Public Release Summary
on

Evaluation of the new active

TRIFLOXYSULFURON SODIUM

in the product

ENVOKE HERBICIDE

National Registration Authority for Agricultural and Veterinary Chemicals

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FOREWORD

The National Registration Authority for Agricultural and Veterinary Chemicals (NRA) is an independent statutory authority with responsibility for assessing and approving agricultural and veterinary chemical products prior to their sale and use in Australia.

In undertaking this task, the NRA works in close cooperation with advisory agencies, including the Department of Health and Ageing (Chemicals and Non-prescription Medicines Branch), Environment Australia (Risk Assessment and Policy Section), the National Occupational Health and Safety Commission (NOHSC)) and State departments of agriculture and environment.

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

The information and technical data required by the NRA to assess the safety of new chemical products and the methods of assessment must be undertaken according to accepted scientific principles. Details are outlined in the NRA's publications *Ag Manual: The Requirements Manual for Agricultural Chemicals* and *Ag Requirements Series.*

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

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

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

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LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
ARfD	Acute Reference Dose
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
d	day
DAT	Days After Treatment
DT_{50}	Time taken for 50% of the concentration to dissipate
EA	Environment Australia
ECD	Electron capture detection
E_bC_{50}	concentration at which the bio mass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
ESI-MS	Electro spray ionisation mass selection
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GC	Gas chromatography
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
K_{oc}	Organic carbon partitioning coefficient
L	Litre
LC_{50}	concentration that kills 50% of the test population of organisms
LD_{50}	dosage of chemical that kills 50% of the test population of organisms
LOD	Limit of Detection – level at which residues can be detected
LOQ	Limit of Quantitation – level at which residues can be quantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
NEDI	National Estimated Daily Intake
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration/Level

OC	Organic Carbon
OM	Organic Matter
PHI	Pre-Harvest Interval
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
SPE	Solid Phase Extraction
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
TRR	Total Radioactive Residues
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
mg	microgram
uv	Ultra violet
vmd	volume median diameter
WG	Water Dispersible Granule
WHO	World Health Organisation
WHP	Withholding Period

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INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of ENVOKE HERBICIDE which contains the new active ingredient, trifloxysulfuron sodium.

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

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

Written comments should be submitted by 23 September 2002 and addressed to:

Ranjit Gajanayake
Agricultural Chemicals Evaluation Section
National Registration Authority
PO Box E240
Kingston ACT 2604

Applicant
Syngenta Crop Protection Pty Ltd

Product Details
It is proposed to register ENVOKE HERBICIDE containing 750g/kg trifloxysulfuron sodium as a water dispersible granule formulation for use on cotton in NSW, Qld and WA. The active constituent trifloxysulfuron sodium and the product ENVOKE HERBICIDE are manufactured overseas and will be imported fully packaged into Australia. It will be packaged in 100g, 500g, 1kg containers.

Trifloxysulfuron sodium is a novel sulfonylurea herbicide which acts by inhibiting biosynthesis of essential amino acids valine and isoleucine (ALS inhibitor). It is exempt from poisons scheduling.

ENVOKE HERBICIDE is a member of the sulfonylurea group of herbicides. For weed resistance management this product is a group **B** herbicide.

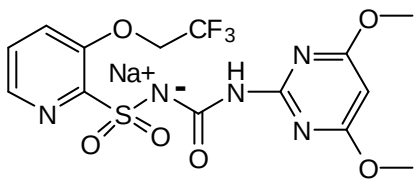
ENVOKE HERBICIDE has been developed as a selective herbicide for the control of a selected range of broadleaf weeds and nutgrass in cotton. This product will give the cotton grower, early season, post-emergence, over the top control of broadleaf weeds which remains a problem in cotton production. The product is currently being evaluated for registration in a number of other countries.

CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent trifloxysulfuron sodium is manufactured at Syngenta Crop Protection AG Monthey Switzerland and is pending approval by the NRA.

Chemical Characteristics of the Active Constituent

Common name:	Trifloxysulfuron sodium (ISO/SA approved)
Synonyms and code number:	CGA 362622
Chemical name:	1-(4,6-dimethoxypyrimidin-2-yl)-3-[3-(2,2,2-trifluoroethoxy)-2-pyridylsulfonyl] urea sodium salt (IUPAC) *N*-[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(2,2,2-trifluoroethoxy)-2-pyridinesulfonamide sodium salt (CAS)
CAS Number:	199119-58-9
Molecular formula:	$C_{14}H_{13}F_3N_5O_6SNa$
Molecular weight:	459.3
Chemical structure:	

Physical and Chemical Properties of Active Constituent

Physical state:	solid, fine powder	
Colour:	white	
Odour:	odourless	
Melting point:	170.2-177.7 °C with thermal decomposition	
Solubility in water at 25 °C:	pH.7.4:.25.7g/L pH 5.4: 102.5 mg/L pH 7.6: 25.5 g/L pH 8.1: 25.5 g/L	
Solubility in organic solvents at 25 °C:	Acetone:	17 g/L
	Dichloromethane:	790 mg/L
	Ethyl acetate:	3.8 g/L
	Hexane:	<1 mg/L
	Methanol:	50 g/L
	Octanol:	4.4 g/L
	Toluene:	<1 mg/L

Vapour pressure at 25 °C:	$<1.3\times10^{-6}$ Pa
Density/specific gravity:	1.63 g/mL
Octanol/water.partition coefficient:	pH 5.0: log P_{ow}=1.4 pH 7.0: log P_{ow}=-0.42 pH 9.1: log P_{ow}=-1.6
Surface tension – 1 g/L solution:	65.8 mN/m
pH – 1% solution in water:	8.9
Dissociation constant in water:	pK_a=4.76 at 20 °C
Henry's Law constant (mean):	2.6×10^{-5} m^3/mol
Corrosive Hazard:	non-corrosive to tin plate, galvanised sheet metal, iron steel and stainless steel
Flammability:	not highly flammable
Explosive properties:	not explosive
Oxidising properties:	not an oxidising substance
Self-ignition:	no self-ignition
Stability:	2 years at 30 °C
Chemical type:	herbicide
Chemical family:	sulfonylurea

Summary of the NRA's Evaluation of Trifloxysulfuron sodium active constituent

The Chemistry and Residues Evaluation Section of the NRA has evaluated the chemistry aspects of trifloxysulfuron sodium (manufacturing process, quality control procedures, batch analysis results and analytical methods) and they are acceptable. On the basis of the data provided it is proposed that the following minimum compositional standard be established for trifloxysulfuron sodium:

Active constituent

Trifloxysulfuron sodium	Not less than 890 g/kg

Product

Distinguishing name:	Envoke Herbicide
Formulation type:	Water dispersible granule
Active.constituent concentration:	750 g/kg

Physical and Chemical Properties of the Product

Physical state:	solid, granules
Colour:	grey beige
Odour:	weak phenolic odour
Bulk density:	0.645 g/cm^3
pH (1% solution):	9.7
Flammability:	Not highly flammable
Corrosive habit:	non-corrosive to tin plate, galvanised sheet metal, iron steel or stainless steel
Oxidising properties:	not an oxidising substance
Explosive properties:	not explosive
Storage stability:	2 years at ambient temperatures

Conclusion

Based on an assessment of chemistry and manufacturing details provided by the applicant, the NRA is satisfied that ENVOKE HERBICIDE will be manufactured to consistent specifications using sources of actives approved by the NRA and will be stable for a minimum of two years

TOXICOLOGICAL ASSESSMENT

Evaluation of Toxicology

The toxicological database for trifloxysulfuron, 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.

Following oral gavage administration in rats trifloxysulfuron was almost completely absorbed and excreted in urine and bile within 48 hours. Less than 0.3% of an orally administered radiolabelled dose was found in tissues seven days later, with blood, liver and kidneys containing the highest amounts of residual radioactivity. O-demethylation, hydroxylation of the pyrimidine ring and rearrangement of the sulfonylurea, were major pathways of metabolism with hydrolysis of the sulfonylurea, oxidative O-deethylation and glucuronide and sulfate conjugation being minor pathways of metabolism. Unmetabolised parent compound found in urine accounted for up to 50% of the administered dose, whereas it represented only up to 3% in bile. Renal excretion was the predominant route of elimination with females (70-80% of dose) excreting more radioactivity in the urine than males (50-60% of dose). The kinetics were similar after a low (0.5 mg/kg bw) or high (100 mg/kg bw) dose and after repeated administration for 14 days.

Acute Studies

Trifloxysulfuron had low acute oral toxicity in both rats and mice (LD_{50} >5000 mg/kg bw) and low acute dermal (LD_{50} >5000 mg/kg bw) and inhalation (LC_{50} >5030 mg/m^3) toxicity in rats. It was a moderate eye irritant but was not a skin irritant in rabbits or a skin sensitiser in guinea pigs.

ENVOKE HERBICIDE had low acute oral (LD_{50} >5000 mg/kg bw), dermal (LD_{50} >2000 mg/kg bw) and inhalation (LC_{50} >2550 mg/m^3) toxicity in rats, was a slight eye and skin irritant in rabbits, and may have slight potential to be a skin sensitiser in guinea pigs.

Short Term Studies

Trifloxysulfuron applied to the skin of rats at doses of 0, 10, 100 or 1000 mg/kg bw/day for 28 days did not result in any deaths, abnormal clinical signs, skin irritation, changes in food consumption, macroscopic changes or microscopic lesions attributable to treatment. Body

weight gain was lower in females at 1000 mg/kg/day and haemoglobin and phosphate were slightly lower in males at 1000 mg/kg bw/day. Thymus weights were lower in males at 100 and 1000 mg/kg bw/day and in females at 1000 mg/kg bw/day.

