Public Release Summary
on

Evaluation of the new active

PYRAFLUFEN-ETHYL

in the product

SUMMIT ECOPAR 20SC HERBICIDE

Australian Pesticides and Veterinary Medicines Authority

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FOREWORD

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

In undertaking this task, the APVMA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Office of Chemical Safety), Department of Environment and Heritage (Risk Assessment and Policy Section), and State departments of agriculture and environment.

The APVMA has a policy of encouraging openness and transparency in its activities and of seeking community involvement in decision making. Part of that process is the publication of public release summaries for all products containing new active ingredients and for all proposed extensions of use for existing products.

The information and technical data required by the APVMA to assess the safety of new chemical products and the methods of assessment must be in accordance with accepted scientific principles. Details are outlined in the APVMA's publications *Manual of Requirements and Guidelines (MORAG)*

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

More detailed technical assessment reports on all aspects of the evaluation of this chemical can be obtained by completing the order form in the back of this publication and submitting with payment to the APVMA. Alternatively, the reports can be viewed at the APVMA Library 18 Wormald Street, Symonston ACT 2609.

The APVMA welcomes comment on the usefulness of this publication and suggestions for further improvement. Comments should be submitted to the Program Manager Pesticides, Australian Pesticides and Veterinary Medicines Authority, PO Box E240, Kingston ACT 2604.

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
CRP	Chemistry and Residues Program
d	day
DAT	Days After Treatment
DM	Dry matter
DT_{50}	Time taken for 50% of the concentration to dissipate
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
F_o	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Haematocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms

LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral
POEM	Predictive Operator Exposure Model (UK)
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
TRR	Total radioactive residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
μg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the registration of the product Summit Ecopar 20SC Herbicide, which contained the active constituent pyraflufen-ethyl. The product is for use in wheat, barley and triticale for control of annual broadleaf weeds.

Responses to the Gazette Notice that foreshadowed the publication of Public Release Summary were considered prior to registration of the product. They were taken into account by the Australian Pesticides and Veterinary Medicines Authority (APVMA) in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling. By posting this document on the Website, the APVMA seeks to remedy an inadvertent oversight of not doing so earlier.

Copies of full technical evaluation reports on pyrafluefen-ehtyl, covering toxicology, occupational health and safety aspects, residues in food and environmental aspects are available from the APVMA on request (see order form on last page). They can also be viewed at the APVMA library located at the APVMA offices, 18 Wormald Street, Symonston ACT 2609.

Applicant: Summit Agro Australia Pty Ltd

PRODUCT DETAILS

The product name is Summit Ecopar 20SC Herbicide, which contains 20g/L of the active constituent pyraflufen-ethyl as a suspension concentrate. The product will be formulated in overseas using pyraflufen-ethyl manufactured in Japan. The product will be packaged in 20L containers.

Pyraflufen-ethyl is a member of the phenyl pyrazole class of herbicides. The product inhibits the activity of protoporphyrinogen IX oxidase. The inhibition of this enzyme in chlorpoplasts leads to subsequent cell membrane destruction and necrosis. For weed resistance management Summit Ecopar 20SC Herbicide is classified as a Group G Herbicide.

The proposed rate of product use was 400mL – 500mL. Summit Ecopar 20SC Herbicide was proposed for registration in all States.

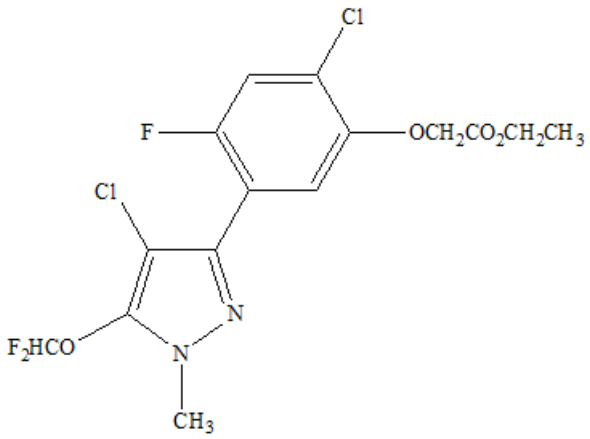
CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent pyraflufen-ethyl is manufactured in Japan by Nihon Nohyaka Co Ltd, Ihara Chemical Industry Co Ltd, 1800 Nakanogo, Fujikawa-Cho, Ihara-Gun, Shizuoka Prefecture, and is approved by the APVMA (Approval Number: 58650).

CHEMICAL CHARACTERISTICS OF THE ACTIVE CONSTITUENT

Common name:	Pyraflufen-ethyl
Synonyms and Code Number:	ET-751
Chemical name (IUPAC):	Ethyl 2-chloro-5-(4-chloro-5-difluoromethoxy-1-methyl-pyrazol-3-yl)-4-fluorophenoxyacetate
(CA):	Ethyl 2-chloro-5-[4-chloro-5-(difluoromethoxy)-1-methyl-1*H*-pyrazol-3-yl]-4-fluorophenoxy acetate
(CAS) Registry Number:	129630-19-9
Molecular formula:	$C_{15}H_{13}Cl_2F_3N_2O_4$
Molecular weight:	413.2
Chemical structure:	



