Australian Pesticides & Veterinary Medicines Authority

Evaluation of the new active

Azimsulfuron

in the product

®

GULLIVER HERBICIDE

Public Release Summary

Australian Pesticides & Veterinary Medicines Authority
Canberra, Australia

July 2006

ISSN1443–1335

Published by the Australian Pesticides and Veterinary Medicines Authority

PO Box E240
KINGSTON ACT 2604
AUSTRALIA

Foreword

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

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

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

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

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

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

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

The Pesticides Program Manager
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
KINGSTON ACT 2604

Contents

List of abbreviations and acronyms

Ac	active constituent
ADI	acceptable daily intake (for humans)
Ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land—und forstwirschaft
Bw	Bodyweight
D	Day
DAT	days after treatment
DT50	time taken for 50 per cent of the concentration to dissipate
EbC50	concentration at which the biomass of 50 per cent of the test population is impacted
EC50	concentration at which 50 per cent of the test population are immobilised
EEC	estimated environmental concentration
ErC50	concentration at which the rate of growth of 50 per cent of the test population is impacted
Fo	original parent generation
G	Gram
GAP	good agricultural practice
GCP	good clinical practice
GLP	good laboratory practice
GVP	good veterinary practice
H	Hour
Ha	Hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	high pressure liquid chromatography or high performance liquid chromatography
id	Intradermal
im	Intramuscular
ip	Intraperitoneal
IPM	integrated pest management
iv	Intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	Kilogram
Koc	organic carbon partitioning coefficient
L	Litre
LC50	concentration that kills 50 per cent of the test population of organisms
LD50	dosage of chemical that kills 50 per cent of the test population of organisms
LOD	limit of detection—level at which residues can be detected
LOQ	limit of quantitation—level at which residues can be quantified

mg	Milligram
mL	Millilitre
MRL	maximum residue limit
MSDS	material safety data sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	Nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	no observable effect concentration/level
OC	organic carbon
OM	organic matter
po	Oral
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
Q-value	quotient-value
RBC	red blood cell count
s	Second
sc	Subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
mg	Microgram
vmd	volume median diameter
WG	Water dispersible granule
WHP	withholding period

Introduction

This publication provides a summary of data reviewed and an outline of the regulatory considerations for the proposed registration of Gulliver® Herbicide, which contains the active constituent Azimsulfuron (a sulfonylurea compound) that has been approved by the APVMA. The APVMA also seeks public comment prior to the chemical product being registered for use in Australia.

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

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

Written comments should be received by the APVMA by 18 August 2006 and addressed to:

Mr J.A.Macdonald
Pesticides Program
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Phone: (02) 6272 3688
Fax: (02) 6272 3218
Email: john.macdonald@apvma.gov.au

Applicant

Dupont (Australia) Ltd

Product details

It is proposed to register Gulliver® herbicide, containing 500g/kg Azimsulfuron, as a water dispersible granule. The product will be formulated in Sydney and packaged in 500 gram size pack and produced at DuPont (Australia) Limited at their formulation plant in Girraween, NSW. The active constituent will be imported for formulation.

Gulliver® herbicide, as a member of the sulfonylurea group of herbicides, has a mode of action of inhibiting of the biosynthesis of essential amino acids insusceptible plants, through the inhibition of acetolactate synthase (ALS). As a member of the sulfonylurea group of herbicides, it is a weed resistance management Group B herbicide.

The proposed use for Gulliver® herbicide is post-emergent control of certain aquatic broadleaf weeds, and the suppression of Barnyard grass in rice.

The rate of product use is 40g mixed with1.6-1.7L MCPA(250g/L sodium & potassium salt)/ha. Gulliver® herbicide is proposed for registration in NSW and Victoria only.

Formulations containing Azimsulfuron are currently registered in Italy, Spain, Portugal, Japan, France, Greece, China, Korea, Brazil, Columbia, Venezuala, Iran, Egypt, Turkey, Uzbekistan and Turkmenistan.

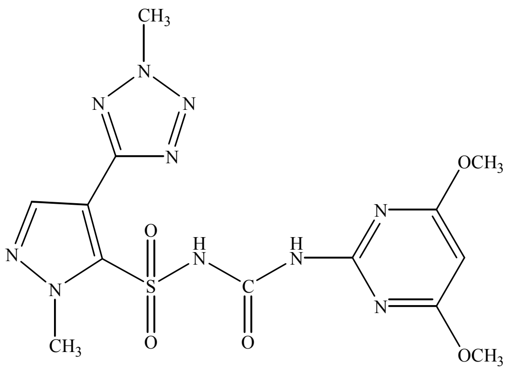
CHEMISTRY AND MANUFACTURE

Azimsulfuron is a sulfonylurea herbicide for the control of certain aquatic broadleaf weeds, and suppression of Barnyard grass in rice.

Chemistry of the active constituent

ISO common name	Azimsulfuron
Chemical name IUPAC	1-[4,6-Dimethoxypyrimidin-2-yl]-3-[1-methyl-4-(2-methyl-2*H*-tetrazol-5-yl)-1*H*-pyrazol-5-ylsulfonyl]urea
CAS registry numbers	120162-55-2
Molecular formula	$C_{13}H_{16}N_{10}O_5S$
Molecular weight	424.4 $gmol^{-1}$
Physical Form	White solid with a phenolic odour
Melting Point	170 °
Density	1.12 ± 0.046 mg/cm^3 (20 °C)
Vapour Pressure	4×10^{-9} Pa (25 °C)
Manufacturer's code	NOA 407855

Structural formula



The Chemistry and Residues Program (CRP) of the APVMA has evaluated the chemistry aspects of azimsulfuron (manufacturing process, quality control procedures, batch analysis results and analytical methods).

Azimsulfuron is a new active constituent and there is no compendial specification available. On the basis of the data provided, it is proposed to establish the following Active Constituent Standard for azimsulfuron:

Constituent	Specification	Level
Azimsulfuron	Azimsulfuron	Not less than 980 g/kg

Chemistry of the product

Name	Du Pont Gulliver Herbicide
Formulation type	Water-dispersible granule
Concentration of active constituents	500 g/kg Azimsulfuron

Physical and Chemical Properties of the Product.

Appearance:	Tan granules with a mild, sweet odour
Bulk density:	0.82±0.02 g/cm^3
PH:	~5.5 (1.0% suspension)

Storage and Stability

The applicant provided the results of real time stability testing conducted using samples stored in an HDPE bottle (the proposed commercial container). The results indicate that the formulated product is expected to be stable for at least two years when stored under normal conditions in the proposed commercial packaging.

Packaging

Gulliver Herbicide will be packaged in HDPE bottles. The packaging is not adversely affected by the product, nor is the product unstable in the packaging.

Recommendation

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

TOXICOLOGICAL ASSESSMENT

Evaluation of Toxicology

The toxicological database for azimsulfuron, 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

Following administration of azimsulfuron to rats, more than 90% of a single oral dose was absorbed in 48 hours. It was almost completely eliminated in 3 days, mainly in the urine (74-81%), and the rest in the faeces via biliary excretion. Azimsulfuron was predominantly distributed in plasma and in tissues responsible for metabolism and elimination such as the liver and kidney, mostly in the form of unchanged azimsulfuron. Twelve metabolites were identified and characterised in rats. The main metabolic pathway was O-demethylation of the dimethoxypyrimidine ring. Minor pathways included hydroxylation or cleavage of the pyrimidine ring, hydrolysis of sulfonylurea linkage and N-demethylation of methylpyrazole or methyltetrazole rings. Repeated dosing had no influence on kinetic parameters or metabolism.

Acute Studies

Azimsulfuron had low acute oral toxicity in mice (LD_{50} 7161 mg/kg in males and 7943 mg/kg in females) and rats (LD_{50} >5000 mg/kg), and low dermal (LD_{50} >2000 mg/kg) and inhalational (LC_{50} >5940 mg/m^3) toxicity in rats. Azimsulfuron was a slight eye irritant in rabbits but was not a skin irritant in rabbits or a skin sensitiser in guinea pigs.

Gulliver Herbicide had low acute oral toxicity (LD_{50} >5000 mg/kg) and low dermal (LD_{50} >2000 mg/kg) toxicity in rats. It was a slight skin and eye irritant in rabbits but was not a skin sensitiser in guinea pigs.

Short-term Studies

Female mice received azimsulfuron by gavage at 0 or 1600 mg/kg/day over a 2-week period (10 doses). Mice dosed at 1600 mg/kg/day showed lethargic behaviour from day 3 to day 12, and one mouse died on day 5 but the cause of death was not determined. Mean bodyweight gain was slightly reduced from day 3 until the end of dosing; leading to mean bodyweights slightly lower than controls until the end of the recovery period. At necropsy, there were no treatment-related changes in organ weights and no treatment-related gross or microscopic lesions were observed.

Male rats were administered azimsulfuron by gavage at 0 or 2200 mg/kg/day over a 2-week period (10 doses). Clinical signs of toxicity were observed from day 3 and included lethargic behaviour, hunched posture, ruffled fur and wet/stained perineum, and allergic oedema of the face and/or hind extremities. Body weight gain was reduced in treated animals during the dosing period, but a group of rats allowed a 2-week recovery period gained weight normally. At necropsy, testes weights were slightly decreased and there was microscopic evidence of mild to moderate degeneration and atrophy of the seminiferous tubules of the testes and oligospermia. The degree of severity of the testicular lesion was less in test rats killed after 14 days of recovery, indicating a potential for reversibility.

Mice received azimsulfuron in the diet at 0, 300, 1000, 3000 or 10000 ppm for 13 weeks. Bodyweight gain and food efficiency for 10000 ppm males were reduced during the study. At necropsy, male mice at ≥1000 ppm had dark livers, males at 3000 and 10000 ppm had increased liver weights, and the livers of males at 1000 and 3000 ppm and both sexes at 10000 ppm showed centrilobular hepatocellular swelling. There were significant increases in the weights of the pancreas of females at 10000 ppm, and males at 3000 ppm and both sexes at 10000 ppm had decreased zymogen granules in acinar cells of the pancreas with or without acinar cell swelling. There was an increase in the weights of the testes of males at 10000 ppm, with intratubular giant cell formation in the testis. Hyaline droplet deposition in epithelial cells of the urinary bladder was observed in some males and females at 10000 ppm. The NOEL was 300 ppm (40 mg/kg/day) for males and 3000 ppm (470 mg/kg/day) for females.