All rats fed trifloxysulfuron at dietary concentrations of 0, 1000, 4000, 12 000 or 20 000 ppm for 28 days survived. There were no abnormal clinical signs, changes in water consumption, changes in body weight or gross morphology. Food consumption was slightly lower in females at 20 000 ppm. Haemoglobin, haematocrit and eosinophil count were lower at 20 000 ppm. Prothrombin time was lower in males at ≥ 4000 ppm. Total bilirubin and plasma AST were lower and cholesterol was elevated at 12 000 and 20 000 ppm. Plasma phosphate was lower at 20 000 ppm and plasma total protein, albumin, globulin and albumin/globulin ratio were slightly elevated in males at 20 000 ppm. Liver weight was higher in males at ≥ 4000 ppm and in females at 20 000 ppm and thymus weights were lower at 20 000 ppm. Hepatocellular hypertrophy was observed at ≥ 4000 ppm with cytoplasmic vacuolation and necrosis observed in males at 20 000 ppm.

Dogs were given trifloxysulfuron at doses of 0, 50, 200 or 500 mg/kg bw/day in gelatin capsules for 28 days. There were no mortalities, changes in food consumption, clinical signs of toxicity or effects on body weight gain. A white material in the faeces of animals at 500 mg/kg bw/day was confirmed by analysis to be the test material. Red blood cell count, haematocrit, haemoglobin, platelet counts and clotting times, plasma bilirubin, protein and albumin were lower and globulin and chloride were higher in both sexes at 500 mg/kg bw/day. Plasma bilirubin was also lower in females at 200 mg/kg bw/day and plasma potassium and calcium were lower in males at 500 mg/kg bw/day. Liver weights were higher in both sexes at 200 and 500 mg/kg bw/day. Thymus weights were marginally lower with one of two males and one of two females at 500 mg/kg bw/day having slight cortical atrophy in the thymus. Testes weight was lower in one of the two males at 500 mg/kg bw/day along with markedly reduced spermatogenesis and some single cell necrosis of tubular cells. This male also had slight follicular hypertrophy in the thyroid. Spleen weights were higher in females at 500 mg/kg bw/day with lymphoid hyperplasia observed in the spleen of males at 200 and 500 mg/kg bw/day and females at all doses. Pneumonia was observed in dogs at 500 mg/kg bw/day.

Dogs were fed trifloxysulfuron at dietary concentrations of 15 000 or 30 000 ppm for 28 days and mean daily test substance intakes were calculated as 343 and 312 (15 000 ppm) and 470 and 457 mg/kg bw/day (30 000 ppm) for males and females respectively. Animals at 30 000 ppm were sacrificed early after showing signs of severe toxicity. Clinical signs included recumbency, weakness of hind limbs, hunched posture, reduced activity, limping and vomiting. These clinical signs were less severe and transient at 15 000 ppm. In neurological examinations at week 2, slightly reduced motility, muscle coordination and muscle tone were observed in males at 30 000 ppm and motility and muscle coordination were slightly reduced in females at 15 000 ppm. Food consumption was almost halved at 30 000 ppm compared to pre-test levels and both sexes had body weight losses. At 15 000 ppm, one female showed slightly reduced food consumption and body weight loss. Compared with pre-test values, red blood cell count, haemoglobin and haematocrit, platelet, neutrophil and eosinophil counts were lower and monocyte and large unstained cell counts were higher in both sexes at both doses. Liver weights were higher and bile duct hyperplasia associated with lymphohistiocytic infiltration was observed in the liver of one female at 15 000 ppm and all animals at 30 000 ppm with some necrosis in one animal of each sex at 30 000 ppm. Spleen weights were higher with lymphoid follicular hyperplasia in the spleen at both doses. Thymus weights were

slightly lower at both doses with slight cortical atrophy in the thymus of all animals. Enlarged cervical lymph nodes with chronic reactive hyperplasia and red popliteal lymph nodes were observed at 30 000. Inflammation, lymphocytic infiltration or pneumonia in the lung and lymphocytic infiltration of the renal parenchyma were found at both doses. Bilateral reduced spermatogenesis at 15 000 ppm and 30 000 ppm was associated with impaction, tubular atrophy and giant spermatic cells.

Subchronic Studies

In mice fed trifloxysulfuron at dietary concentrations of 0, 100, 500, 1750, 3500 or 7000 ppm for 90 days, no treatment-related changes in mortality, clinical signs, food consumption, body weight gain, haematology or gross morphology were observed. Bilirubin was lower at ≥ 1750 ppm. Liver weight was slightly higher in males at 7000 ppm and in females at 3500 and 7000 ppm. Thymus weight was slightly lower in males at 3500 and 7000 ppm. There was a slight increase in the incidence of cytoplasmic vacuolation in the liver of males at 3500 and 7000 ppm and a slight increase in the incidence of ceroid deposition in the adrenal gland of females at 7000 ppm. Based on lower bilirubin observed in mice at ≥1750 ppm, the NOEL in this study was 500 ppm, equal to 68 mg/kg bw/day in males and 102 mg/kg bw/day in females.

In rats fed trifloxysulfuron at dietary concentrations of 0, 1000, 4000, 8000 or 16 000 ppm for 13 weeks, no treatment-related changes in mortality, clinical signs, water consumption or ophthalmology were observed. Body weight gain was lower at 16 000 ppm and was associated with a transient reduction in food consumption. MCH and haemoglobin were slightly lower and platelet count slightly higher in females at 16 000 ppm and prothrombin time was lower at 16 000 ppm. Urea was higher in females at ≥ 8000 ppm and protein, albumin and globulin slightly higher in males at 16 000 ppm and females at ≥ 4000 ppm. Although cholesterol was higher in males at 16 000 ppm triglycerides were lower. Urinary pH was slightly lower at 16 000 ppm. Liver weight was increased in both sexes at 16 000 ppm and hepatocellular hypertrophy was observed in females at ≥ 4000 ppm and in males at ≥ 8000 ppm with single cell necrosis observed in females at 16 000 ppm. A slight increase in the incidence of cholangiofibrosis was observed after the recovery period in males at 16 000 ppm. A higher incidence of small testes associated with lower testes weight and an increased severity of tubular atrophy were observed after the recovery period in males at 16 000 ppm. Based on liver histopathology at ≥ 4000 ppm, the NOEL in this study was 1000 ppm, equal to 66 mg/kg bw/day for males and 76 mg/kg bw/day for females.

Dogs were fed trifloxysulfuron at dietary concentrations of 0, 50, 500, 5000, 10 000 or 20 000 ppm for 90 days. Animals at 20 000 ppm were sacrificed early since all had markedly reduced food consumption, body weight losses and non-specific signs of severe toxicity. Neurological investigations showed no differences between control and treated groups. Food consumption and bodyweight gains were lower in males at ≥ 10 000 ppm and in females at ≥ 5000 ppm. Red blood cell count, haemoglobin, haematocrit and platelet counts were lower in females at 5000 ppm and both sexes at 10 000 and 20 000 ppm. White blood cell counts were lower in both sexes at ≥ 5000 ppm and were characterised by a higher number of large unstained cells and lower numbers of eosinpohils, neutrophils and lymphocytes. Plasma calcium, total bilirubin, albumin and albumin to globulin ratio were lower and plasma chloride and globulin were higher in both sexes at ≥ 5000 ppm. Plasma potassium was slightly lower in males and plasma phosphate was slightly higher in females at 20 000 ppm. The incidence of yellow-

brown discoloured urine was higher at week 8 in both sexes at 20 000 ppm, possibly related to higher bilirubin, urobilinogen and erythrocytes in urine at this time. Urinary pH was slightly lower in females at 5000 and 10 000 ppm and in both sexes at 20 000 ppm. Livers were larger at 20 000 ppm and liver weights were higher in both sexes at 5000 and 10 000 ppm. Extramedullary haematopoiesis was observed in the liver in females at ≥ 5000 ppm and 1/4 males at 20 000 ppm and glycogen deposition was increased in the liver of both sexes at ≥ 5000 ppm. Mottled kidneys were observed at 20 000 ppm with hyaline changes in the kidney tubules in males at ≥ 10 000 ppm and in females at ≥ 5000 ppm. Thymus weights were lower in both sexes at 5000 and 10 000 ppm with the incidence and/or severity of atrophy of the thymus increased in both sexes at ≥ 5000 ppm. Spleens were larger and heavier in females at 5000 and 10 000 ppm. Myeloid hyperplasia of the bone marrow was observed in females at ≥ 5000 ppm and in males at 20 000 ppm. Large mesenteric lymph nodes with suppuration and an increased severity of haemorrhage were observed in both sexes at ≥ 5000 ppm. Red popliteal lymph nodes were observed with haemorrhage and haemosiderosis in males at 20 000 ppm and chronic reactive hyperplasia in females at 20 000 ppm. Small testes was observed in one male at 10 000 ppm and testes weights were lower at 5000 and 10 000 ppm with reduced spermatogenesis observed in all males at ≥ 10 000 ppm and one at 5000 ppm. Prostatic atrophy was observed in one male at 5000 and 10 000 ppm and all males at 20 000 ppm. Masses on the heart, mottled lung and red small intestine were also observed at necropsy. The NOEL in this study was 500 ppm, equal to 19.8 mg/kg bw/day in males and 19.6 mg/kg bw/day in females.

Chronic/Oncogenicity Studies

Mice were fed trifloxysulfuron at dietary concentrations of 0, 50, 200, 1000 or 7000 ppm for 18 months. There were no treatment-related changes in survival, clinical signs, gross morphology or organ weights. Food consumption and body weight gain were lower in females at 7000 ppm. Red blood cell counts, haemoglobin and haematocrit were slightly lower in males at 7000 ppm. There were no histological changes related to treatment and the incidence and time of occurrence of neoplasms was similar in control and treated groups. The NOEL in this study was 1000 ppm, equal to 121 mg/kg bw/day in males and 112 mg/kg bw/day in females.

