Public Release Summary
on

Evaluation of the new active

FLORASULAM

in the product

Torpedo Herbicide

Australian Pesticides and Veterinary Medicines Authority

February 2007

Canberra
Australia

ISSN1443-1335

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

Ranjit Gajanayake
Australian Pesticides and Veterinary Medicines Authority
PO Box E 240
KINGSTON ACT 2604

Ph: (02) 6210 4760
Fax: (02) 6210 4776

FOREWORD

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

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

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

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

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

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

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

[blank page here]

CONTENTS

[blank page here]

LIST OF ABBREVIATIONS AND ACRONYMS

ac	active constituent
ADI	Acceptable Daily Intake (for humans)
AHMAC	Australian Health Ministers Advisory Council
ai	active ingredient
BBA	Biologische Bundesanalstalt fur Land – und forstwirschaft
bw	bodyweight
CRP	Chemistry and Residues Program
d	day
DAT	Days After Treatment
DM	Dry matter
DT_{50}	Time taken for 50% of the concentration to dissipate
E_bC_{50}	concentration at which the biomass of 50% of the test population is impacted
EC_{50}	concentration at which 50% of the test population are immobilised
EEC	Estimated Environmental Concentration
E_rC_{50}	concentration at which the rate of growth of 50% of the test population is impacted
EUP	End Use Product
Fo	original parent generation
g	gram
GAP	Good Agricultural Practice
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
h	hour
ha	hectare
Hct	Heamatocrit
Hg	Haemoglobin
HPLC	High Pressure Liquid Chromatography *or* High Performance Liquid Chromatography
id	intradermal
im	intramuscular
ip	intraperitoneal
IPM	Integrated Pest Management
iv	intravenous
in vitro	outside the living body and in an artificial environment
in vivo	inside the living body of a plant or animal
kg	kilogram
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 dquantified
mg	milligram
mL	millilitre
MRL	Maximum Residue Limit
MSDS	Material Safety Data Sheet
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NOEC/NOEL	No Observable Effect Concentration Level
OC	Organic Carbon
OM	Organic Matter
po	oral

POEM	Predictive Operator Exposure Model (UK)
ppb	parts per billion
PPE	Personal Protective Equipment
ppm	parts per million
Q-value	Quotient-value
RBC	Red Blood Cell Count
s	second
sc	subcutaneous
SC	Suspension Concentrate
SUSDP	Standard for the Uniform Scheduling of Drugs and Poisons
TGA	Therapeutic Goods Administration
TGAC	Technical grade active constituent
T-Value	A value used to determine the First Aid Instructions for chemical products that contain two or more poisons
µg	microgram
vmd	volume median diameter
WG	Water Dispersible Granule
WHP	Withholding Period

INTRODUCTION

This publication provides a summary of the data reviewed and an outline of the regulatory considerations for the proposed registration of the product *TORPEDO HERBICIDE*, which contains the new active constituent florasulam. The product is proposed to be used for the control of broadleaf weeds in barley, triticale and wheat.

Responses to this Public Release Summary will be considered prior to registration of the product. They will be taken into account by the Australian Pesticides and Veterinary Medicines Authority (APVMA) in deciding whether the product should be registered and in determining appropriate conditions of registration and product labelling.

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

Written comments should be received by the APVMA by **26 March 2007**. They should be addressed to:

Ranjit Gajanayake
Pesticides Division
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
KINGSTON ACT 2604

Phone: (02) 6210 4760
Fax: (02) 6210 4776
Email: ranjit.gajanayake@apvma.gov.au

Applicant
Dow AgroSciences Australia Ltd

Product Details
It is proposed to register *TORPEDO HERBICIDE* containing 50g/L of florasulam as a suspension concentrate. The product will be imported fully formulated in New Zealand and packaged in 5L, 10L and 20L containers.

TORPEDO HERBICIDE contains members of the pyridine group of herbicides. The product has the disrupters of plant cell growth and acetolactate synthase (ALS) inhibitor modes of action. For weed resistance management *TORPEDO HERBICIDE* is a Group I & B Herbicide.

The rate of product use is 75mL to 100mL/ha. *TORPEDO HERBICIDE* is proposed for registration in all States.

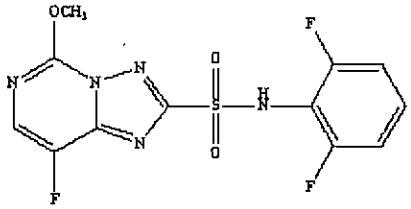
CHEMISTRY AND MANUFACTURE

ACTIVE CONSTITUENT

The active constituent florasulam is manufactured in the USA by Dow AgroSciences LLC, Dow Texas Operations, 2301 Brazosport Boulevard, APB Building, Freeport, Texas, and is pending approval by the APVMA (Approval Number: 59826).

Chemical Characteristics of the Active Constituent

Common name:	Florasulam
Synonyms and Code Number:	XR-570, XDE-570, DE-570
Chemical name (IUPAC):	2',6',8-Trifluoro-5-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidine-2-sulfonanilide
(CA):	*N*-(2,6-Difluorophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-*c*]pyrimidine-2-sulfonamide
Chemical Abstracts Service (CAS) Registry Number:	145701-23-1
Molecular formula:	$C_{12}H_8F_3N_5O_3S$
Molecular weight:	359.3
Chemical structure:	



Physical and Chemical Properties of the Active Constituent

Physical state:	Powder
Colour:	Off-White
Odour:	Odourless
Optical rotation:	not optically active
Melting point (for solids):	193.5-230.5 °C (decomposition)
Boiling point (for liquids):	Not applicable
Relative density (to water at 4 °C):	1.53 g/cm^3
Solubility in water:	At 20°C, (99.7% purity) Purified water 121 mg/L pH 5 (buffer): 84 mg/L pH 7 (buffer): 6.36 mg/L pH 9 (buffer): 94.2 mg/L
Solubility in organic solvents:	Acetone: 123 g/L Acetonitrile: 72.1 g/L Dichloromethane: 3.75 g/L *n*-Heptane: 0.000019 g/L Methanol: 9.81 g/L Ethyl acetate: 15.9 g/L *n*-Octanol: 0.184 g/L Xylene: 0.227 g/L

Vapour pressure:	1 x10^{-5} Pa @ 25 °C (maximum)
Henry's Law Constant:	2.29×10^{-5} pa m^3/mol
Dissociation constant (pKa):	4.54 (at 22-23 °C)
Surface Tension:	71.5 mN/m (at 99 mg/L in water)
Photostability (DT_{50}):	1.82 hours (assuming hydroxyl radical concentration of 1.5×10^6 radicals/cm^3)
Octanol/Water partition coefficient:	K_{ow} = 10.0 at pH 4 K_{ow} = 0.0603 at pH 7 K_{ow} = 0.00871 at pH 10
pH:	4.19 (5% w/v in distilled water) 3.99 (10% w/v in distilled water)
Hydrolysis stability ($t_{½}$):	pH 4-7: stable pH 9: 226 d
Storage stability:	Florasulam is chemically stable at temperatures of 54°C for 2 weeks and is expected to be stable for at least 2 years when stored away from direct sunlight.
Corrosion characteristics:	Non-corrosive
Oxidizing properties:	Not oxidizing
Flammability:	Not flammable
Chemical family:	Triazolopyrimidine

PRODUCT

Distinguishing name:	Torpedo Herbicide
Formulation type:	Suspension concentrate

Physical and Chemical Properties of the Product

Physical state:	Liquid
Colour:	Cream
Odour:	Fragrant
Density (at 20 °C):	1.176 g/mL
Acidity, alkalinity or pH value:	5.3 (neat)
Viscosity (at 20 °C):	350 mPas
Flash point:	>100 °C
Dilution Stability:	No separated material observed
Storage stability:	Stability data provided by the applicant supports a storage life of 2 years when stored under normal conditions in high density polyethylene containers.
Low temperature stability:	No separated material observed

Recommendation

Based on a review of the chemistry and manufacturing details provided by the applicant, registration of Torpedo Herbicide is supported.

TOXICOLOGICAL ASSESSMENT

Evaluation of Toxicology

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

Toxicokinetics and Metabolism Studies

Florasulam technical was rapidly and extensively absorbed after oral administration in rats (Dryzga *et al.*, 1996; Hansen 1997). Up to 92% was absorbed at 10 mg/kg bw and 85% at 500 mg/kg bw in the study of Dryzga *et al.*, 1996. Total GI tract absorption was estimated based on the urinary and biliary excretion data of Hansen (1997). Following an oral florasulam dose of 10 mg/kg bw the GI tract absorption was ~82% comprising a mean of 81% in the urine and 1% in the bile. Maximal plasma and tissue concentrations being achieved within 0.5–1.0 h. The data indicated a saturation of tissue absorption and renal excretion at the high dose level of 500 mg/kg bw. Toxicokinetic and metabolic data for florasulam in rats was not significantly affected by gender or repeat-dose administration. There is little potential for accumulation of florasulam in the tissues. Florasulam was not extensively metabolised; the unchanged parent compound, florasulam, accounted for >80% of the administered dose in the urine. Two other metabolites were identified as 5-hydroxy-florasulam (~3–10% of the administered dose) and a sulphate conjugate of 5-hydroxy-florasulam (~2–4% of the administered dose). Of the tissues, the kidney contained the greatest amount of florasulam per gram tissue weight, followed by the liver. The majority of residue (90%) found in kidneys, liver and blood was unchanged parent florasulam. The metabolite, 5-hydroxy-florasulam was tentatively identified in liver and kidney samples (~1.5% of total recovered radioactivity). Florasulam was rapidly excreted, and the principal route was via the urine with >83% of the administered dose (10 mg/kg bw) excreted in the first 12 h; >90% of the administered dose was excreted in the urine and faeces combined within 24 h.

Percutaneous absorption

There is no available data on the extent of skin absorption for florasulam either in the technical form or when present in Torpedo Herbicide formulation.

In vitro and *in vivo* dermal absorption studies (Perkins & Banks, 2003; Bounds, 1997) were available for a similar SC formulation composition that contains an identical level of florasulam (50 g/L). Results from both studies indicated that florasulam may have a low potential for dermal absorption when administered as either a dilute "spray" (florasulam <0.1 g/L; <1.7 % absorption in 24 h) or undiluted formulation (florasulam 50 g/L; <0.5% absorption in 24 h). In the *in vivo* study, 12-22% of the applied dose remained in the treated skin up to 72 h after dosing. It was determined that the dose of florasulam remaining in skin had the potential to become absorbed even though its removal from the skin may occur through the process of normal epidermal turnover. Therefore,

when included in a similar formulation composition as Torpedo Herbicide, there is a potential for up to 22% of the applied dose of florasulam to become absorbed systemically.

Acute Studies

Active
Acute studies have been conducted with the active constituent, florasulam. Florasulam has low acute oral (LD_{50} of >5000 mg/kg bw in rats and mice), low dermal (LD_{50} >2000 mg/kg bw in rabbits) and low inhalational toxicity (LC_{50} >5000 mg/m^3 4-h nose only exposure in rats). It was slight skin and eye irritants in rabbits, but not a skin sensitiser in guinea pigs.

A metabolite of florasulam in mammals, 5-hydroxy-florasulam, displayed low acute oral (LD_{50} >5000 mg/kg bw) toxicity in rats.

Formulated Product
There were no acute studies performed for Torpedo Herbicide. In the absence of acute toxicity information, the product's hazard profile was extrapolated from data on the individual constituents and their levels in the product. Results of acute toxicological studies performed with an SC formulation of either florasulam at 50 g/L or clopyralid at 300 g/L were also considered in the extrapolation.

An SC formulation containing 50 g/L florasulam, displayed low acute oral (LD_{50} >2000 to >5000 mg/kg bw in rats and LD_{50} >5000 mg/kg bw in mice respectively) and low dermal (LD_{50} >2000 mg/kg bw in rats) toxicity. This formulation was not a skin irritant but was a slight eye irritant in rabbits. It was not a skin sensitiser in guinea pigs.

SC formulations containing 300 g/L clopyralid in the monoethanolamine salt form displayed low acute oral (LD_{50} >2000 to >5000 mg/kg bw in rats), low dermal (LD_{50} >2000 mg/kg bw in rats) and low inhalational toxicity (LC_{50} >4.27 mg/m^3 in rats). The formulation was not a skin irritant but was a slight eye irritant in rabbits. Additionally, no skin-sensitisation was observed in guinea pigs.

Torpedo Herbicide was considered likely to display low acute toxicity by the oral, dermal and inhalation routes of exposure, to be a moderate eye and skin irritant, but unlikely to cause skin sensitisation.

Short-term Studies
Two-week repeat-dose dietary studies were conducted within the same study laboratory for both mice ($B6C3F_1$ strain) and rats (F-344 strain); doses used were 0, 100, 500 and 1000 mg/kg bw/d (Szabo & Davis, 1993). No mortalities were recorded during the course of either study. In mice, females given the high dose exhibited a decrease in body weight gain by the end of the dosing period, which likely reflected lower feed consumption (perhaps due to a degree of florasulam unpalatability) noted throughout the test period in the same animals rather than a toxic effect of florasulam. Female mice exhibited statistically decreased, but not dose-dependent, absolute heart weights at all dose levels (>10%) and decreased absolute liver weights at mid and high doses (>10%) which were all attributable to lower terminal body weights. In females, relative liver and heart weights remained comparable to control and no histological alterations were noted in female liver or heart. The decreased absolute liver and heart weights were therefore concluded to be secondary to reduced weight gain rather than a direct toxicological effect. The NOEL (both sexes) of $B6C3F_1$ mice was the highest tested dose of 1000 mg/kg bw/d.

In the same study laboratory, administration of the high dose to rats resulted in decreased body weight gains (both sexes) by the end of the dosing-period (>20%), related to lower feed

consumption. Although no dose-response pattern was observed, Hct and Hb were statistically lower in both sexes compared to concurrent controls at the high dose. At doses of ≥500 mg/kg bw/d, histopathological alterations characterised as nuclear pleomorphism of renal proximal tubule epithelial cells were detected in both sexes. There was an increased incidence of degeneration/regeneration of renal tubules in females at the mid-dose and in both sexes at the high dose. One of 5 male and 4/5 female rats demonstrated multifocal necrosis of proximal tubule epithelial cells at the high dose. The NOEL for both sexes of F-344 rats was 100 mg/kg bw/d based on the histopathological effects of florasulam on the kidney at doses of 500 mg/kg bw and above.