PHYSICAL AND CHEMICAL PROPERTIES OF THE PURE ACTIVE CONSTITUENT

Physical State:	Powder
Colour:	Cream
Odour:	Odourless
Vapour pressure (25 °C):	1.6×10^{-8} Pa
Henry's Law Constant:	8.1×10^{-5} Pa.m^3/mol
Dissociation Constant:	Does not dissociate
Surface Tension (20 ºC):	74.2 mN/m
Octanol/Water partition coefficient:	Log P_{ow} = 3.49

UV Spectrum (methanol):	Peaks at 205, 243, 293 nm
IR Spectrum:	3066, 3083 cm^{-1} aromatic C-H stretch; 2840-3010 cm^{-1} aliphatic C-H stretch; 1757 cm^{-1} ester C=O stretch; 1430-1560 cm^{-1} aromatic C-C stretch; 1070-1195 cm^{-1} ether and ester C-O stretch; 1200-1330 cm^{-1} C-F stretch; 750-900 cm^{-1} aromatic C-H out of plane bending and C-Cl stretch
^{1}H-NMR Spectrum ($CDCl_3$):	δ 7.26 1H d, 7.06 1H d, 6.7 1H t, 4.71 2H s, 4.27 2H q, 3.83 3H, s, 1.29 3H t
Chemical Type:	Herbicide
Chemical Family:	Phenylpyrazole (Group G herbicide)
Mode of Action:	Inhibitor of the enzyme protoporphyinogen oxidase

CHEMICAL AND PHYSICAL PROPERTIES OF THE TECHNICAL GRADE ACTIVE CONSTITUENT

Purity:	Not less than 956 g/kg
Physical State:	Powder
Colour:	Cream
Odour:	Odourless
Melting Point (for solids):	126.4-127.2 °C
Boiling Point (for liquids):	Not determined (decomposes between 240-288 ºC)
Relative Density (at 24 °C):	1.565 g/cm^3
pH (1% suspension at 25 ºC):	4.27
Solubility in Water (20 ºC):	0.082 mg/L
Solubility in Organic Solvents:	Heptane: 234 mg/L Methanol: 7.39 g/L Dichloromethane: 100-111 g/L Acetone: 167-182 g/L *P*-xylene: 41.7-43.5 g/L Ethyl acetate: 105-111 g/L
Oxidizing Properties:	Not oxidizing
Flammability:	Not considered highly flammable
Explosive Properties:	Not explosive
Storage Stability:	Stable at 54 °C for 2 weeks and is expected to be stable for at least 2 years

PRODUCT

Distinguishing Name:	Summit Ecopar 20 SC Herbicide
Formulation Type:	Suspension concentrate
Active Constituent Concentration:	Pyraflufen-ethyl (20 g/L)
Mode of Action:	Selective post-emergent contact broadleaf herbicide for cereal crops, inhibits the enzyme

	protoporphyinogen oxidase causing photosensitisation

PHYSICAL AND CHEMICAL PROPERTIES OF THE PRODUCT

Physical state:	Liquid
Colour:	White
Odour:	Slight non-specific odour
pH (1% aq at 24 ºC):	6.84
Flash Point:	No flash point observed up to 110 °C
Flammability:	Not flammable (water based)
Explosive Properties:	Not classified as explosive when exposed to heat or mechanical shock
Dangerous Goods Classification:	Not applicable
Viscosity (at 20 °C):	Non-Newtonian
Surface Tension:	Product 39.2 mN/m Working dilution (1:200) 45.9 mN/m
Relative Density:	1.02-1.03
Storage Stability:	Stability data provided by the applicant indicates that the product is expected to remain within specification for at least 2 years when stored under normal conditions in HDPE containers.
Low Temperature Stability:	No separation of suspended material observed

The APVMA's Chemistry and Residues Program concluded that based on their review of the chemistry and manufacturing details provided by the applicant, registration of Summit Ecopar 20SC Herbicide is supported.

Other characteristics of the product Summit Ecopar 20SC Herbicide (toxicology, occupational health and safety etc) are covered in subsequent sections of this Public Release Summary.

TOXICOLOGY ASSESSMENT

EVALUATION OF TOXICOLOGY

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

Summit Agro Australia Pty Ltd provided a package of supporting toxicology data seeking registration of a new agricultural product, Summit Ecopar 20 SC Herbicide containing 20 g/L pyraflufen-ethyl. The product is a suspension concentrate formulation and is designed to be used for the control of certain weeds in wheat, oats, barley, triticale and cereal rye.

Pyraflufen-ethyl belongs to the phenyl pyrazole class of chemicals called protoporphyrinogen oxidase inhibitors (PPO inhibitors). Pyraflufen-ethyl is a novel inhibitor of protoporphyrinogen IX oxidase. The inhibition of this enzyme in chloroplasts causes the accumulation of protoporphyrinogen IX resulting in peroxidation of foliar cell membrane lipid under the presence of light, with subsequent cell membrane destruction and necrosis.

Pyraflufen-ethyl is currently in Schedule 5 of the SUSDP. Pyraflufen-ethyl has an ADI of 0.2 mg/kg bw/d based on a NOEL of 20 mg/kg bw/d established in mouse and rat chronic studies and a rabbit developmental study; and an ARfD of 0.2 mg/kg bw based on a NOEL of 20 mg/kg bw/d in a rabbit developmental study.

