

This work is copyright. Apart from any use permitted under the *Copyright Act 1968*, no part may be reproduced without permission from the Australian Pesticides and Veterinary Medicines Authority. Requests and inquiries concerning reproduction and rights should be addressed to:

The Manager, Communication and Secretariat
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182,
Kingston ACT 2604
Australia.

This document is published by the Australian Pesticides and Veterinary Medicines Authority. In referencing, the APVMA should be cited as both the author and publisher of this document. For further information, please contact:

Ron Marks
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
KINGSTON ACT 2604

Ph: (02) 6210 4772
Fax: (02) 6210 4776
Email: ron.marks@apvma.gov.au

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 [OCS]), the Department of the Environment, Water, Heritage and the Arts [DEWHA] (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 undertaken according to accepted scientific principles. Details are outlined in the APVMA's publications [*AgMORAG: Manual of Requirements and Guidelines for Agricultural Chemicals*: available via the APVMA website at http://www.apvma.gov.au/MORAG_ag/MORAG_ag_home.shtml].

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 which is located at the:

APVMA Building
AMTECH Estate
18 Wormald Street
Symonston ACT 2609.

Office hours are from 9.00am - 5.00pm (EST), Monday to Friday.

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

The Pesticides Program Manager
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604
AUSTRALIA

[This page intentionally left blank]

CONTENTS

Foreword.....	ii
List of Abbreviations and Acronyms.....	v
Introduction.....	1
Chemistry and Manufacture.....	3
<i>Active Constituent</i>	3
<i>Formulated Product</i>	4
<i>Recommendation</i>	5
Toxicological Assessment.....	7
<i>Evaluation of Toxicology</i>	7
<i>Public Health Standards</i>	10
<i>Poisons Scheduling</i>	10
<i>NOEL/ADI</i>	11
<i>Acute Reference Dose (ARfD)</i>	11
<i>Background to the application</i>	13
<i>Metabolism</i>	13
<i>Residue Definition</i>	15
<i>Residues in Foods and Animal Feeds</i>	15
<i>MRLs for Plant Commodities</i>	16
<i>MRLs for Animal Commodities</i>	16
<i>Discussion on Residue Aspects of Rotational Crops</i>	16
<i>Dietary Risk Assessment</i>	17
<i>Conclusions and Recommendations</i>	17
<i>Recommended Amendments to the MRL Standard</i>	18
<i>Withholding Periods</i>	18
<i>Crop Rotation Amendments</i>	18
Assessment of Overseas Trade Aspects of Residues in Food.....	19
<i>Residues related aspects of trade</i>	19
<i>Overseas Registration Status</i>	19
<i>Overseas MRLs</i>	19
<i>Potential Risk to Australian Trade</i>	19
<i>Conclusion</i>	20
Occupational Health and Safety Assessment.....	21
<i>Background</i>	21
<i>Use and exposure</i>	21
<i>Re-entry</i>	22
<i>Recommendations for safe use</i>	22
<i>Conclusion</i>	22
Environmental Assessment.....	23
<i>Environmental Fate (Degradation, Metabolism and Mobility)</i>	23
<i>Environmental Fate Summary</i>	28
<i>Environmental Effects (Hazards)</i>	29
<i>Environmental Effects Summary</i>	36
<i>Environmental Risk Assessment</i>	37
<i>Conclusion with Respect to Environmental Risk</i>	37
<i>Summary of Conclusions</i>	38
<i>Summary of Recommendations</i>	38
Efficacy and Safety Assessment.....	41
<i>Proposed Original Use Pattern of Hero (2002)</i>	41
<i>Justification for Use</i>	41
<i>Evaluation of Efficacy and Crop Safety</i>	42
<i>Recommendation</i>	44
Labelling Requirements.....	45
Glossary.....	53

List of Abbreviations and Acronyms

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ALP	alkaline phosphatase
ALT	alanine aminotransferase
APTT	Activated Partial Thromboplastin Time
AST	aspartate aminotransferase
BBA	Biologische Bundesanstalt für Land – und forstwirtschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DEWHA	Department of the Environment, Water, Heritage and the Arts
DT₅₀	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
E_bC₅₀	concentration at which the biomass of 50% of the test population is impacted
EC₅₀	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC₅₀	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
F₀	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 <i>or</i> 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
LC₅₀	concentration that kills 50% of the test population of organisms
LD₅₀	dosage of chemical that kills 50% of the test population of organisms
LDH	lactate dehydrogenase
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be dquantified
MCH	mean corpuscular (cell) haemoglobin
MCV	mean corpuscular (cell) 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 / No Observable Effect Level
NOHSC	National Occupational Healthy and Safety Commission (now part of OCS)
OC	Organic Carbon
OCS	Office of Chemical Safety (in the Commonwealth Department of Health and Ageing)
OM	Organic Matter
po	oral
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
TRR	Total Radio-active 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
WBC	White Blood Cell
WG	Water Dispersible Granule
WHP	Withholding Period

[This page intentionally left blank]

Introduction

This publication provides a summary of data reviewed and an outline of the regulatory considerations for the proposed registration of Hero® Selective Herbicide (Hero®), which contains the active constituent Ethoxysulfuron. Ethoxysulfuron is a sulfonylurea compound, and is an active that was approved by the APVMA in February 2005.

The APVMA seeks public comment prior to the chemical product being registered for use in Australia.

Responses to public consultation will be considered prior to registration of the product detailed in this document. They will be taken into account by the APVMA in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

Copies of the full technical reports on public health, occupational health and safety, environmental impact and residues in food are available upon request (see order form at the back of this PRS document).

Written comments should be received at the APVMA by Tuesday 28 October 2008 and addressed to:

Mr. Ron Marks
Pesticides Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Phone: (02) 6210 4772

Fax: (02) 6210 4776

Email: ron.marks@apvma.gov.au

Applicant

Bayer CropScience Pty Limited

Product details

It is proposed to register *Hero® Selective Herbicide*, containing 600g/kg ethoxysulfuron, as a water dispersible granule. The product will be formulated by Bayer CropScience GmbH in Frankfurt am Main (Germany). It will be packed in 500 g, 1 kg, 1.5 kg, 2 kg and 5 kg pack sizes, using polyamide/HDPE containers, and imported. The active constituent is manufactured in Switzerland.

Hero® herbicide is a member of the sulfonylurea group of herbicides. Its mode of action is to inhibit the biosynthesis of essential amino acids in susceptible plants, through the inhibition of acetolactate synthase (ALS). With respect to weed resistance, as ethoxysulfuron is a member of the sulfonylurea chemical group, it is classed as a Group B herbicide. It is predominantly a foliar herbicide with less activity via the soil.

It is not expected that this product would increase the rate of evolution of herbicide-resistance or environmental load by sulfonylurea herbicides, as it is expected to replace existing sulfonylureas. Additionally, the product label restricts the application of Hero®, or any other Group-B herbicide, to one per crop-season.

The proposed use for Hero® is post-emergent control of nutgrass in sugar cane. The proposed application method is directed application via “spray droppers” (e.g. an octopus spray head on an Irvin Leg), spraying weeds within and between the rows of sugar cane. The rate of product use is 250g per hectare. Hero® is proposed for registration in Queensland, NSW, WA and NT only.

Ethoxysulfuron in a product was first registered in the world in 1996, in Vietnam. As at 4 August 2008, formulations containing ethoxysulfuron are registered in sugar cane in seven countries (Brazil, Dominican Republic, El Salvador, Guatemala, Nicaragua, Pakistan and Panama).

Formulations with ethoxysulfuron are also registered for use in rice in 31 countries (e.g. China, India, Indonesia, Italy, Japan, Malaysia, Pakistan, the Philippines, Taiwan, Thailand, Turkey and Vietnam). Registrations also exist for use in acacia and oil palm (Indonesia) and also golf courses (Japan).

[This page intentionally left blank]

Chemistry and Manufacture

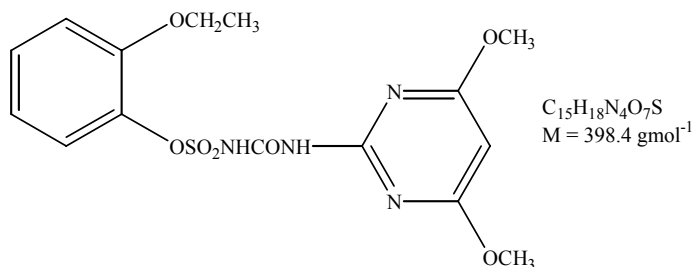
The chemistry and manufacturing aspects of *Hero® Selective Herbicide* and its active constituent are evaluated in this part of the PRS.

Active Constituent

The active constituent known as ethoxysulfuron was approved by the APVMA in February 2005. It is to be manufactured at Lonza AG, in Visp (Switzerland).

Structure

The structure of ethoxysulfuron is shown below:



Physical/Chemical Properties of Active Constituent

The chemical active constituent ethoxysulfuron has the following properties:

Common name (ISO):	ethoxysulfuron
Chemical name:	1-(4,6-dimethoxypyrimidin-2-yl)-3-(2-ethoxyphenoxy)sulfonylurea (IUPAC) 2-ethoxyphenyl[[[4,6-dimethoxy-2-pyrimidinyl]amino]carbonyl]sulfamate (CAS)
Development codes:	AE F095404 (AgrEvo); Hoe 095404 (Hoechst) ; Hoe-404 (Hoechst)
CAS Registry Number:	126801-58-9
Empirical formula:	$C_{15}H_{18}N_4O_7S$
Molecular weight:	398.43 g/mol
Physical form:	Fine powder, partially agglomerated to smooth lumps
Colour:	White to light beige
Odour:	Weak, non-characteristic odour
Melting point:	144 - 147°C
Density:	1.41 g/cm ³ at 20°C
Octanol/water partition coefficient (K_{OW}):	log P = 2.89 (pH 3) ; 0.004 (pH 7) ; -1.2 2.89 (pH 9) [at 20°C]
Henry's Constant* [Pa m ³ mol ⁻¹]:	1.00×10^{-3} (pH 5); 1.94×10^{-5} (pH 7); 2.73×10^{-6} (pH 9); 1.00×10^{-3} (pH 5) [at 20°C]
Solubility in water:	26.4 mg/L (pH 5); 1353 mg/L (pH 7); 9628 mg/L (pH 9) [at 20°C in de-ionised water]
pKa:	5.28 (EU Review Report)
Hydrolytic DT ₅₀ :	65 days (pH 5); 259 days (pH 7); 331 days (pH 9)
Vapour pressure at 25°C:	1.2×10^{-4} Pa [6.6×10^{-2} mPa at 20°C]
Solubility in organic solvents (g/L, 20°C):	n-hexane 0.006 ; toluene 2.5 ; acetone 36 ; ethyl acetate 14.1 ; dichloromethane 107.0 ; methanol 7.7 ; isopropanol 1.0 ; polyethylene glycol 22.5 ; dimethyl sulfoxide >500

* calc

Chemistry of the active constituent

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

Ethoxysulfuron is a new active constituent and there is no compendial specification available. On the basis of the data provided, the following Active Constituent Standard has been established for ethoxysulfuron:

Constituent	Specification	Level
Ethoxysulfuron	Ethoxysulfuron	Not less than 950 g/kg

The details of the APVMA standard for ethoxysulfuron can be viewed on the APVMA website via http://www.apvma.gov.au/actives/standard_ethoxysulfuron.shtml.

Formulated Product

Product name: ***HERO® SELECTIVE HERBICIDE***

Formulation type: Water Dispersible Granule

Active constituent concentration: 600 g/kg ethoxysulfuron

Physical and Chemical Properties of the Product

Physical state: Fine grained granule (nearly dust free)
Colour: Brown
Odour: Slightly acidulous
Density or specific gravity: 610 g/L (before compaction), 680 g/L (after compaction)
pH value: 7.9 (1% dispersion)

The other physical/chemical properties information supplied for *Hero® Selective Herbicide* is acceptable (e.g. flammability, suspensibility, particle size, wettability, dispersability).

Product Formulation

The formulation composition is acceptable for a water-dispersible granular product. Specifications and Material Safety Data Sheets (MSDSs) for the inactive constituents of the product were provided and are acceptable.

Production Process

The formulation process, quality control procedures and product specifications (wettability, dispersability, dust content and flowability) for *Hero® Selective Herbicide* are acceptable.

Analytical Methods

The analytical method and validation data are acceptable.

Batch analysis and stability studies

The batch analysis results are acceptable.

Storage/Shelf-life Stability

A pilot scale batch of 20 kg of *Hero® Selective Herbicide* was stored for 2 weeks at 54°C in the proposed packaging.

The active content of the formulation decreased by less than 5% over the two weeks storage at 54 °C. Provided the product is formulated to contain at least the label amount of ethoxysulfuron, this rate of degradation over 2 years of ambient storage would allow the product to remain within the product specifications.

This rate of degradation complies with FAO requirements, which state that after 2 weeks at 54 °C, a formulation must retain at least 95% of the active content measured before the trial.

Dispersibility decreased very slightly following the stability trials, which is acceptable.

All other physico-chemical parameters did not undergo any significant change during the trial.

The data supplied indicates that the product is expected to remain within specification for up to two years, when stored under normal conditions in the proposed commercial packaging.

Packaging Stability

A sample of *Hero® Selective Herbicide* was stored for 24 months under ambient conditions in an HDPE container. The trial report stated that no detrimental effects on the packaging were noted, there was no sign of any deformation, and the closure seal remained intact.

Packaging

Hero® Selective Herbicide will be packaged in 1, 1.5, 2 and 5 kg polyamide/HDPE containers. A real-time stability trial was conducted in the proposed packaging, which was not adversely affected by the product.

Further, the formulation does not contain any ingredients that are likely to be damaging to HDPE or polyamide on storage, and the packaging material is not expected to be significantly porous to atmospheric moisture.

The packaging material is acceptable.

Labelling

The draft label (dated 19 December 2002) includes instructions to store in the closed original container in a cool, well-ventilated area and not to store for prolonged periods in direct sunlight. The draft label is acceptable from a chemistry perspective.

Recommendation

The Chemistry section of the APVMA has evaluated the chemistry and manufacturing aspects of *Hero® Selective Herbicide* and is satisfied that the data provided support the application for registration.

The APVMA is satisfied that the chemistry requirements of Section 14 (5) of the Agricultural and Veterinary Codes have been met.

[This page intentionally left blank]

Toxicological Assessment

Evaluation of Toxicology

The toxicological database for ethoxysulfuron, 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.

Toxicokinetics and Metabolism Studies

Ethoxysulfuron was almost completely absorbed in **rats** following single oral administration of a low (10 mg/kg-bw) or high dose (350 mg/kg bw). Peak concentrations in the plasma occurred at 1 hour (low dose) or 2-6 hours (high dose) after dosing. 78-95% of the radioactivity was excreted during the first 24 hours after treatment with over 50% in the urine.

Concentrations of radioactivity in tissues were very low with the stomach and liver having relatively higher levels. ¹⁴C-ethoxysulfuron was metabolised principally by O-demethylation and O-deethylation to give the two major metabolites in the excreta. Unchanged parent ethoxysulfuron was the major metabolite in the plasma and liver.

Administration of multiple low doses of ethoxysulfuron resulted in similar kinetics.

Acute Studies

Ethoxysulfuron has low oral (LD₅₀ > 5000 mg/kg bw in **mice** and LD₅₀ = 3270 mg/kg bw in **rats**), dermal (LD₅₀ > 4000 mg/kg bw in **rats**) and inhalation toxicity (LC₅₀ > 3550 mg/m³ in **rats**). It is a slight eye irritant in **rabbits**, but is not a skin irritant in **rabbits** or a skin sensitiser in **guinea pigs**.

In **rats**, the oral, dermal and inhalation LD₅₀'s of Hero Selective Herbicide were 2811 mg/kg bw, >2000 mg/kg bw and >3260 mg/m³, respectively. It was a moderate eye irritant in **rabbits**, but was not a skin irritant in **rabbits** or a skin sensitiser in **guinea pigs**.

Short-term Studies

Ethoxysulfuron was administered in the diet to **mice** for 4 weeks at concentrations of 0, 2000, 4000 and 8000 ppm.

No treatment-related changes were observed in clinical observations, haematology, clinical biochemistry and gross pathology.

Rats received ethoxysulfuron in the diet at concentrations of 0, 1000, 3000 or 10000 ppm for 4 weeks.

Decreased body weight gain, urea, glucose and total protein, and increased liver weight were observed at 10000 ppm. Females at this dose group had increased cholesterol and triglyceride. Slight changes in the protein electrophoretic pattern were also noted at 10000 ppm.

Rats received ethoxysulfuron in water by application to the skin, at doses of 0, 250, 500 or 1000 mg/kg bw/day for 4 weeks.

There were no treatment-related changes in clinical observations, haematology, clinical chemistry, urinalysis and pathology.

Rats were exposed to ethoxysulfuron by inhalation (nose-only) at concentrations of 0, 0.04, 0.2 or 1.0 mg/L for 21 days.

Rats at 1.0 mg/L showed irregular breathing, lowered eyelids and increased salivation, but these signs were reversible. At necropsy, females at 1.0 mg/L had some abnormal cells in the cuboidal epithelium in the larynx, which was accompanied by a minimal increase in cell numbers in 2 animals. This change was also reversible.

Sub-chronic Studies

Mice received ethoxysulfuron at 0, 1000, 3000 or 9000 ppm in the diet for 13 weeks.

Decreased WBC (white blood cells) were observed in males at 9000 ppm. Females at 9000 ppm had increased glucose and liver weights, while males at this dose level had decreased glucose. Increased incidences of enlarged liver cells were observed in both sexes at 9000 ppm. Females at 9000 ppm had an increased incidence of fatty change in the liver.

The **NOEL** was 3000 ppm (492.3 mg/kg bw/day) based on decreased WBC, changes in glucose levels and hepatotoxicity at 9000 ppm.

Rats received ethoxysulfuron at 0, 1000, 3000 or 9000 ppm in the diet for 13 weeks.