Given the unpalatability of florasulam at certain doses, a more focused investigation of florasulam palatability administered *ad libitum* in the diet was evaluated in dogs (beagles) during a 2 to 8-week dietary period (Dalgard, 1995). The maximum target dose level of florasulam for this study (1000 mg/kg bw) exceeded the potential level of human exposure many fold. In this study food consumption at a target level of 1000 mg/kg bw/d was not sufficient to sustain life. At target levels of 500 and 450 mg/kg bw/d in-life body weights and food consumption declined steadily. As a result of the decreased food consumption, actual compound consumption of florasulam was generally below target levels. Animals at target levels of 250 and 350 mg/kg bw/d exhibited compound consumption values that were similar (290 mg/kg bw/d) and stable body weights.

In a 4-week dietary toxicity study in dogs, beagles (2/sex) were fed diets formulated to provide 0, 50, 150 or 450 mg/kg bw/d (Sullivan & Singleton, 1995). No mortalities were reported during the study. Reduced food consumption was noted at the high dose level and consequently body weight gain and florasulam consumption were decreased. Dose-dependent toxic effects were evident in the liver. Alkaline phosphatase (ALP) activity increased in a dose-dependent manner in both sexes, with aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities increased in both sexes given ≥150 mg/kg bw/d at the end of the study period. Hyperplasia of bile ducts was present in both sexes given ≥150 mg/kg bw/d. One high dose male displayed biliary hyperplasia, bile stasis (cholestasis), and hepatocellular necrosis. Increased levels of ALP, ALT, and AST in the affected animals are likely to be linked to this effect, since they can be good indicators of an obstructive condition like cholestasis or hepatocellular disease. A trend for increased relative liver weights was observed at the mid (males only) and high dose level (both sexes) (>10% vs. controls) was linked to decreased terminal body weights. Since effects were observed at the lowest dose administered, a NOEL could not be established for this study.

F-344 rats received repeated dermal applications (25 cm^2) of either 0 (control), 100, 500 or 1000 mg florasulam technical/kg bw/d for 6 h/d, 7 d/wk for 28 d under occlusive conditions (Scortichini & Kociba, 1997). No mortalities or treatment-related systemic effects were observed. The white blood cell (WBC) counts for both sexes were statistically higher than control means at the low-dose. There was no evidence of infection in these animals and there were no statistical outliers, which may have skewed the data on WBC counts. Also at the low-dose, changes indicative of slight anaemia were observed in females (lower red blood cell (RBC) count, haemoglobin (Hb), and haematocrit (Hct)) versus concurrent controls. At the highest dose in females, only Hb levels were statistically lower than concurrent controls. The toxicological significance of reported haematological alterations was not clear, as there was no clear dose-response pattern or histopathological correlates observed. Slight, transient dermal irritation at the application site was observed in male rats at 1000 mg/kg bw/d. The NOEL for systemic toxicity in both sexes of F-344 rats was the test limit dose of 1000 mg/kg bw/d. The NOEL for dermal test site irritancy was 500 mg/kg bw/d in males and the test limit dose of 1000 mg/kg bw/d in females.

Subchronic Studies

Sub-chronic toxicity studies conducted for florasulam were all 13-week dietary studies conducted in mice ($B6C3F_1$), rats (F-344 and CD strain), or dogs (beagles). In addition, the F-344 rat study incorporated a 4-week recovery period within the study protocol to evaluate the reversibility of florasulam effects.

Mice ($B6C3F_1$ strain) received daily dietary doses of 0, 20, 100, 500 or 1000 mg/kg bw/d over 13-weeks duration (Redmond & Johnson, 1996). Although within the normal historical range for this strain and age, statistically decreased blood urea nitrogen (BUN) levels were observed in male mice at ≥500 mg/kg bw/d. Whilst alterations in BUN may indicate changes in kidney function, there were no other kidney function test indicator correlates detected such as changes in creatinine or electrolytes (i.e. sodium, potassium and calcium). Other urinalysis parameters were not examined in this study. Additionally, whilst decreased BUN levels may also indicate abnormal liver function (due to decrease in the formation of urea) and malnutrition, no treatment-related changes in food consumption, body/organ weight changes or liver pathology were noted in this study. Treatment-related renal lesions were found histologically in all male mice at doses of ≥500 mg/kg bw/d, and in 80% of females at the high dose level. The lesions, termed hypertrophy of the collecting ducts, were characterised by enlarged epithelial cells lining the collecting duct that were restricted to the inner stripe of the outer zone of the medulla. Hypertrophied cells were identified as type-A intercalated cells on the basis of their distribution and histological appearance. Under the conditions of the study the NOEL for male and female $B6C3F_1$ mice was 100 and 500 mg/kg bw/d, respectively, based on histopathological findings in the kidneys at higher doses.

Rats (F-344 strain) received daily dietary doses of 0, 20, 100, 500, 800 (females) or 1000 (males) mg/kg bw/d over a 13-week duration (Redmond & Johnson, 1996). After this time, florasulam treatment was ceased and rats were examined after a 4-week recovery period. No mortalities were recorded during the study. At doses of ≥500 mg/kg bw/d, statistically lower body weight gains, perineal urinary soiling and lower food consumption was observed. Feed consumption continued to be lower in high dose animals during the recovery period. In males given ≥100 mg/kg bw/d, there was evidence indicative of slight anaemia (dose-dependent decrease in RBC counts, and lower Hb and Hct levels). At the highest dose in males, serum ALP, total protein and triglycerides were statistically lower whereas cholesterol and potassium levels were higher than controls. RBC counts and serum potassium were the only clinical chemistry parameters that did not normalise in males after the recovery period. At the highest dose in females, serum glucose and phosphorus levels were statistically increased but this effect was reversible after the recovery period. The primary effects of florasulam in this study were on the kidney. At necropsy, absolute and relative kidney weights were statistically higher and renal lesions were evident histopathologically in both sexes at ≥500 mg/kg bw/d. Males had lesions classified as hypertrophy of the collecting ducts, with enlarged epithelial cells lining the collecting duct that were restricted to the inner stripe of the outer zone of the medulla. Hypertrophied cells were identified as type-A intercalated cells on the basis of their distribution and histological appearance. The frequency of hypertrophied cells detected occurred in a dose-responsive manner in males. Gender-related differences were apparent in nature of the lesions. Females had renal lesions that were highly variable with marked intra- and inter-animal variations. The most striking lesion in females involved varying degrees of necrosis and/or degeneration of the epithelium in the descending (straight) limb of the proximal tubules, present in the outer stripe of the outer zone of the medulla, with a variable regenerative response. Although affected to a lesser degree, the second type of lesion in females was a similar form of hypertrophy of the collecting duct epithelium. Additionally, small-foci of mineralised debris were present in the tubules of the papilla in the majority of high dose females. This effect was distinguished from non-treatment related common spontaneous mineralisation of the papilla in F-344 rats by being restricted to the medullary region. Lower urinary pH and specific gravity was observed in both sexes at the high dose. Urinary specific gravity did not normalise to controls levels after the

recovery period. Atrophy of adipose tissue was noted in most animals at the high dose level. The NOEL of florasulam was 100 mg/kg bw/d for both sexes of F-344 rats based on various treatment-related changes at higher doses (500 mg/kg bw/d and above) including histopathological findings in the kidneys, increased kidney weights, and decreased body weight gain.

CD rats (Sprague-Dawley derived) received daily dietary doses of 0, 100, 500 or 1000 mg/kg bw/d over a 13-week duration (Liberacki *et al.*, 1996). Three spontaneous deaths (30%) occurred in high dose males prior to scheduled necropsies that were all attributed to florasulam-associated severe renal papillary necrosis. The necrosis was characterised by coagulation necrosis with congestion and haemorrhage of the entire tip of the papilla. At doses of ≥500 mg/kg bw/d, increased incidences of perineal and/or facial soiling, thin, rough haircoat, reddish urine (high dose males only), lower food consumption and body weight gain were noted. Significant increases in relative kidney weights were noted at the high dose. Treatment-related histopathological changes were noted in the kidneys and included hypertrophy of the cells within the collecting ducts at doses of ≥500 mg/kg bw/d. The effect was dose-responsive, with the moderate grade confined to the high dose group while those given 500 mg/kg bw/d had very slight to slight grades. Renal tubular degeneration/regeneration along with tubular necrosis (females only) and papillary necrosis was present in high dose groups (especially males). Tubular necrosis in females appeared to be an acute effect (a few days) rather than reflecting a 13-week old lesion. These lesion types were distinct from common spontaneous lesions that occur in this strain of rats because the focus of the lesion was larger (more tubules affected), there was less thickening of the basement membrane/fibrosis of the surrounding interstitium, lesions were present more uniformly, and appeared to be centred at the corticomedullary junction rather than randomly scattered throughout the cortex. The NOEL of florasulam in CD rats was 100 mg/kg bw/d for both sexes based on treatment-related histopathological findings on the kidney and clinical signs at higher doses (500 mg/kg bw and above).

Dogs (beagles) received daily dietary doses of 0, 5, 50 and 100 mg/kg bw/d over a 13-week duration (Stebbins, 1995). There were no mortalities recorded during the study. The effects of florasulam were confined to the kidney and liver. Statistically significant decreases in BUN and increases in creatinine (males only) were observed at the high dose in both sexes by the end of the study. The decreased BUN-creatinine ratios in both sexes suggested that extrarenal factors contributed to the decreased BUN and that proportionately more urea than creatinine was excreted by the kidneys. A dose-dependent induction of ALP was detected in both sexes. Total protein tended to be decreased in both sexes (~10%) at ≥50 mg/kg bw/d but was not lower than historical controls for dogs of this age and strain. Histologically, dose-dependent hypertrophy (number of animals affected and incidence of affected cells) of epithelial cells in the inner stripe of the medulla was observed at all doses. The only dog (1 of 2 females) affected at the lowest dose had a congenital absence of one kidney which is thought to have made it susceptible to the renal effects of florasulam compared to other dogs. Under the conditions of this study, the NOEL of florasulam in anatomically normal beagle dogs was 5 mg/kg bw/d in both sexes, based on histopathological findings in the kidney at higher doses (50 mg/kg bw/d and above).

Chronic/Carcinogenicity Studies

Chronic toxicity studies on florasulam were all dietary studies conducted in mice ($B6C3F_1$), rats (F-344) and dogs (beagles).

Mice ($B6C3F_1$ strain) were received daily dietary doses of 0, 50, 500 or 1000 mg/kg bw/d were administered over a 2-year period (Quast *et al.*, 1997). No treatment-related effects on mortality or lifespan were observed. The calculated florasulam intake agreed closely with the target dose level for all dose groups over the course of the study. There was no consistent pattern of treatment-related effects on feed consumption. Overall, body weights and body weight gain for both sexes in the high

dose groups were slightly lower than control values for most of the study. Statistically decreased serum cholesterol and triglycerides were noted at 1 year in high dose males and were interpreted to be secondary to decreased body weight gain and decreased absolute liver weight observed in these mice. Microscopic alterations in tinctorial properties of centrilobular hepatocytes, indicative of decreased glycogen content, were also noted in the same group. Effects on the liver were not noted at 2 years. Decreased absolute and relative kidney weights at 1 and 2 year necropsies were noted in males at doses of ≥500 mg/kg bw/d. Corresponding histopathological findings in kidney included hypertrophy of cells of the collecting duct primarily in the inner and outer stripe of the renal medulla in both sexes at the same doses. Overall, the effect was minimal and was graded as very slight or slight (<5 hypertrophied cells identified in any collecting duct). A dose-related decrease in the amount of cytoplasmic vacuolation of the cortical tubular epithelial cells that are normally present in mature mice on an *ad libitum* diet, was also noted in males given ≥500 mg/kg bw/d. This finding was consistent with decreased kidney weights. A decrease in the normally occurring disease process called renal tubular degeneration with regeneration was also noted in both sexes given ≥500 mg/kg bw/d. There were no clinical chemistry or electrolyte changes to indicate compromised renal function in affected animals. Urinalysis parameters were not measured in this study. The various diagnoses underlying death or moribundity reflected major spontaneously occurring disease processes routinely found in $B6C3F_1$ mice used in 2-year studies. There were no neoplasms in any dose group that were identified as statistically increased or outside the normal historical control range, up to and including the highest tolerated dose of 1000 mg/kg bw/d. Therefore, florasulam did not display any carcinogenic potential. The NOEL of florasulam in both sexes of $B6C3F_1$ was 50 mg/kg bw/d, based on decreased kidney weights, histopathological findings in the kidneys and transient effects on the liver (12 months) at higher doses (500 mg/kg bw/d and above).

In rats (F-344 strain), dietary doses of 0, 10, 125 (females), 250 or 500 (males) mg/kg bw/d were administered over a 2-year period (Johnson *et al.*, 1997). No treatment-related effects on mortality or lifespan were observed. The calculated florasulam intake agreed closely with the target dose level for all dose groups over the course of the study. Perineal urinary soiling was consistently noted during the study in the majority of animals from both sexes at doses of ≥125 mg/kg bw/d. At the high dose, in-life body weights and body weight gains were significantly lower (average of >10%) in males, from ~3 months into the study until termination. This effect corresponded with lower food consumption in the same group, over the same time period. Terminal body weights were also statistically lower at the high dose. To a lesser extent at 250 mg/kg bw/d, there was also a trend for reduced body weights, body weight gains and feed consumption during the second year of dosing. Statistically significant changes in haematological parameters were indicative of slight anaemia (decreased RBC, Hb and Hct) in males at the high dose at 6-12 months but were not apparent at later time points. Also in high dose males, consistently lower serum ALP activities (6 months - 2 years) and transient decreases in serum calcium and phosphorous levels (6 and12 month points only) were detected. Serum bicarbonate levels were slightly increased in high dose males at 2 years (the only time point evaluated) and may have significance with respect to the renal effects found histopathologically in this group. The kidney was the primary target organ for the effects of florasulam in this study. Increases in relative kidney weights (>20%; at 1 and 2-year necropsies) were noted in both sexes. Urinary test parameters affected in high dose males included: decreased urine pH in rats given ≥125 mg/kg bw/d, and lower urine specific gravity, protein and ketone levels. The primary histopathological change was hypertrophy of individual epithelial cells lining the collecting ducts of rats given ≥125 mg/kg bw/d. Other treatment-related effects in male rats given ≥250 mg/kg bw/d included an increased incidence of foci of mineralisation within tubules in the renal papilla (~80% of animals), hyperplasia of the transitional epithelium of the renal papilla (22% of animals) and unilateral papillary necrosis (6% of animals). There were no clear associations made for treatment-related causes of death. The various diagnoses underlying death or moribundity reflected the major disease processes routinely found in older F-344 rats. There were no treatment-related neoplasms in any dose group (no statistical increases or incidence rates outside the normal

historical control range). As such, there was no evidence to indicate any carcinogenic potential of florasulam up to and including the test limit dose. The NOEL of florasulam was 10 mg/kg bw/d for both sexes of F-344 rats based on alterations in urinalysis parameters, organ weight and histopathological alterations in the kidney at higher doses (125 mg/kg bw/d and above).