Rats were fed azimsulfuron in the diet at 0, 300, 1250, 5000 or 20000 ppm for 13 weeks. Bodyweight gain and food efficiency were reduced in females at 20000 ppm. Urinalysis revealed cloudy and/or red urine (females at 5000 and both sexes at 20000 ppm), occult blood (females at 20000 ppm), increased specific gravity (males at 5000 and 20000 ppm), a significant decrease in urine pH and needle-like crystals in the urinary sediment (both sexes at 20000 ppm). There was a decrease in erythrocyte count and increases in MCV, MCH, reticulocytes and lymphocytes at 20000 ppm. Males at 20000 ppm had decreased serum chloride and increased inorganic phosphorus values. At necropsy, both sexes at 20000 ppm and females at 5000 ppm showed increased pancreas weights, with hypertrophy of the pancreatic acinar cells filled with zymogen granules. There were significant increases in the weights of the spleen of both sexes at 20000 ppm. Males at 20000 ppm had dark-coloured spleens and animals of both sexes exhibited a mild increase in extramedullary hematopoiesis of the spleen that was accompanied by congestion in males. Increased hematopoiesis of the bone marrow was also noted in some males at 20000 ppm. Epithelial hyperplasia of the urinary bladder was observed in some males and most females at 20000 ppm. The NOEL was 1250 ppm, equivalent to 75 mg/kg/day for males and 82 mg/kg/day for females.

Dogs were fed azimsulfuron in the diet at 0, 300, 1250, 5000 or 20000/10000 ppm for 13 weeks. The concentration of azimsulfuron was reduced from 20000 to 10000 ppm from week 6, due to severe toxicity. Dogs at 5000 and 20000/10000 ppm had reduced bodyweight gain (with reduced food consumption at 20000/10000), decreased spontaneous motor activity and/or emaciation. Dogs at 5000 and 20000/10000 had moderate to severe anaemia, with bilirubinuria, slightly prolonged blood clotting times (APTT), and increased fibrinogen values. There were increases in the concentration of ALP, total bilirubin, cholesterol and triglyceride at 20000/10000 ppm, and slight decreases in albumin at 5000 and 20000/10000 ppm. Inorganic phosphorus values were decreased at 20000/10000 ppm. These effects were more severe in the males. Dogs at ≥1250 ppm had emaciated condition, pale, yellow or oedematous tissues, with enlarged lymph nodes, and hemorrhagic spots in various organs and tissues. There were increases in the weights of the pancreas (both sexes at ≥5000 ppm), spleen (males at 5000 ppm and both sexes at 20000/10000 ppm) and liver (males at ≥1250 ppm, females at 20000/10000 ppm). Dogs at ≥5000 ppm had acinar swelling of the pancreas and dogs at ≥1250 ppm had diffuse hepatocellular swelling. Females at 1250 ppm and both sexes at ≥5000 ppm had extramedullary haematopoiesis of the spleen. Males at 1250 ppm and both sexes at ≥5000 ppm had hypercellularity of the bone marrow. Other treatment-related findings in some dogs at ≥1250 ppm included thymic atrophy, lymphocyte hyperplasia in the lymph nodes, hepatocellular degeneration/necrosis and mononuclear and polymorphonuclear cell infiltration in the liver, increased mucous secretion (males) or hypertrophic mucosa (females) of the gallbladder, and hyaline droplet degeneration of the renal proximal tubular cells. The NOEL was 300 ppm, equivalent to 8.8 mg/kg/day for males and 9.7 mg/kg/day for females.

Long-term Studies

In a carcinogenicity study, mice were fed azimsulfuron in the diet at 0, 100, 750, 2500 (m) or 5000 (f) ppm for 78 weeks. The only evidence of toxicity was a significantly increased incidence of amyloid deposition in the heart, small intestine, ovary and kidney in females at 5000 ppm. The incidences of tumours in the treated groups were comparable to controls. The NOEL was 2500 ppm (247 mg/kg/day) for males and 750 ppm (70 mg/kg/day) for females.

In a chronic toxicity/carcinogenicity study, rats were fed azimsulfuron in the diet at 0, 125, 1000, 5000 or 8000 ppm for 104 weeks. Male rats at 8000 ppm had slightly reduced bodyweight gain. Slight but statistically significant increases in MCV, MCH and MCHC were observed in males at 8000 ppm, at some of the interim kill timepoints. Males at 8000 ppm had macroscopic hypertrophy of the pancreas with an increase in pancreas weights, but no significant histopathological changes. Females at 5000 ppm had an increase in the incidence of early change of chronic nephropathy in the kidney. There was no effect of azimsulfuron treatment on the incidence of neoplastic lesions. The NOEL was 1000 ppm (34 mg/kg/day for males and 44 mg/kg/day for females).

In a chronic toxicity study, dogs were fed azimsulfuron in the diet at 0, 50, 150, 750 or 3000 ppm for 12 months. At 3000 ppm, males showed slightly reduced bodyweight gain during the last half of the treatment period, leading to terminal bodyweights about 9% lower than controls. Females at 3000 ppm had increased serum creatinine values, and both sexes had increased brown pigment deposition in hepatocytes. The NOEL was 750 ppm (18 mg/kg/day for males and 19 mg/kg/day for females).

Reproduction Study

Rats were fed azimsulfuron in the diet at 0, 125, 1000 or 8000 ppm, from 77 days prior to mating until weaning of the offspring, throughout two successive generations. In parental animals, the bodyweight gain of F0 males was significantly reduced at 1000 and 8000 ppm. All F0 males and females at 8000 ppm had increased pancreas weights with hypertrophy of the acinar cells of the pancreas. F1 males at 8000 ppm had slightly decreased sperm counts, but there was no effect of treatment on the reproductive performance of animals in any group. At 8000 ppm, the bodyweights of F1 and F2 pups were significantly decreased from birth throughout lactation (F1) or from lactation days 14 to 21 (F2). The NOEL was 1000 ppm (87 mg/kg/day) for adult animals and their offspring.

Developmental Studies

Pregnant rats received azimsulfuron by gavage at 0, 50, 200 or 1000 mg/kg/dav, from days 6 to 15 of gestation. At 1000 mg/kg, maternal toxicity was manifested by an increased incidence of salivation during the dosing period, decreased body weight gain, decreased food consumption, and an increased incidence of hypertrophy of the pancreas. At 1000 mg/kg, foetal weights of both sexes were significantly reduced and the incidences of skeletal variations (lumbar ribs and 25 presacral vertebrae) were significantly increased at 1000 mg/kg/day. There was no increase in the incidence of external, visceral or skeletal malformations in any group. The NOEL for maternal and foetal toxicity was 200 mg/kg/day.

Pregnant rabbits received azimsulfuron by gavage 0, 50, 150 or 500 mg/kg/day from day 6 to 18 of gestation. At 500 mg/kg, 7/18 females died and 4 of these aborted on days 19-25 of gestation. These effects occurred in animals exhibiting severe weight loss as well as a rapid decrease in food consumption during the later half of the dosing period. Examination of foetuses revealed no significant increases in the incidences of malformations or variations in the treated groups. The NOEL for maternal toxicity was 150 mg/kg/day and for foetal toxicity was 500 mg/kg/day.

Genotoxicity Studies

Azimsulfuron was not genotoxic in a range of studies, including bacterial mutagenicity (Ames) tests using the following strains: *S. typhimurium* TA97, TA98, TA100, TA1535 & TA 1537 and *E. coli WP2uvrA*; an in *vitro* forward mutation test (HGPRT locus) in CHO cells; an *in vitro* chromosome aberration assay in CHO cells; an *in vitro* unscheduled DNA synthesis test in rat hepatocytes; a DNA repair test using *Bacillus subtilis;* and an *in vivo* mouse bone marrow micronucleus test.

Gulliver Herbicide was not genotoxic in an *in vitro* bacterial mutagenicity (Ames) test or an *in vivo* mouse bone marrow micronucleus test.

Mechanistic studies

Effects on the pancreas.

Male rats were fed diets containing 0, 300, 10,000, or 30,000 ppm azimsulfuron for 28 days. Rats at 30,000 ppm had decreased body weight gain from test day 7 onward, due to reduced food consumption and food efficiency, but bodyweight gains in the recovery group were high and final bodyweights in this group were higher than pair-fed controls. Pancreas weights were increased at 10,000 and 30,000 ppm, and this effect was completely reversible following a 28-day recovery period. It was demonstrated that azimsulfuron increases plasma cholecystokinin (CCK) levels and is able to act as trypsin-inhibitor activity. which accounts for its ability to increase pancreas weight and pancreatic acinar cell proliferation. Both of these responses were mediated by increased plasma CCK levels.

Effects on the testis.

Male rats were fed diets containing 0, 300, 10,000, or 30,000 ppm azimsulfuron for 28 days. Cauda epididymal sperm counts were significantly decreased at 30,000 ppm azimsulfuron on day 28. Changes in sperm counts were associated with microscopic changes of degeneration in the testes and oligospermia/germ cell debris in the epididymides. Neither sperm counts nor microscopic changes in the testes/epididymides were fully reversible following 28 days of recovery. The mechanism for the effect on spermatogenesis is not known but it is unrelated to an induced increase in plasma estradiol levels.

Studies on metabolites and impurities

INJ290-1 is an impurity in the active constituent. It is a metabolite in rice plants and is probably a metabolite in mammals, although it was not identified in metabolism studies. INJ290-1 had low acute oral toxicity in rats (approximate LD 2250 mg/kg), and was a slight eye irritant in rabbits but was not a skin irritant in guinea pigs. In a 10-dose oral gavage study in rats, 450 mg/kg/day produced initial weight loss and salivation, followed by recovery. INJ290-1 was not mutagenic in a S. typhimurium reverse mutation assay.

IN-E6758, a minor impurity, was not mutagenic in a mouse micronucleus test.

Conclusion

Although Azimsulfuron is new to the Australian market, it is closely related to compounds such as bensulfuron methyl that has been registered for use in herbicidal preparations for some time. It is readily absorbed from the gastrointestinal tract of rats and was rapidly and almost completely eliminated, mainly in the urine and mostly as unchanged compound. It had low acute oral toxicity in mice and rats, low dermal and inhalational toxicity in rats, and low potential for irritation and sensitisation. Similarly the product, Du Pont Gulliver Herbicide, has a low acute oral and dermal toxicity in rats, is a slight skin and eye irritant in rabbits but is not a skin sensitiser in guinea pigs.

In repeat dose studies, the main target organs for toxicity were the pancreas, liver, testes and epididymides. The effects in the pancreas were fully reversible in rats and, although azimsulfuron has some effects on the testes and epididymides in rats, these effects are also likely to be reversible and there was no functional effect on reproductive performance. Mild anaemia was also observed leading to secondary effects such as increased spleen weight and increased formation of new red blood cells. Azimsulfuron was associated with minor variations in the development of rat fetuses, but only at doses also toxic to the mother and there was no effect on the development of rabbit fetuses. A range of special studies demonstrated that azimsulfuron did not damage genetic material and long-term studies in mice and rats showed no increase in the incidence of cancer

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

PUBLIC HEALTH STANDARDS

Poisons Scheduling

The National Drugs and Poisons Schedule Committee (NDPSC) considered the toxicity of the product and its active ingredients and assessed the necessary controls to be implemented under States' poisons regulations to prevent the occurrence of poisoning.