Decreased food consumption, body weight gain, bilirubin and potassium were noted at 9000 ppm. Females at 3000 ppm also had decreased bilirubin. Decreased triglyceride, glucose, AST (aspartate aminotransferase), and prolonged thromboplastin time (PT) were observed in males at 3000 and/or 9000 ppm. Males at all dose levels had decreased γ -globulin, while females at 9000 ppm had decreased γ -globulin and protein.

All these changes were reversible, except for decreased glucose.

A **NOEL** was not established based on decreased γ -globulin in males at 1000 ppm and above.

Dogs received ethoxysulfuron at 0, 400, 2000 or 5000 ppm in the diet for 13 weeks.

Decreased food consumption was recorded in both sexes at 5000 ppm. Males at 5000 ppm had increased MCV (mean corpuscular [cell] volume) and MCH (mean corpuscular [cell] haemoglobin) and decreased albumin, while females at this dose level had increased monocytes and decreased LDH (lactate dehydrogenase) and γ -globulin.

These changes were reversible after a 4-week recovery period. Increased liver weight was observed at 5000 ppm and higher thyroid gland weight was recorded in all dose groups. The latter change was associated with thyroid follicular hyperplasia at all dose levels, which was not reversed after the recovery period.

A **NOEL** was not established, based on increased thyroid weight and follicular hyperplasia in the thyroid across all dose levels.

Dogs received ethoxysulfuron at 0, 20, 200 or 2000 ppm in the diet for 13 weeks.

Decreased APTT (activated partial thromboplastin time) and increased total lipids, cholesterol, phospholipid, α_2 -globulin and ALT (alkaline phosphatase) were observed in females at 2000 ppm. Males at 2000 ppm had decreased T₄ and increased γ -globulin, while both sexes at this dose level had increased glutamate dehydrogenase.

All these changes were reversed at the end of the recovery period.

Increased liver weight (female only) and higher incidences of increased numbers of parafollicular cells in the thyroid gland (male only) were observed at 2000 ppm.

The **NOEL** was 200 ppm (6.2 mg/kg bw/day) based on decreased APTT, changes in clinical chemistry, and increased liver weight and higher incidences of increased parafollicular cells in the thyroid gland at 2000 ppm.

Chronic/Carcinogenicity Studies

Mice received ethoxysulfuron at 0, 70, 700 or 7000 ppm in the diet for 52 or 101/102 weeks.

Decreased food consumption (female only) and body weight gain and increased RBC (male only) were observed at 7000 ppm. Reduced platelets and WBC were observed at 7000 ppm in males and females, respectively. Females had decreased adrenal weights, increased incidences of corneal ulcer in the eyes and atrophy in the mandibular glands at 7000 ppm. Males had increased pigment deposits in the liver at 7000 ppm.

The **NOEL** was 700 ppm (100 mg/kg bw/day) based on decreased food consumption, body weight gain and adrenal weight, haematology changes, corneal ulcer and atrophy of the mandibular glands at 7000 ppm.

Rats received ethoxysulfuron at 0, 80, 800 or 8000 ppm in the diet for 52, 104 or 118 weeks.

Decreased food consumption, body weight gain, bilirubin, cholesterol, T₃, T₄, γ -globulin and α_2 -globulin, and increased lactate dehydrogenase and TSH were observed at 8000 ppm. Higher incidences of sinus congestion and histiocytosis in the mesenteric lymph nodes, distended bursa in the ovary, and congestion in the thymus were observed at 8000 ppm. Increased incidences of bile duct proliferation and enlarged centrilobular cells in the liver, at week 52 only, were observed in male rats at 8000 ppm.

Females had higher incidences of luminal dilation and congestion in the uterus, inflammation in the exorbital lacrimal gland, and granulopoiesis and congestion in the bone marrow at week 118. Neoplastic findings at 8000 ppm included increased uterine adenocarcinoma in females but the incidence of these tumours was higher than normal in the control group as well.

The **NOEL** was 800 ppm (38.94 mg/kg bw/day) based on decreased body weight gain and changes in clinical chemistry and pathology at 8000 ppm.

Dogs received ethoxysulfuron at 0, 125, 500, 2000 or 8000 ppm in the diet for 52 weeks.

Decreased food consumption (female only) and body weight gains were observed at 8000 ppm. MCV and MCH were increased in males at 8000 ppm and in females at 2000 and 8000 ppm. Females at 2000 ppm had increased triglycerides, while both sexes at 8000 ppm had elevated total lipids, triglycerides, ALP and iron, and reduced creatinine and albumin.

At necropsy, higher liver, thyroid and kidney weights, and decreased prostate weights were observed in males and/or females at 8000 ppm. Higher incidences of granulated bile in the gallbladder and increased septal hepatitis (male dogs only) and bile duct proliferation were also recorded at 8000 ppm.

The **NOEL** was 500 ppm (15.5 mg/kg bw/day) based on haematological and clinical chemistry changes at 2000 ppm and above.

Reproduction Studies

In a preliminary study, ethoxysulfuron at concentrations of 0, 400, 2000 or 8000 ppm in the diet was administered to **rats** during a 3-week pre-mating period and throughout the mating, gestation and lactation periods.

Decreased food consumption and body weight gain were observed in adults at 8000 ppm. Reduced implantation sites and lower pup body weight gain were observed at 8000 ppm. Decreased ovary weight was observed in dams at 2000 ppm and above, while increased liver weight was seen in 8000 ppm parents and lower liver weight was evident in 8000 ppm pups.

Ethoxysulfuron at concentrations of 0, 200, 1000 or 5000 ppm in the diet was administered continuously to two successive generations of **rats**.

Decreased food consumption and body weight gain were observed at 5000 ppm in both F0 and F1 adults. During the lactation period, lower body weight gain was noted in F1 and F2 pups at 5000 ppm.

The **NOEL** was 1000 ppm (91.5/128.8 mg/kg bw/day) for general and reproduction toxicity based on decreased food consumption and body weight gain in adults and pups at 5000 ppm.

Developmental Studies

Pregnant **rats** received ethoxysulfuron by gavage at concentrations of 0, 200, 400, or 800 mg/kg bw/day on day 7 through day 16 of gestation.

Increased urinary excretion and hairloss, reduced food consumption and body weight gain were observed in dams at 400 and/or 800 mg/kg bw/day. In the 800 mg/kg- bw/day group, foetuses showed lower placental and body weights and shorter body length. Skeletal examinations revealed increased foetuses at 800 mg/kg bw/day with partial or absent ossification of various bones and higher incidences of extra vertebra/ribs. Foetuses at 400 mg/kg bw/day also showed increased incidences of non-ossified or partially ossified sternebra.

The maternal and foetal **NOEL** was 200 mg/kg bw/day based on increased urinary excretion and hairloss, reduced food consumption and body weight gain in dams, and retarded foetal development at 400 mg/kg bw/day and above.

Pregnant **rabbits** received ethoxysulfuron by gavage at concentrations of 0, 25, 63, or 160 mg/kg bw/day on days 6 through 18 of gestation.

One dam at 25 mg/kg bw/day was killed moribund. Three **rabbits** in the 160 mg/kg bw/day group were found to have vaginal haemorrhage and two of them were killed before the end of the study. Decreased or no faeces was observed in dams at 63 and 160 mg/kg bw/day. Dams at 160 mg/kg bw/day lost body weight. Increased abortion or premature delivery were seen at 160 mg/kg bw/day, which resulted in reduced dams with viable foetuses. Increased post-implantation loss and late intrauterine deaths were observed at 160 mg/kg bw/day, which led to decreased mean live foetuses. At 160 mg/kg bw/day, there were twice as many female as male foetuses. Decreased placental and body weight, shorter body length and higher neonatal mortality were observed in foetuses at 160 mg/kg bw/day.

Also at this dose level, there were increases in haematoma in the apex of the heart, enlarged stomach filled with fluid or soft mass, fused or longitudinally displaced sternebra and a short and/or abnormally long rib on one or both sides of the 13th thoracic vertebra. Dead or prematurely delivered foetuses were severely stunted.

The maternal **NOEL** was 25 mg/kg bw/day based on decreased or no faeces at 63 mg/kg bw/day and above.

The foetal **NOEL** was 63 mg/kg bw/day based on embryotoxicity, retarded foetal development and foetal abnormalities at 160 mg/kg bw/day.

Genotoxicity Studies

Ethoxysulfuron was not genotoxic in a battery of genotoxicity studies including the Ames test, *in vitro* HGPRT mutation test, unscheduled DNA synthesis in rat hepatocytes and chromosome aberration tests in cultured mammalian cells and bone marrow in mice.

Other Studies

Tests with four impurities of ethoxysulfuron showed low acute oral toxicity with LD_{50s} = 2669, 2568, 1876 and 606 mg/kg bw, respectively.

Six metabolites/impurities of ethoxysulfuron showed negative results in the Ames test.

Public Health Standards

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients.

On the basis of its toxicity, the NDPSC has included ethoxysulfuron in **Schedule 5** of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate first-aid instructions and safety directions on the product label.

NOEL/ADI

The Acceptable Daily Intake (ADI) is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime, and is based on the lowest NOEL obtained in the most sensitive species.

This NOEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The **ADI** for ethoxysulfuron was established at 0.06 mg/kg bw/day based on a **NOEL** of 6.2 mg/kg bw/day in the 3-month **dog** study. A 100-fold safety factor was used in recognition of the extensive toxicological database available for ethoxysulfuron.

Acute Reference Dose (ARfD)

The acute reference dose is the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event.

The ARfD is derived from the lowest single or short term dose which causes no effect in the most sensitive species of experimental animal tested, together with a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The **ARfD** is 0.2 mg/kg bw/day based on a **NOEL** of 25 mg/kg bw/day in the development study in **rabbits**, using a 100-fold safety factor.

[This page intentionally left blank]

Background to the application

Ethoxysulfuron, in the product *Hero® Selective Herbicide* (56831), is a sulfonylurea herbicide used overseas for the control of broad-leaved and sedge weeds in cereals, rice and sugarcane.

The maximum use rate proposed for the product in Australia is 250 g product/ha (150 g ethoxysulfuron/ha). As at March 2004, there were no MRLs present for the use of ethoxysulfuron in any commodity.

Metabolism

The applicant provided metabolism studies conducted in sugar cane, rice and rats. The results of these data are summarised as follows:

Sugar Cane: [2-¹⁴C-pyrimidyl]-ethoxysulfuron was applied directly to leaves of sugar cane plants growing in pots inside a greenhouse. In a separate experiment the same test substance was applied to the soil around the plants. Treatments were applied to simulate field application rates at 90 g ai/ha. All treatments were applied when cane plants were 60-70 cm tall.

Samples of treated and untreated leaves from the foliar treatment were collected 0, 7 and 32 days after application. Samples of cane were collected at normal harvest 139 days after treatment. Samples of leaves and cane were collected from the soil treatment 139 days after treatment.

A small amount of translocation was observed with approximately 1.6% of the foliar applied radioactivity found in untreated leaves at harvest. Translocation of foliar or soil applied radiolabel into cane stalks was negligible. In leaves the predominant residue component was the parent compound accounting for 79%, 37% and 33% of the TRRs at 7, 32 and 139 days respectively.

Several minor metabolites were observed in leaves, at levels between 0.2%-4.3% of TRR.

Total radioactive residues (TRR) in cane stalks were <0.01 mg equiv./kg and the nature of the radioactivity was not investigated further.

Paddy Rice

Paddy rice grown in containers was treated with [2-¹⁴C-pyrimidyl]-ethoxysulfuron at 0.22-0.46 kg ai/ha, 45 days after sowing.

Mature rice (with husk) contained <0.1 mg equiv./kg total radioactive residues. The nature of the radioactivity in the rice was not investigated further.

Samples of leaves and straw collected 14, 28 and 82 days after application were analysed with the parent compound accounting for 68-75% of the TRR in leaves and straw.

A total of 8 minor metabolites were present with no individual component accounting for >5% of the TRR.

Rats: In rats dosed with radio-labelled ethoxysulfuron, greater than 90% of the dose was absorbed from the gastrointestinal tract. Urinary excretion was the main route of elimination (approximately 60% of the dose) with significant faecal excretion (30-40% of the dose) via the bile. The parent compound was metabolised mainly by O-demethylation and O-deethylation with the O-deethyl metabolite also excreted as a sulfate conjugate.

Additional plant data (rice): Studies were undertaken on rice, that were harvested 120 days after the application of pyrimidinyl-¹⁴C-ethoxysulfuron and benzyl-¹⁴C-ethoxysulfuron to the paddy water.

In both cases, the radio-label remained in the soil and paddy water, comprising over 59% of the applied radio-activity. Less than 7% of the total radio-active residues (TRR) were identified in the shoot or rice straw and less than 0.15% of the TRRs were located in the rice grain.

¹ This assessment includes a metabolism and toxicokinetics assessment in crop plants: e.g. sugar cane, rice.

Metabolites in the soil were not measured, however in the straw the parent compound accounted for <10% of the TRRs. Two metabolites were identified which comprised 2.2-15.1% and 26.9-34.7% of TRR. Other metabolites were isolated but were not characterised, and a significant proportion of the metabolites were bound to the lignin, cellulose or other bound fractions.

As negligible amounts of radioactivity were isolated from rice grain and husk, metabolites in these commodities were not characterised any further.

Additional animal data: Apart from the rat study, no additional animal metabolism studies were provided. The Office of Chemical Safety also reviewed these data, and it was concluded that the unchanged parent compound was the major metabolite in the plasma and liver.

Rotational crops: Soil was treated with pyrimidinyl-2-¹⁴C-ethoxysulfuron, any further into which rotational crops (potatoes, wheat, spinach, carrots and little radish) were planted 30, 120 or 364 days after treatment.

Depending on the interval between soil treatment and planting, the spinach, carrot and little radish crops did not emerge due to the phytotoxicity of ethoxysulfuron. After 364 days between treatment and planting, only the spinach crop did not emerge.

The carrot, little radish, potato were fractionated into leaves and root/tuber (for the root crops), and fractionated into the grain and straw for the wheat crop. The radioactivity was slowly transported to the deeper soil layers over the study period, due mostly to irrigation and rainfall.

Metabolism of ethoxysulfuron in the soil was noted, giving rise to a number of metabolites with different R_f values after TLC analyses. These metabolites were not characterised.

The maximum residue in the edible portions of all these crops was 2.7 µg equiv./kg. Up to 40.2 µg equiv./kg of the TRRs were recovered from the wheat straw, 26.8 µg equiv./kg from potato vine and 67.2 µg equiv./kg from carrot leaves. In all of these fractions the parent compound was metabolised, however the metabolites were not characterised further.

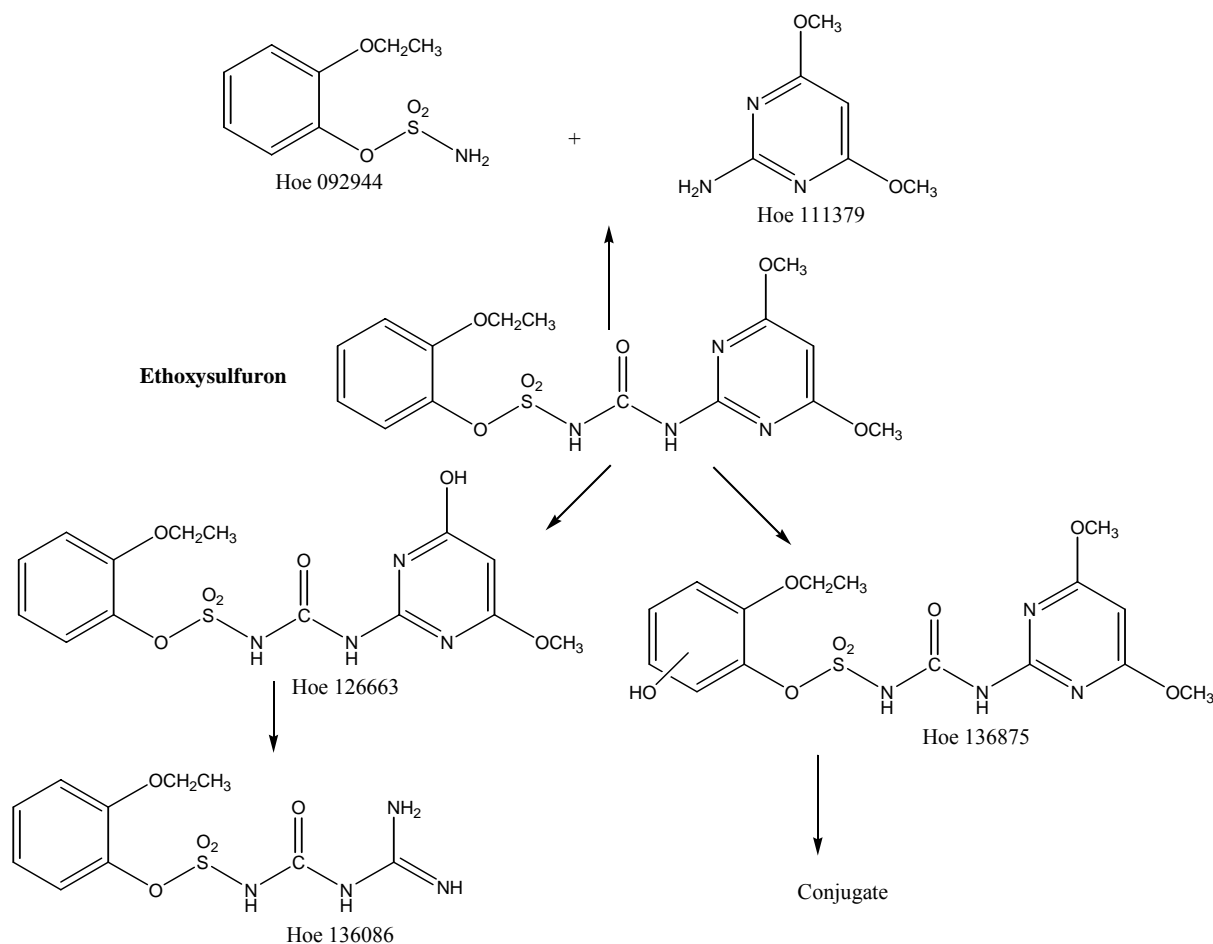
Summary:

In plant studies, the parent compound ethoxysulfuron was present as well as a number of metabolites.

