metabolism studies in rats, mice, goats and hens were provided. In rats/mice, oral administration of single and multiple doses of ^{14}C-labelled parent led to elimination of the majority of the dose in urine (60 – 76% of the administered dose) and faeces (10.5 – 26%) within 24 hours after the final dose. For the low dose groups (5 mg/kg bw), none of the tissues contained ^{14}C residues in excess of 0.009 mg/kg. The animals given a single high dose (1000 mg/kg bw), the highest residues were in liver (1.101 mg/kg parent equivalents) and kidney (0.811 mg/kg parent equivalents). Urinary metabolites identified were 3-hydroxy carfentrazone, the cinnamic acid derivative of carfentrazone and its 3-hydroxy analogue, a dechlorinated derivative of carfentrazone (F8426-propionic acid) and 3-hydroxy F8426-propionic acid. The metabolism of carfentrazone-ethyl was rapid and extensive in rats/mice. Metabolism occurred through hydrolysis of the ester moiety to form carfentrazone, followed by oxidation of the methyl group to form 3-hydroxy carfentrazone or dehydrochlorination to form a cinnamic acid. Dechlorination of carfentrazone leads to F8426-propionic acid and hydroxylation of the methyl group of this metabolite provides 3-hydroxy-F8426-propionic acid.

In goats the majority of the orally administered ^{14}C-labelled parent compound (87 – 88 ppm in the feed) was eliminated in urine (78.3 – 81.3% of the administered dose) and faeces (4.5 – 6.8%). Milk contained 0.12 – 0.13% of the applied dose and at sacrifice all tissues contained <0.01% of the administered dose with the exception of liver which accounted for 0.02% of the dose. The presence of carfentrazone, F8426-propionic acid and the cinnamic acid derivative of carfentrazone were confirmed in liver and kidney. The major metabolite in these tissues was carfentrazone.

In hens after administration of ^{14}C-labelled carfentrazone-ethyl (10 ppm in the feed), the level of radioactive residue in all tissues except liver, and in eggs were less than 0.01 ppm (<0.1% of

the administered dose). In liver the average residues found were 0.045 – 0.055 mg/kg parent equivalents. The major metabolite identified in liver was carfentrazone [63.3 – 72.9% of the Total Radioactive Residue (TRR)]. Two minor components were also identified. They comprised 2.2% to 5.0% of the TRR and were identified as 3-hydroxy carfentrazone and F8426-propionic acid. The TRR in eggs and other tissues were at very low levels; therefore there was no further characterisation of the radioactivity. Based on the identified metabolites it can be concluded that the metabolic pathways for carfentrazone-ethyl in hens are similar to those elucidated in goats.

Animal Transfer Studies:
Lactating cows were fed at levels equivalent to 1, 3 and 10 ppm in the diet for 28 consecutive days. No detectable residues (<0.005 ppm) of carfentrazone-ethyl, carfentrazone or F8426-propionic acid were found in any of the milk samples taken, except for low concentrations of carfentrazone (0.005 – 0.008 ppm) in three isolated samples from the 10 ppm dose group. No detectable residues (<0.01 ppm) of carfentrazone-ethyl, carfentrazone or F8426-propionic acid were found in any of the tissue or cream samples with the exception of kidney samples where trace amounts of carfentrazone (0.012 – 0.013 ppm) were found in samples from the 10 ppm dose group. There were no detectable residues of carfentrazone in kidney from cows fed clean feed for 7 days after dosing for 28 days, indicating that this residue was readily cleared from the kidney and excreted from the animal over a relatively short period of time. Milk and tissues from the 1 ppm dose group were not analysed when samples from the 3 ppm dose group failed to show residues. It was concluded that no accumulation of residues occurred in milk or tissues during feeding of cows over 28 days at rates of up to 10 ppm in the feed.

MRL Standard

The following amendments to the *MRL Standard* are recommended:

Table 1

Compound	**Food**	**MRL (mg/kg)**
ADD:		
Carfentrazone-ethyl		
GC 0080	Cereal grains	*0.05
MO 0105	Edible offal (mammalian)	*0.05
PE 0112	Eggs	*0.05
MM 0095	Meat (mammalian)	*0.05
ML 0106	Milks	*0.025
PM 0110	Poultry meat	*0.05
PO 0111	Poultry, edible offal of	*0.05

Table 3

Compound	***Residue***

ADD:

Carfentrazone-ethyl	Carfentrazone-ethyl

Table 4

Compound	Animal feed commodity	MRL (mg/kg)
ADD:		
Carfentrazone-ethyl		
	Cereal grain forage and fodder	*0.05

* at or about the limit of quantitation

The following Withholding Periods (WHPs) in relation to the above MRLs are recommended:

CEREALS: DO NOT ALLOW STOCK TO GRAZE TREATED AREAS FOR 14 DAYS AFTER APPLICATION

Assessment of Overseas Trade Aspects of Residues in Food

Commodities Exported

Export statistics for cereal crops from the 1998/9 financial year are tabulated below:

Commodity	Total Australian Production (tonnes)	Total Export (tonnes)
Barley	5680	4654
Oats	1874	229
Triticale	483	0
Wheat	22108	16387

Countries Where Exported

Major export markets for Australian wheat crop are Iran, Iraq, South Korea, Pakistan, Indonesia, Japan and Egypt. Major export markets for sorghum are Japan and Chinese Taipei. Major export markets for oats are Japan, Germany and the Philippines. Of these countries, only Pakistan and the Philippines have registrations for carfentrazone-ethyl based products in wheat and rice, respectively. Neither of these countries have introduced tolerances for carfentrazone-ethyl in the relevant crops.

International MRLs

The following table lists the MRLs established for carfentrazone-ethyl in various countries.

Crop	Country	Residue tolerance (mg/kg)
Wheat	USA	0.1
	Czechoslovakia	0.1
	Switzerland	0.1
	United Kingdom	0.1
Corn	USA	0.1
Rice	USA	0.1 (due to expire 31.10.99)
Barley	Czechoslovakia	0.1
	Poland	0.1
	Switzerland	0.1
	United Kingdom	0.1
Triticale	Czechoslovakia	0.1
Soy bean	USA	0.1

Overseas Registrations and Use Patterns

Registrations of carfentrazone-ethyl based products have been obtained in China, Czechoslovakia, Pakistan, the Philippines, Poland, Switzerland, the U.K. and the U.S.A.

The maximum use-pattern currently registered in other countries is a single application at 40 g ai/ha applied at early post-emergence. This use-pattern is roughly double that proposed for Australia (24 g ai/ha). Some countries, such as the U.K. and the Philippines have a maximum use pattern of 20 g ai/ha for barley and wheat in the case of the former and 20 g ai/ha for rice in the case of the latter.

CODEX Alimentarius Commission MRL

No CODEX MRLs have been established for carfentrazone-ethyl.