In dogs (beagles), dietary doses of 0, 0.5, 5, or 100 (reduced to 50 after 3 months dosing during study due to animal welfare concerns) mg/kg bw/d were administered over a 1-year period (Stebbins & Haut, 1997). There were no mortalities recorded during the study. Treatment-related effects on haematological (slight anaemia and effects on WBC counts) and clinical chemistry parameters (ALP, ALT, albumin, total protein, total bilirubin) occurred during the first 3 months of dosing in both sexes at 100 mg/kg bw/d. These alterations were restored to control levels following a reduction of the dose level to 50 mg/kg bw/d. Lesions in the kidney characterized as a slight hypertrophy of epithelial cells of collecting ducts (above the spontaneous degree of hypertrophic change noted for this species) in the inner and outer stripe of the outer zone of the medulla were present in one-quarter of the animals from the high dose group in both sexes. These lesions were identical to those observed at the end of a separate 13-week dietary study in dogs (Stebbins, 1995) and hypertrophied cells were identified as type-A intercalated cells on the basis of their distribution and histological appearance. No treatment-related effects on urinalysis parameters were noted in either sex. A histopathological alteration of the adrenal glands, characterised as slight vacuolisation of the zona reticularis and zona fasciculata, was present in both sexes at the high dose. Under the conditions of study, the NOEL of florasulam was 5 mg/kg bw/d for both sexes of beagle dogs based on histopathological alterations in the kidneys at higher doses (50 mg/kg bw/d and above).

Reproduction Study

Rats (CD strain) were given diets that provided 0, 10, 100 or 500 mg/kg bw/d florasulam, 7 days a week for two generations (one litter/generation) (Liberacki *et al.*, 1997). Treatment-related observations noted in both sexes of P1/P2 animals included soiling of the perineal/inguinal area and reddish urine. At the high dose, parental effects consisted of decreased food consumption (P1 females, P2 both sexes), and significantly lower body weights of P2 males and P1/P2 females of the high dose group during most of the pre-mating, gestation, and lactation periods. Body weight gains of the high dose group P1/P2 females were also significantly lower during gestation (days 0-21). Parental effects (P1/P2) observed in the kidneys of both sexes, at high dose levels, were considered to be treatment-related and included increases in relative kidney weights, hypertrophy of renal tubular collecting ducts of the inner stripe of the outer zone of the medulla (multifocal and very slight in >70% of animals), necrosis of renal papilla with accompanying inflammation (bilateral, multifocal and slight in ~10% of animals) and haemorrhagic casts present in the lumen of the urinary bladder (~10% of animals).

No treatment-related effects were observed on any reproductive indices measured including gestation length and survival, litter size, pup survival indices or pup sex ratios. No treatment-related clinical or physical observations or organ weight changes were noted for F1/F2 pups. There were no treatment-related effects on F1/F2 pup body weight at birth. However, transient decreases in F1/F2 pup body weights (~10%) from high dose P1/P2 animals were noted between lactation days 4-7 and were considered to be secondary to decreased food consumption of the maternal (P1/P2) animals early in the lactation period. Under the conditions of the study, the parental NOEL of florasulam for systemic effects was 100 mg/kg bw/d for both sexes of CD rats based on histopathological findings in the kidneys, lower body weight and gains, and increased kidney weights at higher doses. Based upon transient decreases in pup body weights, the foetal NOEL was determined to be 100 mg/kg bw/d. The NOEL for reproductive effects was the test limit dose of 500 mg/kg bw/d.

Developmental Studies

Oral gavage teratology studies, including preliminary studies, were carried out in time-mated rats (Liberacki *et al.*, 1996; Liberacki & Carney, 1997) and rabbits (Zablotny & Quast, 1996; Zablotny & Carney, 1997).

In the preliminary study (Liberacki *et al.*, 1996), florasulam was administered by oral gavage to rats (CD strain) on days 6-15 of gestation at dose levels of 0 (vehicle), 100, 500 or 1000 mg/kg bw/d. The high dose group was terminated on gestation day 13 as excessive maternal toxicity was observed and a new high dose study group given 750 mg/kg bw/d was substituted, alongside a concurrent vehicle control group. Feed consumption of dams at the high dose (750 mg/kg bw/d) was decreased on gestation days 6-12. Statistically decreased body weight gains (~30%) were identified within the same time period. Treatment-related increases in absolute and relative kidney weights (>10%) were observed in dams given 750 mg/kg bw/d. There were no other significant treatment-related differences in maternal or developmental test-parameters. Under the conditions of the study, the NOEL for maternal toxicity was 500 mg/kg bw/d for effects on decreased food consumption, decreased body weight gain and increased kidney weights at higher doses. The NOEL for foetal toxicity was the test dose limit of 750 mg/kg bw/d.

Oral gavage doses of 0, 50, 250 or 750 mg/kg bw/d were given to rats on gestation days 6-15 in the main CD rat study (Liberacki & Carney, 1997). Four of 25 dams given the high dose died prior to scheduled necropsy. Three of the deaths were attributed to gavage error based upon pathology findings in the lungs whilst the fourth death was not determined and may have been treatment-related. All 4 dams had normal developing embryos respective to gestational age. Observations in surviving dams at high dose included increased salivation immediately after dosing and perineal urinary soiling. Feed consumption in high dose dams was decreased on gestation days 6-12 and correlated with decreased body weight gains during the same time period. Treatment-related increases in absolute and relative kidney weights (~10%) were observed for dams given 750 mg/kg bw/d. Under the conditions of the study, the NOEL of florasulam for maternal toxicity was 250 mg/kg bw/d in CD rats based on decreased feed consumption, decreased body weight and gain, and increased kidney weights at higher doses. The NOEL for foetal toxicity was the test limit dose of 750 mg/kg bw/d.

In the preliminary rabbit study (Zablotny & Quast, 1996), florasulam was administered by oral gavage on days 7-19 of gestation at dose levels of 0, 100, 300, 600 or 1000 mg/kg bw/d (in 0.5% Methocel A4M vehicle). One dam dosed with 600 mg/kg bw/d and three dams on the high dose were found dead between days 10-19 of gestation, these were considered to be treatment-related. Dams at 1000 mg/kg bw/d were sacrificed on gestation day 17 due to excessive maternal toxicity. A decrease in body weight gain observed in dams given ≥600 mg/kg bw/d corresponded with decreased mean food consumption during days 7-16 of gestation. The decreased weight gains resulted in lower body weights in high dose dams on gestation day 16. Although not statistically identified, absolute and relative kidney weights in all dose groups were ~10% higher than concurrent controls. This was not a dose-responsive effect and all weight values were within the historic range of recent studies in NZW rabbits of the study laboratory. There were no other significant treatment-related differences in maternal or developmental test-parameters. Under the conditions of the study, the NOEL of florasulam for maternal toxicity was 300 mg/kg bw/d in NZW rabbits based on decreased body weights, lower body weight gains and food consumption during gestation at higher doses (600 mg/kg bw/d). The NOEL for foetal toxicity was the test limit dose of 600 mg/kg bw/d.

Oral gavage doses of 0, 50, 250 or 500 mg/kg bw/d (in 0.5% Methocel A4M vehicle) were given to rabbits on gestation days 7-19 in the main NZW rabbit study (Zablotny & Carney, 1997). One dam out of 20 at the high dose was found dead on day 19 due to gavage error. No treatment-related

effects on feed consumption, in-life body weights and gains, terminal weights or organ weights were observed at any dose level. In the preliminary NZW rabbit study, effects on body weight and food intake were only seen at doses above the highest dose used in this study. There were no treatment-related differences in other maternal or developmental test-parameters. Under the conditions of the study, the NOEL of florasulam for maternal and foetal toxicity was the test limit dose of 500 mg/kg bw/d in NZW rabbits.

Genotoxicity Studies

The mutagenic potential of florasulam was tested in a battery of *in vitro* tests (bacterial *Salmonella*-Ames test and *E.coli* reverse mutation assays, mammalian cell forward mutation assay, chromosomal aberration assay) and an *in vivo* micronucleus test. The weight of evidence from these tests indicated that florasulam lacks genotoxic potential.

5-hydroxy florasulam, the major metabolite resulting from the hydroxylation of the florasulam phenyl moiety in mammals, displayed no genotoxic potential when tested in both bacterial and mammalian *in vitro* mutation assays.

Neurotoxicity Studies

There were no significant treatment-related findings in the acute (Mattsson *et al.*, 1997) or subchronic (Shnkar & Johnson, 1996) neurotoxicity screening studies in the rat (F-344). Both studies are summarised below. Under test study conditions, florasulam was not considered to be neurotoxic.

In an acute neurotoxicity study, F-344 rats were given a single oral gavage dose of florasulam at 0, 200, 1000 or 2000 mg/kg bw/d (in aqueous methylcellulose vehicle) (Mattsson *et al.*, 1997). One high dose male rat died on day 2 post-dosing from undetermined causes and no data from this rat was reported. Treatment-related perineal urinary soiling occurred in both sexes at the mid and high doses from the second day of dosing onwards. On the day of dosing (day 1), a slight transient decrease in motor activity, an increased incidence of minimal level of activity in the open field and decreased responsiveness to sharp noise in high dose males was detected. These functional observational battery (FOB) and motor activity findings were no longer observed in high dose males on day 8 post-dosing. The overall pattern of effects on the day of dosing suggested a slight transient decreased activity and reactivity in the high dose males on the day of dosing. In the absence of any (histo-) pathological or neuropathological correlates in the central or peripheral nervous system, the FOB and motor activity findings on the day of dosing in high dose males were not considered to be due to neurotoxicity *per se*. Under the conditions of this study, a single dose of florasulam given to F-344 rats up to 2000 mg/kg bw inclusive did not evoke any changes indicative of neurotoxicity during a 2-week observation period after dosing. The NOEL for systemic toxicity was 1000 mg/kg bw for males, based on decreased activity and reactivity of rats at the higher dose. A NOEL for systemic toxicity of 200 mg/kg bw for females was based on clinical signs (perineal urinary soiling) at the next highest dose (1000 mg/kg bw/d and above). The NOEL for neurotoxicity was 2000 mg/kg bw, the test dose limit, in both sexes.

In a chronic neurotoxicity study (Shnkar & Johnson, 1996), F-344 rats were fed diets containing 0, 10, 250 or 500 mg/kg bw/d (males) and 10, 125 or 250 mg/kg bw/d (females) of florasulam for 12 months. There were no affects on various test parameters that would be indicative of neurotoxicity (FOB, forelimb and hindlimb grip performance testing, landing footsplay testing, automated motor activity testing, and auditory brainstem response testing). High dose male rats had statistically significant decreases in body weights and body weight gains compared to concurrent controls at 6, 9 and 12-month test points. Perineal urinary soiling was a treatment-related effect seen in both sexes at the mid and high dose. Cumulative incidences of observations of urinary soiling for the year of treatment for males were in sequence from control to high dose: 1/10, 4/10, 8/10 and 10/10. For females, from control to high dose: 1/10, 0/10, 9/10 and 9/10. Treatment-related perineal soiling may have been associated with a slight tendency towards urination observed in treated rats in the

open field. The NOEL for neurotoxicity was the highest dose level tested on each sex, which was 250 mg/kg bw/d for females and 500 mg/kg bw/d for males. The NOEL of florasulam for systemic toxicity in both sexes was 10 mg/kg bw/d based on clinical signs (perineal urinary soiling) in both sexes at the next higher dose level of 250 mg/kg bw/d.

Other Studies

Repeat-dose dietary studies with florasulam consistently demonstrated treatment-related microscopic changes in the kidneys of rats, mice and dogs. The microscopic changes were primarily identified as hypertrophy of the type-A intercalated cells of the collecting ducts. As a possible mechanism for florasulam-induced type-A intercalated cell hypertrophy, the potential for florasulam to act as an inhibitor of carbonic anhydrase (CA) was investigated in a study by Stott (1997). In this study, bovine erythrocyte CA activity was assessed using p-nitrophenylacetate as a substrate and measuring the rate of *p*-nitrophenol formation via spectrophotometric methods. CA esterase activity was inhibited ~50% relative to the controls at the highest concentration of florasulam tested, 6.2 mM. Full CA activity was evident at concentrations of 0.62 mM florasulam or lower. In contrast, the positive control acetozolamide completely abolished CA activity at a concentration of 0.01 mM or greater. Approximately 50% CA activity was noted at the lowest concentration of acetozolamide tested (0.001 mM). The findings of this study indicated that florasulam has a relatively low capacity for inhibiting carbonic anhydrase *in vitro* when compared with the potency of a known inhibitor, acetazolamide.

Conclusion

Based on the adequacy of the toxicological database, the approval of florasulam as a new active constituent and registration of Torpedo Herbicide are supported. The proposed use of Torpedo Herbicide will not be an undue health hazard to humans according to the criteria stipulated in Section 14 (5)(e) criteria of the Ag/Vet Code Act of 1994.

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.

At its 46th meeting, on 21-23 February 2006, the NDPSC agreed, having regard to the slight skin and eye irritancy potential, that florasulam be included in Schedule 5 of the SUSDP. No cut-off to another Schedule was proposed for florasulam when present at 50 g/L in Torpedo Herbicide SC formulation.

No-observed-Effect-Level (NOEL) and Acceptable Daily Intake (ADI)

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

An ADI of 0.05 mg/kg bw/d has been established for florasulam, based on a NOEL of 5 mg/kg bw/d in a one-year dog study, using a safety factor of 100.