Each of the metabolites was present at less than 4.3% of the applied radioactivity.

The major proportion of the radioactive residue was the parent compound, ethoxysulfuron.

The structure and relationship of the major metabolites to ethoxysulfuron are shown in the diagram below.



Analytical methods

Analytical data were provided for and evaluated for this assessment. The analytical methods used for residues in plant and animal commodities were validated, and found to be acceptable.

The validated LOQs for animal commodities were 0.01 mg/kg for milk and 0.05 mg/kg for eggs and muscle. The ability of the method to determine residues in offal was not investigated.

The validated LOQs for plant commodities were 0.01 mg/kg for sugarcane, sugar cane fodder [fresh weight] and also for sugar cane forage.

Residue Definition

The parent compound was the predominant residue in plant commodities. The analytical method provided for determination of residues in sugar cane commodities determines the parent compound. A residue definition of “ethoxysulfuron” is appropriate for commodities of plant origin.

The analytical method for animal commodities measures ethoxysulfuron as the hydrolysis product 2-amino-4,6-dimethoxypyrimidine (Hoe 092944). A residue definition of “2-amino-4,6-dimethoxypyrimidine, expressed as ethoxysulfuron” is appropriate for commodities of animal origin.

Residues in Foods and Animal Feeds

The applicant provided 4 Australian residue trials on sugarcane conducted in Queensland and New South Wales.² Summaries of 2 trials conducted in Brazil were also provided.

In the Australian trials, plant sugarcane was treated with ethoxysulfuron at 150 or 300 g ai/ha at different stages, between pre-emergence to out-of-hand (~ 100 cm tall) stage of crop development.

² Radunz, L., Determination of residues of ethoxysulfuron in sugarcane (billets, forage, sugarcane juice and bagasse) after early post-emergence applications of 150 or 300 g ai/ha, Laboratory Report No. AQ-02-029, 26 November 2002, Bayer CropScience.

Samples of cane tops (top 30 cm of canes) and cane billets (equal portions of top, middle and bottom sections) were collected at 133, 238, 272 or 293 days after application.

Residues of ethoxysulfuron in samples of billets, tops, juice and bagasse from crops treated at 150-300 g ai/ha (1-2x) were all <0.01 mg/kg. No correction for dry matter content was applied to the results for cane tops. The LOQ of the method was 0.01 mg/kg.

For the 2 trials conducted in Brazil, residues of ethoxysulfuron in billets harvested 153-159 days after application at 150-300 g ai/ha were <0.05 mg/kg.

MRLs for Plant Commodities

The minimum interval between application and harvest in the trials was 133 days (19 weeks). Residues in billets and cane tops were <0.01 mg/kg (fresh weight).

Therefore the following MRLs are appropriate, with an associated **harvest**-withholding period of 19 weeks:

Table 1			
GS	0659	Sugar cane	*0.01 mg/kg
Table 4			
AM	0659	Sugar cane fodder [fresh weight]	*0.01 mg/kg

MRLs for Animal Commodities

The applicant proposed a grazing withholding period of 19 weeks. This effectively precludes grazing of failed crops, although it is understood that grazing of failed cane crops would be extremely rare.

In the sugar cane metabolism study total radioactive residues in treated leaves were 9.4, 10.6, 4.2 and 15.7 mg equiv./kg at 0, 7, 32 and 132 days respectively after treatment at 90 g ai/ha. It should be noted that the results reflect residues only in leaves that were directly treated with radiolabel, rather than a sample from a sprayed plant.

In the absence of animal transfer data livestock dietary exposure must be negligible.

Residues in tops harvested 19 weeks after application (just prior to out-of-hand stage) were <0.01 mg/kg. Livestock consuming tops from mature cane crops should be exposed to negligible levels of ethoxysulfuron.

Therefore it is appropriate to establish the following MRLs for commodities of mammalian origin at the limits of analytical quantitation (LOQ), with an associated **grazing** withholding period of 19 weeks:

Table 1			
MO	0105	Edible offal (mammalian)	*0.05 mg/kg
MM	0095	Meat (mammalian)	*0.05 mg/kg
ML	0106	Milks	*0.01 mg/kg

Discussion on Residue Aspects of Rotational Crops

As described above, the applicant provided data for rotational crops (potato, wheat, spinach, carrots and little radish) planted 30, 120 and 364 days after treating the soil with ¹⁴C-ethoxysulfuron. The majority of the radioactive residue remained in the soil, slowly being transported to the deeper layers as the time between the soil treatment and planting increased.

Harvest residues: The highest concentration of residue in the edible portions of the crops trialled were <0.0027 mg equiv./kg, seen in the 120-day trial. These values are well below the validated LOQs as shown in the analytical methods, and consequently would be expected to have non-detectable residues in these commodities.

Ethoxysulfuron was metabolised to a number of different metabolites in the soil and in the wheat straw and husk, carrot leaves and potato vine over the 120 and 364-day studies. The metabolites comprised up to 40% of the TRRs, however, the actual concentrations were <0.0158 mg equiv./kg. Characterisation of the metabolites was not undertaken due to the low concentrations of these metabolites.

Consequently, it is **not** expected that residues of ethoxysulfuron or its metabolites would translocate to plants from the treated soil (providing that these plants are not the target of the herbicide) or to the edible commodities of these plants.

Grazing residues: Detectable residues may be present in the new crops as a result of planting in a treated area and as such, grazing by cattle or sheep on these new crops may result in detectable residues of ethoxysulfuron in grazing animals.

There are no animal feeding studies in support of definitive MRLs for grazing animals, and also no re-cropping studies undertaken at 90 days (3 months) relevant to the use of ethoxysulfuron. The latter time period is proposed as a re-cropping interval for the crops guar beans and Dolichos lab-lab, so an assessment of ethoxysulfuron residues in these crops was not possible for a 3month delay in planting.

However, there is residue data on potential ethoxysulfuron residues in following crops, when they were planted 120 days after soil treatment with ethoxysulfuron. These data showed that whilst residues were maximised in the following crops at 120 days after soil treatment, there were not significant. Hence there is very little or no potential for significant transfer of ethoxysulfuron residues to animals that eat such crops, 120 days after soil treatment.

Hence it is recommended by the APVMA Residues section that the minimum re-cropping period be extended to 4 months (120 days) for guar beans and Dolichos lab-lab, because of potential transfer of plant residues to animals that consume them.

Dietary Risk Assessment

The **chronic** dietary exposure to ethoxysulfuron is estimated by the National Estimated Daily Intake (**NEDI**) calculation, encompassing all registered/temporary uses of the chemical and the mean dietary consumption data derived from the 1995 National Nutrition Survey of Australia. The NEDI calculation is made in accordance with international guidelines (*Guidelines for predicting dietary intake of pesticide residues*. Geneva, WHO 1997).

The **NEDI** for ethoxysulfuron is equivalent to 0.3% of the ADI. It is concluded that the chronic dietary exposure is small and the risk is acceptable.

The **acute** dietary exposure is estimated by the National Estimated Short Term Intake (**NESTI**) calculation. The NESTI calculations are made in accordance with the deterministic method used by the JMPR, with 97.5th percentile food consumption data derived from the 1995 National Nutrition Survey of Australia.

As seen in the below table, the **NESTIs** for all relevant commodities are less than the ARfD. It is concluded that the acute dietary exposure is small and the risk is acceptable.

NESTIs Calculations for Ethoxysulfuron in Food Commodities.

Commodity	%Acute Reference Dose (ARfD)	
	2-6 years	2+ years
Meat (mammalian)	0.34	0.19
Edible offal (mammalian)	0.021	0.07
Milks	0.30	0.08
Sugarcane	0.04	0.02

Conclusions and Recommendations

The Residues section of the APVMA has evaluated the residues aspects of *Hero® Selective Herbicide*.

Metabolism, residue trials, analytical methodology, and fate in storage and processing data, including that submitted by Bayer CropScience Pty Ltd to support their application for registration of the product, have been considered, and the following recommendations³ are made:

³ These recommendations ensure that the residues aspects of Section 14(5) Agricultural and Veterinary Chemicals Codes are satisfied

Recommended Amendments to the MRL Standard

1. The following amendments be made to the MRL Standard:

Table 1

Compound	Food	MRL (mg/kg)
Ethoxysulfuron		
DELETE		
MO 0105	Edible offal (mammalian)	T*0.05
MM 0095	Meat (mammalian)	T*0.05
ML 0106	Milks	T*0.01
GS 0659	Sugarcane	T*0.01
ADD:		
MO 0105	Edible offal (mammalian)	*0.05
MM 0095	Meat (mammalian)	*0.05
ML 0106	Milks	*0.01
GS 0659	Sugarcane	*0.01

Table 3

Add:	Ethoxysulfuron	Commodities of plant origin: Ethoxysulfuron Commodities of animal origin: Sum of all ethoxysulfuron and metabolite residues hydrolysed to 2-amino-4,6-dimethoxypyrimidine, expressed as ethoxysulfuron
-------------	----------------	---

Table 4

Compound	Animal Feed Commodity	MRL (mg/kg)
Ethoxysulfuron		
DELETE		
AM 0659	Sugar cane fodder [fresh weight]	T*0.01
ADD		
AM 0659	Sugar cane fodder [fresh weight]	*0.01
AV 0659	Sugar cane forage	*0.01

* value is the Limit of Quantitation (LOQ) for that commodity

Withholding Periods

2. The following withholding periods are required in conjunction with the above MRLs:

Harvest: DO NOT HARVEST FOR 19 WEEKS AFTER APPLICATION

Grazing: DO NOT GRAZE OR CUT FOR STOCKFOOD FOR 19 WEEKS AFTER APPLICATION.

Crop Rotation Amendments

3. Amendments to the Crop Rotation Recommendations:

For Guar bean and Dolichos lab-lab, that the crop rotation recommendation be extended from 3 months to 4 months, due to concerns regarding potential residue transfer to animals that eat these crops.

Assessment of Overseas Trade Aspects of Residues in Food

Residues related aspects of trade

Export of treated produce containing finite residues of ethoxysulfuron may pose a risk to Australian trade in situations where (i) no residue tolerance (import tolerance) is established in the importing country or (ii) where residues in Australian produce are likely to exceed a residue tolerance (import tolerance) established in the importing country.

There are no CODEX tolerances for ethoxysulfuron. Hence the APVMA conducted a risk assessment for ethoxysulfuron, with respect to possible adverse effects on trade between Australia and places outside Australia.

Overseas Registration Status

The applicant has provided a statement that as at 4 August 2008, formulations containing ethoxysulfuron are registered in sugar cane in seven countries (Brazil, Dominican Republic, El Salvador, Guatemala, Nicaragua, Pakistan and Panama).

It is also registered for use in rice in 31 countries (e.g. China, India, Indonesia, Italy, Japan, Malaysia, Pakistan, the Phillipines, Taiwan, Thailand, Turkey and Vietnam). Registrations also exist for use in acacia and oil palm (Indonesia) and also golf courses (Japan). Ethoxysulfuron was first registered in the world in 1996, in Vietnam.

Overseas MRLs

The recommended MRL is 0.01 mg/kg for sugarcane (and its fodder/forage). As mentioned above, rice is a commodity for which ethoxysulfuron is also registered, with MRLs of 0.05, 0.01 and 0.1 mg/kg in Brazil, Italy and Japan, respectively.

Potential Risk to Australian Trade

Sugar is considered to be a major export commodity for Australia. Approximately 80% of Australia's sugar is exported, with the export quantity being in the order of 4.1 million tonnes annually (2002/3 to 2005/6). The total value of sugar exported in this period of time is equivalent to \$A1.2 - 1.6 billion.

Australian Commodity Statistics (2002) published by ABARE Economics has listed the major importers of Australian sugar for the 2001-2002 fiscal year:

- Malaysia (772 kt) [~19%],
- Japan (763 kt) [~19%],
- Republic of Korea (570 kt) [~14%],
- Canada (477 kt) [~12%],
- New Zealand (246 kt) [~6%],
- China (230 kt) [~6%],
- Saudi Arabia (169 kt),
- Taiwan (123 kt) and
- USA (83 kt).

Major importers of Australian sugar for 2005/6 were:

- Republic of Korea (~25% of exports),
- Malaysia (~12%),
- Indonesia (~12%),
- Japan (~12%) and
- Taiwan (~8%).

Finite residues are not expected to occur in sugar cane or processed sugar commodities. Finite residues are not expected to occur in cane tops after the proposed grazing withholding period. It is expected that livestock dietary exposure to ethoxysulfuron will be negligible.

The proposed use of ethoxysulfuron is unlikely to unduly prejudice trade, however comment will be welcomed by the APVMA as a part of the public consultation process.

Conclusion

The Residues section of the APVMA has considered whether the proposed use of *Hero® Selective Herbicide* would unduly prejudice trade and commerce between Australia and places outside Australia, as required by section 14(3)(e)(iv) of the Agricultural and Veterinary Chemicals Codes.

Detectable residues are not expected to occur in commodities relevant to the current application and are expected to be below the relevant standards of key export markets.

Therefore, the APVMA is satisfied that the proposed use of *Hero® Selective Herbicide* would not unduly prejudice trade between Australia and places outside Australia.

Occupational Health and Safety Assessment

Background

Ethoxysulfuron is not on the NOHSC *List of Designated Hazardous Substances*. Based on its potential for eye-irritating effects, Hero Selective Herbicide is classified as hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances*.

The product containing ethoxysulfuron (*Hero® Selective Herbicide*) has low acute oral and dermal toxicity in rats. It was a moderate eye irritant to the rabbit, but was not a skin irritant in rabbits or a skin sensitiser in guinea pigs. Based on the available toxicological data, the Office of Chemical Safety (OCS) classified Hero Selective Herbicide as hazardous according to NOHSC⁴ *Approved Criteria for Classifying Hazardous Substances* (NOHSC 1999), and assigned the following risk phrase:

R36 Irritating to eyes

Based on the toxicology assessment of *Hero® Selective Herbicide*, the main hazards associated with repeat exposure to the product are systemic effects on the liver and thyroid and changes in haematology parameters.

Hero® Selective Herbicide will be formulated overseas and imported into Australia in sale packs. Transport workers, store persons and retailers will handle packaged product and could only become contaminated if packaging were breached.

The product will be packed in 1, 1.5, 2 and 5 kg polyamide/HDPE containers with 63 mm diameter neck.

Use and exposure

Hero® Selective Herbicide is a wettable granule formulation, and will be used for the control of nutgrass and certain broadleaf weeds in sugarcane crops. It will be applied only by ground application either as a broadcast (by boom spray) or directed application (octopus head attachment) depending on the growth stage of the sugarcane.

The recommended application rate is 250 g/ha in a minimum spray volume of 250 L/ha of water (0.1% EUP, 0.06% ethoxysulfuron). Only one spray application will be made per crop season.

A withholding period of 19 weeks is recommended for grazing and harvesting or using the treated plants as stockfeed.

End-users may be exposed to the product when opening containers, preparing spray, applying spray, maintaining equipment and clearing up spills. In addition, workers re-entering treated crops to carry out crop management practices can be exposed to product residues.

Exposure during mixing and loading will be largely through dermal contact with the product and the mix solution. The main routes of exposure during application are likely to be dermal and inhalation.

There were no worker exposure studies available for assessment.

In the absence of worker exposure data, OCS used the Predictive Operator Exposure Model (POEM) and the Pesticide Handlers Exposure Database (PHED) to estimate worker exposure to ethoxysulfuron during mixing/loading and application.

The POEM data indicated unacceptable risk (Margin of Exposure⁵ [MOE] <100) to mixer/loaders when gloves were not worn. MOE became acceptable when workers wore gloves (i.e. MOE >100). Risks were acceptable for applicators even without gloves.

When PHED was used, MOE were acceptable without gloves for mixing/loading as well as boom spray (open cab) application. Both exposure models assume that workers wear at least one layer of clothing (cotton overalls or equivalent clothing) when performing these tasks.

⁴ NOHSC = National Occupational Health and Safety Commission. Its functions are now within the OCS.

⁵ The MOE measure as used here is more a Measure of Safety: a low MOE (<100) is considered to indicate lack of safety, whereas a high MOE (>100) is considered to indicate operator safety.

The risk assessment indicates that cotton overalls buttoned to the neck and wrist or equivalent clothing, elbow-length PVC gloves and face shield or goggles should be worn when opening the container and preparing spray.

Additional information is available in the *Hero® Selective Herbicide* Material Safety Data Sheet (MSDS).

Re-entry

There were no worker exposure data available to assess exposure during re-entry activities. Workers entering treated areas can be exposed to product residues and degradation products during crop irrigation, manual harvesting or other crop management activities.

In the absence of re-entry data, OCS estimated risk for re-entry workers by using the US EPA Occupational Post-Application Risk Assessment Calculator Version 1 (8/9/00)-US EPA Policy 003.1.

Based on this model, a worker re-entering treated areas may not be at risk and therefore, OCS does not recommend any re-entry statement.

Recommendations for safe use

Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length PVC gloves and face shield or goggles when opening the container and preparing spray.

The full safety directions recommended by the OCS for *Hero® Selective Herbicide* are presented below:

Ethoxysulfuron	WG all strengths	<i>Hazard Statements</i>
	161 162	Will irritate the eyes
	210 162	Avoid contact with eyes
	340 343	If product in eyes, wash it out immediately with water
	351	Wash hands after use
		<i>Personal Protection</i>
	279 280 281 290 292b 294 299	When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length PVC gloves and face shield or goggles
	360 361 365 366	After each day's use, wash gloves face shield or goggles and contaminated clothing

The PPE recommended above should meet the relevant standards determined by *Standards Australia*.