Australian MRLs

The MRLs recommended for inclusion in the Australian *MRL Standard* are as follows:

Cereal grains	*0.05
Edible offal (mammalian)	*0.05
Eggs	*0.05
Meat (mammalian)	*0.05
Milks	*0.025
Poultry meat	*0.05
Poultry, edible offal of	*0.05
Cereal grain forage and fodder	*0.05

Potential Risks to Australian Export Trade

Risks to trade on the basis of carfentrazone-ethyl residues in cereal crops are not anticipated. Residues in these crops have been shown to be consistently non-detectable and the Australian MRL in cereal grains of *0.05 mg/kg is justified. Of those countries which have established tolerances for carfentrazone-ethyl in cereal grains, Australia has the lowest. The maximum use-pattern registered overseas involves application of the active at higher rates than the use-pattern proposed for Australia, except for the UK and Philippines where the registered use-pattern is slightly lower than that proposed for Australia (20 g ai/ha vs. 24 g ai/ha). In general, carfentrazone-ethyl residues in grains from cereal crops were below the Limit Of Quantitation (LOQ) at crop maturity.

Animal transfer data were presented with the application. These data establish carfentrazone-ethyl residues in animal commodities resulting from feeding of grain, forage and fodder are below the LOQ in animal tissues, milk and eggs for feeding at 100% in the diet. Animal MRLs, set at the LOQ for the analytical method in animal tissues and other animal commodities, have been established for carfentrazone-ethyl as part of this application to register *Affinity*. Carfentrazone-ethyl residues should not present a risk to meat exports as use of the product in crops is likely to result in non-detectable residues.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Carfentrazone-ethyl is not on the NOHSC *List of Designated Hazardous Substances*. Based on the NOHSC *Approved Criteria for Classifying Hazardous Substances*, carfentrazone-ethyl is classified as non-hazardous.

Carfentrazone-ethyl TGAC is in the form of yellow orange viscous liquid. It has low acute oral, dermal and inhalation toxicity in rats and rabbits. It is a slight eye irritant in rabbits but not a skin irritant. It is not a skin sensitiser in guinea pigs.

Affinity cannot be classified as hazardous according to NOSHC criteria based on the information supplied to NOHSC.

Affinity is a dry flowable formulation. It is expected to possess low acute oral and inhalation toxicity and low acute dermal toxicity. The product is a slight skin irritant and a moderate eye irritant in rabbits but not a skin sensitiser in guinea pigs. The product will be supplied in 2 kg containers.

Formulation, transport, storage and retailing

Affinity will be formulated overseas and imported into Australia in sale packs. Transport workers, storepersons and retailers will handle the packaged product and could only become contaminated if the packaging were breached.

Use of the Product

Affinity is proposed for the post emergence control of broadleaf weeds in winter cereals such as wheat, barley, oats and triticale. It will be applied by boomspray. The proposed application rate is 40 to 60 g of product/ha (16-24 g active ingredient/ha) in 50-100 L of water.

The main routes of exposure to the product are inhalational and dermal. The product is a dry flowable formulation, workers are likely to be exposed to the product while loading spray equipment. Workers may also be exposed to spray mist from the product spray. Functions that can lead to exposure to the product include opening containers, mixing/loading, application, cleaning up spills, cleaning/maintaining equipment.

Re-entry Statement

Based on the toxicity of the product and its use pattern, a re-entry statement is not recommended.

Recommendations for Safe Use

Workers involved in transport, storage and retailing should be protected by safe work practices and training. Users should follow the instructions on the product label. Based on the toxicity of the active ingredient and the product, elbow-length PVC gloves and face shield or goggles are recommended for users of *Affinity*.

The personal protective equipment recommended should meet the relevant Standard Australian standards specified below:

AS 2161-1978	Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)
AS 1337-1992	Eye Protection for Industrial Applications

Conclusions

Affinity can be used safely if handled in accordance with the instructions on the product label. Additional information is available on the MSDS.

ENVIRONMENTAL ASSESSMENT

Introduction

FMC International AG has applied for registration of *Affinity 400 DF Herbicide* (Affinity), which is a 400 g ai/kg dry flowable formulation containing the new Technical Grade Active Constituent (TGAC) carfentrazone-ethyl. It is to be used for early post emergence control of certain broadleaf weeds in winter cereals, such as wheat, barley, oats and triticale. Carfentrazone-ethyl belongs to the aryl triazolinone group of herbicides, which act in a complex way by inhibiting the enzyme protoporphyrinogen oxidase (an enzyme involved in the formation of chlorophyll and heme).

Environmental Fate

Hydrolysis
A study of the hydrolysis of carfentrazone-ethyl at ~20°C to meet OECD Guidelines and a similar study at ~25°C conducted to meet USEPA Guidelines were provided. These studies indicated that carfentrazone-ethyl hydrolyses only slightly at pH 5.0 (DT50 > 30 d), but hydrolyses moderately at pH 7.0 (DT50 = 13.7 d and 8.6 d, respectively) and very rapidly at pH 9.0 (DT50 = 0.21 d and 0.15 d, respectively). The only significant hydrolysis product was the chloropropionic acid formed by removal of the ester ethyl group ("F8426-chloropropionic acid"). Hence carfentrazone-ethyl may hydrolyse at moderate to very rapid rates in the environment where pH is neutral to alkaline, but the product formed is relatively stable to further hydrolysis.

Photolysis
An aqueous photolysis study with carfentrazone-ethyl conducted to meet USEPA Guidelines was provided. The study used continuous irradiation from a lamp simulating natural sunlight wavelengths and was conducted at pH 5.0, where only slight hydrolysis occurs. The results indicated photolysis DT50s of ~70 h under the test conditions (DT50 = 24-96 h - readily photodegradable). This was estimated by different methods to correspond to ~7.3 d or ~8.3 d under natural sunlight conditions at 40°N latitude in summer. Various photoproducts were identified, indicating that photolysis caused chlorine and fluorine atoms on the phenyl ring or ester sidechain of the molecule to be replaced. However, the phenyl and triazolinone rings in the molecule remained intact and attached.

Similar studies with the hydrolysis product F8426-chloropropionic acid indicated photolysis DT50s for this product of 45.6 h to 87.0 h at pH 5.0, 7.0 and 9.0 (ie readily photodegradable at all 3 pHs). This was estimated by different methods to correspond to ~3.8 d to ~10.4 d under natural sunlight conditions at 40°N latitude in summer. Various products were identified, indicating that in addition to causing chlorine and fluorine atoms on the phenyl ring or ester sidechain of the molecule to be replaced, photolysis of this hydrolysis product rather than the parent molecule led to opening and separation of the phenyl and triazolinone rings and a substantial degree of mineralisation.

A soil photolysis study conducted to meet USEPA Guidelines with cyclic illumination from a lamp simulating natural sunlight wavelengths indicated that carfentrazone-ethyl is stable to photolysis in soil.

Photolysis in water is likely to be the most rapid means of mineralisation, but may be reduced to some extent where the water is turbid. Photolysis on soil is not expected to be significant.

Soil and Water Metabolism Studies

Aerobic and anaerobic soil metabolism: A 121 day aerobic soil metabolism study to USEPA Guidelines (20°C, soil moisture 75% of field capacity [0.33 bar], in the dark) using a single soil indicated that degradation of carfentrazone-ethyl was biphasic, with a DT50 of 2.2-2.5 days over the first 8 days (DT90 = 7.3-8.3), followed by much slower degradation of the carfentrazone-ethyl residues remaining (half-life 43-71 days for ~10% of the initially applied substance).