Rats were fed trifloxysulfuron at dietary concentrations of 0, 50, 500, 2000 or 10 000 ppm for 24 months. There were no treatment-related changes in survival, clinical signs, water consumption, ophthalmology, gross morphology or organ weights. Food consumption and body weight gains were lower in both sexes at 10 000 ppm. MCH and MCV were lower throughout the study in females at 10 000 ppm. The incidence of flaccid testes and Leydig cell hyperplasia was higher at 2000 and 10 000 ppm and relative testes weights were higher at 10 000 ppm. The incidence of uterine and liver cysts was higher in females at 10 000 ppm. The incidence of kidney tubule atrophy was higher in females at 2000 and 10 000 ppm. The NOEL in this study was 500 ppm, equal to 20.2 mg/kg bw/day for males and 23.7 mg/kg bw/day for females.

Dogs were fed trifloxysulfuron at dietary concentrations of 0, 50, 200, 500, 1500 or 4000 ppm for 12 months. There were no deaths and clinical signs, food consumption, eye and neurological examinations and urine parameters were similar in control and treated groups. Lower body weight gain was seen in males at 1500 and 4000 ppm. Slightly lower red blood cell count, haemoglobin and haematocrit were observed in both sexes at 4000 ppm. Total bilirubin was lower in both sexes at 1500 and 4000 ppm and albumin, albumin to globulin

ratio and calcium were lower at 4000 ppm. Plasma AST was higher in males at 4000 ppm. Liver weights were higher in females at 1500 and 4000 ppm. Thymus weights were lower and the severity of thymic atrophy was increased at 1500 ppm and 4000 ppm in males and at 4000 ppm in females. All males at 4000 ppm had a fibrous thickening of the pleura correlating with gray white foci or nodules observed on the lung at necropsy. The NOEL in this study was 500 ppm, equal to 15.0 mg/kg bw/day in males and 14.9 mg/kg bw/day in females.

Reproduction Study

Rats were fed trifloxysulfuron at dietary concentrations of 0, 500, 1000, 8000 or 12 000 ppm for 10 weeks prior to mating, during the mating period and until sacrifice. There were no adult mortalities and no clinical signs related to treatment in any generation. At 8000 and 12 000 ppm, food consumption and body weight gain were lower at most stages in adults and pups at 8000 and 12 000 ppm. In F_0 and F_1 adults liver weights were higher at 8000 and 12 000 ppm with a higher incidence of hepatocellular hypertrophy. Spleen and thymus weights were generally lower in F_1 and F_2 pups and adults at 8000 and 12 000 ppm. There were no necropsy observations related to treatment and no histopathological observations in reproductive organs. Vaginal opening in F_1 females at 8000 and 12 000 ppm was slightly delayed, consistent with the lower body weights observed in these groups. All other reproductive parameters were similar in control and treated groups. There were no effects on reproduction at the highest dose tested. The NOEL for general toxicity was 1000 ppm, equal to 83.4 mg/kg bw/day.

Developmental Studies

Trifloxysulfuron was given to pregnant rats by oral gavage at 0, 30, 300 or 1000 mg/kg bw/day on days 6 to 15 of gestation. There were no treatment-related deaths and no gross morphological findings in dams. Food consumption and body weight gain were slightly lower at 300 and 1000 mg/kg bw/day. Post-implantation losses were similar in control and treated groups. Fetal body weights were lower at 1000 mg/kg bw/day. There were no external or visceral findings in fetuses that could be attributed to treatment, but there was an increased incidence of poor, absent or irregular ossification at 300 and 1000 mg/kg bw/day. The NOEL for maternal and fetal toxicity in this study was 30 mg/kg bw/day.

Trifloxysulfuron was given to pregnant rabbits (20 per group) by oral gavage at 0, 50, 100, 250 or 1000 mg/kg bw/day on days 7-29 of gestation. Although no deaths occurred at 500 mg/kg bw/day in a dose-range finding study, all but one doe at 500 mg/kg bw/day were found dead, sacrificed moribund or sacrificed after abortion in the main study. Two does at 250 mg/kg bw/day and one at 100 mg/kg bw/day were sacrificed after spontaneous abortion. Clinical signs included bloody vaginal or ano-genital discharge, blood in the cage and pallor at doses of 250 and 500 mg/kg bw/day. Lower food consumption and body weight loss were observed in does at 500 mg/kg bw/day. Post-implantation losses, fetal sex ratios, fetal viability and fetal body weight were similar in control and treated groups. At necropsy, solid stomach contents and evidence of haemorrhage in the caecum and large intestine were observed at 500 mg/kg bw/day. Haemorrhage in the urinary bladder and uterus were also observed at 500 mg/kg bw/day. The incidence of fetal external, visceral and skeletal anomalies was similar between control and treated groups. The NOEL for maternal toxicity was 100 mg/kg bw/day and the NOEL for fetuses was 250 mg/kg bw/day.

Genotoxicity Studies

Trifloxysulfuron was not mutagenic at concentrations up to 5000 µg/plate in microorganisms or at concentrations up to 4000 µg/mL in Chinese hamster V79 cells. At concentrations up to 250 µg/mL it did not induce an increase in DNA repair activity in primary cultures of rat hepatocytes. At concentrations up to 4000 µg/mL it did not increase the frequency of chromosomal aberrations in CHO-CCL61 cells and single oral doses up to 5000 mg/kg bw did not change the ratio of polychromatic to normochromatic erythrocytes or the number of micronucleated polychromatic erythrocytes in an *in vivo* mouse micronucleus assay.

ENVOKE HERBICIDE was not mutagenic in bacteria at concentrations up to 5000 µg/plate.

Other Studies

Studies on impurities in the TGAC

NOA 451576 and NOA 452296, both impurities in the TGAC, were of low acute oral toxicity (LD_{50} >2000 mg/kg bw) in rats. NOA 447769, also an impurity in the TGAC, was not mutagenic in bacteria at concentrations up to 5000 µg/plate.

Neurotoxicity studies

In an acute oral neurotoxicity study, there were no deaths, body weight gains were not affected by treatment and there were no macroscopic findings at necropsy after treatment with trifloxysulfuron at 2000 mg/kg bw. Reduced motor activity was limited to the period 1-2 hours after dosing. There were no effects indicative of specific neurotoxicity.

After acute oral dosing with 200, 600 or 2000 mg/kg bw trifloxysulfuron, there were no mortalities, no clinical signs in treated groups and no effect of treatment on food consumption or body weight gain. Functional neurological parameters were similar in control and treated groups. Motor activity tended to be higher in males and lower in females shortly after dosing at 2000 mg/kg bw. There were no effects on motor activity at ≤ 600 mg/kg bw.

In a 90-day neurotoxicity study, rats were fed trifloxysulfuron at dietary concentrations of 0, 2000, 8000 or 16 000 ppm. There were no clinical signs, changes in the battery of functional tests, changes in motor activity, gross morphological changes or histopathological changes that could be attributed to treatment. Food consumption was lower at ≥ 2000 ppm, recovering to control levels after a few weeks at 2000 and 8000 ppm. Body weight gain and body weights were lower in males at 8000 and 16 000 ppm.

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 decided that trifloxysulfuron sodium is not required to be in a schedule of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). There are provisions for appropriate warning statements and first-aid directions on the product label.

NOEL/ADI

The 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 trifloxysulfuron was established at 0.2 mg/kg bw/day based on a NOEL of 1.5 mg/kg bw/day in a 12-month dog dietary study, and using a 100-fold safety factor in recognition of the extensive toxicological database available for trifloxysulfuron.

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.

An ARfD of 6 mg/kg bw was established using the dose (600 mg/kg bw) at which no effects were observed in an acute oral neurotoxicity study in rats, and using a safety factor of 100.

RESIDUES ASSESSMENT

The Chemistry and Residues Evaluation Section of the NRA has undertaken a residues assessment of ENVOKE HERBICIDE, a new product based on the active constituent, trifloxysulfuron sodium. Data concerning trifloxysulfuron sodium metabolism in plants and animals and residues in cotton commodities were considered as part of the residues evaluation of the product.

Metabolism

Adequate data concerning the metabolism of trifloxysulfuron sodium in cotton (target plant), other plants (sugar cane) and animals (rats, lactating goats and laying hens) were provided.

Plants: Absorption of trifloxysulfuron sodium in plants occurs rapidly and plateaus within 4 days of application. The absorbed trifloxysulfuron is immobile in plant tissues, with minimal translocation from treated tissues to untreated tissues within the same plant. Trifloxysulfuron sodium is extensively metabolised in plants, with the parent compound comprising less than 10% of the total residue in studies conducted with radio-labelled tracers. The major metabolic pathways of trifloxysulfuron sodium in plants involve Smile's rearrangement of the sulfonylurea bridge, *O*-desmethylation, oxidation of the pyrimidine ring and hydrolysis of the sulfonylurea bridge.

Animals: Following oral administration to rats, lactating goats and laying hens, trifloxysulfuron sodium undergoes rapid absorption and elimination *via* the excreta. Less than 1% of the trifloxysulfuron dose administered was associated with edible tissues, milk and eggs in lactating goats and laying hens after treatment for 4 and 8 days respectively. Trifloxysulfuron sodium residues did not accumulate in the milk of lactating goats and plateaued in egg white after 3-5 days. The residues began to plateau in egg yolk after 7-8 days. The parent trifloxysulfuron and the pyridine metabolite resulting from hydrolysis of the sulfonylurea bridge were the major residues identified in all tissues, milk and eggs of lactating goats and laying hens. The rank order for trifloxysulfuron residues in tissues from treated goats is: kidney > liver > muscle > fat. In laying hens, the rank order for trifloxysulfuron residues is liver > muscle > fat.