On the basis of its low toxicity, the NDPSC has made azimsulfuron exemptfrom the requirements of scheduling in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate safety directions on the product label.

Acceptable Daily Intake (ADI)

The Acceptable Daily Intake is that quantity of an agricultural compound which can safely be consumed on a daily basis for a lifetime and is based on the lowest NOEL obtained in the most sensitive species. This NOEL is then divided by a safety factor which reflects the quality of the toxicological database and takes into account the variability in responses between species and individuals.

The ADI for azimsulfuron was established at 0.2 mg/kg bw/day based on a NOEL of 18 mg/kg bw/day in a 12-month dietary study in male dogs and using a 100-fold safety factor in recognition of the extensive toxicological database available for azimsulfuron.

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 highest short-term dose of azimsulfuron at which no evidence of toxicity was detected was 150 mg/kg bw in a developmental study in rabbits. The ARfD was established at 1.5 mg/kg bw mg/kg bw on the basis of this NOEL and using a 100-fold safety factor.

RESIDUES ASSESSMENT

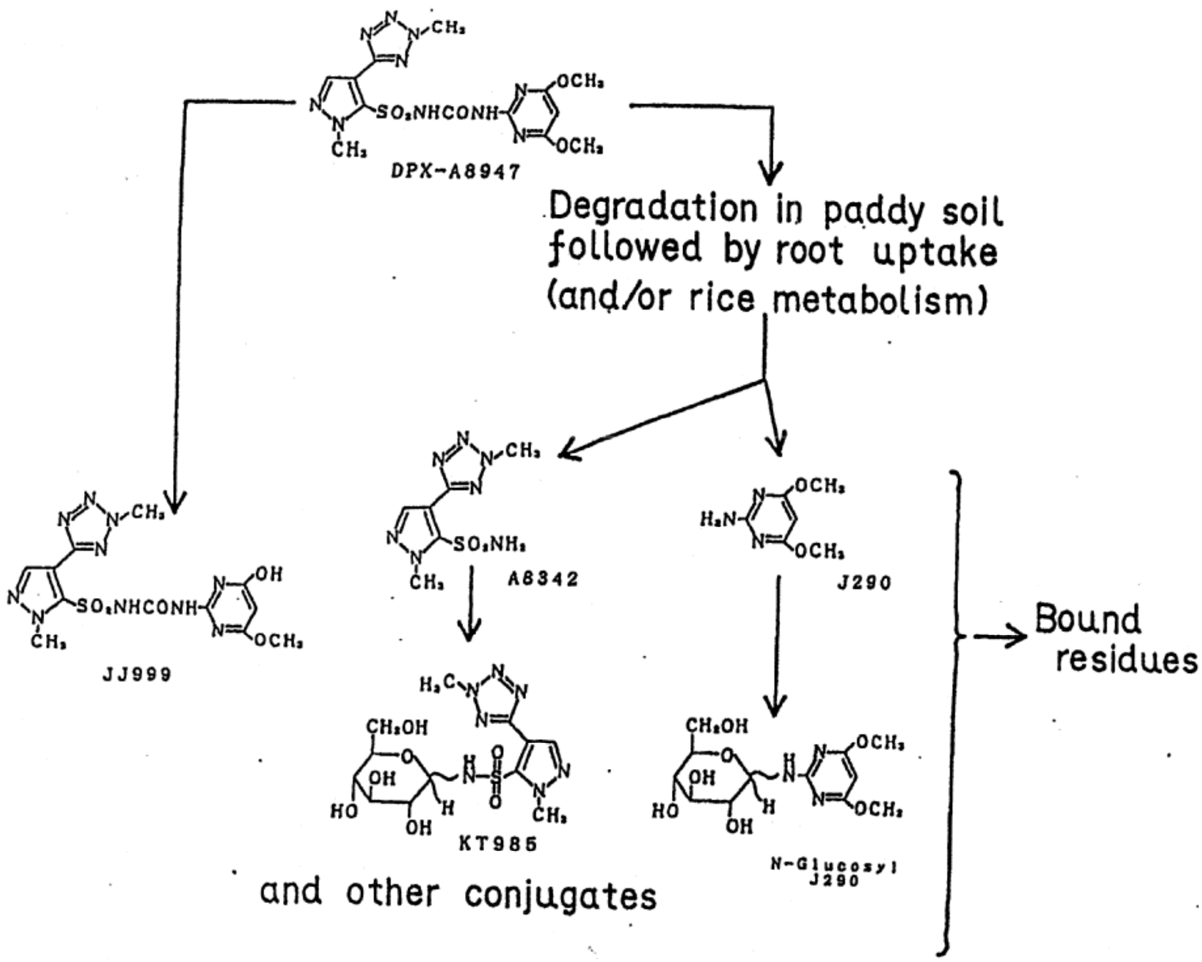
Introduction

Residue data for rice; metabolism studies for rice and animals (rats); environmental fate and chemistry were considered as part of the residue evaluation of azimsulfuron.

Metabolism

Plant metabolism studies were conducted on rice. Rice was subjected to [pyrazole-2-^{14}C]-azimsulfuron or [pyrimidine-2-^{14}C]-azimsulfuron by various treatments and the uptake and distribution of radioactivity was monitored. The principle metabolic pathway of azimsulfuron in rice plants was O-demethylation of one of the methoxy groups on the pyrimidine ring, forming the JJ999 metabolite. Additional metabolites absorbed in plant tissues are thought to arise from hydrolysis of the sulfonylurea bridge and/or the uptake of degradation products found in the soil, including metabolites A8342, J290, KT985 and N-glucosyl J290, amongst other conjugates.

Figure 1: Metabolic pathways of azimsulfuron in rice



Animal metabolism studies were conducted on rats fed either [pyrazole-^{14}C] and [pyrimidine-^{14}C] labelled azimsulfuron at 5 mg/kg (low dose), and 1000 mg/kg (high dose). The majority of radioactivity from oral dosing was eliminated within 3 days following administration. The recovered dose was found mainly in the urine (74-81%), and in the faeces (16-25%). There was no discernable difference in the metabolic profile from either labelled starting material, indicating that the metabolic route was independent of the radioactive label used.

Metabolites identified in the urine, faeces and tissues consisted predominantly of unchanged azimsulfuron. The low dose rate of azimsulfuron was not retained in any tissues, and less than 0.2% of the high dose was retained in tissues, the highest level of radioactivity was found in the liver and erythrocytes. Twelve metabolites were identified and characterised in rats following treatment. Based upon the identified metabolites, the metabolic pathways show various mechanisms of breakdown, being predominantly O-demethylation of the dimethoxypyrimidine ring. Second phase conjugation, being sulfate- or glucuronide- was also observed.

In summary, the radioactive profiles show that azimsulfuron in rice is metabolised via O-demethylation of one of the methoxy groups on the pyrimidine ring, forming the JJ999 metabolite. Additional metabolites absorbed in plant tissues are thought to arise from hydrolysis of the sulfonylurea bridge and/or the uptake of degradation products from the soil. In animals, there is initial absorption of azimsulfuron, followed by rapid elimination. Low levels of radioactivity remained in rat tissues.

Residue definition

As no detectable residues are expected to be found in rice and in animal commodities, the residue definition will be established as parent only. This definition will ensure that Good Agricultural Practice has been adhered to when azimsulfuron is applied to rice. Therefore, the residue definition for compliance and for dietary assessment is as follows:

Azimsulfuron azimsulfuron

Analytical methods

Determination of residues in plant tissues

Analytical determination was performed using HPLC with UV detection at 245 nm. The reported limit of quantification (LOQ) for grain was 0.01 mg/kg, and for fodder and straw was 0.02 mg/kg. The reported LOQ for rice grain from trials conducted in Australia was 0.02 mg/kg. The method is appropriately validated for the determination of azimsulfuron residues in rice grain, fodder and straw commodities.

Determination of residues in animal tissues

Although animal transfer studies were not provided, a validated analytical method for the determination of azimsulfuron residues in meat, eggs, milk and fat was submitted. Determination was performed by HPLC with UV detection at 245 nm. The reported LOQ was 0.02 mg/kg for all matrices (whole milk, eggs, beef muscle, poultry muscle). The average recovery from samples fortified with 0.02-0.1 mg/kg of azimsulfuron was 83%. Testing was not conducted on offal (liver or kidney) as sulfonylurea herbicides are not known to concentrate in liver and kidney tissues. Furthermore, azimsulfuron is not fat-soluble and has a low octanol/water partition coefficient (K_{OW} = 0.038 at pH 7) and so method validation in cream and fat commodities was not conducted. The method is appropriately validated for the determination of azimsulfuron residues in animal commodities.

Storage stability

The storage stability of residues has been determined on rice commodities, and in animal tissues (rat). Residues of azimsulfuron remained stable in rice straw and grain for a minimum of 18 months when stored under freezer conditions (-15 °C). The metabolic profile in rat tissues (plasma, erythrocytes, liver pancreas, bile) was stable for 244-250 days when stored frozen (-30 °C). The rat studies confirm that residues in animals are reflective of those present at the time of sampling, following freezer storage for up to 8 months.

Residue trials

Rice-grain

There were eleven trials conducted on rice grown in Australia, Italy, Spain and Malaysia. Azimsulfuron was applied at 1-1.5 × the proposed Australian rate. The data show that azimsulfuron residue levels in harvested grain are below the limit of quantification of 0.01-0.02 mg/kg when azimsulfuron was applied according to GAP. The calculated STMR is <0.02 mg/kg. The results support establishment of the following MRL for azimsulfuron:

GC 0649	Rice	*0.02 mg/kg

In association with this MRL, a harvest withholding period is not required when Dupont Gulliver Herbicide is used as directed.

Rice-forage

There were five trials conducted on rice forage in Italy, Spain and Australia. These results indicate that following Dupont Gulliver Herbicide treatment, residues in rice forage collected at the proposed withholding period of 2 weeks contain negligible residues, ie <0.05 mg/kg. Rice forage may be used as an animal feed, particularly in failed crop situations. The data support the following animal feed commodity MRL for azimsulfuron:

	Rice forage (fresh weight)	*0.05 mg/kg

Rice-straw and fodder

There were ten trials conducted on rice straw in Italy, Spain and Australia. In the European trials, azimsulfuron was applied at 30 g ai/ha (1.5 ×) according to GAP. In the Australian trials, azimsulfuron was applied as Dupont Gulliver Herbicide in accordance with GAP at the proposed rate of 20 g ai/ha. Straw collected at harvest, 90-140 days after treatment, contained residues of <0.02-<0.05 mg/kg. The results support the following animal feed commodity MRL for azimsulfuron:

AS 0649	Rice straw and fodder, dry	*0.05 mg/kg

In association with the animal feed MRLs for forage and straw, a two week grazing withholding period should be observed when Dupont Gulliver Herbicide is used as directed.