Conclusion

The OCS supports the registration of *Hero® Selective Herbicide*, containing 600 g/kg of ethoxysulfuron, as a wettable granule formulation, for the control of nutgrass and certain broadleaf weeds in sugarcane crops.

Hero® Selective Herbicide can be safely used by workers when handled in accordance with the instructions on the product label and any other control measures described above.

Environmental Assessment

The data package presented in support of the application for the registration of *Hero® Selective Herbicide* (600 g/L ethoxysulfuron as a wettable dispersible granule [WG]), addresses the environmental fate and toxicity of ethoxysulfuron and its relevant metabolites.

Environmental Fate (Degradation, Metabolism and Mobility)

NOTE: To view the structure of most of the degradation products of ethoxysulfuron referred to in this environmental assessment, see page 15.

Hydrolysis

Ethoxysulfuron hydrolyses faster under moderately acidic conditions: at pH 4, half-life was approximately 16 days and at pH 5, half-life was 64.6 days in one study (and of the order of 96 days in a second study). However, it is more stable under neutral to more alkaline conditions. For example, at pH 6, pH 7 and pH 9, half-lives were greater than 18 months, 259 and 331 days respectively.

Hence significant stability is expected at neutral or near environmental pH values.

Under the hydrolysis conditions, parent and three degradation products were identified:

- 2-amino-4,6-dimethoxypyrimidine (Hoe 092944),
- 2-ethoxyphenol (Hoe 110068) and
- 2-ethoxyphenol sulfamate (Hoe 111379).

Hydrolysis is not expected to be a significant degradation mechanism at environmental pHs.

Aquatic photolysis

When ¹⁴C-ethoxysulfuron was dissolved in natural river water and also in distilled, sterile water, and then irradiated (142 to 192 hours) using an artificial light similar to that of sunlight, up to five degradation products were detected in the surface water and three in the distilled water.

Apart from residual ethoxysulfuron, identified degradates in the surface water were:

- 3-(4,6-dimethoxypyrimidin-2-yl)-1-(2-phenoxy sulfonyl)-urea (Hoe 136087), formed by de-ethylation of the ethoxyphenyl moiety;
- which in turn underwent cleavage at the sulphonylurea linkage to form, sequentially, the three pyrimidines,
 - sulfonic acid of 3-(4,6-dimethoxypyrimidine-2-yl)-urea (no Hoe code number assigned),
 - 4,6-dimethoxypyrimidin-2-yl-urea (Hoe 099095) and
 - 2-amino-4,6-dimethoxypyrimidine (Hoe 092944).

In distilled water, three photoproducts were identified in some samples, with the maximum value reached being 6.5% of the applied radioactivity. No degradates were identified in either dark control.

At the end of the irradiation periods, ethoxysulfuron made up an average of 44% of the applied radioactivity in the river water and an average of 92.3% of the applied radioactivity in the distilled water.

Half-lives in surface water were of the orders of 30 sunshine days in surface water and 275 to 304 days in sterile water.

While direct photolysis of ethoxysulfuron in natural waters is not indicated as a significant degradation process, the presence of photosensitisers in such waters is expected to result in a slow degradation of ethoxysulfuron in natural water systems.

Photodegradation in air

The calculated half-life for ethoxysulfuron degradation in the atmosphere, by reaction with hydroxyl radicals, was ~1.7 hours. Hence ethoxysulfuron would readily degrade in the atmosphere as a result of reaction with photogenerated hydroxyl radicals.

Aerobic soil metabolism

Study 1: Two Korean clay loam soils (1.46 and 2.09% organic matter contents) were treated in the laboratory at a rate of 1 mg ethoxysulfuron/kg soil and residues of ethoxysulfuron determined over the following 90 days. The half-lives determined were 13 and 15 days.

Study 2: In a second laboratory study, a Brazilian light clay was treated with pyrimidyl-2-¹⁴C-ethoxysulfuron at a rate of 90 g ethoxysulfuron/ha and incubated under aerobic conditions for 100 days. Sterilised soil samples were similarly prepared and incubated.

In the non-sterile soil at 100 days:

- ethoxysulfuron was present at 12.2% of the applied radioactivity
- along with two other metabolites as the major radioactive constituents at that time, namely
 - 1-(N-hydroxymethylcarbonyl-N'-methoxycarbonylguanyl)-3-(2-ethoxyphenyl-sulfonyl)urea [identified only as Metabolite M-3 and with no Hoe number assigned] (17.1% of the applied radioactivity and
 - 1-(2-ethoxyphenoxy sulfonyl)-3-guanylurea⁶ (19.8% of the applied radioactivity).

In the sterile soil after 100 days,

- ethoxysulfuron (44.3% of the applied radioactivity) and
- the metabolite, 2-amino-4,6-dimethoxypyrimidine [or Hoe 092944] (44.3% of the applied radioactivity)

were the only identifiable residues.

Formation of volatile material was negligible for both soils.

The DT₅₀ values in the non-sterile soil and sterile soil were, respectively, 6 and 169 days. The respective DT₉₀ values were 72 and 335 days.

However, there was substantial deviation from first order kinetics degradation.

Study 3: Radio-labelled ethoxysulfuron was used to treat a sandy loam soil under aerobic conditions in a third laboratory study, with the treatment rate being about 86 g/ha. The treated soil was incubated in the dark under aerobic conditions for up to 91 days.

At the end of the incubation period, non-extractable residues made up 55% of the applied radioactivity. Mineralisation to carbon dioxide increased over the incubation period to a maximum of 7.7% of the applied radioactivity at day 91. By day 91, the metabolites made up 33.8% of the applied radioactivity in the soil extracts and ethoxysulfuron, 6.8%.

The DT₅₀ was 17.7 days (first order kinetic degradation) and the DT₉₀, 58.7 days.

Study 4: Three Japanese soils (two light clays, 10.52 and 6.19% organic matter and a clay loam, 3.38% organic matter) were fortified with the ethoxysulfuron soil metabolite 1-(2-ethoxyphenoxy sulfonyl)-3-guanylurea⁶ at 2 ppm, and analysed for this metabolite over a 246 day period.

Residues declined over this period with half-lives in the three soils between 35 and 40 days, values indicative of the metabolite not being persistent in aerobic soils.

Anaerobic soil/sediment metabolism

Study 1: Degradation of radiolabelled ethoxysulfuron in the laboratory was studied using:

- two Japanese soils (an alluvial sandy loam and a volcanic loam) under paddy field conditions, and
- an Italian soil (a sandy loam) under water/sediment conditions.

The soils were treated at the equivalent to a field rate of 90 g ethoxysulfuron/ha and were covered with water during the incubation period of 100 days, with the water/soil open to the atmosphere during this time.

In the Japanese soils at 100 days, non-extractable residues made up 25.3 and 56% of the applied radioactivity. Mineralisation (formation of carbon dioxide) at that time accounted for 3.02 and 4.58% of the applied radioactivity in the two soils.

For the Italian soil, at 100 days, non-extractable residues made up 39.5% of the applied radioactivity with 3.02% of the applied radioactivity being carbon dioxide.

⁶ Also called Hoe 136086 or 3-amidino-1-(2-ethoxyphenoxy sulfonyl)urea

In sterilised soils at 100 days, non-extractable residues in the three soils were significantly lower in the Italian and one Japanese soils: 7.38 and 3.76% of the applied radioactivity, respectively. In contrast, the second Japanese sterile soil had 30.56% non-extractable residues.

In one of the Japanese and the Italian (non-sterile) soils:

- ethoxysulfuron,
- 2-amino-4,6-dimethoxypyrimidine (Hoe 092944),
- 1-(2-ethoxyphenoxysulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea (Hoe 126663), and
- 1-(2-ethoxyphenoxysulfonyl)-3-guanylurea

were identified.

In the other non-sterile Japanese soil only Hoe 092944 and Hoe 126663 were identified as metabolites. In the sterilised soils, only ethoxysulfuron and Hoe 092944 were identified.

In the soils, the half-lives ranged from 10 to 62 days and DT_{90} s from 33 to 207 days.

In the overlaying waters, the dissipation half-lives ranged from 1.5 to 9.0 days for the Japanese waters with DT_{90} s of 17 to 30 days. In the Italian water, the DT_{50} was 30.5 days (first order kinetics) and the DT_{90} was 94.8 days.

Aerobic Aquatic Metabolism

Two equilibrated river and lake water/sediment systems were treated with radio-labelled ethoxysulfuron (1 mg/L) and then incubated in the dark for 140 days.

Redox potentials showed the treated water columns remained aerobic and the sediments anaerobic throughout the acclimatisation and incubation phases. Movement of radioactivity from the water column to the sediment took place in both cases, with formation of carbon dioxide identified in both systems. After 140 days, 34.8% of the applied radioactivity in the river system and 60.1% of the lake system were associated with the sediment and were unextractable. The rates of disappearance of ethoxysulfuron and its metabolite AE F126663⁷ were determined using non-linear first-order, one-compartment model reaction-kinetics.

Ethoxysulfuron was degraded to at least eleven radioactive components in the aquatic systems with the same metabolic pathway followed in both river and pond systems. The main degradation products were:

- AE F126663⁷, which reached maxima of 24.2% (river) and 21.5% (pond) of the applied radioactivity (within 56 and 28 days respectively) and
- AE F 136086⁸ was the second most important metabolite, present at maximum concentrations of 15.8% (river) and 10.3% (pond) of the applied radioactivity at 126 days of incubation.

Mineralisation occurred in both systems, with maxima (as percentages of the applied radioactivity) of 10% in the river system and 4.6% in the pond system, both at day 126 of the incubation period.

Half-lives for ethoxysulfuron in the river system were 23 days in the water phase, 42 days in the sediment and 35 days in the whole system. In the lake system, the corresponding DT_{50} s were, respectively, 11, 38 and 24 days.

The half-lives for the metabolite, AE F126663 were also determined for the entire systems and reported as 35.4 days for the river system and 17.8 days for the lake system.

Soil Adsorption/Desorption

The adsorption/desorption behaviour of ethoxysulfuron on five soils was determined using the batch equilibrium method. The soils were a silt loam, a sand (S 2.1), two loamy sands (Arizona A and LS 2.2) and a sandy loam. Organic carbon content of the soils ranged from 0.16 (the loamy sand, Arizona A) to 2.96% (the loamy sand, LS 2.2).

Except for soil LS 2.2, to which ethoxysulfuron was adsorbed relatively strongly, all other soils showed a rather weak adsorption.

⁷ AE F126663 = 1-(2-ethoxyphenoxysulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)urea = Hoe 126663.

⁸ AE F 136086 = 1-(2-ethoxyphenoxysulfonyl)-3-guanylurea or 3-amidino-1(2-ethoxyphenoxysulfonyl)-urea = Hoe 136086.

Adsorption isotherms were determined and the adsorption coefficients K_d range from 0.10 to 7.19. Normalising these values to the organic carbon content of each soil resulted in K_{oc} values ranging from 57 (the silt loam) to 243 (the loamy sand LS 2.2).

Such values are indicative of the ethoxysulfuron not being strongly bound to soils and ethoxysulfuron can be classified as having medium to high soil mobility.

The adsorption/desorption behaviour of a major ethoxysulfuron metabolite, Hoe 136086⁹ (radiolabelled carbon), was determined in four soils using the batch equilibrium method. The soils were a sand, two loamy sands and a silt loam. The soils had organic carbon contents of 0.16 to 2.96%.

The K_{oc} values determined ranged from 27 to 55 with non-determinable for the loamy sand with 0.16% organic carbon content.

This metabolite does not strongly bind to soil and is classified as having high to very high mobility.

Soil Column Leaching Studies - Aged Soil

In an aged soil column leaching study, a standard loamy sand soil (0.91% organic carbon content) was treated with ethoxysulfuron at a rate equivalent to 60 g/ha, thoroughly mixed and stored in darkness at 18-22°C over 21 days (one degradation half-life). Evolved carbon dioxide and volatile organic materials were trapped during this period and analysis of the soil was conducted at 21 days.

The aged soil was added to columns packed with a standard sandy loam (1.07% organic carbon content) or a standard sand (1.25% organic carbon content) and calcium chloride solution (equivalent to 200 mm of precipitation) run through the columns over a period of two days. Leachates and soil fractions were analysed for the presence of ethoxysulfuron and its metabolites.

Extractable materials from the aged soil were made up of ethoxysulfuron (44.6% of the applied radioactivity) and five metabolites (a combined total of 30.9% of the applied radioactivity). The two metabolites identified were:

- Hoe 136086⁹ at 8.5% of the applied radioactivity and
- Hoe 126663¹⁰, at 15.7% of the applied radioactivity.

After leaching, most of the applied radioactivity remained in the upper soil layers of the columns with approximately 75% of the applied radioactivity located in the 0 to 17 cm soil portion. Two metabolites, identified as Hoe 126663 and Hoe 136086, and ethoxysulfuron were identified in the column extracts from both soils.

The majority of the ethoxysulfuron was in the 0 to 7 cm layer but was measurable down in the 12 to 17 cm layer. Ethoxysulfuron was present from 37.2 to 45.2% of the applied radioactivity in the soil cores of the two columns. Levels of Hoe 126663 in all the soils were less than 4% of the applied radioactivity and, of Hoe 136086, less than 2% of the applied radioactivity.

Leachate contains only a small percent (<5%) of the applied radioactivity. No ethoxysulfuron was detected in the leachates. Three metabolites were isolated. Two were identified as Hoe 126663 and Hoe 136086 and the third (less than 2% of the applied radioactivity) was not identified.

Aged residues of ethoxysulfuron show only a slight tendency to leaching and that such leachate is not expected to contain parent ethoxysulfuron.

Field Dissipation Studies

Study 1: Two Korean clay loam soils (1.46 and 2.09% organic matter contents) were treated (field conditions) with one or two applications of ethoxysulfuron, as a formulated product, at 40 g ethoxysulfuron/ha and sampled over a period of 90 days from the date of the last application.

The half-lives for the field studies were:

- 28 and 32 days after a single application and
- 41 and 48 days after two applications.

⁹ Hoe 136086 = 3-amidino-1-(2-ethoxyphenoxy-sulfonyl)-urea

¹⁰ Hoe 126663 = 1-(2-ethoxyphenoxy-sulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea

Degradation curves were characterised by a rapid degradation in the first 7 to 15 days followed by a slower degradation over the remaining period of time, i.e. there was a deviation from simple exponential degradation after about 15 days.

Study 2: A granular formulation of ethoxysulfuron was added to two Japanese small rice flooded paddies, one based on a diluvial volcanic ash soil (a light clay, 6.19% organic matter) and the other, on an alluvial clay lowland soil (a clay loam, 3.6% organic matter) at a rate of 320 g ethoxysulfuron/ha.

There were two applications, 20 days apart with paddy soils sampled (0-10 cm depth) from 0 to 120 days after the last application.

Ethoxysulfuron residues were below the level of detection (0.002 ppm) in both soils by 60 days after the last application. DT₅₀s were, respectively, 14 and 21 days with the DT₉₀ being 46 and 69 days.

The ethoxysulfuron soil metabolite Hoe 126663¹¹ was not detected (less than 0.002 ppm). In the same field study, residues of a second ethoxysulfuron soil metabolite (Hoe 092944¹²) were analysed for, over the 120 day period the two soils were sampled. At all times, residues of this metabolite were <0.002 ppm. Consequently, Hoe 092944 is not expected to be a significant field metabolite.

With the same field conditions with the same volcanic ash light clay and the alluvial clay loams and sampling over a 259 day period, a third ethoxysulfuron soil metabolite, Hoe 136086¹³, was only identified after a long period of time. It was first measurable at approximately 90 days after the last application in both soils and then degraded to be non-measurable (<0.002 ppm) at 259 (light clay) or 254 (clay loam) days after the last application. This metabolite is not expected to be present in measurable quantities in treated soils as a result of yearly carryover.

Sugar Cane Run-off Studies

Study 1: In an Australian sugarcane runoff study, six sites with varying cane growth in the Burdekin irrigation district in Queensland were treated with Hero 600 WG formulation at the proposed rate of 150g ethoxysulfuron per hectare and the cane allowed to grow with two irrigation events. Irrigation was conducted to ensure runoff occurred (i.e. not good agricultural practice) so that levels of ethoxysulfuron in the runoff could be determined.

The first irrigation events occurred between 1 and 19 days after the Hero treatment and the second set at 13 to 35 days after the treatment. Based on an integrated analysis of the ethoxysulfuron concentrations in the runoff waters, between 0.0015 and 0.45% of the applied ethoxysulfuron moved off-site in a runoff event. The maximum runoff concentration was 25.6 µg ethoxysulfuron/L and the maximum time weighted average runoff concentration was 5.6 µg ethoxysulfuron/L.

Study 2: A second Australian study on the offsite movement of ethoxysulfuron via irrigation/rainfall runoff and deep drainage and its leaching through the soil profile was conducted at Ayr, North Queensland, in the Burdekin region. There were seven irrigation events over a period of 106 days after the application of Hero 600 WG formulation at 145 g ethoxysulfuron/ha. Soil, deep drainage and runoff waters (when they occurred) were analysed for ethoxysulfuron. This study was conducted to normal agronomic practices and represent the more typical irrigation practices for sugarcane.

The maximum soil concentration was 41.3 µg ethoxysulfuron/kg soil reported in the 0-10 cm soil layer three days after application and located in the top part of the treated field. The maximum mean soil concentration (0 to 10 cm soil layer) was measured at the same time and equalled 23 µg ethoxysulfuron/kg soil.

While the maximum concentrations were associated with the 0-10 cm soil depth, measurable ethoxysulfuron residues to a depth of 100 cm were measured during the study, the maximum concentration in the 30 to 100 cm soil profile being 0.8 µg/kg soil, at a depth of 50-75 cm soil and occurring after the fourth irrigation event and 29 days after treatment. However, after the last irrigation, residues in the 30 to 100 cm depth were all less than 2 µg/kg soil, the concentration in the untreated soil.