A similar study with 4 other soils with 12 months incubation (20°C, moisture content 50% or 75% of field capacity, in the dark) indicated DT50s of <0.1 days to 1.3 days, fitted using non-standard mathematical models because the degradation rate slowed greatly with increasing incubation time. The range of soil moisture content tested had relatively little effect on the degradation rate, but differences in degradation rate between the soils tested became increasingly evident with longer duration of incubation. Estimated DT90 values ranged widely, from ~0.2-1.2 days in 2 of the soils to 8.5-17 days in a third soil and 220-299 days in a fourth soil. One of the soils was also incubated for 102 days at 10°C (moisture content 75% field capacity), for which the estimated DT50 and DT90 were 0.1 and 482 days (extrapolated), indicating degradation was still rapid initially under cool conditions.

Thus, under aerobic laboratory test conditions, initial degradation of carfentrazone-ethyl in these soils proceeded readily and a high percentage of applied carfentrazone-ethyl (~73-97%) was degraded within 8 d of application. However, under the test conditions degradation of the remaining residues then proceeded much more slowly, and at 20°C residues of carfentrazone-ethyl remaining at 12 months ranged between soils from undetectable to ~10% of applied.

A further soil metabolism study to USEPA Guidelines with carfentrazone-ethyl and one of the above soils investigated degradation when anaerobic conditions were imposed before application of the test substance to the soil, followed by incubation in the dark under continuing anaerobic conditions for 12 months at 20°C. Estimated DT50 and DT90 values in this case were 1.0-1.1 days and 3.3-3.6 days. Thus carfentrazone-ethyl also degrades readily under anaerobic conditions.

Analyses of metabolites indicated that under aerobic test conditions, carfentrazone-ethyl hydrolysed to F8426-chloropropionic acid and transformations then followed on the acid side-chain to form F8426-propionic acid, F8426-cinnamic acid and F8426-benzoic acid. Hydroxylation of the methyl group on the triazolinone ring also occurred. Under anaerobic conditions, F8426-chloropropionic acid and F8426-propionic acid were formed, but further changes to the acid side-chain occurred very slowly and hydroxylation of the methyl group on the triazolinone ring was absent. No ring separation metabolites were identified and mineralisation of the molecule to CO_2 occurred very slowly (<3% of applied after 12 months).

Aerobic aquatic metabolism: An aerobic aquatic metabolism study to German and UK Guidelines was provided, with 2 water/sediment systems incubated for 100 days. Both systems were tested at 20°C and one also at 10°C. This study was conducted in the dark, excluding the possibility of aqueous photolysis. Carfentrazone-ethyl degraded readily in both water/sediment systems at 20°C (DT50 in whole system = 0.25-0.37 days, DT90 = 0.84-1.22 days). Degradation was almost as rapid in the water/sediment system at 10°C (DT50 in whole

system = 1.33-1.50 days, DT90 = 4.42-5.00 days). The great majority of the applied carfentrazone-ethyl and metabolites forming from it remained in the water phase rather than partitioning to sediment. A similar metabolic pathway (again with very slow mineralisation and no evidence of ring separation metabolites) was indicated to that in soil under aerobic conditions, except that hydroxymethyl metabolites did not reach significant levels during the 100 day incubation period.

Mobility Studies

Chemical and physical data indicate that carfentrazone-ethyl is very slightly volatile and unlikely to evaporate significantly from soil or water.

Soil adsorption/desorption studies were not possible with carfentrazone-ethyl because of its instability under the test conditions, but studies were provided with five major metabolites of carfentrazone-ethyl. Batch equilibrium studies to USEPA Guidelines of the adsorption and desorption of these metabolites on five soils found that three had very high mobility in all five soils and two had medium to very high mobility, depending on soil type. Mean K_{OC} values for adsorption ranged from 4.3 (mean of only 3 soils - too low to determine in 2 cases) for 3-hydroxymethyl-F8426-benzoic acid to 17 for F8426-benzoic acid, 23.4 for F8426-chloropropionic acid, 98 for F8426-propionic acid, and 142 for F8426-cinnamic acid. However, adsorption of carfentrazone-ethyl metabolites to soil was not well correlated with organic carbon content (OC%) range 0.23-3.4%. Hence it is more appropriate to consider the untransformed K_d values, where the range in mean values was 0.11 (mean of only 3 soils) for 3-hydroxymethyl-F8426-benzoic acid to 2.85 for F8426-cinnamic acid. Adsorption of each soil was strongest in a soil with a very low pH (pH = 4.6-4.8, other soils pH 5.7-6.4), which may reflect the degree of dissociation present with these acid metabolites. Once adsorbed, residues were slightly more strongly held (K_d and K_{OC} values for desorption were slightly higher than for adsorption).

An aged soil column leaching study to USEPA Guidelines was provided. The study used the same 5 soils treated with ^{14}C-carfentrazone-ethyl and incubated ("aged") for 10 days before placement on soil columns of the corresponding soil. The soil columns were then leached with ~51 cm of water within 24 hours. The amount of radioactivity present in the leachate of the five different soils varied from 8.8% to 91.5% of applied. Radioactivity remaining on the soil columns was distributed down the whole column, but in each case a large proportion was present in the surface layer. Analysis of the leachates indicated that no parent substance had leached through the soil columns, whereas all the major metabolites evaluated were found in leachate to some extent. Carfentrazone-ethyl had degraded to a large degree (~87-98% of applied) over the 10 day aging period, and the main metabolite present after aging was F8426-cinnamic acid in four of the soils and F8426-chloropropionic acid in the other. F8426-chloropropionic acid was the main metabolite present in leachate from the latter soil, whereas F8426-benzoic acid rather than F8426-cinnamic acid was the main metabolite in leachate from the other 4 soils. Thus little or no mobility of carfentrazone-ethyl itself was evident, whereas major metabolites of carfentrazone-ethyl were mobile to very mobile under the test conditions. F8426-cinnamic acid was less mobile than the other metabolites in 4 of the soils, consistent with the results of the batch equilibrium studies on the same soils.

The Gustafson Ubiquity Score (GUS) assesses the leaching potential of a chemical by considering both its mobility (K_{OC}) and its persistence in soil (DT50). Because it degrades too rapidly under the test conditions, measured K_{OC} data are not available for carfentrazone-ethyl, and it is likely that carfentrazone-ethyl would also degrade too rapidly under field conditions

for significant leaching to occur. GUS values calculated by Environment Australia for major metabolites of carfentrazone-ethyl using the above mean K_{OC} data and assuming a DT50 of 30 days in each case were 2.7 for F8426-cinnamic acid ("transitional leacher") and 3.0, 3.9, 4.1 and 5.0, respectively, for F8426-propionic acid, F8426-chloropropionic acid, F8426-benzoic acid and 3-hydroxymethyl-F8426-benzoic acid (ie "probable leachers").

Field Dissipation

Field Dissipation Study With Carfentrazone Ethyl
In field dissipation studies to USEPA Guidelines at two sites in the USA, carfentrazone-ethyl was applied to bare soil on a single occasion at a target rate of ~104 g ai/ha (5x the proposed rate for cereal crops in Australia). Soil samples were taken over a 280 day period at one site and 356 days at the other. These samples were analysed for carfentrazone-ethyl and four major metabolites (F8426-chloropropionic acid, F8426-propionic acid, F8426-cinnamic acid and F8426-benzoic acid).