Analytical methods

Details were provided for the validated analytical methods used to determine trifloxysulfuron sodium residues in plant commodities (cotton commodities and sugarcane). Method details were provided for determination of trifloxysulfuron sodium residues in animal tissues, milk and eggs. The methods involve extraction of the trifloxysulfuron residues from sample matrices, followed by extensive purification procedures. Quantification of the residue was conducted by reverse phase HPLC with UV detection at 250 nm. Validation data were generated for the plant sample matrices, and the levels of recoveries from fortified samples were acceptable. The limit of quantitation (LOQ) is 0.01 mg/kg for all plant and animal commodities.

Storage stability

Stability trials showed that trifloxysulfuron sodium residues in cotton seed oil are stable for at least 5 months when samples are stored frozen. Storage stability data for animal commodities were generated in metabolism trials and showed no appreciable change in trifloxysulfuron residues in animal tissues when the samples are stored frozen for at least 8 months. The results obtained in the residue trials are considered an accurate reflection of the residues present at sampling.

Residue definition

On the basis of the results from metabolism studies, plus the availability of appropriate analytical methods for monitoring good agricultural practice, it is considered appropriate that the residue definition for trifloxysulfuron sodium remain as trifloxysulfuron *i.e.* the parent compound.

Residues

ENVOKE HERBICIDE is to be used as an early post-emergent spray for the treatment of broadleaved weeds and nutgrass in cotton. Australian and overseas residue trials were provided for cotton commodities. In Australian trials (6 trials), a single application of ENVOKE HERBICIDE (30, 37.5, 60 and 75 g ai/ha) was made to cotton at rates higher than the proposed label rate (22.5 g ai/ha). Cotton commodities (cotton seed, cotton trash) were sampled at commercial harvest (at least 60 days after application). Residues in/on cotton seed were at or about the LOQ (0.01 mg/kg) as were residues is cotton trash (LOQ 0.04 mg/kg). In overseas residues trials conducted in the USA and Argentina (14 and 3 trials respectively), three applications of trifloxysulfuron sodium were made to cotton at 7.5, 15, 20 and 100 g ai/ha. Cotton seed was sampled at harvest (generally not less than 60 days after last application) with two decline studies present where cotton seed was sampled at days 0. 46, 53, 60 and 67. In general, trifloxysulfuron sodium residues in cotton seed were below the LOQ (0.01 mg/kg) when sampled. Residues were detected in cotton seed in two trials: in one trial where cotton was treated with three applications of 100 g ai/ha, residues of up to 0.032 mg/kg were detected in undelinted seed, with delinted seed having residues below the LOQ at 61 days after last treatment. In the second trial, residues of 0.037 mg/kg were detected in cotton seed following three applications of 20 g ai/ha. On the basis of the data provided, an MRL of *0.01 mg/kg is supported for cotton seed.

Cotton seed oil was produced in 7 of the overseas trials. In all cases, the residues detected in crude and refined oil were below the LOQ (0.01 mg/kg). These data support an MRL of *0.01 mg/kg in cotton seed oil (crude and edible).

No MRLs were established for cotton foliage, cotton/gin trash, hulls or meal as it is not considered Good Agricultural Practice (GAP) to feed cotton forage or trash to animals. The following grazing restraint has been recommended: DO NOT GRAZE OR CUT TREATED PLANTS FOR STOCK FEED

Animal transfer studies and MRLs

Cotton seed may be fed to livestock and poultry. No animal transfer studies were provided to demonstrate the likely extent of trifloxysulfuron residues in animal commodities few treated

cotton commodities. On the basis of metabolism studies and trifloxysulfuron residues determined in crop residue trials, it was estimated that residues in animal commodities (edible tissues, eggs and milk) fed treated cotton commodities would be below the LOQ (0.01 mg/kg). The argument provided and associated analytical method supports animal commodity MRLs of *0.01 mg/kg.

Estimated dietary intakes

The chronic dietary risk is estimated by the National Estimated Daily Intake (NEDI) calculation encompassing all registered/temporary uses of the chemical and dietary intake data from the 1995 National Nutrition Survey of Australia. The Acceptable Daily Intake (ADI) for trifloxysulfuron is 0.2 mg/kg bw/day. The NEDI calculation is performed in accordance with accepted guidelines[?].

The NEDI for trilfoxysulfuron sodium is equivalent to 0.08 % of the ADI. It is concluded that the chronic dietary exposure is small, and the risk is acceptable.

An acute reference dose of 6 mg/kg bw has been set for trifloxysulfuron. Using 97.5th percentiles for infants (2-6 years old, body weight 19 kg) and the adult population (7 years and above, body weight 70 kg), the acute intake of trifloxysulfuron was estimated. The results are summarised in the following table. The highest acute dietary intake was estimated at less than 1% for infants and adults. The acute exposure is therefore considered to be low and the risk is acceptable.

Commodity	**% ARfD**	
	Kids	**Adults**
(1) Cotton seed oil	0.000	0.000
Sugar cane molasses	0.001	0.001
Meat (mammalian)	0.002	0.001
Edible offal (mammalian)	0.000	0.001
Milks	0.013	0.005
Poultry meat	0.002	0.001
(2) Poultry, edible offal of	0.000	0.001
Eggs	0.001	0.000

(1) Dietary intake for vegetable oil, edible used in calculation
(2) Consumption figure for edible offal (mammalian) used in calculation

[?] Guidelines for predicting dietary intake of pesticide residues (revised), World Health Organisation, 1997.

Recommended amendments to the MRL Standard:

Table 1

Compound	Food		MRL (mg/kg)
Trifloxysulfuron sodium			
DELETE:	SO 0691	Cotton seed	T*0.01
	OC 0691	Cotton seed oil, crude	T*0.01
ADD:	SO 0691	Cotton seed	*0.01
	OC 0691	Cotton seed oil, crude	*0.01
	OR 0691	Cotton seed oil, edible	*0.01
	MM 0095	Meat (mammalian)	*0.01
	MO 0105	Edible offal (Mammalian)	*0.01
	ML 0106	Milks	*0.01
	MF 0100	Mammalian fats	*0.01
	PM 0110	Poultry meat	*0.01
	PF 0111	Poultry fats	*0.01
	PO 0111	Poultry, edible offal of	*0.01
	PE 0112	Eggs	*0.01

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

A withholding period of 8 weeks is recommended in relation to the above MRLs for ENVOKE HERBICIDE.

The following grazing restraint is recommended: DO NOT GRAZE OR CUT TREATED PLANTS FOR STOCK FEED

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Commodities exported and main destinations

Australia produced 1062 kt of cotton seed in 2000/2001, 657.8 kt of which were exported as cotton seed and 0.64 kt as cotton seed oil.(ABARE Commodity Statistics 2001).

Overseas registration status

The applicant states that trifloxysulfuron sodium is currently not registered for use in any other country although is being currently undergoing registration in many overseas countries

CODEX Alimentarius Commission MRL

Trifloxysulfuron sodium has not been reviewed by the JMPR. Therefore, no Codex MRLs have been established for trifloxysulfuron in any edible commodities. Please note that Codex does not consider chemicals unless it can be demonstrated that there are finite residues in produce moving in trade.

Potential risk to Australian export trade

Trifloxysulfuron sodium residues in cotton seed and cotton seed oil are expected to be below the LOQ (0.01 mg/kg) and are therefore unlikely to cause any undue prejudice to Australian trade. Trifloxysulfuron residues in animals fed treated cotton seed products are expected to be well below the LOQ and are therefore unlikely to cause any undue prejudice to Australian trade.

The NRA is satisfied hat the proposed use of trifloxysulfuron sodium on cotton would not unduly prejudice trade between Australia and places outside Australia.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Trifloxysulfuron sodium is not listed in the NOHSC List of Designated Hazardous Substances. Trifloxysulfuron sodium and ENVOKE HERBICIDE are not hazardous according to NOHSC Approved Criteria for Classifying Hazardous Substances.

Trifloxysulfuron sodium is a fine white powder of low acute oral, dermal and inhalation toxicity in rats. It is not a skin irritant or skin sensitiser, but it is a moderate eye irritant. Trifloxysulfuron sodium shows no reproductive or developmental toxicity in rats. It was not genotoxic in a range of *in vitro* and *in vivo* assays and showed no neurotoxicity in acute oral rat studies.

ENVOKE HERBICIDE is a grey beige water dispersible granule formulation of low acute oral, dermal and inhalation toxicity in rats. It is a slight skin and eye irritant and may have some potential to be a skin sensitiser.

The product will be packed in 100 g, 500 g and 1 kg high-density polyethylene bottles.

Formulation, repackaging, transport, storage and retailing

The product will be formulated overseas and imported fully packaged. Transport workers, store personnel and retailers will handle the packaged product and will only become contaminated if the packaging is breached.

Advice on safe handling of the product during routine use is provided in the Material Safety Data Sheet (MSDS) for ENVOKE HERBICIDE.

Use and exposure

ENVOKE HERBICIDE is proposed for use on cotton for the post-emergence control of broadleaf weeds and nutgrass. It will be applied a maximum of two times per season at a rate of 15-30 g/ha (7.5-22.5 g trifloxysulfuron/ha) in a minimum of 100 L water/ha. Applications will be by boom spray; ideally using 2 directed flat fan nozzles mounted to droppers positioned either side of the plant row.

Workers may be exposed to ENVOKE HERBICIDE during preparation of spray, application by ground boom and clean up operations. The main route of exposure during mixing/loading and application will be dermal. During mixing and loading, inhalation exposure will be minimal as the product is a water dispersible granule with relatively large particle size and low volatility. During application, some inhalation exposure may occur as a result of airborne spray droplets or mist.

The main acute hazards associated with the product are slight skin and eye irritation as well as some potential for skin sensitisation. The final spray is not expected to pose any significant acute hazards to workers given the low level of product (0.03%). The assessment of acute risks indicated that workers should wear elbow-length PVC gloves when preparing spray.