The maximum runoff concentration of ethoxysulfuron was in the first runoff event where, after runoff had been proceeding for 2 h 15 m, the ethoxysulfuron concentration was 0.5 µg/L. Unfortunately, samples between the start of the runoff event and this time were accidentally broken and there is uncertainty as to whether the 0.5 µg/L value was the maximum recorded.

¹¹ Hoe-126663 = 1-(2-ethoxyphenoxy-sulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea

¹² Hoe 092944 = 2-amino-4,6-dimethoxypyrimidine

¹³ Hoe 136086 = 3-amidino-1-(2-ethoxyphenoxy-sulfonyl)urea

The maximum AE F126663⁷ concentration was 0.64 µg/L, which was measured in the second runoff event at 15 and 30 minutes after the event started.

Deep drainage samples collected at a depth of 1.5 metres give some evidence of downward movement of ethoxysulfuron in the field for at least 77 days after treatment.

As noted by the study authors, this is consistent with the low levels of ethoxysulfuron found in the deeper soil layers. The maximum concentration determined was 0.92 µg ethoxysulfuron/L at 1.5 metres, 27 days after treatment. By 85 days after treatment, the concentration at this depth was <0.2 µg ethoxysulfuron/L.

Analytical methodology

Two Japanese soils were fortified with ethoxysulfuron and its metabolites Hoe-126663¹⁴ and Hoe-092944¹⁵ at 0.05 ppm for each chemical.

The HPLC/UV analytical method used to extract and determined the ethoxysulfuron and its metabolites gave satisfactory recoveries (>70%), and had a detection limit for the three chemicals of 0.002 ppm.

A second method validation study for ethoxysulfuron in which two soils, a volcanic ash and an alluvial soil, were spiked at 0.5 to 2.0 mg ethoxysulfuron/kg soil also produced satisfactory recoveries. Here the overall mean recovery, over the fortification levels used, was 78.7%.

Bioaccumulation

The bioaccumulation of ethoxysulfuron in common carp, *Cyprinus carpio*, and the bio-concentration factor after eight weeks was determined for two exposure concentrations, 1 and 10 µg ethoxysulfuron/L.

Visual examination indicated no obvious adverse effects in the lengths and weights of the exposed and control fish. The concentrations of ethoxysulfuron in the fish were less than 10 µg/kg in all cases.

Such results indicate that no bioaccumulation of ethoxysulfuron occurred in the exposed carp. Because the concentrations of ethoxysulfuron in the fish were all <10 µg/kg (i.e. reported as under the detection limit for both exposed and control fish), bio-concentration did not occur.

Environmental Fate Summary

Ethoxysulfuron is stable to hydrolysis at environmental pH values but undergoes indirect photolysis in the presence of photosensitisers. Ethoxysulfuron should readily degrade in the atmosphere.

In the laboratory, ethoxysulfuron readily degraded in aerobic soils with half-lives from 6 to 17.7 days in two clay loams, a light clay and a sandy loam soil. In anaerobic soil conditions (simulated paddy fields), soil half-lives in two sandy loams and a loam soil ranged from 10 to 62 days. In the overlying water, the half-lives were from 1.5 to 30.5 days.

In two river and lake water/sediment systems, ethoxysulfuron underwent extensive degradation with respective half-lives of:

- * 23 and 11 days in the water phases,
- * 42 and 38 days in the sediment and
- * 35 and 24 days in the whole systems.

The adsorption/desorption behaviour of ethoxysulfuron on five soils (a silt loam, a sand, two loamy sands and a sandy loam) indicated ethoxysulfuron was not strongly bound to soils and has medium to high soil mobility.

However, aged residues of ethoxysulfuron show only a slight tendency to leach with the leachate containing parent ethoxysulfuron.

Field dissipation studies with two clay loams gave half-lives for ethoxysulfuron of 28 and 32 days. In two flooded rice paddies, ethoxysulfuron half-lives were 14 and 21 days.

¹⁴ Hoe 126663 = 1-(2-ethoxyphenoxysulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea

¹⁵ Hoe 092944 = 2-amino-4,6-dimethoxypyrimidine

In an Australian sugarcane runoff study, up to 0.45% of the applied ethoxysulfuron moved off-site in runoff events with the maximum concentration in the runoff being 25.6 µg ethoxysulfuron/L. Another Australian study on the offsite movement of ethoxysulfuron from treated sugarcane fields showed that significant movement of ethoxysulfuron through the soil profile is not expected to occur.

Bio-concentration of ethoxysulfuron in fish did not occur.

Environmental Effects (Hazards)

Avian toxicity

Bobwhite quail: No mortalities occurred in the bobwhite quail orally given single doses of ethoxysulfuron equivalent to 2000 mg ethoxysulfuron/kg body weight. The median lethal LC50 was >2000 mg ethoxysulfuron/kg body weight and ethoxysulfuron is practically non-toxic to the bobwhite quail.

Japanese quail: After oral administration of ethoxysulfuron to Japanese quail at a single oral dose of 2000 mg ethoxysulfuron/kg body weight, one male and two females of the ten birds treated died within three days of dosing. While no clinical signs were observed in the male quail, all five female birds showed adverse effects. The symptoms disappeared by second day in the three female birds which survived.

These results imply that ethoxysulfuron is practically non-toxic to the Japanese quail.

When Japanese quail were given doses of either 500 or 2000 mg 60% formulation/kg body weight, there were no mortalities in any of the treated birds at either exposure levels. No clinical signs of intoxication were recorded in the birds exposed to 500 mg formulation/kg bw. At the higher dose, all birds showed clinical signs such as reduced spontaneous activity, increased respiration, squatting positions and uncoordinated gait between 30 minutes and 6 hours after dosing. For the remaining time (up to 15 days), no further clinical signs were seen.

Ethoxysulfuron, as a 60% Water Dispersible Granule is practically non-toxic to the Japanese quail. If expressed as ethoxysulfuron, the LD50 would be >1200 mg/kg body weight, indicative of slight toxicity.

Japanese quail chicks were fed ethoxysulfuron in their diets at 312.5 to 5000 mg ethoxysulfuron/kg feed (ppm) for five days followed by a three day period with untreated feed. No mortalities occurred in the ethoxysulfuron exposed birds up to and including the 2500 ppm birds. One chick in the 5000 ppm group died on day 2 of the study. No clinical signs of intoxication were seen in any of the exposed birds, even in the chick which died. Feed consumption and body weight gain appeared unaffected by exposure to the ethoxysulfuron in all test groups.

The results indicate ethoxysulfuron is practically non-toxic (LC50 >5000 mg/kg feed) to the Japanese quail. On the basis of the death of one chick at 5000 ppm, the NOEC (mortality) is set at 2500 ppm.

Mallard ducks: Mallard ducklings (ten ducklings per test group) were fed ethoxysulfuron in their diets for five days at concentrations of 312.5 to 5000 mg ethoxysulfuron/kg feed (ppm), followed by a five day period with untreated feed. No mortalities occurred in ducklings exposed to 312.5 and 1250 ppm. Mortalities were seen in the 625 (one duckling, during the treatment period), 2500 (one duckling during the treatment period and one during the follow-up period) and 5000 (one duckling during the treatment period) ppm exposed birds. However, a dose response was not considered present. No clinical signs of intoxication were seen in any of the exposed birds, even in the ducklings which died during the exposure and post-exposure phases. Feed consumption and body weight gain appeared unaffected by exposure to the ethoxysulfuron in all test groups.

The results indicate ethoxysulfuron is practically non-toxic (LC50 >5000 mg/kg feed) to the mallard duck. On the basis of the death at 625 ppm, the NOEC (mortality) is set at 312.5 ppm.

Japanese quail - reproduction: Effects on reproduction of ethoxysulfuron was examined by feeding adult male and female Japanese quail a daily diet containing 0 (control), 40, 200 and 1000 mg/kg feed (ppm) for a period of six weeks. Chicks which were born during the study were fed a diet without ethoxysulfuron. Apart from a cock and a hen from two of the 16 pairs exposed to the 200 ppm treatment, there were no other mortalities. Nor were there clinical signs attributable to the ethoxysulfuron exposure. Body weights and feed consumption was unaffected by the exposure to ethoxysulfuron at the 40 and 200 ppm levels. At the 1000 ppm level, body weights of the hens were significantly reduced and feed consumption at that level was also significantly reduced at some times. However, the overall means of the weekly feed intakes per feed level were not significantly different at any of the test levels including 1000 ppm.

In the six weeks exposure period, the ethoxysulfuron caused no reduction in egg production in the hens from any of the treatment groups and the numbers of normal eggs laid/hen were also comparable between the test groups and the controls. Mean egg shell thicknesses and mean egg weights were not affected in any of the treatment groups. Similarly, fertility, hatching rates, numbers of 14 day chicks which survived, chick body weights and chick feed consumptions showed no dose related responses with respect to any of the ethoxysulfuron exposures.

The data presented indicated that, compared to control values, there were no overt adverse effects on reproduction and the NOEC is set at 1000 mg ethoxysulfuron/kg feed.

Fish toxicity

Rainbow trout – effects of active under static conditions: Rainbow trout were exposed to nominal concentrations of 1.0 to 100 mg ethoxysulfuron/L for 96 hours under static conditions. No mortalities or symptoms of intoxication were seen in the nominal test concentrations of 1.0 to 32.0 mg/L over the 96 hours. At 100 mg ethoxysulfuron/L, one fish died at 72 hours and the remaining six fish showed signs of intoxication at 72 and 96 hours.

The 96 hour LC₅₀ is set at >80 mg/L (mean measured) and ethoxysulfuron is considered, at worst, slightly toxic to the rainbow trout.

Carp – effects of active under static conditions: Carp were also exposed to the same nominal concentrations of ethoxysulfuron under static conditions over a 96 hour period and no mortalities or symptoms of intoxication were seen in any of the fish exposed to the nominal test concentrations of 1.0 to 100.0 mg/L over the 96 hours.

The 96 hour LC₅₀ is set at >85.7 mg/L (mean measured). Ethoxysulfuron is considered, at worst, slightly toxic to the carp.

Rainbow trout– effects of product under static conditions: Rainbow trout were exposed to nominal concentrations of 4.6 to 100 mg formulation/L of a 60% water dispersible granule formulation for 96 hours under static conditions. No mortalities or symptoms of intoxication were seen in the nominal test concentrations of 4.6 to 46.0 mg/L over the 96 hours. At 100 mg/L, adverse reactions and death were observed from 48 hours with six of the seven fish dead after 96 hours.

As a result, the 96 hour LC₅₀ is set at 72.4 mg formulation/L (based on nominal concentrations) or 45.7 mg ethoxysulfuron/L. Ethoxysulfuron, as the formulated product, is considered slightly toxic to the rainbow trout under the tested conditions.

Rainbow trout– effects of product under flow through conditions: To determine the (chronic) effect of ethoxysulfuron on the growth of rainbow trout, the fish were exposed to nominal concentrations of 0.32 to 32 mg ethoxysulfuron/L in a flow through system for 28 days. Low recoveries of ethoxysulfuron were obtained at all concentrations (34 to 71% of nominal) except 0.32 and 1.0 mg/L (respectively, 94 and 97%). There was undissolved ethoxysulfuron present in the 10 mg/L from day 4 onwards and 32 mg/L nominal solutions for the entire period.

Mortality and symptoms were not seen in any of the ethoxysulfuron exposed fish over the 28 days and there were no adverse effects on their growth (lengths and weights).

The 28 day NOEC (for survival and effects on growth) was set at 22.8 mg/L (based on mean measured concentrations) and classifies ethoxysulfuron as very slightly toxic to fish with respect to chronic exposure.

Aquatic invertebrate toxicity

Daphnia – effects of active under static conditions: Daphnia neonates were exposed to nominal concentrations of 10 to 1000 mg ethoxysulfuron/L for a 48 hour period under static conditions.

There were no mortalities or signs of intoxication in daphnids exposed up to ≤320 mg/L test solutions. There was 5% mortality at 560 mg/L replicates and 85% mortality at 1000 mg/L after 48 hours. However, at concentrations above 100 mg/L, the ethoxysulfuron did not dissolve completely and that there was precipitate in the test vessels.

As a result, the 48 hour LC₅₀ is set at >100 mg ethoxysulfuron/L (nominal) and ethoxysulfuron is classified as practically non-toxic to daphnia.

In a second study, daphnia neonates were also exposed to nominal test concentrations of 10 to 1000 mg ethoxysulfuron/L and immobility determined at 24 and 48 hours. At concentrations of 100 to 1000 mg/L, the media was turbid because of the high concentration of suspended ethoxysulfuron, with ethoxysulfuron also observed at the surface of the test media.

At 24 hours, there was 5% immobility at 320 mg/L and 30% at 1000 mg/L and at 48 hours, 20% and 100% immobility at these concentrations. There was no immobility in the lower concentrations.

The 48 hour EC₅₀ was set at 307 mg/L (mean measured concentrations) and ethoxysulfuron is classified as practically non-toxic to daphnia.

Daphnia – effects of product under static conditions: Neonate daphnia were exposed to nominal concentrations of a 60% water dispersible granule formulation of 10 to 1000 mg/L for 48 hours. There was:

- 10% and 100% immobilisation at, respectively, 320 and 1000 mg/L after 24 hours and
- 15%, 25%, 100% and 100% immobilisation at, respectively, 32, 100, 320 and 1000 mg/L after 48 hours.

At 320 and 1000 mg/L, the solutions were turbid.

Based on nominal concentrations, the 48 hour EC₅₀ was set at >115 mg formulation/L (or expressed as ethoxysulfuron, >72.6 mg/L) on the basis of this concentration being the highest in which no undissolved ethoxysulfuron was taken as being present. The 60% ethoxysulfuron formulation is considered practically non-toxic to daphnia.

Daphnia – effects of ethoxysulfuron metabolites under static conditions: Daphnia neonates were exposed to nominal 18 to 100 mg/L concentrations of the ethoxysulfuron metabolite AE F126663¹⁶ under static conditions for 48 hours.

There were no mortalities at 24 hours but at 48 hours there were 20% mortality in the 56 mg/L concentration and 50% at 100 mg/L. Daphnids were observed swimming at the water surface at 24 hours in the 56 and 100 mg/L solutions and at 48 hours in the 18 to 100 mg/L solutions.

The 48 hour EC₅₀ is 96 mg/L and this metabolite is rated as slightly toxic to daphnia.

In another study, Daphnia neonates were exposed to nominal concentrations of 10 to 100 mg/L of a second ethoxysulfuron metabolite AE F136086¹⁷, under static conditions for 48 hours. No mortalities or symptoms of intoxication were observed.

As a result, the 48 hour EC₅₀ for the metabolite was set as >100 mg/L and this metabolite is rated as practically non-toxic to daphnia.

Mysid shrimp – effects of ethoxysulfuron under static conditions: Neonate mysid shrimp were exposed to concentrations of 12, 19, 32, 54, 90 and 150 mg ethoxysulfuron/L of seawater for 96 hours under static conditions.

Mean cumulative mortalities at 24, 48, 72 and 96 hours were, respectively, 15, 45, 70 and 75% with all surviving mysids being lethargic at 48 to 96 hours. All exposure solutions (nominal 12 to 150 mg ethoxysulfuron/L) were reported as clear and colourless.

The reported 24, 48, 72 and 96 hour LC₅₀ values were, respectively, >140, >140 (161 mg/L as determined by DEWHA), and 120 and 110 mg ethoxysulfuron/L. It is concluded that ethoxysulfuron is practically non-toxic to the mysid.

Daphnia – effects of ethoxysulfuron on reproduction under semi-static conditions: Exposure of daphnia to ethoxysulfuron over a 21 day period in a semi-static system, with exposure to nominal concentrations of 1.0 to 100 mg ethoxysulfuron/L, resulted in 10 to 20% mortality.

Such values show the survival rate was not significantly reduced up to the nominal test concentration of 100 mg/L. However, there were statistically significant reductions on daphnid reproduction at all concentrations above 1.0 mg/L.

As a result, the 21 day NOEC (reproduction) was 1.0 mg/L and ethoxysulfuron is classed as slightly toxic to daphnid reproduction.

¹⁶ AE F126663 = 1-(2-ethoxyphenoxysulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea [= Hoe 126663]

¹⁷ AE F136086 = 3-amidino-1-(2-ethoxyphenoxysulfonyl)-urea [= Hoe 136086]

Benthic toxicity

In the absence of benthic ecotoxicity data, it is not possible to state what the effects of such sediment concentrations would be.

There is significant partitioning to sediment, with ethoxysulfuron half-lives in the sediment reported as 42 days in the river sediment and 38 days in the lake sediment. Hence there is a potential for benthic dwelling organisms being exposed to ethoxysulfuron, following runoff or spraydrift events.

However, a chronic toxicity study on the sediment dweller, *Chironomus riparius*, is reported to have set a NOEC of 3.2 mg ethoxysulfuron/L. This value is indicative of only very slight chronic toxicity.

Algal, diatom and plankton toxicity

Green alga, Scenedesmus subspicatus -- effect of active: The green alga, *Scenedesmus subspicatus*, was exposed to nominal test concentrations of 0.046 to 1.0 mg ethoxysulfuron/L for 72 hours.

This resulted in significant biomass and growth rate inhibitions after 72 hours at all concentrations except the nominal 0.046 mg/L (0.03 mg/L mean measured).

Based on mean measured concentrations, the 0-72 hour biomass EC₅₀ (EbC) was determined as 0.19 mg/L and the 0-72 hour growth rate EC₅₀ (ErC) was determined as 0.72 mg/L. Hence ethoxysulfuron is highly toxic to this algal species.

Green alga, Ankistrodesmus falcatus var. aciculari - effect of active: The green alga, *Ankistrodesmus falcatus* var. *acicularis*, was exposed to nominal concentrations of 0.13 to 1.0 mg ethoxysulfuron/L for a period of 96 hours.