Mean total residues in soil at the two sites on the day of application (day 0) were ~58 ppb and ~30 ppb in the surface 10 cm (~53 ppb at this site on day 7). At day 0, mean levels of carfentrazone-ethyl were only 3.6 and 5.9 ppb in the surface 10 cm, declining to <1 ppb by 7-15 days after treatment (DAT). Thus carfentrazone-ethyl degraded very rapidly on the first day of application, and the DT50 from initial concentrations in soil calculated from the limited data available was ~2 days at one site and ~5 days at the other.

The dominant metabolite present was F8426-chloropropionic acid (peak ~45-49 ppb in the surface 10 cm on day 0). The other metabolites measured were present over the course of the studies at much lower peak levels (2.2-14.2 ppb in the surface 10 cm). Total residues of carfentrazone-ethyl plus these measured metabolites dissipated relatively rapidly initially, but dissipation then slowed and total residues remaining in the surface 10 cm at the final sampling were ~4 ppb. The calculated half-life DT50 for total residues of carfentrazone-ethyl and these measured metabolites over the first 9 weeks was 17 days at one site and 32 days at the other (note that these are not mineralisation half-lives and that other metabolites still retaining both rings may have remained, such as 3-hydroxymethyl-F8426-benzoic acid).

At a sandy site regarded as a “worse case" scenario for downward migration of residues, residues of carfentrazone-ethyl and F8426-chloropropionic acid first appeared in the 10-20 cm layer on day 3 after treatment (3 DAT). Carfentrazone-ethyl was not found at 10-20 cm at later samplings, but F8426-chloropropionic acid, F8426-benzoic acid and/or F8426-cinnamic acid were found at that depth at various later samplings. Leaching below 20 cm was not observed at all at this site. At the other site, leaching of residues below 10 cm was not observed.

Thus, rapid degradation of carfentrazone-ethyl and the pattern of metabolites found in these field studies was consistent with laboratory studies, to the extent the metabolites were investigated. The results suggest little leaching in field situations of metabolites known to be mobile to very mobile from laboratory studies.

Confined Rotational Crop Study
Soil analysis results from a confined rotational crop study with lettuce, radish and wheat crops planted 1, 3, 6 or 9 months after application of ^{14}C-carfentrazone-ethyl were consistent with

soil laboratory studies in the rapid degradation rate of carfentrazone-ethyl evident, the metabolites formed, and their relatively slow degradation. Only limited mobility in soil was evident, similar to the field dissipation study results. The study indicated that carfentrazone-ethyl metabolites and the small amount of carfentrazone-ethyl which remained in soil at 1-9 months after application are taken up from the soil by various plant species, with by far the highest concentration of residues being found in wheat straw. 3-hydroxy-F8426-benzoic acid was the major metabolite present in plant tissue and F8426-cinnamic acid was not present, whereas F8426-benzoic acid was generally the major metabolite in the soil, followed by F8426-cinnamic acid. No metabolites formed by ring opening or ring separation were identified in either the plants or soil.

Accumulation Potential In Soils

The low rate of application of carfentrazone-ethyl together with its degradation behaviour mean that little or no carryover from year to year is expected of the parent substance. Laboratory studies indicated that ring separation and mineralisation of carfentrazone-ethyl occurs slowly except where residues are exposed to aqueous photolysis, and that the metabolites which are produced are mobile to very mobile in soil. However, field dissipation trials showed that residues of carfentrazone-ethyl did not persist in soil, and did not leach at detectable concentrations below 20 cm. Environment Australia concludes that at most very low levels of carfentrazone-ethyl metabolites may persist in soil.

Bioaccumulation In Aquatic Organisms

A rainbow trout bioaccumulation study to USEPA Pesticide Guidelines was provided, with two carfentrazone-ethyl exposure concentrations (mean measured concentrations 18 µg ai/L and 171 µg ai/L, for 41 or 28 days, respectively). The results indicated that the Bioconcentration Factor (BCF) of total radioactive residues from ^{14}C-labelled carfentrazone-ethyl with this species was 28-34, 349-379 and 159-176, respectively, in edible tissue, non-edible tissue and whole fish. This would indicate that carfentrazone-ethyl is moderately bioconcentrating, but initial depuration occurred very rapidly (>80% of whole body tissue and >50% of edible tissue residues present on the final day of exposure eliminated by day 1 of depuration) and little residues remained in fish tissue by 14 days of depuration (~1-2% of original whole body residues). Furthermore, bioaccumulation of carfentrazone-ethyl was affected by rapid degradation both in the test water and within the fish. Despite flow-through conditions, in the presence of fish ~60-65% of radioactive residues in water were parent carfentrazone-ethyl, with F8426-chloropropionic acid the dominant metabolite present. Carfentrazone-ethyl was not detected in fish tissue, but F8426-chloropropionic acid was present at high levels (~90-94% of extracted residues), together with other minor metabolites and/or conjugates of them.

Environmental Toxicity

Birds
Toxicity tests conducted to USEPA Guidelines showed that carfentrazone-ethyl is practically non-toxic to bobwhite quail with acute oral exposure (LD50 > 2250 mg/kg) and to both bobwhite quail and mallard ducks with subacute dietary exposure (LC50 > 5620 ppm in both cases). Avian reproductive studies to USEPA Guidelines indicate No Observed Effect Levels (NOELs) of 1000 ppm for both bobwhite quail and mallard ducks.

Aquatic
Acute toxicity tests conducted to USEPA Guidelines under flow-through conditions found that carfentrazone-ethyl is moderately toxic to rainbow trout (96 h LC50 in the range 1.1-2.1 mg ai/L), bluegill sunfish (96 h LC50 in the range 1.5-4.4 mg ai/L) and tidewater silverside (96 h LC50 = 1.14 mg ai/L). Acute toxicity tests to USEPA Guidelines under flow-through conditions found that carfentrazone-ethyl is slightly toxic to *Daphnia magna* (48 h EC50 >9.8 mg ai/L) and moderately toxic to mysid shrimp (96 h LC50 = 1.17 mg ai/L) and eastern oyster (96 h EC50 = 2.30 mg ai/L). Acute toxicity tests with major carfentrazone-ethyl metabolites to OECD Guidelines under static conditions found they were at most slightly toxic to rainbow trout (96 h LC50 > 25.4 mg ai/L to >99.2 mg ai/L) and *Daphnia magna* (48 h EC50 >10.7 mg ai/L to >102 mg ai/L).

In contrast, as may be expected from its herbicidal activity, carfentrazone-ethyl was found to be very highly toxic (EC50 < 100 µg ai/L) to the algae, diatom and aquatic plant species tested according to USEPA or OECD Guidelines. Results were based on measured initial concentrations, due to the rapid decline in carfentrazone-ethyl concentration under the static test conditions. The EC50s for algal and diatom species (freshwater green alga *Selenastrum capricornutum*, marine alga *Skeletonema costatum*, freshwater diatom *Navicula pelliculosa* and blue-green alga *Anabaena flos-aquae*) were in the range 7.7-17 µg ai/L (72 or 120 h incubations). The aquatic macrophyte duckweed (*Lemna gibba*) was the most sensitive species under the test conditions (14 d EC50 = 5.7 µg ai/L). Similar tests with the alga *Selenastrum capricornutum* showed that three early metabolites of carfentrazone-ethyl (F8426-cinnamic acid, F8426-propionic acid and F8426 chloropropionic acid) retain significant activity towards algae (72 h EC50 = 37.2 µg ai/L, 139 µg ai/L and 534 µg ai/L, respectively). A fourth metabolite (F8426-benzoic acid) had slight toxicity to this algal species (72 h EC50 = 12.6 mg ai/L).