The main hazards associated with repeat exposure to product are systemic effects (effects on liver, haematopoietic system and testes). No worker exposure data were available for trifloxysulfuron sodium or ENVOKE HERBICIDE. NOHSC used UK POEM to estimate mixer/loader and applicator exposure. The repeat dose risk assessment indicated that workers should wear elbow-length PVC gloves when preparing spray.

Entry into treated areas

Workers may be exposed to product when entering fields that have been treated with product. Re-entry may be required for a number of reasons including irrigation, scouting, thinning, and weeding. Harvesting is conducted mechanically and is not expected to involve significant exposure to treated plants. No post-application worker exposure data were available.

Given the low application rate of the product (0.0225 kg ai/ha) and the relatively low toxicity of the product, NOHSC does not consider re-entry workers to be at risk following the application of ENVOKE HERBICIDE once the spray has dried.

Recommendations for safe use

Users should follow the instructions and Safety Directions on the Product label. Safety Directions include the use of elbow-length PVC gloves when preparing the spray.

The personal protective equipment recommended should meet the relevant Standards Australia standards specified below:

> AS 2161-1978 Industrial Safety Gloves and Mittens (Excluding Electrical and Medical Gloves)

To ensure there is no risk from exposure to wet spray, the following re-entry statement should be included on the product label.

> Do not allow entry into treated areas until the spray has dried. When prior entry is necessary and if exposure to treated foliage is likely, wear cotton overalls buttoned to the neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each days use.

Information provision

Syngenta Crop Protection Pty Ltd has produced a MSDS for ENVOKE HERBICIDE. which contains information relevant to Australian workers, as outlined in the NOHSC National Code of Practice for the Preparation of Material Safety Data Sheets. Employers should obtain the MSDS from the supplier and ensure that employees have ready access to it.

Conclusion

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

ENVIRONMENTAL ASSESSMENT

Environment Australia has assessed the data provided by Syngenta Crop Protection Pty Limited in support of registration of their product ENVOKE HERBICIDE. The product is for the control of certain broadleaf weeds and suppression of nutgrass in cotton. Environmental fate studies indicate that trifloxysulfuron sodium is unstable in acid but is more persistent in alkaline solutions. In the laboratory, metabolism in soils and natural water-sediment systems is relatively fast with half-lives between 30-78 days. Initial half-lives in field studies were faster; however, residues were still measurable in soil about 23 months after treatment. Laboratory mobility of trifloxysulfuron sodium through soils is rated as high to very high but movement in the field was limited. Trifloxysulfuron sodium is not expected to bioaccumulate.

Environmental Chemistry and Fate

Hydrolysis

Trifloxysulfuron sodium hydrolyses relatively quickly at acidic pH values with a half-life of 5.6-6.0 d at pH 4 and 20°C. At pH 5, the half-life was longer at 11.5-12 d while at environmentally relevant pH 7 it was slow at 37-41 d. The main degradation products at pH 4 and 5 were the urea CGA 368732, the pyrimidine amine CGA 53052 and the sulfonamide CGA 382997.

Photolysis

Photolysis was not an important removal process in aqueous solution as half-lives of 14-17 and 18-19 d for irradiated and dark control treatments, respectively, showed that hydrolysis was more dominant in the pH 7 buffered solutions. Photolysis on soil surfaces was slower with irradiated and dark control half-lives of 34-35 and 54-60 d, respectively.

Aerobic soil metabolism

The metabolism of trifloxysulfuron sodium when applied to a loam soil at 0.03 mg ai/kg soil was biphasic with an initial rapid disappearance with a 5.3-5.4 d half-life followed by a slower 96-108 d half-life. The overall DT50 and DT90 values were 30-50 and 250-300 d, respectively. Main metabolites were CGA 53052, CGA 382997, the amine CGA 368733 and CGA 368732 with the proposed pathway the same as for hydrolysis. When applied to four soils (two loams and two loamy sands) at 0.2 mg ai/kg soil, the DT50 and DT90 values were 66-78 and 220-260 d. A silt loam treated with 0.2 mg ai/kg soil and incubated aerobically had DT50 and DT90 values of 49 and 164 d, respectively, at 20°C and 40% maximum water holding capacity (MWC); when the MWC was reduced to 20%, these values increased to 123 and 408 d, respectively. The major metabolites were CGA 368732, CGA 368733, the sulfonyl guanidine NOA 440735, CGA 382997 and the guanidine NOA 443300.

In the proposed main pathway for metabolism, parent trifloxysulfuron sodium is metabolised to CGA 368732 which was further degraded via CGA 368733 to the bridge contracted amine NOA 436664, which were further degraded to NOA 443300. In a second pathway, the opening of the pyrimidine ring yielding NOA 440735 was observed. Additionally, parent compound and NOA 440735 degraded to CGA 382997 by cleavage of the urea bridge.

Anaerobic soil metabolism
Trifloxysulfuron sodium degraded with DT50 and DT90 values of 19 and 65 d, respectively, in a loam soil that had been flooded with water and anaerobically incubated. The DT50 in water only was 13 d. In a similar study with another loam soil, the DT50 and DT90 values for the whole soil-water system were 20 and 65 d, respectively, with values of 19 and 31 d for the water only. In both of these studies, only two metabolites (NOA 436664 and CGA 368732) reached >10% of the originally applied radioactivity.

The proposed degradation pathway involved bridge contraction resulting in initial loss of the sulfur dioxide (CGA 368732) and subsequent loss of NH_2CO (CGA 368733). Concurrent degradation involved cleavage of the pyrimidine ring from the pyridinyl ring to yield CGA 382997. Anaerobic microbial degradation produced the major degradate, NOA 436664, which is the mono demethylated structure of CGA 368733.

Aerobic-anaerobic soil metabolism
Under aerobic and anaerobic conditions in the same soil, trifloxysulfuron sodium degraded with half-lives of 50-55 and 45-60 d, respectively. After 52 d of aerobic incubation followed by flooding to establish anaerobic conditions, the DT50 was 82 d. Only one main metabolite was found (the sulfonyl guanidine NOA 440735) which peaked at 13% at 224 DAT. In the aerobic treatment, the urea metabolite CGA 368732 had a DT50 of 187 d which was greater than three times longer than for parent. However, under anaerobic conditions, the metabolite degraded faster than parent with a DT50 of 39 d.

Metabolism in natural sediment-water
Natural river and pond water-sediment systems dosed at 0.05 mg ai/L degraded trifloxysulfuron sodium with DT50 values of 5.2-10.6 d in the water only and 23-26 d in the whole systems. Major metabolites were CGA 368732 (with a DT50 of 29-67 d in the whole system) and NOA 436664 in both systems.

A natural lake water-sediment system treated at 0.029 mg ai/L showed DT50 and DT90 values of 14 and 48 d in the whole water-sediment system, respectively, and 16 and 58 d in the water only. Metabolites were similar to other studies.

Mobility
In adsorption/desorption studies in five soils, the mobility of trifloxysulfuron sodium was high to very high. The desorption K_{OC} values were higher than the adsorption values, indicating that once adsorbed to soil, the compound does not desorb as easily. When trifloxysulfuron sodium was aged for 85 d in other soils, the parent compound's mobility decreased to medium in three soils and low to immobile in two others. Despite the reduced mobility, residues aged for 14-30 d in five soil columns and saturated with 1 L of $CaCl_2$ solution still leached primarily parent compound making up 6-24% of the originally applied radioactivity. Most of the total radioactivity (38-77%) remained in the top 6 cm of the soil columns but 0.6-38% was found in the leachate. This was confirmed in a similar study when residues aged for 24-30 d were leached as 20-46% remained in the top 6 cm of the soil columns while 10-44% was found in the leachate; the majority of radioactivity in the leachate was made up of parent in the loamy sand while the metabolite CGA 382997 dominated in the leachates of three other soils.

Volatility
Although no studies were submitted on volatility, the low vapour pressure is expected to preclude volatility being a major factor in trifloxysulfuron sodium's mobility.

Field Dissipation
Trifloxysulfuron sodium was applied 3 times at 60 g ai/ha with 14 day intervals to cotton and bare soil plots – the total is 8 times the proposed maximum Australian rate of 22.5 g ai/ha for cotton. The soil was classified as loamy sand. Both plots were irrigated using overhead sprinklers in accordance with typical commercial practices for cotton. Soil samples were collected to a depth of 120 cm (48 inches) from treated and untreated control plots and the soil sections analysed by HPLC for parent and metabolites with a limit of quantification of 0.5 ppb. The results show that under field conditions, trifloxysulfuron degrades with a short half-life of approximately 13 days in cotton field under commercial practice and 8 days in bare soils. Environment Australia notes a two compartment model was used and there was no calculation of the DT_{90}, which we estimated as about 250 days demonstrating considerable slowing with time. There was some movement through the soil profile but this did not extend below 45 cm. While most of the metabolites did not show any leaching behaviour beyond that of the parent compound, a sulfonamide metabolite CGA 382997 did show significant leaching and was found down to 90 cm deep in the soil profile. Note that the rate is significantly higher than that proposed and the sulfonamide metabolite is unlikely to show significant herbicidal activity.

Trifloxysulfuron sodium was applied 3 times at 60 g ai/ha to sugarcane and bare soil plots – again the total rate is 8 times the proposed maximum Australian rate for cotton.. The first 30 cm of soil was classified as silt loam with lower layers either a clay loam or a silty clay loam; these soils are considered to be poorly drained. Both plots were irrigated using overhead sprinklers to ensure that the monthly moisture input was >120% above the 30 year monthly average. Soil samples were collected to a depth of 120 cm (48 inches) from treated and untreated control plots and sections analysed by HPLC for parent and metabolites with a limit of quantification of 0.5 ppb. The results show that under field conditions, trifloxysulfuron degrades with a short half-life of approximately 8 days in sugarcane field and 5 days in bare soils liable proportion ie bioavailable fraction, using a two-compartment non-linear model. There was no movement of parent through the soil profile. While most of the metabolites did not show any leaching behaviour beyond that of the parent compound, the sulfonamide CGA 382997 did show significant leaching down to 30-45 deep in the soil profile and was found once at 60-75 cm. These results are similar to those for cotton above but there was less overall leaching, considered to be mainly due to the limited drainage in the heavier clay soils.