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.

An ARfD for florasulam was not established since it was considered unlikely to present an acute hazard.

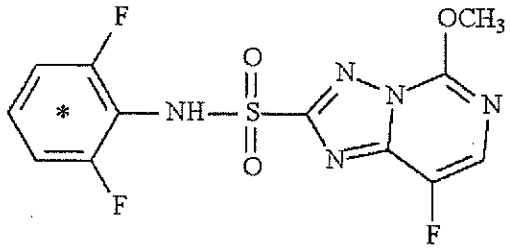
RESIDUES ASSESSMENT

Introduction

The following sections relate to the metabolism and residue aspects of florasulam only. Clopyralid has previously been considered as part of the registration of Lontrel Herbicide. As the proposed use of clopyralid in Torpedo Herbicide is similar to that approved for Lontrel Herbicide, no further consideration of clopyralid is required as part of the current assessment.

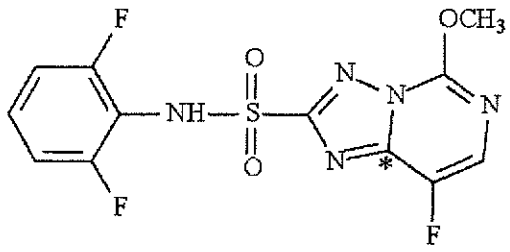
Metabolism

The metabolism of florasulam was investigated in wheat, rats, goats and hens using ^{14}C "phenyl" and "TP" labelled florasulam, as shown in the following diagram.



[UL-phenyl-^{14}C]-florasulam

"Phenyl" label



[9- triazolopyrimidine-^{14}C]-florasulam

"TP" label

In a wheat metabolism study, ^{14}C florasulam (both labels) was applied to crops at either BBCH 30 (stem elongation) or BBCH 49 (post flag-leaf emergence) at a rate of 50 g ai/ha. The application at BBCH 30 reflects the proposed use of the herbicide in Australia. Samples of whole plant material (forage) were collected at 0 and 30 days after application and grain and straw were collected at normal harvest (129 or 65 DAT).

TRR in whole grain were 0.001 and 0.002 mg/kg florasulam equivalents for the phenyl and TP labels, respectively, following both application timings. As the levels of radioactivity were low, no further characterisation or identification was conducted.

Residues of parent florasulam in whole plants sprayed at BBCH 30 at 0 days after treatment (0 DAT) accounted for 63% and 71% of the total radioactive residues (TRR) for the TP and phenyl labels, respectively. At 30 DAT, florasulam comprised 27% and 29% of the TRR for the TP and phenyl labels, respectively. By comparison, florasulam comprised 80% and 84% of the TRR for the TP and phenyl labels, respectively at 0 DAT and 32% and 27% of the TRR at 30 DAT, following application at BBCH 49.

In wheat straw sampled at 65 DAT, residues of florasulam comprised 7 and 14% of the TRR for the TP and phenyl labels, respectively only after application at BBCH 49; no florasulam was detected in mature straw (129 DAT) following application at BBCH 30.

Following extraction and analysis using HPLC and TLC, unconjugated 4-OH-(phenyl)-florasulam metabolite was identified in all samples of forage and straw. Residues of the metabolite in forage samples at 0 DAT following application at BBCH 30 were 0.84 and 0.9 % TRR and 15.1 and 6.8 %TRR at 30 DAT for the TP and phenyl labels, respectively. Following application at BBCH 49, residues were 0.4 and 1.2% TRR at 0 DAT for the TP and phenyl labels, respectively. No metabolite was detected in the 30 DAT samples.

The glucose conjugate of 4-OH-(phenyl)-florasulam compromised 24% and 19% of the TRR at 0 DAT and 13% and 21% of the TRR at 30 DAT for the TP and phenyl labels, respectively, following application at BBCH 30. Similarly, following application at BBCH 49, the glucose conjugate comprised 8.5% of the TRR (both labels) at 0 DAT and 19% and 42% of the TRR at 30 DAT for the TP and phenyl labels, respectively. In mature straw, both the 4-OH-(phenyl)-florasulam metabolite and its conjugate accounted for <10% of the TRR. The only other identified metabolite was 2-sulphonamide which appeared in the TP labelled samples only, accounting for up to 4.7% of the TRR in mature straw and ranging 0.7 to 1.5% TRR in forage samples.

Lactating goats were dosed for 5 days with ^{14}C phenyl or TP labelled florasulam at 0.48 mg/kg bw, equivalent to 11 ppm in the diet. The feed consumption was ~2 kg/day. The majority of the administered dose (83-89%) was recovered from excreta and cagewash. TRR in tissues were 0.12 and 0.14% of the administered dose for the phenyl and TP labels, respectively. Residues in the composite milk samples (AM and PM milkings) during the study period were 0.016 and 0.033 mg/kg equivalents for the phenyl and TP labels, respectively. Residues in the morning milk samples were generally higher than in the afternoon samples, however little variability was observed throughout the dosing period.

The highest concentration of radioactive residues in tissues was found in the kidneys, at 0.069 and 0.039 mg/kg equivalents for the phenyl- and TP-labelled samples, respectively. The concentration of TRR in other tissues for the phenyl and TP labels, respectively, were (mg/kg equivalents): liver (0.033 and 0.023); muscle (0.0016 and 0.0009); and fat (0.0016 and 0.0017)

Parent florasulam was the major component identified in milk and kidney. It comprised 87 and 89% of the TRR in milk (0.015-0.028 mg/kg equivalents), and 98 and 96% of the TRR in kidney samples for the TP and phenyl labels, respectively. In liver, a large proportion of the radioactivity remained un-extracted, even following enzyme digestion. The results of the goat study indicate that florasulam is readily absorbed and eliminated from the goat.

Laying hens were dosed for 5 days with ^{14}C phenyl- and TP-labelled florasulam at 0.76 mg/kg bw, equivalent to 10.7 ppm in the diet. The average feed consumption was 0.13 kg/day.

The majority of the administered dose was excreted; 91 and 97% of the phenyl and TP labels, respectively. The radioactivity in excreta was identified as parent compound. The TRR found in the tissues and egg samples were approximately 0.01% of the administered dose. A large proportion of the radioactivity in eggs and skin (81 – 95%) was mainly attributed to parent compound. The highest concentration was found in the skin, 0.0066 mg/kg equivalents (0.002% of the administered dose) and 0.005 mg/kg equivalents (0.002% of the administered dose) of phenyl and TP labels respectively. Residues in eggs were ~0.004 mg equiv./kg for both the phenyl and TP labels. TRR in muscle, fat and liver were less than limit of quantitation (<0.001 mg/kg equivalents). There was no significant difference in the metabolism of either labelled florasulam by hens, indicating no significant sulfonanilide-bridge cleavage had occurred.

Rats received a single oral dose of ^{14}C florasulam at 10 and 500 mg/kg bw. Most of the florasulam was readily absorbed and eliminated. The principal route of excretion was the urine, which contained 81-92% of the administered dose. Due to its rapid elimination, florasulam appears to have little potential for accumulation upon repeated administration. For further details see the toxicology section of this document.

Analytical methods

- ***Determination of florasulam residues in plant tissues***

Various chromatographic methods were used to determine florasulam residues in cereal matrices, namely forage, fodder, straw and grain. In all cases, samples were extracted using an acetic acid/acetone/water solution. Clean-up of the extract was conducted using liquid-liquid partitioning between acetonitrile and MTBE or by C-18 SPE cleanup. The clean extract was derivatised to form N-methyl florasulam, and the resulting extract was cleaned-up by silica SPE. Analysis for N-methyl florasulam was conducted using HPLC with UV absorption at 260 nm or GC/MSD.

Samples were also analysed by LC/MS/MS. The initial MTBE solution containing florasulam residues was solvent exchanged with ethyl acetate, before strong anion exchange (PE-AX) SPE cleanup. No derivatisation was required and samples were prepared in water/methanol/formic acid or acetonitrile/methanol/water/acetic acid solution prior to injection.

Each method was validated with LOQs of between 0.01-0.02 mg/kg for grain samples, and 0.05 mg/kg for forage and fodder samples. Recoveries were conducted with fortification at concentrations of 0.01 to 1.0 mg/kg and ranged 76.3 to 104%.

An ELISA (enzyme-linked immunosorbent assay) method was also provided which involved specific antibiotic test reagents to bind florasulam in the test sample. A colourimetric test was used to determine the amount of bound florasulam-antibody complex in the sample. The method was validated with a LOQ of 0.01 mg/kg. It is unknown whether this method will be commercially available in Australia for monitoring purposes.

- ***Determination of florasulam residues in animal tissues***

A method for the determination of florasulam in bovine tissues (muscle, kidney, live, fat) and milk by reverse-phase HPLC coupled with tandem mass spectrometric detection (MS/MS) was available. Samples are extracted with ethyl acetate and ethanol solution. The extract was centrifuged and evaporated. For samples other than fat, the extract was cleaned-up with a polymeric sorbent SPE cartridge and the florasulam residue was eluted with acetonitrile. For fat samples, the extract was cleaned-up by partitioning with acetonitrile and hexane. The acetonitrile layer containing florasulam residues was analysed. For milk samples, florasulam residues were extracted with acetonitrile. All samples were prepared in methanol/water for analysis by HPLC/MS/MS. The LOQ for bovine tissues and milk is 0.01 and 0.005 mg/kg, respectively. Recoveries were conducted by fortification at concentrations of 0.01 to 0.1 mg/kg for tissues and 0.005 to 0.05 mg/kg for milk and ranged 87 to 109%.

Residue definition

Due to the extensive metabolism of florasulam in plants and rapid elimination occurring in animal tissues, residues are unlikely to be detected when Torpedo Herbicide is used as proposed according to label directions and Good Agricultural Practice. Analytical methods are available for the determination of florasulam in plant and animal commodities with an LOQ of 0.01 mg/kg. Therefore, the following Residue Definition is recommended for florasulam for the purposes of dietary exposure assessment and for compliance and monitoring:

Florasulam *Florasulam*

Storage stability

Storage stability of florasulam residues in various plant matrices was conducted for up to 16 months. Stability of residues in forage, grain and straw samples was satisfactory for up to 15 months at -15°C, with recoveries remaining above ~70%. The results of the study show that

residues in stored samples are representative of the residues present in commodities at the time of sampling.

Residue trials

The proposed use of Torpedo Herbicide in Australia is application to barley, triticale and wheat from 2-leaf stage to 1st node (up to BBCH 30/31) at a rate of 5 g ai/ha and a withholding period of "Not Required When Used As Directed".

- ***Grain***

Overseas trials were conducted on wheat, barley, oats and rye treated with a single application of florasulam at rates ranging 4.2-10 g a.i./ha (0.8-2 × rate) at crop stage BBCH 21 to 61 (beginning of tillering to first tiller detectable to the beginning of flowering: first anthers visible). Residues in grain samples at 48-113 days after application were <0.01 mg/kg (n=122).

In similar trials, wheat, barley and oats were treated with two applications of florasulam at 4.2-10 g a.i./ha (0.8-2×) at crop stages BBCH 31-32 (first or second node) and 49-52 (first awns visible to beginning of heading). Residues in grain samples at 48-78 days after application were <LOD =0.002 mg/kg (n=12). The validated LOQ in grain was 0.01 mg/kg.

The following MRL is recommended for cereal grains in conjunction with the proposed WHP of "NOT REQUIRED WHEN USED AS DIRECTED".

Table 1

Compound	Food		MRL (mg/kg)
Florasulam	GC 0080	Cereal grains	*0.01

Animal feeds

Fodder/straw

Fodder (straw) samples were collected at harvest from cereals crops treated as described above. Residues in all straw samples at harvest were <LOD =0.01 mg/kg in all samples (n=132).

Forage

Forage samples were collected from cereal crops treated as described above and harvested at 0-64 DAT. Residues in 40 samples at 0 DAT (from crops treated with a single or double application) ranged from <0.05 (LOQ) – 0.15 mg/kg (n=40) on a dry weight basis.

Residues in samples collected 3 DAT were <LOD - <LOQ (ie <0.01-<0.05 mg/kg) (n=38). Only 5 out of 82 samples contained detectable residues beyond 3 DAT. Residues in these samples, all treated with a single application at 1-2× the proposed rate, were 0.05 and 0.06 mg/kg in winter soft wheat at 6 DAT, 0.05 mg/kg in winter soft wheat at 11 DAT, and 0.06-0.09 mg/kg (estimated based on moisture content of 22-50%) in oats at 7 DAT. The remaining samples harvested with a WHP of 6 days or more had residues <LOQ =0.05 mg/kg (n=77). On the basis of a weight-of-evidence approach and recognising that double the proposed rate was employed in some trials, an MRL of *0.05 mg/kg is recommended for cereal forage.

The data support the following MRLs for cereal forage and fodder in conjunction with a 7 day withholding period for grazing and cutting for stockfeed:

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
Florasulam	AF 0081	Forage of cereal grains [fresh weight]	*0.05
	AS 0081	Straw and fodder of cereal grains (dry)	*0.05

Crop rotation

Crop rotation studies were conducted on wheat, sunflower, cabbage and carrots, planted at 30 days after application to soil with ^{14}C florasulam. No detectable residues were found in crops harvested at maturity (156-195 DAT). These data show that residues remaining in the soil following cereal treatment are not likely to incur detectable residues in subsequent crops, therefore no further consideration from a residues perspective is required. The label has appropriate crop safety advice for plant back periods, which account for clopyralid residues following use of Torpedo Herbicide. These are similar to those found on the reference product, Lontrel Herbicide.

Processing studies

No processing studies were required or submitted in the current application. Residues in harvested grain and seed are below the limit of quantification and processing is unlikely to result in detectable residues in grain and seed fractions.