The data package provided in the present submission consisted of 26 studies. Twenty were toxicology studies. Six of them characterised the acute hazard profile of the formulated product and were conducted in accordance with the contemporary test guidelines, and the data provided in these studies were relied on to enable the recommendations for the product to be developed. Two mechanistic studies were considered to be supplementary data for the existing toxicological database and were also relied on. The remainder of the submitted studies had been previously evaluated (8 studies), or were related to residue levels in crops/farm animals (4 studies) or to

chemistry and manufacture (6 studies). These studies were not evaluated in this report.

Based on the findings of toxicological assessment, Summit Ecopar 20SC Herbicide is expected to have low acute oral, dermal and inhalational toxicity. The product is not expected to be a skin or eye irritant, or a skin sensitiser. Based on the present evaluation, hazard based safety directions are not needed for the product.

An occupational health and safety risk assessment was based on a consideration of the toxicological hazard and the product use pattern. Based on acute and repeat dose risk assessments, personal protective equipment has not been recommended. A re-entry statement was not recommended, as re-entry activities are not expected except for harvesting (mechanical).

The toxicology data and other information on the product provided and considered in this assessment justify no Safety Directions for the product Summit Herbicide. Furthermore, the proposed use of 'Summit Herbicide' will not be an undue health hazard to humans according to the criteria stipulated in Section 14 (5)(e) criteria of the Ag/Vet Code Act of 1994. Based on the toxicity profile of pyraflufen-ethyl, the registration of the product, Summit Ecopar 20SC Herbicide, is supported.

- There are no objections on public and occupational health grounds to the registration of the product Summit Ecopar 20SC Herbicide, containing 20 g/L of pyraflufen-ethyl.

PUBLIC HEALTH STANDARDS

- The submitted data did not warrant a change to the existing ADI or ARfD for pyraflufen-ethyl.
- The existing poison schedule classification for pyraflufen-ethyl remains appropriate.

LABEL STATEMENTS

- **First Aid Instructions**

  The following first aid instruction has been recommended and should appear on the product label.

  New Entry Pyraflufen-ethyl

  a

  The code above refers to the following first aid instruction:

  If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 131126; New Zealand 03 4747000.

- **Safety Directions**

Based on the acute toxicology profile of the product, use patterns and an occupational health and safety risk assessment no safety directions recommended (hazard based or personal protective equipment). The following entry will be included in the FAISD Handbook.

New entry

Pyraflufen-ethyl	SC 25 g/L or less	Nil

- **Re-entry statement**

A re-entry statement is not recommended.

- **Warning Statements and General Safety Precautions**

No warning or precautionary statements are required.

HAZARD CHARACTERISATION

Ddiscussion of Toxicity data

Active constituent

Toxicology of pyraflufen-ethyl has been considered by the OCS previously. It has low acute oral (LD_{50} >5000 mg/kg bw in mice and rats; no deaths), dermal (LD_{50} >2000 mg/kg bw in rats; no deaths) and inhalation toxicity (LC_{50} >5030 mg/m^3 in rats; no deaths). It was a slight eye irritant in rabbits, but not a skin irritant in rabbits or a skin sensitiser in guinea pigs.

Product

Six acute toxicology studies conducted using an identical formulation (2% SC ET-751) were submitted with the application. This data indicated that the formulated product has low acute oral (LD_{50} >5000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalational (LC_{50} >5030 mg/m^3) toxicity in rats. The product was not a skin or eye irritant in rabbits or a skin sensitiser in guinea pigs.

SELECTION OF A NOEL FOR OHS RISK ASSESSMENT

Summit Ecopar 20 SC Herbicide (Summit Herbicide) is an early post-emergence herbicide for the control of certain weeds in winter cereals and the product will be applied only once per season between May and August. Therefore, the maximum use of product will be for 120 days in one year. For long-term exposure (i.e. $\geq$ 3 months continuous daily exposure in any one year), the most appropriate NOELs are drawn from studies of approximately 12 months duration. Furthermore, since occupational exposure to pyraflufen-ethyl will be predominantly via the dermal route, the most appropriate NOEL is derived from repeat-dose dermal toxicity studies.

However, subchronic dermal toxicity study is not available for pyraflufen-ethyl. A 28-day dermal toxicity study (application on 5 days/week for 4 weeks) is available for pyraflufen-ethyl. There were no local or systemic effects observed in rats who received pyraflufen-ethyl by dermal application at 100, 300 or 1000 mg/kg bw/day for 4 weeks. Therefore, based on above, a NOEL of 1000 mg/kg bw/d (the highest tested

dose in a 28-day dermal toxicity study in rats), was considered the most appropriate NOEL for OH&S risk assessment of Summit Herbicide considering the proposed use pattern of the product.

POISONS SCHEDULE CONSIDERATIONS

Pyraflufen-ethyl is currently in Schedule 5 of the SUSDP. The existing poisons scheduling classification for pyraflufen-ethyl remains appropriate.

The statement codes above translate into the following safety directions:

Harmful if inhaled. Do not inhale spray mist	129 132 220 223
Will damage eyes	207 162
Will irritate the skin	161 164
Avoid contact with eyes and skin	210 211
When opening the container and preparing spray	279 280 281
Wear cotton overalls buttoned to the neck and wrist and a washable hat, elbow-length PVC gloves and face shield or goggles	290 292 294 299
If product on skin, immediately wash area with soap and water	340 342
If product in eyes wash it out immediately with water	340 343
After each day's use, wash gloves, face shield or goggles and contaminated clothing	360 361 365 366
Wash hands after use	351

- **Re-entry Statement**

No re-entry statement is required.