Non-target Invertebrates
In studies conducted to USEPA Guidelines, carfentrazone-ethyl was found to have very slight toxicity to bees by acute contact or acute oral exposure (24 h LD50 > 200 µg/bee in both cases). At most slight toxicity to earthworms was indicated in a study to OECD Guidelines with carfentrazone-ethyl (14 d LC50 > 820 mg/kg soil, measured initial concentration). Limit tests with four major carfentrazone-ethyl metabolites showed they were all very slightly toxic to earthworms (LC50 > 1000 mg/kg soil, nominal initial concentrations). No studies on the potential effect of carfentrazone-ethyl on predators or parasites were available, but low toxicity to bees and earthworms makes effects on other non-target invertebrates unlikely under the proposed use at very low per hectare rates once per annum. Similarly, no studies have been provided regarding the toxicity to soil micro-organisms, but significant effects are unlikely under the low frequency and rate of use.

Phytotoxicity
Carfentrazone-ethyl is a selective herbicide absorbed by foliage, with limited translocation and limited root absorption. Certain metabolites may also be phytotoxic to susceptible plants via foliar or soil exposure. A study was provided of the effects of carfentrazone-ethyl on the germination of seeds exposed in petri dishes, emergence and early growth of plants sprayed shortly after sowing in pots, and vegetative vigour of plants sprayed as seedlings. The results show that exposure of the 10 crop species tested to carfentrazone-ethyl resulted in various degrees of response depending on the species, stage of development and exposure by foliage or roots. The chemical had little or no effects on germination of 8 of the 10 species. In general, effects on emergence were relatively low, except for some species at the highest rate (~3.5x the proposed rate for winter cereals). The highest response to the chemical was observed in actively growing seedlings in the vegetative vigour tests, where the only species showing little or no effects were corn, ryegrass and wheat, while soybean was affected to a relatively minor degree.

Environmental hazard

It is proposed that Affinity 400 DF Herbicide will be sprayed on winter cereal crops via ground-based boomspray equipment at a rate of 40, 50 or 60 g product/ha (16, 20 or 24 g ai/ha), in general only once per year. Residues would be expected in the crop area on plant and soil surfaces and direct overspray, spray drift and run-off are potential means of contamination of adjacent areas and surface water. Laboratory data indicate that carfentrazone-ethyl is unlikely to leach significantly because of rapid degradation and possibly some adsorption to soil. However, its metabolites are mobile to highly mobile in soil and to differing degrees retain some herbicidal activity.

Terrestrial Hazard
The hazard to birds from application of carfentrazone-ethyl as proposed is low, based on estimates of residues resulting in the field relative to the typical diet of bobwhite quail and mallard ducks and the available dietary toxicity data. Estimates of the maximum dose per bee from direct contact with spray are well below toxic levels to bees and a low hazard to bees and other non-target insects and mites is expected from use as proposed. Maximum expected concentrations of carfentrazone-ethyl and its metabolites in soil are well below toxic levels to earthworms and are not expected to be harmful to soil micro-organisms.

However, carfentrazone-ethyl is a selective herbicide absorbed by foliage, with limited translocation and limited root absorption. Phytotoxic effects are likely in susceptible species where foliage is reached by direct overspray or potentially by spray-drift. Phytotoxic effects to susceptible plants exposed via residues of carfentrazone-ethyl or certain of its metabolites in soil may occur, but mobility and degradation in soil to less toxic metabolites is expected to minimise any hazard from soil residues.

Aquatic Hazard
Direct overspray: *Environment Australia* assessed the aquatic hazard from direct overspray of Affinity 400 DF by considering the expected environmental concentration of carfentrazone-ethyl and its major metabolites in a static, shallow (15 cm deep) pond following direct overspray at the proposed application rate to winter cereals of 20 g ai/ha on a single occasion, as specified on the label. The estimated EEC was then compared with acute toxicity data for

carfentrazone-ethyl and its metabolites to aquatic organisms to determine the hazard quotient (Q = EEC/EC50 or LC50).

This indicated that only a low hazard exists to fish and aquatic invertebrates (Q < 0.02), but indicated an unacceptable hazard from direct overspray to algae, diatoms and aquatic plants (Q = 0.94-2.81). Carfentrazone-ethyl degrades rapidly in water, but one of its metabolites was also potentially hazardous to algae (and a potential hazard from at least this metabolite presumably also applies to diatoms and aquatic plants). Chronic exposure of aquatic organisms to carfentrazone-ethyl or its metabolites is not expected due to rapid degradation of the parent substance, mineralisation of metabolites in the presence of sunlight, and infrequent use.

Hence *Environment Australia* concludes that direct overspray of aquatic areas should be avoided. Affinity 400 DF is expected to be applied to winter cereals by ground based equipment, where direct overspray of waterbodies or streams is unlikely. Aerial application to winter cereals is unlikely and is not recommended for efficacy reasons, and the applicant has advised against it for winter cereals on the product label. The label also carries a standard warning against contamination of waterbodies with the product or used container.

Spray drift: A similar procedure was then followed for algae, diatoms and aquatic plants exposed to 10% spray drift in a similar pond. This indicated a mitigable hazard to the 5 test species, hence the AgDRIFT™ Tier I model was used to estimate water concentrations reached through spray drift to a 15 cm deep, 3 m wide waterbody 10, 30 or 100 m downwind from a cereal crop where Affinity 400 DF was applied by boomspray. Only a low hazard was indicated to even the most sensitive species (*Lemna gibba*) at these distances, hence there is only a low aquatic hazard with application of the product by boomspray. Furthermore, water depths are likely to be greater than 30 cm, further reducing the hazard. The spray drift warning provided on the draft product label requires amendment to refer to aquatic areas. The applicant has added a label comment advising against aerial application to winter cereals.

Run-off:
Carfentrazone-ethyl metabolites are mobile to highly mobile according to laboratory studies and may therefore enter waterways in run-off waters. However, this is likely to occur to a lesser extent with the most toxic metabolite (F8426-cinnamic acid) and there is evidence that carfentrazone-ethyl itself has little mobility in soil. As very much a worst case scenario, it was assumed that 2% of the applied substance runs off from a 10 ha cereal crop into a 15 cm deep, 1 ha waterbody. This indicated a mitigable hazard to algae, diatoms and aquatic plants (Q = 0.19-0.56), but Environment Australia expects concentrations of carfentrazone-ethyl and its metabolites in run-off water will not reach toxic levels due to interception and absorption of spray by foliage, rapid degradation to less toxic metabolites, partial adsorption by soil and greater dilution in water free of herbicide residues.