Animal commodity MRLs

Animal feeding studies have not been conducted on florasulam. The metabolism studies show that florasulam is rapidly and extensively metabolised in goats and hens, and residues in animal tissues, milk and eggs are likely to be below the LOQ of 0.01 mg/kg following exposure to treated crops and crop portions. Based upon these data and the residues data for cereal crops, the following animal commodity MRLs are recommended:

Edible offal (mammalian)	*0.01 mg/kg
Eggs	*0.01 mg/kg
Meat (mammalian)	*0.01 mg/kg
Milks	*0.01 mg/kg
Poultry meat	*0.01 mg/kg
Poultry, edible offal of	*0.01 mg/kg

Estimated dietary intake

The chronic dietary intake risk for florasulam has been assessed. The ADI for florasulam is 0.05mg/kg bw/day, based upon a NOEL of 5 mg/kg bw/day and a 100 fold safety factor. The NEDI of florasulam is equivalent to <1% of the ADI. With respect to acute dietary intake, no acute reference dose (ARfD) has been set for florasulam as it was considered unlikely to present an acute hazard. It is concluded that the dietary exposure to florasulam is low and the risk from residues in food is acceptable when Torpedo Herbicide is used according to label directions.

Bioaccumulation potential

The Log K_{ow} of florasulam is 1.00 at pH 4.0 and 1.22 at pH 7.0, indicating that florasulam (parent) is unlikely to be fat-soluble. The low values are in line with results from the poultry and goat metabolism studies, where the feeding of radio-labelled parent compound resulted in little, if any residue in tissues, fat, milk or eggs. It is considered that the potential for florasulam to bio-accumulate is low.

Recommendations

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

Table 1

Compound	Food		MRL (mg/kg)
DELETE:			
Florasulam	GC 0080	Cereal Grains	T*0.01
ADD:			
Florasulam	GC 0080	Cereal Grains	*0.01
	MO 0105	Edible offal (mammalian)	*0.01
	PE 0112	Eggs	*0.01
	MM 0095	Meat (mammalian)	*0.01
	ML 0106	Milks	*0.01
	PM 0110	Poultry Meat	*0.01
	PO 0111	Poultry, edible offal of	*0.01

Table 3

Compound	Residue
ADD:	
Florasulam	Florasulam

Table 4

Compound	Animal feed commodity		MRL (mg/kg)
DELETE:			
Florasulam	Forage and fodder of cereal grains (dry)		T*0.05
ADD:			
Florasulam	AF 0081	Forage of cereal grains [fresh weight]	*0.05
	AS 0081	Straw and fodder of cereal grains (dry)	*0.05

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

HARVEST WITHHOLDING PERIOD

BARLEY, TRITICALE and WHEAT: Not required when used as directed.

When using Torpedo in a tank mix with another product, observe the Harvest Withholding Period of the other product.

GRAZING WITHHOLDING PERIOD

DO NOT graze or cut for stock feed for 7 days after application of Torpedo Herbicide.

When using Torpedo Herbicide is in a tank mix with another product, observe whichever Stockfeed Withholding Period is the longer.

ASSESSMENT OF OVERSEAS TRADE ASPECTS OF RESIDUES IN FOOD

Overseas registration status

Codex MRLs have not been determined for florasulam. The Applicant has indicated that florasulam is registered in 42 countries for weed control in cereals at similar application rates proposed for Australia. The following overseas MRLs are established for florasulam:

Country	Commodity Group	MRL Value (mg/kg)
Canada	Cereal Grains	0.01
Denmark	Cereal Grains	0.01
EU	Cereal Grains	0.01
France	Cereal Grains	0.01
Germany	Cereal Grains	0.01
Italy	Cereal Grains	0.01
Japan	Wheat, barley	0.01 (prov.)
Netherlands	Cereal Grains	0.01
Poland	Cereal Grains	0.01
Spain	Cereal Grains	0.01
Sweden	Cereal Grains	0.01
Switzerland	Cereal Grains	0.01
United Kingdom	Cereal Grains	0.01

Potential risk to Australian export trade

No detectable residues of florasulam are expected to occur in cereal grain, and therefore, unlikely to unduly prejudice trade in cereal gains. Furthermore, no Export Intervals are required for florasulam as there will be no detectable residues in the exported commodity; wheat and barley grain or processed wheat and barley foods.

Forage and fodder of treated crops, as well as grain, may be used as livestock feeds. Residues of florasulam in all of these commodities are expected to be below the LOQ. The feeding of these commodities to livestock is not expected to result in detectable residues in animal commodities, and thus prejudice trade in animal commodities.

The overall risk to export trade in cereal and animal commodities from the registration of Torpedo Herbicide is considered to be negligible.

OCCUPATIONAL HEALTH AND SAFETY ASSESSMENT

Formulation, packaging, transport, storage and retailing
The active constituent florasulam is to be manufactured by Dow Agrosciences LLC at the Dow Texas Operations Plant in Freeport, Texas, USA. Torpedo Herbicide is to be formulated by Dow Agrosciences NZ Ltd, New Zealand. Therefore, Australian workers will not be involved in the manufacture of dichlorprop-P technical or formulation of Torpedo Herbicide. Once imported, Australian workers may be involved in unloading and unpacking activities at the dock and in transporting and storing activities.

Torpedo Herbicide will be available in 5, 10 and 20 L HMW polyethylene jerry cans that are made by a blow moulding process. The neck sizes of these containers are 24, 35 and 55 mm, respectively.

Use pattern
Torpedo Herbicide is a suspension concentrate formulation for post-emergent control or suppression of broadleaf weeds in cereals crops including barley, triticale and wheat. Broadleaf weeds listed for control by Torpedo Herbicide include Bedstraw (*Galium spp.*), Indian hedge mustard (*Sisymbrium orientale*), Snail medic (*Medicago scutellate*), Turnip weed (*Rapistrum rugosum*), Wild radish (*Raphanus raphanistrum*),Vetches (*Vicia spp.*), Capeweed (*Arctotheca calendula*), Doublegee (*Emex australis*) and Volunteer legumes (including Chickpea, Faba bean, Field pea, Lentil and Lupin). According to the product label, Torpedo Herbicide is to be used with Uptake Spraying Oil (Dow Agrosciences) adjuvant and is compatible with Bromoxynil, bromoxynil-MCPA, metsulfuron, MCPA LVE and MCPA amine.

The recommended application rate in cereal crops is 75-100 mL/ha (3.75-5 g/ha florasulam + 22.5-30 g/ha clopyralid) using only ground boom spraying equipment. The product is to be applied from 2 leaf up to 1st node of the crop as a single application per season, using a spray volume of 50–100 L/ha. The undiluted product contains 5% florasulam and 30% clopyralid. The most concentrated spray (0.2% Torpedo Herbicide) preparation will contain 0.01% florasulam and 0.06% clopyralid. The area to be treated per day may vary from 50-300 ha per day. The product is intended to be used up to 5 days per year by farmers and up to 60 days per year by contractors. In the maximum usage scenario, a contractor may handle as much as 1.5 kg florasulam and 9 kg clopyralid and treat an area of 300 ha per day. Application of product to cereal crops will be performed between July and September in all climatic regions of Australia.

The draft label does not specify any re-entry interval following Torpedo Herbicide application. The types of workers that are likely to re-enter fields after spray application of Torpedo Herbicide include farmers, salesmen, technicians, crop inspectors, agronomists, farm managers. The work undertaken during re-entry is likely to involve visual assessment of crop, a walk through of plants, hand contact and parting of crops. The reasons for undertaking these tasks may be to check efficacy and selectivity, to check for weeds, pests and disease and to plan the next application.

As livestock may graze on or be supplied with Torpedo Herbicide treated crops, a stockfood withholding period may also be required following application of this product. The proposed first date of trial is August 2006, with trials likely extending to August, 2007. According to the draft product label, it is stated that no harvest withholding period is required for barley, triticale and wheat when used as directed. Also when using, Torpedo in a tank mix with another product the label advises that the harvest withholding Period of the other product should be observed. A stockfood withholding period is listed on the product label. The label advises that livestock are not

to graze and treated crops are not to be cut for stockfeed for 7 days after application of Torpedo Herbicide. Also, when using Torpedo in a tank mix with another product, the label advises that the longest stockfood withholding period is to be observed.

Exposure during use

Farmers and their employees (including contract spray workers) will be the main users of the product and may become contaminated with the product/spray when opening containers, mixing and loading, application, and cleaning up spills and equipment. The main routes of exposure to the product/spray will be dermal, and to a much lesser extent inhalational and ocular.

The acute hazards associated with undiluted Torpedo Herbicide are moderate skin and eye irritation. These hazards were identified based on the extrapolation of toxicity data from individual constituents present in the product and from similar SC product formulations that contain either active at the current product strength (50 g/L florasulam or 300 g/L clopyralid). In order to prevent health effects in workers which may occur following a single acute exposure to Torpedo Herbicide, personal protective equipment including goggles and elbow-length PVC gloves are recommended when opening product container and preparing spray.

The final spray may contain up to 0.2% Torpedo Herbicide (0.01% florasulam and 0.06% clopyralid). The concentrations of active ingredients are very dilute and below the cut-off concentrations for National Occupational Health and Safety Commission (NOHSC) classification as a hazardous substance. Therefore, handling of the final spray was not considered likely to be associated with any acute hazards.

No worker exposure studies on florasulam or Torpedo Herbicide were provided or available for assessment. In the absence of worker exposure data, the OCS used the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (1998) to estimate worst-case worker exposure based on maximum product use according to the Australian use pattern. Based on a comparison of the repeat-dose toxicity profiles for the active constituents (florasulam and clopyralid) and their levels in product form, clopyralid was considered to present the greater hazard. Toxicological endpoints based on clopyralid were therefore used in the OHS repeat dose risk assessment for Torpedo Herbicide. In the maximum usage scenario a contractor may handle as much as 9.0 kg of clopyralid per day (100 mL product/ha x 300 ha/d = 30 L product/d = 9 kg clopyralid) and will use a ground boom applicator in either open or closed cab situation during mixing/loading and application. No further PPE was recommended because the risk of systemic effects occurring after repeated exposure to clopyralid, in Torpedo Herbicide, was considered to be negligible. The assumption of the surrogate exposure modelling (PHED) used in this risk assessment is that workers will wear PPE including a single layer of clothing (including a full-length shirt and full length pants). No specific recommendations for this were made, since this particular PPE requirement is assumed to be part of prudent risk management on the farm when working with chemicals.

Exposure during re-entry

The types of workers that are likely to re-enter fields after spray application of Torpedo Herbicide include farmers, salesmen, technicians, crop inspectors, agronomists, farm managers. Re-entry activities for cereals crops include scouting and mechanical harvesting and involve minimal contact with treated foliage. Scouting may involve visual assessment of crops, a walk through of plants, hand contact and parting of crops. The main route of exposure during these various activities will be dermal through the transfer of florasulam and clopyralid residues product residues, photodegradates and degradation products present on plants and soil.

Torpedo Herbicide is to be applied from second leaf up to first node of the crop and will not be sprayed over mature crop foliage. Based on this information it is unlikely that there will be any significant transfer of residues during post-application activities in the later crop maturation stages.

The applicant did not provide any information regarding worker exposure when re-entering Torpedo Herbicide treated areas. In the absence of data, a single assessment for re-entry exposure was undertaken for clopyralid based on the maximum usage scenario for Torpedo Herbicide and the US Occupational Post-Application Risk Assessment Calculator Version 1 (8/9/00) (US EPA Policy 003.1). No specific re-entry interval period was established as the risk to workers in re-entry scenarios was determined to be low from 'day 0'.

Based on the proposed use pattern and risk assessment the following re-entry statement is recommended for placement on the product label: "Do not allow entry into treated areas until the spray has dried, unless wearing cotton overalls buttoned to neck and wrist (or equivalent clothing) and chemical resistant gloves. Clothing should be laundered after each day's use."

Recommendations for safe use
Users should follow the instructions and Safety Directions on the product label. Safety Directions include the use of goggles and elbow-length PVC gloves when opening the container and preparing spray.

The PPE recommended should meet the relevant Australian Standards.

Re-entry statement:

"Do not allow entry into treated areas until the spray has dried unless wearing cotton overalls (or equivalent clothing) and chemical resistant gloves. Clothing must be laundered after each day's use."

Conclusions
Torpedo Herbicide can be used safely if handled in accordance with the instructions and Safety Directions on the product label and in accordance with relevant OHS and public health standards and regulations.

ENVIRONMENTAL ASSESSMENT

Introduction

Dow AgroSciences Australia Limited has applied to the Australian Pesticides and Veterinary Medicines Authority (APVMA) for registration of Torpedo Herbicide (a suspension concentrate containing 300 g clopyralid, as the monoethanolamine salt/L and 50 g florasulam/L) for post-emergent broadleaf weed control in barley, triticale and wheat.

Environmental Fate

Florasulam

- ***Hydrolysis***

Two hydrolysis studies showed that florasulam is hydrolytically stable over the pH range of 4 to 7, but hydrolysed at pH 9 with degradation half-lives of 2 days (50°C), 100 days (25°C) and 226 days (20°C). The major hydrolysis product observed was 5-hydroxy-florasulam.

- ***Photolysis***

Four photolysis studies were performed with sterile pH 5 buffer and three with natural waters. These showed half-lives of 46-64 days in summer at 40°N in sterile water, but half-lives were much lower in natural waters (as low as 3.3-15.2 days in spring – summer sunlight). The soil photolysis study gave a half-life estimated as 62 days with 5-hydroxy-florasulam the major product (reaching ~47% of the applied radioactivity in light exposed samples and ~68% in the dark samples).

- ***Aerobic soil metabolism***

Seven aerobic soil degradation studies showed that florasulam degraded through microbiological process producing a number of metabolites, non-extractable residues and CO_2. Generally, florasulam's estimated DT50s ranged from ~1-10 days and its DT90s up to 81 days with longer times associated with lower temperatures. Such results showed florasulam's rate of biodegradation was strongly affected by temperature, indicating 3 or 4 fold decrease in half-live with every 10°C rise in temperature. The results showed that soil moisture does not play a significant role in altering the degradation rate of ^{14}C-florasulam. The main degradation by-product was 5-hydroxy-florasulam with estimated DT50s ranging from 7 to 286 days. Other metabolites observed were DFP-ASTCA, DFP-TSA ASTCA, TSA, STCA, and STA. Soil degradation studies of DFP-ASTCA and ASTCA showed faster degradation for DFP-ASTCA (half-life of 8 to 25 days to form ASTCA) and much slower degradation for ASTCA (half-life of 158 to 502 days).

- ***Anaerobic soil metabolism***

No anaerobic soil studies conducted. Instead an anaerobic water/sediment study (see below) provided information on the fate of florasulam in anaerobic soils.