- **Warning Statements and General Safety Precautions**

No warning or precautionary statements are required.

RESIDUES ASSESSMENT

INTRODUCTION

Summit Agro Australia Pty Limited has submitted two applications (Category 3) for the registration of two new products, SUMMIT ECOPAR 20SC HERBICIDE and SUMMIT ETEE COTTON DEFOLIANT AND HERBICIDE, which contains pyraflufen-ethyl (20 or 25 g/L, respectively) as the active constituent. The products are to be used as a broadleaf herbicide in winter cereals or as a defoliant in cotton.

METABOLISM

In plants pyraflufen-ethyl is rapidly absorbed and hydrolysed to its primary bioactive acid metabolite (E-1). In susceptible plants inactivation of this metabolite is slow in comparison to resistant plants which rapidly degrade E-1 to several bio-inactive molecules.

Plants are unlikely to contain residues of the parent compound greater than 0.01 mg/kg unless they are collected shortly after application of pyraflufen-ethyl.

The metabolism data supports a residue definition encompassing both the parent molecule and bioactive metabolite E-1.

In animals following ingestion, pyraflufen-ethyl is rapidly absorbed and quantitatively metabolised to its carboxylic derivative (E-1). A minor proportion ~10% remains unabsorbed and undergoes faecal elimination. Metabolite E-1 undergoes rapid elimination in urine. Further metabolism of E-1 to form both the N-des-methyl and phenolic derivatives of the parent is also observed. These secondary metabolites individually constitute less than 10% of the metabolites observed and are not considered relevant to the residue definition.

The data support a residue definition based on the parent and the metabolite E-1.

ANALYTICAL METHODS

In animals pyraflufen-ethyl and its metabolites are extracted from tissue using acetonitrile/water solution. The extract is acidified and salted. The aqueous phase is discarded and the fat eliminated by back extraction into hexane. The solution is cleaned using SPE and the residues methylated using diazomethane, prior the final SPE cleanup and GC/MS analysis. The limits of quantitation (LOQ) were 0.02 mg/kg for individual analytes in mammalian and avian (tissues, milk and eggs, where appropriate).

In plants pyraflufen-ethyl and its metabolites are extracted from commodities using acetonitrile/1N HCl water solution. The extract is salted and quantitatively extracted with hexane/ethyl acetate or dichloromethane. The solution is cleaned using SPE and methylated using diazomethane, prior the final SPE and florisil cleanup. The samples are assayed using GC/MS analysis. The limit of quantitation is 0.02 mg/kg for

individual analytes in the commodities of concern (cereal grain, forage and fodder, cotton seed, oil and trash).

The methods were fully validated for analysis of fortified cereals, fodder and forage, cotton seed, trash and oil and animal commodities (tissue, milk and eggs).

The methods were found to be acceptable for the determination of residues (as per the residue definition) in the commodities of concern.

Residue Definition

The following residue definition is supported. Sum of pyraflufen-ethyl and its acid metabolite (2-chloro-5-(4-chloro-5-difluromethoxy-1-methylpyrazol-3-yl)-4-fluorophenoxyacetic acid)

RESIDUE TRIALS

Cereals

Residues in cereal grain and fodder following the application of pyraflufen-ethyl in accordance with the use pattern were nondetectable at crop maturity. As both the parent and E-1 metabolite residues were individually below the LOD the data support an MRL at the LOQ for the individual analytes (0.02 mg/kg) rather than the combined analyte LOQ (0.04 mg/kg).

The data support a WHP of "not required when used as directed " and an MRL of 0.02 mg/kg for cereal grains when associated with the use of *SUMMIT ECOPAR 20SC HERBICIDE*.

The applicant has assayed forage to establish an acceptable forage grazing withholding period. These data demonstrate total residues of 0.93 mg/kg in the dry forage 14 days following application at the maximum proposed rate. Animal transfer data obtained during feeding trials indicate that lactating goat and hens fed 10 mg ai/kg feed demonstrated very low level residues in bodily tissues 24 hours post dose. In laboratory animals fed 5 mg ai/kg feed levels of radioactivity had declined to near background level within 96 hours of dose. The crop residue data coupled with the metabolism data support the Applicants proposal for a 14 day crop grazing restraint on *SUMMIT ECOPAR 20SC HERBICIDE* and a forage MRL of 1.0 mg/kg. Given that both forage and fodder may be used as animal feeds an MRL of 1.0 mg/kg will be established to cover both commodities.

Cotton

Residues in cotton seed were below the limit of detection following the application of pyraflufen-ethyl at rates up to 4x the maximum proposed application rate. The data support an MRL at the limit of quantitation for the residue definition (0.04 mg/kg) and a WHP of 7 days when S*UMMIT ETEE COTTON DEFOLIANT AND HERBICIDE* is used as directed. Given CODEX conventions the MRL will be rounded to 0.05 mg/kg.

Following application of pyraflufen-ethyl at the maximum proposed rate the level of pyraflufen-ethyl and its E-1 metabolite in cotton trash were a maximum of 0.34 mg/kg in dry trash. This level will result in nondetectable levels of pyraflufen-ethyl in

animals fed treated crops. However, as the Applicant has proposed a feeding restraint this issue is not considered further.