Trifloxysulfuron sodium applied to a bare sandy loam resulted in 11-15 µg ai/kg soil immediately after the first 20 g ai/ha application, to 71-99 µg ai/kg soil after a total of 60 g ai/ha application. By the time of first planting of wheat, radish and mustard at 30-90 DAT, residues had decreased to 24-55 µg ai/kg soil. By 365 DAT, soil residues had decreased to 16-22 µg ai/kg soil prior to planting. However, about 23 months after treatment (including wheat planted 365 DAT and harvested at maturity), radioactive residues were still measurable at 13-18 µg ai/kg soil. Radioactivity in wheat planted at various intervals was 1-42 µg ai/kg wheat (highest when planted 240 DAT) for both radiolabels. Residues for radish (leaves and tubers) and mustard ranged from 2-3 µg ai/kg tissue at 240 DAT to 25-30 µg ai/kg tissue at 30 DAT.

Bioaccumulation
Based on the low octanol/water partition coefficient (log K_{OW} = -0.42 at pH 7 and 25°C), trifloxysulfuron sodium is expected to have a low potential to bioaccumulate in aquatic organisms.

Accumulation in soils
Based on a worst case aerobic soil biodegradation DT50 of 78 d, Environment Australia calculated that the proposed annual application rate of 22.5 g ai/ha would cause an annual carryover of about 4%. If annual applications were to be made to the same plot of land, accumulation of trifloxysulfuron sodium in soils would amount to about 20 µg ai/kg soil in the top 10 cm of soil presuming a bulk density of 1.2 g/mL.

Environmental Toxicology

Birds
Trifloxysulfuron sodium was practically nontoxic to both bobwhite quail and mallard duck adults in single oral dose tests with the LD50 > 2,250 mg ai/kg bw. This was also true with quail chicks and ducklings in 5-d dietary exposures with the LC50 > 5,620 mg ai/kg food. In one generation dietary exposures for both species, the NOEC was the highest dose tested of 200 mg ai/kg food.

Fish
Juvenile rainbow trout were not sensitive to trifloxysulfuron sodium in static or flow-through exposures with the 96-h LC50 > 103 mg ai/L. This was also true for bluegill sunfish and sheepshead minnow in flow-through tests. The urea metabolite CGA 368732 and sulfonamide metabolite CGA 382997 were also practically nontoxic to trout with 96-h LC50 values of >104 mg/L and >96.7 mg/L, respectively. A chronic exposure of 95 d to trout early life stages also indicated very slight toxicity with a NOEC of 9.5 mg ai/L.

Aquatic invertebrates
Water fleas were not sensitive to formulated or technical trifloxysulfuron sodium in static or flow-through exposures with 48-h EC50 values of >104 mg ai/L. The marine mysid shrimp was slightly more sensitive with a 96-h LC50 of 62.4 (51.6, 76.9) mg ai/L which is considered only slightly toxic. The eastern oyster showed no adverse effects after 96 h to 103 mg ai/L. The urea metabolite CGA 368732, amine CGA 368733 and sulfonamide CGA 382997 were all practically nontoxic to water fleas with 48-h EC50 values of >99.5 mg/L. After 21 d chronic exposure, water fleas had NOEC and LOEC values of 0.549 and 1.23 mg ai/L, respectively, which is slightly toxic. This gives a high acute to chronic ratio of 131.

Aquatic plants
As expected, trifloxysulfuron sodium was very highly toxic to the green alga *Pseudokirchneriella subcapitata* with a 120-h IC50 of 6.6 (5.5, 7.5) µg ai/L and 72-h IC50 of 5.5 (4.3, 6.5) µg ai/L for technical and formulated forms, respectively. The technical grade was highly toxic to the blue-green alga *Anabaena flos-aquae* with a 120-h IC50 of 256 µg ai/L but only very slightly toxic to the freshwater diatom *Navicula pelliculosa* (120-h IC50 > 139 mg ai/L) and slightly toxic to the marine diatom *Skeletonema costatum* (120-h IC50 = 85.4 (61.9, 102.7) mg ai/L). The metabolites CGA 368732, CGA 368733 and CGA 382997 were slightly toxic to *P. subcapitata* with 72-h IC50 values of 20.3 (15.9, 24.4), 10.9 (6.3, 14.0) mg/L and >95.8 mg/L, respectively.

Trifloxysulfuron was very highly toxic to duckweed (*Lemma gibba*), with 14 day IC50s of 25 ng ai/L (24-26), 0.55 µg ai/L (23-65) and 0.52 µg ai/L (45-62) for semi-static (renewed every 2 days), static-renewal (renewed after 7 days) and static conditions respectively. The plants from the static-renewal exposure recovered after exposure to <1.0 µg ai/L when placed into clean growth media. Recovery from the semi-static exposures were significantly less at <0.056 µg ai/L after 14 days of growth in clean conditions.

The semi-static test was approximately 20 times more sensitive than the static or static renewal conditions and it is unclear whether this is due to the lower pH in the semi-static test or if it is a result of the constant renewal of testing solutions compared to the other two tests. However, Environment Australia notes that the static or static renewal conditions are closer to expected field conditions and therefore considers that the static results as more representative of the expected environmental conditions.

Terrestrial invertebrates

Earthworms were relatively insensitive to trifloxysulfuron sodium with the 14-d LC50 > 748 mg ai/kg soil. Similarly the metabolites CGA 368732 and CGA 382997 had 14-d LC50 values of >995 mg/kg soil. Honeybees were also insensitive with the 48-h oral and contact LD50 of >25 µg ai/bee. The predatory mite *Typhlodromus pyri* showed adverse effects at an application rate of 46.1 g ai/ha (LOEC) but the 14-d LD50 was >76.9 g ai/ha. Parasitic wasps were unaffected by application rates up to 74.8 g ai/ha.

Soil microorganism processes

Soil concentrations of 0.8 mg ai/kg soil (equivalent to about 600 g ai/ha application rate, 27 times proposed rate) caused deviations in nitrate and total soil nitrogen from controls of ~25% on 14 and 28 DAT, and then declined to ~5% by 102 DAT. No adverse effect on soil microbial respiration was observed. However in two soils in another experiment, adverse effects (>25% deviation from control) in nitrate (both soils) and nitrite (one soil only) concentrations persisted by 28 DAT at 0.03 mg ai/kg soil, making this the LOEC.

Terrestrial plants

A Tier 2 study on the effect of trifloxysulfuron on seedling emergence and vegetative vigour was conducted according to USEPA Guidelines using a number of dicotyledon and monocotyledon seedling species. All seedlings showed some phytotoxic effects or reduced dry weights after 21 days at some treatment levels, with radish and lettuce seedlings the most sensitive, EC50 of 0.09 and 1.57 g ai/ha respectively, and tomato the least affected. Emergence of seedlings from seed was affected; again with radish being the most sensitive with a NOEC at 1.9 g ai/ha but ryegrass had the lowest EC50 at 15.23 g ai/ha. Phytotoxic effects on the emerging seedlings were noted with the most sensitive being radish and lettuce with EC50s of 3.9 and 4.7 g ai/ha respectively. It is concluded the sensitive non-target plants could be significantly affected with the principal effects related to phytoxicity and growth rather than seedling emergence.

Environmental Hazard

Registration is sought for the control of certain broadleaf weeds and nutgrass in cotton as a post-emergent spray as per the directions for use. The label states that ENVOKE HERBICIDE is to be applied either as an over the top spray before or as as a directed spray after the 8 leaf cotton growth stage. All applications are expected to be made using spray boom, most likely to be tractor mounted using medium to coarse droplets. The label

precludes application by air and under cool overcast conditions. The term directed spray is used when the spray is to be targeted to the weeds between the rows with spraying either side of the plant row up to the cotton plants, without the spray coming into contact with the cotton plants. The spray is therefore directed under the foliage without touching it. Generally a directed spray will cover about 60% of the total ground area.
Residues from application would be expected on plant (weeds) surfaces and soil. Surface water, uncultivated land and nearby non-target plants (e.g. trees and grasses) may be contaminated through overspray, spray drift and/or run-off.

Concentration in soil
The maximum application rate of ENVOKE HERBICIDE is 22.5 g ai/ha as a directed spray or at 11.25 g ai/ha ideally as a band spray either side of the cotton row, once per year. Given a direct application to bare soil at the maximum rate, the estimated environmental concentration (EEC) of trifloxysulfuron sodium in treated soil is 0.019 mg ai/kg soil. With only one application per year and using a DT50 of 78, no significant accumulation is expected.

Concentration in water
In a worst-case scenario of a direct overspray of a 15 cm deep body of water with the maximum single application rate of 22.5 g ai/ha, the EEC would be 15 µg ai/L. As only one application per year is to be made and the dissipation DT50 in natural water-sediment systems is relatively fast (23-26 d), no accumulation is expected.

Hazard to Terrestrial Organisms

Birds
Based on the typical diet of northern bobwhite quail and the EEC of trifloxysulfuron sodium in food items, the concentration of trifloxysulfuron sodium in the diet was calculated as 2.4 mg ai/kg food. The most sensitive chronic NOEC for quail is significantly higher (83X) and no hazard is expected.

Earthworms
The 14-d LC50 for the earthworm was significantly higher than the worst case soil EEC of 0.019 mg ai/kg soil for ENVOKE HERBICIDE in the top 10 cm of soil. Thus the proposed use of trifloxysulfuron sodium is not expected to be an acute hazard to earthworms. The 14-d NOEC of the metabolites CGA 368732 and CGA 382997 were >995 mg/kg soil and therefore no hazard is expected from these metabolites. Given the low acute hazard, it is expected that the chronic toxicity will also be low.