Processing studies

No rice processing studies were included in the product submission. On the basis of non-detectable residues being found in unprocessed rice (paddy rice), the rice MRL of *0.02 mg/kg will account for residues in processed rice commodities, including rice bran.

Animal commodity MRLs

No animal feeding studies were included in the product submission. On the basis of non-detectable residues resulting in animal feed commodities (ie grain, forage, straw and fodder) following the proposed use on rice, it is unlikely that residues will be found in animal commodities. Metabolism studies conducted on rats show that azimsulfuron is rapidly absorbed and eliminated from animals. Following an oral dose of 1000 mg/kg of radio-labelled azimsulfuron, there was less than 1% of radioactivity remaining in the body after three days. The majority of the radioactivity was eliminated in the urine and faeces.

Analytical methodology has been provided for determining azimsulfuron residues in meat, milk and egg commodities, with an LOQ of 0.02 mg/kg. On the basis of non-detectable residues resulting in animal commodities, the following animal commodity MRLs are recommended:

MO	0096	Edible offal (mammalian)	*0.02
PE	0112	Eggs	*0.02
MM	0095	Meat [mammalian]	*0.02
ML	0107	Milks	*0.02
PO	0111	Poultry, edible offal of	*0.02
PM	0110	Poultry meat	*0.02

Estimated dietary intake

The theoretical chronic and acute dietary intakes for azimsulfuron has been assessed. The ADI for azimsulfuron is 0.2 mg/kg bw/day, based upon a NOEL of 18 mg/kg bw/day and a 100 fold safety factor. The NEDI of azimsulfuron is equivalent to <1% of the ADI. With respect to the acute dietary intake, the acute reference dose (ARfD) for azimsulfuron is 1.5 mg/kg bw/day. The highest acute dietary intake was estimated at <1%. It is concluded that chronic and acute dietary exposure to azimsulfuron is low and the risk from residues in food is acceptable.

Bioaccumulation potential

Azimsulfuron has shown little indication that it will bio-accumulate in animals and the environment. Rat metabolism data show that it does not accumulate in fat tissue.

Recommendations

The following amendments to the *MRL Standard* are recommended in relation to the proposed use of Dupont Gulliver Herbicide:

Table 1

Compound	Food			MRL (mg/kg)
ADD: Azimsulfuron				
	MO	0096	Edible offal (mammalian)	*0.02
	PE	0112	Eggs	*0.02
	MM	0095	Meat [mammalian]	*0.02
	ML	0107	Milks	*0.02
	PO	0111	Poultry, edible offal of	*0.02
	PM	0110	Poultry meat	*0.02
	GC	0649	Rice	*0.02

Table 3

Compound	Residue
ADD:	
Azimsulfuron	Azimsulfuron

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
ADD:			
Azimsulfuron	AS 0649	Rice straw and fodder, dry	*0.05
		Rice fodder (fresh weight)	*0.05

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

Grazing: DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 2 WEEKS AFTER APPLICATION.

Harvest: NOT REQUIRED WHEN USED AS DIRECTED.

Conclusions

Consideration of the residues of Azimsulfuron in food leads to the conclusion that the use of Azimsulfuron is unlikely to be an undue risk to human helth from a dietary perspective. The proposed use of Azimsulfuron for the control of certain Aquatic broadleaf weeds, and suppression of Barnyard grass in rice is unlikely to unduly prejudice trade.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD.

Overseas registration status

There are no Codex MRLs established for azimsulfuron. Japan has established an MRL of 0.1 mg/kg for rice. The USEPA has no established tolerances for azimsulfuron, including import tolerances.

Potential risk to Australian export trade

Export of treated produce containing finite (measurable) residues of azimsulfuron 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.

MRLs are not established in any of Australia's major export markets for rice. However, the proposed use of Dupont Gulliver Herbicide on rice is unlikely to prejudice Australian trade as there are no detectable residues expected on rice. Similarly, there are no residues expected in/on animal commodities as a result of animal feed exposure to rice (forage, straw and grain) from treated crops.

Conclusion

In summary, based upon the proposed use-pattern and the residue data submitted, the proposed use of Dupont Gulliver Herbicide is unlikely to unduly prejudice trade.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Azimsulfuron is on the NOHSC *List of Designated Hazardous Substances* as an environmental hazard. Risk phrases or cut-off concentration have not been assigned to azimsulfuron. Based on the available data, Du Pont Gulliver Herbicide could not be classified as hazardous according to NOHSC *Approved Criteria for Classifying Hazardous Substances.*

Du Pont Gulliver Herbicide has low acute oral and dermal toxicity in rats. Based on the toxicity of azimsulfuron, the product is expected to have low inhalation toxicity. The product is a slight skin and eye irritant in rabbits, and is not a skin sensitiser in guinea pigs. The main hazards associated with repeat exposure to the product are systemic effects on the liver and changes in haematology parameters.

Formulation, Packaging, transport, storage and retailing.

Du Pont Gulliver Herbicide will be formulated and packaged in Australia by Du Pont (Australia) Limited at their formulation plant in Girraween, NSW. The active constituent will be imported for formulation.

The product will be packed in 500 g high-density polyethylene (HDPE) containers. Workers will be exposed to the active constituent and the product during formulation and packaging.

Use and exposure

Du Pont Gulliver Herbicide is a dry flowable formulation, and will be used for the control of Barnyard grasses and certain aquatic annual weeds in rice crops.

The product will be mixed with water and applied by boom spray or aerial application. The recommended application rate is 40 g/ha in a minimum spray volume of 40 L/ha of water (0.1% EUP, 0.05% azimsulfuron). Only one spray application will be made per crop season.

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, NOHSC used the Predictive Operator exposure Model (POEM) and the Pesticide Handlers Exposure Database (PHED) to estimate worker exposure to azimsulfuron during mixing/loading and application.

The POEM data indicated unacceptable risk (MOE<100) to mixer/loaders when gloves were not worn. MOE became acceptable when workers wore gloves. Risk to applicators was acceptable even without gloves. The PHED data indicated low risk to workers while mixing/loading and application. Both exposure models assume that workers wear at least one layer of clothing (cotton overalls or equivalent clothing) when performing these tasks.

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. The risk assessment indicates that cotton overalls or equivalent clothing should be worn when applying the prepared spray by ground application method.

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, NOHSC 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, NOHSC 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. Safety Directions include the use of cotton overalls buttoned to the neck and wrist (or equivalent clothing) when applying the prepared spray.

The PPE recommended should meet the relevant *Standards Australia*.

NOHSC recommends the following precautionary statement on the product label:

PRECAUTION

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

Conclusion

NOHSC supports the registration of Du Pont Gulliver Herbicide, containing 500 g/kg of azimsulfuron, as a dry flowable formulation, for the control of Barnyard grasses and certain aquatic weeds in rice crops.

Du Pont Gulliver 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.

Additional information is available in the Du Pont Gulliver Herbicide MSDS.

ENVIRONMENTAL ASSESSMENT

Introduction

DuPont has applied for registration of Gulliver Herbicide containing the new active ingredient azimsulfuron (500 g ac/kg) for the control of a range of weeds in rice. Gulliver will be applied at 40 g/ha (20 g ac/ha) tank mixed with MCPA and a non-ionic surfactant as a foliar spray only. The label gives directions to apply in a minimum of 40L/ha for aerial application and 120 L/ha for groundrig applications. This implies most application would use medium droplet sizes of 250-350 µm vmd for all applications. Almost all applications (~95%) are expected to be aerially applied with just ~5 % by groundrigs There is no limitation on repeat applications, but the company has indicated that in most instances only one application per rice crop would occur and only occasionally two. The first application would be early in the rice crop with the latter a 'salvage' treatment only if required.

Environmental Fate

Hydrolysis

In a study conducted to meet US EPA Guidelines the hydrolysis of azimsulfuron was pH-dependent and followed first order kinetics. The half-lives were 89, 124 and 132 days at pH 5, pH 7 and pH 9. The sulphonylurea bridge was cleaved during hydrolysis, resulting in the formation of the pyrazole sulfonamide and the corresponding pyrimidine as the only hydrolysis products.

Photolysis

In a test conducted to meet US EPA requirements, aqueous irradiation of azimsulfuron with a simulated solar spectrum showed that photolysis was pH dependent. The average half-lives under irradiated conditions were calculated as 48, 71 and 84 days for pH 5, 7 and 9 respectively and for the dark control half lives were 89, 124 and 132 day respectively. As for hydrolysis, the primary degradates were from cleavage of the sulphonylurea bridge giving pyrazole sulfonamide and the corresponding pyrimidine.

The half-life of photolysis was determined at pH 7 as 164 days by the difference between the observed photolysis and hydrolysis rates. Using a US EPA model and the molar absorption of azimsulfuron, the half-lives of azimsulfuron at 30, 40 and 50° latitude in summer, integrated over the full day/night, was determined as 487, 496 and 524 days respectively.

In a study conducted to US EPA requirements using natural water, the average half-lives of azimsulfuron in irradiated sterile and non-sterile natural water were 12.2 and 12.0 days, respectively, approximately 6 times faster than reported in the above study using purified water. This also indicates that microbial activity was not a significant factor in the more rapid degradation. This increase in the rate of photolysis is well known due to the dissolved organic matter in natural waters acting as an activator. Apart from the major degradates due to hydrolysis, there were also a number of minor metabolites.

Using the rate constant for reaction of azimsulfuron with hydroxyl radicals, determined under laboratory conditions, and assuming steady rate concentration of hydroxyl radical in natural waters (about 10^{-15} to 10^{-16} M), the predicted half-life for indirect photolysis of azimsulfuron in natural water ranges from 2–23 days. These results suggest that azimsulfuron would be rapidly degraded by indirect photolysis processes in shallow or near-surface water.

Metabolism

Aerobic soil

The metabolism of azimsulfuron was studied in an agricultural soil, classified as silt loam, under aerobic conditions according to US EPA Guidelines. Metabolism was relatively fast, with the average DT_{50} calculated as 21 days. The main metabolites were due to cleavage of the sulfonylurea together with a range of unknowns, and non-extractable soil bound products that reached 39% after 270 days.

The degradation of azimsulfuron in 4 European soils was studied at 20°C according to BBA and EC Guidelines. Two soils (a clay and a silt clay) were taken from rice fields in Spain while the other 2 soils (sandy loam and a silt loam) were from rice growing regions of Italy. After 120 days of incubation, the DT_{50}s were calculated as 18 and 26 days for Italian soils and 98 and 134 days for the clayey Spanish soils, which could be due to low biological activity in the Spanish soils during the incubation. The Department of the Environment and Heritage concludes that in microbially active soils azimsulfuron degrades fairly rapidly and based on the Italian results is rated as fairly degradable.