Conclusions
Environment Australia has assessed data in support of the use of AFFINITY 400 DF HERBICIDE on winter cereal crops and believes that the application contains adequate environmental fate and toxicity data to demonstrate that use according to the label is unlikely to result in primary poisonings of wildlife, fish etc. Environmental fate studies indicate that the active ingredient carfentrazone-ethyl degrades rapidly in water and soil to a sequence of metabolites. Laboratory studies indicate that in surface water aqueous photolysis is expected

to lead to rapid mineralisation, but that in soil these metabolites may persist and may be mobile to highly mobile. However, field dissipation studies show the parent substance and metabolites dissipated to low levels within one year and did not leach detectably below 20 cm. Furthermore, the product is used infrequently (expected to be once per annum with the proposed use in winter cereals) and at very low application rates. Carfentrazone-ethyl and certain of its metabolites have very high toxicity to algae and aquatic plants and may be toxic to various terrestrial plants, hence aquatic contamination or spray drift onto non-target plants should be avoided. At the proposed rates of application an adequate safety margin exists as long as the product is not applied by air. Environment Australia has recommended suitable label advice to minimise the hazard from direct overspray or spray drift, which appear to be the greatest hazards with the proposed use regime.

EFFICACY AND CROP SAFETY ASSESSMENT

This summarizes the trials conducted in Australia with *Affinity* (containing the active constituent carfentrazone-ethyl), providing information in relation to weed control, crop safety, and re-cropping studies.

Affinity is a post-emergence, broadleaf herbicide for use in winter cereals. It is a rapid knockdown herbicide with activity observed 1 to 4 days after treatment. The product degrades quickly in the soil and does not provide any residual activity against weeds. Its mode of action results in membrane disruption, which ultimately kills sensitive weeds by interfering with the chlorophyll biosynthetic pathway. Carfentrazone-ethyl belongs to the aryl triazolinone group and is included in group G for the herbicide mode of action.

Justification for the use of *Affinity* arises primarily from its relatively benign environmental characteristics and the opportunity to use a different mode of action against weeds prone to develop herbicide resistance. *Affinity* does not appear to be particularly effective alone against some of the weeds listed on the label and relies heavily on the synergistic or additive effects of the phenoxy MCPA, another broadleaf herbicide.

Weed Control Efficacy

Carfentrazone-ethyl has been evaluated under a wide range of Australian winter cereal growing conditions and in all major winter cereal growing areas. A total of 48 efficacy and crop tolerance trials have been completed since 1990. Apart from the normal development requirements of establishing the use rates, generating weed efficacy and crop safety data, the development of carfentrazone-ethyl has been complicated by two changes in formulation and the need to develop this product with a tank mix partner.

Rate Range

Initial trials conducted in 1990 to '93 were undertaken with a 240 g/L EC formulation of carfentrazone-ethyl. These established the basic rates range of carfentrazone-ethyl and showed that carfentrazone-ethyl had a limited weed control spectrum within the confines of acceptable crop tolerance. Use rates of 30 g ai/ha and above were found to cause unacceptable crop injury, while to achieve control of many weed species these higher rates were required. Rates of below 15 g ai/ha did not provide useful weed control.

The efficacy of carfentrazone-ethyl was typified by extremely rapid knockdown (1 to 4 days). However, if the weeds were not killed by the rapid knockdown, they tended to regrow. This knockdown capability was considered desirable and an ideal tank mix partner was sought to broaden control. The optimum use rate range of *Affinity* without compromising crop safety was found to be 40 to 60 g/ha, with or without a surfactant at 0.05% v/v.

Environmental conditions at the time of application play a significant role in influencing the activity of carfentrazone-ethyl. Extremes in environmental conditions e.g. temperature and moisture, soil conditions and cultural practices may affect the activity of *Affinity*. Under warm moist conditions, herbicide symptoms may be accelerated. While under very dry conditions,

the expression of herbicide symptoms is delayed, and weeds hardened off by drought are less susceptible to *Affinity*.

Addition of Surfactants

Surfactants, when added to *Affinity*, were found to be a key determinant in crop selectivity, particularly when combined with extremes of environmental conditions. *Affinity* is responsive to the addition of spray adjuvants such as crop oils and oil/surfactant blends, increasing crop phytotoxicity as well as increasing early knockdown of weeds. Rapid knockdown does not always convert to good control. Increased knockdown can result in the regrowth of a greater number of plants.

The addition of oil/surfactant blends (eg Uptake) to any *Affinity* treatment resulted in excessive crop injury and therefore they are not recommended.

The addition of the standard rate of a commercially available non-ionic surfactant (eg BS 1000) at 100 mL/100L was found to cause excessive early crop injury, despite rapid crop recovery. The use of a "half rate" of a non-ionic surfactant at 50 mL/100L provided acceptable crop safety as well as improved weed control in most cases.

When application is made in less than ideal conditions i.e. “drier growing conditions at time of application" a non-ionic surfactant should be added to ensure optimum control. While some herbicide symptoms may appear on the crop, the crop quickly recovers with no significant yield loss.

MCPA amine as a Mix Partner

The issue of crop selectivity was a significant factor in the selection of a mix partner for *Affinity*. MCPA amine was found to be the best, providing broadened weed control without increasing crop injury. The combination of *Affinity* and the low volatile ester (LVE) formulation of MCPA consistently increased crop phytotoxicity to unacceptable levels and it is not recommended.

Trial work was undertaken with various ratios of *Affinity* and MCPA amine to determine the recommended 500 mL/ha of MCPA with *Affinity*. This rate is the lowest recommended rate required for robust weed control. Higher MCPA amine use rates may be tank mixed with *Affinity* in accordance with the specific label of the MCPA amine product to be used.

Application Timing

As *Affinity* is a contact, foliar herbicide, good coverage is essential to ensure good control. Later applications to crops at the Zadoks scale 28 tended to achieve poorer control than earlier applications to crops at Zadoks scale 13. Reduced efficacy can be attributed to an increase in weed size and the increase in crop “shading" (interception of herbicide by shielding) as crops moved towards canopy closure. The combination of *Affinity* plus MCPA amine provides a more robust control option, as weed and crop stages advance, compared to *Affinity* alone. However the general recommendation is to treat weeds and crops early at the 3 leaf to early tillering stage, rather than later at mid to late tillering.

Crop Safety

Affinity activity is rapid and any crop injury is first noticed within four to seven days of application. The severity of the injury is rate responsive and can be significantly increased by the addition of surfactants, oils and adjuvants such as oil/surfactant blends. Symptoms of *Affinity* crop injury vary from minor cases of crop injury such as leaf spotting/scalding and plant stunting, to severe cases of total leaf yellowing/whitening and leaf abortion. Recovery from injury is rapid and generally occurs within 14 to 21 days after application. Crop injury from *Affinity* does not negatively impact on crop yields.

The major trends in crop phytotoxicity are:

- Rates of 30g ai/ha and above of *Affinity* provide unacceptable crop selectivity.
- The addition of a surfactant to *Affinity* increases crop phytotoxicity.
- The higher the rate of surfactant the greater the crop phytotoxicity. The addition of the standard 100 mL/100 Lrate of surfactant consistently caused unacceptable crop injury while a lower rate of 50 mL/100L proved acceptable.
- The tank mix of *Affinity* plus MCPA amine provided commercially acceptable crop selectivity even when a non-ionic surfactant at 50 mL/100L was added.

Yield Summary
Of the 48 efficacy trials conducted, 31 were taken through to yield. The results showed that when *Affinity* is applied alone or in tank mix with MCPA for in-crop weed control, the net affect between weed control and crop phytotoxicity effects is positive in terms of final yield.