Processing studies and storage stability

Two studies were submitted examining the concentration of pyraflufen-ethyl residues in the processed fractions of cotton. Given the highly water-soluble nature of the free acid metabolite no accumulation of residues were observed in the processed commodities made available for either human or animal consumption.

Residues of pyraflufen-ethyl remained stable in undelinted cottonseed and trash at periods of up to 6 months when stored at –20 ^{o}C. Residues of the E-1 metabolite were stable in undelinted cottonseed and trash up to 15 months post harvest when stored below –15 ^{o}C. Significant degradation of pyraflufen-ethyl was observed in cotton trash 15 months following harvest when stored below –15 ^{o}C, however this instability was not observed in the seed. The residues of pyraflufen-ethyl demonstrate acceptable stability within the time scale encompassed by the residue trials.

Animal transfer Studies and associated MRLs

The applicant has provided one metabolism study in lactating goat and one metabolism study in laying hens. The Applicant did not provide livestock feeding studies.

A lactating goat was orally administered [^{14}C-pyrazole]-ET-751 by capsule once daily for 3 days at a dose rate was equivalent to 10.0 mg ET-751/kg feed (0.6 mg/kg bw/day). Milk was collected twice daily. Slaughter occurred 23 hours following cessation of the final dose. Samples of blood, kidney, liver, muscle and fat were taken, frozen and assayed for the radio-metabolites of pyraflufen-ethyl.

Following the course of administration the TRR recovered from all sources accounted for 79.8% of the administered dose. Within 23 hours of oral administration, absorbed pyraflufen-ethyl was quantitatively hydrolysed to metabolite E1 in liver, kidney and milk. Two other minor metabolites (E-2 and E-9) where observed in liver and kidney at less than 10% of the total. In milk no significant metabolite E-2 was observed and only E-9 was detected at any significant concentration (<10% total). No significant residues were observed in muscle or fat. Residues had declined to a maximum of 0.08 mg/kg in kidney at slaughter

Laying hens (n=6) were orally administered [^{14}C-pyrazole]-ET-751 by capsule once daily for 3 days at a dose rate was equivalent to 10.5 mg ET-751/kg feed (0.9 mg/kg bw/day). Eggs where collected daily. Slaughter occurred 23 hours following cessation of the final dose. Samples of blood, kidney, liver, muscle and fat were taken, frozen and assayed for the radio-metabolites of pyraflufen-ethyl.

Following the course of administration the TRR recovered from all sources accounted for 90.4% of the administered dose. Within 23 hours of oral administration, absorbed pyraflufen-ethyl was quantitatively hydrolysed to metabolite E1 in chicken tissue and egg. One other minor metabolite (E-9) was observed in liver and egg yolk near the LOD. While this metabolite appears to form a significant component of the residue given the extremely low levels observed the ratio of metabolites cannot be accurately determined. No significant residues were observed in muscle or fat. The highest

residue observed at slaughter was in liver at 0.019 mg/kg and is below the analytical LOQ.

Given the rapid absorption, metabolism and elimination of pyraflufen-ethyl, residues occurring in animal commodities at slaughter are expected to be below the analytical LOQ. As such, the data support the establishment of animal MRLs at the LOQ (0.02 mg/kg)

Grazing of green fodder and forage commodities
The grazing of green cereal crops following the proposed WHP (14 days) is not expected to result in detectable animal residues.

Spray drift modelling
Pyraflufen-ethyl concentrations grazing animals may ingest following spray drift will not result in detectable tissue residues.

Dietary risk
The chronic dietary exposure of pyraflufen-ethyl is less than 1% of the Acceptable Dietary Intake (ADI).

The acute intake for pyraflufen-ethyl constituents less than 1% of the acute reference dose (ARfD).

Trade risk
Residues in the commodities of plants and animals exposed to *SUMMIT ECOPAR 20SC HERBICIDE* are expected to remain below LOQ and will not constitute a prejudice to trade.

ENVIRONMENTAL ASSESSMENT

INTRODUCTION

Summit Ecopar 20 SC Herbicide is a new product containing the active constituent pyraflufen-ethyl, for use to control certain weeds in wheat, oats, barley, triticale and cereal rye. No additional environmental fate or ecotoxicity reports were provided, hence this assessment has used summaries prepared for the initial assessment of pyraflufen-ethyl from studies provided previously. The available data are considered adequate to evaluate the environmental safety of the proposed new use.

Fate studies in the laboratory and field indicate that in the environment, pyraflufen-ethyl is likely to degrade rapidly under both aerobic and anaerobic conditions in water and soil to the ester hydrolysis metabolite E1. From there, degradation is expected to continue to produce various metabolites retaining both the phenyl and pyrazole rings, and ultimately to cleavage products and CO_2, the rate and extent of this depending on conditions. Abiotic hydrolysis may contribute to this at neutral to alkaline pH, as well as aqueous and soil photolysis and biotic processes. Pyraflufen-ethyl and E1 are both very slightly volatile and unlikely to evaporate significantly from soil or water. Column leaching studies in the laboratory and field dissipation studies indicate that pyraflufen-ethyl and its metabolites are unlikely to leach in soil or move significantly in run-off, though soil adsorption coefficient (K_{OC}) values indicate E1 has medium to high mobility potential in soil. Pyraflufen-ethyl and its metabolites are unlikely to accumulate significantly in soil or to bioaccumulate.