Aerobic aquatic metabolism

The aerobic aquatic metabolism of azimsulfuron was conducted according to BBA Guidelines using two sediment-water systems from the UK, one a pond and the other a moving water site. The applied radioactivity moved from the water into the sediment and after 100 days incubation between 32.7% and 38.5 % of the applied radioactivity was measured in the water and between 54.1% and 64.1% of the applied radioactivity in the sediment. The DT_{50} for dissipation from water compartments was similar at 44 and 54 days.

The main degradates indicated that azimsulfuron was degraded by hydrolytic cleavage of the sulphonylurea bridge and a minor metabolite by cleavage of one of the methoxyl groups of the pyrimidine ring.

Anaerobic aquatic metabolism

The anaerobic aquatic metabolism of azimsulfuron was conducted according to a US EPA Guideline using a silt loam sediment. The soil was flooded with water then incubated for 32 days under nitrogen before being dosed with azimsulfuron and incubated at 25°C under anaerobic conditions. The applied radioactivity moved from the water into the sediment with 23 and 25% of the applied radioactivity in the water, and sediment respectively after 162 days. The major degradation products were from cleavage of the sulfonylurea bridge. The average half-life was determined using first order analysis as 80 days.

Metabolism in rice paddy soils

The soil metabolism of azimsulfuron in two different Japanese paddy soils (Iwate and Ushiku light clays) was performed to meet Japanese requirements. Each soil was dosed and then incubated under 3 aerobic conditions: non-sterilized flooded, sterilized flooded, or non-sterilized upland conditions (~50% maximum moisture holding capacity of the soils) for 84 days.

In the flooded soils, the applied radioactivity rapidly moved from the water into the sediment and after 3 days incubation only 9-18 % of the applied was measured in the water.

The amount of bound radioactivity increased during the study in the non-sterile system (42-51%) but not in the sterilized soils. Two degradation products were identified in the flooding water and soil extracts of non-sterilized flooded soils together with sulfonylurea cleavage products. In the sterilized soils, the only metabolites were due to hydrolysis (cleavage) of the sulfonylurea bridge. The half lives in non-sterilized soils ranged from 24 to 26 days while those in sterilized soils ranged from 78 to 90 days using first order kinetics. These results clearly indicated that the rate of chemical hydrolysis was slower than that of the microbial decomposition.

In the upland systems, there was some evolution of CO_2 with a maximum of 13 and 3% of applied radioactivity for Ushiku and Iwate soils respectively. After 84 days between 41-65% of applied radioactivity was still extractable, which is less than the levels found in the non-sterilized flooded soils. Major degradation products were from cleavage of the sulfonylurea bridge and were higher than those in the flooded soils. Degradation of azimsulfuron was analysed using bi-phasic first order kinetics (two compartment model) with half-lives of 11 days and 96 days for the first and second phase respectively. The Department of the Environment and Heritage re-analysed the data using first order kinetics to give half-lives of 41.5-52.1 days with acceptable correlations with r^2 from 0.93 to 0.96.

Mobility

Volatility

The volatilisation behaviour of azimsulfuron was studied in accordance with the BBA Guidelines. Azimsulfuron was applied to a sandy soil and bean plants, then the losses due to volatilisation determined over a 24 hour period. Under the test conditions volatilisation after application from leaves was 2.7% and for soil loss of radioactivity, 12.9%. The study demonstrated that volatilisation is <20% for 24 hours and therefore according to BBA Guidelines, volatilisation is not considered a significant pathway for dissipation of azimsulfuron.

Adsorption/desorption

The adsorption/desorption of azimsulfuron was studied by the batch equilibrium method using 4 agricultural soils. Azimsulfuron weakly adsorbed onto all soils with K_{oc}s ranging from 61 to 86 and was classified as having high to very high mobility (McCall classification). Desorption showed that between 63 to 97% readily desorbed from the soils.

The adsorption/desorption of azimsulfuron to 4 Japanese soils was also studied by the batch equilibrium method. The study demonstrated that azimsulfuron is moderately to weakly adsorbed and classified as of low to medium and high to very high mobility (McCall classifications) with Kocs ranging from 77 to 1000. The adsorption for two rice soils was higher than for other soils which could have been due to the lower pH and the high ion exchange capacity of these soils.

The adsorption/desorption of 4 metabolites of azimsulfuron was studied as before in the four European soils used previously. The results show that the hydrolysis cleavage products are slightly less mobile in these European soils than the other two degradates that retain the sulfonylurea bridge. Given that hydrolysis is the major degradation pathway, this indicates the major degradates are in general less mobile than the parent compound.

The mobility of 4 metabolites of azimsulfuron was studied by soil TLC in the four Japanese soils used previously. As before, the results show that the major degradates from cleavage of the sulfonylurea bridge are less mobile than parent.

Field Dissipation

Dissipation at 2 Italian sites.

The dissipation of azimsulfuron was studied under field conditions (rice paddies) at two locations in Italy that had been arably farmed for a number of years. One application of Gulliver (25 g ac/ha) was made at each site with 3-10 cm of standing water and rice growing in the paddies. The results of the chemical analysis (HPLC) showed that the azimsulfuron residues dissipated in the water from 25-33 μg/L (27.9; 38.2 μg/L) at 3 hours after application to <0.1 μg/L after at 21 days. The half-lives were 2.4 and 3.0 days for water in the paddies under still conditions. No residues of azimsulfuron were found in the soil samples from the both locations, apart from only one sample per test that contained 1.0 and 1.4 μg/kg azimsulfuron residues respectively.

Dissipation Spain.

The dissipation of azimsulfuron was studied at a single site in Spain. The azimsulfuron residues dissipated from 29 μg/L to 5 μg/L after 14 days. A half-life of 4.5 days in water was determined (r^2 = 0.9193, first order kinetics) but as there were two conditions during sampling (closed and outrunning water) and the half-life is based on the combined data set, the half-life has to be used with caution.

The degradation in the field is significantly faster that would be expected based on the laboratory data. However, literature reports indicate that indirect aquatic photolysis (reaction of azimsulfuron with hydroxyl radicals formed from photolysis) is a very fast reaction and is responsible for ~75% of the observed fast degradation in the rice paddy studies.

Soil Residues Trial in Europe – 1993 and 1994

The purpose of these studies was to determine the magnitude of residues of azimsulfuron in rice grown in Europe following a single application of azimsulfuron at 25.9 g ac/ha. The trials sites were in Spain and Italy. Soil sample cores were sampled at harvest (approximately 100 day after application) and prior to next crop sowing (~280 days after application). Traces of azimsulfuron residues were occasionally detected at harvest but below the limit of quantification (10 μg/kg). There were no other detections.

Environmental Toxicity

Avian

Azimsulfuron was practically non-toxic to bobwhite quail and mallard ducks by the single oral dose route with NOEC values greater than 2,250 mg ac/kg bw. This was also true for the 5-day dietary exposures resulting in an NOEC of 5620 mg ac/kg bw for both bobwhite quail chicks and mallard ducklings. Tests using the formulation Gulliver also showed that it was not toxic to bobwhite quail and mallard ducks.

Aquatic

Under static conditions in a test conducted to meet US EPA requirements, technical azimsulfuron is rated as practically non-toxic to rainbow trout with a 96 h LC_{50} of 154 mg/L and to bluegill sunfish with a LC_{50} of >1000 mg/L. It is also practically non-toxic to carp, with a LC_{50} of >300 mg ac/L and a NOEC of 300 mg/L, and to sea bream with a NOEC of

100 mg/L (limit test). The formulated product Gulliver is also rated as practically non-toxic to rainbow trout with the LC_{50} = 492 mg/L (equivalent to 246 mg ac/L).

A short term sublethal and an early life stage study were conducted using rainbow trout and technical azimsulfuron according to OECD guidelines under flow-though conditions. The NOEC in the sublethal study was 23 mg ac/L and LOEC 45 mg ac/L. For the early life stage study the no observable effects level was 25 mg/L and LOEC 49 mg/L, with sublethal effects of reduced body length of hatchlings, delays in hatching, increased number of abnormal hatchlings and decreased larval survival from hatch to thinning noted at 49 mg/L.

For aquatic invertebrates the acute 48 h daphnia toxicity test conducted according to US EPA and OECD Guidelines using technical azimsulfuron gave an EC_{50} of 945 mg ac/L and azimsulfuron was rated as practically non-toxic. Using the formulated product Gulliver, again tested according to US EPA and OECD Guidelines, the acute 48 h daphnia toxicity test gave an EC_{50} of >1030 mg/L and NOEC of 1030 mg/L, equivalent to 550 mg ac/L, and was rated as practically non-toxic. In the chronic 21 days study, conducted according to US EPA and OECD guidelines, the NOEC and LOEC for daphnia were 5.4 and 20 mg ac/L respectively with effects on reproduction being the effect observed in the study.

For green neon shrimp tested according to Japanese guidelines, a 96 h limit test showed there were no observable effects at a nominal concentration of 100 mg ac/L. Using a freshwater shellfish, azimsulfuron was also rated as practically non-toxic with an EC_{50} of >100 mg ac/L and the NOEC = 100 mg ac/L.

Technical azimsulfuron was rated as very highly toxic to the green alga *(Selenastrum capricornutum*) with a 96-h E_bC50 of 21 µg/L and an E_rC50 of 12 µg/L in a test conducted according to US EPA Guidelines. When the algae were transferred to clean medium at the end of the test, the algae grew normally and thus the effects of azimsulfuron were determined to be algistatic at <130 µg/L. In limit tests at 19.7 µg/L (nominal) it affected blue-green algae and freshwater diatoms, with 14 and 20% inhibition of growth respectively, but did not affect marine diatoms. An acute 72-h toxicity test using the formulated product Gulliver (50% ac) and the same green alga gave an E_rC50 of >75 µg/L and an E_bC50 of 43 µg/L of Gulliver. One metabolite, IN-A8342 showed no effect on the green algae *S. capricornutum* at 1.0 mg/L.

Technical azimsulfuron was rated as very highly toxic to duckweed *(Lemma gibba*) with a 96-h EC50 (fronds) of 0.93 µg/L and an EC50 (biomass) of 0.80 µg/L in a test conducted according to US EPA Guidelines. Plants from the highest treatment (1.8 µg/L) were transferred to clean medium and grown for 7 days where they resumed normal growth relative to control replicates. The metabolite, IN-A8342, showed no effect on duckweed at 1.0 mg/L.