- ***Aerobic aquatic metabolism***

Two aerobic water/sediment metabolism studies showed that florasulam biodegradation is an important route of transformation of florasulam producing a number of metabolites and carbon dioxide. The studies indicate that, at 20 or 25°C, florasulam is not persistent in aerobic water/sediment systems with 5-hydroxy-florasulam, a major degradation product, persists in both the water and sediment phases. Florasulam's estimated DT50s ranged from 3 to 6 days in a natural water and sediment system or 6.5 to 29 days in natural water over sandy loam or clay loam sediment systems. DT90s in these latter cases were 30 to 59.2 days, while 5-hydroxyflorasulam had estimated DT50s from 38 to 193 days (169 to 193 days at 5°C) in the natural water sediment system and 69 and 244 days in the natural water sandy loam system. Degradation rates were strongly affected by temperature. DFP-ASTCA and STCA were the main metabolites observed with DFP-ASTCA remaining up to a year at lower temperature in the sample in the dark.

- ***Anaerobic aquatic metabolism***

In anaerobic water and soil or water and sediment, florasulam had a half-life of <2 (flooded sediment) to 13 days (flooded soil), indicating it was not persistent. This contrasts to the major degradation product, 5-hydroxy-florasulam, which persists with further slow degradation. Mineralisation to carbon dioxide is minimal and no significant amounts of volatile materials were detected.

- ***Biodegradation***

The ready biodegradability of both florasulam and the 5-hydroxyflorasulam metabolite were tested using the CO_2 evolution test. After 28 days, both molecule resulted in cumulative production of CO_2 and therefore not considered readily biodegradable.

- ***Mobility***

Volatility

A study on the volatilisation from soil and plant surfaces showed that after 24 hours, there was 1.3% volatilisation from plants and 0.8% volatilisation from soil. These results show volatilisation is unlikely to be an important route of environmental exposure of florasulam.

Florasulam's estimated Henry's Law Constant of 2.29×10^{-5} Pa.m^3/mol is equivalent to a dimensionless value of 9.24×10^{-9}, which indicates florasulam would be very slightly volatile from water. Modelling of the fate of florasulam in the atmosphere indicates degradation with hydroxyl radicals would occur with a half-life estimated as 20.5 hours.

Adsorption/desorption

Three batch equilibrium studies showed florasulam was likely to be very mobile in a range of soils with Koc values of 2 to 69. High to very high mobility would be expected from the metabolites formed in degradation processes with Koc values for the 5-hydroxy-florasulam degradate ranging from 7 to 32 and other metabolites having Koc values ranging from 24 to 159.

Leaching

Column leaching studies confirmed the mobility of the chemicals and its main metabolite, 5-hydroxyflorasulam in soil columns. With non-aged residues, between 67.7 and 92.1% the applied radioactivity was recovered in the leachates. In aged residues, extensive degradation of florasulam was observed and 32 to 36% of the applied radioactivity was recovered in the leachate and 66.5 to 69% remaining in the soil column. 5-Hydroxy-florasulam was the major degradate found in the leachate (50.8 to 56% of the applied radioactivity) while florasulam accounted for 6.10 to 12.7% of the leachate radioactivity.

Two lysimeter studies measured residues in leachate and soil residues over 2 to 3 years. Application rates (4 to 5 g/ha) were generally at or around those expected in Australia. The majority of the applied radioactivity remained in the soil column in the first test with 32 to 70.5% remaining in the top 30 cm depending on soil type. At the end of the study, very little radioactivity was attributed to florasulam.

In the second study, 44 to 53% of the applied radioactivity was found in the leachate but with none of this being florasulam. At the end of the study, 16 to 20% of the applied radioactivity remained in the lysimeter soil. Very small concentration of florasulam (0.11 to 1.7% of the applied radioactivity) was found in the wheat crop grown in the lysimeter soils in both studies. The degradation products 5-hydroxy-florasulam, DFP-ASTCA, DFP-TSA, ASTCA were identified in the leachate.

Although florasulam is not expected to leach given the low use rate and rapid degradation expected,

metabolite leaching may be expected to occur.

Field dissipation

Field dissipation studies from seven European sites and a single study which considered five sites in the US and Canada were provided. The studies were generally conducted at rates of approximately 15 g/ha and were of 7 to 18 months duration. Florasulam had field half-lives of 2 to 19 days while the 5-hydroxy-florasulam had field half-lives of 9 to 96 days except for two values of 206 and 342 days in two Canadian soils. These values were attributed to low soil moisture conditions, which would limit soil microbial activity and increase soil adsorption, which in turn would reduce the metabolite's bio-availability. Florasulam and 5-hydroxy-florasulamresidues were generally found mainly in the top 30 cm of the soil profile.

Accumulation/bioaccumulation

Bioaccumulation testing on rainbow trout under flow conditions at 5 and 50 ppb showed that florasulam is unlikely to accumulate after application. The bioconcentration factors for whole fish were 0.8 and 2.2 mL/g (low and high concentration exposures respectively) and 1.4 and 2.5 mL/g for muscle and remainder tissue (high concentration exposure). These results confirmed the expectation of negligible bioaccumulation potential indicated by the log Kow value of -1.22 at pH 7. Depuration whole fish half-lives of 6.4 and 5.9 days were determined for the low and high exposure levels respectively, suggesting that fish exposure to florasulam is quickly overcome with time.

Environmental toxicity summary

- ***Avian toxicity***

Based on a Japanese quail study, florasulam is slightly acutely toxic to birds (acute LD50 1046 mg florasulam/kg body weight). Short term dietary toxicity studies with the mallard and Japanese quail showed florasulam was practically non-toxic (5 day dietary LC50 >5000 mg florasulam/kg feed). In subchronic (6 week screening tests) and reproductive (21 weeks) toxicity studies, bobwhite quail were not affected by florasulam (NOECs ≥1500 mg florasulam/kg feed) while mallards were more sensitive in a six week screening test (NOEC of 800 mg florasulam/kg feed compared to >1500 mg florasulam/kg feed in the longer study. Based on acute oral data for the rat and mouse, florasulam is expected to be at worst slightly toxic to native animals.

- ***Aquatic toxicity***

Limit tests on two freshwater and one saltwater fish species showed no effects with the 96 hour LC50s being >96 mg/L, indicating florasulam was at worst slightly toxic to fish based on measured concentrations or practically non-toxic based on nominal concentrations. Chronic (28 day) testing with rainbow trout also showed no effects with the NOEC at least 119 mg/L, indicative of, at worst, very slight toxicity. The 5-hydroxy-florasulam metabolite had a 96 hour LC50 of >91 mg/L to the rainbow trout, also indicating, at worst, slight toxicity. Florasulam was practically non-toxic to aquatic invertebrates with *Daphnia magna*, grass shrimp (*Palaemonetes pugio*) and eastern oyster (*Crassostrea virginica*) all having LC50/EC50 values >100 mg/L. A chronic test with daphnids resulted in a 21 day LC50 of 169.2 mg/L and a NOEC of 38.9 mg/L based on length and weight of progeny. These results show florasulam was very slightly toxic under the test conditions. Metabolites showed no effects at the tested concentrations in static limit tests. A 28 day midge study to determine the effects of florasulam on larval to adult midge development was undertaken with a NOEC for development rate of 4.6 mg florasulam/L and a NOAEC of 10 mg/L determined. Such results indicate florasulam is very slightly toxic to this species.

Florasulam was very highly toxic to the freshwater green alga *Selenastrum capricornutum* and highly toxic to the blue-green alga *Anaebaena flos-aquae* and moderately toxic to the freshwater diatom *Naviculla pelliculosa.* It was slightly toxic to the salt water alga *Skeletonema costatum.*

Duckweed was the most sensitive organism tested with a 14 day IC50 of 1.18 ppb (frond number) and a 14 day NOEC for frond number of 0.616 µg florasulam/L and florasulam is chronically highly toxic to duckweed. Testing showed there was an ability for the duckweed to recover once exposure ceased. Metabolites were indicated as less toxic to the freshwater green alga and duckweed.

- ***Toxicity to beneficial species***

No effects were observed on honey bees tested orally and by contact with concentrations up to 100 µg florasulam/bee. Consequently, florasulam is rated as very slightly toxic to the honey bee via the oral and contact exposure routes.

Earthworms were exposed to florasulam at concentrations of up to 1300 mg/kg soil with no effects being seen and the 7 and 14 day LC50s were set at 1320 mg florasulam/kg soil (dry weight) based on measured concentrations and florasulam is rated as very slightly toxic to the earthworm *Eisenia foetida*. The NOEC (change in mean body weight with respect to controls) was set at 336 mg florasulam/kg. The 5-hydroxy-florasulam was very slightly toxic with the 7 and 14 days LC50s >1120 mg/kg soil (dry weight) and the NOEC set at 1120 mg/kg soil for absence of mortality and other sublethal effects. Exposure to other metabolites resulted in mortalities that were normal when compared to the controls (92.5 to 100% survival for both control and exposed worms). Lethargy was noted on worms exposed to some metabolites and the NOEC for these was set at 10 μg metabolite/kg of soil with the LC50s >100 μg metabolite/kg of soil.

Florasulam was harmless to three non-target arthropods (adult carabid beetle, *T. pyri* protonymphs and hoverfly larvae, at rates of 5 to 15 g/ha, cf. the proposed 5 g florasulam/ha. While exposure to 7.5 g florasulam/ha as a 50% SC formulation was slightly harmful to green lacewing larvae and harmful at 15 g florasulam/ha under laboratory, an extend laboratory study using fresh residues of the formulated material applied to maize seedlings at a rate of 7.5 g florasulam/ha showed the exposure was not harmful to the larvae of the lacewing (with respect to mortality and resultant fecundity).

Screening of another six insects and one mite species where there was foliar contact, root systemicity, stomach poison, contact or topical contact depending on the species being tested resulted in no harmful effects following exposure to 800 ppm florasulam (50 ppm for a beetle species). Florasulam had no significant long-term impacts on soil microbial processes (respiration or nitrogen turnover) at 7.5 g florasulam/ha or 5 X that rate.

- ***Phytotoxicity***

Florasulam applied pre-emergence at up to 10 g/ha showed no significant activity on nine of ten plant species. The exception was radish with respect to visual phytotoxicity on the emerged plants with an EC25 of 4.3 g florasulam/ha established.

When applied to plant foliage at rates of up to 10 g florasulam/ha, significant post-emergence activity was seen on many of the ten terrestrial plant species tested. Dicotyledons were most affected with visual phytotoxicity EC25s of 0.02 (tomatoes) to 0.35 g florasulam/ha (cucumbers). The lowest EC25 for plant deaths was 0.24 g florasulam/ha for radish. With respect to shoot length and weight, florasulam again caused significant effects. Tomato and sunflower were most sensitive with each having an EC25 of 0.06 g florasulam/ha with regard to shoot length while carrot had an EC25 of 0.06 g florasulam/ha with respect to plant weight.

Of the metabolites associated with florasulam degradation, only the 5-hydroxy-florasulam was associated with adverse effects – transient stunting and chlorosis on broadleaf plants from post-emergence applications but this metabolite had no significant effects when applied pre-emergence being 100 times less phytotoxic than florasulam. Other metabolites were considered unlikely to

cause plant damage.

A screening test with thirteen broadleaf species, eleven grasses and a sedge showed florasulam had "potent" post-emergence herbicidal activity on numerous broadleaf plants at rates of 1 ppm florasulam or less with all broadleaf plants moderately to highly sensitive to pre- and post-emergence applications of florasulam with an average pre-emergence GR80 (value causing 80% reduction in growth) for broadleaf plants of 36 g florasulam/ha and, for post-emergence, 1.8 ppm.

Environmental risk summary

The proposed use of Torpedo Herbicide is not likely to present either an acute or dietary risk to birds ingesting residues on plants or insects. While risk to fish and aquatic invertebrates from florasulam is acceptable there is a potential risk to algae and aquatic plants. Adherence to the proposed 5 metre buffer distance for waterbodies would be expected to result in acceptable risk to algae and aquatic plants from the presence of florasulam.

Because florasulam is expected to be moderately to readily soluble at environmental pHs, it could show mobility in soils. There is a potential for it to enter aquatic habitats as a result of dissolution in runoff from treated land and a potential risk exists to aquatic flora, Mitigation of this risk, based on use of more realistic considerations, including allowance for adsorption of florasulam to soil and the observation that duckweed exhibited an ability to recover once florasulam exposure ceased indicates that risk from runoff to aquatic plants from the proposed use of florasulam in Torpedo Herbicide is expected to be acceptable. While florasulam has mobility in soils, its short field half-lives and essentially absence from leachates indicate movement to groundwater is unlikely.

Exposure of honeybees should not pose unacceptable risk. Risk to earthworms from the proposed use pattern appears acceptable. The principal florasulam metabolite, 5-hydroxy-florasulam, is non-toxic to earthworms. Risks to beneficial insect predators and parasites from the proposed use of Torpedo Herbicide are expected to be acceptable. The proposed use of Torpedo Herbicide is not expected to have adverse or lasting effects on soil respiration or nitrification processes.

With respect to spraydrift on to non-target vegetation, the draft label's 10 metre buffer distance between the downwind edge of the boom and the closest edge of non-target native vegetation is expected to result in acceptable risk from spraydrift to such vegetation.

Conclusion

Environmental fate studies indicate that florasulam is not expected to persist in aquatic systems. This lack of persistence coupled with the low application rate means that levels of florasulam in the environment from the proposed use will be low. The proposed use of florasulam is not likely to present unacceptable risk to birds, mammals, aquatic species other than algae and aquatic plants, beneficials, soil respiration processes or non-target plants. Risk to algae and aquatic plants is expected to be acceptable as a result of mitigation resulting from the specification of buffer distances with respect to water bodies and non target vegetation.

EFFICACY AND SAFETY ASSESSMENT

Justification for use

Torpedo Herbicide is a mixture of the existing herbicide active clopyralid (Group I) and florasulam, a new herbicide active from the triazolopyrimidine sulfonanylide family of ALS herbicides (Group B). As such the application must justify registration of florasulam, as well as the mixture.

Torpedo Herbicide is a proprietary mix of 300g clopyralid and 50g florasulam. This has been recommended for use between 75ml/ha (22.5g a.i. clopyralid + 3.75g a.i. florasulam) and 100ml/ha (30g a.i. clopyralid + 5g a.i. florasulam). For most of the weeds listed on the label it is recommended that additional herbicides be tank-mixed with Torpedo Herbicide.