Pyraflufen-ethyl technical is practically non-toxic to birds with acute oral or sub-acute dietary exposure. The NOEC to bobwhite quail and mallard ducks in avian reproductive studies is 5000 ppm and 500 ppm, respectively. Pyraflufen-ethyl technical is not toxic with acute exposure to fish or the waterflea *Daphnia magna* up to its limit of solubility in water (NOECs = 82-106 µg ac/L). The 2.5% EC formulation of pyraflufen-ethyl is moderately toxic to fish and highly toxic to *Daphnia magna* with acute exposure, but this appears to be due to components other than the pyraflufen-ethyl active constituent as similarly high toxicity resulted from formulation blank controls. With acute exposure, the metabolite E1 was not toxic to fish or *Daphnia magna* up to its limit of solubility in water (NOECs = 90-120 mg/L, at most slightly toxic), but was slightly toxic to eastern oyster and moderately toxic to mysid shrimp. E1 was very slightly toxic to fathead minnow with chronic exposure (early life stage toxicity test). As may be expected from its herbicidal activity, pyraflufen-ethyl as the 2.5% EC formulation was very highly toxic to algae, diatoms and aquatic plants (the most sensitive endpoint being a 96 h EC50 = 2.1 µg ac/L for the freshwater diatom *Navicula pelliculosa*). Pyraflufen-ethyl technical was very slightly toxic to bees and earthworms and had negligible effects on nitrogen turnover or respiration by soil microflora. It is a selective contact herbicide to terrestrial plants.
The proposed new product Summit Ecopar 20 SC Herbicide adds significantly to the situations and locations where pyraflufen-ethyl may be used. The rate of active constituent per hectare proposed for pyraflufen-ethyl in this product is slightly less than the maximum rate for the cotton product for which an environmental assessment has already been conducted. On the basis of previous assessments at a higher field

rate (10 g ac/ha compared to 8 g ac/ha), the risks to birds, bees and other insects and mites, earthworms, and soil microbial activity from use of pyraflufen-ethyl as a herbicide in cereal crops are considered low. Assessments were conducted of the risks to aquatic and terrestrial organisms with ground application by low boomspray, noting aerial application is forbidden on the draft label. A risk was indicated to algae and aquatic plants in shallow waterbodies from direct overspray and from 10% spray drift, but the spray drift risk is readily mitigated. Direct overspray or spray drift may also be toxic to susceptible terrestrial plants by foliar exposure, but a low risk 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 risks. With one minor label amendment, that was incorporated on the label the Department of the Environment and Water Resources recommended that the APVMA be satisfied that the proposed use of Summit Ecopar 20 SC Herbicide to control certain weeds in wheat, oats, barley, triticale and cereal rye, in accordance with the instructions for use on the product label, would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

EFFICACY AND CROP SAFETY ASSESSMENT

JUSTIFICATION OF USE

This application seeks registration of product, Summit Ecopar 20 SC Herbicide for the post-emergence control of certain broadleaf weeds in cereals. Summit Ecopar 20 SC contains 20 g/L pyraflufen-ethyl, and is a group G herbicide that will increase the options available to growers.

Reports were provided in relation to forty-two efficacy and crop safety trials and five specific crop safety variety screens which have been conducted in Australia over three growing seasons from 2002 to 2004. Trials were continuing in the 2005 season, but no data were available at the time of preparation of this application. The results from the first season (2002) showed that pyraflufen-ethyl alone, at the rates tested, was inadequate for the control of the listed target plants. However, the addition of MCPA LVE improved the control of many of these species.

On the basis of this data generated, it was decided that 2003 trials should include treatments of mixtures with MCPA amine to investigate weed control efficacy with an anticipated reduction in crop damage. As an over-all conclusion it was shown that a higher rate of Ecopar is required in mixtures with MCPA amine than with MCPA LVE to produce equivalent efficacy. It was also shown that the substitution of MCPA amine for the LVE formulated reduced the previously seen transient but still significant crop phytotpoxicity to a minor level.

The 2004 trials standardised the rate of amine, and discontinued any further use of LVE formulation and the 25 g/L formulation of pyraflufen-ethyl.

The trials (Appendix 2 to Appendix 43), were all set out as randomised complete block experiments with four replicates in each case. Plot size was generally 2 m by 10 m, with 0.5 m buffers. In most of the trials treatments were applied using a hand held gas operated 2 metre boom incorporating four Spraying systems 80067 flat fan nozzles. Using a walking speed of 1 metre per second and a pressure of 220 kPa, the treatments were applied in a volume of 70 L/ha. In some trials there were minor variations mainly with application pressures and volumes. In addition, in some trials with wheat, the treatments were applied at a various nominated Zadoks growth stages.

All trials were statistically analysed, showing significant variations between treatments and untreated controls. Throughout the trials assessments were conducted between three and five occasions, these ranging from first assessment at 7 DAT and the final assessment at 57 DAT. Crop damage and weed control were assessed using a 0 – 100 scale, and were clearly outlined for each of the trials. The trials were all conducted in the major cereal growing areas including New South Wales, Victoria, South Australia and Western Australia.