Non-Target Terrestrial Invertebrates

The NOEC for azimsulfuron (technical) to bees was 25 and 100 µg/bee for the oral and contact exposure routes respectively, tested according to US EPA Guidelines. The formulated product Gulliver was also rated as harmless to bees with an oral NOEC of 350 µg/bee (175 µg ac/bee) and the contact NOEC is 400 µg/bee (200 µg ac/bee). There were no effects on parasitic wasps, green lacewings, predatory mites and ground dwelling beetles when tested according to standard procedures to dry residues of Gulliver on glass at ~60 g/ha (30 g ac/ha: proposed rate for Australia is 20 g ac/ha). Azimsulfuron can be rated as harmless to bees, parasitic wasps, green lacewings, predatory mites and ground beetles and presumably to other terrestrial insects in the field.

Earthworms

In tests on the effect of azimsulfuron technical on earthworms conducted according to OECD Guidelines using artificial soil as a limit test at 1000 mg ac/ha, there was 18% mortality and the LC_{50} was determined as > 1000 mg ac/kg. In the same OECD test using Gulliver at 1000 mg/kg soil, there was only 2% mortality (corrected) and the LC_{50} was determined as > 1000 mg/kg.

Soil micro-organisms

Investigations into the effects of Gulliver on soil microbial activity were conducted according to EU Guidelines at twice the European field rate (120 g/ha). There was no significant effect on respiration or on nitrogen turnover after 28 days.

Non-target vegetation

The effect of azimsulfuron on non-target plants was evaluated in a seedling emergence and vegetative vigour study at rates from 1 to 62 g ac/ha, the maximum single field rate. The results showed that azimsulfuron is more herbicidal to dicotyledons than monocotyledons and has higher toxicity post-emergent than pre-emergent. Five dicotyledon species (sugarbeet, rape, cotton, pitted morninglory and cocklebur) show more than 80% inhibition (assumed to be inhibition of growth) at 1 g ac/ha in the post-emergent test with the first 2 having 100% inhibition. Unfortunately the study did not determine endpoints, either NOEC or IC50, for the most sensitive plants tested and a more accurate determination is needed. The study is a discovery screening trial and was not conducted to GLP requirements or to any regulatory requirements.

An Australian field study was conducted where aerial applications of Gulliver Herbicide in combination with MCPA were performed over a spread of districts under typical conditions with most using a medium (270-300 μm) spray quality. Observations of off-target plant damage were on neighbouring crops such as grapes, stone fruit, tomatoes and citrus (all sensitive to MCPA), as well as maize (not sensitive to MCPA). In addition, at 3 sites potted plants were also placed at 0, 50 and 200 m downwind immediately prior to application. These consisted of corn, tomatoes, capsicum, onions, melons, vines/grapes, citrus, silver beet, red gum, blue gum, yellow box and lemon gum. Immediately after application plants were removed for care and observation. Control and untreated plants were also kept.

As the age and size of the plants was not given, although photographs showed that the vines and trees appear to be close to the sizes seen in most nurseries, the result are not directly comparable to the seedling emergence and vegetative vigour studies.

Very little information could be drawn from the neighbouring crops situations, as almost all of these are sensitive to MCPA and aerial operators avoid spraying downwind of these crops. Of the potted plants, toxic symptoms were observed for tomatoes and watermelons where in both cases 6 weeks after application the plants had died. These two species were only placed at the edge of the field and it is unknown how they might have been affected at 50 or 200 m.

Grape vines, citrus and eucalypts trees were present at all three sites at 0 and 50 m and eucalypts at 200 m at all sites but grapes and citrus only at one site each at 200 m. At 0 and 50 m there was increasing leaf damage and by 6 weeks most vines and trees at 0 m had died but at 50 m the vines and trees were actively growing after 6 weeks. The effects seen were consistent with damage due to MCPA. At 200 m there was no visible damage to the vines or citrus and eucalypts trees.

Hazard to Terrestrial Organisms

Birds

Based on the typical diet of northern bobwhite quail and the calculated of azimsulfuron in food items, the concentration in the diet was calculated as 2.1 mg/kg. As the dietary LD_{50} for quail and mallards of >5620 mg ac/kg and a NOEC of 5620 mg ac/kg, clearly there is no hazard to birds from worst case single dose. Even with two applications, the hazard remains low.

Earthworms

The concentration of azimsulfuron in top 5 cm of soil following 2 applications was calculated as 0.06 µg/kg, which is at least 1000 times lower than the 14-d LC_{50} for the earthworm of >1000 mg ac/kg soil. Thus the proposed use is not expected to pose an acute hazard to earthworms. There were no studies on chronic toxicity to earthworms but given the large safety margin for acute effects, chronic effects are unlikely.

Beneficial arthropods

The hazard to honey bees is expected to be low as the single application rate of 20 g ac/ha (equivalent to 0.2 µg ac/cm^2) is 125 times lower than the most sensitive contact NOEC of 25 µg ac/bee, assuming that a honeybee is approximately 1 cm^2 in surface area. Effects on species such as predatory mites, parasitic wasps, green lacewing and ground beetles are not expected as applications at rates similar to that proposed had no or limited effect.

Soil micro-organisms

The soil micro-organisms were not affected at 60 g ac/ha in the laboratory test and therefore a hazard to soil micro-organisms and soil processes is unlikely at the proposed rate of 20 g ac/ha.

Hazard to Aquatic Organisms

Contamination outside the target area is likely to result from spraydrift, particularly from small droplets. As the label excludes releasing water from the treated rice paddies, contamination from run-off is unlikely except in cases of accidents.

Direct overspray

The worst-case scenario of a direct overspray of a 15 cm deep body of water with an application rate of Gulliver Herbicide of 20 g ac/ha would result in an EEC of 13.3 µg ac/L. Using the most sensitive acute adverse effect on fish was for rainbow trout with the 96-h LC_{50} of 154 mg ac/L and NOEC of 49 mg ac/L the hazard to fish was calculated as low. The EEC is also below the 97-day no observable adverse effects level (NOAEL) for early life stages of rainbow trout (25 mg ac/L) and indicates no hazard for chronic exposure. The risk to fish does not need to be examined further.

Similarly, acute effects on water fleas are also unlikely, with a 48 hour EC_{50} of >100 mg ac/L. The chronic NOEC (5.4 mg ac/L) is also significantly above the EEC and indicates that chronic exposure is unlikely pose a hazard from direct overspray. The risk to daphnia and other aquatic invertebrates is low and does not need to be examined further.

For algae, the lowest EC_{50} (cell density) for algae was 12 µg ac/L and the resulting quotient (EEC/EC_{50}) of 1.1 shows that acute effects on algae are possible from direct overspray. The EC50 (biomass) for aquatic plants was just 0.8 µg ac/L and the quotient of 16 indicates a potential high hazard. The risk to algae and aquatic plants was high and the hazard assessment was considered further.

Spraydrift

There is potential for Gulliver to contaminate surface waters via spraydrift. However, the resulting EEC is expected to be considerably lower than that from direct overspray. The risk and extent of spraydrift can be minimised if applications are made under suitable meteorological conditions and with appropriate equipment, as advised on the label. However, it must be assumed that some spraydrift will occur and hence contamination of soil and water outside the target areas.

In the case of application by ground rig, rice bays will be dry so that no physical movement of water occurs during application as such movement may cause the applied chemical to be washed off the target plants leading to reduced efficiency of the chemical. Water supply to bays will commence 24 h after application. It is expected that a single application will be used in most cases but two applications are possible.

Assuming a worst-case scenario of 10% of a single application reaching the aquatic environment via spraydrift (Urban and Cook 1986), the resulting EEC would be 1.3 µg ac/L. The risk for algae would be reduced and the Q = 0.11, ie ~0.1 and effects on these organisms from spraydrift is unlikely. In addition, the actual spraydrift is expected to be significantly less than 10% of the application rate and therefore the risk is considered below the level of concern. For duckweed, the most sensitive organisms tested, the quotient is 1.6 and a hazard is indicated. However, the test showed that duckweed recovers from single exposures at 1.8 µg/L and therefore any effects from exposure are short term. While there is unlikely to be long-term effects, the quotient remains greater than 1 and further refinement is needed.

Aerial Application

Aerial application was evaluated using the AgDrift model. The results clearly indicated a potential hazard and to achieve an acceptable hazard for most sensitive aquatic organisms (ie Q < 0.1) using a fine/medium spray (vdm = 245 µm) a buffer of 300 metres is indicated. However, the NOEC was 0.46 µg ac/L and as the EEC from the Agdrift model is less than the NOEC at 50 metres, the hazard is acceptable with this distance as a buffer. As duckweed recovers from single exposures at 1.8 µg ac/L, any effects from exposure are likely to be short term.

The draft label has a downwind spraydrift buffer of 50 metres for aerial applications and warnings not to allow spraydrift to contaminate any off-target water bodies (eg ponds, streams, lakes, rivers or waterways).

The hazard to non-target aquatic organisms from single aerial application of azimsulfuron is acceptable provided a downwind spraydrift buffer of 50 m as required by the draft label is used. With the rapid degradation due to indirect photolysis together with degradation, there is not expected to be any carryover if a second application is made 21 days after the first and therefore no increase in environmental effects.

Ground-rig

Two models were used to evaluate the spraydrift from ground-rig application to rice, the German or Ganzelmeier model and Agdrift. It is assumed that the rice is sprayed with the ground boom at 50 cm or less in height. Using the German model calculations showed that there is unlikely to be a hazard to duckweed at 5 metres but with the US EPA model a slight hazard out to 20 metres was indicated. However, as the EEC from the Agdrift model at 5 metres was less than the NOEC for duckweed, effects from spraydrift on duckweed are unlikely. In addition, there are label warnings not to allow spraydrift to contaminate any off-target water bodies (eg ponds, streams, lakes, rivers or waterways). There is unlikely to be any effect on non-target aquatic organisms from ground applications of azimsulfuron.

Run-off – release of tailwater

Run-off from rice paddy soils is considered not to occur due to levies around the paddies but tailwater could be released. The label for Gulliver has several restraints not to release tailwater from treated rice paddies into local drains, waterways or water systems. During the growing season release of water from the bays only occurs after prolonged heavy rainfall or if the water becomes cloudy. In such events, overflow is directed either into a recirculation system or onto adjacent fields where the water is absorbed into the soil. Overflow is unlikely to enter river systems. Treated water will not normally be released into drainage within 21 to 28 days after application, as specified by local irrigation authorities. However, water may be deliberately drained from the rice crop during very wet weather. The Rice Growers Association website indicates that, in this case, the water is held in recycling storages on the property and does not re-enter the river system. This is also in line with the label restraint that states "Do not release tail-water from the treated paddies into local drains, waterways or water systems."