Significant inhibition occurred at all concentrations greater than 0.13 mg/L with respect to growth and growth rate.

The 0-72 and 0-96 hour EbC₅₀ values were, respectively, 0.31 and 0.27 mg/L (based on mean measured concentrations). It is concluded that ethoxysulfuron is highly toxic to this alga.

Saltwater diatom, Skeletonema costatum - - effect of active: Ethoxysulfuron was slightly toxic to the saltwater diatom, *Skeletonema costatum*, after a 72 hour exposure to test concentrations of 6.25 to 100 mg/L with mean measured concentrations of 58.4 and 115 mg/L.

The study showed statistically significant decreases in cell density, biomass and growth rate over this period.

The respective values for the ErC₅₀, EbC₅₀ and EC₅₀ (cell density) were, 86.7, 42.6 and 45.0 mg/L (all based on mean measured concentrations).

Green alga, Scenedesmus subspicatus – effect of product: When the green alga, *Scenedesmus subspicatus*, was exposed to nominal concentrations of 0.02 to 2.0 mg of 60% water dispersible ethoxysulfuron formulation/L for 72 hours, statistically significant reductions in biomass and growth rate were obtained at all concentrations greater than 0.02 mg formulation/L. The 0-72 hour EbC₅₀ was 0.33 g formulation/L (95% confidence limits 0.26 to 0.41 mg/L) and the study determined 0-72 hours ErC₅₀ was 1.22 mg formulation/L.

On the basis of the growth rate value, the 60% ethoxysulfuron formulation is moderately toxic to the tested alga.

Planktonic alga, Pseudokirchneriella subcapitata - effect of ethoxysulfuron metabolites: The unicellular, planktonic alga, *Pseudokirchneriella subcapitata*, was exposed to the ethoxysulfuron metabolite AE F126663¹⁸ (which still contains the sulfonylurea moiety), at concentrations of 1 to 32 mg of metabolite/L for a period of 96 hours.

Algal biomass and growth rates were all significantly reduced at concentrations of greater than 1.0 mg metabolite/L.

The 96 hour ErC₅₀ of 15.6 mg/L identifies the metabolite AE F126663 as slightly toxic to *Pseudokirchneriella subcapitata*.

¹⁸ AE F126663 = 1-(2-ethoxyphenoxy-sulfonyl)-3-(6-hydroxy-4-methoxypyrimidin-2-yl)-urea [= Hoe 126663]

Pseudokirchneriella subcapitata was exposed to the ethoxysulfuron metabolite AE F136086¹⁹, at nominal concentrations of 1.0 to 32 mg metabolite/L for 96 hours.

This resulted in significant reductions in algal reproduction and growth rate at all exposure concentrations. The 96 hour EbC₅₀ was < 1 mg of AE F136086/L, and the 96 hour ErC₅₀ was > 32 mg of AE F136086/L.

At worst, the 96 hour ErC₅₀ identifies the metabolite AE F136086 as slightly toxic to *Pseudokirchneriella subcapitata*.

Duckweed toxicity

Ethoxysulfuron: Duckweed was exposed to ethoxysulfuron in a static test system for 14 days, at nominal concentrations of 0.13 to 1.0 µg/L.

There were statistically significant reductions in frond numbers at all concentrations greater than 0.191 µg/L and the 14 day EC₅₀ for reduction in frond number was 0.24 µg ethoxysulfuron/L. It was concluded that ethoxysulfuron is very highly toxic to duckweed.

In an exposure and recovery test with ethoxysulfuron, duckweed were exposed to nominal concentrations of 0.244 to 1.00 µg ethoxysulfuron/L for 7 days, and then placed in growth medium without any ethoxysulfuron for 21 days. The 168 hour (7 day) EC₅₀ for total frond numbers as 0.32 µg ethoxysulfuron/L, with mean frond numbers from all ethoxysulfuron concentrations identified as statistically significantly less than the control mean.

In the recovery phase, growth rates from frond numbers and total frond areas indicated the duckweed had recovered for all test levels within the seven days of recovery period. By the fourteenth day of the recovery period, there were no visual effects remaining in the duckweed exposed to ethoxysulfuron at all concentrations except the 1.00 mg/L where the fronds were identified as “small”. By the twenty-first day, these effects were no longer visible.

Duckweed has the ability to recover from prolonged ethoxysulfuron exposure up to 1 µg/L.

Ethoxysulfuron metabolites: Duckweed was exposed to the ethoxysulfuron metabolite AE F126663¹⁸ at nominal concentrations of 0.1 to 3.2 mg/L for seven days, with renewal of the test concentrations at days 3 and 5. There were significant inhibition of frond numbers and biomass at concentrations of 0.56 mg/L and above, with intoxication symptoms (colonies not fully separating and/or colonies with vaulted surfaces) seen at days 3, 5 and 7 at concentrations of and above 0.56 mg/L.

The ErC₅₀ (frond number) and EbC₅₀ (biomass) after 7 days were both 1.0 mg of AE F126663/L and the 7 day NOEC (growth rate/frond number) was 0.32 mg of AE F126663/L.

Based on the ErC₅₀, the metabolite is highly toxic to duckweed.

Duckweed was exposed to the ethoxysulfuron metabolite AE F092944²⁰ at nominal concentrations of 10 to 100 mg/L for 7 days, with renewal of the test solutions at days 3 and 5. This resulted in no intoxication symptoms and no significant inhibition of either growth rate or biomass.

The ErC₅₀ (frond number) and EbC₅₀ (biomass) after 7 days were both >100 mg AE F092944/L.

It is concluded that the metabolite is practically non-toxic to duckweed.

Non-target beneficial terrestrial invertebrates

Honeybees: Honey/water solutions of ethoxysulfuron were prepared over the range of 0.01 to 10.0% ethoxysulfuron, and fed to honeybees for a period of five hours and then untreated sucrose/water thereafter.

There was between 2 and 8% mortality after 48 hours.

The 48 hour LC₅₀ for oral toxicity was calculated as > 254 µg ethoxysulfuron/L i.e. ethoxysulfuron is very slightly toxic to the honeybee via the oral route.

¹⁹ AE F136086 = 3-amidino-1-(2-ethoxyphenoxy-sulfonyl)-urea [= Hoe 136086]

²⁰ AE F092944 = 2-amino-4,6-dimethoxypyrimidine [= Hoe 092944]

Application of ethoxysulfuron to the ventral thoraxes of honeybees at doses of 0.1 to 200 µg ethoxysulfuron/bee, resulted in 2 to 10% mortality of the treated honeybees after 48 hours.

Consequently, the acute contact LD₅₀ for bees exposed to ethoxysulfuron was > 200 µg/honeybee and ethoxysulfuron is very slightly toxic to the honeybee via the dermal contact route.

Earthworms: Earthworms exposed to an artificial soil containing 100 to 1000 mg ethoxysulfuron/kg soil (dry weight basis) for 14 days exhibited cramping at 560 and 1000 mg/kg.

There were, however, no mortalities in this period and no significant effects on the weights of the exposed earthworms at any concentration.

The 14 day LC₅₀ was >1000 mg ethoxysulfuron/kg soil (dry weight) and ethoxysulfuron is very slightly toxic to earthworms.

When earthworms were exposed to an artificial soil containing a 63.1% water miscible ethoxysulfuron formulation at concentrations of 0.1 to 1000 mg formulation/kg soil (dry weight) for 14 days, mortalities ranged from 0% to 5% and no dose response was evident.

There were no significant adverse effects on the bodyweights of the exposed worms over the 14 days.

The 14 day LC₅₀ was set at >1000 mg 63.1% ethoxysulfuron formulation/kg soil (dry weight) and the formulated material is very slightly toxic to earthworms. The data provided do not trigger the need for chronic toxicity results.

Predacious mites (*Typhlodromus pyri*): Freshly hatched predacious mites (*Typhlodromus pyri*) were exposed to leaf discs treated with a water dispersible granular formulation (600 g ethoxysulfuron/kg, close to that proposed for Australian use), at a rate of 100 g formulation/ha (= 60 g ethoxysulfuron/ha) for 18 days.

The juvenile mortality after 8 days was 41.8%. The number of eggs/female was determined for the remainder of the exposure period and, in conjunction with the corrected mortality used to calculate an overall reduction in beneficial effectivity of 54.3%.

Ethoxysulfuron, as a 60% water dispersible granule formulation is slightly harmful to the predatory mite at the doses tested in the laboratory.

In a second study, protonymphs of *Typhlodromus pyri* were exposed to glass plates sprayed with a 60% water dispersible granular formulation with the equivalents of 24 to 150 g ethoxysulfuron/ha for 14 days. Numbers of living mites, number of males and females, eggs and juveniles determined.

There were no significant differences between the mortalities of the exposed mites with respect to concentration or time (mean mortalities were all ≤ 27%) and no dose effect was apparent. Similarly, there was no significant reduction of reproduction at any of the test concentrations compared to the control rate.

The 14 day LD₅₀ was set at > 150 g ethoxysulfuron/ha and significant adverse effects on predatory mites are not expected. As the same formulation is proposed, this result will be used in the risk assessment.

Pardosa spiders: Field collected *Pardosa* spiders were placed in sand trays and sprayed with a 60% solid ethoxysulfuron formulation, equivalent to that for Australian use, at a rate equivalent to 60 g ethoxysulfuron/ha.

The spiders showed no behavioural effects, changes in feed consumption or mortalities over a 14 day period.

Ground beetles, *Poecilus cupreus*: Adult ground beetles, *Poecilus cupreus*, were exposed to the same 60% water dispersible granule as the spiders (above), at a rate equivalent to 60 g ethoxysulfuron/ha. There were no mortalities or adverse effects seen in any of the exposed beetles over a 26 day period.

Parasitoid wasp, *Aphidius rhopalosiphi*: The parasitoid wasp, *Aphidius rhopalosiphi*, was exposed to glass plates that had been sprayed with a 60% water dispersible granular ethoxysulfuron formulation (close to the one proposed for Australia), at a rate equivalent to 60 g ethoxysulfuron/ha.

This resulted in 40% mortality after 24 hours and 83.3% after 48 hours. The ability of surviving female wasps to parasitise aphids was then determined with the mean number of parasitised aphids/female being 7.53 compared to a control value of 10.

The reduction in beneficial effectiveness was determined as 79.8% and the laboratory exposure was moderately harmful to the wasps.

In a second study with *Aphidius rhopalosiphi*, the wasps were exposed to glass plates treated with ethoxysulfuron, as a 61% wt/wt water dispersible granule formulation (as proposed), at rates equivalent to 24 to 150 g/ha. Mortality after 48 hours was determined as not more than 15%.

The 48 hour LD₅₀ was > 150 g ethoxysulfuron/ha.

Surviving females were allowed to parasitise aphids for 24 hours and the number of mummies determined after 12 days. The maximum reduction in reproduction relative to the untreated controls was 33.5% at the 150 g ethoxysulfuron/ha concentration. In this study, rates of up to 150 g ethoxysulfuron/ha were not found to be statistically significantly detrimental to the parasitoid wasp.

When both corrected mortality and reproduction in the exposed and unexposed wasps are considered, an ethoxysulfuron exposure of 150 g/ha is rated as being slightly harmful to beneficial effectivity. Again, as this latter study used the proposed formulation, this result will be used in the risk assessment.

Microbial soil processes

When a loamy sand and a silty loam from Germany were supplemented with nitrogen (lucerne) and treated with ethoxysulfuron at 0.09 to 36.0 kg/ha (equivalent to 0.6 to 240 times the proposed Australian rate), effects of the ethoxysulfuron on microbial soil nitrification processes were measured at 28 days.

All concentrations in the loamy sand were still within 15% of the control values. In the silty loam at this time, the effect was negligible at the 0.09 kg/ha level (an increase of not more than 15% had occurred). While significant increases had occurred at all higher levels, the 1.8 kg/ha treatment level (12 times the proposed Australian rate), results had returned to within 15% of the control at 90 days.

While the results indicated sometimes excessive changes in particularly ammonium nitrogen levels, with respect to the control, the treatment rates were greatly in excess of that proposed for Australia in all cases but one.

In a further study, a German loamy sand was treated with 0.09 to 36.0 kg ethoxysulfuron/ha and, after supplementation with glucose, respiration rates were determined over 91 days.

Over 28 days, effects on microorganisms in aerobic soil (carbon transformations) processes at 90 g/ha and 1.8 kg/ha (0.6 and 12 times the proposed Australian rate) were within 25% of control respiration values. Therefore ethoxysulfuron is not indicated as likely to have an a substantial or lasting adverse effect on soil nitrification processes.

An activated sludge test with ethoxysulfuron at concentrations of 250 to 1000 mg/L showed a maximum 31% inhibition of respiration at the 1000 mg/L level.

The EC₅₀ for ethoxysulfuron was set at >1000 mg/L, indicative of ethoxysulfuron not being expected to inhibit respiration in activated sewage sludge.

Non-target terrestrial plants

In a non-standard study, seeds of eight different crop species were incorporated into soil treated with a 20% ethoxysulfuron wettable powder formulation at rates of 0.078 to 83 g ethoxysulfuron/ha and visual herbicidal efficacy assessed after 38 days.

Effects on graminaceous crops such as wheat and maize were considered minimal (in maize at low treatment doses) with much higher activity against dicotyledonous crops (sunflowers, rapeseed, cucumber and alfalfa). Within the dicots, soybean and tomatoes being least affected.

In a second non-standard study, paddy water (prepared in the laboratory) was treated with a 20% ethoxysulfuron wettable powder formulation at rates equivalent to 15 and 30 g ethoxysulfuron/ha and the paddy water used to irrigate five pre-cultivated dicotyledonous vegetable crops. Assessment of plant damage after 28 days showed that tomatoes, beans and peas tolerated even a triple irrigation reasonably well. Radish and spinach, however, showed >50% damage after even a single irrigation.

A standard seedling emergence and seedling growth test was conducted with mono and dicotyledonous plants, using a 60% ethoxysulfuron water dispersible granular formulation at rates of between 0.5 and 250 g formulation/ha.

This study showed that ER₅₀ values for seedling emergence and survival in the dicotyledonous plants were all >15.6 mg formulation/ha. In contrast, for biomass after 14 days, the ER₅₀ values ranged from 0.5 g product/ha for oilseed rape to 28.9 g product/ha for soybean (0.3 to 17.3 g ethoxysulfuron/ha).

Monocotyledonous plants had ER₅₀s for emergence, survival and biomass reduction of >250 g product/ha in all cases except for corn, where the ER₅₀ for biomass reduction was 97.7 g product/ha. All the species showed phyto-toxicity symptoms with the severity dependent on the sensitivity of the species and the treatment rate.

Vegetative vigour of mono and dicotyledonous plants was examined in a standard test, in which the plants were treated with between 1 to 250 g of a 60% ethoxysulfuron water dispersible granular formulation/ha and vegetative vigour assessed over a 21 day period.

All the species showed phytotoxicity symptoms with the severity dependent on the sensitivity of the species and the treatment rate.

For the dicotyledonae, the most sensitive EC₅₀ for survival was 12.9 g product/ha (equivalent to 7.6 g ethoxysulfuron/ha) for oilseed rape.

For biomass reduction, the most sensitive EC₅₀ was 7.1 g product or 4.2 g ethoxysulfuron/ha for soybean.

The monocotyledonae corn and oats had survival and biomass reduction EC₅₀ of >250 g product/ha while the onion had a survival and biomass reduction EC₅₀ of, respectively, 60.8 and 13.4 g product/ha.

Environmental Effects Summary

Avian species: Ethoxysulfuron is practically non-toxic to birds following acute oral exposure. Ethoxysulfuron in a 60% water dispersible granule formulation is slightly toxic to birds after acute oral exposure.

Ethoxysulfuron is indicated as practically non-toxic to birds via short-term dietary exposure. Ethoxysulfuron exhibited no overt adverse on avian reproduction.

Vertebrate and invertebrate aquatic species: Ethoxysulfuron is, at worst, slightly acutely toxic to representative **fish** species. As a 60% water dispersible granule formulation, it is slightly acutely toxic to fish and very slightly toxic to fish, with respect to chronic exposure.

On an acute basis, ethoxysulfuron is practically non-toxic to freshwater and marine **invertebrates** such as daphnia and the mysid shrimp. Also on an acute basis, as a 60% water dispersible granule formulation, it is practically non-toxic to daphnia.

Acute exposure of daphnia to two metabolites of ethoxysulfuron retaining the sulfonyl urea function, was slightly to practically non-toxic to daphnia, depending on the metabolite concerned.

Chronic exposure of daphnia to ethoxysulfuron did not affect parental survival rates but was slightly toxic to daphnid reproduction.

Sediment dwellers: A chronic toxicity study on the sediment dweller, *Chironomus riparius*, is reported to indicate only very slight chronic toxicity.

Freshwater algae: Ethoxysulfuron is highly toxic to representative freshwater algae, but only slightly toxic to the marine diatom, *Skeletonema costatum*. A 60% water dispersible ethoxysulfuron formulation was moderately toxic to a freshwater green alga.

Two metabolites retaining the sulfonylurea function were, at worst, slightly toxic to a freshwater alga.

Duckweed: Ethoxysulfuron is very highly toxic to duckweed but recovery on cessation of exposure is expected. An ethoxysulfuron metabolite retaining the sulfonylurea function was highly toxic to duckweed whereas an ethoxysulfuron metabolite lacking the sulfonylurea function was practically non-toxic.

Honeybees: Ethoxysulfuron exhibited very slight toxicity to honeybees via the contact and oral exposure routes.

Worms: Ethoxysulfuron, as the active constituent or a 63.1% water miscible formulation, is very slightly toxic to earthworms.

Predatory mites and spiders: Ethoxysulfuron, as a 60% water dispersible granule formulation is slightly harmful to the predatory mite. However, exposure to the proposed formulation caused no significant mortality or reduction in reproduction.

Exposure of spiders to a 60% solid ethoxysulfuron formulation, showed no behavioural effects, changes in feed consumption or mortalities at concentrations up to 60 g ethoxysulfuron/ha.