This report consolidates data generated from the trials on the efficacy of Summit Ecopar 20 SC herbicide in controlling certain broadleaf weeds in cereals when tested alone and with MCPA, at a range of rates in both cases. The report details the study data assessments for each of the trials as well as the specific crop safety variety screens.

In the application it is stated that the registration of this product would provided growers with an alternative to Affinity, which is the only other Group G herbicide

available to growers. The data were adequate to demonstrate that the product, Summit Ecopar 20 SC Herbicide justify the label claim, direction for use and other label instructions relevant to product efficacy, and therefore label claims are supported.

Information is presented on the efficacy of Summit Ecopar 20 SC herbicide for the control of certain broadleaf weeds in cereals. The report discusses information by trial and specific variety screens for the proposed label rates. Justification for registration of Summit Ecopar 20 SC Herbicide in these instances is based in the trial data provided and supported by the forty-eight trials conducted over the three season period in New South Wales, Victoria, South Australia and Western Australia.

LABELLING REQUIREMENTS

CAUTION
KEEP OUT OF REACH OF CHILDREN

Summit
ECOPAR 20 SC Herbicide

ACTIVE CONSTITUENT: 20 g/L PYRAFLUFEN-ETHYL

GROUP	**G**	HERBICIDE

For the control of annual broadleaf weeds in winter cereals as per the Directions For Use Table.

IMPORTANT: READ THE ATTACHED LEAFLET BEFORE USE.

Summit Agro Australia Pty Ltd

Contents: 20 L

APVMA Approval No.: 60493/20/0607

Back Panel

STORAGE AND DISPOSAL
Keep out of reach of children.
Store in the closed original container in a cool, well ventilated area. Do NOT store for prolonged periods in direct sunlight.
Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do NOT dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no local authority 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.

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

MATERIAL SAFETY DATA SHEET
Additional information is listed on the Material Safety Data Sheet for Summit ECOPAR 20 SC Herbicide. These can be obtained at www.summitagro.com.au. For emergency situations only, call 1800 033 111, all hours.

CONDITIONS OF SALE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purpose stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under abnormal conditions.

Date of manufacture:

Batch No:

IN A TRANSPORT EMERGENCY
DIAL 000
POLICE OR FIRE BRIGADE

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

Summit Agro Australia Pty Ltd

ABN: 29 105 302 298
Suite 3, Level 7, 111 Elizabeth Street
SYDNEY NSW 2000
Telephone (02) 8236 6902

Leaflet

CAUTION
KEEP OUT OF REACH OF CHILDREN

Summit
ECOPAR 20 SC Herbicide

ACTIVE CONSTITUENT: 20 g/L PYRAFLUFEN-ETHYL

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

This leaflet is part of the label.

APVMA Approval No.: 60493/20/0607

Summit Agro Australia Pty Ltd

ABN: 29 105 302 298
Suite 3, Level 7, 111 Elizabeth Street
SYDNEY NSW 2000
Telephone (02) 8236 6902

DIRECTIONS FOR USE: All States

RESTRAINTS:
DO NOT tank mix Summit ECOPAR 20 SC Herbicide plus MCPA amine with any wetter, crop oil concentrates or blended oil/surfactant adjuvants. (see compatibility section)
DO NOT tank mix MCPA LVE with Summit ECOPAR 20 SC Herbicide.
DO NOT tank mix Summit ECOPAR 20 SC Herbicide plus MCPA amine treatments with selective grass herbicides.
DO NOT apply the tank mix of Summit ECOPAR 20 SC Herbicide plus MCPA amine before the two leaf crop stage.
DO NOT apply Summit ECOPAR 20 SC Herbicide plus MCPA amine by aircraft.
DO NOT apply if rain is expected within 6 hours of application.
DO NOT apply to weeds suffering from stress caused by conditions such as frost, drought, soil water logging etc.

Crop	Weeds Controlled	Rate/Ha	Critical Comments
Wheat, barley, triticale	Bedstraw (*Galium tricornutum*), capeweed (*Arctotheca calendua*), Indian hedge mustard (*Sisymbrium orientale*), long storks bill (*Erodium botrys*), prickly lettuce (*Lactuca serriola*), volunteer canola (*Brassica napus*), volunteer lupin (*Lupinus* sp), wild radish (*Raphanus raphanistrum*), wild turnip (*Brassica tournefortii*)	400 mL plus 500 mL MCPA amine (500 g/L product)	**Apply as a post-emergence treatment to actively growing weeds up to the 6 leaf stage and/or not more than 12 cm in diameter and when the crop is between 2 leaves and mid-late tillering (Zadoks 12-25). Always tank mix with MCPA amine.** **Under favourable growing conditions some weed regrowth may occur. A follow up application of a suitable herbicide e.g.,** **2,4-D amine, may be required as part of a good weed management strategy.**

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

WITHHOLDING PERIOD:

HARVEST: NO WITHHOLDING PERIOD REQUIRED WHEN USED AS DIRECTED.

GRAZING AND FEEDING OF DRY FODDER/STRAW: NO WITHHOLDING PERIOD REQUIRED WHEN USED AS DIRECTED.

GRAZING: DO NOT GRAZE OR CUT GREEN FORAGE FOR STOCK FOOD FOR 14 DAYS AFTER APPLICATION.