Crop Tolerance
Seven crop tolerance variety screens were conducted with *Affinity*. These trials were conducted over a number of seasons in NSW, Vic, SA, and WA. All trials were installed in weed free sites with application timings ranging from Zadoks 14 to 28. In total 75 wheat, 22 barley, 10 oat and 8 triticale crop screens were conducted.

Results showed no adverse effects on yield while some cases of slight stunting, leaf whitening and/or minor leaf scald were recorded.

In conclusion, given the similar growth habits of the winter cereals and the proposed use pattern of *Affinity*, this data supports the labelling of *Affinity* for use in winter cereals such as wheat, barley, oats and, triticale.

Safety to Following Crops
Carfentrazone-ethyl is a non residual herbicide. As such, the use of *Affinity* will not restrict rotation to following crops. Trial results were presented to substantiate this. When mixing with MCPA amine any recropping restrictions identified on the MCPA label must be observed.

Suitability to Aerial Application

No data has been generated to support an aerial application claim. Application of *Affinity* will be restricted to conventional ground rig, boom spray application.

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 label. As long as the product is used according to label instructions and Good Agricultural Practice it should be suitable for the proposed purpose.

Proposed Draft label

Main Panel

Affinity 400 DF

HERBICIDE

ACTIVE CONSTITUENT: 400 g/kg CARFENTRAZONE-ETHYL

GROUP	G	HERBICIDE

For the control of certain annual broadleaf weeds in Winter cereals as per the Directions For Use Table

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE

2 kg

FMC International A.G.
Suite 7, 36 Bryants Road
Loganholme QLD 4129

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.

Spillage - In case of spillage, confine spilled product with material such as sand or clay. Dispose of waste as indicated below or according to the Australian Standard 2507 - Storage and Handling of Pesticides. DO NOT allow spilled product to enter sewers, drains, creeks or any other waterways. Keep out animals and unprotected persons. Vacuum, shovel or pump waste into an approved drum. To decontaminate spill area, tools and equipment, wash with a suitable solution (ie organic solvent, detergent, bleach or caustic) and add the solution to the drums of wastes already collected. Label for contents. Dispose of drummed wastes, including decontamination solution, in accordance with the requirements of Local or State Waste Management Authorities.

Triple or preferably pressure rinse container 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, 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 and skin. Avoid contact with eyes and skin. If product in eyes, wash it out immediately with water. Wash hands after use. When opening the container, preparing spray and using the prepared spray wear 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. Phone Australia 13 11 26.

Additional information is listed in the **MSDS FMC/AFF/1**, which is available from the supplier.

WARRANTY

FMC makes no warranty express or implied, concerning the use of this product other than that indicated on the label. Except as so warranted the product is sold as is. Buyer and user assume all risk of use and/or handling and/or storage of this material when such use and/or handling and/or storage is contrary to label instructions.

TRADEMARKS

"BS1000" – Registered Trademark.

DOM:

Batch Number:

NRA Approval No:

Draft Leaflet

Affinity 400 DF

HERBICIDE

ACTIVE CONSTITUENT: 400 g/kg CARFENTRAZONE-ETHYL

GROUP	G	HERBICIDE

For the control of certain annual broadleaf weeds in Winter cereals as per the Directions For Use Table

IMPORTANT: READ THIS LEAFLET BEFORE USE

2 kg

FMC International A.G.
Suite 7, 36 Bryants Road
Loganholme QLD 4129

Directions For Use

RESTRAINTS

DO NOT tank mix Affinity 400 DF with crop oil concentrates or blended oil/surfactant adjuvants (See compatibility section).

DO NOT tank mix MCPA LVE with Affinity 400 DF.

DO NOT tank mix Affinity 400 DF treatments with selective grass herbicides.

DO NOT apply the tank mix of Affinity 400 DF+ MCPA amine before the three-leaf crop stage.

DO NOT apply to cereals under sown with legumes.

DO NOT apply Affinity 400 DF to winter cereals by aircraft.

CROP	TARGET WEED	RATE/ha		WEED STAGE	CRITICAL COMMENTS
		Affinity 400 DF	**Affinity 400 DF + MCPA amine**		
Winter cereals (wheat, barley, oats, triticale)	Bedstraw/Cleavers *Galium tricornutum*	50g		Up to 6 whorls	**General** Apply as a post-emergence treatment for the control of small actively growing weeds. Tank mix with MCPA amine to improve control of larger weeds or when weed populations are high. The MCPA amine rate recommended on this label is a minimal rate required for control. Refer to the specific MCPA amine label for higher use rates. The addition of a non-ionic surfactant at a maximum rate of 50mL/100L of final spray volume to Affinity 400 DF alone or in tank mix with MCPA amine may be used to improve weed control under drier growing conditions at time of application. Refer to General Instructions and compatibility directions for further application details.
			50g + 500mL	6 to 10 whorls	
	Bifora *Bifora testiculata*		50g + 500mL	Up to 6 leaf	
	Capeweed *Arctotheca calendula*		50g + 500mL	Up to 8 leaf	
	Climbing Buckwheat *Fallopia convolvulus*		50g +500mL	Up to 6 leaf	
	Crassula *Crassula sieberana*	50g		Up to 4 leaf	
			50g + 500mL	Up to 8 leaf	
	Fumitory (Dense flower) *Fumaria densiflora*		50g + 500mL	Up to 8 leaf	
	Indian hedge mustard *Sisymbrium orientale*	50g		Up to 6 leaf	
			50g + 500mL	Up to 8 leaf	
	Lupins *Lupinus angustifolius*		40g + 500mL	Up to 4 leaf	
			50g + 500mL	Up to 8 leaf	
	Prickly Lettuce *Lactuca serriola*	50g		Up to 4 leaf	
			50g + 500mL	Up to 8 leaf	
	Rough Poppy *Papaver hybridum*		50g + 500mL	Up to 8 leaf	
	Shepherd's Purse *Capsella bursa-pastoris*		50g + 500mL	Up to 8 leaf	
	Sowthistle *Sonchus oleraceus*		50g + 500mL	Up to 6 leaf	
	Spiny Emex *Emex australis*		50g + 500mL	Up to 4 leaf	
	Turnip Weed *Rapistrum rugosum*		50g + 500mL	Up to 8 leaf	
	Wild Radish *Raphanus raphanistrum*		60g + 500mL	Up to 4 leaf	
	Wild Turnip *Brassica tournefortii*	50g		Up to 4 leaf	
		60g	50g + 500mL	Up to 6 leaf	
	Wireweed ***Polygonum aviculare***		50g + 500mL	Up to 8 leaf	

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

WITHHOLDING PERIOD

Winter cereals **DO NOT ALLOW STOCK TO GRAZE TREATED AREAS FOR 14 DAYS AFTER APPLICATION.**

GENERAL INSTRUCTIONS
Affinity 400 DF Herbicide is an early post-emergence herbicide for the control of certain broadleaf weeds in winter cereals. Affinity 400 DF is a fast acting contact herbicide and controls weeds through a process of membrane disruption. The foliar uptake of Affinity 400 DF is rapid and plant desiccation can occur within 1 to 4 days of application. Application of Affinity 400 DF should target small actively growing weeds. Subsequent germinations will not be controlled.