Torpedo Herbicide is for use in wheat, barley and triticale and aims to control broadleaf weeds such as wild radish, which can be very difficult to manage even in cereals.

In Western Australia many broadleaf weeds have developed herbicide resistance. For instance wild radish is commonly resistant to herbicides in Group B and F and resistance to Group C and I is on the increase. Populations with multiple resistance of up to three groups is not unusual and growers are keen to use tank-mixtures to control wild radish and other weeds in an attempt to find a mode of action that still works. Torpedo Herbicide offers a good option by combining a Group B and a Group I herbicide in a package, which is compatible with a number of other herbicides. Clopyralid alone is not active against a number of the weeds listed on the label such as wild radish. However, the label provides a range of tank-mix options including MCPA (Group I) and bromoxynil-MCPA (Groups C + I) that would be suitable for suspected resistant populations.

Adequacy of efficacy data

A range of different herbicide rates and mixture options are proposed for the Torpedo Herbicide label to optimise control of different weeds.

The bulk of the weeds require Torpedo to be tank-mixed with either MCPA LVE or bromoxynil-MCPA. Different rates can be useful, but limited evidence for the different rates has been provided in the application. A large number of efficacy references are provided which show that either florasulam alone or the Torpedo Herbicide provide excellent control of most of the weeds; Capeweed being the most notable exception. There are often several references showing efficacy for florasulam or Torpedo Herbicide and only one or two suggesting a tank-mix is required.

Claims

The claims made for broadleaf weed control by Torpedo Herbicide are fair and reasonable across a range of troublesome weeds species. It appears to provide good control of most of the weeds; Capeweed is the notable exception.

Control of wild radish appears to be excellent considering how important a weed it is. However, with much of the Radish in Western Australia now resistant to Group B herbicides this product will not add much value when compared with the option of tank-mixing the current clopyralid and MCPA +- bromoxynil products already available on the market. Although it will help growers attempting to tackle multiple weed problems who are forced to combine as many actives as possible.

Safety to target and non target species

Target

The Torpedo Herbicide is for use in wheat, barley and triticale crops.

The label includes substantial crop safety warnings for barley.

> "Barley – Transient stem shortening and crop yellowing may occur, although yields are normally unaffected. However, where crop stress occurs a longer period may be required for crop recovery, especially if the crop is stressed by root or foliar disease, poor nutrition, water logging,

drought or cold stress. In severe cases and seasons where a dry spring occurs, yields may be reduced."

A number of references are presented to illustrate the crop safety of barley, wheat and triticale. For wheat and triticale there is virtually no concern. Most trials showed wheat was less likely to be damaged than barley. However, a very few trials demonstrated damage to wheat greater than to barley, and even then it was transient and was within the acceptable range.

Barley is at times unaffected by Torpedo or florasulam and at other times suffers quite substantial transient crop injury. For instance florasulam (3.5 to 5g) caused between 18 and 33% crop injury in a drought stressed trial in NSW in weeks 1, 2 and 3 and finally zero damage in week 8. This significant injury was comparable to the currently registered Broadstrike (another sulfonamide) which was tested in the same trial. In another trial conducted under more normal seasonal conditions in South Australia florasulam (5g) damage to 4 barley varieties was 24-28% at 13 days and 18% at 5 weeks, with no further data supplied. A range of cultivars were tested across all of the reports and in one case 9 cultivars were directly compared with the worst 3 showing up to 22% injury and the worst 2 (a different 2) showing up to 15% yield penalty.

The bulk of the crop safety reports demonstrate that florasulam, Torpedo or Torpedo + MCPA LVE or bromoxynil-MCPA do not cause any long term damage to barley. Injury tends to peak at about 2-4 weeks depending on the trial as would be expected from a slow acting sulfonamide herbicide. Barley maturity is delayed by about 1 week. Some references imply that clopyralid and MCPA slightly improve crop safety of florasulam, but this is only marginally demonstrated.

Importantly, florasulam appears to cause less injury to barley than the current alternative Group B herbicides: metsulfuron and metosulam. For this reason the crop safety of the Torpedo Herbicide is considered to be acceptable, particularly as the applicant has included a significant warning on the label to protect themselves under difficult conditions.

Non-target

Florasulam does not add any great risks to non-target species beyond the area sprayed when compared to clopyralid, which is already registered.

The Group B chemistry is a family of herbicides known for soil persistence and leaching. Florasulam is highly soluble in water, particularly with increasing soil pH, and is highly mobile in soil. However, it has a half-life (DT_{50} 2-18 days) which is considerably shorter than another triazolopyrimidine sulfonanylide herbicide metosulam (DT_{50} 14-50 days) that is already used in Australia with no issues for recropping. Sensitive crops include oilseed rape (canola), lucerne, beans, clover, sugar beet and lentils, with oilseed rape the most sensitive.

Recropping trials with florasulam at Nimes, France in pH 8.2 silt loam showed a considerably shorter recropping interval than for metsulfuron even at very high rates of florasulam. In some trials there was some damage (0-6.7% injury) to oilseed rape sown in the following season but no loss of yield. In 32 trials across Europe there was some loss of vigour in oilseed rape not associated with yield loss in just 4 trials, however this was mainly with 15g/ha, with late application and drier than usual conditions. In selected trials soil residue tests were conducted at harvest and in most cases residues were below the level of quantification. Similar plantback trials in North America, including Canada, included a range of soil types and demonstrated recropping intervals considerably shorter than for the sulfonylurea, metsulfuron. Recropping trials across Europe only produced occasional visual damage to oilseed rape at very high rates (30g/ha). In Australia metsulfuron has a recropping period of 9 months.

Based on the data presented florasulam is assessed to be of low risk for carryover damage to following crops. The applicant have chosen to use the recropping intervals from the current clopyralid label on the grounds that recropping issues from florasulam are of less concern. While it is feasible that low levels of florasulam could aggravate the potential for clopyralid to damage crops, it is unlikely that florasulam residues would still be an issue at the end of the clopyralid recropping period of 9 months for canola and a range of legumes. Clopyralid has recognised recropping issues in Australia and this is a valid action under the circumstances. The recropping

intervals currently recommended for clopyralid should be more than sufficient to safeguard from damage by florasulam residues.

Recommendation
The applicant has adequately justified the registration of the product and reasons for the particular tank-mix recommendations. The applicant's satisfactory explanation of the case for tank-mixes and the concessions made in the case of two specific weeds (bedstraw and turnip weed) recommendations allow the registration to be supported.

It is recommended that on the basis of efficacy and crop safety Torpedo Herbicide be considered for registration.

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Dow AgroSciences™

Torpedo*

Herbicide

ACTIVE CONSTITUENTS: 300 g/L CLOPYRALID present as the monoethanolamine salt
50 g/L FLORASULAM

GROUP I B HERBICIDE

A suspension concentrate formulation for post-emergent control or suppression of broadleaf weeds in barley, triticale and wheat as specified in the Directions for Use.

IMPORTANT: READ THE ATTACHED BOOKLET BEFORE USE.

Dow AgroSciences Australia Limited
A.B.N. 24 003 771 659
20 Rodborough Road
FRENCHS FOREST NSW 2086
www.dowagrosciences.com.au
CUSTOMER SERVICE TOLL FREE: **1-800 700 096**

Contents: 5L

GMID:

STORAGE AND DISPOSAL

- Store in the tightly closed original container in a securely locked place, out of direct sunlight.
- DO NOT store near food, feedstuffs, fertilisers or seed.
- This container can be recycled if it is clean, dry, free or visible residues and has the ***drum****MUSTER* logo visible. Triple or pressure rinse containers for disposal. Dispose of rinsate by adding it to the spray tank. Do not dispose of undiluted chemicals on site. Wash outside of the container and the cap. Store cleaned container in a sheltered place with the cap removed. It will then be acceptable for recycling at any ***drum****MUSTER* collection or similar container management program site. The cap should not be replaced but may be taken separately.
- If not recycling break, crush or puncture and bury empty packaging in a local authority landfill. If no landfill is available, bury the packaging below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty packaging and product should not be burnt.

SMALL SPILL MANAGEMENT

Wear appropriate clothing whilst cleaning up small spills (see SAFETY DIRECTIONS). Apply absorbent material such as earth, sand, clay granules or cat litter to the spill. Sweep up material and contain in a refuse vessel for disposal. Disposal of the contaminated material must be done in accordance with STATE and/or LOCAL regulations.

SAFETY DIRECTIONS

- May irritate the eyes & skin. Avoid contact with eyes & skin when opening the container and preparing spray. Wear elbow-length PVC gloves and goggles.
- Wash hands after use. After each day's use, wash gloves and goggles.

FIRST AID

if poisoning occurs contact a doctor or Poisons Information Centre.
(Ph: Australia13 1126)

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet for Torpedo Herbicide which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1-800 700 096 or visit www.dowagrosciences.com.au

NOTICE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under off-label permits not endorsed by Dow AgroSciences, or under abnormal conditions.

EMERGENCY RESPONSE
(All Hours)
RING FROM ANYWHERE IN AUSTRALIA
1-800 033 882
(LOCAL CALL FEE ONLY)

Barcode for stock identification

DrumMuster logo

D.O.M./Batch No.:

APVMA Approval No. 59789/5/0307

Made in New Zealand

CAUTION

KEEP OUT OF REACH OF CHILDREN

READ SAFETY DIRECTIONS BEFORE OPENING OR USING

Dow AgroSciences™

Torpedo*

Herbicide

ACTIVE CONSTITUENTS: 300 g/L CLOPYRALID present as the monoethanolamine salt
50 g/L FLORASULAM

GROUP I B HERBICIDE

A suspension concentrate formulation for post-emergent control or suppression of broadleaf weeds in barley, triticale and wheat as specified in the Directions for Use.

IMPORTANT: READ THIS BOOKLET BEFORE USE.

Dow AgroSciences Australia Limited
A.B.N. 24 003 771 659
20 Rodborough Road
FRENCHS FOREST NSW 2086
www.dowagrosciences.com.au
CUSTOMER SERVICE TOLL FREE: **1-800 700 096**

* Trademark of Dow AgroSciences

GMID:

APVMA Approval No. 59789/5/xxx

DIRECTIONS FOR USE

For Application to Barley, Triticale and Wheat only; from 2 leaf up to 1st node of the crop.

RESTRAINTS

DO NOT apply to crops or weeds which may be stressed due to prolonged periods of extreme cold, moisture stress (water-logging or drought) or previous herbicide treatment, as crop damage or reduced levels of control may result (see bottom of table below for additional comments on barley).

DO NOT sow susceptible crops into paddocks treated the previous season with Torpedo Herbicide until after the required plantback period has elapsed - see under label heading "**PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS**" below.

DO NOT spray if rain is likely to occur within three hours.

DO NOT apply later than the 1st node stage of the crops.

DO NOT apply by air and **DO NOT** apply this product by mister within a Chemical Control Area in Victoria without a valid permit.

Use of Adjuvant with Torpedo* Herbicide:
Always use Uptake Spraying Oil at 0.5% v/v (except when tank mixing with metsulfuron)

WEED	WEED STAGE	RATE (mL Torpedo/ha)	CRITICAL COMMENTS
Volunteer legumes, (including Chickpea, Faba bean, Field pea, Lentil & Lupin)	***Cotyledon to 4 leaf***	**75 to 100**	***When using Torpedo* Herbicide alone:*** Always use a higher rate for larger weeds or high weed density. ***When using Torpedo* Herbicide in a tank mix as recommended:*** Apply tank mixes from the 3 leaf crop stage onwards. Where a range of rates is labelled, use the higher rates of Torpedo* Herbicide and its tank mix partner when weeds are large, at high density, crop is non-competitive, weeds are stressed or any of these situations in combination. **Control of Doublegee** may be improved by a tank mix with metsulfuron. Do not use Uptake* Spraying Oil if using metsulfuron; use what is recommended on the metsulfuron label. **With Capeweed**, large weeds at treatment time may not be completely controlled. Only treat small rosette weeds.
Bedstraw (*Galium* spp.)	***Cotyledon to 4 whorl***	**100 (alone) or 75** + either 0.5L MCPA LVE or 0.35 - 0.5L Bromoxynil-MCPA	
Turnip weed (*Rapistrum rugosum*)			
Vetches (*Vicia* spp.)		**100 (alone) or 75** + either 0.5L MCPA LVE or 0.5L Bromoxynil-MCPA	
Doublegee (*Emex australis*)		**100 (alone) or 75** + 5g Metsulfuron (600g/kg)	
Indian hedge mustard (*Sisymbrium orientale*) Snail medic (*Medicago scutellata*) Wild radish (*Raphanus raphanistrum*)		**75 to 100** + either 0.5L MCPA LVE or 0.35 to 0.5L Bromoxynil-MCPA	
Capeweed (*Arctotheca calendula*)		**100** + either 0.5L MCPA LVE or 0.35-0.5L Bromoxynil-MCPA	

***CROP SAFETY: Barley** - Transient stem shortening and crop yellowing may occur, although yields are normally unaffected. However, where crop stress occurs, a longer period may be required for crop recovery, especially if the crop is stressed by root or foliar disease, poor nutrition, water logging, drought or cold stress. In severe cases and seasons where a dry spring occurs, yields may be reduced.*

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

HARVEST WITHHOLDING PERIOD

BARLEY, TRITICALE and WHEAT: None required when used as directed.

When using Torpedo in a tank mix with another product, observe the Harvest Withholding Period of the other product.

STOCKFOOD WITHHOLDING PERIOD

DO NOT graze or cut treated crops for stock feed for 7 days after application of Torpedo Herbicide. When using Torpedo Herbicide in a tank mix with another product, observe whichever Stockfood Withholding Period is the longer.

GENERAL INSTRUCTIONS

MIXING: Torpedo Herbicide is a suspension concentrate which may show some separation on storage. Roll, shake or invert the container several times to ensure that Torpedo has completely resuspended before measuring to mix. Torpedo Herbicide should be added to the spray tank with simultaneous agitation. If agitation is limited, premix the Torpedo Herbicide in a bucket before adding to the main tank. Once diluted correctly, Torpedo Herbicide remains in suspension. **If tank mixing with other products, the following order should be followed:**

1. Quarter fill the spray tank, maintaining agitation, then:
2. Add Torpedo Herbicide (as described above).
3. Add water to half fill the spray tank.
4. Add wettable powders, water dispersible granules or other suspension concentrates.
5. Add emulsifiable concentrates.
6. Add Uptake* Spraying Oil when spray tank is half-full.
7. Add water to bring to the final spray volume.