Ground beetles: Adult ground beetles, *Poecilus cupreus*, were unaffected by exposure to a 60% water dispersible granule at 60 g ethoxysulfuron/ha.

Parasitoid wasp: Exposure of the parasitoid wasp, *Aphidius rhopalosiphi*, to 60% water dispersible granular ethoxysulfuron formulation was moderately harmful to the wasps, however, when the wasp was exposed to the proposed formulation at the Australian use rate, there was only a slightly harmful effect on beneficial effectivity.

Soil micro-organisms: The proposed Australian use pattern is not expected to result in any substantial or lasting effects on soil microorganism activity.

Non-target terrestrial plants: Phytotoxic effects on seedling emergence, plant survival, biomass reduction on non-target terrestrial plants would be expected from the proposed Australian use pattern.

Environmental Risk Assessment

Preliminary Comments

The following risk assessments are essentially based on:

- the environmental fate and ecotoxicity data initially provided in support of the Bayer CropScience application for registration of Hero Selective Herbicide and
- on data subsequently supplied in response to issues identified by DEWHA, in its assessments of permit applications for use of ethoxysulfuron on sugarcane.

The risk assessment has also taken account of recent changes promulgated by the APVMA with respect to spraydrift determination (APVMA, 2008).

The proposed maximum application rate of ethoxysulfuron is 250 g Hero Selective Herbicide/ha or 150 g ethoxysulfuron/ha for sugarcane per season, with only one application of Hero to a crop per season. Application by aircraft is prohibited by the draft label. Metabolites toxicity is considered where appropriate data have been presented.

Conclusion with Respect to Environmental Risk

Risk to birds and mammals from dietary exposure to ethoxysulfuron, resulting from the proposed use pattern, is acceptable. Similarly for the risk to avian reproduction.

Risk to fish, aquatic invertebrates and algae is also acceptable from the proposed use pattern.

Risk to aquatic plants from spray drift is expected to be acceptable when directed sprayers are used and no downwind no-spray zone need to be specified in that case.

With irrigation only to the point of runoff or with runoff waters kept on site, risk to aquatic plants is expected to be acceptable following use of Hero Selective Herbicide on sugarcane at the proposed use rates. Runoff following rainfall events is expected to produce, at worst, transient effects on aquatic plants as a result of the larger water volumes leaving the treated fields in such circumstances.

Honeybees and earthworms are not expected to be at risk as a result of the proposed use pattern on sugarcane.

While significant adverse effects on predatory mites are not expected as a result of the proposed use pattern, some adverse effects on wasp parasitoids, and perhaps spiders and ground beetles, might result following the proposed use of Hero Selective Herbicide.

The proposed use pattern is not expected to significantly affect micro-organisms associated with soil nitrification and respiration processes.

Spraydrift from the proposed use pattern would result in adverse effects on seedling emergence, survival and biomass and also on vegetative vigour in non-target terrestrial plants. Such risk is expected to be acceptable when directed sprayers are used, as off-target spray drift is expected to be effectively eliminated. Hence downwind no-spray zones do not need to be established.

Controls/Labelling

The proposed label contains standard APVMA storage and disposal statements.

To aid in the prevention of runoff into waterbodies, DEWHA recommends that the following be added to the draft label's Directions for Use:

After application of Hero Selective Herbicide, **DO NOT** irrigate crop to the point of run-off, unless it can be retained on the farm.

Summary of Conclusions

Ethoxysulfuron will be applied using ground equipment only to sugarcane. Environmental exposure is expected to primarily involve the crop and the underlying soil, with aquatic exposure also possible through spray drift and runoff.

Ethoxysulfuron is stable to hydrolysis at environmental pH values, but undergoes indirect photolysis in the presence of photosensitisers.

In two river and lake water/sediment systems, ethoxysulfuron underwent extensive degradation with respective half-lives of 23 and 11 days in the water phases, 42 and 38 days in the sediment and 35 and 24 days in the whole systems.

Ethoxysulfuron does not strongly bind to soils and has medium to high soil mobility, although aged residues of ethoxysulfuron show only a slight tendency to leach. Field dissipation studies with two clay loams gave half-lives for ethoxysulfuron of 28 and 32 days.

An Australian sugarcane runoff study showed that up to 0.45% of the applied ethoxysulfuron moved off-site in runoff events. Another Australian study on the offsite movement of ethoxysulfuron from treated sugarcane fields, showed significant movement of ethoxysulfuron through the soil profile is not expected to occur.

Ethoxysulfuron is not expected to bioaccumulate.

Ethoxysulfuron is practically non-toxic to birds, mammals, fish and aquatic invertebrates toxicity.

Ethoxysulfuron is highly toxic to representative freshwater algae but only slightly toxic to the marine diatom, *Skeletonema costatum*. A 60% water dispersible ethoxysulfuron formulation was moderately toxic to a freshwater green alga. Two metabolites retaining the sulfonyleurea function were, at worst, slightly toxic to a freshwater alga.

Ethoxysulfuron is very highly toxic to duckweed but recovery on cessation of exposure is expected. An ethoxysulfuron metabolite retaining the sulfonyleurea function was highly toxic to duckweed.

Ethoxysulfuron exhibited very slight toxicity to honeybees via the contact and oral exposure routes and is very slightly toxic to earthworms. No significant mortality or reduction in reproduction of predatory mites is expected and exposure of spiders and ground beetles showed no behavioural effects, changes in feed consumption or mortalities at concentrations up to 60 g ethoxysulfuron/ha. Exposure of the parasitoid wasp, *Aphidius rhopalosiphi*, to the proposed formulation at the Australian use rate showed there was only a slightly harmful effect on beneficial effectivity.

The proposed Australian use pattern is not expected to result in any substantial or lasting effects on soil microorganism activity.

Phytotoxic effects on seedling emergence, plant survival and biomass reduction on non-target terrestrial plants would be expected from the proposed Australian use pattern.

Summary of Recommendations

Based on DEWHA's risk assessment, risk to non-target terrestrial plants following application by a fine/medium spray, as recommended by the draft label, results in an un-acceptable risk.

Consequently, DEWHA can not recommend to the APVMA that the proposed use of *Hero® Selective Herbicide*, using a fine/medium spray application would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

Similarly, irrigation waters containing ethoxysulfuron moving would be expected to result, on occasion, in risk to aquatic plants.

However, risk in both cases is expected to be acceptable if the draft label is amended to:

- restrict application to directed spraying and
- include a statement that the sugarcane is not to be irrigated to the point of run-off unless it can be retained on the farm.

Consequently, DEWHA recommended to the APVMA that, if:

- ❖ the present draft label's "Application and Equipment" statement of,
"For broadcast application apply with a standard ground-driven boom sprayer fitted with by-pass or mechanical agitation. Where crop stage warrants directed spraying, use an Irvin leg or octopus head attachment."

is deleted and replaced by the following,

"Apply only by directed spraying." and

- ❖ the following restraint is added to the draft label's "Directions for Use",

"After application of Hero Selective Herbicide, DO NOT irrigate crop to the point of run-off, unless it can be retained on the farm."

then the proposed use of *Hero® Selective Herbicide* would not be likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

[This page intentionally left blank]

Efficacy and Safety Assessment

This efficacy and crop safety assessment, and the associated recommendations, are based on the submission overview, efficacy and crop safety studies that were included in the submission and professional expert opinion²¹.

Note that the assessment is also based on the use pattern proposed in the application (in 2002). That use pattern is shown below.

Proposed Original Use Pattern of Hero (2002)

DIRECTIONS FOR USE

RESTRAINTS

DO NOT use if rainfall or irrigation is expected to occur within 2 hours of application.

DO NOT apply to weeds under severe moisture stress.

CROP	WEED	STATE	WEED STAGE	RATE g/ha	CRITICAL COMMENTS
Sugarcane	Nutgrass (<i>Cyperus rotundus</i>)	Qld, NSW, WA, NT only	4 – 6 leaf	250	Hero may be applied as a broadcast or directed application, depending on sugarcane growth stage.
	Bellvine (<i>Ipomoea plebeia</i>)		2 – 6 leaf		Addition of a non-ionic wetting agent is recommended. Apply the equivalent of 100 mL/100 L of a 1000 g/L formulation of non-ionic wetting agent.
	Red convolvulus (<i>Ipomoea hederifolia</i>)		cotyledon – 6 leaf		Thorough coverage of the weeds is essential for good weed control. Apply in a minimum of 250 L/ha of water.
	Star of Bethlehem (<i>Ipomoea quamoclit</i>)		2 leaf - 30 cm runners		DO NOT apply more than one application of Hero or other group B herbicide to a crop in one season.

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

WITHHOLDING PERIODS

Harvest: DO NOT HARVEST FOR 19 WEEKS AFTER APPLICATION

Grazing: DO NOT GRAZE OR CUT FOR STOCKFOOD FOR 19 WEEKS AFTER APPLICATION

Justification for Use

The introduction of green cane trash blanketing (GCTB) in the early 1970's and more recently minimum tillage and zero tillage in the sugar industry has resulted in a considerable shift in the methods used for effective weed control. Weed populations are generally lower in a minimal tillage situation, however application timing and the use of additional weed control methods are now critical to manage or prevent the initial growth of weeds in the crop (McMahon, Lawrence & O'Grady, 2000²²).

Problem weeds such as Nutgrass cause several difficulties for the sugar industry, because of their difficulty in management and very few registered herbicides are available for effective control in crop. The use of cultivation for weed management where cane trash exists is difficult, because the machinery is not able to function normally.

²¹ For example: O'Grady T and Sluggett R, (2000) BSES Herbicide Manual 2000, Bureau of Sugar Experiment Stations, Queensland.

²² McMahon G, Lawrence P and O'Grady T, (2000) 'Weed Control In Sugarcane - Manual of Cane Growing', in Hogarth M & Allsopp P, Bureau of Sugar Experiment Stations, Brisbane.

Under the current submission, approval is sought for the use of *Hero® Selective Herbicide* (active constituent: 600 g/L ethoxysulfuron) as a post-emergent herbicide for the control of nutgrass and certain broad leaf weeds in sugarcane (*Hero®* Draft Label, 2002). *Hero®* is a member of the sulfonylurea group of herbicides (in Group B). The herbicide can be applied using a broadcast or directed spray depending on the sugarcane growth stage.

Evaluation of Efficacy and Crop Safety

Adequacy of Efficacy Data

Review of the efficacy and crop safety reports included with the submission indicates that a total of thirteen trials were conducted in sugarcane growing regions of Queensland and New South Wales during 2000 to 2002. Aventis CropScience conducted the majority of the field trials (twelve trial sites), with one field trial conducted by an independent researcher.

Trial sites were established using suitable trial designs for thorough assessment, with replications, control treatments, varying product doses, appropriate standards and trial site details included in all experiments.

Standard plot sizes were used in the trials, varying from 10m x 3m (2 rows) to 10m x 4.5 (3 rows). Commercial size trials are not included in this submission. Although not necessary, commercial size trials may be beneficial for company interests by ensuring that all areas at application are fully investigated to ensure the desired results under normal user conditions.

The main weed species investigated in the trials were nutgrass (*Cyperus rotundus*), Bell vine (*Ipomoea pledeia*), Star of Bethlehem (*Ipomea quamoclit*) and Red convulvulus (*Ipomoea hederifolia*).

A considerable amount of nutgrass efficacy data is presented in the submission with predominantly high (19 - 475 plants/m²) weed pressures across all trial sites. A limited amount of efficacy data is presented on Bellvine, Star of Bethlehem and Red convulvulus. Weed populations of Bellvine were low/moderate ranging from 4 - 14 plants/m² across the two trial sites. Star of Bethlehem weed pressure was low, with weed pressures ranging from 0.1 - 2 plants/m² across the two trial sites.

The majority of the treatments were applied during the early growth stages of cane when the plant is generally most susceptible to herbicide damage and yield effects from weed competition. Trials conducted in plant cane by BSES have shown that weeds left uncontrolled for 4 weeks after spiking stage can result in yield losses up to 11 per cent. Delayed weed control until 8 and 12 weeks after spiking stage resulted in yield losses of 23% and 34% respectively (McMahon, Lawrence and O'Grady, 2000²¹).

Twelve trials were applied as a broadcast spray using standard application equipment in cane ranging from spiking to 6-leaf stage. One trial was applied using a directed spray with octopus heads at the out-of-hand stage. The application techniques and timing are typical of those currently used under commercial conditions and accurately reflect the time period when these weed species are generally a problem in sugarcane.

The *Hero®* trials were conducted on soil types that typically display high populations of nutgrass, thereby enabling accurate efficacy assessment. Soil types ranged from light sands, sandy loams to sandy clay loam. Details on the environmental conditions were also recorded during and post-application of the treatments. Trials were conducted during various environmental conditions, ranging from very dry to good soil moisture and rainfall following treatment application.

Efficacy and crop safety data collected at each trial site was analysed using the analysis of variance test ($p < 0.05$) to determine if statistical differences occurred between treatments.

Claims

Efficacy data was collected using two methods, the first being a visual assessment of percentage biomass reduction and the second being a plant count per m² at each plot.

The product is specified as a post-emergent herbicide, therefore pre-emergent use is not considered in the evaluation of the product. The symptoms of sulfonylurea (Group B) herbicides are gradual and the plant may not show significant visual discoloration until five weeks after treatment application (Bayer CropScience Pty Ltd, 2002). Because of the characteristics of sulfonylurea herbicides, these assessment methods are considered to be most accurate for recording efficacy data.

The 'claims of use' statement outlines that *Hero®* is a post-emergent herbicide used for the control of nutgrass and certain broad leaf weeds in sugarcane as specified in the 'direction for use' statement (*Hero®* Draft Label, 2002). The weeds specified for control in the 'Directions for Use' section of the draft label are Nutgrass, Bellvine, Red convulvulus and Star of Bethlehem.

Trial results in the Bayer CropScience submission details that Hero® has effective post-emergent control on **nutgrass** weeds between 4 - 6 leaf stage. From the thirteen trials conducted across Queensland, a considerable amount of data is presented on the efficacy effect on nutgrass. Nutgrass control using Hero® is relatively consistent across all trials and equal to that of halosulfuron-methyl. Halosulfuron-methyl was considered to be the industry standard for nutgrass control. In 2003, the latter product was not available in the sugar industry.

The efficacy of Hero® on **Bellvine** was assessed in two trial sites (OC04/01 and OC13/01) in New South Wales and Queensland. Weed pressures ranged from low (41 m²) at trial site QC04/01 to moderate numbers (141 m²) at trial site OC13/01. The results provided in the submission indicate that Hero® generally provided adequate control of Bell vine at various product rates (including the rate stated on draft label), however there was some efficacy inconsistencies in OC04/01 where product dose increases displayed lower efficacy results.

The submission outlines that two trial sites (0001/01 and 0004/01) evaluated the efficacy of Hero® on **Star of Bethlehem**. Trial site 0001/01 displayed very low weed pressure and inconsistency in density across the trial site. Unfortunately, a comparison with a control treatment (no product application) was not possible due to extremely low pest pressure, however Hero treatments did display a reduction in weed numbers suggesting effective control of the pest. Trial site 0004/01 contained low weed pressures at application. Trial results displayed effective control of Star of Bethlehem across all treatments with a significant reduction in weed numbers.

From the limited efficacy data provided, it is expected that Hero® should provide consistent efficacy results on Bellvine and Star of Bethlehem. However, further trials need to be conducted in scenarios of higher Bellvine and Star of Bethlehem weed pressure to allow for a thorough assessment on product efficacy, and to provide a larger range of efficacy data for further evaluation. At this stage, the claim for these two weeds is not supported.

The efficacy of Hero® on **Red convolvulus** was also assessed at two trial sites (0014/00 and 0001/01) against standards Actil OS and Sempra. Weed pressures ranged from low (1.6/m²) at trial site 0001/01 to moderate (20/m²) at trial site 0014/00. Trial results indicate that effective control was achieved using Hero® at the nominated product rate on the herbicide draft label. Like Bell vine and Star of Bethlehem, additional trial work is required to provide a larger set of data for accurate evaluation of Red convolvulus. At this stage, the claim for Red convolvulus is not supported.

Directions For Use

The efficacy data provided in the submission adequately supports the nominated application rate (150g ai/ha) on the product draft label for effective nutgrass control. The limited efficacy data provided on Bellvine, Star of Bethlehem and Red Convolvulus also indicates that the nominated product rate will be sufficient for effective control of these weed species.

The product rate of 150g ai/ha was established using variable rate trials and statistical analysis to determine the level of active ingredient that achieved optimal efficacy under normal application conditions.

Trial results also indicated that the addition of wetting agent generally improved efficacy, probably as a result of increased target coverage through reduced surface tension of the spray liquid. Review of the submission indicates that there should be no implications with the addition of a non-ionic wetting agent (1000 g/L formulation) at the standard recommended rate of 100mL/100 L of water.

The 'Application and Equipment' section of the draft label outlines the use of a standard ground-driven broadcast spray or directed spray with nozzles that produce a fine/medium spray droplet. These spraying practices are standard for the sugar industry and the recommended water rate of 250 L/ha would be needed to achieve coverage in dense stands of nutgrass.

Based on the information provided in the submission, the Hero draft label sufficiently outlines the application method and timing required to achieve good target coverage and control.

Safety to Target and Non Target Species, Adequacy of Precautionary Advice

Crop Safety evaluation was recorded using visual observations and a percentage scale system (0% = no effect, 100% = plant killed). Crop phyto-toxicity is usually affected by the product used, variety, application method and environmental conditions pre- and post- application.

Herbicide tolerance can vary significantly across different variety types and growth stage. Trial results in the submission indicate that eight varieties were assessed for crop damage when Hero® was applied as a broadcast or directed spray in plant sugarcane.

Sugarcane is generally most susceptible to herbicides in the young plant cane stage when the plant is actively growing. Cultivars are rated for their general ability to withstand herbicide application; ratings include susceptible, intermediate and tolerant.