Beneficial arthropods
The hazard to honey bees was calculated to be relatively low as the maximum application rate of 22.5 g ai/ha (equivalent to 0.225 µg ai/cm^2) is at least 100 times lower than the most sensitive contact and oral LD50, assuming that a honeybee is approximately 1 cm^2 in surface area. Predatory mites are not expected to be adversely affected at the proposed rates of as no effect was seen at a similar rate (23.1 g ai/ha) under worst case conditions. Parasitic wasps are also expected to be unaffected as the LOEC was least 3.3 times higher than the application rate.

Terrestrial plants
As trifloxysulfuron sodium is a sulfonylurea herbicide, it is expected to cause adverse effects

to a wide range of non-target broadleaf plants. At the maximum application rate of 22.5 g ai/ha direct overspray is expected to be phytotoxic to a range of non-target plants (Q>1). However, after allowing for directed spraying, spray drift (German spray drift figures and noting that the height of the spray head is lowered) and interception by the cotton plants, a downwind spray drift buffer of 10 metres is considered to be satisfactory to limited effects on non-target plants.

It is noted that the current Best Management Practices Manual (BMPM) for cotton growers has as a guideline for ground rig spraying a spray drift buffer of 100 metres from sensitive areas.

Soil microorganisms

The proposed use of trifloxysulfuron sodium may be a hazard to soil microorganisms as the LOEC for adverse effects on nitrogen mineralisation was only slightly higher than the soil EEC. Any buffer zone recommended to protect terrestrial plants would reduce any potential adverse effect outside the treated area.

Hazard to Aquatic Organisms

Water bodies adjacent to cotton plots may be contaminated through direct overspray. Contamination outside the target area is likely to result from spray drift and from run-off of material dissolved in the water or sorbed to soil and organic matter particles.

The worst-case scenario of a direct overspray of a 15 cm deep body of water with ENVOKE HERBICIDE would result in an EEC of 15 µg ai/L. The EC50s for fish, daphnia and mysid shrimp are significantly above this level and indicate an acceptable hazard for these organisms. However, there is an unacceptable risk to green algae and duckweed. Using similar methodology, the hazard from the metabolites CGA 368732 and CGA 382997 for trout and water fleas is acceptable. As well, the hazard for CGA 368733 (the most toxic metabolite) to green alga was low.

Despite the risk to algae and duckweed, indicated by the Q-values, the likelihood of a direct overspray of natural waterways is minimal given the layout of cotton fields, particularly if best management and good agricultural practices are followed (aerial application is already prohibited on the label). Thus most water would be exposed through spray drift or run-off rather than direct overspray, particularly as it will only be applied by ground boom sprayer.

Spray drift

The risk and extent of spray drift 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 spray drift will occur and hence contamination of soil and water outside the target areas. Assuming that 10% of a single application reaches the aquatic environment via spray drift as a worst case the risk to algae was just acceptable but the risk to duckweed remained unacceptable.

As the likelihood of a 10% spray drift from an application is expected to be low, the results of German studies for field crops were used to more closely refine the EEC. For an acceptable hazard to duckweed, a distance of >5 m from a 15 cm deep body of water is required to reduce the risk to an acceptable level. However, as noted above for terrestrial plants, these tables are expected to give an overestimate of the spray drift since droppers will lower the

height of the nozzles to below the height of the plants.

Therefore, a buffer zone of at least 5 m downwind of all areas to be treated with ENVOKE HERBICIDE would reduce the hazard to duckweed to an acceptable level and presumably to other aquatic macrophytes. Again the use of cotton BMPM would clearly reduce any hazard.

Run-off

Trifloxysulfuron sodium is soluble in water and has high to very high mobility in soil. The metabolite CGA 382997 was also found in the leachate from soils. Therefore, it is reasonable to expect that heavy rainfall or irrigation shortly following trifloxysulfuron sodium application would result in residues in run-off from treated areas.

While NSW cotton farms are known to practice water recycling and thus movement off farm would be limited, this is not the case for QLD. Environment Australia notes that even in NSW, more northern farms have much less capacity, if any, to retain storm events, particularly when irrigation has just occurred. In addition, use of ENVOKE HERBICIDE in dry land cotton crops, where there is limited capture of run-off could lead to contamination of nearby natural watercourses.

In a worst case scenario, using the maximum application rate the EEC in water was calculated as 0.86 µg ai/L. This assumes 10% runs off and the dilution results from the 15 cm deep water, 100 mm of rain and 10 mm of runoff water, total depth of 26 cm. This EEC indicates an unacceptable hazard for green algae and duckweed. A more realistic scenario is that ENVOKE HERBICIDE is applied as a directed spray and that runoff from several areas enters an area of environmental significance, ie a natural wetland. Assuming that 10% of the catchment is treated, then the concentration in runoff becomes 0.052 µg ai/L and the risk for duckweed is acceptable. It should be noted that in the duckweed fully recovered from exposures at 0.089 µg ai/L and therefore any effects are expected to be of short duration.

The label does not prohibit spraying if rain is forecast but there is the statement "DO NOT apply under cool, overcast conditions". In order to reduce the risk of run-off and leaching of parent and/or metabolites to groundwater with subsequent recharge to surface water, the label should also prohibit application if heavy rainfall is forecast.

Coupled with at least a 10 m buffer zone for ENVOKE HERBICIDE, the recommendation not to apply before heavy rain should reduce the potential hazard to aquatic plants resulting from run-off. Treated areas should also not be irrigated within a period of 48 hours after treatment.

EFFICACY AND SAFETY ASSESSMENT

Justification for Use

ENVOKE HERBICIDE will offer cotton growers an early season, post emergence over the top control of broadleaf weeds that remains a problem in cotton production. This new herbicide offers efficacy against a new range of problem weeds.

Adequacy of Efficacy Data

The trials appear to have been undertaken appropriately, with adequate replication and control. Generally the trials appear to cover a wide range of weeds and conditions and are acceptable.

However, it is apparent that a large number of trials were conducted on a relatively small number of properties heavily concentrated around three areas. It would be preferable to have a wider range of soil types and climatic conditions covered. The analysis and interpretation of data appear to be adequate.

Claims

The sheer bulk of data and inefficient method of reporting make the review of the data quite demanding. The presented data do not adequately support the label claim in some instances.

Directions for Use

The trial data do not generally support control of some weeds at the proposed dose rates. Therefore in the directions for use “control” was replaced with “suppression” for certain weeds.

Safety to Target and Non Target Species

Directions are in place on the product label and are appropriate.

Conclusion

The efficacy data of the submission was not adequate to recommend the control of all the proposed weed species; therefore suppression was recommended for some of them.

LABELLING REQUIREMENTS

CARTON LABEL:

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

ENVOKE®

HERBICIDE

ACTIVE CONSTITUENT:
750 g/kg TRIFLOXYSULFURON SODIUM

GROUP	B	HERBICIDE

For the control of certain broadleaf weeds and the suppression of nutgrass in Cotton as per Directions for Use.

IMPORTANT: Read the attached booklet before use.

The bottle must not be sold separately.
DO NOT destroy box while product still remains.

100 g,
(500g, 1 kg) NET

Syngenta Crop Protection Pty Limited
140-150 Bungaree Road Pendle Hill NSW 2145 **NRA Approval no. _____/_____**
In a transport emergency dial 000, Police or Fire Brigade. N1
For specialist advice in an emergency only, call 1800 033 111 (24 hrs)

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well ventilated area out of direct sunlight.
Rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. Dispose of at a local authority landfill. If no landfill is available, bury the containers below 500mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty containers and product should not be burnt.

SAFETY DIRECTIONS
Will irritate the eyes and skin. Avoid contact with eyes and skin. When preparing spray wear:

- **cotton overalls buttoned to the neck and wrist (or equivalent clothing) and**
- **elbow-length PVC gloves.**

After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water. After each day's use wash gloves and contaminated clothing.

FIRST AID
If poisoning occurs, contact a doctor or Poisons Information Centre. Phone 131 126.

MATERIAL SAFETY DATA SHEET
If additional hazard information is required refer to the Material Safety Data Sheet. For a copy phone 1800 067 108 or visit our website at www.syngenta.com.au

MANUFACTURER'S WARRANTY AND EXCLUSION OF LIABILITY
Syngenta has no control over storage, handling and manner of use of this product. Where this material is not stored, handled or used correctly and in accordance with directions, no express or implied representations or warranties concerning this product (other than non-excludable statutory warranties) will apply. Syngenta accepts no liability for any loss or damage arising from incorrect storage, handling or use.

Batch No.	
Date of Manufacture	

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BAR CODE

UN NO. 3077	**Environmental hazardous substances, solid, N.O.S. (contains trifloxysulfuron sodium)**
In a Transport Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 033 111** ALL HOURS - AUSTRALIA WIDE
PG III	**HAZCHEM 2 X**

Insert Miscellaneous Dangerous Goods 9 symbol

BOOKLET:

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

ENVOKE®

HERBICIDE

ACTIVE CONSTITUENT:
750 g/kg TRIFLOXYSULFURON SODIUM

Group	B	Herbicide

For the control of certain broadleaf weeds and suppression of nutgrass in Cotton as per Directions for Use.

Syngenta Crop Protection Pty Limited
140-150 Bungaree Road Pendle Hill NSW 2145
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In a transport emergency dial 000, Police or Fire Brigade.
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L1

Directions for Use

Restraints:

DO NOT apply by air.
DO NOT apply under cool, overcast conditions.
DO NOT apply when the crop or weeds are not actively growing.
DO NOT apply within 48 hours of forecast rainfall or irrigation.
DO NOT make more than 1 application per season.