COMPATIBILITY

Torpedo Herbicide is compatible with the following:
Broadleaf Herbicides: Bromoxynil, bromoxynil-MCPA, metsulfuron, MCPA LVE, MCPA amine.
Adjuvants: Always use Uptake Spraying Oil, except when using metsulfuron in a tankmix.

- **APPLICATION**

Boom Spraying: Apply Torpedo Herbicide in sufficient water to obtain good coverage. It should be applied by an accurately calibrated ground rig using a water volume of 50 – 100 L/ha. Sprayers should aim to apply medium quality spray based on BCPC specifications and in accordance with ASAE standard S-572.

CLEANING SPRAY EQUIPMENT:

After using Torpedo Herbicide, empty the tank completely and drain the whole system. Thoroughly wash inside the tank using a pressure hose, drain the tank and clean any tank, pump, line and nozzle filters.
Partial Cleaning **(Rinse only** -before using rig to spray barley, triticale and wheat):
After cleaning the tank as above, quarter fill the tank with clean water and circulate through the pump, line, hoses and nozzles. Drain and repeat procedure twice.
Complete Cleaning **(Decontamination** -before using rig to spray crops that are susceptible to Torpedo Herbicide): After cleaning the tank as above, quarter fill the tank with clean water and add a liquid alkali detergent (e.g. Surf®, Omo®, Drive®) at 500 mL/100 L water and circulate throughout the system for at least fifteen minutes. Drain the whole system. Then remove filters and nozzles and clean separately. Finally rinse inside the tank thoroughly using a pressure hose and flush system with clean water and allow to drain. ***Note:*** If using a concentrated laundry detergent use 250 g (or mL)/100 L water. Do not use chlorine based cleaners.

Rinse water should be discharged onto a designated disposal area or, if this is unavailable, onto unused land away from desirable plants and their roots and watercourses.

RESISTANT WEEDS WARNING

GROUP	I	B	HERBICIDE

Torpedo Herbicide contains members of the pyridine and triazolopyrimidine sulfonanilide group of herbicides. The product has the disrupters of plant cell growth and acetolactate synthase (ALS) inhibitor modes of action. For weed resistance management, the product is a Group I + Group B herbicide. Some naturally occurring weed biotypes resistant to the product and other Group I and/or B 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 this product or other Group I or Group B herbicides. Since the occurrence of resistant weeds is difficult to detect prior to use, Dow AgroSciences accepts no liability for any losses that may result from the failure of the product to control resistant weeds. Strategies to minimise the risk of herbicide resistance are available. Contact your farm chemical supplier, consultant or local Department of Agriculture.

Torpedo Herbicide is a broadleaf herbicide with no grass weed activity and exerts no selection pressure on annual ryegrass.

PROTECTION OF CROPS, NATIVE AND OTHER NON-TARGET PLANTS

Do not apply under weather conditions or from spraying equipment that may cause spray drift onto nearby susceptible plants/crops, cropping lands or pastures.

Composts and Mulches

Compost, mulch or mushroom substrate made from plant material treated with Torpedo Herbicide may cause damage to susceptible crops or plants. Do not apply Torpedo Herbicide to crops or pastures that will be used for the production of compost, mulches or mushroom substrate.

Stubble from Treated Crops

Ensure that harvesters effectively spread crop straw and do not leave a heavy 'header trail' after harvest. Burn (if legal in the area) or bale and remove, slash or incorporate stubble as soon as practical after harvest and for as long as possible before planting next year to allow microbial breakdown of any residues in straw. Heavy stubble loads may carry more residue into the following season. Where heavy stubble burdens and/or non-wetting soils exist and less than the recommended amount of rain has fallen from application to planting the susceptible crop (see below), only plant a winter or summer cereal or canola.

Susceptible crops and plants include, but are not limited to, chickpeas, cotton, faba beans, field peas, fruit trees, lentils, lupins, lucerne, medics, ornamentals, potatoes, safflower, sub-clover, tomatoes, vegetables, vetches, vines (grape and kiwifruit), wattles and white clover. Field peas, faba beans, lentils and vetches are particularly susceptible.

Where Torpedo Herbicide residue carryover is suspected and susceptible crops are to be planted, test the treated area as follows:

Field bioassay – where rain allows, plant a small area of the susceptible crop four to six weeks before desired planting date and take note of any symptoms of injury. If any herbicide symptoms are observed, only plant either canola or a cereal (see recommendations for northern and southern Australia below).

Pot bioassay – where not practical to do field bioassay, plant a small number of seeds of the susceptible crop into pots containing soil from the treated field. Do this test four to six weeks before desired planting date. If any herbicide symptoms are observed, only plant either canola or a cereal (see recommendations for northern and southern Australia below).

Planting Crops Following Use of Torpedo Herbicide in Previous Cereal Crop

Planting crops 'dry' without appropriate rain (see below) in the fallow prior to planting increases the risk of injury to susceptible crops. This practice should be avoided or only plant a cereal or canola. In severely dry conditions, where less than 30% of average annual rainfall and/or less than the minimum rain has fallen between application and planting the next year (see below), only plant a cereal or canola.

Plantback Periods

Area/State	Minimum Rain/Water requirements before sowing crops following use of Torpedo Herbicide	Crops to be planted	Plantback Interval
Sth NSW, Vic, SA, WA (**Winter dominant rainfall areas**)	At least 25 mm of rain or irrigation in the summer to autumn period, with a subsequent extended period of soil wetting (at least 1 week)	Clover, chickpea, faba bean, field pea, lentils, lucerne, lupins, medics and vetch.	9 months
		Barley, canola, triticale, wheat, oats	1 week
Nth NSW and Qld (**Summer dominant rainfall areas**)	***For susceptible summer crops;*** at least 100 mm rain or irrigation. ***For susceptible winter crops***; at least 150 mm rain or irrigation. This rain or irrigation should wet the soil for an extended period of 1 week or more.	Lucerne	9 months
		Chickpea, cotton, soybean, sunflower	6 months
		Maize, sorghum	2 weeks
		Canola, barley, oats, wheat	1 week
For all situations, sufficient rainfall to enable soil wetting for at least one week is essential to enable residue breakdown before planting following crops.			

PROTECTION OF WILDLIFE, FISH, CRUSTACEANS AND ENVIRONMENT

Torpedo Herbicide has low toxicity to fish, birds, honey bees, livestock, earthworms and aquatic organisms.

Overspray or drift to sensitive habitats should be avoided. For ground application, a buffer zone of 15 metres is required between the downwind edge of the boom and the closest edge of non-target vegetation and a buffer zone of 5 metres is required between the downwind edge of the boom and the closest edge of waterbodies.

Florasulam is very highly toxic to algae and aquatic plants. **DO NOT** contaminate streams, rivers or waterways with chemical or used containers.

STORAGE AND DISPOSAL

Store in the tightly closed original container in a securely locked place, out of direct sunlight.

DO NOT store near food, feedstuffs, fertilisers or seed.

This container can be recycled if it is clean, dry, free or visible residues and has the ***drum****MUSTER* logo visible. Triple or pressure rinse containers for disposal. Dispose of rinsate by adding it to the spray tank. Do not dispose of undiluted chemicals on site. Wash outside of the container and the cap. Store cleaned container in a sheltered place with the cap removed. It will then be acceptable for recycling at any ***drum****MUSTER* collection or similar container management program site. The cap should not be replaced but may be taken separately.

If not recycling break, crush or puncture and bury empty packaging in a local authority landfill. If no landfill is available, bury the packaging below 500 mm in a disposal pit specifically marked and set up for this purpose clear of waterways, desirable vegetation and tree roots. Empty packaging and product should not be burnt.

SMALL SPILL MANAGEMENT

Wear appropriate clothing whilst cleaning up small spills (see SAFETY DIRECTIONS). Apply absorbent material such as earth, sand, clay granules or cat litter to the spill. Sweep up material and contain in a refuse vessel for disposal. Disposal of the contaminated material must be done in accordance with STATE and/or LOCAL regulations.

SAFETY DIRECTIONS

May irritate the eyes & skin. Avoid contact with eyes and skin when opening the container and preparing spray. Wear elbow-length PVC gloves and goggles.

Wash hands after use. After each day's use, wash gloves and goggles.

FIRST AID

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

MATERIAL SAFETY DATA SHEET

Additional information is listed in the Material Safety Data Sheet for Torpedo Herbicide which is available from Dow AgroSciences on request. Call Customer Service Toll Free on 1-800 700 096 or visit www.dowagrosciences.com.au

NOTICE

Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. No warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of the product contrary to label instructions, or under off-label permits not endorsed by Dow AgroSciences, or under abnormal conditions.

EMERGENCY RESPONSE
(All Hours)
RING FROM ANYWHERE IN AUSTRALIA
1-800 033 882
(LOCAL CALL FEE ONLY)

Barcode for stock identification

*Trademark of Dow AgroSciences, ®Registered Trademark

GLOSSARY

Active constituent	The substance that is primarily responsible for the effect produced by a chemical product.
Acute	Having rapid onset and of short duration.
Carcinogenicity	The ability to cause cancer.
Chronic	Of long duration.
Codex MRL	Internationally published standard maximum residue limit.
Desorption	Removal of an absorbed material from a surface.
Efficacy	Production of the desired effect.
Formulation	A combination of both active and inactive constituents to form the end use product.
Genotoxicity	The ability to damage genetic material
Hydrophobic	Water repelling
Leaching	Removal of a compound by use of a solvent.
Log P_{ow}	Log to base 10 of octonol water partioning co-efficient.
Metabolism	The conversion of food into energy
Photodegradation	Breakdown of chemicals due to the action of light.
Photolysis	Breakdown of chemicals due to the action of light.
Subcutaneous	Under the skin
Toxicokinetics	The study of the movement of toxins through the body.
Toxicology	The study of the nature and effects of poisons.

References

Goring, C.A.I. et al. 1975, 'Principles of pesticide degradation in soil', in *Environmental Dynamics of Pesticides*, edited by R. Haque and V.H. Freed, Plenum Press, New York, pp 135-72.

Matthews, G.A. 1992, *Pesticide Application Methods*, 2nd ed., Longman, London.

Australian Pesticides and Veterinary Medicines Authority 1996, *Ag Manual: The Requirements Manual for Agricultural Chemicals*, APVMA, Canberra.

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

Australian Pesticides and Veterinary Medicines Authority 1996, *MRL Standard: Maximum Residue Limits in Food and Animal Feedstuffs*, APVMA, Canberra. (See footnote below)

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

Dryzga MD, Stewart HS, Hansen SC & Brzak KA (1996) XR-570: Tissue distribution and metabolism of ^{14}C-labeled XR-570 in Fischer 344 rats. Study No. DR 0312-6565-014 (unpublished). Study date: 14 November 1996. The Toxicology Research Laboratory, Health and Environmental Research Laboratories, The Dow Chemical Company, Michigan USA.

Perkins JM & Banks G (2003) Dermal absorption of [^{14}C] DE-570 through rat skin (in vitro) following exposure to undiluted EF-1343 and a spray solution. Study ID: P97-003. Report No. GHE-P-10262 (unpublished). Study date: 17 March 2003. Agricultural Research and Development Centre, Dow Agrosciences, Letcombe Laboratory, Oxon, UK.

Sullivan JM & Singleton NC (1995) XDE-570: Exploratory four-week dietary toxicity study in beagles. Study No. DR-0312-6565-018. Derbi No. 31415 (unpublished). Study date: 7 June 1995. The Toxicology Research Laboratory, Health and Environmental Sciences. The Dow Chemical Company. Indianapolis, IN 46268-0470, USA.

Redmond JM & Johnson KA (1996) XDE-570: 13-week dietary toxicity study in $B6C3F_1$ mice. Study ID: DR-0312-6565-010 (unpublished). Study date: 30 January 1996. The Toxicology Research Laboratory, Health and Environmental Sciences. The Dow Chemical Company. Midland, Michigan 48674. USA.

Stebbins KE (1995) XDE-570: 13-week dietary toxicity study in beagles. Study ID: DR-0312-6565-021 (unpublished). Study date: 13 September 1995. Amended study date: 20 November 1997. Health and Environmental Sciences. The Dow Chemical Company. Midland, Michigan 48674. USA

Liberacki AB, Carney EW & Kociba RJ (1997) XCE-570 Two-generation dietary reproduction study in CD rats. Study ID: 960030 (unpublished). Study date: 13 November 1997. Health and Environmental Research Laboratories. The Dow Chemical Company. Midland, Michigan. 48674. USA.

Zablotny CL & Quast JF (1996) XDE-570: Oral gavage teratology probe study in New Zealand White rabbits. Study ID: DR-0312-6565-023 (unpublished). Study date: 27 November 1996. The Toxicology Research Laboratory. Health and Environmental Research Laboratories. The Dow Chemical Company. Midland, Michigan. 48674. USA.

Mattsson JL, McGuirk RJ &Yano BL (1997) XDE-570: Acute neurotoxicity study in Fischer 344 rats. Study ID: DR-0312-6565-022 (unpublished). Study date: 6 January 1997. The Toxicology Research Laboratory, Health and Environmental Research Laboratories. The Dow Chemical Company. Midland, MI. 48674. USA.

Shnkar MR & Johnson KA (1996) XDE-570: Chronic neurotoxicity study in Fischer 344 rats. Study ID: DR-0312-6565-019N (unpublished). Study date: 25 September 1996. The Toxicology Research Laboratory. Health and Environmental Sciences. The Dow Chemical Company. Midland, MI. 48674. USA.

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

APVMA PUBLICATIONS ORDER FORM

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

David Hutchison
Pesticides Division
Australian Pesticides and Veterinary Medicines Authority
PO Box E240
Kingston ACT 2604

Alternatively, fax this form, along with your credit card details, to:
David Hutchison at 02 6210 4748.

Name (Mr, Mrs, Ms, Dr)_____

Position _____

Company/organisation _____

Address _____

Contact phone number (___) _____

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

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

___ Bankcard ___ Visa ___ Mastercard

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

Signature_____ Date _____