If, after heavy rainfall, the excess water in a paddy is released, the concentration of azimsulfuron is dependent on several factors. Assuming a half-life of 5 days, in-line with the field half-lives, and that release occurs after 28 days (label requirement and NSW Authorities recommended period on holding water in rice paddy before release), the concentration in the released water is calculated as 0.14 μg/L and the hazard to algae and duckweed is considered to be low.

Leaching

Azimsulfuron is relatively water soluble, with limited binding to soil and a relatively long half-life in soil (20-134 days). However, as indicated by the applicant, the potential concentrations in groundwater are likely to be extremely low due to the low application rate, interception by the crop (50%), rapid degradation of azimsulfuron in rice paddies (half-life <5 days) and that water leakage though the underlying clay layer in rice paddies is generally low. The applicant has calculated the peak concentration in shallow groundwater (2-3 metres below the bottom of the rice paddies) as 0.05 μg/L.

Leaching potential can be easily predicted using a nomogram based on the mobility and persistence. Using this nomogram, azimsulfuron was in the transitional extending into the probable leacher range. Given that the longest half-life was due to loss of biological activity during the study incubation and the low permeability soils used in Australian rice paddies, significant leaching under field conditions appears unlikely.

Multiple Applications

The label does not give any direction as to the maximum number of applications but 2 applications are the maximum likely. Given that azimsulfuron degrades in water/sediment and with 21 days between applications, the maximum concentration from spraydrift in water was calculated to increase by just 6% (half-life of 5 days). The increase in the hazard is relatively minor and therefore the additional hazard from 2 possible applications per year is considered very low.

Chronic hazard

Azimsulfuron is unlikely to be a chronic toxicant. After application to a rice paddy, it is likely to remain in the paddy for several months (NSW requirement is for treated water to be held for at least 28 days) where it will degrade in the water/sediment system via indirect photolysis together with degradation. Given the low hazard already, azimsulfuron (Gulliver) is not expected to cause a chronic hazard.

Desirable vegetation

At the proposed maximum spray rate of 20 g ac/ha, adverse effects on non-target plants are considered possible. When used according to label directions, the exposure to non-target vegetation should be limited to spraydrift. In tests using both dicotyledon and monocotyledon seedlings, there was significant (>80%) inhibition at 1 g ac/ha (equal to 5% spraydrift) to sugarbeet, rape, cotton, pitted morninglory, and cocklebur. As there were no clear endpoints, a safety factor of 10 was used to estimate the lowest EC50 for terrestrial plants as 0.1 g ac/ha. For aerial application calculations showed that a spraydrift buffer of 400 metres gives a Q = 1.0 using the EC50 of 0.1 g ac/ha. In order to obtain a quotient of <0.1, needed due to the uncertain endpoints (note that this is equivalent to a safety factor of 100 for 1 g ac/ha), the spraydrift buffer would need to be >1500 metres (for aerial application) and this is impractical. For ground applications the Ganzelmeier data for field crops show that a spraydrift buffer of at least 200 metres for Q = 0.1 would be required and with AgDrift (medium spray, low boom) the required spraydrift buffer is out of range of the model (maximum range is 300 metres).

However, the field information presented showed that there was little damage to non-target vegetation when placed at 200 metres downwind with aerial application (aerial drift at 200 meters is estimated to be 1.5% of application rate, based on AgDrift using fine/medium droplets). For ground rigs, 1.5% of application rate corresponds to 7 and 5 meters from AgDrift and Ganzelmeier respectively. Further, given that the rice is grown in bays surrounded by soil banks and paddocks, the likelihood that desirable non-target vegetation outside the rice bays will be adversely affected by spraydrift from ground rig applications is considered low. A spraydrift buffer of 10 metres is considered appropriate for ground rigs.

Therefore, based on the limited field data, the Department of the Environment and Heritage recommends minimum spraydrift buffers of 200 metres for aerial application to protect non-target vegetation and 10 metre for groundrigs.

Conclusion

It was concluded by the Department of the Environment and Heritage that provided the product is applied according to the proposed label use patterns and the following (minimum) downwind spray drift buffers are used:

- for aerial applications a 50 metre buffer for non-target natural aquatic areas and 200 metres from the treated area and sensitive crops, native or other non-target vegetation.
- for ground application a 10 metre buffer from the treated area and sensitive crops, native or other non-target vegetation

then there is unlikely to be an unintended effect that is harmful to animals, plants or things or to the environment.

EFFICACY AND SAFETY ASSESSMENT

Justification for Use

Azimsulfuron – Gulliver® - is a low use rate herbicide for the control of barnyard grasses and a range of aquatic weeds in rice.

The availability of Gulliver®, when used in combination with MCPA, will assist in the management of herbicide resistance. The efficacy of Gulliver® on barnyard grasses (*Echinichloa* spp) will provide an alternative mode of action on barnyard grasses to the two main herbicide groups used for barnyard grasses in rice, either by the use of Gulliver® in the same season as another grass herbicide, to provide a second mode of action, or alternating herbicides with different modes of action between seasons. This will enhance the recommended programs for the control of barnyard grasses and the management of the potential development of herbicide resistance in barnyard grasses in rice fields.

The modes of action of the Gulliver®/MCPA tank mix on aquatic weeds provides the two modes of action recommended by the Rice Weed Management Working Group for the management of herbicide resistance in aquatic weeds in rice.

In addition, the availability of Gulliver® will widen the application window for the control of barnyard grasses. Herbicides currently registered for the control of barnyard grasses in rice are generally restricted to application in the presow up to 3 or 4 leaf weed stage. The availability of the Gulliver®/MCPA tank mix will extend this application window up to the 4 tiller stage of the barnyard grass weeds. This will provide greater flexibility of weed control programs, particularly when conditions result in poor barnyard grass control in the earlier application window of currently used herbicide programs.

There is more than adequate justification for the registration of this proposed product label. The availability of this product will provide potential benefits to the NSW rice industry.

Adequacy of efficacy data.

Adequacy of efficacy data as it relates to:

- **Trial design in relation to provision of controls, treatment group size, number of replicates, age and type of animal, plant varieties and stage of growth etc:** The design of the trials, number of replicates, provision of controls, treatment group size and treatment stages of growth were satisfactory. The trial data listed covered the main varieties.
- **Experimental conditions in relation to relevant variables, such as pest/disease pressure, weather conditions, soil type etc:**
  The trials covered a satisfactory range of weather, soil, and weed environments.
- **Analysis of trial data and its interpretation, including efficacy relative to dose/application rate and application/administration:** The analysis of the trial data and it interpretation were generally satisfactory.
- **Trial validation with respect to the person responsible for the trial, location of the trial, date of trial:** The personnel/companies responsible for the experimental work and the trial locations are experienced in this work and is well accepted.

- **General applicability of the trial data to the use of the candidate preparation under commercial conditions:** In general the trial data can be applied to commercial conditions.

Claims

In general the efficacy data supports the label claims proposed for the use of Gulliver® Herbicide.

Safety to Target and Non-Target Species including adequacy of precautionary advice.

- **Target Crop Safety.** Crop phytotoxicity has been observed as transient crop yellowing and growth retardation. The data supports the view that this phytotoxicity is within acceptable limits, is transient and likely to have no significant affect on yields. The effects may be due to the Gulliver® and/or the MCPA. In the 32 crops treated with the Gulliver®/MCPA mix in the 2002/03 rice season only minimal crop damage was observed, attributable to MCPA.

  Crop phytotoxicity is not seen to be an issue. The precautionary advice is accepted as adequate.

- **Non-Target Damage**. Gulliver® is active at low concentrations and may damage non-target crops. Precautionary advice to avoid drift and not to sow treated fields to other crops within 7 months of application is considered adequate. The data provided on the re-cropping study was minimal, but as significant, minor effects were only observed at 3X the commercial rate the recommendation is **accepted**.

Conclusion.

The proposed Gulliver® label claims have generally been shown to provide acceptable control of the weed species of rice listed in the Direction for Use and acceptable crop safety within the conditions and limitations outlined**.** It is recommended that on the basis of efficacy and crop safety Gulliver® Herbicide be considered for registration.

Labelling Requirements

READ SAFETY DIRECTIONS BEFORE
OPENING OR USING

DuPont™
Gulliver®
herbicide

ACTIVE CONSTITUENT: 500 G/KG AZIMSULFURON

GROUP **B** HERBICIDE

For the control of certain Aquatic broadleaf weeds, and suppression of Barnyard grass in rice as per Directions for Use.

IMPORTANT:
READ THE ATTACHED LEAFLET BEFORE USE

Net Contents 500 g

DUPONT®
The miracles of science™

STORAGE AND DISPOSAL

KEEP OUT OF REACH OF CHILDREN.

Store in the closed, original container in a dry, well-ventilated area, as cool as possible out of direct sunlight. Store in a locked room or place away from children, animals, food, foodstuffs, seed and fertilisers. Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. **DO NOT** dispose of undiluted chemical 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 and skin. Avoid contact with eyes and skin. Wash hands after use. 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. When using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing). After each day's use wash gloves, face shield or goggles and contaminated clothing.

FIRST AID

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26.

IN A MEDICAL EMERGENCY CALL
1800 674 415 All hours

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet.

NOTICE TO BUYER

To the extent permitted by law all conditions and warranties and statutory or other rights of action which buyer or any other user may have against DuPont or Seller are hereby excluded. DuPont hereby gives notice to buyer and other users that it will not accept responsibility for any indirect or consequential loss arising from reliance on product information or advice provided by DuPont or on its behalf unless it is established that such information or advice was provided negligently and that the product has been used strictly as directed. DuPont's liability shall in all circumstances be limited to replacement of the product or a refund of the purchase price paid therefore.

Batch No.

DOM:

APVMA Approval No: 56017/500/

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Du Pont (Australia) Ltd
A.C.N. 000 716 469
168 Walker Street
North Sydney NSW 2060
(02) 9923 6111 or 1800 257 169
http://www.dupont.com.au/ag/

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

DuPont™ Gulliver®

herbicide

ACTIVE CONSTITUENT: 500 G/KG AZIMSULFURON

GROUP **B** HERBICIDE

For the control of certain Aquatic broadleaf weeds, and suppression of Barnyard grass in rice as per Directions for Use.

IMPORTANT:
READ THIS LEAFLET BEFORE USE

Net Contents 500 g

DUPONT®
The miracles of science™

DIRECTIONS FOR USE

NSW and Vic Only

RESTRAINTS

DO NOT apply to crops under stress (Refer to Crop Safety Section for details).
DO NOT apply if rain is likely within 6 hours.
DO NOT use on drill sown rice (combine seeding or sod seeding).
DO NOT apply directly into floodwater, as in the SCWIIRT (Soluble Chemical in Water Injection Into Rice Technique) or the aerial Bickley boom techniques. Apply only as a foliar spray.
DO NOT store DuPont Gulliver® herbicide suspensions for more than 2 days.
DO NOT store tank mixes of Gulliver®.