The BSES Variety Guide (2003) identifies Q174A as an intermediate rating. Treatments were applied as a broadcast spray over the top of Q174A plant cane (trial AR AvCypro01) during the early stages of growth and no phyto-toxicity was recorded. The submission indicates that Hero® was applied to plant cane at various growth stages and no visual phyto-toxicity was recorded. Crop yields were not included in the submission. However it is unlikely that any effects will occur if no visual effects were noticed in either crop vigour or discoloration of the leaves.

The selection of suitable application methods is necessary to reduce herbicide drift. Specifications could be made on the draft label to ensure the user selects the correct nozzle type and pressure (within the recommended nozzle operating pressure) to minimize spray drift, thus improving environmental safety.

The disposal of spray waste is sufficiently outlined in the product draft label. The reviewer does not agree with the first statement in the disposal procedure, as it is preferable to spray remaining product in the crop.

Compatibility of Proposed Withholding Periods (WHP) With Good Agricultural Practice

The proposed withholding periods provided in the draft label are in line with good agricultural practices in the sugar industry.

However, it is considered inappropriate to set a WHP (harvest) of 19 weeks as the crop needs to be harvested when the crop has maximum sugar content. The WHP (harvest) would be much better to be defined in terms of growth stage of the crop. Information provided by the reviewer suggests that the application would be made between planting and out of hand stage when the crop is between 70-80cm high. The label at present does not comment on the timing of the application. It is recommended that the timing of the application be added to the draft label. The WHP (harvest) can then be set in terms of growth stage such as "Do not apply after the out of hand stage of the crop"

During the drought of 2002, some canegrowers were selling their crop for stockfeed rather than to the mill. The current proposed WHP (grazing) of 19 weeks inhibits this practice. The applicant should provide justification for a 19 week WHP (grazing). (*Note: This was based on the earliest residue samples that were collected for residue trials. These samples were collected at 133 days [19 weeks] after application: see Residue Assessment in this document.*)

Crop rotation and re-cropping intervals for Guar bean, Dolichos Lab-Lab, Navy beans and sugarcane are also outlined in the draft label. The data for following crops demonstrates crop safety for such crops, if the re-cropping intervals are followed. Further studies in re-cropping intervals are planned to commence in 2003.

Special Consideration

There are no special considerations.

Presentation of Data

The review provided by Bayer CropScience Pty. Ltd is thorough and in the case of nutgrass, provides sufficient context to determine whether the subject preparation is considered to be effective for the purpose nominated.

Recommendation

A sufficient amount of efficacy data is presented in the submission to support the registration of Hero® *Selective Herbicide* as a post-emergent herbicide for control of nutgrass in sugarcane. Trial results in the Bayer CropScience submission details that Hero® has effective post-emergent control on nutgrass weeds between 4 - 6 leaf stage.

It is recommended that additional trial work be conducted on Bell vine (*Ipomoea pledeia*), Star of Bethlehem (*Ipomea quamoclit*) and Red convolvulus (*Ipomoea hederifolia*) in order to provide a larger range of data for more thorough assessment. A limited amount of efficacy data is provided in the submission on these weed species and therefore a recommendation cannot be made to support the requested label registration of Bell vine, Star of Bethlehem and Red convolvulus.

This submission for registration is supported for control of nutgrass in sugarcane provided additional information is made on the draft label to:

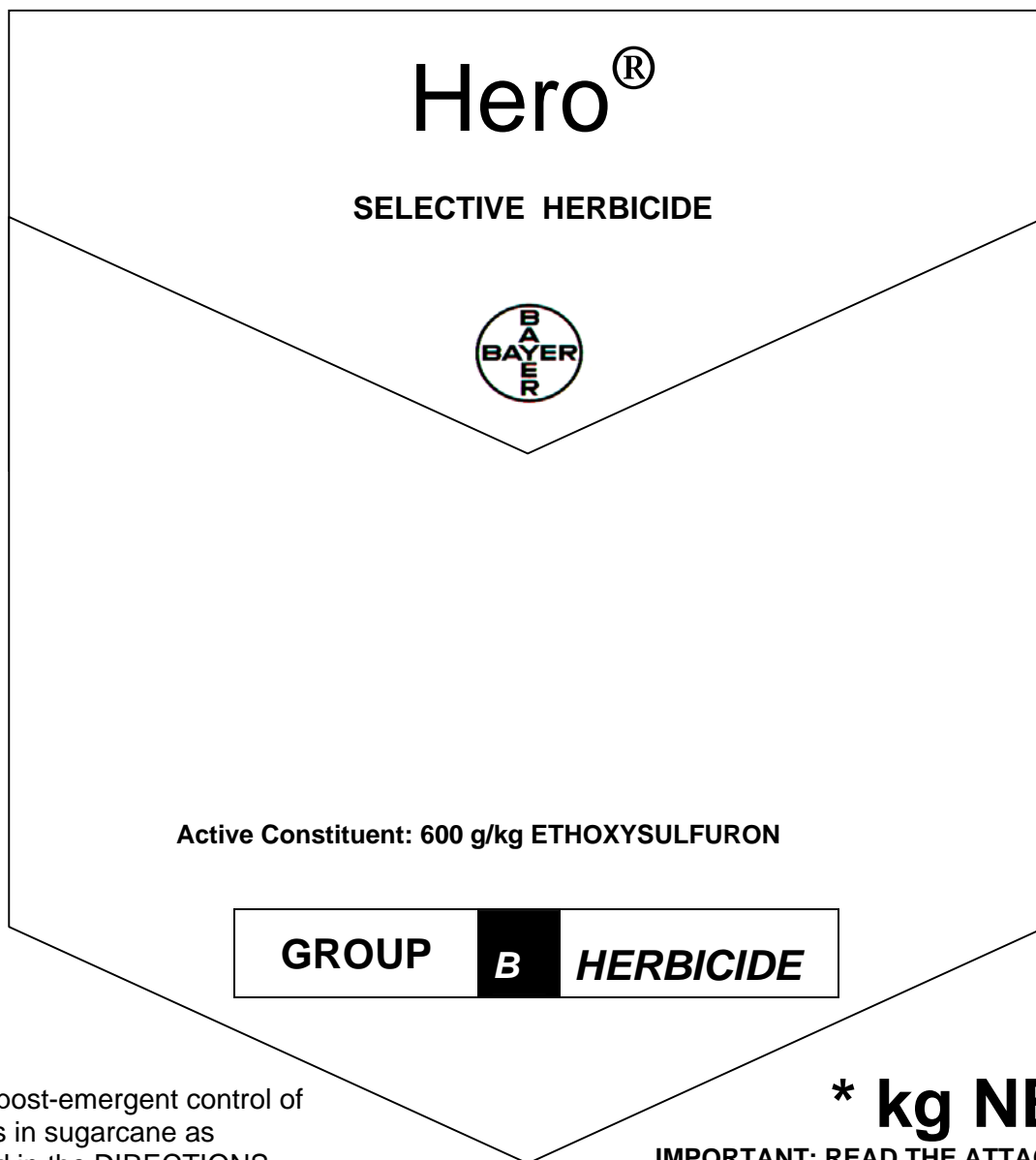
- ❖ ensure the user selects the correct nozzle type and pressure (within the recommended nozzle operating pressure) to minimize spray drift, thus improving environmental safety.

MAIN PANEL

Text above this line does not form part of the label

Label-Page 1 of 8

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



For the post-emergent control of
nutgrass in sugarcane as
specified in the DIRECTIONS
FOR USE table.

*** kg NET**
**IMPORTANT: READ THE ATTACHED
BOOKLET BEFORE USE**

(label code)

Text below this line does not form part of the label

* 0.5, 1, 1.5, 2 and 5 kg

²³ Label changes as a result of the various assessments appear in *bold italics*.

HERO SELECTIVE HERBICIDE

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Keep from contact with fertiliser, other pesticides and seeds. Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS

Will irritate the eyes. Avoid contact with eyes. If product in eyes, wash it out immediately with water. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length PVC gloves and face shield or goggles. Wash hands after use. After each day's use, wash gloves face shield or goggles and contaminated clothing.

FIRST AID

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

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet, which can be obtained from www.bayercropscience.com.au.

EXCLUSION OF LIABILITY

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

APVMA Approval No.: 56831/**/1008

Hero® is a Registered Trademark of Bayer.

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE

Text below this line does not form part of the label

** = pack-id = 0.5, 1, 1.5, 2 or 5 (depending on pack size involved)

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



BAR

Bayer CropScience Pty. Ltd.
A.B.N. 87 000 226 022
391-393 Tooronga Rd
East Hawthorn Vic. 3123



Phone: (03) 9248 6888
Fax: (03) 9248 6800
www.bayercropscience.com.au
Technical enquiries: 1800 804 479

Batch Number:
Date of Manufacture:

(label code)

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

HERO SELECTIVE HERBICIDE

Active Constituent: 600 g/kg ETHOXYSULFURON

GROUP B HERBICIDE

For the post-emergent control of nutgrass in sugarcane as specified in the DIRECTIONS FOR USE table.

STORAGE AND DISPOSAL

Store in the closed, original container in a cool, well-ventilated area. Do not store for prolonged periods in direct sunlight. Keep from contact with fertiliser, other pesticides and seeds. Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. Do not dispose of undiluted chemicals on site. If recycling, replace cap and return clean containers to recycler or designated collection point. If not recycling, break, crush, or puncture and bury empty containers in a local authority landfill. If no landfill is available, bury the containers below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS

Will irritate the eyes. Avoid contact with eyes. If product in eyes, wash it out immediately with water. When opening the container and preparing spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing), elbow-length PVC gloves and face shield or goggles. Wash hands after use. After each day's use, wash gloves face shield or goggles and contaminated clothing.

FIRST AID

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

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet, which can be obtained from www.bayercropscience.com.au.

EXCLUSION OF LIABILITY

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

APVMA Approval No.: 56831/1008

Hero® is a Registered Trademark of Bayer.

IMPORTANT: READ THIS BOOKLET BEFORE USE

DIRECTIONS FOR USE

Restrictions

DO NOT use if rainfall or irrigation is expected to occur within **48** hours of application. Refer to **General Instructions – PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT.**

DO NOT apply to weeds under severe moisture stress.

DO NOT apply in crop under stress from drought, waterlogging, frost or disease.

After application of Hero Selective Herbicide, DO NOT irrigate crop to the point of run-off, unless run-off water can be retained on the farm.

CROP	WEED	STATE	WEED STAGE	RATE g/ha	CRITICAL COMMENTS
Sugarcane	Nutgrass (<i>Cyperus rotundus</i>)	Qld, NSW, WA, NT only	4 – 6 leaf	250	<p>Apply in plant or ratoon crops, up to the out-of-hand stage (i.e. when crop is less than 100 cm tall).</p> <p>DO NOT apply by broadcast spray. Hero must be applied as a directed application, e.g. by an octopus head attached to an Irvin leg, or by appropriate dropper/nozzle configurations to minimise movement of spray off target.</p> <p>Addition of a non-ionic wetting agent is recommended. Apply the equivalent of 100 mL/100 L of a 1000 g/L formulation of non-ionic wetting agent.</p> <p>Thorough coverage of the weeds is essential for good weed control. Apply in a minimum of 250 L/ha of water.</p> <p>DO NOT apply more than one application of Hero or other group B herbicide to a crop in one season.</p>

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

WITHHOLDING PERIODS

Harvest: DO NOT HARVEST FOR 19 WEEKS AFTER APPLICATION

Grazing: DO NOT GRAZE OR CUT FOR STOCKFOOD FOR 19 WEEKS AFTER APPLICATION

GENERAL INSTRUCTIONS

Hero is a selective sulfonylurea herbicide. It is predominantly a foliar herbicide with less activity via the soil. Hero will not reliably control weeds that emerge after spraying. Results are best under good growing conditions and application to weeds or crop under stress should be avoided.

Resistant Weeds Warning

GROUP	B	HERBICIDE
--------------	----------	------------------

Hero Selective Herbicide is a member of the sulfonylurea group of herbicides and has the inhibitor of acetolactate synthase (ALS) mode of action. For weed resistance management Hero is a Group **B** herbicide. Some naturally-occurring weed biotypes resistant to Hero, and other Group **B** herbicides, may exist through normal genetic variability in any weed population. These resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by Hero or other Group **B** herbicides.

Do not rely exclusively on Hero for weed control. Use as part of an integrated weed management program involving herbicides with other modes of action and non-chemical methods of control. Avcare resistance management strategies are available from your local agricultural chemical supplier. Refer to these strategies for details of how to manage the build up of resistant weeds on your farm.

Since occurrence of resistant weeds is difficult to detect prior to use Bayer CropScience Pty. Ltd. accepts no liability for any losses that may result from the failure of Hero to control resistant weeds.

Crop Rotation Recommendations

For advice on re-cropping intervals for crops other than sugarcane or those listed below, contact your local Bayer CropScience representative.

Crop	minimum recropping interval
Guar bean, Dolichos Lab-Lab	4 months
Navy beans	6 months
Sugarcane	0 days

Application and Equipment**Ground Sprayers**

DO NOT apply as a broadcast spray. Apply only through directed spraying equipment, for example an Irvin leg fitted with an octopus head attachment. It is recommended that a minimum of 250 L water/ha is applied. **USE ONLY** a **MEDIUM** spray droplet classification according to ASAE S572 definition for standard nozzles. Refer to the nozzle manufacturer's specification for information on the spray droplet classification associated with your spray nozzles. To obtain effective results thorough coverage is essential.

Aircraft

DO NOT apply Hero by aircraft.

Mixing

Before spraying calibrate equipment to determine the quantity of water necessary to uniformly cover the measured area to be treated. Half fill the spray tank with clean water then, with agitators in motion, add the correct amount of Hero directly into the spray tank, then add wetting agent as recommended. Complete filling the tank with agitators in motion. Agitation must continue before and during spraying.

Use Of Surfactant / Wetting Agent

Addition of a non-ionic wetting agent is recommended. Use the equivalent of 100 mL/100 L of a 1000 g/L formulation of non-ionic wetting agent.

Sprayer Clean Up

The sprayer must be decontaminated before being used to spray crops other than sugarcane. Ensure that the following operation is carried out in an area that is clear of waterways, desirable vegetation and tree roots, and preferably in an area where drainings can be contained.

- **Apply unused spray to an untreated crop area, or untreated part of the paddock. DO NOT drain unused spray to a single point on the ground, but rather apply it to untreated crop or soil at 250 g product/ha as for treatment of crop.**
- Drain sprayer of remaining spray mix **in spray lines** and wash out tank, boom and hoses with clean water.
- Drain again.
- **If drainings and rinsings cannot be contained, make sure they will not drain towards sensitive areas such as waterways, desirable vegetation or tree roots.**
- Fill the tank with clean water and add 300 mL of chlorine bleach (containing 4% chlorine) per 100 L of water with agitator in motion.
- Flush some bleach solution through booms and hoses and allow remainder to agitate in tank for 10 minutes.
- Remove nozzles and filters and leave to soak in a bleach solution of 500 mL per 10 L of water while tank cleaning is in progress.
- Drain tank and repeat the procedure of flushing with bleach solution.
- Flush the tank, boom and hoses with clean water.

Compatibility

Compatibilities are under evaluation. Contact your local Bayer CropScience representative for the latest information on compatible products.

PRECAUTION

Re-entry Period

Treated fields should not be re-entered until spray deposits have completely dried. If prior entry is necessary wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and elbow-length PVC gloves. After each day's use wash gloves and contaminated clothing.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Very toxic to aquatic plants. DO NOT contaminate streams, rivers or waterways with the chemical or used container.

Application must be planned to avoid run-off. Run-off water from treated fields (from irrigation or its equivalent volume of natural precipitation) must be prevented from entering natural waterways. Application should not be made to wet/waterlogged soils. Application should not be made if heavy rains are expected within 48 hours. Irrigation should not occur within 48 hours of application.

Vegetative buffer zones between treated fields and natural waterways are recommended. Headlands and spoon drains should be well maintained so that runoff flow is not accelerated. Steady gradients, even profiles and grassed surfaces on headlands and drains reduce off-farm movement of runoff.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

DO NOT apply under weather conditions, or from spraying equipment, that may cause spray to drift onto nearby susceptible plants/crops, cropping lands, pastures, waterways or wetlands.

Hero® is a Registered Trademark of Bayer.

Bayer CropScience Pty Ltd.
A.B.N. 87 000 226 022
391-393 Tooronga Rd
East Hawthorn Vic. 3123



Phone: (03) 9248 6888
Fax: (03) 9248 6800
Website: www.bayercropscience.com.au
Technical enquiries: 1800 804 479

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 partitioning co-efficient.
Metabolism	The conversion of food into energy
Photo-degradation	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.

References

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, APVMA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *Vet Manual: The Requirements Manual for Veterinary Chemicals*, APVMA, Canberra.

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Ag Requirements Series: Guidelines for Registering Agricultural Chemicals*, APVMA, Canberra. (See footnote below)

National Registration Authority for Agricultural and Veterinary Chemicals 1997, *Vet Requirements Series: Guidelines for Registering Veterinary Chemicals*, APVMA, Canberra. (See footnote below)

National Registration Authority for Agricultural and Veterinary Chemicals 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, APVMA, Canberra. (See footnote below)

National Registration Authority for Agricultural and Veterinary Chemicals 2001, *Ag Labelling Code—Code of Practice for Labelling Agricultural Chemical Products*, APVMA, Canberra. (See footnote below)

National Registration Authority for Agricultural and Veterinary Chemicals 2001, *Vet Labelling Code—Code of Practice for Labelling Veterinary Chemical Products*, APVMA, Canberra. (See footnote below)

Footnote:

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

APVMA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of [active constituent] in the product [product name], please fill in this form and send it, along with payment of \$30 to:

The Contact Officer
Pesticide Program
Australian Pesticides and Veterinary Medicines Authority
PO Box 6182
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
The Contact Officer(Pesticides Program) at (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 _____