GENERAL INSTRUCTIONS

Summit ECOPAR 20 SC Herbicide is an early post-emergence contact herbicide with rapid foliar uptake. Herbicide effects on susceptible weeds can occur within 1 to 7 days of application. Subsequent germinations will not be controlled. Summit ECOPAR 20 SC HERBICIDE should always be tank mixed with MCPA amine to improve the weed control spectrum compared to either product applied alone.

Compatibility

Summit ECOPAR 20 SC Herbicide plus MCPA amine is compatible with metsulfuron and triasulfuron.

Do NOT mix Summit ECOPAR 20 SC Herbicide with selective grass herbicides as grass weed control will be 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 spraying Summit ECOPAR 20 SC Herbicide and grass herbicide applications.

Do NOT add wetters, spray oils or oil/surfactant adjuvants to the tank mix of Summit ECOPAR 20 SC Herbicide plus MCPA amine. The addition of wetters, spray oils or oil/surfactant blends will greatly increase crop injury without any significant improvement in weed control. Prior to applying Summit ECOPAR 20 SC Herbicide, clean the spray tank to remove any wetters or adjuvants remaining from previous spray operations otherwise crop injury may result.

RESISTANT WEEDS WARNING

GROUP	**G**	HERBICIDE

Summit ECOPAR 20 SC 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, Summit ECOPAR 20 SC Herbicide is a Group G herbicide.

Some naturally occurring weed biotypes resistant to Summit ECOPAR 20 SC Herbicide 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 Summit ECOPAR 20 SC Herbicide or other herbicides that inhibit the enzyme protoporphyrinogen oxidase.

Since the occurrence of resistant weeds is difficult to detect prior to use, Summit Agro Australia Pty Ltd accepts no liability for any losses that may result from the failure of Summit ECOPAR 20 SC Herbicide or other herbicides that inhibit the enzyme protoporphyrinogen oxidase.

MIXING

Add half the required volume of water to spray tank and start agitation. Add the required amount of Summit ECOPAR 20 SC Herbicide followed by the MCPA amine. Metsulfuron or triasulfuron should be added last if including these in the tank mix. Add the remaining water. Maintain good agitation at all times until spraying is completed.

APPLICATION

Apply Summit ECOPAR 20 SC Herbicide plus MCPA amine as a broadcast application. Use conventional boom sprayers with either mechanical or bypass agitation. Spray equipment should be properly calibrated to to ensure correct application. Use a spray volume of 70 to 150 litres per hectare. This is particularly important on hard-to-control weeds. Use the higher volume if weed infestation is heavy or the crop cover is dense. The best application conditions are when soil is moist, weather fine and rain unlikely within 6 hours.

CROP SAFETY

Some herbicidal symptoms may appear on the crop in the form of leaf spotting due to environmental conditions. However the crop recovers quickly usually within 2-3 weeks of treatment .

SPRAYER CLEAN OUT

Do not allow the spray solution to dry in the application equipment. After application and before using the sprayer equipment for any other applications, the sprayer must be thoroughly cleaned. Applicators must ensure proper equipment clean-out for any other products mixed with Summit ECOPAR 20 SC Herbicide as provided on the other product label(s). Immediately following application, clean all

equipment thoroughly with detergent or a spray tank cleaner and water as described below. Should residues of Summit ECOPAR 20 SC Herbicide remain in inadequately cleaned equipment, they may be released in subsequent applications and cause injury to crops.

1. Drain sprayer tank, hoses and spray boom and thoroughly rinse with clean water the inside of the spray tank, sprayer hoses, boom, and nozzles to remove any sediment or residues.
2. Fill the tank with clean water, add an alkaline detergent or boom cleaner (follow manufacturer's directions for use). Fill tank to capacity and operate the sprayer with agitation for 15 minutes to flush hoses, boom and nozzles.
3. Drain the sprayer tank, lines, and booms. Rinse the tank with clean water and flush through the hoses, boom and nozzles. Remove and clean spray nozzles, tips and screens.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

Do NOT apply under meteorological conditions or from spraying equipment that could be expected to cause spray to drift on to nearby susceptible plants, adjacent crops and pastures or on to wetlands, waterbodies or watercourses. Summit ECOPAR 20 SC Herbicide does not provide residual activity, therefore no crop rotational restrictions apply.

PROTECTION OF WILDLIFE, FISH, CRUSTACEA AND ENVIRONMENT

Very highly toxic to algae and aquatic plants. Do NOT contaminate streams, rivers or waterways with the chemical or used container.

STORAGE AND DISPOSAL

Keep out of reach of children.

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

Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no local authority 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.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Telephone 131 126 Australia-wide.

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CONDITIONS OF SALE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purpose stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under abnormal conditions.

IN A TRANSPORT EMERGENCY
DIAL 000
POLICE OR FIRE BRIGADE

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

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 octanol water partioning co-efficient
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light
Photolysis	Breakdown of chemicals due to the action of light
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body
Toxicology	The study of the nature and effects of poisons

APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of pyraflufen-ethyl in the product Summit Ecopar 20SC Herbicide please fill in this form and send it, along with payment of $30 to:

Colin McCormack
Pesticides Division
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to: Colin McCormack 02 6210 4776.

Name (Mr, Mrs, Ms, Dr)_____

Position

_____

Company/organisation

_____

Address

_____

Contact phone number (___)

_____

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

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

___ Bankcard ___ Visa ___ Mastercard

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

Signature_____ Date _____