CROP	**WEEDS CONTROLLED**	WEED STAGE	**RATE/ha**	**CRITICAL COMMENTS**
Rice (4 to 5 leaf up to 4 stems or shoots)	Barnyard grass (*Echinochloa* spp.) – suppression only	4 leaf to 4 stems or shoots	40 g + 1.6 L - 2.7 L MCPA (250 g/L sodium & potassium salt) (such as Nufarm MCPA 250 Selective Herbicide) + non-ionic surfactant	For population and resistance management, always apply an alternate mode of action grass herbicide as a pre or at sowing treatment.
	Alisma (seedlings) (*Alisma lanceolatum*)	4 to 6 leaves		**Always** mix with MCPA (250 g/L sodium salt) and add a non-ionic surfactant (see USE OF SURFACTANT/ WETTING AGENT section). For rice, use 1.6 L MCPA 250 at 4 to 5 leaf stage, and 2.7 L MCPA 250 at 1 to 3 tillers. If resistance to Group B herbicides is suspected use 2.7 L MCPA 250 on tillered rice. Foliar apply to crop and weeds where water has been lowered to expose the weed foliage to the spray. **Important** see WATER MANAGEMENT section for managing water levels before and after treatment. Observe local laws and regulations relating to water management in **rice growing areas.**
	Arrowhead (*Sagittaria montevidensis*)	4 to 8 leaves		
	Dirty Dora (*Cyperus difformis*)	3 to 6 leaves		
	Spikerush (*Eleocharis acuta*)			
	Starfruit (*Damasonium minus*)	4 leaf to bolting		
	Water Plantain (seedlings) (*Alisma plantago-aquatica*)	4 to 6 leaves		

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

WITHHOLDING PERIODS
RICE HARVEST: NOT REQUIRED WHEN USED AS DIRECTED.
GRAZING / STOCK FOOD: DO NOT GRAZE OR CUT FOR STOCK FOOD FOR 2 WEEKS AFTER APPLICATION.

GENERAL INSTRUCTIONS

DuPont™ Gulliver® herbicide is a dry flowable herbicide used for early post emergence control of Barnyard grass, certain aquatic broadleaf and sedge weeds in rice. Application of Gulliver® should target small actively growing weeds. **Subsequent weed germinations will not be controlled.**

CROP SAFETY

DO NOT apply to crops that are stressed by any cause (such as severe weather conditions, excessive water salinity, soil acidity or alkalinity, poor nutrient status, disease or insect damage) as crop injury may result. When treatment is followed by severe stress, crop yellowing or growth retardation may occur. Crops normally recover without loss in yield.

WATER MANAGEMENT

Proper water management is essential for maximum weed control with DuPont Gulliver® herbicide. Before herbicide application, ensure that water levels are lowered in the bays and at least three-quarters of the weed growth exposed (on the low side of the bay) enabling direct foliar contact by the spray. Water depth should be no more than 1 - 2 cm deep (on the low side of the bay), or at least the soil should be kept saturated. **DO NOT** allow the soil to dry out. Weeds covered by water may not be controlled. For ground application, the presence of water can result in a “wash” from the vehicle that will reduce efficacy.

Commence raising water levels 12 - 24 hours following spraying. Reach permanent water levels within 2 days.

Water from treated paddys must be kept in the rice paddy after application.
DO NOT drain water from Gulliver® treated paddys into regional drains, or local waterways or systems for 28 days, or for the period set by the local irrigation Authority and/or State governmental Agency, which ever is the greater.

RESISTANT WEEDS WARNING **GROUP B HERBICIDE**

DuPont™ Gulliver® herbicide is a member of the sulfonylurea group of herbicides. Gulliver® has the ALS inhibitor mode of action. For weed resistance management Gulliver® is a Group B herbicide, and should always be mixed with MCPA (250 g/L sodium & potassium salt) a Group I herbicide.

Some naturally occurring weed biotypes resistant to one or both of the modes of action of Gulliver®, MCPA or other ALS inhibitor and disruptors-of-plant-cell-growth herbicides may exist through normal genetic variability in any weed population. The resistant individuals can eventually dominate the weed population if these herbicides are used repeatedly. These resistant weeds will not be controlled by either Gulliver® or MCPA, and other Group B and Group I herbicides.

Since the occurrence of resistant weeds is difficult to detect prior to use, Du Pont (Australia) Limited accepts no liability for any losses that may result from the failure of Gulliver® or MCPA to control resistant weeds.

Strategies to minimise the risk of herbicide resistance are available. Consult your farm chemical supplier, consultants, local Department of Agriculture or Primary Industries, or local DuPont representative.

SPRAY PREPARATION
DuPont™ Gulliver® herbicide is a dry flowable formulation to be mixed with water and applied as a foliar spray. Partially fill the tank with water. Measure the amount of Gulliver® required for the area to be sprayed. Add the correct amount of Gulliver® to the spray tank with the agitation system engaged. Top up to the correct volume of water. THE MATERIAL MUST BE KEPT IN SUSPENSION AT ALL TIMES BY CONTINUOUS AGITATION.

Gulliver® must be in suspension before adding MCPA 250, other companion herbicides or non-ionic surfactant.

SURFACTANT/WETTING AGENT
Always add a non-ionic surfactant (1000 gai/L) at 100 mL/100 L of final spray volume (0.1% volume/volume).

COMPATIBILITY
DuPont™ Gulliver® herbicide is compatible with the herbicide, Londax®.

APPLICATION INSTRUCTIONS
Avoid spraying in still conditions and in winds likely to cause drift onto adjacent sensitive crops. Turn off application equipment whilst passing over irrigation channels, creeks and dams.

DO NOT apply when a temperature inversion is likely to occur.

Ground Spraying: Use a boom properly calibrated to a constant speed and rate of delivery to ensure thorough coverage and a uniform spray pattern. Avoid overlapping and shut off spray booms while starting, turning, slowing or stopping as injury to crop may result. Apply a minimum of 120 L water /ha.

Aerial Spraying: Apply in a minimum of 40 L water /ha using a medium spray quality (VMD droplet size of 250 - 350 μm. Use of Micronaire* equipment is **not recommended** due to greater drift potential.

Sprayer Cleanup
To avoid subsequent injury to crops immediately after spraying thoroughly remove all traces of DuPont™ Gulliver® herbicide from mixing and spray equipment as follows:

1. Immediately after spraying, drain tank completely. Any contamination on the outside of the spraying equipment should be removed by washing with clean water.

2. Rinse inside of tank with clean water and flush through boom and hoses using at least one-tenth of the spray tank volume. Drain tank completely.

3. Half fill tank with clean water adding household ammonia to give a 1% solution (equivalent ratios include 1/3 litre household ammonia product (containing 9.5% ammonia) for each 100 litres of tank volume. Agitate, and then flush the boom and hoses with the cleansing solution. Top up with water making sure the tank is completely full and allow to stand for 15 minutes with agitation engaged. Again flush the boom and hoses and drain tank completely.

4. Nozzles and screens should be removed and cleaned separately with ammonia solution at the same concentration as used for the sprayer.

5. Rinse the tank with clean water and flush through boom and hoses using at least one-tenth of the spray tank volume. Drain tank completely.

6. **DO NOT** spray the tank rinsate onto sensitive crops or land intended for cropping with sensitive crops.

NOTE: If not possible to drain the tank completely, step 3 must be repeated before going on to step 4.

PRECAUTION

DO NOT use human flaggers/markers unless they are protected by engineering controls such as enclosed cabs.

PROTECTION OF CROP, NATIVE AND OTHER NON-TARGET PLANTS

Injury to or loss of desirable trees or vegetation may result from failure to observe the following.

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

DO NOT apply unless there is a downwind buffer distance (200 m by air, or 20 m by ground) between the treated area and sensitive crops, native and other non-target vegetation. As DuPont™ Gulliver® herbicide is applied in combination with MCPA, avoid spray drift onto susceptible crops such as cotton, tobacco, tomatoes, vegetables, vines, lucerne, legume crops/pastures, oil seed crops, lupins, fruit trees, ornamentals and trees (such as Kurrajong and Belah).

DO NOT apply irrigation tail waters to crops other than rice.

DO NOT apply or drain or flush equipment on or near desirable trees or other plants or on areas where their roots may extend or in locations where the chemical may be washed or moved into contact with their roots.

DO NOT sow Gulliver® treated paddies to any other crop for seven (7) months following Gulliver® application, as crop injury may result.

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

HIGHLY TOXIC TO ALGAE AND AQUATIC PLANTS

DO NOT apply unless there is a 50 m downwind buffer distance between the treated area and nearby ponds, streams, lakes, rivers or waterways.

DO NOT contaminate any off-target body of water (e.g. ponds, streams, lakes, rivers or waterways) by spraying, spray drift, cleaning of equipment or disposal of waste (including used containers). **DO NOT** drain rice field water into regional drains for 28 days, or for the period set by the local irrigation Authority and/or State governmental Agency, which ever is the greater.

STORAGE AND DISPOSAL

KEEP OUT OF REACH OF CHILDREN.

Store in the closed, original container in a dry, well-ventilated area, as cool as possible out of direct sunlight. Store in a locked room or place away from children, animals, food, foodstuffs, seed and fertilisers. Triple or preferably pressure rinse containers before disposal. Add rinsings to spray tank. **DO NOT** dispose of undiluted chemical 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 and skin. Avoid contact with eyes and skin. Wash hands after use. 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. When using the prepared spray, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing). After each day's use wash gloves, face shield or goggles and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26.

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MATERIAL SAFETY DATA SHEET
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NOTICE TO BUYER
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APVMA Approval No: 56017/

A00621483/06-06SAP CODE

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Du Pont (Australia) Ltd
A.C.N. 000 716 469
168 Walker Street
North Sydney NSW 2060
(02) 9923 6111 or 1800 257 169
http://www.dupont.com.au/ag/

Glossary

active constituent	The substance that is primarily responsible for the effect produced by a chemical product
acute	Having rapid onset and of short duration
carcinogenicity	The ability to cause cancer
chronic	Of long duration
Codex MRL	Internationally published standard maximum residue limit
desorption	Removal of an absorbed material from a surface
efficacy	Production of the desired effect
formulation	A combination of both active and inactive constituents to form the end use product
genotoxicity	The ability to damage genetic material
hydrophobic	Water repelling
leaching	Removal of a compound by use of a solvent
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient
metabolism	The conversion of food into energy
photodegradation	Breakdown of chemicals due to the action of light
photolysis	Breakdown of chemicals due to the action of light
subcutaneous	Under the skin
toxicokinetics	The study of the movement of toxins through the body
toxicology	The study of the nature and effects of poisons

References

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

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