SYMPTOMS
Affinity is rapidly absorbed through the foliage of plants. Within a few hours following application, the foliage of susceptible weeds shows signs of desiccation, and in subsequent days necrosis and death of the plant. Due to environmental conditions and certain spray tank additives, some herbicidal symptoms may appear on the crop in the form of leaf spotting. However, the crop recovers quickly, usually within two to three weeks of treatment.

Extremes in environmental conditions, e.g. temperature and moisture, soil conditions and cultural practices may affect the activity of Affinity 400 DF. Under warm moist conditions, herbicide symptoms may be accelerated. While under very dry conditions, the expression of herbicidal symptoms is delayed, and weeds hardened off by drought are less susceptible to Affinity 400 DF. Under dry conditions the addition of a non-ionic surfactant may be used to improve weed control.

COMPATABILITY
Affinity 400 DF should be tank mixed with formulations of MCPA **amine** to broaden the weed control spectrum compared to either product applied alone. Do not tank mix Affinity 400 DF with MCPA **LVE** formulations or ester formulations of other herbicides or with oil/surfactant blends, as excessive crop injury may occur.

Annual Grass (wild oat, ryegrass etc.) Control
Affinity 400 DF should not be mixed with selective grass herbicides as grass weed control is significantly reduced and excessive crop injury may occur. Increased crop injury is caused by the crop oil concentrates and oil/surfactant blends used with these grass herbicides. Instead, allow a 10 to 14 day interval between separate broadleaf and grass herbicide applications.

Use of Surfactant/ Wetting Agents
The addition of a non-ionic surfactant (1000 gai/L) such as BS1000, at a maximum rate of 50 mL/100 L of final spray volume (0.05% volume/volume) may be used to improve weed control under drier growing conditions at time of application. At this use rate some leaf spotting may appear on the crop, however the crop recovers quickly, usually within two to three weeks of treatment.

The addition of oils and oil/surfactant blends will reduce crop selectivity and increase crop injury. Increasing the rate of these adjuvants results in increased (excessive) herbicide symptoms. Do not tank mix Affinity 400 DF with spray oils or oil/surfactant blends.

RESISTANT WEEDS WARNING | **GROUP** | **G** | **HERBICIDE**

Affinity 400 DF Herbicide is a member of the Aryl triazolinone group of herbicides. Its mode of action is through a process of membrane disruption, which is initiated by the inhibition of the enzyme protoporphyrinogen oxidase. This inhibition interferes with the chlorophyll biosynthetic pathway. For weed resistance management Affinity 400 DF is a Group G herbicide.

Some naturally occurring weed biotypes resistant to Affinity 400 DF and other herbicides that inhibit the enzyme protoporphyrinogen oxidase may exist through normal genetic variability in any weed population and increase if these herbicides are used repeatedly. These resistant weeds will not be controlled by Affinity 400 DF or other herbicides that inhibit the enzyme protoporphyrinogen oxidase.

Since the occurrence of resistant weeds is difficult to detect prior to use, FMC International A.G. accepts no liability for any losses that may result from the failure of Affinity 400 DF or other herbicides that inhibit the enzyme protoporphyrinogen oxidase.

TIMING
Application should be made to small, actively growing weeds less than 6 to 8 leaf in stage. As Affinity 400 DF is a contact herbicide, best control is achieved when weeds are exposed and are not shielded by other weeds and or the crop. Ideally crops should be at the 3 leaf to early/mid tillering stage (Zadoks code 13 to 25), prior to crop canopy closure.

MIXING
Add half the required volume of water to spray tank and start agitation. Add the measured amount of Affinity 400 DF next, followed by MCPA amine if tank mixing. Add balance of water to tank and add non-ionic surfactant at recommended rate if necessary. Maintain good agitation at all times until spraying is completed.

APPLICATION
Apply Affinity 400 DF as a broadcast application. Use conventional boom sprayers with either mechanical or by-pass agitation. Flat fan nozzles should be used. Spray equipment should be properly calibrated to ensure correct application. Use a spray volume of 50 to 150 litres per hectare. Use the lowest pressure and boom height, which provides uniform coverage. Use the higher volume if weed infestation is heavy or the crop cover is dense. Do not apply Affinity 400 DF to winter cereals by aircraft.

Tank mix with MCPA amine: When mixing Affinity 400 DF with MCPA amine it is important to follow the MCPA label directions for use in relation to weed and crop size and application timing. The MCPA amine use rate recommended for tank mix with Affinity 400 DF on this label is a minimum rate required for control. Higher MCPA amine rates may be used in accordance with the specific MCPA amine label to improve results in difficult situations.

The best application conditions are when soil is moist, weather fine and rain unlikely within one hour (Affinity 400 DF alone) or 6-8 hours when tank mixed with MCPA amine.

Under dry growing conditions, a low rate of a non-ionic surfactant (1000 gai/L) such as BS1000 may be added at a maximum rate of 50mL/100L of final spray volume (0.05% v/v) to improve weed control.

Extremes in environmental conditions eg. temperature and moisture, soil conditions and/or cultural practices may affect the activity of Affinity 400 DF. Under warm moist conditions, herbicide symptoms may be accelerated. While under very dry conditions, the expression of herbicidal symptoms is delayed, and weeds hardened off by drought are less susceptible to Affinity 400 DF. Under dry conditions the addition of a non-ionic surfactant may be added to improve weed control.

CROP ROTATION RECOMMENDATIONS
Affinity 400 DF Herbicide does not provide residual activity, therefore no crop rotational restrictions apply.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
Do not apply under weather conditions, or from spray equipment, which may cause spray drift onto nearby susceptible plants, adjacent crops, or pastures, or onto wetlands, waterbodies or watercourses.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS, AND ENVIRONMENT
Highly toxic to algae and aquatic plants. DO NOT contaminate streams, rivers or waterways with Affinity 400 DF or used container.

STORAGE AND DISPOSAL
Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight.

Spillage - In case of spillage, confine spilled product with material such as sand or clay. Dispose of waste as indicated below or according to the Australian Standard 2507 - Storage and Handling of Pesticides. DO NOT allow spilled product to enter sewers, drains, creeks or any other waterways. Keep out animals and unprotected persons. Vacuum, shovel or pump waste into an approved drum. To decontaminate spill area, tools and equipment, wash with a suitable solution (ie organic solvent, detergent, bleach or caustic) and add the solution to the drums of wastes already collected. Label for contents. Dispose of drummed wastes, including decontamination solution, in accordance with the requirements of Local or State Waste Management Authorities.

Triple or preferably pressure rinse container 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, 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 and skin. Avoid contact with eyes and skin. If product in eyes, wash it out immediately with water. Wash hands after use. When opening the container, preparing spray and using the prepared spray wear 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. Phone Australia 131126.

Additional information is listed in the **MSDS FMC/AFF/1**, which is available from the supplier.

WARRANTY
FMC makes no warranty express or implied, concerning the use of this product other than that indicated on the label. Except as so warranted the product is sold as is. Buyer and user assume all risk of use and/or handling and/or storage of this material when such use and/or handling and/or storage is contrary to label instructions.

TRADEMARKS
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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.

Bibliography/Further Reading

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United States Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances (OPPTS), Office of Pesticide Programs (OPP). http://www.epa.gov/OPPTS_Harmonized/

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