Crop and Growth Stage	Weeds Controlled	Weed Growth Stage at Application	Rate/ha	Critical Comments
Cotton 2 leaf to row closure	Dwarf Amaranth (*Amaranthus macrocarpus*) Burr Medic (*Medicago polymorpha*) Noogoora Burr (*Xanthium occidentale*) Sesbania Pea (*Sesbania cannibina*) Yellow Vine (*Tribulus micrococus)*	up to 40 cm diameter up to 15 cm diameter up to 8 leaf up to 8 leaf up to 15 cm diameter	15 g plus BS1000 or Agral at 0.25%	Apply post-emergent in a minimum of 100 L water per ha when crop and weeds are actively growing. Apply over the top of cotton from 2 leaf until 8 leaf. Apply as a directed application for cotton from above 8 leaf to row closure.
	Suppression of: Budda Pea (*Aeschynomena indica*) Italian Cockleburr (*Xanthium italicum*) Peach Vine (*Ipomoea lonchophylla*)	up to 8 leaf up to 4 leaf up to 8 leaf		
	Suppression of: Nutgrass (*Cyperus rotundus*)	3 to 6 leaf	30 g plus BS1000 or Agral at 0.25%.	**Apply as a directed application only.** Envoke should be used as part of a program including other weed control techniques to manage nutgrass.

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

WITHHOLDING PERIOD:
GRAZING/STOCK-FOOD: DO NOT GRAZE OR CUT TREATED PLANTS FOR STOCK FEED
HARVEST: : DO NOT HARVEST FOR 8 WEEKS AFTER APPLICATION

GENERAL INSTRUCTIONS

ENVOKE Herbicide is a water dispersible granule herbicide for the control of certain broadleaf weeds and nutgrass in cotton. Symptoms of control of nutgrass appear over 1 to 2 weeks.

ENVOKE should be used as part of a weed management program. It is recommended to use a range of management tools to control weeds, including herbicides, cultivation, machinery hygiene and crop competitiveness. Refer to the CRC weed management guidelines for the latest information on the best strategies to control weeds in cotton and use ENVOKE as one part of a management program.

Since crops other than cotton may be sensitive to low soil concentrations of ENVOKE, careful consideration should be given to crop rotations prior to using the product. (see Crop Rotation Guidelines).

Some yellowing of terminal growth may occur following an early post-emergent application of ENVOKE. Avoid spraying under cool, overcast conditions or in situations where crops are not actively growing or under stress due to drought, cold weather, hail, water-logged soil, disease infection, insect damage or nutrient deficiency. Crop effects are usually of short duration and under normal conditions produce no detrimental effects on yields.

Mixing
ENVOKE Herbicide mixes readily with water - no pre-mixing is required.
This product must be mixed with water and applied by suitable spray equipment.

1. Fill vat no more than 25% full with clean water before adding ENVOKE. Begin agitating vat contents vigorously and continue agitation during entire mixing and spraying operations.
2. Pour required amount of ENVOKE steadily into vat. Allow vigorous bypass agitation to completely disperse product. DO NOT dump product into vat all at once.
3. After adding required quantity of ENVOKE and obtaining complete dispersion, continue to fill vat to desired level for spraying.
4. Add required quantity of BS1000 or Agral (0.25%) with continued agitation.
5. Thorough agitation (preferably mechanical) of the spray liquid is essential during the addition of the product and during the entire spraying operation.
   Recirculate if left to stand.

N.B. Spray solution should NOT be left standing in the vat overnight.

Application
Apply by boom spray, applying a minimum of 100 litres of water per hectare. Avoid overlapping of spray runs. ENVOKE will primarily be applied as a band spray. **ENVOKE should be applied using 2 directed flat fan nozzles mounted on droppers positioned either side of the plant row. This ensures adequate coverage of all weeds in the band width and reduces the amount of product intercepted by the cotton foliage**.

ENVOKE should be applied as a directed spray from the 8 leaf to row closure crop growth stage or when using rates above 15 g/ha.

Sprayer Cleanup
Thoroughly clean spray equipment using the following procedure when you have finished spraying highly active materials such as sulfonylurea products. Start with a thoroughly cleaned sprayer before beginning the next job.

1. **Mix only as much spray solution as needed. Immediately after spraying, clean equipment thoroughly using this procedure. Wear appropriate protective clothing.**
   As a first step, flush tank, hoses, boom and nozzles with clean water.
2. Prepare a cleaning solution of 300 mL of household chlorine bleach (containing 4% chlorine) per 100 L of water. Ensure bleach used is fresh as it can degrade significantly over time resulting in a reduction in cleaning ability.
3. When available, use a pressure washer to clean the inside of the spray tank with this solution. Take care to wash all parts of the tank, including the inside top surface and lid.
4. Completely fill the sprayer with the cleaning solution to ensure contact of the cleaning solution with all internal surfaces of the tank and plumbing. Start agitation in the sprayer and thoroughly recirculate the cleaning solution for at least 15 minutes. All visible deposits must be removed from the spraying system and in cases where there is the possibility of heavy build up of residues the cleaning solution may need to be left in the tank for extended periods to ensure adequate decontamination of the tank.
5. Flush hoses, spray lines and nozzles for at least one minute with the cleaning solution.
6. Dispose of rinsate from steps 1 to 5 in an appropriate manner.
7. **Repeat steps 2 to 5.**
8. Remove nozzles, screens and strainers and clean separately in the cleaning solution after completing the above procedures. Be careful with filters, as they are a main source of contamination.
9. Rinse the complete spraying system with clean water.

The above method is only effective if the cleaning solution comes into contact with every surface or contact point that may contain even minute sulfonylurea herbicide residues. In some boom sprayers this may not be physically possible and hence it may be advisable to use a different boomsprayer, that has not been used to spray sulfonylurea herbicides, when spraying sensitive crops such as legumes and especially Canola.

Compatibility
ENVOKE is compatible with Staple*.
Crop Rotation Guidelines
Where the product is applied at recommended rates the ENVOKE treated area can be replanted after the interval indicated in the table below. These recommendations are made on the assumption that ENVOKE is applied in a cotton crop that reaches maturity in the season of application.

Replanting Interval	**Crop**
6 months	Wheat, Oats and Barley
7 months	Faba Beans
9 months	Mung Beans and Cotton
15 months	Soybean and Pigeon Peas
18 months	Chickpeas
22 months	Sunflower, sorghum and maize

For all other crops a replanting interval of 22 months should be observed.

Resistant Weeds Warning **GROUP B HERBICIDE**

ENVOKE Herbicide is a member of the sulfonylurea group of herbicides and has the ALS Inhibitor mode of action. For weed resistance management this product is a Group B herbicide. Some naturally occuring weed biotypes resistant to ENVOKE Herbicide and other sulfonylurea 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 ENVOKE Herbicide or other Group B herbicides. Since the occurrence of resistant weeds is difficult to detect prior to use, Syngenta Crop Protection Pty Limited accepts no liability for any losses that may result from the failure of ENVOKE Herbicide to control the resistant weeds. Advice as to strategies and alternative treatments that can be used should be obtained from your local supplier, consultant, local Department of Agriculture, Primary Industries Department or a Syngenta representative.

PRECAUTION

Re-entry Period: DO NOT enter treated areas without protective clothing until spray has dried.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS
This product is very highly toxic to non-target plants including aquatic plants. DO NOT apply under weather conditions or from spraying equipment that may cause spray to drift onto nearby susceptible plants/crops, cropping lands, pastures and other non-target plants or natural and impounded lakes, dams oro ther waterways. All applications should be made in accordance with the Best Management Practices Manual for cotton.

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

STORAGE AND DISPOSAL
Store in the closed, original container in a dry, cool, well-ventilated area out of direct sunlight.
Rinse containers before disposal. Add rinsings to spray tank. DO NOT dispose of undiluted chemicals on site. Dispose of at a local authority landfill. If no landfill is available, bury the containers below 500mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots.
Empty containers and product should not be burnt.

SAFETY DIRECTIONS
Will irritate the eyes and skin. Avoid contact with eyes and skin. When preparing spray wear:

- cotton overalls buttoned to the neck and wrist (or equivalent clothing), and
- elbow-length PVC gloves.

After use and before eating, drinking or smoking, wash hands, arms and face thoroughly with soap and water. After each day's use wash gloves and contaminated clothing.

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UN NO. 3077	**Environmental hazardous substances, solid, N.O.S. (contains trifloxysulfuron sodium)**
In a Transport Emergency Dial **000** Police or Fire Brigade	SPECIALIST ADVICE IN EMERGENCY ONLY **1800 033 111** ALL HOURS - AUSTRALIA WIDE
PG III	**HAZCHEM 2 X**

Insert Miscellaneous Dangerous Goods 9 symbol

BOTTLE LABEL:

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

ENVOKE®

HERBICIDE

ACTIVE CONSTITUENT:
750 g/kg TRIFLOXYSULFURON SODIUM

GROUP	**B**	**HERBICIDE**

For the control of certain broadleaf weeds and suppression of nutgrass in Cotton as per Directions for Use.

BEFORE USING PRODUCT, READ DIRECTIONS ON OUTER PACK.
SALE OF THIS BOTTLE EXCEPT IN OUTER PACK IS ILLEGAL.

100 g,
(500 g, 1 kg) NET

Syngenta Crop Protection Pty Limited
140-150 Bungaree Road Pendle Hill NSW 2145
NRA Approval no. _____/_____
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Insert Miscellaneous Dangerous Goods 9 symbol

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.

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Footnote:
Updated versions of these documents are available on the NRA website http://www.nra.gov.au.

NRA PUBLICATIONS ORDER FORM

To receive a copy of the full technical report for the evaluation of trifloxysulfuron sodium in the product Envoke Herbicide, please fill in this form and send it, along with payment of $30 to:

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

Alternatively, fax this form, along with your credit card details, to the above contact person: (06) 6272 3218.

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

Make cheques payable to 'National Registration Authority'.

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Signature_____ Date _____